

Practical Nutrition Workbook

Krispin Sullivan, CN
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Nutrition Workbook

FOR THE 21ST CENTURY

PRACTICAL NUTRITION 'HOW TO' GUIDE

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When you read a report on nutrition in your newspaper or weekly magazine or see information at your health food store or physician's office, please remember that we are still learning about nutrition and human health. Nutrition information is yet evolving. Truly, one man's food is another man's poison. A food that is beneficial for your neighbor may not be a beneficial food for you. Your body must be the final authority. Listen to your body.

Use this workbook. Mark it up. Use stickums, bookmarks, whatever it takes to get the information you need and make it yours. Read the table of contents and go to the sections that interest you. Come back as you need for more information.

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CHAPTER 1 INTRODUCTION TO NUTRITION

This workbook has been designed for my clients. 'Everything' is not and cannot be in this manual. If you have a serious or chronic condition, PLEASE call or email and request the information packet with forms. Allow me to help you resolve your health issue's faster than 'going it alone'. I have many years of experience to help you 'listen to your body' and understand what it is trying to tell you about what it may need. 1-775-831-0292 krispin@krispin.com

You need to acquire the wisdom to determine what is right for you.

Listen to your body.

Each person must discover for her or himself what kind and quantity of food to eat.

This workbook offers information about the current findings in nutrition research and basic guidelines to help you make wise choices.

Less than three generations (150 years) ago most people were born, grew up, married, had children and died within a one hundred miles radius. They ate food available locally, in season, without benefit of long-term storage (fresh food). Foods were in their natural state, not processed, refined, canned or frozen (except in the Arctic). Refrigeration and refrigerated trucks did not exist so foods were consumed truly fresh (not what the word means today).

Our ancestors' genes developed in response to local foods' quality, quantity, and kind. The food they consumed also developed genetically in response to the environment; conditions of sun, soil, minerals, nutrients, and water. In addition local bacteria and other commensal microbes carried by humans, animals, soil and water modified genes in all life forms.

Some examples: Fish living distant from the equator, far north and far south and fish living deep under the sea, where sunlight is scarce and the temperature cold, have large amounts of omega-3 fats and vitamin D. Tropical fish also have omega-3 and D but much less. Cold water fish, high in omega-3 fatty acids and vitamin D, are a primary source of these nutrients for humans and other mammals living in the far north and far south, distant from sourcing adequate UV-B.

Grains, nuts and other plants grown nearer the equator, such as corn in Mexico, are higher in saturated fats than the same grain grown in Illinois or Canada. Plants grown further from the equator contain more polyunsaturated fats. Examples of products high in polyunsaturated fatty acids include flax grown in Canada and sunflower seeds in Russia. The composition of fatty acids found in these nuts and seeds will vary by location (UV-B sunlight exposure) and plant genes.

In the mountains iodine is often lacking in the soil requiring the addition of sea vegetables to maintain health and prevent goiter (thyroid disease). Valleys, especially river valleys, often have high mineral content in the soils from yearly flooding providing our ancestors with produce high in mineral and trace mineral content. Some soils may be naturally low in a given mineral, zinc, manganese, iodine or other trace element or conversely they may have high amounts of a given mineral or minerals such as dolomitic soils high in calcium and magnesium. The quantity of minerals contained in the plants grown on these soils will, to a great extent, reflect soil content.

Our genes and those of our microbiome determine the nature of our digestive tracts, and the expression of other genes and hormones. If our genes descend from an ancestor living in an area high in calcium or other minerals, we will, genetically, be poor absorbers of these elements or we will have kidneys designed to rapidly excrete them. These genetic variations would protect us from mineral excess. If our modern diet has little of an essential nutrient which was abundant in our ancestors' diet we are predisposed to a deficiency.

If our genes are from an ancestor who lived in an area with low levels of a critical element we will likely have a tendency to high absorption and/or retention which in another environment may lead to an overload of this element. These genetic traits allowed our ancestors to survive in a wide range of conditions as long as they remained within those conditions.

Example: hemochromatosis is the result of unchecked absorption of iron leading to iron overload, liver damage, and death. It is prevalent in certain gene pools and, in those with the condition, may initiate other disorders including cancer. Genes for this trait likely developed in areas of low iron or carriers would not have survived to bear offspring.

Chronically low or high levels of nutrients in an environment alter all body systems. An example includes our kidneys and kidney regulating hormones. In some, hypertension is genetically associated with salt retention, or salt sensitivity. If your ancestors came from an area with less access to sodium in foods or water, or in areas that were hot or dry resulting in sodium loss in perspiration, salt retention would be a survival benefit. In modern society, with easy access and an overabundance of sodium the sodium retaining property of your genes may contribute to disease.^(1,2,3,4)

Our ancestors' genes are with us still and it is from these genes we get our likes, dislikes, tolerances, needs, and intolerances. When I suggest *you* must determine your personal program, I am asking you to monitor your body's response to various dietary changes. 'Listen' to your body. We need to rediscover the 'intuition' that has evolved within us all. Your senses are the channels through which these instincts perform. Honor them.

Intuition-the power of knowing without reasoning.

Over 40 years of teaching and consulting have taught me that students and clients have or can develop a perfect sense about what foods they need, or should avoid, but ONLY if they follow the FOOD RULES, and count protein and potassium intake.

It has become a common habit to associate nutrition with nutritional 'supplements'.

Nutrition is about FOOD, your food.

The best way to determine if a food is 'yours':

- Look at it; if it looks good
- Smell it; if it smells good
- Taste it; if it tastes good
- Eat it
- If it feels good today and tomorrow, keep eating it.

This method only works with real food (see Rule One next).

VERY SIMPLE FOOD RULES

Rule One: EAT REAL, FRESH, FOOD. Real food is food that is alive or was recently alive. Real food is found around the edges of your supermarket, at farmer's markets or in your garden. Many foods found in your grocery or health food store are processed foods, including soy-based foods and powdered foods, and do not come under the category of real food. Fresh food means the ingredients are fresh. Whole wheat may be real but it may also have been ground months ago and rancid before being incorporated into the cracker or bread. Fresh means fresh (not preserved).

Rule Two: EAT ANY REAL FOOD THAT YOU LIKE and THAT LIKES YOU. Food is for pleasure. Eating a food you do not like because it is 'good for you' is not. Food that likes you is food that feels good today and tomorrow. Food allergies are easy to spot. You will have symptoms. Mood changes, behavior changes, skin reactions, respiratory symptoms, or bowel changes indicate this food is not for you. Always some negative symptom will suggest a food does not like you and you will be healthier if you avoid it.

Rule Three: EAT ENOUGH WHOLE REAL FRESH FOOD TO SATISFY YOUR HUNGER. Once you have determined the best way for you to get your daily requirement of potassium/fiber and protein and have begun consuming them daily you will be able to know what and how much you need. Overeating often occurs because cravings, caused by missing nutrients, drive you to over consume. Consuming foods that provoke an excess of insulin or mistaking thirst for hunger can confuse your appetite too.

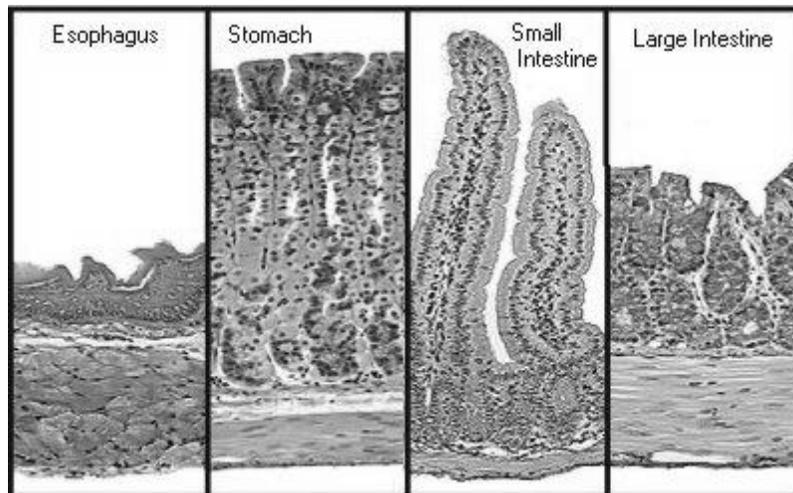
Rule Four: DO NOT EAT ALL DAY LONG Confine your eating to a period of time not to exceed 12 hours, 8-10 hours may be better. (More on Time Restricted Feeding pg.159)

Not a rule but, PLEASE, stuff in jars, cans, bottles, OR POWDERS called raw or organic or whole or any other similar name are NOT real, whole, fresh food. EVER.

CHAPTER 2 DIGESTION

It is important to have a basic understanding about how your body turns food into 'self'. Your digestive tract is your 'feeding tube', as well as your 'inside wall' which runs from your mouth to your anus. This tube changes size, pH, texture and even temperature along its length. The digestive tract, from mouth to anus, in an adult human is typically about 30-40 feet long.

Figure 2-1 Surfaces typical of various parts of the digestive tract



The Parts of You That Aren't You- Our Living Shield

Digestive Helpers/Immune Protectors

The human digestive tract (GIT, gastrointestinal tract) is lined with mucous membranes. A key to healthy immunity is healthy mucous membranes (those inside walls). Mucous membranes secrete mucous but also other substances that protect us from virus, pathogenic bacteria, and potential allergy producing lectins (see chapter on lectins).

The Mucosal immune system is that portion of the immune system which provides protection to an organism's various mucous membranes from invasion by potentially pathogenic microbes. It provides three main functions[1]: protecting the mucus membrane against infection, preventing the uptake of antigens, microorganisms, and other foreign materials, and moderating the organism's immune response to that material.

At birth, the neonate's mucosal immune system is relatively undeveloped, but the colonization of intestinal flora accelerates its development[2].

Because of its front-line status within the immune system, the mucosal immune system is being investigated for use in vaccines for various afflictions[3], including AIDS and allergies[4].
http://en.wikipedia.org/wiki/Mucosal_immune_system

The human body has been estimated to contain about 37.2 trillion cells. The amount of bacteria we host, on all our surfaces and within our digestive tract, equates to greater than 100 trillion, 2.68 times as many bacteria as the total number of individual body cells. So the cells comprising 'us' (however many that may turn out to be) are mostly bacteria, primarily living throughout our digestive tract.

From Todar's Online Textbook of Bacteriology Kenneth Todar, PhD
http://www.textbookofbacteriology.net/normalflora_3.html

The normal flora of humans are exceedingly complex and consist of more than 200 species of bacteria...

It has been calculated that a human adult houses about 10 trillion bacteria on the skin, 100 billion in the mouth, and 100 trillion in the gastrointestinal tract. The latter number is far in excess of the number of eucaryotic cells in all the tissues and organs which comprise a human...

That's an estimated 100+ trillion living organisms that may or may not be 'friendly'. Healthy digestion or health in general cannot be addressed without understanding the symbiotic relationship between us and our bacteria.

Extracted from BACTERIA: MORE THAN PATHOGENS Trudy M Wassenaar
<http://www.actionbioscience.org/biodiversity/wassenaar.html> © 2002, American Institute of Biological Sciences. Educators have permission to reprint articles for classroom use.

We house millions of bacteria on our skin and in our nose, mouth, and gut: up to 500 species can be found as normal oral flora: there can easily be 25 species living in a single mouth; a milliliter of saliva can contain as many as 40 million (4×10^7) bacterial cells; 108 bacterial cells present in the cecum (the initial part of the colon) per milliliter of content is normal and many of these species are different from those found in the mouth
Antibiotics can wipe out our body's beneficial bacteria, causing unwanted health consequences. Strictly speaking, the inside of our mouth, stomach and intestines are part of our outer surfaces. Although they are inside our body, their surfaces are in direct contact with the outside world, and as food particles pass the mucosal inner lining of our intestines, hitchhiking bacteria can stay there and multiply. We are born sterile (free of bacteria) but within hours we are colonized by our little friends, not to be left alone again.
Without bacteria we would not survive. They help us digest our food, produce vitamins, and occupy niches that would otherwise be available for competing pathogens. This competitive effect becomes apparent when we wipe out a large proportion of our intestinal flora, for instance by an antibiotic that is prescribed to treat a bacterial infection. Diarrhea is frequently the unwanted result, as 'foreign' bacteria take their chance to occupy the 'empty' niches. Healthy bacteria take over in time, so that in most cases the side effects of antibiotics are soon gone. Bacterial populations grow into a state of equilibrium until some external factor disturbs it again.

Having the right bacteria in your nose, mouth and throat will prevent cavities, protect from food and airborne pathogens (including lowering your risk for bacterial and viral infections) and improve the health of your mouth and sinus mucous membranes.

This beneficial symbiosis applies throughout the digestive tract. 'Good' (meaning friendly and helpful, supporting our immunity, protecting and even nourishing our inner barrier) bacteria should line your mouth, throat, stomach, upper and lower digestive tract, in varying amounts and types (called strains).

Having enough of the 'right' bacteria has been associated with caries protection^(5,6,7,8,9,10,11,12,13), lowered risk for infection and not just in the gut^(14,15,16,17,18,19,20,21,22,23,24), reduced metabolic disease (ALL obese persons have a form of dysbiosis)^(25,26,27,28,29,30), less cancer throughout the digestive tract^(31,32,33,34,35,36,37,38,39,40), and improved immunity and longevity.^(41,42,43)

Some of us may be blessed with diverse strains (kinds) and quantities (amounts) of friendly bacteria;^(41,43) others may have lost or never had this critical, beneficial, balance of bugs (good bugs). Our microbiome is inherited from our parents, and modified by food, water and soil. It is damaged, imbalanced or destroyed by antibiotics, antimicrobials, chemotherapy, radiation, lack of growth factors (prebiotics), NSAIDs and PPIs (proton pump inhibitors) as well as infection agents, pathogenic bacteria and other substances that damage bacterial balance including GMO foods and pesticides.

Feeding our good bacteria and using probiotics will help restore or maintain our microbial balance throughout our lives. Particular types of fiber in our diet will help maintain the aerobic and anaerobic bacteria. Regular use of probiotics will maintain the balance of friendly aerobic microbes. There are two important qualifications for a useful probiotic supplement. 1) It must contain 8 or more strains of beneficial bacteria, the more strains the better. 2) It must contain enough potency to be easily taken in amounts of 250-500 billion organisms per dose. 3) It must be alive.

Think about the implications of your body hosting more than 100 trillion symbiotic bacteria. A supplement containing 1 billion or even 3.5 billion bacteria won't do much to change the balance of things. In ulcerative colitis research it took 900 billion friendly bacteria three times a day (2.7 trillion)^(20,44,45,46,47,48) to shift the balance of power and normalize inflammation and gut immunity.

If you think you might not have the right mix of beneficial bacteria, or if you have any 'mucous membrane sensitivity' issues before you do anything else, read the Special Protocols section Immune Restoration pg. Chapter 0222. Restoration of normal body microbiota changes everything. Good bacteria in the mouth and throat increase or normalize salivation and improve salivary enzyme production and may improve one's sense of taste. Good bacteria in the nose protect us from inhalant allergies and infection and may improve a failing sense of smell. Imbalanced bacteria contribute to obesity and insulin resistance. Friendly bacteria are a critical part of your mucous membrane functioning and its immune system, but also play a major role in healthy digestion. Make sure your immune and digestive system have the probiotics they need and support them with appropriate dietary fibers..

The Immune Restoration Protocol has been designed to support the growth of anaerobic (cannot tolerate oxygen) bacteria composing 90% of the bacteria in your gut and additionally add probiotics known to be beneficial but which do not normally grow in your intestinal tract.

Repeated or long term use of antibiotics may permanently destroy beneficial anaerobes which may lead to serious bowel conditions including colitis, Crohn's and IBS. Currently the only way to rapidly restore anaerobic bacteria is a Fecal Transplant. The Immune Restoration Protocol has been designed to help restore anaerobic bacteria if at all possible.

Stage One- Seeing, Smelling, Tasting (not stressing)

Digestion begins when we see, smell, or even just begin thinking about food. This 'awareness' starts the production and secretion of digestive enzymes, pepsin, and hydrochloric acid. Chewing alters the size of the food particles so they may freely mix with digestive juices starting in your saliva, which contains enzymes to digest some carbohydrates, and continuing throughout the digestive tract. Eating fast or not chewing your food will contribute to maldigestion. It is not beneficial to eat when stressed.

The best way to begin a meal is to say a prayer of thanks (adopt an attitude of gratitude). The mental and spiritual position of being grateful, consciously feeling gratitude, brings about a state of receptivity in both mind and body. The 'state' of gratitude is always a relaxed and peaceful state, which contributes to optimum digestion and absorption of food.

Watching the news, arguing at the table, or bringing your problems and fears to your meal will make your mealtime less pleasant, your digestion disturbed and your meal less nutritious. Eating in your car, on the run, or in other stressed situations will not support health even if the food you choose is healthy food. When you must eat on the run soups, stews, pre-digested protein drinks, and other easy to digest foods are your best food choices. Give your body a break and don't ask it to do more than it is able to do.

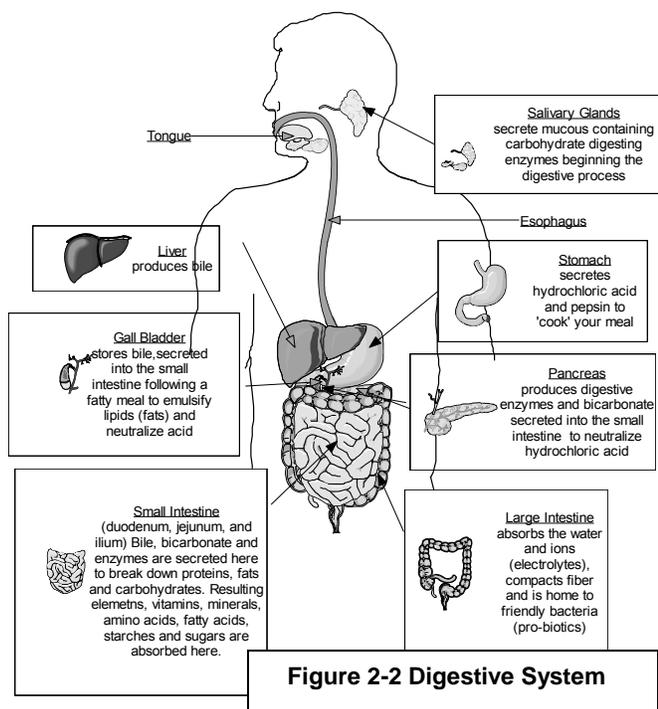
It is important to thoroughly chew your food to prepare it for your stomach. Slow down and enjoy your meal. Much indigestion may be caused by 'wolfing' your food. Conscious eating, actually being mentally 'present' at your meal, will reduce your calorie intake, improve your digestion, solve some symptoms of GERD and allow you to experience greater pleasure at your meals. Food, good food, contributes to a 'sensuous' experience.

Stage Two- Stomach, Here It Comes

Your stomach is a widening of the digestive tract with a sphincter muscle located at the upper, cardia, and lower, pylorus, ends. A sphincter muscle is a ring like band of muscle fibers that constrict a passage or close a natural opening. Food passes down your esophagus through the cardia (esophageal sphincter) into the stomach.

An adult stomach holds about 2 liters (8 ½ cups). In your stomach, hydrochloric acid and pepsin, produced in the stomach lining, chemically 'cook' your food. As acid increases and the pH in the stomach drops, the complex amino acid chains composing proteins and fiber complexes are weakened. This 'cooking in acid' begins the process of denaturing consumed proteins so your body can

The Human Digestive System



harvest individual amino acids and polypeptide chains for use as essential body proteins, neurotransmitters, and immune fractions.

During this stomach phase of digestion, hydrochloric acid destroys many pathogenic bacteria and parasites that might be harmful to you. ⁽⁴⁹⁾ Sufficient stomach acid is important to digestion and to your immune system. ^(50,51,52) Medications which prevent production of stomach acid 24 hours a day may relieve symptoms of acid reflux but, when use is chronic, cause indigestion, gas, bloating, diarrhea or constipation. In addition, these medications contribute to malabsorption of many nutrients including calcium and zinc. ^(53,54) Anti-acids also leave you vulnerable to pathogenic gut bugs that may be lurking in your meal. ^(55,56) Recent studies have found proton pump inhibitors reduce contractibility of the heart, increase heart attack and stroke and increase incidence and symptomology of lupus. ^(57,58,59,60) Protein pump inhibitors change your microbiota and not in a good way. ^(61,62,63)

TOO MUCH STOMACH ACID: Some people feel or have been told they have too much acid but in reality they are suffering from esophageal reflux (GERD). They do not have too much stomach acid. In GERD the stomach acid being produced, the right amount for a stomach, pushes up through the esophageal sphincter where acid does not belong and ‘burns’ the esophageal tissues, at times leaving serious scarring or even shortening of the esophagus.

GERD: Stands for Gastroesophageal Reflux Disease, a disorder in which there is recurrent return of stomach contents back up into the oesophagus, frequently causing heartburn, a symptom of irritation of the oesophagus by stomach acid. This can lead to scarring and stricture of the oesophagus, which can require stretching (dilating). 10% of patients with GERD develop Barrett's oesophagus which increases the risk of cancer of the oesophagus. 80% of patients with GERD also have a hiatal hernia.

Hiatal hernia: when a portion of the stomach protrudes through the diaphragm (where the oesophagus passes through). Obesity, chronic constipation and smoking are considered risk factors. It also may occur during pregnancy. Hiatal hernia is associated with reflux oesophagitis, see above.

If the suggestions below do not relieve symptoms, chronic GERD patients should be tested for Helicobacter Pylori, a pathogen that lives in the stomach and is the primary cause of gastritis and ulcers. Certain foods and alcohol may react to relax the esophageal sphincter leading to reflux. Consider lectin intolerance (lectin chapter). Often avoiding offending lectin containing foods, especially wheat and products containing wheat, will immediately reverse the symptoms.

GERD may be corrected by:

Complete a minimum of 30 days of the Immune Restoration Protocol page 218
Avoiding alcohol or other substances that bring on reflux
Simple exercises, which strengthen the esophageal sphincter***
Using a digestive enzyme such as a papaya chewable or Twinlab Super Enzyme
Taking a high potency probiotic, minimum 300 billion CFU, with every meal, such as Jarro-dophilus Ultra
Stopping the use of any over the counter or prescribed antacid; chronic use of these medications lower stomach pH making one more susceptible to gut pathogens and may lead to overgrowth of bacteria in the small bowel, cell hyperplasia, and stomach cancer. ^(53,55,56,64)
If a hernia is present, it must be repaired, sometimes by a simple manipulation and specific physical exercise or by surgery if necessary.
Regular use of melatonin 3-6 mg nightly, melatonin is critical to healthy gut function ^(65,66,67,68,69,70,71,72)

Table 1 GERD may be corrected by

The fastest way to reverse GERD in an adult is to take 3-6 mg of melatonin every night at the same time. Never take melatonin multiple times a night. If you miss your ‘time’, wait until the

next night. Melatonin is very important to normal gut function and in research has reversed GERD, working better than antacids or Protein Pump Inhibitors (PPI).^(69,70,73,74)

***A weakened esophageal sphincter may be strengthened by diaphragmatic breathing exercises, which exercise the esophageal sphincter. These breathing exercises may be found in any book teaching yoga breathing, breathing for singers, Pam Grout's book Supercharge Your Metabolism, or fitness programs which focus on breathing, such as OxyCise and BodyFlex. Google 'exercises to strengthen the diaphragm' for free choices.

TOO LITTLE STOMACH ACID: Low production of stomach acid is a frequent occurrence in the elderly^(75,76) but can occur at any age. Inability to produce sufficient stomach acid may cause constipation, indigestion, reflux, overgrowth of bacteria in the small intestine (SIBO) and susceptibility to food borne pathogens as well as an increase in food allergy reactions.^(77,78)

Table 2 Common Causes of Hypochlorhydria

lack of B vitamins, especially thiamin (B-1)
lack of estrogen post menopause
aging with degenerative changes in mucous membranes
hypothyroidism
lectin intolerance
lack of vitamins, C, A, or D
dysbiosis (those gut bugs again) so do complete 30 days of the Immune Restoration Protocol
lack of or loss of sodium, chloride, or other electrolytes from diarrhea or vomiting
low dietary zinc
lack of sufficient protein
dehydration

A person with low stomach acid, caused by diarrhea or vomiting, may need electrolytes such as chloride, potassium, magnesium, or sodium. The simple addition of a physiologic solution of electrolytes, such as Trace Mineral Research Electrolyte Stamina Tablets, taken with water or juice one or more times a day may correct the condition in a matter of hours or days. If TMR Electrolyte Stamina Tablets are unavailable Pedialyte will work (but not as well).

If protein is deficient, it takes longer for the condition to be corrected. Protein digesting enzymes such as bromelain or papaya enzymes may be needed at each meal for 1-2 weeks. Pancreatin 8X or a strong vegetarian enzyme complex, such as Absorb Aid powder, may also make sense (stronger than the bromelain or papain). Take according to instructions on the label.

If you suspect your bacteria are out of balance, not enough friends, perhaps a few enemies (pathogens), do begin the Immune Restoration Protocol page **Error! Bookmark not defined..**

Low stomach acid contributes to pernicious anemia, a deficiency of vitamin B₁₂, because there is not sufficient acid to stimulate the production of intrinsic factor for B₁₂ absorption.^(79,80) Consider a B-12 supplement for several months while you work on restoring your gut function.

The addition of vinegar or lemon, on food or in water taken with the meal, may sometimes improve digestion temporarily. The use of 'bitters' common in Europe and an earlier America, stimulates digestive juices.^(81,82)

Make sure you are fully hydrated. Hydrochloric acid is a 'secretion' and all body secretions rely on sufficient hydration Read the section on water and dehydration page 36. Poor digestion often improves when fully hydrated. 8 glasses of water a day may not be enough.

A digestive aide that contains hydrochloric acid should not be used without careful monitoring by a healthcare professional.

The natural microbes of the stomach include lactobacilli (*L. reuteri*, *L. delbrueckii*, *L. gastricus*, *L. antri*).

Stage Three- Enzymes, Bile, Bacteria, and pH

As food leaves the stomach, your pancreas secretes bicarbonate and your gallbladder secretes concentrated bile to raise the pH and neutralize the stomach acid now mixed with the food. Raising the pH allows the digestive enzymes secreted by your pancreas to work. Digestive enzymes are inactive at low pH. An insufficiency of bicarbonate (alkaline reserve) or bile will impair the process of neutralizing acid.

Pancreatic enzymes work in a more alkaline (higher pH) environment so if bicarbonate or bile are lacking even though you produce enzymes they may remain inactive and as a result you will experience partially digested food and often gas and/or diarrhea or find food particles in your stool.

Lack of sufficient protein may reduce the amount of digestive enzymes produced. Whether the pH is wrong or the enzymes are insufficient, digestion and absorption of nutrients is impaired.

Lack of sufficient alkalization (bicarbonate or bile) or lack of sufficient digestive enzymes, from insufficient protein or essential minerals, may produce symptoms of gas and bloating, at times with diarrhea rather than constipation. Insufficient vitamin D and calcium, zinc, or other vitamins or minerals may also contribute to failures of the digestive system.

Digestive enzymes may help temporarily but do not correct the underlying condition. Expensive 'digestive enzymes' advertised to improve health and suggested for daily, lifelong, use are not advised.

For temporary relief use bromelain (2,000 GDU) 1,000 mg or chewable papaya enzymes (papain and bromelain are protein digesting enzymes), 3 or 4 as needed with food; or Twinlab Super Enzymes (contains all enzymes for fats, protein and carbohydrates, and hydrochloric acid) may be appropriate. One that works for everyone (including your pets) and is reasonably priced is Absorb Aid powder. The powder mixes more freely with your food and is likely to produce better results than others. Enzymes should be taken exactly as suggested on the label. Pick one of the above, not several. Find the one that helps. Use it only when needed to help correct your digestion, not long term.

The bulk of enzymatic digestion takes place in the upper intestine, which is composed of the jejunum and ileum. This is where most nutrients, that is amino acids from proteins, fatty acids found in fats, vitamins and minerals are extracted from your food (broken down, see note below) and absorbed. The jejunum averages 5-7 feet long and the ileum 10-12 feet long. This portion of your intestine contains 'villi' pictured in Figure 1 which greatly increase the surface absorptive capacity of your digestive tract. This is also the portion of the gut where lectins may do damage (see chapter on lectins page 40).

Active bacteria in the jejunum and ileum also participate in digestion and protect this portion of your GIT from pathogens. Chronic use of antibiotics or consumption of inappropriate (for you) lectins alter the quantity and variety of microbiota and appear to weaken GIT integrity. Persons in less developed countries have a more natural balance of bacteria throughout the GIT and lower incidence of allergy and autoimmunity.

SIBO stands for Small Intestine Bacterial Overgrowth. While small amounts of certain bacteria help digestion in the small intestine, large amounts of inappropriate bacteria in the small intestine cause digestive impairment and malabsorption. Symptoms include bloating and pain within one hour after a meal, slow or incomplete digestion, constipation or diarrhea, sometimes nausea and burping. The condition is serious because large amounts of bacteria do not belong in the small intestine and may rob your body of essential nutrients as well as causing malabsorption. The most common causes are over use of antibiotics, low stomach acid or use of proton pump inhibitors (anti-acid medication) but diet may also play a role.^(83,84,85,86,87,88,89)

It is this portion of the intestine that is partially removed during some types of obesity surgery to prevent absorption of calories. Unfortunately, when this part of your digestive tract, critical for absorption of nutrients, is partially or totally removed or damaged as occurs in celiac disease and Crohn's disease, nutritional deficiencies may abound even if you eat all the right foods. Nutrition, that is the food we eat, only works if digestion works.

Our dietary foods thousands of different molecules, but the bulk of the ingested nutrients are in the form of huge (as compared to the size of the transport sites on your gut wall) macromolecules. These macromolecules cannot be absorbed into blood and lymph without first being reduced to much simpler, smaller forms - even table sugar (sucrose) cannot be absorbed without first being enzymatically uncoupled into glucose and fructose.

When the gut barrier is yet only partially formed as in newborns, during the first 18 months of life⁽⁹⁰⁾, or has been damaged by lectins, including soy, dairy and/or grain lectins, gut pathogens, which include pathogenic bacteria, parasites or fungus, or drugs/medications such as aspirin or NSAIDs (non-steroidal anti-inflammatory drugs), large macromolecules are able to cross the gut wall.⁽⁹¹⁾ These large molecules send out a danger signal, 'foreign invader present', to the immune system and a series of reactions begin that may lead to production of immune factors contributing to generalized inflammation, allergy, asthma or more serious immune and autoimmune disorders.

Macromolecules that are able to cross the gut wall may be responsible for profound food allergy reactions and other serious immune problems.^(92,93) Your gut barrier is important. Make sure you keep it healthy.⁽⁹⁴⁾

Some authorities believe changes in gut bacteria and gut permeability may be a primary cause of the current increase in allergies worldwide.⁽⁹⁵⁾ Having sufficient and correct good bacteria (both anaerobes and probiotics) protect from many of these problems and will restore the gut barrier and immunity. (See Immune Restoration)

Another role for probiotics, primarily in the small intestine, is detoxification. It has been known for some time appropriate bacteria reduce cholesterol levels in hypercholesterolemia.^(96,97,98,99,100,101,102,103,104,105,106,107,108) A recent study found bacteria in the human digestive tract break down and remove xenobiotics and thereby improve liver function by reducing the load of metabolic waste.

Without adequate and diverse 'good' bacteria, the gut mucosa (in this case the lining of the lower or large intestine) begins to alter many of its characteristics, losing its 'integrity' and becoming permeable and even ulcerated with a loss of ability to perform its important barrier functions and reducing its production of important immune proteins and healthy new cells.

Probiotics (good-bacteria) aren't just protectors. They are necessary elements of normal digestion as well as key components of your immune system.^(14,114,115,116,117,118,119,120,121,122) Loss or imbalance of these good bacteria can lead to chronic constipation or diarrhea, maldigestion, chronic fatigue, and/or food allergy reactions. Probiotics have been used to reverse food allergy reactions.^(123,124)

Balanced bacteria protect women from vaginal and urinary tract bacterial and fungal infections. Bacteria, both good and not so good, are the bulk of the stool, more than 60% of wet weight. Good bacteria produce butyric acid upon which newly forming gut mucosal cells feed. Butyric acid may prevent colon cancer and reverse pre-cancerous changes in colon cells.⁽¹²⁵⁾

While taking probiotics is necessary if you have taken antibiotics or lost your gut bug balance (dysbiosis) in any other way, the best way to keep the digestive tract healthy is to farm your probiotics by feeding them. Gut bacteria are fed by the fiber in your diet. Certain fibers are better at feeding the good bacteria than others. Foods containing fructo-ogliosaccarides, including asparagus, and onions, increase good bacteria. Whole fruits, dried fruits, gum arabic, acacia fiber, guar, and pectin all support healthy bacterial growth.

Probiotic supplements AND specific fibers which promote the growth of anaerobic bacteria should always be taken during and after use of antibiotics, including natural ones such as berberine, after serious diarrhea, and prophylactically once or twice a year. In some individuals they may be needed on a daily or weekly basis.

Fiber is key to microbial farming. All bacteria rely on undigested carbohydrate/fiber to survive. Types of fiber include soluble, such as found in oatmeal, oat cereal, lentils, apples, oranges, pears, oat bran, strawberries, nuts, flaxseeds, beans, dried peas, blueberries, psyllium, cucumbers, celery, and carrots and insoluble found in whole grains, wheat bran, corn bran, seeds, nuts, barley, couscous, brown rice, bulgur, zucchini, celery, broccoli, cabbage, onions, tomatoes, carrots, cucumbers, green beans, dark leafy vegetables, raisins, grapes, fruit, and root vegetable skins. In addition resistant starch supports several types of beneficial microbes. Resistant starch is found in green bananas, raw potato starch, and cooked and cooled potatoes and rice. (think potato salad and sushi)

Your microbial inhabitants require a significant amount of all 3 types every day. Some sources suggest 50-80 grams of fiber daily. Many 'fiber charts' are available online. Eating the suggested 3 pounds of whole plant foods daily will typical cover your basic fiber requirement.

Bacterial restoration is important for children as well as adults. These friendly symbiotes play a role in preventing asthma, allergy and even autism.^(35,126,127,128,129,130,131)

When the gut wall is damaged by NSAIDs (non-steroidal anti-inflammatories), ibuprofen, or aspirin (or acetaminophen in high doses) the microbial balance may shift so that good bacteria may no longer be able to maintain gut health. If you need to take any of these medications always take them with 1 rounded teaspoon of lecithin granules which will enhance their anti-

inflammatory action and prevent gut damage. Also use the Immune Restoration Protocol drink several times a week to keep gut flora healthy.

If you need to be on any of these medications daily consider taking PepZin GI which is zinc-l-carnosine twice a day, and a modified version of the Immune Restoration Protocol. A balanced microbiota has been shown to reduce inflammation, not just in the gut, and protect the gut wall from NSAIDS damage. ^(132,133,134,135,136,137) Zinc-l-carnosine helps protect the gut lining in a different way than prebiotics/probiotics or lecithin. They work together to make NSAID and aspirin use much less damaging.

The natural microbes of the large intestine are anaerobic (cannot live in high oxygen). They may be difficult to replace if destroyed by antibiotics or NSAID therapies.

The Unhappy Digestive Tract

ULCERS? Irritable Bowel Syndrome? SIBO (small intestine bacterial overgrowth)?

In the past, many digestive problems were thought to be psychological. While stress can play a role in gut symptoms, emotional/psychological triggering of symptoms because of increased production of various hormones and/or neurotransmitters, any person with chronic symptoms of indigestion, such as gas, especially gas with strong odor on a daily basis, bloating, burning, reflux, stomach or intestinal pain, constipation or diarrhea should order the ubiome test <http://ubiome.refr.cc/XL3MGSK> and begin the Immune Restoration Protocol.

Pathogenic bacteria (bad guys) may cause symptoms anywhere along the digestive tract; A bug called Helicobacter Pylori causes most stomach and duodenal ulcers. ⁽¹³⁸⁾ Some 60-90% of IBS patients have overgrowth of one or more pathogens, bacterial, fungal or parasitic. ^(139,140) More recently researchers suggest IBS may be a 'post-infection' condition which remains even after pathogenic organisms are removed. ^(141,142,143) Pathogens can change the 'ecology' of your gut so that unfriendly bacteria thrive and healthy bacteria are unable to grow. If the Immune Restoration Protocol does not rebalance your microbiota you may need a course of natural antibiotics to remove pathogens.

Lectins have been strongly associated with gastrointestinal problems from IBS to 'gas' to colitis and even Crohn's Disease. ⁽¹⁴⁴⁾ Make sure to read the section on lectins carefully if you suffer from any of these unhappy gut conditions. Certain probiotics may bind some lectins allowing persons who believed they were intolerant to certain foods to begin to eat them again BUT some lectins just really aren't 'our food'.

People with gut complaints often are given barium enemas, colonoscopy, or other invasive procedures and get a diagnosis of 'nothing' or 'colitis' which means inflamed colon, Recently colonoscopies have been implicated in CAUSING chronic gut infections leading to IBS, a term simply meaning your bowel is irritated. The diagnostic problem is the testing method employed. A well done stool test can tell what enzymes are present, whether you have sufficient stomach acid and balanced gut flora (bacteria), whether you have pathogens present, such as candida, pathogenic bacteria or a parasite, status of the gut immune system, gut antibodies and much more.

When symptoms are overwhelming, or longstanding, testing is important to determine the true condition of digestive tract. Ulcers were thought to be caused by 'stress' until a scientist, Barry

Marshall, AC, FRACP, FRS, FAA, DSc, followed his hunch and produced gastritis in his own stomach by ingesting a common pathogenic bacteria, helicobacter pylori. He then killed the bacteria using antibiotics and cured the gastritis. Twenty years after his experiment he was awarded the Nobel Prize for his discovery. A simple breath test can determine presence of this bug which is responsible for damage to the stomach wall and a primary cause of stomach cancer. Now gastritis and/or ulcers are treated with antibiotics, probiotics, and an antacid in just 10 days. The treatment protocol will cause dysbiosis so it should be followed by a minimum of 30 days on the Immune Restoration Protocol.

Diarrhea or constipation, or chronic 'smelly' gas is NEVER normal, NEVER tolerable. If a person with any combination of symptoms of maldigestion or malabsorption does not find the cause and correct the condition, changing the diet and taking supplements will do little good. The first step to improved health is improved digestion. Please see the section on Immune Restoration.

Colonoscopies- Beware

A note on colonoscopies: More than a few of my clients have had chronic bowel problems following colonoscopies. Please read:

UNSTERILE DEVICES PROMPT WARNINGS; Use of dirty endoscopes in colon and throat exams can pass along infections, activists say

- By John M. Gionna. The Los Angeles Times. Feb 13, 2003. pg. B.1

The nation's leading manufacturer of endoscopes has known for a decade that some scopes contain cavities inaccessible to cleaning by hand but has failed to fix the oversight, said David Lewis, a University of Georgia research microbiologist who has conducted research for the federal Environmental Protection Agency on the issue of dirty endoscopes.

There is wide consensus that it is difficult to sterilize the devices, which can cost \$28,000 each, without using temperatures so high that the scopes themselves become damaged. The scopes have numerous cavities that are difficult to clean, even by hand, critics say.

Acknowledged Timothy Ulatowski, an FDA official who oversees endoscope compliance: "When these things were designed, cleaning and sterilization was obviously an afterthought."

Even the government can't agree on how long is needed to clean the devices. The FDA says endoscopes should be disinfected for 45 minutes to kill tuberculosis bacteria, but the Centers for Disease Control believes the job can be done in 20 minutes, Lewis says.

He and other microbiologists advocate sterile disposable parts for endoscopes as well as the use of a condom-like sheath for each new patient. But they say manufacturers and health-care providers have resisted such solutions because of added costs.

Lewis says Olympus, which provides 70% of endoscopes on the U.S. market, has long been aware of cleaning problems associated with its product. In a patent filed in 1993, he says, the company wrote that at times "satisfactory cleaning cannot be achieved."

You can read this newspaper article in full at: <http://www.sheller.com/NewsDetails.asp?NewsID=22>

To find out what to do about it please read

Meals- Many or Few?

Time Restricted Feeding

In 2009 Martin Berkhan <http://leangains.com> began using and writing about Intermittent Fasting (IF). As a body builder and personal trainer his goal was to be as lean as possible yet maintain muscle. Using a program of daily feast and fast, 8 hours eating and 16 hours of zero calorie fasting, plus an intense training program he has managed to keep his muscles quite huge and body fat at 4%.

I am discussing Martin's work not because any of my clients are likely to become body builders nor do I think you need to lower your body fat to 4%. What I learned from Martin led me to the research. Why can he do what he does? Why doesn't his body hold on to fat like so many do or loose muscle when he 'goes lean'?

There isn't much clinical research but what there is is exciting and to me, profound. Time Restricted Feeding (8 hours feasting/16 hours fasting) and Intermittent Fasting 24 hours feasting and 24 hours fasting, work as well as severe low calorie diets to regenerate the human body and keep it lean. There are several different versions of Intermittent Fasting and many books on Amazon. What they all have in common and why they do what they do is they allow the digestive tract to rest.

Just as sleep is a necessity and impaired sleep lowers the immune system and increases degeneration and inflammation we need to rest from eating. For quite some time experts have suggested smaller meals more often, always eat breakfast, don't skip meals. We have been encouraged to eat from dawn to dusk.

Your distant ancestors likely ate meals late morning and evening. Without a refrigerator or restaurant they ate lightly (or not at all) on arising and had a light (and early) evening meal (leftovers). This is still the ideal. Commonly Americans, and most of the developed world, eat all day long and eat their largest, heavy meal at night which forces calorie storage AND disturbs deep sleep. This pattern of eating also reduces cellular autophagy. More on autophagy later but reducing it is not a good idea.

Historically breakfast happened after gathering the eggs or catching the fish, rather a brunch/lunch, likely a hearty meal to provide the energy needed for completing the day's work or celebrating the hunt. There were no refrigerators to open and 'eat' or grocery stores to easily replenish the refrigerator or all night restaurants to 'eat any time'. The evening meal invariably consisted of leftovers.

We (my self included) have blamed the Western diet, processed foods, bad fats, and/or lack of exercise, for the condition in which we find ourselves; Type II diabetes has increased 90% in the last 10 years. And it isn't just the US. Worldwide the increase in Metabolic Syndrome is almost unimaginable, 50% of the population of urban Southern India, 40% of Saudi Arabia. Obesity, just one part of Metabolic Syndrome is present in 31% of Americans and 32% of Mexicans.

Metabolic syndrome is a combination of the medical disorders that, when occurring together, increase the risk of developing cardiovascular disease and diabetes. Metabolic syndrome is also known as metabolic syndrome X, cardiometabolic syndrome, syndrome X, insulin resistance syndrome, Reaven's syndrome (named for Gerald Reaven), and CHAOS (in Australia) Wikipedia

What if we got here for a quite different reason, we eat too much, sometimes very bad foods, but even if we make healthier food choices we may just eat too much food during too many meals over too many hours. 24 hour access to food may be our demise.

In the mice study discussed in the chapter on hyperinsulinemia page 156, eating ad libitum, all day and night, whether the food was great or not so great, did NOT maximize health. Time Restricted Feeding, whether the food was healthy or not so healthy, did maximize health.

Enough of my clients have now tried the 8/16 feeding/fasting plan, a milder version of Martin's IF, to offer an opinion. Whether in their 20's or 70's they love the new found energy and mental clarity. There are two key benefits, likely more will be discovered.

Time Restricted Feeding-

1. **Lowers fasting insulin reversing insulin resistance** which dramatically reduces incidence of cancer, hypertension, heart disease, Benign Prostatic Hypertrophy, Thyroid reverse T3 syndrome, Alzheimer's, PCOS, obesity, Type II Diabetes, and much more.
2. **Increases the process of autophagy.** Sounds weird but it is wonderful. During the fasting period autophagy degrades damaged cells, virus including HIV, bacteria, damaged DNA; ... "Autophagy (auto - self, phagy - eating) is defined as a fundamental lysosomal catabolic pathway responsible for degrading long-lived proteins, protein aggregates, oxidised lipids, damaged organelles, and even microbial invaders." It is absolutely necessary for regeneration.^(145,146,147,148,149,150) With impaired autophagy we become cellular hoarders, keeping the junk that really needs to go.



When elevated insulin from over consumption, too much food or too many meals, or poor sleep with lower melatonin, or stress suppress the process of cellular housekeeping we are rapidly overwhelmed with dead and dying material that will lead to premature aging and disease. Health requires we keep our bodies clean inside and out. Autophagy is our internal housecleaner.

Autophagy regulates food intake, adipose tissue development, and plays a protective role against fat toxicity in beta cells (pancreatic cells). Autophagy may be suppressed or enhanced in various conditions from Metabolic Syndrome^(151,152,153,154,155,156) to cancer^(157,158,159,160,161,162,163,164,165) or Alzheimer's^(166,167,168,169,170,171,172).

Infants and young children should not be included in Time Restricted Feeding. For children above 9 the window is likely 10-12 hours depending on age and growth rate. For pre-menopausal women the window is likely 10-12 hours and for adult males and post-menopausal women 8-10 hours. Honestly, I feel the LOWER number is best in every category.

You may pick any 8-10 hour block. Eat all your required nutrients within that time. Eat your largest meal of the day when you break your fast. For the rest of the 24 hours consume zero calories. Coffee if tolerated, tea, clear broth and water are allowed. You might miss your 'window' once a week or so without issue as long as generally you keep your feeding time restricted. I promise you will be healthier and happier, do let me know.

Over the last year clients have commenting on meeting seniors in excellent health who have told them they never eat after 4PM. Time restricted feeding has been around for a long time.

If you decide to body build do visit Martin's page as in my opinion he is the very best.

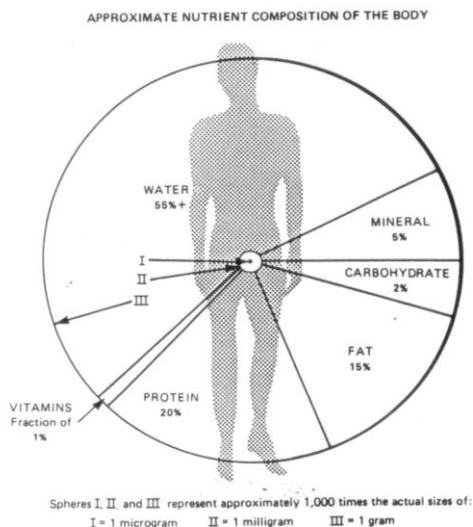
<http://leangains.com>

Checklist and Notes:

- Do I keep my feeding window within acceptable limits
- Do I feel satisfied after meals without fullness?
- Do I depend on 'digestive aids' or work to improve my own digestive function?
- Do I regularly use an anti-acid or reflux medication? If so have I been tested for helicobacter?
- Do I have a minimum of one and not more than 3 bowel movements daily resulting in full evacuation? Vegetarians will tend to more bowel movements daily due to the higher content of fiber in the diet.
- Are my stools fully formed, easy to pass and dark brown in color?
- Is the odor of my stool normal? That is not excessively odorous and without odorous gas?
- Am I free of noticeable gas unless eating unusual foods?
- When using antibiotics do I routinely re-implant the 'good' bacteria and use fiber to regrow my anaerobes?
- Am I free of belching, burping and reflux?
- When I experience symptoms of a possible gut pathogen do I immediately treat with Tricycline and a probiotic (see Special Protocols)? Symptoms include loud stomach 'noises', excess gas, unusually odorous gas, diarrhea, explosive diarrhea, any other dramatic and unusual change in bowel function.

CHAPTER 3 START WITH THE BASICS

Figure 3-1 Body Composition



Besides our bacteria the primary components of the human body are water, protein and fat. These elements are required daily in significant amounts and a section is devoted to proteins and a separate section/chapter to fats and water.

Vitamins and minerals are found in whole foods and to fulfill your daily need of these essential nutrients you only need counting potassium, an essential element. Eating suggested amounts, as found in fresh whole food, will ALSO provide significant amounts of all other vitamins and minerals.

Healthy bodies are about 55-65% water, higher in athletes than in sedentary persons because water is associated with muscle

mass and muscle metabolism, not fat. Adequate water, fresh, clean, is a primary need. Physical activity, dry climate or hot weather increase the need for water consumption. Often thirst is mistaken for hunger. Try drinking 8 ounces of water when you feel hungry and see what happens. Read the section on water page 36 to make sure you stay fully hydrated.

Protein comprises about 15-20% of body mass and fat from 15-25% in healthy men and women.

Carbohydrates are used for fuel. Carbohydrates (and proteins) not 'burned' are converted to fat so total body carbohydrate is very low, about 2%. Refined high carbohydrate foods may provide fuel (calories) but little of essential nutrients to build and repair the human body. Very little space is devoted to carbohydrates as they are found in all foods and are not essential for building body mass and are rarely deficient in the modern diet. Excess and refined carbohydrates are primarily responsible for the dramatic rise in degenerative diseases.

Minerals comprise about 5%-7% and vitamins less than 1/10 of 1%. Clearly, taking a multivitamin and mineral, if you did not also consume adequate protein, sufficient potassium in foods, high quality fat and clean water, would do little to improve your health. FOOD (and water) must come FIRST.

Food provides raw materials to replace body parts and calories for energy. Proteins and high quality fats are of first importance in determining a healthy diet as these will make up the replacement parts for new cells. Some high carbohydrate foods may provide a source of vitamins and minerals. For most Americans the need for carbohydrates is quite low, the exception being athletes and persons whose work requires intense physical energy such as firefighters or field workers.

Rather than consider carbohydrate 'counting' or trying to figure out the vitamin and mineral content of each food I use the 'potassium count'. To get adequate potassium requires consumption of whole fruits and vegetables. The most concentrated sources of potassium are typically vegetable/fruit carbohydrates high in vitamins and minerals as well as fiber. If you reach your potassium goal you will get more than enough carbohydrate (and vitamins, minerals and fiber too).

- Make sure you drink enough good tasting, fresh, high quality water. See page 110 for information on water consumption.
- Make sure you meet your protein and potassium food goals. These two values are your keys to long-term health. Don't skip this step. You may believe you 'eat enough'. Count and make sure. Evaluating the potassium and protein content of the food you eat takes some learning but once you learn you won't forget.
- Evaluate your fat choices, kind is more important than amount. Get rid of bad fats. I do not encourage counting fat grams. Eat the fat found naturally in the 'real food' you eat. Use added fats per the fat section sparingly, as seems pleasing and tasty.
- Check your vitamin D status and meet your mineral goals.

Be patient with yourself and be willing to spend the time you need to find out about the nutrient content of the food you eat. Use a food journal for the first few weeks and a good protein and potassium food content book to make sure you get your daily minimums.

There are only TWO CATEGORIES YOU NEED TO COUNT to insure you are getting enough of the RIGHT foods to keep you well. One category is PROTEIN, the building block of muscles, cells, bone, hair, teeth, enzymes, neurotransmitters, hormones, your DNA and RNA and much, much more. The second is POTASSIUM, which will give you significant amounts of MANY nutrients and all the carbohydrates you could possibly need. Counting potassium should also insure you consume enough indigestible carbohydrates to feed your microbiota.

FATS

No need to count. Further you will find a section on omega-6 and omega-3 fats. In general let fat be your LARGEST food intake. It will typically be in the whole foods you eat, meat with fat, poultry with skin, fish with skin, nuts and seeds, eggs, cream, etc. You do not need to count fat grams. DO NOT use processed or hydrogenated fats, ever. Do not eat foods containing them. Use full fat dairy including full fat yogurt. Acceptable added fats- extra virgin olive oil, butter, cream, nut butters, ghee, non-hydrogenated lard, avocado oil, coconut oil. DO NOT use protein

bars of power bars or other processed foods with fat, ever. Processed fats are dangerous to human (and animal) health.

PROTEIN

I have included several ways to determine your protein needs but will tell you all three methods give nearly the same answer. Once you determine your need keep within the boundaries. More protein is not needed and excess not healthy. If you are still hungry increase your NATURAL fat intake.

The easiest, for adults male or female, is simply 'THREE PALMS FULL OF PROTEIN A DAY' (your palm, no one else's).

Your daily total can be eaten all at once or over the course of the day. You decide. Just make sure you get three palms full of protein. While fruits and vegetables do contain some protein I do not include these when counting daily totals

Your body depends on DIETARY proteins to provide the amino acids necessary for the production of hormones, prostaglandins, neurotransmitters, immune system components, digestive enzymes, other digestive fluids, blood and bile. Your muscles, bone matrix, joint collagen, skin, hair and nails (and more) are composed primarily of proteins and they are constantly being broken down and rebuilt.

Amino acids are a part of every cell of your body. They are a major structural component of skin, hair, nails, and bone. Amino acids are necessary to make enzymes that provide the chemical reactions for every function of your body including production of energy, digestive functions, reproductive functions, immune functions and more.

Amino acids are necessary for the production of neurotransmitters that affect your mind and mood. Protein (with fat) is the basis of the immune system. Without the amino acids found in protein there is no life. Used proteins are not recycled in the body but are broken down and excreted through the kidney as nitrogenous wastes.

You cannot make essential amino acids. They must be consumed every day by eating sufficient quantities of complete proteins to replace daily losses.

Many persons suffering from depression and prescribed medication are simply deficient in adequate protein. The amount of serotonin or dopamine you have today, as you read this, is proportional to your protein intake of the prior two or three days. Protein does not store in the human body. You need protein for all vital processes. More than just your muscles will be destroyed if intake is insufficient. Do not avoid protein foods.

3 Ways to Calculate Your Daily Minimum Protein Requirement

Quick calculations for the math impaired, slackers, and the wise who have better things to do with their time:

Ideal body weight divided by 2.

For 150 pounds this would mean about 75 grams per day.

Even simpler: Look at the palm of your hand.

Eat enough protein every day to cover the palm of your hand three times.

Pile it high, very high, if from non-meat protein sources or about 1.5-2 inches high if using meat, fish or poultry sources.

Advanced Calculations to make your life more complicated (who needs this?):

Ideal body weight in kilos X 0.8 grams ⁽¹⁷³⁾ to 1.3 grams (very active); in pounds X 0.36 grams (inactive) to 0.6 grams (very active).

Calculations As Percent Of Calories (to make your life totally complicated and make eating less fun but put here for the sticklers who need to see that the number is the same any way you calculate. There is no reason to determine carbohydrates as your potassium number will cover carbohydrates and fat is determined by taste and fat content of proteins):

Desired body weight times 14-28 (calories used per pound per day) times 0.15-0.3 (percent of calories 15-30) divided by 4.5 (number of grams per calorie). Example: A woman, 45 years of age, healthy body weight 130-- 130 X 15 X 0.2 divided by 4.5=86 grams per day. (20% protein)

Choose 14 calories per pound if you are sedentary; spend most of your time sitting down. Increase the number as activity increases. A professional athlete could use more than 28 calories per pound. The average for an active male or female exercising 4+hours per week and spending most of your time on your feet is 20. Do not go under 14 calories. You cannot reduce body fat by reducing calories. You will end up losing muscle and further reducing your capacity to burn fat.

If you are in good health, not under stress, not pregnant, not preparing for surgery or recovering from injury use 0.15 (15%). If you have some stress, frequent infections, fatigue, moodiness or impaired digestion multiply by 0.2 (20%). If you are a competitive athlete, under great emotional or physical stress including chronic illness, injury, pre or post-surgery or are pregnant or nursing, multiply by 0.25 (25%)-0.3 (30%). Athletes who have increased the protein and fat in their diets have improved endurance performance over 30%.

MY PROTEIN REQUIREMENT IS _____ GRAMS A DAY.

Getting Protein

Not all of these are preferred. They are listed to show general amounts.

Table 3 Protein Content of Common Foods

Adzuki beans, cooked	17 grams per cup
Bread	2-11 grams per slice (check the label)
Bulgur, cooked	8 grams per cup
Cheddar/jack	7 grams per oz.
Corn meal, cooked	2 grams per cup
Cream cheese	2 grams per oz.
Egg	6 grams per each

Kidney beans, cooked	15 grams per cup
Lean meat, fish, poultry	25-30 grams per 3 1/2 oz.
Low fat 2% cottage cheese	31 grams per cup
Milk	8-9 grams per cup-8oz.
Most fruits	1 gram per fruit
Nutritional yeast, flakes	4 grams per heaping tablespoon
Nuts and seeds	2-3 grams per level tablespoon
Oatmeal, cooked	5 grams per cup
Parmesan	10 grams per oz.
Potato, baked with skin, medium	5 grams
Rice, cooked	5 grams per cup
Tempeh	30 grams per cup-8oz.
Tofu	20 grams per cup- 8oz.
Vegetables	1-3 grams per 1/2 cup
Wheat germ, toasted	8 grams per 1/4 cup
Yogurt	8-10 grams per cup-8oz.

Protein foods also contain fat and/or carbohydrate. Beans and grains are protein-carbohydrate combinations. Meat, fish, poultry, and eggs are primarily protein-fat combos as are nuts and seeds. When choosing proteins keep the fat/protein ratio in mind and be a label reader. Use a food value table when necessary until you get used to estimating. Use a book with protein values or visit the USDA site online at <http://www.nal.usda.gov/fnic/foodcomp/search/> or download the USDA software for free here <http://www.nal.usda.gov/fnic/foodcomp/Data/SR17/sr17.html>

Nuts and seeds and some fish and wild game are high in fat but these fats are readily converted into fuel to be used by the body for energy. The fats in natural food, including wild game, are higher in the beneficial and often hard to get omega-3 fatty acids. The omega-3 fatty acids found in wild game and fish are used to manufacture other essential substances and are critical for healthy functioning of brain and nerve.

An easy way to estimate the protein to fat ratio of a food is by texture. Fat gives a creamy or juicy texture. Low fat, high protein foods are usually dry and chewy. Fats become liquid with heat. Proteins become drier and tougher. Mozzarella is a better source of protein than cream cheese or brie. Round steak has more protein per ounce than pot roast.

To make lean protein foods more palatable use liquids in serving and preparation- salsa, wine, water mixed with a small amount of oil, fat-free sauces. Use a slow cooker, convection oven, steamer, or microwave. Steaming, microwaving, and slow cooking keep proteins moist and tender making them more digestible. Do not overcook proteins.

Bacon, hot dogs, 'lunch meats', and other processed meats (including processed ham turkey and chicken products) are not typically good sources of protein. They often contain excess processed fat, salt and chemical preservatives. Oscar Meyer makes lean hot dogs preserved with vitamin C (ascorbic acid) for a once-in-awhile treat. You may find other brands as well.

Vegetarians and even vegans (persons who eat no dairy or eggs as well as no meat or fish) can get sufficient protein but they must consume much larger quantities of food to get adequate amounts of all of the essential amino acids. Total number of grams and the kinds of amino acids the proteins contain equal the quality.

When using vegan or vegetarian sources for protein the 'three palms full' rule does not apply. You will have to count your grams.

If you are a vegetarian you should be eating at least 4 meals per day of whole, fresh food. The vegetarian/vegan diet is fiber rich, bulky. Eating 3 or less times a day will not provide adequate nutrients. Vegetarian animals graze all day. Meat eating animals eat infrequently and often fast. The difference is the nutrient density of the foods being consumed.

Vegetarians/vegans need to include legumes, nuts, and seeds to balance proteins. These foods are high in lectins so make sure that the sources you choose for protein are from lectins you tolerate. Read the chapter on lectins carefully.

Grains do not have the complete complement of essential amino acids necessary to support life nor are they nutrient dense. They are primarily a source of calories. It may be difficult for some vegetarians to get enough protein. If you are vegan/vegetarian make sure to count your daily protein grams and learn how to get your minimum daily requirement.

Protein, from food, is broken down in the gut into polypeptides and slowly released into the bloodstream allowing for maximum utilization of amino acids. In countries outside the US people eat four or more meals per day. Traditionally the largest meal is consumed before 4 PM. Eat sufficient protein early in the day and smaller amounts at more than one meal to feed your body well.

When proteins (or minerals or other nutrients) are 'loaded' into your system, such as when people use amino acid supplements or highly concentrated protein powders, your kidney will work overtime to remove the excess from your blood. Proteins in food are 'time-released' as the foods are digested.

Protein powders or supplements are not advised for daily use but may be supportive during times of illness or stress.

Current food fads encourage imbalanced eating such as high carbohydrate, or low fat or low protein or more recently low carbohydrate. Dietary imbalance will not lead to long-term health. Consider moderation in all things. The body must have wholesome, natural, unrefined proteins, carbohydrates and fats with all accessory nutrients to function properly.

The best diet, including protein choices, for you is one that mimics the food of your ancestors, what your forbearers ate 200-300 years ago.

The largest dietary failings in the American diet are lack of real food, lack of genetically appropriate food, food processing/refining, food preservation (eating foods that are not fresh) and genetic engineering of proteins. Avoid processed, preserved, and genetically engineered foods as much as possible. Avoid foods your ancestors would not have had access to.

Children and Protein:

Researchers in Japan studied the effects of the L-tryptophan content in the diet of children from birth to 15 years of age. L-tryptophan is found in high quality protein foods such as meat, fish, eggs, poultry and dairy. L-tryptophan is important because it is the precursor for production of serotonin and melatonin. Serotonin affects your mood, melatonin your sleep.

On the days dietary l-tryptophan content was low 'at the breakfast meal' children 8 and under suffered from altered mood, were more easily angered, found learning more difficult and had difficulty going to sleep at night and waking up the next morning.^(174,175,176)

Low BREAKFAST protein altered behavior and learning IMMEDIATELY. Children's growth is so rapid from birth to eight no 'spare' proteins were available for neurotransmitter or hormone production.

Think about the implications for American children. You aren't just what you eat, you are what you ate this morning, especially if you are 8 years old or younger, and if it wasn't quality protein who is to blame?

Currently the national government run school breakfast programs allow ½ ounce of protein foods and ¾ cup of milk for children 3-5; ½ cup of milk for children 1-2. Even assuming children eat what they are given it is unlikely these values would meet the minimum l-tryptophan requirement determined by the Japan researchers.

In the US it seems our primary concern is 'low fat' which means none of the programs provide eggs (an excellent source of iron, protein, and lecithin for brain development) or meat (iron, protein, copper, zinc, l-carnitine). The switch from 'fat' to a carbohydrate obsession not only is increasing obesity and early onset diabetes it is also depriving our children of the amino acids needed for growth, development, and sleep.

Women and Protein:

Men as hunters, women as gatherers, he eats the meat and she has a salad. Hmmm... It may be a bad idea. Margaret Mead found a tribe where the fruits of the hunt were presented to the women and children; and the fruits of the gatherers, likely nuts, seeds, berries and fruits, were presented to the men. The tribe was very healthy.

Beneficial outcomes- 1. Women and children need more protein per pound of body weight because of growth and fertility. 2. Men, because of testosterone, spare proteins. They have a high need for other nutrients and antioxidants. 3. Sharing benefits mind and body.

In my 40+ years of practicing/teaching nutrition, I have come to believe women, from puberty to menopause, need more protein, per pound of body weight, than men to attain and maintain the same level of health.

Many cases of depression, PMS, symptoms of menopause, fatigue and other chronic complaints have disappeared, completely, with an increase in daily protein.

There has been some attention given to the idea that protein may increase the risk of osteoporosis. Newer research shows the risk for osteoporosis is strongly tied to the amount of potassium and magnesium consumed. Adequate protein protects bone, especially when vitamin C is adequate^(177,178,179,180,181,182,183) (to build collagen, the matrix of bone)..

Nutr Rev. 2002 Oct; 60(10 Pt 1): 337-41.

Elderly women need dietary protein to maintain bone mass.

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Excess dietary protein is considered a risk factor for osteoporosis owing to the potential for renal acid load. Researchers who conducted a recent prospective study of older adults reported that animal protein had a protective role for bone, especially in elderly women, whereas plant protein was negatively associated with bone mineral density. An interaction between protein and calcium suggested protein alone was not the important factor. Other studies confirm the beneficial effect of increasing dietary protein intake in older women to reduce bone mineral density loss and risk of fracture, suggesting that emphasis should be placed on promoting adequate protein intake in elderly women.

The three key components of the healthy diet are protein, magnesium, and potassium. They must all be considered when planning a program. Elderly women consuming extra animal based protein had higher bone density. Women of all ages NEED adequate, high quality protein.

Protein and Seniors

Two important studies using nitrogen balance found an increased need for protein in seniors. ^(184,185,186,187) In these well done studies both men and women 65 and older needed at least 1 gram of high quality protein for each kilo (2.2 lbs.) of body weight, more than the 0.8 grams RDA. Seniors eating adequate protein do not lose muscle mass or bone mass (collagen core) or lose it more slowly than seniors consuming lower amounts. Seniors need more than 1 gram per kilo a day during and after illness, injury and stress. While a number of studies have suggested protein needs in seniors do not increase and may even decrease, the markers used in these studies for protein sufficiency are not as accurate as the nitrogen balance studies.

POTASSIUM FOR VITAL ENERGY

The role of potassium, a primary electrolyte in the human body, is played out in the muscle and in the blood. Muscle cells are the primary residence of potassium. Potassium is key to muscle energy and also helps keep cells 'plump'. Think of cells as bathyspheres.

A bathysphere is a spherical deep-sea diving submersible which is lowered into bodies of water with a cable. Bathyspheres have a variety of uses, usually including the study of underwater life.

To keep the 'roundness' a cell must have equal pressure inside and out. Potassium and magnesium within the cell and calcium and sodium outside the cell are the regulators of cell integrity. An inappropriate change in pressure, caused by a shift in intra and extra cellular electrolytes may cause implosion or explosion. Muscle cells are able to withstand an 80% loss in potassium but they are greatly weakened and susceptible to damage which we experience as a vascular incident or stroke. Potassium is one of the most important elements in our diets.

Potassium is equally critical in plant health. Your local nursery sells it as potash. Potassium has many functions in plant growth. In plants it

is essential for photosynthesis,

activates enzymes to metabolize carbohydrates for the manufacture of amino acids and proteins,
facilitates cell division and growth by helping to move starches and sugars between plant parts,
adds stalk and stem stiffness,
increases disease resistance,
increases drought tolerance,
regulates opening and closing of stomates,
gives plumpness to grain and seed,
improves firmness, texture, size and color of fruit crops, and
increases the oil content of oil crops.

Although not an integral part of cell structure, potassium regulates many metabolic processes required for growth, fruit, and seed development. Many vegetable and fruit crops are high in potassium, which is vital for animal and human nutrition. Indeed, the health and survival of man and beast is dependent on potassium. M Ray Tucker, Agronomist NCDA&CS AGRONOMIC DIVISION Mailing address: 1040 MAIL SERVICE CENTER, RALEIGH NC 27699-1040

What you see in plant nutrition is true for our cells as well. Potassium makes our cells more resistant to 'drought' and disease. It stiffens our stalk (cells' integrity). It is likely potassium also plays other roles such as in cell regulation not yet researched. Potassium for humans is critical for bone health.^(188,189,190,191)

The primitive, or "natural", whole food diet contained 2 mg. or more of potassium for each calorie consumed. A 2,000 calorie diet would naturally contain a minimum of 4,000 mg of potassium.

Carbohydrate foods, such as sugar and wheat, are rich sources of potassium in their whole unprocessed state but lose some or all of their potassium through refining.

Foods high in potassium are also rich in all other nutrients. Rather than count carbohydrates, count potassium.

That last statement is REALLY important. Foods high in potassium are fruits and vegetables. FRESH fruits and vegetables. There are numerous studies showing a relationship between fruit and vegetable intake and a reduction in ALL degenerative diseases, especially cancer.^(192,193,194,195,196,197,198,199,200,201,202,203)

This relationship is not about RDA vitamin and mineral requirements but about the interesting components found in fresh fruits and vegetables. Citrus contains vitamin C and many different bioflavonoids found to be regulators of cell replication. Adequate intakes of these elements reduce incidence of all cancers.

ZEST: One of my favorite sources of bioflavonoids, especially d-limonene which is an anti-cancer nutrient, is known as zest, made from the outer skin of citrus fruits including lemons, limes, grapefruit. and oranges. To make zest you need a zester, my favorite being the Microplane Zester, available from amazon.com. Use it daily to make a delightful and healthy addition to your smoothie, tea, dessert, or even your coffee.

Zest has been clinically shown to reduce incidence of skin cancers.^(204,205) This is interesting because it is found in the skin of the fruit. Perhaps what protects the fruit skin also protects our skins? An element found in zest, d-limonene, may prevent and even reverse cancers of the stomach, liver, pancreas, colon, skin, prostate and breast.^(204,204,206,206,207,207,208,208,209,209,210,210,211,211,212,212,213,213,214,214)

There are lots of reasons to eat your fruits and vegetables. Counting potassium (and getting enough) guarantees you'll get the essential elements, vitamins and minerals to keep you healthy and active throughout your life.

As you begin counting your potassium intake you'll wonder how your ancestors got enough. Their 'secret' was simply unrefined whole food 'one pot cooking'.

Our ancestors had few cooking utensils and no refrigeration. Whatever food they had was consumed whole, raw, or put in a pot over the fire and simmered until eaten. Gathered foods, squash, potato, apples, pears, fruits and berries, were smaller as no modern agricultural methods were applied whether artificial watering or fertilizing. Potassium is higher in the skin or peel. Eating two small apples would provide much higher potassium than eating one larger apple of equivalent weight and calories.

As previously mentioned, potassium is an intracellular nutrient. When the cell wall is broken potassium leaks out. One pot cooking retains nutrients that are lost when foods are roasted, broiled, boiled (with water tossed out) or steamed (losses in the 'drip'). In past years much of the potassium would be retained by using the drippings for sauces or gravies, a practice not in common use now in the USA.

One pot cooking had other benefits. Open fires just don't get very hot. Low heat moist cooking, in a single pot, destroys pathogens, preserves the nutrients, breaks down proteins to make digestion easier and as most pots also contained bones of some kind, whether from domesticated animals, wild game, or fish, it also provided essential minerals and fats.

This cooking method is similar to today's crock-pot or slow cooker. Unless you truly love salad or juicing you may find utilizing a crock-pot or slow cooker is the easiest way to increase your potassium intake.

By eating potassium rich foods you will be getting all of the trace elements and other elements that researchers will discover cure or prevent something next month or next year and you won't have to wait or buy it in a pill.

Persons who consume 4,000 mg. of potassium or more DAILY, regardless of calorie intake, have a much lower incidence of all degenerative diseases, have better bones, lower incidence of cancer, have fewer incidences of stroke and are less likely to become obese or develop adult onset diabetes.^(188,191,215,216,217,218,219,220,221,222,223,224,225,226,227,228,229,230,231)

When we began refining foods, increasing the number of 'pots', and using new methods of cooking the amount of potassium in the finished meal dropped precipitously. The modern food consumer is lucky to get ½ mg. of potassium for each calorie consumed.

One of the greatest benefits of the vegan/vegetarian diet is simply that there is typically a huge increase in the daily amount of potassium consumed.⁽²³²⁾ All of the dietary programs that successfully lower cholesterol, normalize weight, or improve blood pressure, contain high amounts of potassium.

You may choose the sources of potassium that you like but make sure you get a minimum of 2 mg. per calorie and try to get even more.

Whole foods such as vegetables, legumes and fruits all have high amounts of potassium. Grains have very little potassium except in the germ and bran. Adding oat, rice, corn or wheat bran to foods can increase the potassium content but watch for lectin response. (see lectin chapter)

Domesticated meats trimmed of visible fat and poultry without the skin have about 1:1 ratio calories: potassium. Fruits, vegetables, wild game and most lean fish have 1:2 calories:potassium.

Many of my clients use vegetable juices, potassium broth, bone stock plus veggies, or high potassium soups to get their daily quota of potassium. They are not used to consuming the quantity of food necessary to get 4,000-10,000 mg. of potassium a day. Making vegetable soup and eating the veggies would provide both potassium and fiber needed by our microbiota. In all situations vegetable soup is better than vegetable broth.

Another potassium trick is to use tomato sauce, juice, paste, or salsa if tolerated. Tomatoes are high in potassium. If tolerated buy low or sodium-free tomato based products. They can contribute significantly to your potassium intake. Added to spaghetti, tomato based sauce can help balance the lack of potassium in pasta (pasta is refined flour boiled and drained, having little value other than calories, not even fiber).

Sodium increases the need for potassium. ^(229,233,234,235,236,237) So if you add salt you work against yourself and must also increase potassium. This is not true if you are a vegan or vegetarian. The healthy vegan/vegetarian diet, if composed of abundant fruits and vegetables, is high in potassium and low in sodium and requires additional sodium for health. Vegetarian animals always need a 'salt lick'.

If you tolerate the lectins in beans, all types of beans are high potassium, kidney, lentil, garbanzo, black or pinto being the highest. Beans add color, flavor and texture as well as potassium and protein to any meal. Using beans, in chili, soup or salad, increases the amount of potassium, protein and complex carbohydrates. Blackstrap molasses added to your bean recipes further increases potassium content. Beans are also a good source of soluble fiber.

Potassium containing foods may be eaten raw (whole) or cooked by slow cooking (crock pot or pressure cooker) or stir-frying. Use soups, stews and casseroles frequently because they retain the natural potassium found in the food. Remember, potassium is an intracellular nutrient (inside the cell). When the cell wall is broken during thawing or heating the potassium leaks out. If you broil or steam and don't use the 'juices' that have escaped you will lose much of the potassium.

Fresh peas have a significant amount of potassium, canned peas including the 'water' have 2/3 the original amount. If you toss the 'water' in the can the amount of potassium is again reduced, leaving little of the original value. Processing also removes the fiber needed by our microbiota.

Fresh foods, prepared from scratch, are best. Frozen foods should be prepared in a way that retains the 'juice' or frozen berries mixed in a smoothie without thawing.

I understand this way of shopping and food preparation may be a change for you. Some clients may not be great cooks. Some of you may not cook at all.

Honestly, if you rely on prepared foods or restaurant cooking you will not be able to regain or maintain your health.

Will changing your life style to eat high potassium be tough? YES.

We are used to looking at foods differently. Some people see everything as food. Others eat no fat or no dairy or low cholesterol. Still others avoid any food that is not in a container (can, box or tray). The idea that you can eat as much as you like as long as the food is real and is balanced by potassium to calories 2:1 can be labor intensive at first. Soon after you begin this program you will see that it works and habit makes it easy.

The Other Reason to Consume High Potassium Foods- FIBER to Feed Microbes-Eating for Two (ourselves and our microbiota)

All potassium containing foods, that is whole fruits and vegetables, contain fiber required by your microbes (gut bugs) for health. We need to eat for our microbiota as well as our body. Fibers needed by our microbes include resistant starch (RS2 and RS3), soluble and insoluble fiber.

Foods high in both potassium and the fiber we need to grow our friendlies include (daily) onions, leeks, garlic, tubers (root vegetables like sweet potato, parsnips, carrots), potato with skin (always with skin), , green bananas (for RS2), legumes, berries (very high in fiber), all types of squash, roasted and cooled potato with skin (for RS3), cooked and cooled rice (for RS3). Include significant amounts daily for healthy microbiota

Both insoluble fiber and RS3 are found in lentils, peas, and legumes. Other root vegetables and tubers are also abundant in either RS3 (sago, cassava, taro, heirloom potatoes) or insoluble fiber (turnips, okra).

Consuming 3 or more POUNDS of plant foods including tubers (potato) and a few whole fruits will typically contain both enough potassium and enough fiber to keep us and our bugs healthy.

Sample Protein - Potassium Meals

Breakfasts (should be a moderate meal, or even skipped by adults):

- Anytime Smoothie (see Potassium Recipes)
- One or two eggs and 1 whole orange or other whole fresh fruit Muesli with dark muscovado sugar, or maple syrup grade B or C, for sweetening, with 1/4 cup whole organic milk or cream or coconut milk.
- One or two eggs, sausage, bacon, or ham, sprouted grain or gluten free toast. A side of sauted vegetables, onion, squash, etc.
- Cooked oatmeal with fresh berries or other fresh fruit, topped with whole organic raw (if possible) milk, cream, or full fat coconut milk. Add cottage cheese for extra protein (about two heaping tablespoons) and a natural sweetener such as grade C maple syrup, dark muscovado sugar, Billington's Dark Molasses Sugar, or panela.

Lunches (ideally should be your largest meal):

- Large salad with turkey or tuna 4-6 oz. and tomatoes, carrots, cucumber, sprouts, kidney or garbanzo beans, if tolerated, sweet red pepper, red cabbage, lettuce or mixed greens, onions and home-made extra virgin olive oil dressing (with bleu cheese or?)
- Always make extra virgin olive oil dressings. Do not use dressings containing seed oils such as soy or safflower or sunflower seed oil. See chapter on fats.

- 1-2 cups brown rice and 5-8 oz. fish or poultry or lean red meat and 2+ cups vegetable such as asparagus or green beans plus 1-2 fruits or 1-2 cups mixed fruit for dessert.
- A sandwich (use sprouted fat free whole grain breads like Alvarado or Ezekiel or gluten free bread), or salad, or soup or stew with lots of vegetables and protein such as beans or chicken or beef. Fruit for dessert.

Dinners (should be your lightest meal):

- Soup, stew or casserole with moderate protein from poultry, fish, legumes (if tolerated) and vegetables , sprouted whole grain or gluten free bread, butter or no bread or grain if you're intolerant or inactive or dieting.
- 2-6 oz. of protein with rice (mixed white and wild) or spaghetti squash (use a tomato based sauce, high in potassium)
- Baked potato with the skin and 3-6-oz. protein and 2+ cups of cooked vegetables; or salad with lots of vegetables and protein in it and 1-2 cups or servings of fruit.
- Protein smoothie with berries for potassium

Condiments:

Salsa, adds C, bioflavonoids and potassium; low salt, low sugar ketchup or make your own with molasses sugar; tomato sauces; Parmesan cheese; Feta cheese; all spices and herbs; Wysong mixed salt or VegeSalt; soy sauce without preservatives if soy is tolerated; butter; cream cheese; sour cream; mustard; home-made barbecue sauce; chutney. Use 'real' not processed versions of these products.

Total daily potassium intake should meet a minimum of 2 mg. potassium per calorie consumed. No matter what your caloric intake you should strive to get **not less than 4,000 mg.** of potassium per day as an adult. In repeated studies men and women consuming 4,000 mg. or more of potassium daily had dramatically reduced incidences of stroke, hypertension and associated heart conditions. This figure held true even among smokers.⁽²³⁰⁾

Potassium Calculator- Daily Optimum:

My daily goal for potassium is my ideal body weight in pounds X 40 milligrams

per day or in kilos X 88 milligrams per day = _____ milligrams per day.

Getting Potassium

Table 4 Potassium Content of Common Foods

FOOD GROUP	500+ milligrams	300-499 milligrams	100-299 milligrams
DAIRY			
		Buttermilk, 1 cup 370	
		Nonfat fortified milk, 1 cup 450	Cottage cheese, 2%, ½ cup 110
		Whole milk, 1 cup 350	Whey, sweet, dry 1 tbsp. 155
		Yogurt, plain, 1 cup 380	
MEAT, FISH POULTRY	Roasted, braised or broiled		

FOOD GROUP	500+ milligrams	300-499 milligrams	100-299 milligrams
	Cod, 4 oz., 580	Beef liver, 4 oz. 430	Chicken, meat only, 4 oz. 275
	Flounder or sole, fillet, 6 oz. 750	Haddock, 4 oz. 450	
	Salmon, 6 oz., farmed 650, wild, 735-855	Ham, lean, 4 oz. 325	Round steak, lean, 4 oz. 250
	Sardines, canned, 6 oz. 675	Lamb, lean, 4 oz. 365	
		Perch, 4 oz. 390	
		Pork chop, lean, 4 oz. 370	
		Tuna, albacore, water pack, 1 can 410	
		Turkey, meat only, 4 oz. 340	
LEGUMES & NUTS			
	Adzuki beans, cooked, 1 cup 1225		
	Baked beans, canned, 1 cup 550		Almonds, dry roasted, ¼ cup 255
	Baked beans, homemade, 1 cup 900	Tofu, firm, ½ cup 300	
	Black beans, canned, 1 cup 610		Cashews, dry roasted, ¼ cup 195
	Garbanzo beans, cooked, 1 cup 480		Coconut milk, ½ cup 250
	Kidney beans, canned, 1 cup 610		Macadamia nut, 1 oz. 100
	Lima beans, cooked, 1 cup 730		Peanut butter, chunky, 1 tblspn.120
	Pinto beans, cooked, 1 cup 740		Pecans or pecans, 1 oz. 125
VEGETABLES			
	Broccoli, 1 med stalk whole, cooked, 520	Beans, green, cooked, 1 cup 375	Carrot, raw, 1 med. 195
	Lettuce, red, 1 head 580	Beets, each, 2" dia 300	
	Lettuce, iceberg, 1 head 6" dia 760	Cauliflower, raw, small, 4" dia, ½ head 400	Celery, 1 stalk 8" 100
	Lettuce, romaine, ½ head, 775	Lettuce, butter, 1 head 390	Mushrooms, raw, sliced, 1 cup 120
	Potato, mashed, w/ milk, 1 cup 600	Potato, mashed, instant prepared w/milk, 1 cup 300	
	Potato w/skin, baked, 1 med. 925	Peas, raw, 1 cup 350	Mustard Greens, boiled, 1 cup 280
	Spinach, raw, 1 bunch 1900		Peas, frozen, boiled, drained, 1 cup 260
	Spinach,, cooked, 1 cup 840		Spinach, New Zealand, cooked, 1 cup 195
	Sweet Potato, baked, 2"X5" 525		Tomato, cherry, each 40
	Squash, winter, baked, 1 cup 890	Squash, summer, boiled, sliced, 1 cup 340	Tomato, 1 med, 2.5" dia. 290
	Yam, baked, cubed, 1 cup 910		Zucchini, cooked, sliced, 1 cup 230
FRUITS			
	Apricots, dried, ½ cup 850	Apricots, 4 fresh 360	Apple, 1 med (3 per lb) 150 Apple juice, 1 cup 295

FOOD GROUP	500+ milligrams	300-499 milligrams	100-299 milligrams
	Avocado, 1 each, California 880, Florida 1070	Banana, 1 med (7-8") 420	Cherries, sweet, raw, 10 150
	Cantaloupe, ½, med (5" dia) 725	Orange juice, fresh, 1 cup 490	Grapefruit, 1 (3 ¾" dia) 175
	Currants, dried, ½ cup 650	Peach, 1 med (2 ½ per lb). 300	Orange, 1 large (3 ½" dia). 330
	Dates, dried, ½ cup 600		Pear, 1 large (2 per lb). 250
	Honeydew (7" dia), ¼, 725	Watermelon, diced, 2 cups, 340	Pineapple, raw, 1 cup 180
	Peaches, dried, ½ cup 800	Prune juice, ½ cup 350	Plum, 1 each, 110
	Prunes, pitted, ½ cup 750		Strawberries, med., 6 whole 120
	Raisins, ½ cup 575		Tangerine, med. 1 each, 140
GRAINS			
	Rice Bran, crude, ½ cup 875	Bran Buds or All Bran ½ cup 450	Brown rice, cooked, 1 cup 155
			Oatmeal, cooked 1 cup 130
OTHER FOODS			
	Tomato juice, 1 cup 560	Blackstrap molasses 1 tbsp. 350-585 (check label, batches vary)	Nutritional Yeast, heaping tablespoon 157
	Low Sodium V8 6 oz. 560		Panela, chancaca, muscovado dark, jaggery sugars, 3 tablespoons packed level (1 oz.) 295 (calories 87)
	Coconut water 11 oz. .670		Maple syrup, 3 tablespoons, 122 (calories 157)
			Brown sugar, 3 tablespoons packed, 143 (calories 156)

Values taken from USDA Nutrient Database SR17. Values are approximate as nutrients vary by season, crop, location and fertilization. All food values on labels or in this database are estimates and should not be consider absolute.

Potassium Quickie Recipes

<p>YEAST DRINK 1 cup fresh orange or other juice or 1 cup Very Veggie or 1 cup low sodium V8 2-6 heaped tablespoons Red Star yeast flakes or Lewis Labs International Brewer's Yeast with Selenium (start with smaller amount) Potassium 800-1,800mg. Protein 8-24 grams depending on amount of and type of yeast</p>	<p>ANYTIME SMOOTHIE 1 cup fresh orange juice or other whole juice (not from concentrate) 1 banana, apple, or other ripe fruit (ok to use green banana for resistant starch) 1 cup fresh or frozen strawberries, blueberries, blackberries, or raspberries or a mix. Optional: Your favorite protein powder Optional: inulin, fos and acacia fiber Potassium 1300-1500mg. If added: Protein 15-30 grams</p>
<p>MOLASSES HOT COCKTAIL 1 tablespoon blackstrap molasses Optional--1 tablespoon natural apple cider vinegar 6-8 oz. hot water Potassium 350-625 mg</p> <p>BANANA SMOOTHIE 1 cup milk 1 GREEN banana (RS2) Added fiber: insulin, fos and acacia fiber 1 tablespoon blackstrap molasses Potassium 1200mg Protein 9 grams May add protein powder to increase protein</p>	<p>POTASSIUM BROTH 8 cups water in stock pot, or crock pot 6 large potatoes with skin, cut in large pieces 6 med. carrots 8 med. stalks celery, cut in large pieces 2 bunches parsley, whole 1 large onion, cut in large pieces Season with garlic, tarragon or other herbs. Bring to boil, reduce heat Simmer slowly 120 or more minutes Strain - Throw out veggies, reduce to 6 cups 1 cup without the vegetables contains approx. 1200-1400 mg potassium</p> <p>Option: <u>Triple</u> the recipe. Reduce, slowly, to about 1 ½ cups liquid. Cool, pour in standard ice cube tray. Freeze. Serving size- One cube added to just less than 1 cup boiling water.</p>

The original Yeast Drink was a bit different. I still enjoy it. It is almost a meal.

Apple, grapefruit, or orange juice.6-8 ounces
 2-4 heaped tablespoons Red Star Nutritional Yeast Flakes (protein, trace minerals and B vitamins)
 ½-1 teaspoon ascorbic acid powder (1 teaspoon is 4,000 mg C)
 ½-1 teaspoon Kal dolomite powder (1 teaspoon is 1000 mg calcium, 500 mg magnesium)

For a complete list of nutrient content of foods get Food Values of Portions Commonly Used, Bowes and Church, used copy available at most bookstores. Or get an app for your phone. My Fitness Pal for iphone and android gives basic nutritional data including potassium.

The USDA database can be found here, USDA Search, <http://ndb.nal.usda.gov/>

IT IS BEST and SAFEST TO GET YOUR POTASSIUM FROM FOOD.

POTASSIUM SUPPLEMENTS ARE NOT ADVISED FOR GENERAL USE

- Do not take potassium supplements on an empty stomach.

- Do not take supplemental potassium if you are taking aspirin or any other non-steroidal anti-inflammatory. It can exponentially increase the danger of gut damage.
- Do not take supplemental potassium without checking with your physician if you are taking any kind of prescription drug, have kidney disease or have had kidney problems or digestive problems (such as IBS or ulcers) in the past.
- Do not take potassium supplements if you are being treated for hypertension with a prescribed diuretic, unless advised to do so by your prescribing physician. Many modern diuretics are potassium sparing and potassium supplementation could lead to dangerously high levels of potassium in the blood.
- Do not use diuretics unless a physician monitoring their use prescribes them. Do not self-prescribe an herbal diuretic (natural does not necessarily mean safe).
- If you decide to try potassium supplements do not take more than 200-300 mg. of potassium in supplement form at one time. All available non-prescription potassium supplements, by law, may contain no more than 99 mg. of active potassium. The maximum daily amount of potassium, in supplement form, should not exceed 300 mg at a time and no more than 1500 mg. total per day. Some clients have tolerated Alacer K Factors or Now Foods potassium gluconate powder.
- If you have symptoms of any kind when using a potassium supplement stop the supplement and get your potassium from food. pH (acidity/alkalinity) imbalance may cause serious indigestion and pain.

While potassium is good for us and necessary for life please understand that in supplement form it may be harmful. We want increased body stores of potassium (potassium stores in muscle). Besides, getting potassium from fresh whole food also gives us fiber (to feed your microbiota), protein, vitamins, and minerals not present in supplements.

Artificially raising blood levels of potassium, with supplements of any kind, may cause serious side effects including death. Though no deaths have been recorded from potassium pills, high amounts of potassium chloride salt and intravenous potassium have caused death. The 'lethal injection' used to terminate the life of pets and death row prisoners is potassium. Potassium supplements have caused intestinal bleeding and ulceration.

WATER

Water is an essential part of your daily diet. You will feel and function best when you get used to consuming 1 ounce of water for each 2 pounds of actual, current, body weight daily. For a 150 lb. person this is about nine 8-ounce glasses daily. In hot weather or when you exercise you will need more than this amount. At first you may have difficulty drinking the suggested amount. Take in a cup or two every one or two hours. Limit intake of liquids, including water, after 6-7 PM. Juice-not from concentrate, tea and coffee-fresh ground, if tolerated, may be counted in this calculation.

Unless you have your own spring or well your water should be filtered, preferably by reverse osmosis plus double carbon filters. This water tastes great. Be careful about bottled water. Many bottled waters contain excessive amounts of sodium or other minerals or contaminants from the container.

Most tap water in the US contains chlorine and fluoride; both are halogens, potentially deadly gases that have been indicated as possible promoters of thyroid disease.⁽²³⁸⁾ A UK study found higher incidence of hypothyroidism in highly fluoridated areas. The only way to

remove these toxins from your drinking water is with reverse osmosis. Filtration won't do it. Whatever minerals are lost are easily replaced with good food and perhaps a mineral supplement.

Find a container or containers that hold your total daily amount and fill them each morning. Make sure they are empty by 7 PM. Urination may increase at first but will normalize within one week.

It is possible for a person to drink too much water. I have clients who have done this. Excess water consumption may impair health and cause further loss of minerals. Drinking more water than you need is diuretic, increasing loss of electrolytes. If your blood test shows low sodium or potassium or if you do not sweat easily, water may, temporarily, be toxic for you. Increase your electrolyte intake if you are significantly increasing water intake, have diarrhea or vomiting.

Drink water with your meal if desired. Water stimulates digestion. It promotes the production of stomach acid and digestive juices. It does not dilute stomach acid as some have believed in the past. The exception to this is if your electrolytes are low. In this condition water can be toxic as mentioned. Make sure to get your trace minerals and electrolytes. Stews and soups using vegetable and bone broths are great sources of these essential elements.

Dehydration-Avoid

It has been estimated that at any given moment up to 90% of Americans are dehydrated. Even mild dehydration has many negative health impacts. Common symptoms of mild dehydration, just 1-2%, may include any of the following-

- Headache
- Impaired digestion
- Dry eyes
- Dry mouth
- Changes in mood
- Depression
- Cognitive impairment/confusion
- Fatigue
- Joint pain/general inflammation
- Water retention
- Elevated histamine (with increase in allergic response)
- Decreased urine volume
- Dark or cloudy urine
- Irritability,
- Lack of tears when crying
- Dizziness when standing due to orthostatic hypotension,
- Insomnia. Other possible symptoms include cloudy urine and stinging during urination

Hydration and cognition- Do NOT shrink your brain.

A UK study found teenage boys losing 1-2% during athletic activity suffered from noticeable brain shrinkage on MRI. The shrinkage was equivalent to 3 months progression of Alzheimer's. Other studies have found even mild dehydration impairs cognition and mood in children and adults. Some dementia symptoms may simply be chronic dehydration. Whether you are an athlete, a 6 year old in school, a senior trying to avoid memory loss or an airline pilot staying sharp while flying, water intake matters, every day.
(239,240,241,242,243,244,245,246,247,248,249)

Staying hydrated

Hydration is a primary element in long term health. There is no substitute for water. The chart below is from the Army and shows amounts needed to move about under load at higher temperatures. Please note it is amounts per HOUR not whenever. Elevated temperatures may require the addition of electrolytes, especially if you sweat profusely. Using Trace Mineral Research Electrolyte Stamina Tablets (2-4 with each quart of water consumed) may be the best way to rehydrate for those performing physical labor/exercise/athletics in temperatures above 75°.

No amount of training or acclimatization can reduce your bodies need for water.

Heat Category	WBGT Index, °F	Water Intake	Water Intake	Water Intake
1	78° - 81.9°	½	¾	¾
3	85° - 87.9°	¾	¾	1
4	88° - 89.9°	¾	¾	1
5	> 90°	1	1	1
Body armor = +5° mOpp 4 = +10° rest - sitting or standing in the shade if possible		easy Work – walking on a hard surface at less than 2 mph with less than a 30 pound load, weapon maintenance,	moderate Work – patrolling, walking in the sand at 2.5 mph with no load, calisthenics; patrolling; individual movement	hard Work – walking in the sand at 2.5 MPH with a load, field assaults
The fluid replacement volumes will sustain performance and hydration for at least 4 HOURS of work in the specified heat category. Fluid needs can vary based on individual differences and exposure to full sun or full shade.				
CAUTION: Hourly fluid intake should never exceed 1.5 quarts. Daily fluid intake should never exceed 12 quarts.				

Hydration tests

There are two easy tests to determine if you are adequately hydrated at any given time.

The easiest is the turgor test. Rest one hand or your knee or lightly on a table or desk. With the other hand lift/pinch the skin from the top of the resting hand for a few seconds and then release. If the skin does not return to flat/normal within 3 seconds, whatever your age, you are underhydrated.

The second test is urine color. Email me for a copy of the color sheet. There is also a copy in the back pocket of this workbook. The first urine after taking a multi-vitamin or B-complex may be brighter yellow from the riboflavin but that should pass. Check your first AM urine if you aren't sure.

Checklist and Notes:

- Do I regularly check to make sure my daily intake of potassium and protein foods is adequate to my current need?
- Do I add more protein when under stress?
- Do I eat more potassium containing foods when physically active and/or when the weather is hot?
- Do I make an effort to consume minimum daily amounts with rare exceptions?
- Do I consume most of my calories in the morning and mid-day, eating lightly at night?
- Do I make sure to consume adequate water/fluids under all conditions? Do I check my turgor and/or urine color regularly to make sure I am hydrated?

CHAPTER 4 LECTINS- GLYCOPROTEINS AND DISEASE

Proteins are essential for long-term health. When you are determining your protein needs consider whether a particular source of protein is safe for you or other family members. Lectins are glycoproteins with a few rare exceptions. Human response to lectins can be positive, negative or neutral. Virus and bacteria can contain lectins or have lectin-like properties. Many probiotics bind lectins, reducing their potential reactivity.

Most foods contain glycoproteins, but amounts and types vary widely. While research in lectinology is in its infancy, this information is critical to your health and it is important to begin to understand lectins NOW. Read the following report carefully. I'll get specific about how this all applies to you. *Lectins that do not agree with you (cause damage to your digestive tract, like gluten, a lectin) should NOT be consumed and do not contribute to daily protein needs.*^(144,250,251)

Lectin-The Definition

ID: lectin

PART OF SPEECH: n

SYNONYM: Plant Hemagglutinin

TERM ELEMENT: Hemagglutinin

DEFINITION

Protein or glycoprotein substances, usually of plant origin, of non-immunoglobulin nature, capable of specific recognition of and reversible binding to, carbohydrate moieties of complex glycoconjugates without altering the covalent structure of any of the recognized glycosyl ligands. This group includes monovalent lectins (i.e. bacterial and plant toxins). These lectins bind to sugar moieties in cell walls or membranes and thereby change the physiology of the membrane to cause agglutination, mitosis, or other biochemical changes in the cell. (agglutination- clumping; mitosis-multiplication or division of a cell forming two daughter cells)

Lectins were first described in 1888 by Stillmark working with castor bean extracts. Many members of the lectinic protein family agglutinate (clump together) red blood cells. Research done by Ehrlich, considered to be the father of immunology, has shown that feeding small amounts of lectin containing seeds to rabbits caused partial immunity to the toxicity demonstrating lectins are also antigenic (able to induce antigen antibody reactions).

High levels of lectins (glycoproteins) may be found in grains (also known as cereals or pulses), legumes (that is 'beans' including peanuts), dairy and plants in the nightshade family. Many other foods contain lectins but are less well studied and the amounts of lectins present are not thought to be as high or as potentially toxic.

Lectins purified from the germinating seeds of wheat (*Triticum* spp.); bind to carbohydrate moieties on cell surface glycoproteins and are used to identify certain cell populations and inhibit or promote some immunological or physiological activities.

Lectins purified are used to determine one's blood type (ABO). Lectins from the castor bean are highly toxic and can kill if ingested in even small amounts. Lectins from kidney beans have been implicated as cause in an outbreak of 'food poisoning' with no known pathogen.

Think of a lectin as a protein containing a key that fits a certain type of lock. This lock is a specific type of carbohydrate. All life forms, plant and animal, insect and fungus have cell membranes that contain carbohydrates that sit within and project from the membrane. If a lectin with the right key comes in contact with one of these 'locks' on the gut wall or artery or gland or organ it 'opens the lock', that is disrupts the membrane and damages the cell and may initiate a cascade of immune and autoimmune events leading to cell death.

Lectins can be inactivated by specific carbohydrates (technically known as mono and oligosaccharides) which can bind the 'key' and prevent the protein from attaching to the carbohydrate 'lock' within the cell membrane. Glucosamine is specific for wheat lectin and it is this specificity that may protect the gut and cartilage from cell inflammation and destruction in wheat (or gluten) responsive arthritis.

While various foods and supplements may inactivate some of these toxic lectins it is impossible for such substances to protect the body from them completely. The safest path is avoidance of known toxic lectins. Common foods with known lectin common reactions include all soy and wheat products including oils from these substances.

I have always promoted adequate protein in my dietary programs with moderate 'good' fats and moderate complex carbohydrates including plenty of fresh fruits and vegetables. For some clients eating enough protein was and is difficult. They (and the culture in which we currently reside) tend to diminish protein's important contribution to our health, both mental and physical. When protein intake is maximized clients find this moderate, easy to follow program has aided in restoring function of body and mind.

For some of my most difficult clients this simple basic program just hasn't given them the level of health and well-being they so very much desire. Over time I have noted that some of these most difficult clients have reported improvement in health using high protein, low carbohydrate diets.

Some of the best results came when switching to the Paleolithic Diet. These programs included The Specific Carbohydrate Diet from Breaking the Vicious Cycle by E Gottschall; the Paleo Diet as written in It Starts with Food, Hartwig and Hartwig, The Primal Blueprint, Sisson, Primal Body Primal Mind, Gedgaudas, Charles Hunt's Diet Evolution and Neanderthin by Audette. The commonality is higher natural, unprocessed protein (and naturally occurring unprocessed fats), fresh vegetables and fruits and a reduction in carbohydrates, especially carbohydrates high in lectins like grains and legumes.

In the 1970s research on lectins, called lectinology, began increasing worldwide. For a more scientific overview see the end of this report.

BMJ 1999;318:1023-1024 (17 April) Editorials

Do Dietary Lectins Cause Disease?

The evidence is suggestive and raises interesting possibilities for treatment. In 1988 a hospital launched a "healthy eating day" in its staff canteen at lunchtime. One dish contained red kidney beans, and 31 portions were served. At 3 PM one of the customers, a surgical registrar, vomited in theatre. Over the next four hours 10 more customers suffered profuse vomiting, some with diarrhea. All had recovered by next day. No pathogens were isolated from the food, but the beans contained an abnormally high concentration of the lectin phytohaemagglutinin.¹ Lectins are carbohydrate-binding proteins present in most plants, especially seeds and tubers like cereals, potatoes, and beans. Until recently their main use was as histology and blood transfusion reagents, but in the past two decades we have realized that many lectins are (a) toxic, inflammatory, or both; (b) resistant to cooking and digestive enzymes; and (c) present in much of our food.² It is thus no surprise that they sometimes cause "food poisoning." But the really disturbing finding came with the discovery in 1989 that some food lectins get past the gut wall and deposit themselves in distant organs.^{3 4} So do they cause real life diseases?

This is no academic question because diet is one part of the environment that we can manipulate and because lectins have excellent antidotes, at least in vitro. Because of their precise carbohydrate specificity, lectins can be blocked by simple sugars and oligosaccharides. Wheat lectin, for example, is blocked by the sugar N-acetyl glucosamine^{and} its polymers.⁵ These natural compounds are potentially exploitable as drugs should lectin induced diseases be identified.

Wheat gliadin, which causes coeliac disease, contains a lectin-like substance that binds to human intestinal mucosa,⁶ and this has been debated as the "coeliac disease toxin" for over 20 years.⁷ But coeliac disease is already managed by gluten avoidance, so nothing would change were the lectin hypothesis proved. On the other hand, wheat lectin also binds to glomerular capillary walls, mesangial cells, and tubules of human kidney and (in rodents) binds IgA and induces IgA mesangial deposits. This suggests that in humans IgA nephropathy might be caused or aggravated by wheat lectin; indeed a trial of gluten avoidance in children with this disease reported reduced proteinuria and immune complex levels.⁸

Of particular interest is the implication for autoimmune diseases. Lectins stimulate class II HLA antigens on cells that do not normally display them, such as pancreatic islet and thyroid cells.⁹ The islet cell determinant to which cytotoxic autoantibodies bind in insulin dependent diabetes mellitus is the disaccharide N-acetyl lactosamine,¹⁰ which must bind tomato lectin if present and probably also the lectins of wheat, potato, and peanuts. This would result in islet cells expressing both class II HLA antigens and foreign antigen together a sitting duck for autoimmune attack. Certain foods (wheat, soya) are indeed diabetogenic in genetically susceptible mice.¹¹ Insulin dependent diabetes therefore is another potential lectin disease and could possibly be prevented by prophylactic oligosaccharides.

Another suspect lectin disease is rheumatoid arthritis. The normal human IgG molecule possesses carbohydrate side chains, which terminate with galactose. In rheumatoid arthritis much of the galactose is missing, so that the subterminal sugar N-acetyl glucosamine is exposed instead. These deficient IgG molecules feature strongly in the circulating immune complexes that cause fever and symptoms.¹² In diet responsive rheumatoid arthritis one of the commonest trigger foods is wheat, and wheat lectin is specific for N-acetyl glucosamine the sugar that is normally hidden but exposed in rheumatoid arthritis. This suggests that N-acetyl glucosamine oligomers such as chitotetraose (derived from the chitin that forms crustacean shells) might be an effective treatment for diet

associated rheumatoid arthritis. Interestingly, the health food trade has already seized on N-acetyl glucosamine as an anti-arthritis supplement.¹³

Among the effects observed in the small intestine of lectin fed rodents is stripping away of the mucous coat to expose naked mucosa and overgrowth of the mucosa by abnormal bacteria and protozoa.¹⁴ Lectins also cause discharge of histamine from gastric mast cells,¹⁵ which stimulates acid secretion. So the three main pathogenic factors for peptic ulcer acid stimulation, failure of the mucous defense layer, and abnormal bacterial proliferation (*Helicobacter pylori*) are all theoretically linked to lectins. If true, blocking these effects by oligosaccharides would represent an attractive and more physiological treatment for peptic ulcer than suppressing stomach acid. The mucus stripping effect of lectins¹⁶ also offers an explanation for the anecdotal finding of many allergists that a "stone age diet," which eliminates most starchy foods and therefore most lectins, protects against common upper respiratory viral infections: without lectins in the throat the nasopharyngeal mucus lining would be more effective as a barrier to viruses.

But if we all eat lectins, why don't we all get insulin dependent diabetes, rheumatoid arthritis, IgA nephropathy, and peptic ulcers? Partly because of biological variation in the glycoconjugates that coat our cells and partly because these are protected behind a fine screen of sialic acid molecules, attached to the glycoprotein tips.¹⁰ We should be safe. But the sialic acid molecules can be stripped off by the enzyme neuraminidase, present in several micro-organisms such as influenza viruses and streptococci. This may explain why diabetes and rheumatoid arthritis tend to occur as sequelae of infections. This facilitation of lectins by micro-organisms throws a new light on postinfectious diseases and makes the folklore cure of fasting during a fever seem sensible.

Alternative medicine popularizers are already publishing articles about dietary lectins,¹⁷ often with more enthusiasm than caution, so patients are starting to ask about them and doctors need to be armed with facts. The same comment applies to entrepreneurs at the opposite end of the commercial spectrum.

Many lectins are powerful allergens, and prohevein, the principal allergen of rubber latex, is one. It has been engineered into transgenic tomatoes for its fungistatic properties,¹⁸ so we can expect an outbreak of tomato allergy in the near future among latex sensitive individuals. Dr Arpad Pusztai lost his job for publicizing concerns of this type (20 February, p 483).

David L J Freed, Allergist.

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Gilbert RJ. Healthy eating day. *Communicable Disease Report* 1988; 33: 3-4.

Van Damme EJM, Peumans WJ, Pusztai A, Bardocz S. *Handbook of plant lectins: properties and biomedical applications*. London: Wiley, 1998:31-50.

Pusztai A, Greer F, Grant G. Specific uptake of dietary lectins into the systemic circulation of rats. *Biochem Soc Trans* 1989; 17: 481-482.

Wang Q, Yu L-G, Campbell BJ, Milton J, Rhodes JM. Identification of intact peanut lectinin peripheral venous blood. *Lancet* 1998; 352: 1831-1832

Goldstein IJ, Poretz RD. Isolation and chemical properties of lectins. In: Liener IE, Sharon N, Goldstein IJ, eds. *The lectins*. Orlando: Academic Press, 1986.

Kolberg J, Sollid L. Lectin activity of gluten identified as wheat germ agglutinin. *Biochem Biophys Res Comm* 1985; 130: 867-872

Weiser MM, Douglas AP. An alternative mechanism for gluten toxicity in coeliac disease. *Lancet* 1976; i: 567.

Coppo R, Amore A, Roccatello D. Dietary antigens and primary IgA nephropathy. *J Am Soc Nephrol* 1992; 2(10 suppl): S173-S180

What triggers auto-immunity? *Lancet* 1985; ii: 78-79.

Uchigata Y, Spitalnik SL, Tachiwaki O, Salata KF, Notkins AL. Pancreatic islet cell surface glycoproteins containing Gal (1-4)GNAC-R identified by cytotoxic monoclonal antibodies. *J Exp Med* 1987; 165: 124-139

Scott FW, Kolb H. Cow's milk and insulin-dependent diabetes mellitus. *Lancet* 1996; 348: 613.

Bond A, Kerr MA, Hay FC. Distinct oligosaccharide content of rheumatoid arthritis derived immune complexes. *Arthr Rheum* 1995; 38: 744-749

Toohey L. Natural substances combat arthritis with "immune power". *Nutri Notes* 1997; 2: 1-6.

- Banwell JG, Howard R, Kabir I, Costerton JW. Bacterial overgrowth by indigenous microflora in the PHA-fed rat. *Can J Microbiol* 1988; 34: 1009-1013
- Greer F, Puzstai A. Toxicity of kidney bean (*Phaseolus vulgaris*) in rats: changes in intestinal permeability. *Digestion* 1985; 32: 42-46
- Freed DLJ, Buckley CH. Mucottractive effect of lectin. *Lancet* 1978; i: 585-586.
- Anonymous, but attributed to D'Adamo P. Blood type: the link with diet and disease. *What Doctors Don't Tell You* 1998; 9: 1-4.
- Lee HI, Raikhel NV. Prohevein is poorly processed but shows enhanced resistance to a chitin-binding fungus in transgenic tomato plants. *Braz J Med Biol Res* 1995; 28: 743-750

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Lectins In Plain English

Lectins are found in ALL foods, certain foods more than others, and the same food may contain varying amounts of lectins depending on processing, when and where the plant was grown, and species.

The major known potentially allergenic lectin containing food groups are

1. Grains, especially wheat and wheat germ but also quinoa, rice, oats, rye, barley, millet and corn.
2. Legumes (all beans, including pea, soy, and peanuts),
3. Dairy (perhaps more so when cows are fed grains instead of grass, a speculation based on research showing transference of lectins into breast milk and dairy and potentially more harmful in pasteurized, processed milk because of the reduction of S-IgA, an immunoglobulin that binds dangerous lectins, [Biol Neonate 1991;59\(3\):121-5 Davin JC et al The high lectin-binding capacity of human secretory IgA protects nonspecifically mucosae against environmental antigens.](#) NOTE: Only breast milk is good for babies.)
4. Nightshade (includes potato, tomato, eggplant and pepper).

Each of these lectin groups has a history of being implicated as allergenic. A lectin group includes all foods containing any amount of the particular lectin, (all forms- milled grains, flours, oils), peanut butter, cereal or legume oils (soy, canola, corn), additives, thickeners, grain vinegar and products containing grain vinegar, grain alcohol including grain based vodka, and all beers and ales. The only non-grain based alcohol is 100% Agave tequila or potato vodka (but potatoes can also cause lectin responses, a nightshade) . Grape based alcoholic beverages are probably allowed if you know you tolerate them.

There has been some information that lectins may be inactivated or removed by soaking, sprouting, cooking or fermenting. Soaking legumes overnight, draining the water, rinsing and draining again does seem to remove many of the lectins in legumes. Heating seems to remove others in some foods but not all. There is little data to prove that any of these methods remove lectins completely as few foods have been tested and of those that have, many lectins seem to remain after processing.

Excerpt from [Plant Lectins](#), Puzstai A, Cambridge University Press 1991 pg.108

Nachbar and Oppenheim (1980) found 30% of fresh and PROCESSED foods contained active lectins. Lectins from green salads, fruits, spices, seeds, dry cereals and nuts (even after roasting) showed activity of toxic lectin. Some of these lectins interact with serum or salivary components and bacteria from the oral cavity (Gibbons & Dankers, 1981).

Another example of the hardness of lectins- Klurfeld DM and Kritchevsky D Lipids 1987 Sep:22(9):667-8, Isolation and quantitation of lectins from vegetable oils. Results-Unrefined soy oils contained 858-2983 mcg/kg, after refining oils still contained 24-55 mcg/kg of soy lectins. **IMPORTANT-Both refined and unrefined soy oil contained lectins.**

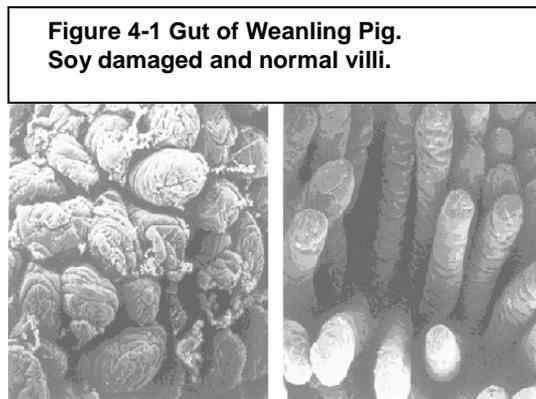
From Plant Lectins A Pusztai 1991 Table 6.9 page 179 Picture is not from the book.

Common features of toxic (non-nutritive) effects in lectin-gut interactions-

High degree of resistance to gut proteolysis (breakdown of protein).

Binding to brush border cells; damage to microvillus membrane; shedding of cells; reduction in the absorptive capacity of the small intestine.

Increased endocytosis; induction of hyperplastic growth of the small intestine; increased turnover of epithelial cells. (my note-means stimulation of gut cells resulting in overgrowth of cells) Picture shows damaged gut villi, left, from soy consumption, and normal gut villi, right. This is leaky gut.



Interference with the immune system; hypersensitivity reactions.

Interference with the microbial ecology of the gut; selective overgrowth. (this means changes in the probiotic status of the gut, not in a good way)

Direct and indirect effects (hormones, etc.) on systemic metabolism.

Especially note #5. The popular Candida Diet is essentially a high protein, low carbohydrate diet, which limits starches and sugars and thereby limits certain potential offending lectins. If lectins are a problem for this person (the so-called 'candida' patient) lectin ingestion may be associated with overgrowth of various gut pathogens that may include yeasts. Removal of lectins would restore the gut ecology and the gut immune system. If this is true, the diet works because it relieves the person from symptoms and pathogenic consequences caused by ingestion of lectins to which he or she is intolerant.

Lectins are hardy proteins that do not break down easily. They are resistant to stomach acid and digestive enzymes.

Lectins may bind to the gut wall and damage the gut lining, are not altered by digestive enzymes, and may alter gut permeability and pass through the gut into general circulation.

Lectins can cause alterations in gut function that may be related to colitis, Crohn's Disease, Celiac-Sprue, IBS and gut permeability.

Lectin damage to the gut wall may allow other non-lectin proteins to cross undigested into general circulation and cause allergic reactions, including anaphylaxis.

Having gained access to general circulation various lectins may bind to the surface of cell membranes in arteries and vessels, organs and glands, including the thyroid, pancreas, kidney and adrenals, in susceptible animals and humans. This binding may begin antigen antibody reactions leading to autoimmune disorders and so-called degenerative diseases.

Different lectins have been implicated in different diseases. Dairy lectins have been implicated in juvenile onset type I diabetes.^(252,253,254,255) Wheat lectins have been implicated in juvenile nephropathy (kidney disease).^(256,257,258,259)

Type or types of lectin and one's susceptibility (genetic susceptibility) cannot be determined by blood type. D'Adamo tested lectins with blood cells. Lectin intolerance reactions occur in the gut, general circulation (artery walls and the like), brain, gland or organ as well as red blood cells. Sensitivity of one type of cell does not necessarily determine whether another type cell will or will not react. Our lectin intolerances have more to do with our ancestors 'location' than blood type.

S-IgA, and other immune factors may, if sufficient in quantity, help protect against some exposure to toxic lectins. See abstract at end of report.

GM (genetically modified foods) are modified by splicing 'lectins' from one plant family to another. This is extremely problematic. If you know you react to a particular plant family but that lectin has been put in a plant not of that family you may consume the 'toxic to you' lectin, have the reaction/response and not know the cause.

We are or become lectin sensitive because:

Genetics, we have binding sites that precipitate immune reactions to the offending lectin.

Early introduction to lectins, before 18 months of age when the gut barrier is fully formed

A failure of S-IgA barrier protection, genetic or environmentally induced

Bacterial or virus infection. Certain bacteria and virus, including the influenza virus, can damage our cells making them susceptible to lectin antibody/antigen reactions. Some virus and bacteria have lectin activity, including HIV.^(260,261)

The use of NSAIDS (non-steroidal anti-inflammatory) or other drugs that increase gut permeability and allow lectins to enter general circulation.

Celiac-Sprue is caused by 'gliadin' or gluten sensitivity. Gliadin, a lectin, is found in wheat, rye, barley, oats, buckwheat and foods containing these grains (including beer, grain based alcohols, mayonnaise, grain vinegar, etc.). Some celiacs did not respond to elimination of

gluten/gliadin. In 1951 Drs. Sidney V. and Merrill P. Haas published Management of Celiac Disease documenting treatment and cure of persons given the diagnosis of 'celiac' and cystic fibrosis of the pancreas. Merrill and Haas used a carbohydrate limiting diet introduced as the 'Specific Carbohydrate Diet'.

More information about this diet can be gotten from Breaking the Vicious Cycle E Gottschall, BA, MSc. Kirkton Press Ltd. Baltimore, Ontario, Canada 1998.

In many cases cited in Gottschall's book, elimination of certain carbohydrates 'cured' diagnosed celiacs after one year and they were able to return to eating gluten-containing foods. In hindsight many of the foods eliminated in this plan are high lectin foods known to be associated with gut and systemic inflammatory reactions.

If all cases of lectin intolerance were gene-based, reversal of intolerance would not be possible. There must therefore be a subgroup of IBS, Crohn's, Celiac, and colitis that is related to sensitization to food lectins. This type of sensitivity can be reversed by avoidance of these lectins and a restoration of gut barrier function including Secretory IgA and other immune protectors. Bacteria, virus, fungus medications, or injurious substances acting directly on the gut wall may cause sensitization. Probiotics may help prevent or protect the gut from sensitization. ^(123,124,262,263,264)

Tests are available to determine SIgA levels, and gut immune reactions to soy, dairy, wheat and egg. These tests do not cover the entire family of lectins, nor would blood or skin tests necessarily show sub-clinical sensitivity reactions. Most of the conditions associated with sub-clinical lectin intolerance appear to be degenerative, often taking extended periods of time to appear and longer to reach life threatening or painful (such as arthritis) stages. Many lectin related conditions may be considered to be 'autoimmune'.

Awareness of genetically based intolerance to one or more lectin groups is important family information. If you or another family member has such intolerance, other family members need to be made aware and test themselves to prevent problems before they begin.

Eating foods to which you show intolerance, whatever the cause, raises serum markers of inflammation. ^(265,266,267,268) ***General inflammation is a marker for heart disease, obesity, diabetes and cancer.***

Pathogen or drug induced food intolerance responses need to be prevented or reversed. These antigen/antibody responses may be reversible but this is not always true. Food reactions caused by gut permeability require avoidance of offending lectins for a minimum of one year before reintroduction. If on reintroduction symptoms return it is likely the intolerance is genetic and the food or food group should henceforth be avoided.

Lectinology, the study of lectins and their possible involvement in degenerative and autoimmune disease, is a relatively new science. This report, as presented, is hypothesis, not yet fully supported by clinical trials and not yet at a stage where we have any idea of how to connect 'family' with lectin response. What facts can be supported include-

Lectins institute most allergic and antigenic responses.

Lectins are glycoproteins found in large amounts in the foods we eat.

Lectins are not easily removed from foods or rendered harmless to animals and humans.

Lectins from pea, soy, peanut and other beans, wheat germ and wheat, milk, peanut oil (and perhaps other seed oils including soy oil) and nightshades, in a variety of clinical studies have shown varying damage to gut lining, joints, kidney, pancreas and brain (some even able to cross the blood-brain barrier).

Lectins found in peanut oil have been implicated in atherosclerosis leaving open the possibility that other seed oils contain damaging lectins and that trans fats, polyunsaturation and free radicals may not be the full picture on the dangers of polyunsaturated fats.

You may react to lectins due to genetics, intensity of lectin exposure, failure of immune factors to protect you, viral infection, bacterial infection or gut permeability induced by medication or infection.

Lectin toxicity (antigen-antibody response) can be 'sub-clinical' not showing obvious symptoms for many years.

What Does Lectin Intolerance Mean To Me?

Lectin intolerance is not an allergy. A person may be lectin intolerant and not have antibodies to the suspect food when given an allergy test whether blood or skin or saliva. A person may be lectin intolerant and because of the damage done by lectins end up having allergic reactions to food (that does not contain the initiating lectin but may have other lectins), other chemicals, or the environment.

Genetic lectin intolerance means having binding sites on cell surfaces, whether located in your gut, artery, organ, gland or brain, for the toxic (to you) lectin and producing anti-bodies to the exposed protein. The immune response damages the cell to which the lectin attaches and possibly surrounding cells. This antigen/antibody response may be the key to many or even most autoimmune diseases and many degenerative diseases may need to be reclassified as autoimmune. There is evidence heart disease is strongly associated with markers of inflammation which are common in lectin intolerance.

If you or other family members are suffering from any of the symptoms, conditions or diseases mentioned consider an elimination diet to test for lectin sensitivity.

Most persons are aware that there are certain foods that 'do not like them'. Symptoms could be obvious, such as gas, bloating, diarrhea or constipation (or both, alternating). Less obvious symptoms may include asthma, headache, fatigue, 'indigestion', skin problems including hives, psoriasis, swollen joints, arthritis, or generalized edema (water retention).

Some symptoms may occur chronically and may seem unrelated to a gut/food or lectin intolerance reactions. This group of symptoms includes the so-called degenerative diseases and autoimmune diseases like those mentioned in the list at the beginning of this chapter including atherosclerosis, hypertension, osteoporosis, senile dementia, osteoarthritis and rheumatoid arthritis, inflammatory joint diseases, fibromyalgia, chronic fatigue, adult onset diabetes, autoimmune thyroid disorders and even obesity.

If your condition responds to elimination of one or more of the lectin groups, consider your intolerance to be at minimum, induced by the environment (infection or medication induced), and continue to restrict your diet for one year before testing a food-lectin group for re-inclusion. If you again react consider your intolerance a probable genetic inheritance and avoid this type of lectin containing food group as completely as you are able.

For severe symptoms or conditions eliminate all of the major suspect groups, all grains, all legumes, and all dairy. Add the nightshades, potato, tomato, eggplant and pepper, to your restricted list if your symptoms are associated with rheumatic or arthritic complaints or if other eliminations don't help.

Determining Intolerance To Lectins and Treatment

Books mentioned at the beginning of this report by Eades, Rosedale, Jaminet, Audette , or Hunt are good resources for menus. Check on Amazon for 'paleo diet' for more. Eades has some recipes that include dairy, soy and nightshade, some of the suspect foods so don't use those recipes. None of Audette's or Hunt's recipes use any major lectin groups. They do have some recipes with nightshades. Watch out for those recipes if you think it is a group you may react to.

Rarely will anyone need to eliminate every major lectin group. Lectin problems are typically associated with a limited number of foods. You have to experiment and see 'who' you are and 'what' your ideal foods are. It is a process. For those with lectin intolerances Fallon and Enig's Nourishing Traditions is still a great cookbook just watch out for the lectin containing foods in recipes and avoid them if you suspect or find you are intolerant.

There are support groups for gluten intolerance, dairy intolerance and soy intolerance but since the idea of lectin intolerance and the broadness of the groups is so new you will have difficulty finding support and information in one place.

Lectins are in most foods, with plant foods containing the highest levels of known toxic lectins. While they have existed as long as life has existed they are not yet well researched or understood. Lectins can be extremely toxic, causing rapid death or, conversely, may be useful in preventing or reversing conditions and illnesses such as cancer or viral infections. Most lectins fall somewhere in between these two extremes allowing the possibility of subclinical conditions which appear over time and don't seem to be directly related to lectin exposure.

Lectin Research Abstracts

J Biol Neonate 1991;59(3):121-5

The high lectin-binding capacity of human secretory IgA protects nonspecifically mucosae against environmental antigens.

Davin JC, Senterre J, Mahieu PR

Department of Pediatrics, State University of Liege, Belgium.

The anti-infectious role of human milk may be, at least partly, ascribed to its content in secretory IgA. As lectins are present in various infectious antigens, the binding of different types of IgA to three lectins (concanavalin A, peanut agglutinin, wheat germ agglutinin) was studied by Elisa. The specificity of those bindings was assessed by inhibitory experiments performed with the corresponding oligosaccharides. The following were found for the three lectins: (1) the lectin-binding capacity of colostrum secretory IgA was markedly greater than that of normal plasma IgA1 (p less than 0.001); (2) the lectin-binding capacity of polymeric IgA1 was greater than that of monomeric IgA1 (p less than 0.001). This property of mucosal IgA may be responsible for a nonimmune opsonization able to prevent the early step of some infectious mucosal diseases, i.e. the attachment of bacteria to epithelial cells by lectin-like bonds and also the penetration into the body of some antigens able to favor the development of allergy. Milk mucosal IgA, present in significant amounts in human colostrum and mature milk - but not in infant formulas - may therefore play an important polyvalent protective role in newborns.

IgA antibodies to dietary antigens and lectin-binding IgA in sera from Italian, Australian, and Japanese IgA nephropathy patients.

Coppo R;Amore A;Roccatello D;Gianoglio B;Molino A;Piccoli G;Clarkson AR;Woodroffe AJ;Sakai H;Tomino Y

We studied serum IgA as antibodies to dietary antigens (Ag), as lectin-binding molecules, and as conglutinin-binding immune complexes (IgAIC) in people from geographical areas in which IgA nephropathy (IgAGN) is particularly frequent. Sera from 63 Italian, 21 Australian, and 25 Japanese patients affected by IgAGN and 24 Italian, 20 Australian, and 40 Japanese healthy controls were studied. Increased values of IgAIC were detected in 42.8% of Italian patients, while only in 23.8% and 8% of Australian and Japanese patients, respectively. Mean values were significantly increased only in Italian patients (P less than 0.0001). Positive values of IgA antibodies against dietary Ag had variable prevalences, but again Italian patients showed the highest frequency, from 19% to 28.5% versus 0 to 38% in Australians and 0 to 16% in Japanese. Mean values of these antibodies were not significantly increased in any patient groups in comparison to the corresponding healthy populations. However, patients with elevated values of IgAIC had significantly higher serum concentrations of antibodies to alimentary components and a linear correlation was found between IgAIC and some IgA antibodies to food components. The relationship between these two series of data was particularly evident for Italian and Australian IgAGN patients. Moreover, the patients with positive data tended to have a cluster of increased levels of IgA antibodies against several alimentary Ag at the same time. A linear correlation was evident between values of IgA antibodies to gluten fractions and to heterologous albumins. None of these correlations was evident among healthy controls.

Invest Ophthalmol Vis Sci 1991 Dec;32(13):3277-84

Identification of lectin binding proteins in human tears.

Kuizenga A, van Haeringen NJ, Kijlstra A

Biochemical Laboratory, Netherlands Ophthalmic Research Institute, Amsterdam.

The identity of glycoproteins in stimulated normal human tears was investigated by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) of tears onto minigels, blotting, and subsequent incubation with different biotinylated lectins (concanavalin A [Con A], peanut agglutinin [PNA], glycine max agglutinin [SBA], Phaseolus vulgaris agglutinin, wheat germ agglutinin [WGA, native form], Artocarpus integrifolia agglutinin [Jacalin], and Pisum sativum agglutinin). Control proteins included purified secretory immunoglobulin A (sIgA) from human colostrum, human milk lactoferrin, and chicken-egg lysozyme. All samples were prepared in a denaturing (SDS) buffer under nonreducing and reducing conditions. The sIgA in tears and IgA (alpha) heavy chain fragments (reduced sample) were identified with most of the lectins tested. A particular high molecular weight (greater than 200 kD) protein fraction in tears that just entered the separation gel

on SDS-PAGE was detected with WGA and Jacalin. This fraction stain poorly with silver. Tear lactoferrin was identified with all lectins used, although binding was low with SBA. Purified milk lactoferrin showed a poor reaction with Jacalin, but a protein in tears of similar mobility bound this lectin (nonreduced samples). Under both nonreducing and reducing conditions, tear-specific prealbumin in tears did not bind any of the lectins tested. Tear lysozyme only reacted with lectin after reduction. The techniques described may provide additional valuable information in addition to commonly used methods for tear protein analysis and further knowledge concerning the role of glycoproteins on the ocular surface.

Testing for Lectin Intolerance

Pick the most suspect food or food group (for you). Eliminate everything containing that food/group for 7 days. Sometimes only one particular food will be on your list. It is possible to react to potato and not react to tomato or eggplant. You may tolerate black beans but not kidney or soy bean

On day 8 eat foods from that group at each meal. Example: Testing wheat- Have some cereal or toast, later spaghetti or other noodle or pizza or other wheat containing food.

On day 9 and 10 again avoid all foods from this group. Carefully record your moods, bowel function, hunger, energy, sleep and mental functioning (alert, focused, good memory recall, or not) on the day of the test and for the following two (lectin free) days.

You will see specific and obvious changes if the tested lectin food or family is your foe. .

Keep a record of your experiment.

Life is an adventure. You are discovering what foods are 'yours'. Once you know, remain a good steward. love your body and only eat 'your' food. ***When marriages are between persons genetically disparate it is possible that each family member may have equally disparate requirements.***

Make sure before you test lectins you have adequate and appropriate good bacteria in your digestive tract. Do consider the Immune Restoration Protocol as your first step. Many of the strains of probiotics bind lectins and reduce or eliminate lectin intolerance. On rare occasions you may eat or have eaten an unfriendly lectin. Larch Arabinogalactins bind unfriendly lectins and reduce or prevent symptoms of lectin intolerance. Not to be used ongoing but handy to have around 'in case':

VRP Lectin Lock <http://vrp.com> or Source Natural's Wellness Larch Extract <http://iherb.com> or Arabinogalactin Powder from <http://beyondacenturyonline.com>

Arabinogalactin is great for your gut too as it promotes the growth of beneficial bifido bacteria.

Checklist and Notes:

- Have I noticed any symptoms of food intolerance?
 - Generalized inflammation (general body or joint ache)?
 - Moodiness?
 - Fatigue after eating?
 - Insatiable hunger after a full meal?
 - Chronic constipation or diarrhea without apparent pathogens?
- Before testing for an intolerance did I make sure my gut bacteria were friendly and abundant?
- When testing did I test the entire food 'group'?
- Did I enlist the aid of a family member or friend for an objective view of any symptoms?
- Is there a particular food (example: wheat) I can't even think about 'doing without'? This may signal an allergic/addictive response.
- Am I clear that infrequent use of the food or food group may not produce symptoms but may still have consequences regarding gut integrity and furtherance of autoimmune processes?
- If I have not always reacted to a lectin group have I considered gut interactions and completed 21 days of the Immune Restoration Step Two?

CHAPTER 5 ABOUT FATS

As fats are 15-25% of total body mass, a primary component of the human central nervous system including bone marrow, and 60% of non-water brain mass, and as they are being used and replaced regularly, quality and quantity are critical.

The 'fat problem' is one of type and quality (freshness). Fats are saturated or unsaturated, short chain or long chain. Dietary fats and oils supply the material to keep your joints lubricated, your skin soft, your hair shiny and your mood pleasant.

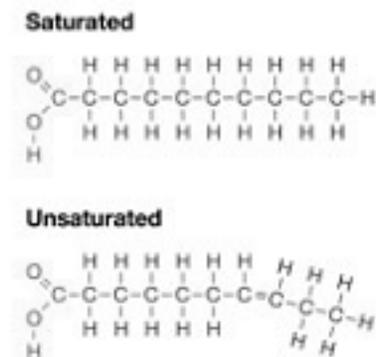
Fats are composed of fatty acids. These fatty acids are generally classified into three groups; saturated, monounsaturated, and polyunsaturated. Foods contain a mixture of fatty acids. In nature no food is a pure source of only one type of fatty acid. Pure 'fatty acids' only occur in the laboratory.

Mono and poly-unsaturated fatty acids having missing hydrogen atoms (H in the diagram) resulting in a 'carbon double bond' at one or more locations. Monounsaturates have one missing hydrogen, polyunsaturates more than one.

The location of the missing hydrogen/s, carbon double bond/s give/s the fatty acid its specific qualities. Omega-3 fatty acids have the first missing hydrogen carbon double bond on the third carbon; omega-6 on the 6th carbon. (See Naming the Fatty Acids)

These structural differences, while seemingly slight, have profound effects within living systems. Fatty acids can and do substitute for one another within cells but cells have fatty acid preferences that allow optimal cell performance.

Figure 5-1 Fat Structure



From The Need for Fat, John Whitfield

<http://www.nature.com/horizon/livingfrontier/background/fat.html>

The terms saturated and unsaturated lipids refer to the number of bonds on each carbon atom that makes up the fatty-acid tail of the molecule. Saturated lipids are so-called because they have single bonds between all the carbon atoms, and therefore all the carbons are bonded to the maximum number of hydrogen atoms. These chains are fairly straight and can pack closely together, making these fats solid at room temperature. Other fats have some double bonds between some of the carbons in the tail, causing the molecule to bend. As carbon atoms with double bonds are not bonded to as many hydrogens as possible, they are called unsaturated fats. The kinks in the tails mean that unsaturated fats can't pack as closely together,

making them liquid at room temperature.

When dietary lack or overabundance of a specific fatty acid occurs cells pay a price in any number of ways. Utilization of an inappropriate fatty acid may result in-

- abnormal cell replication, as in cancer or psoriasis
- early cell death
- cell membrane permeability
- cell membrane resistance, as found in insulin resistance
- cellular DNA damage from free radicals
- cell to cell messaging insufficiency found in depression
- cell inflammation, found in heart disease, cancer, arthritis and osteoporosis

Figure 5-2 Per capita consumption of fats USDA 1909-1972

hydrogen atom to one or more available carbons in mono or poly unsaturated fatty acids.

As evident from the chart on the left intake of hydrogenated fats represented by margarine and shortening (also known as hydrogenated or partially hydrogenated) increased steadily from 1909 to the present day (later another graph).

It is also clear from this data that the intake of saturated fats FROM FOOD SOURCES such as butter and lard, not from processed shortenings and margarine, has steadily declined. This is the reverse of what we read in health literature and hear in the media.

Over the last 100 years our intake of animal fats has steadily declined while our intake of vegetable fats has dramatically increased. Part of this increase is from vegetable oils used in processed foods and in our homes for cooking. Since the late 1940's intake of rancid polyunsaturated fatty acids has grown from almost 50% to greater than 75% of total fat intake.

As polyunsaturated fats are easily destroyed by light, air and heat most of the processed oils we intake are rancid before they enter our bodies. It is the over-consumption, of these rancid, processed, vegetable oils high in omega-6 fats, that parallels the incidence of degenerative disease in our society.

rancid

Having a rank smell or taste, from chemical change or decomposition; musty; as, rancid oil or butter.

Origin: L. Rancidus, fr. Rancere to be rancid or rank.

Source: Websters Dictionary

rancidification

Hydrogenation is the process of adding a

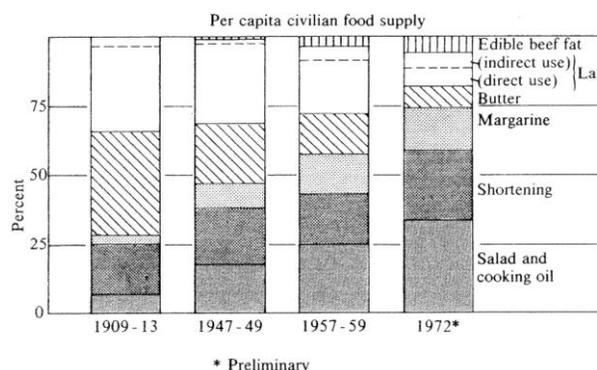


Figure 5-3: Sources of dietary fats and oils from 1909–1913 to 1972. From *Fat Content and Composition of Animal Products* (Washington, D.C.: National Research Council, 1976).

The decomposition of fats and other lipids by oxidation. Rancid foods and oils develop highly reactive chemicals which produce unpleasant and obnoxious odors and flavors, and destroy nutrients in food. Under some conditions, rancidity, and the destruction of vitamins, occurs very quickly.

In essence eating rancid fat is eating rotten food. There are other problems besides flavor and smell.

Nahrung. 1975;19(9-10):911-20.

[Interaction between proteins and oxidized lipids]

[Article in German]

Pokorny J, Janicek G.

Oxidized lipids react with proteins to form lipoprotein complexes in which the lipids are bound to the proteins in part by physical forces, in part by covalency. The free radicals resulting from the cleavage by hydroperoxides are the major precursors of the lipoprotein complexes. The interaction is associated with protein denaturation and oligomer formation. The lipids contained in the lipoprotein complexes are only in part extracted by chloroform-methanol; in part not until after acid or alkaline hydrolysis. The nutritive value of the protein moiety is diminished by the reaction of the hydroperoxides with methionine and cysteine and by the reaction of the peroxidic radicals and aldehydes with lysine and other basic amino acids. Secondary reactions of the lipoprotein complexes lead to brown coloured, only partly soluble compounds which often impair the organoleptic value. The rancidity products of the fats are neutralized by the reaction with proteins. The action of highly unsaturated oxidized lipids on proteins results in the development of a fishy aroma.

Our ancestors consumed fresh foods as no refrigeration or preservation was available. The large addition of polyunsaturated omega-6 fats began during World War II when dairy farms were badly understaffed due to large numbers of farm workers being drafted and deployed. Margarine was inexpensive and quickly gained in popularity. Margarine is made by the hydrogenation of vegetable oil.

Diets high in hydrogenated fats and processed, rancid oils, and low in omega-3 fatty acids, promote heart disease, adult onset diabetes, all forms of cancer including breast, prostate, colon and melanoma, mood disorders, depression, ADD, learning disorders and nerve and brain degenerative diseases from Multiple Sclerosis to Alzheimer's.

Because fats play such an important part in the cells of your body quality fats must be a large consideration in meal planning. So, do read and apply the guidelines in this section.

Check your refrigerator and cupboards and remove all the processed foods, packaged foods, frozen foods, canned or jarred foods containing the fats and oils in the Do Not Consume list.

Become a label reader and do not bring these fats and oils home.

When eating out ask what oils are used. If they use vegetable oil eat only foods prepared without oil. If the salad dressing contains vegetable oil bring your own made from extra-virgin olive oil or use vinegar or a non-fat dressing.

In the refining of polyunsaturated, omega-6 (vegetable) oils, the natural antioxidants such as vitamin E are dramatically reduced or destroyed. We lose the benefit of the antioxidant, and the oil becomes even more readily susceptible to oxidative damage (rancidity).

Eating oils that have lost their natural antioxidant content and that have been stored and heated and partially oxidized is the primary cause of cellular free radical damage in the body, thought to be of importance in both cancer and heart disease.

Do not consume. Avoid always

- Do not use refined or so-called cold pressed vegetable oils, sunflower, soy, canola, corn or cottonseed oils.
- NO Hydrogenated fats such as Crisco, margarine, all brands.
- NO Vegetable shortening (shortening is an hydrogenated omega-6 fat)
- NO Hydrogenated and partially hydrogenated fats in processed foods (these fats are everywhere, check your cupboards)
- NO Soy, sunflower, cottonseed, corn and canola oils, or other omega-6 oils whether from a regular store or the health food store.

Margarine, shortening, hydrogenated and partially hydrogenated fats of any kind are not included in this food plan. While trans fats are now recognized as dangerous by government health sources^(269,270,271) they have yet to admit the dangers of overuse of omega-6 fats. Excellent research studies, available for the past 20 years, have concluded that these fats contribute significantly to the incidence of degenerative disease in the USA and other countries..

Sircar, S. and Kansra, U. 1998 *J.Indian Med.Assoc.* 96 304-307

Choice of cooking oils--myths and realities

In contrast to earlier epidemiologic studies showing a low prevalence of atherosclerotic heart disease (AHD) and type-2 dependent diabetes mellitus (Type-2 DM) in the Indian subcontinent, over the recent years, there has been an alarming increase in the prevalence of these diseases in Indians--both abroad and at home, attributable to increased dietary fat intake. Replacing the traditional cooking fats condemned to be atherogenic, with refined vegetable oils promoted as "heart-friendly" because of their polyunsaturated fatty acid (PUFA) content, unfortunately, has not been able to curtail this trend. Current data on dietary fats indicate that it is not just the presence of PUFA but the type of PUFA that is important--a high PUFA n-6 content and high n-6/n-3 ratio in dietary fats being atherogenic and diabetogenic. The newer "heart-friendly" oils like sunflower or safflower oils possess this undesirable PUFA content and there are numerous research data now available to indicate that the sole use or excess intake of these newer vegetable oils are actually detrimental to health and switching to a combination of different types of fats including the traditional cooking fats like ghee, coconut oil and mustard oil would actually reduce the risk of dyslipidaemias, AHD and Type-2 DM

Dubnov, G. and Berry, E. M. 2004 *Curr.Atheroscler.Rep.* 6 441-446

Omega-6 fatty acids and coronary artery disease: the pros and cons

Polyunsaturated fatty acids have long been recommended as a beneficial substitute for atherogenic saturated fat. The connection between dietary lipids and blood cholesterol is still under debate, as is the connection between dietary fat and coronary artery disease. Thus, the lipid hypothesis is still a hypothesis. The major dietary polyunsaturated fatty acid, linoleic acid of the omega-6 family, has several properties that render it hyperinsulinemic and atherogenic. The potential benefits of linoleic acid intake regarding coronary artery disease, and its possible harms, are discussed

Maillard, V., Bougnoux, P., Ferrari, P., Jourdan, M. L., Pinault, M., Lavillonniere, F., Body, G., Le Floch O., and Chajes, V. 3-1-2002 *Int.J.Cancer* 98 78-83

N-3 and N-6 fatty acids in breast adipose tissue and relative risk of breast cancer in a case-control study in Tours, France

Experimental studies have indicated that n-3 fatty acids, including alpha-linolenic acid (18:3 n-3) and long-chain n-3 polyunsaturated fatty acids inhibit mammary tumor growth and metastasis. Earlier epidemiological studies have given inconclusive results about a potential protective effect of dietary n-3 polyunsaturated fatty acids on breast cancer risk, possibly because of methodological issues inherent to nutritional epidemiology. To evaluate the hypothesis that n-3 fatty acids protect against breast cancer, we examined the fatty acid composition in adipose tissue from 241 patients with invasive, nonmetastatic breast carcinoma and from 88 patients with benign breast disease, in a case-control study in Tours, central France. Fatty acid composition in breast adipose tissue was used as a qualitative biomarker of past dietary intake of fatty acids. Biopsies of adipose tissue were obtained at the time of surgery. Individual fatty acids were measured as a percentage of total fatty acids, using capillary gas chromatography. Unconditional logistic regression modeling was used to obtain odds ratio estimates while adjusting for age, height, menopausal status and body mass index. We found inverse associations between breast cancer-risk and n-3 fatty acid levels in breast adipose tissue. Women in the highest tertile of alpha-linolenic acid (18:3 n-3) had an odds ratio of 0.39 (95% confidence intervals [CI] = 0.19-0.78) compared to women in the lowest tertile (trend p = 0.01). In a similar way, women in the highest tertile of docosahexaenoic acid (22:6 n-3) had an odds ratio of 0.31 (95% CI = 0.13-0.75) compared to women in the lowest tertile (trend p = 0.016). Women in the highest tertile of the long-chain n-3/total n-6 ratio had an odds ratio of 0.33 (95% confidence interval = 0.17-0.66) compared to women in the lowest tertile (trend p = 0.0002). In conclusion, our data based on fatty acids levels in breast adipose tissue suggest a protective effect of n-3 fatty acids on breast cancer risk and support the hypothesis that the balance between n-3 and n-6 fatty acids plays a role in breast cancer

You will need to read labels carefully and ask about fats used in restaurants. You will be amazed to find out how many foods contain these fats. Always avoid them. If you use a cookbook that recommends them substitute butter, please, or convert the recipe to nonfat.

Edem, D. O. 2002 *Plant Foods Hum.Nutr* 57 319-341

Palm oil: biochemical, physiological, nutritional, hematological, and toxicological aspects: a review

*The link between dietary fats and cardiovascular diseases has necessitated a growing research interest in palm oil, the second largest consumed vegetable oil in the world. Palm oil, obtained from a tropical plant, *Elaeis guineensis* contains 50% saturated fatty acids, yet it does not promote atherosclerosis and arterial thrombosis. The saturated fatty acid to unsaturated fatty acid ratio of palm oil is close to unity and it contains a high amount of the antioxidants, beta-carotene, and vitamin E. Although palm oil-based diets induce a higher blood cholesterol level than do corn, soybean, safflower seed, and sunflower oils, the consumption of palm oil causes the endogenous cholesterol level to drop. This phenomenon seems to arise from the presence of the tocotrienols and the peculiar isomeric position of its fatty acids. The benefits of palm oil to health include reduction in risk of arterial thrombosis and atherosclerosis, inhibition of endogenous cholesterol biosynthesis, platelet aggregation, and reduction in blood pressure. Palm oil has been used in the fresh state and/or at various levels of oxidation. Oxidation is a result of processing the oil for various culinary purposes. However, a considerable amount of the commonly used palm oil is in the oxidized state, which poses potential dangers to the biochemical and physiological functions of the body. Unlike fresh palm oil, oxidized palm oil induces an adverse lipid profile, reproductive toxicity and toxicity of the kidney, lung, liver, and heart. This may be as a result of the generation of toxicants brought on by oxidation. In contrast to oxidized palm oil, red or refined palm oil at moderate levels in the diet of experimental animals promotes efficient utilization of nutrients, favorable body weight gains, induction of hepatic drug metabolizing enzymes, adequate hemoglobinization of red cells and improvement of immune function. However, high palm oil levels in the diet induce toxicity to the liver as shown by loss of cellular radial architecture and cell size reductions which are corroborated by alanine transaminase to aspartate transaminase ratios which are higher than unity. The consumption of moderate amounts of palm oil and reduction in the level of oxidation may reduce the health risk*

believed to be associated with the consumption of palm oil. Red palm oil, by virtue of its beta-carotene content, may protect against vitamin A deficiency and certain forms of cancer

Consumable Fats

Use small amounts of nuts and seeds sprouted or lightly dry-roasted for omega-6 essential fatty acids. Raw nuts and seeds contain anti-digestive enzymes. Sprouting or roasting destroys the anti-digestive enzymes making them more digestible.

Use fish oil capsules for omega-3 fatty acids. Buy capsules not liquid because omega-3 is fragile and exposed to oxygen, or light or heat rapidly oxidizes. Keep your fish oil in the freezer. Eating enough fish to get your omega-3 would be mercury toxic.

Acceptable fats for consumption and food preparation include extra virgin olive oil, (you can use pan spray but do not use those containing hydrogenated fats), fresh ground peanut butter, unprocessed palm oil, cream cheese, sour cream, butter, ghee, natural non-hydrogenated lard, coconut milk and coconut oil and salad dressings that you make from extra virgin olive oil.

Acceptable store brands of mayonnaise should contain high oleic safflower oil. High oleic oil means the oil contains the more stable monounsaturated fatty acids. These oils are processed and should be used sparingly. Homemade mayonnaise is preferred. Nourishing Traditions (see reading list) has a great recipe using olive oil. You may also use any mayonnaise recipe and substitute high oleic safflower oil.

Fats and Oils: Rules for Handling and Storage

Polyunsaturated fatty acids
Nut and seed oils that are made into liquid vegetable oils, these oils do not become solid when refrigerated. <u>It is preferable to not use these oils at all.</u> Such oils include soy, canola, corn, flax, soy, walnut, safflower, cottonseed and sunflower oil.
Adding nuts or seeds in small amounts to recipes or eating some 'trail munch' on occasion is a safe way to consume the omega-6 polyunsaturated fatty acids. Oils out of the nut or seed degrade in quality rapidly. Even cold pressed oils are heated to 350 degrees and exposed to air and light.
Monounsaturated fatty acids
Found in the new HIGH OLEIC oils and olive oil, peanut oil and avocado oil. Use extra virgin olive oil with moderation. Use fresh ground peanut butter. Cold pressed or 'virgin' peanut and avocado oil are also good choices. DO NOT USE CANOLA OIL.
May be kept at room temperature in a closed container. Do not expose to light. Good for cooking but do not overheat. Do not allow oil to smoke while cooking. Do not reuse oil for cooking. Dispose of this oil (if in opened container) after 6 months. If your container is closed these oils keep for about a year. Fortunately to live near olive territory we purchase a year's supply of extra virgin olive oil at harvest, bottled in 8 oz.(small) containers.
Saturated fatty acids
Found in meat, dairy, poultry including eggs, non-hydrogenated coconut oil, coconut milk, non-hydrogenated palm oil, cocoa butter, non-hydrogenated lard, non-hydrogenated palm oil, butter and ghee.
Very stable to heat, light and air. Saturated fats have a low oxidation rate so these fats are excellent for cooking. Saturated fats will keep more than a year without oxidative damage. Light, heat and air (oxygen) exposure is not as damaging though these fats should not be overheated.

May not be suitable in more than minimal quantities for persons with high blood lipids or imbalanced hdl/lDL ratios or for those with a history of certain types of heart disease however research in this area is mixed.

If it agrees with you and you like it, minimally processed coconut oil or coconut milk may be consumed daily. If you suffer from chronic illness or virus the medium chain fats found in coconut will contribute to improving your health. Coconut fatty acids burn rapidly for energy, and are anti-viral, anti-fungal and anti-bacterial. Coconut oil must be NON hydrogenated. Make sure of your source. Coconut milk must be whole NOT 'lite' and preferably contain no preservatives. Coconut does NOT keep well. Once your jar or bottle is open, refrigerate and use up quickly.

Non-hydrogenated lard and grass-fed dairy butter can be ordered from organic farms. Check with the Weston A. Price Foundation for information and sources for good fat and grass-fed meats. You can reach them at 1-202-333-HEAL organic butter is available from many groceries these days but most of it comes from cows fed corn, back to our 'bad' fat profile. Try to find a grass-fed source for butter if possible

Lard from your local market is hydrogenated. Coconut and palm oils used in the confectionary trade are also hydrogenated. Avoid hydrogenated fats

Table 5 Terms Used- Fatty Acids

Terms Used	
Omega-6 or n-6	Any of the fatty acids in the omega-6 family, short or long-chain. Also designated as n-6. These fats are polyunsaturates with multiple double bonds beginning on carbon 6.
Linoleic Acid	Short-chain omega-6 fatty acid also designated by LA. Can be converted into arachidonic acid.
Arachidonic acid	Long-chain essential omega-6 designated AA
Decosapentanoic Acid	Long-chain omega-6 designated DPA (may displace DHA in the brain- not a good thing)
Omega-3 or n-3	Any of the fatty acids in the omega-3 family, short or long-chain. Also designated by n-3. These fats are polyunsaturates with multiple double bonds beginning on carbon 3.
Linolenic Acid	Short-chain omega-3 fatty acid designated by ALA or LNA or alpha linolenic acid. Can be converted into EPA and DHA.
Eicosapentanoic	Acid: Long-chain omega-3 designated EPA
Decosahexanoic Acid	Long-chain conditionally essential omega-3 designated DHA. The most important fatty acid for brain development and function.
Monounsaturated Fatty Acid	Fats containing one double bond on carbon 9. Designated omega-9 or n-9 or oleic acid.
Saturated fat	Fats with no double bonds. They can be short or long-chained. They are ubiquitous (in all life). Several are critically important to health and may be anti-viral and antibacterial. Natural saturated fats are stable to heat and light and safe for higher heat cooking. They do not oxidize readily.
Trans-fats	Trans-fatty acids are created when seed and grain oils are processed such as in the making of margarine and the hydrogenated fats used in most processed foods. Trans-fats also occur in vegetable and grain oils when they are heated.

Seed, nut, and grain oils	Corn, soy, safflower, sunflower, sesame, cottonseed, canola, walnut, peanut, flax
Fruit oils	Olive, avocado.

	nickname	abbreviation used in book	shorthand	structural formula	
Saturated Fatty Acids	Butyric Acid	BA	4:0		
	Caproic Acid		6:0		
	Caprylic Acid		8:0		
	Capric Acid		10:0		
	Lauric Acid		12:0		
	Myristic Acid		14:0		
	Palmitic Acid	PA	16:0		
	Stearic Acid	SA	18:0		
	Monounsaturated Fatty Acids	Palmitoleic Acid	P OA	16:1w7	
		Oleic Acid	OA	18:1w9	
Essential Fatty Acids (EFA's)	Linoleic Acid	LA	18:2w6		
	Linolenic Acid	LNA	18:3w3		
Fatty Acid's made from linolenic acid	Gamma-Linolenic Acid	GLA	18:3w6		
	Arachidonic Acid	AA	20:4w6		
	Stearidonic Acid	SDA	18:4w3		
	Eicosapentaenoic Acid	EPA	20:5w3		
	Docosahexaenoic Acid	DHA	22:6w3		

SOME SCIENTIFIC FATTY ACID STUFF YOU NEED TO KNOW

Figure 5-3 Naming the Fatty Acids

Naming the Fatty Acids shows representative fatty acid chains from short chain saturated fatty acids to the very long chain super unsaturated fatty acids. Each of these fatty acids play a different role in living organisms.

The EFAs (essential fatty acids, we must eat them our bodies can't make them) and the substances the body makes from these EFAs are essential to health and life and must be consumed on a daily basis. The best sources of the essential fatty acids, linoleic and linolenic acid, are eggs, nuts, seeds and fish.

There is some information suggesting omega-3 fatty acids as eicosapentaenoic acid and docosahexaenoic acid are conditionally essential. The thought had been these fatty acids could be made from linolenic acid. Newer findings suggest we are unable to make sufficient EPA or DHA and must consume it directly.

Varying fatty acids comprise the lipid membranes enclosing every cell in your body. These fatty acids give the cell its ability to selectively choose what is absorbed and what is excreted.

They also change the way your cells respond to the environment. When the fats in your diet are the wrong kind the integrity of every cell suffers.

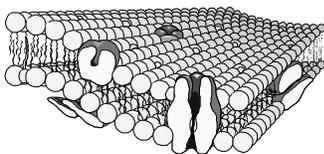


Figure 5-4 Cell Membrane

From chapter 9, *The Plasma Membrane*, Nutrition an Integrated Approach, Pike and Brown, 1986

All cells are units separated from their environment by a membrane. This a barrier whose presence determine the shape and encloses the substance of the cell. Despite the variability and potential hostility of the outside environment, it is the membrane on which the constancy of the internal chemistry of the cell is dependent. The discharge of this responsibility is made possible by the ability of the membrane to discriminate among those organic and inorganic molecules in the surrounding medium, permitting the entrance to some and rebuffing others. This is a truly vital task since either mass invasion of potentially toxic material or rejection of essential nutrients can lead to cellular death by asphyxiation,

hydration, desiccation, poisoning, starvation, or other equally effective means. The cell, thus dependent on the external environment for all the raw materials from which it is made and with which it operates, by means of the membrane barrier and its fastidious selectivity, can enjoy a distinct and separate existence.

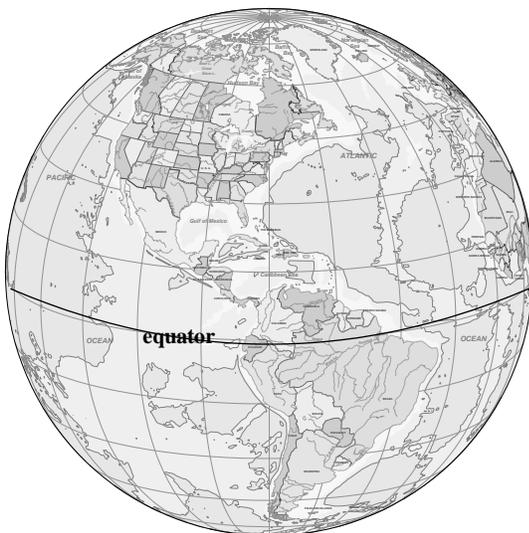
A cell in equilibrium with its environment is a dead cell.

Cell membranes have a lipid bilayer, two layers primarily composed of fatty acids. The fats you eat are critical to the health of your cell walls. Without healthy walls your cells die prematurely or conversely may multiply excessively as in cancer.

Fats and Light

Fatty acids develop in plants in relation to latitude and altitude, that is, in relationship to the sun. Plants nearer the equator produce higher levels of saturated fats such as the coconut and palm and the macadamia nut. Highly polyunsaturated flax is grown in Canada. Oil seeds such as safflower, sunflower, canola, corn and the like vary in fatty acids by strain and by where they are grown.

Figure 5-5 Globe



The fats produced and incorporated into cell membranes of plants are induced by sunlight. Sunlight produces both light and heat. Plant fats are modulated by UV-B intensity and temperature which are determined by latitude and altitude. Plants use fatty acids (as waxes and fats) to modulate the plant cells exposure to light (UV-B) and to give stability and flexibility.

Living things all contain a variety of fatty acids but amounts and ratios of these fats are altered by genes and location. Near the equator the preponderance of fats produced by plants are saturated. In the mid-latitudes monounsaturates are abundant. Polyunsaturates as found in flax and canola oils appear in the more northern and southern latitudes.

Saturated fats, higher in tropical plants exposed to intense heat and light, stiffen the cell membrane and moderate the intensity of UV-B, protecting the plant DNA. In plants grown more distant from the equator fatty acids produced by the plant change becoming less saturated and thereby allowing the entrance of more light as the overall intensity of light is diminished. Increasing levels of unsaturation keep cell membranes flexible as temperatures drop in more northern and southern latitudes.

Qualities of fats:

Saturated fats are solid at room temperature. Saturated fats are stable to heat and light. They oxidize slowly remaining stable without refrigeration. They are safe to use in higher heat cooking.

Monounsaturated fats are liquid at room temperature. They are somewhat stable to heat and light. If kept in a closed container they remain fresh from harvest to harvest without refrigeration. They oxidize more rapidly than saturated fats but less rapidly than polyunsaturated fats. They are suitable for cooking with moderate heat.

Poly unsaturated fats are liquid at room temperature and in the refrigerator. They are unstable to heat and light. They oxidize readily. These fats are best used fresh. Once an oil is pressed from the grain or seed rancidity will progress even when refrigerated. This group includes fish oil and flax which should always be kept in the refrigerator or even the freezer.

Animal cells are composed of the fats consumed. Humans and animals historically had fatty acids patterns similar to local plants. In equatorial regions the cells of animals and humans contained higher amounts of saturated fats, in the mid-regions, such as the Mediterranean, more monounsaturated fats and in the far north or south more polyunsaturated fats.

Living near the equator, higher intakes of locally available saturated fats protect cells and do not contribute to heart disease, obesity or diabetes. Consider ghee in India, coconut in Hawaii and Thailand and palm oil in other tropical countries.^(272,273)

Fats are produced and incorporated into flesh and skin of plants, animals, and humans offering protection suitable to location.

We, all living things, have developed over thousands of years in relationship to our location, in relationship to light. Our skins (largest cell membrane of them all) qualities are genetically set for the land and light of our ancestors and nutritional needs reflect the locally grown plants, resident animals and fish to provide proportionally correct fatty acids and other nutrients.

When humans first transported themselves and then their food and finally introduced man-created processed food, the intimate relationship of plant, animal, man, and light was destroyed. Few know where the food they eat was grown or whether it is suitable for their genetics or location. If processed foods are consumed the fats the foods contain have no relationship to any 'real' genetics or environment.

It is important to eat fats according to location and ancestry. If your ancestry is coastal or island expect to need high levels of omega-3 fats. Inlanders depend more on grains and seeds with some omega-3 from fresh water fish. Tropical, sub-tropical or desert ancestry suggests other choices such as coconut or palm oil. Your ancestral saturated fat may be coconut oil, palm oil, butter, ghee, tallow (beef fat) or lard. Make sure whatever fats you use the are NEVER hydrogenated.

While omega-3 fats are found in all locations, higher levels of polyunsaturated fats of the omega-3 family are natural, in plants, animals, and fish, in the latitudes of the Far North Monounsaturated fatty acids predominate in the middle latitudes.

In moderate climates it is appropriate to increase saturated fats in spring and summer months as dietary fats are incorporated into the skin and become a part of our cell barrier, the stratum corneum.^(274,275,276) When winter approaches adding small amounts of

polyunsaturated nuts or seeds and reducing intake of saturated fats get us ready for the cold dark months ahead.

When the out layer of our skin, the stratum corneum, is healthy and underlying skin containing fatty acids appropriate to sunlight intensity, we have the most potent protection from damaging effects of UV light.^(277,278,279,280) Extra virgin olive oil, coconut oil and palm oil (unprocessed) are skin protective as sunbathers can attest.⁽²⁸¹⁾

Fats, like sun exposure, have important implications but avoidance is not safety. It is knowing how much, type, and location.

Fats and Degenerative Disease

Omega-6 fatty acids as found in vegetable oils made from corn, soy, canola, sunflower and safflower are implicated in the development of heart disease, cancer, diabetes type 2, allergy and asthma. High levels of omega-6 fatty acids are present in mood disorders, prostate cancer, benign prostatic hypertrophy, melanoma, other skin cancers, breast cancer, ADD, ADHD, Alzheimer's, senile dementia, obesity, insulin resistance, hypertension, and associated degenerative conditions. Other studies show a connection with learning disabilities, schizophrenia and bipolar disease.

The research is quite strong in all of these areas. Whether the problem is the fragility of these oils or omega-6 balance, enough but not too much, these fatty acids should be consumed in very small amounts as present in fresh foods, never from added oils. There are supplements containing a combination of omega-6 and omega-3. These supplements should be avoided. It is very easy to get omega-6 and additional omega-6 actually inhibits the body's use of omega-3.

Omega-6 fatty acids are the base for inflammatory prostaglandins, substances that promote inflammation in our bodies. Omega-3 fatty acids are the base of anti-inflammatory prostaglandins. We don't need large amounts of either of these fats but we do need some of each and in the right ratio.

The ratio of omega-6 to omega-3 in the hunter-gatherer diet was 1:1. Current ratios in the US are 12-50:1. For us to get the benefit of omega-3 fats, omega-6 must be dramatically reduced from all sources.

Omega-6 (vegetable oils) and Cancer

Dietary polyunsaturated fatty acids and cancers of the breast and colorectum: emerging evidence for their role as risk modifiers. Carcinogenesis 1999 Dec;20(12):2209-18

Bartsch H, Nair J, Owen RW.

Division of Toxicology and Cancer Risk Factors, German Cancer Research Center (Dkfz), Im Neuenheimer Feld 280, D-69120 Heidelberg, Germany. H.Bartsch@Dkfz-Heidelberg.De

The hypothesis that a high-fat diet promotes the development of postmenopausal breast cancer is supported by international data showing a strong correlation between fat intake and breast cancer rates and a modest positive association with high-fat diet in case-control studies. Dietary fat intake was found to be unrelated to the risk of breast cancer in cohort studies. In view of these conflicting findings it has been difficult to make nutritional recommendations for the prevention of breast cancer. **Studies in animal models and recent observations in humans, however, have provided evidence that a high intake of omega-polyunsaturated fatty acids (PUFAs), stimulates several stages in the development of mammary and colon cancer,** from an increase in oxidative DNA damage to effects on cell proliferation, free estrogen levels to hormonal catabolism. In contrast, **fish oil-derived omega-3 fatty acids seem to prevent cancer by influencing the activity of enzymes and proteins** related to intracellular signaling and, ultimately, cell proliferation. In this commentary, current evidence from experimental and human studies is summarized that implicates a high intake of omega-6 PUFAs in cancer of the breast, colon and, possibly, prostate and which indicates that omega-3 PUFAs and monounsaturated fatty acids such as oleic acid (omega-9) are protective. Plausible mechanisms for modulation of steps in the multistage carcinogenesis process by fats are discussed. Properly designed epidemiological studies are now needed, that integrate relevant biomarkers to unravel the contributions of different types of fat, their interactions with hormonal catabolism, protective nutritional factors and human cancer risk.

ESSENTIAL FATS FOR HUMANS

Fatty acids play critical roles in human health and disease. Cell membranes (all cells) are composed of a double layer of fats. Your brain cells are about 60% fat. The fats you eat strongly influence the ability of your cell membranes and your brain to function.

Cholesterol is an alcohol, not a fat. Natural saturated fats are found in most foods to some degree. Saturation of a fat may be natural or from processing as is done to make margarine solid. Naturally occurring saturated fats are not associated with disease unless they are imbalanced by inadequate intake of the polyunsaturate essential fatty acids, especially the omega-3 fats.

Linoleic Acid is an omega-6 that is 20 (or more) times too high in the American diet and strongly implicated in degenerative diseases. Linoleic acid is the precursor to arachidonic acid.

Arachidonic Acid is found in meat and fish and eggs and dairy and made in our bodies from linoleic acid. It is critical for the growth of the body and brain and immune function but needed in very small amounts.

Linolenic Acid is a short chain omega-3, first double bond on the third carbon, found in perilla, canola and flax. It has been considered to be important as a precursor for production of long chain omega-3 DHA and EPA but many Americans suffer from poor conversion, an enzyme insufficiency, or impaired genetic ability to elongate the fatty acid to its active EPA and DHA forms. A vitamin B-6 deficiency also prevents conversion.

EPA, eicosapentanoic acid and DHA, decosahexanoic acid, are found in fish, grass-fed beef and poultry and wild game. Some may be made from linolenic acid, depending on your genetics, your liver function and other as yet unknown factors.

Omega-3 (Fish Oil, not flax) Fatty Acid

Omega-3 fatty acids, DHA and EPA, are essential to brain and nerve function. In cell membranes they enhance cell response (to insulin, neurotransmitters and other messengers), and facilitate repair when cells are damaged. Omega-6 fats contribute to membrane resistance, altering mood, insulin response, learning and cell repair in a negative way.

There is a chart located on the last following showing fat types, omega-3, omega-6 found in foods. You may use this as a reference guide.

Some anthropologists believe the human brain would not have developed as it did without access to high levels of DHA found in fish and shellfish and to a lesser degree in wild game.^(282,283,284,285,286,287) Just two generations of high omega-6 and low omega-3 can lead to profound alterations in brain size and brain function in animals and probably in man.

Other anthropologists believe that the human brain formed as it is today, large in proportion to body size, and that its capacity is being diminished as the diet becomes deficient in omega-3 fats.

A relative omega-3 fat deficiency can be created by an overabundance of omega-6 fats, a lack of omega-3 fats, alcohol consumption or the consumption of trans-fats as has been increasingly occurring in the US for the past 50 years.

Breast milk contains DHA and EPA, equivalent to amounts present in the mother's diet (what mom eats is critical). Formulas typically contain no omega-3. Raising children on formula or mother's milk deficient in omega-3 fats contributes to impaired visual development, poor spatial development, slower learning, decreased comprehension and early allergies and asthma.

The amount of **omega-6 fats** in the American diet need to be decreased and **omega-3 fats** increased. I have suggested the use of butter, unprocessed coconut and extra virgin olive oil for many years and this recommendation continues. The next step is intentional avoidance of added, processed, omega-6 fats. Omega-3 fats must be sought out and consumption increased.

Avoid all vegetable seed oils. Do not use sunflower, corn, soy, safflower, canola, or products that contain these oils; that is, no hydrogenated or partially hydrogenated fats, no margarine, no vegetable oil, no shortening, no bottled dressing.

Acceptable oils are extra virgin olive oil, peanut or avocado oil in moderate quantities. High oleic (omega-9) safflower or sunflower oil is acceptable in minimal quantity, but not preferred. Natural (non-hydrogenated) saturated fats are NOT a problem. Use butter, coconut oil, palm oil and non-hydrogenated lard in moderate amounts.

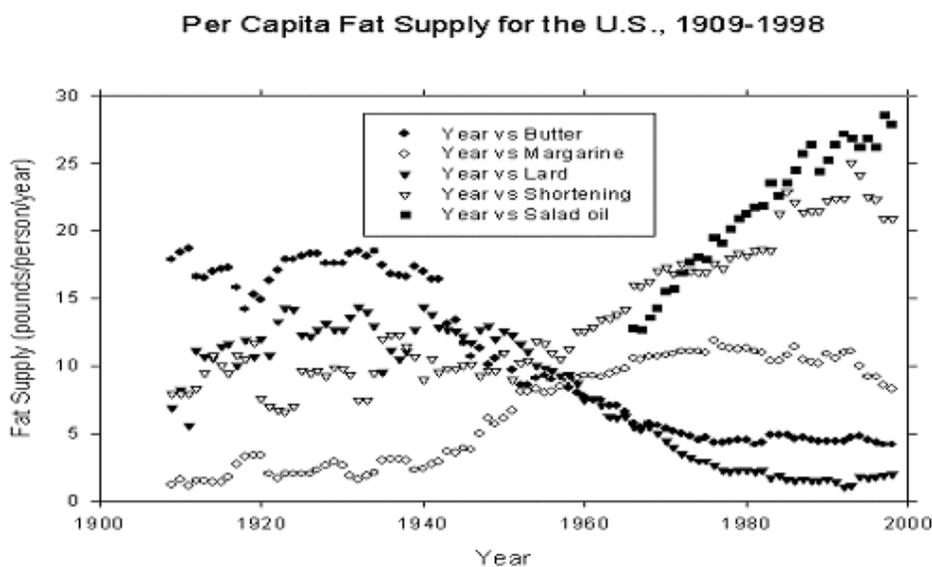
Foods are never composed of a single type of fatty acid. Coconut oil has saturated and polyunsaturated fats and olive oil has monounsaturated and saturated fats. In nature fats are always mixed. Fish oil, high in omega-3 also contains saturated fat and cholesterol.

Do not worry about naturally occurring cholesterol in fish, shellfish, eggs or lean meats. Do not worry about total fat intake as long as it is from actual food, whole-fat milk, real butter, the fat naturally present in fish, poultry, meat.

If you haven't already, reduce ADDED FAT, eliminating as much omega-6 added fat as possible. Do your best to avoid obvious omega-6 fats. If you suffer from elevated cholesterol it is even more important that you increase your omega-3 fats and avoid omega-6. Keep your total added fat, dressings, cooking, added to vegetables or popcorn, to less than 2 tablespoons daily.

Between 1903 and 1998 ADDED FATS rose from 34 pounds per person per year, mostly butter and lard, to more than 66 pounds per person per year. All of the fat increase was in the form of omega-6 as salad dressing, margarine, shortening and hydrogenated fat added to processed foods and candies. See the figure that follows.

Figure 5-6 Per Capita Fat Supply US 1909-1998



USDA and WB Grant PhD

The ratio of omega-6 to omega-3 in the U.S. diet is somewhere between 25-50:1. The ideal ratio is somewhere between 4-1:1. To correct this imbalance you will need to severely restrict omega-6 fats and add fatty fish daily making sure to eat the skin and fat under the skin. Remember, the fish must not be cooked in an omega-6 fat, vegetable oil or margarine, nor dipped in mayonnaise, also an omega-6.

Supplementing Omega-3

Supplemental Dose: If you are not eating fatty portions (skin with fat, fat at the tail) of fish such as mackerel, sardines (packed in salmon oil, eat the oil), or salmon, a minimum of three times a week you will need to use fish oil supplements. We need the equivalent of about 8-10 tablespoons per week of fish oil.

The daily maintenance dose of fish oil is probably 2,000-3,000 mg of combined DHA-EPA, more if you are obese and less if you are a child under 10 years of age. As fish oil soft gels (or liquid) contain more than just DHA and EPA you will need to calculate how many soft gels this works out to be.

The pharmacological dose, to treat omega-3 deficiency, is 300 mg combined EPA-DHA for each 10 pounds of actual body weight, for both children and adults. To alter tissue levels of omega-3 fatty acids it is necessary to increase omega-3 and avoid most sources of omega-6 fats for 1-3 months after which 2,000-3,000 mg daily is probably adequate.

Fish oil can be taken with or without food. Many clients find that there is less reflux when taken on an empty stomach. **Keeping your fish oil in the FREEZER keeps the oil fresh AND may also reduce burping/reflux.** Fish oil can be taken all at once or split up into two or three doses. For some, fish oil may be very energizing and best taken in the morning or mid-afternoon. If you determine you need a higher dose but it causes gastrointestinal distress (gas, bloating or diarrhea) take 1 rounded tablespoon of lecithin granules, a natural emulsifier, with your full daily dose of fish oil.

In July 2013 a retrospective analysis of an earlier cancer risk trial suggested omega-3 fatty acids increased the risk of aggressive prostate cancer. This conclusion cannot actually be drawn from the study though it was widely reported as TRUE. This happens, news headlines dooming us without actual solid science to back it up. You need omega-3 fats and they are safe if purchased from reputable suppliers and kept fresh in your fridge or freezer. Do not consume rancid fats of any kind.

An inexpensive source of omega-3 fish oil is the Kirkland brand from Price-Costco. It is the freshest (due to high product turnover), good quality and a great price, 300 soft gels for about \$10. It is not concentrated so the daily dose is 8-10 soft gels. Now Foods Super EPA Double Strength is concentrated, so you'll need only 5 per day.

Table 6 Fish Oil Safety

Selected Environmental Toxin Content of 5 Preparations of Fish Oil		
Brand Name	Polychlorinated	
	Biphenyls, ppb	Organochlorine, ppb
CVS	None detected	None detected
Kirkland	None detected	None detected
Natrol	None detected	None detected
Omega Brite	None detected	None detected
Sundown	None detected	None detected

Mercury Content of 5 Preparations of Fish Oil	
Fish Oil Brand Name	Mercury Level, mg/L
CVS	10
Kirkland	.6
Nordic Ultimate	.6
Omega Brite	12
Sundown	.6

I frequently get questions from clients about products advertising they have the only fish oil (or other element) that is pure and effective; that their manner of production is more natural or preserves more elements, or the element is more absorbable. As a rule all supplement companies get their raw materials from a relatively few manufacturers of the element/s in question.

All fish oil is either molecularly distilled or undergoes ultra-filtration. Both remove toxins and fat-soluble vitamins from fish body oil. Look for price and convenience not inflated advertising claims.

Omega-3 and 6 fats move into cell membranes, particularly the membranes of epithelial cells- cells that compose skin, the lining of the arteries and lungs, the linings of the ducts in the breast and testes. They also are components of nerve and brain cells. The preferential fat for these cell membranes is omega-3 but n-3 will be replaced by n-6, if n-3 is not available. Cells where omega-3 is displaced by omega-6 are less able to repair themselves, perform poorly, and potentially the DNA may be altered.

The brain and nerves so need omega-3 that they will rob it from every other cell to maintain optimum brain levels. Some of the brain and nerve conditions associated with high omega-6 and low omega-3 include, alcoholism, depression, manic depression, memory loss, impaired night vision, anxiety, insomnia, dementia, Parkinson's, ADD, ADHD, dyslexia, stress induced hostility and schizophrenia.^(288,289,290,291,292,293,294,295,296)

Recently research indicated omega-3 fats are primary in the prevention of Alzheimer's disease.^(297,298,299,300,301,302) Humans need long chain omega-3 fish fat.

In the following table of US per capita fat consumption 1909-1998 it is clear that both our overall intake of fats and intake of omega-6 fats has dramatically increased. There is no indication our intake of natural unprocessed saturated fats has increased over this period of time.

Table 7 Added Fats Per Capita Consumption 1909-1998

From the USDA	1909	1945	1970	1980	1998	
Butter In 1909 butter and cream was from grass-fed cows.	17.9	11.7	5.4	4.5	4.2	Butter from grass-fed cows is high in omega-3
Lard In 1909 natural lard, not hydrogenated, contained poly fats including omega-3	6.9	12.2	4.5	2.3	2.0	Most is now hydrogenated or from grain-fed (omega-6) pigs
Margarine	1.2	3.9	10.8	11.3	8.3	All Omega-6 and trans-fats
Shortening, Crisco, added hydrogenated and partially hydrogenated fats. (In 1909 shortening contained less omega-6. It had coconut or palm oil, safer)	8.0	10.0	17.3	22.2	20.9	All Omega-6 and trans-fats
Salad Oils Most Omega-6, often rancid, containing trans-fats.	N/A	N/A	15.5	21.3	27.9	In 1998 a small amount was omega-9 olive oil (<0.5 lb)
Edible Tallow	N/A	N/A	N/A	1.1	3.2	
Total Pounds of Added Fat Per Capita	34	37.8	53.5	62.7	66.5	Almost double by 1998, mostly omega-6

The following paper was presented in 2000 at the National Institute of Health in Washington, DC. The BOLD text is my emphasis. Keywords in understanding fats- Linoleate is omega-6, linolenate is omega-3 as is DHA and EPA and oleic is omega-9. Linoleate, DHA, EPA and linolenate are all polyunsaturated fats. Oleic omega-9 is monounsaturated fat.

Fats and Disease- The Importance of Omega-3

Choice of n-3, Monounsaturated and Trans-fatty Acid-Enriched Oils for the Prevention of Excessive Linoleic Acid Syndrome

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Excessive linoleic acid (omega-6) intake and relative n-3 deficiency syndrome

Animal experiments and epidemiological studies have revealed that excessive intake of linoleic acid (omega-6) (LA, n-6) is a major risk factor for cancers of western type, allergic hyper-reactivity, coronary heart disease (CHD) and cerebrovascular disease (CVD) (1). Although epidemiological studies performed in the USA failed to reveal a positive correlation between LA intake and breast cancer mortality, this is probably because the proximate marker for breast cancer is the proportion of n-6 eicosanoid precursors in phospholipids, which is saturated both in the high and low LA intake groups in the USA. Empirical equations presented by Lands indicate that both increasing the intake of n-3 fatty acids and decreasing that of n-6 fatty acids are necessary for effectively decreasing the n-6 eicosanoid precursors in phospholipids and thereby decreasing cancer mortality. On the other hand, high n-6/n-3 ratio but not hypercholesterolemia has been proved clinically to be a major risk factor for thrombotic diseases. Over-production of inflammatory lipid mediators of n-6 series has been shown to be a major cause for the rapid increase in allergic hyper-reactive patients in Japan.

President's Summary 1997 from the Japan Society for Lipid Nutrition

After discussion through several annual meetings of the Japan Society for Lipid Nutrition, Presidents Summary 1997 was published (in Japanese) as a review article (J. Lipid Nutr. 6:5-42, 1997), in which 20% as total fat energy was recommended for those with moderate physical activity. For healthy populations, saturated plus monounsaturated : n-6 : n-3 = 2.5 : 0.8 : 0.2 (n-6/n-3 4) was recommended.

For the primary and secondary prevention of those diseases described above, an n-6/n-3 ratio of 2 was recommended. The latter value was based on: 1) even the n-6/n-3 ratio of Danes was 3 in a well-known epidemiology of Greenland natives; 2) the ratio of current Japanese is 4 but the incidence of **cancers** of western type has been increasing rapidly, and the ratio of 4 or above cannot be recommended; 3) **animal experiments have shown the effectiveness of decreasing n-6/n-3 ratio to below 2 for the suppression of carcinogenesis and metastasis**; and 4) the safety of n-6/n-3 ratio of 1 has been established in animal experiments and in a retrospective study on hunters and gatherers foods.

In order to meet the recommendations described above, vegetable oils with n-6/n-3 ratios of 2 or below and those with very low n-6 fatty acid contents (e.g., high-oleic type) are useful. However, there was another criterion to be considered; the presence of minor components, which affect animal physiology seriously.

Survival time-shortening and renal injury induced by some vegetable oils and partially hydrogenated oils in SHRSP rats

Using soybean oil as a control, some oils were found to **prolong the mean survival time** of SHRSP rats by 10% (e.g., **DHA-rich fish oil, perilla seed oil, flaxseed oil**) while some others shortened it dose-dependently by 40% (double-low rapeseed oil, evening primrose oil, high-oleate safflower oil, high-oleate sunflower oil, olive oil and partially hydrogenated rapeseed and soybean oil). When the rapeseed oil was lipase-treated, the resulting free fatty acid fraction was almost free of such activity, indicating that the survival-time shortening activity is due to minor components other than fatty acids in these oils. Free fatty acid fraction from partially-hydrogenated soybean oil exhibited a survival time between those of the original oil and soybean oil. It should be emphasized that **lard and sesame oil were relatively safe** for the SHRSP rats.

Those oils with survival-time shortening activity were found to cause renal injury; lesions in blood vessels, accelerated proteinuria, decreased platelet count and elevated gene expression for TGF β , fibronectin and renin.

Choice of n-3, monounsaturated and trans-fatty acid-enriched oils

In order to decrease the n-6/n-3 ratio of our current foods to 2 or below, the intake of high-n3 linolenate oils such as perilla seed oil and flaxseed oil as well as seafood and vegetables should be increased. **High-linoleate (omega-6) oils are inappropriate for human use as foods.** For deep-frying and preservation purpose, high-oleate vegetable oils are useful but all the high-oleate vegetable oils and hydrogenated vegetable oils we have examined so far exhibited the survival time-shortening activity, and I cannot recommend people to have these oils in large quantities. **Instead, lard was safe for this animal model, and could be used in quantities not to induce obesity;** animal fats as well as a high-LA vegetable oil intake caused insulin resistance in a NIDDM model of rats.

Reference

Okuyama, H., Kobayashi, T., and Watanabe, S. (1997) Dietary fatty acids ñ The n-6/n-3 balance and chronic, elderly diseases. **Excess linoleic acid (omega-6) and relative n-3 deficiency syndrome seen in Japan.** Prog. Lipid Res. 35: 409-457.

Key Facts Regarding n-3 and n-6

Omega-6 fats in amounts more than essential promote cancer, heart disease, autoimmune disorders including arthritis, diabetes and allergy/asthma.

Omega-6 fats must be dramatically reduced. Eliminate all obvious sources.

Omega-3 fats are protective and may prevent or reverse the listed conditions.

Omega-3 is not necessarily available from flax or perilla oil.

Omega-3 is available from fatty fish (when consuming the fat) but daily intake may be a problem due to fish toxicity from chemicals, pesticides, etc.

Fats are incorporated into skin and all other tissues and organs- you are what you eat- a combination of **omega-3** fats and natural saturated fats including coconut oil, butter and lard offer the **best protection** from disease, including skin **cancer**.

Omega-6 fats, in high amounts, promote inflammation of tissue so that the skin, linings of the lungs, gut, breast, prostate, and bone are more susceptible to damage from UV light, carcinogens, mutagens, allergens and toxins

Omega-3 fats including all parts of the fish oil, both DHA and EPA and even the cholesterol it contains protect these same cells.

HDL cholesterol in its own right has powerful antioxidant activity.

Omega-6 decreases and omega-3 increases HDL cholesterol.

Omega-3 DHA is the major fat in the eye and is replaced (if available) every 10 days. Increasing omega-3 with fish oil improves night vision and color vision.

Omega-3 fats are associated with the ability to smell and for seniors who have lost their sense of smell fish oil may restore it in 1-2 months.

Omega-3 fats improve memory. Just two days after increasing omega-3 the phosphatidylserine content of the brain is dramatically increased.

HDL has long been known as the good cholesterol, protecting against heart disease and atherosclerosis. It was recently discovered that HDL has powerful antioxidant properties similar to vitamin C, vitamin E, and coenzyme Q-10. An HDL associated enzyme, lecithin-cholesterol acyltransferase, which forms part of HDL, is a powerful antioxidant enzyme that blocks the oxidization of LDL cholesterol. Cholesterol is beneficial and without harm if it is not first oxidized. Vohl MC, Neville TA, Kumarathasan R, Braschi S, Sparks DL: A novel lecithin-cholesterol acyltransferase antioxidant activity prevents the formation of oxidized lipids during lipoprotein oxidation. Biochemistry; 1999 May 11;38(19):5976-81

Oleic acid is an omega-9 such as found in olive oil and avocado oil. Some sunflower and safflower oils are bred to be high in this fat, safe for cooking and mayonnaise. Look for the words High Oleic on the bottle and a high number for omega-9 on the label.

Extra Virgin Olive Oil- Nature's Tree of Life

In the last 20 years significant research on the health properties of the olive has shown benefits far beyond its omega-9 content.

Olives and olive oil contain a number of substances that are anti-oxidant, anti-bacterial, anti-viral, anti-osteoporotic, anti-atherogenic and even anti-cancer.
(281,303,304,305,306,307,308,309,310,311,312,313,314,315,316,317,318,319)

The amount of these beneficial elements is dependent on growing conditions and the type of olives used to make the oil. Fortunately for us these elements impart flavor and color to the oil. For the highest amounts of these life-promoting elements choose extra virgin olive oil that is dark and has an intense odor and flavor.

Fielding, J. M., Sinclair, A. J., DiGregorio, G., Joveski, M., and Stockmann, R.
2003 Asia Pac.J.Clin.Nutr. 12 Suppl S36

Relationship between colour and aroma of olive oil and nutritional content

Background - **Olive oil** contains some minor constituents including, characteristic phenolic compounds which contribute to the stability of the oil, antioxidant properties, lipoxygenase activity inhibition and microbial activity. Objective - To determine differences between olive and sunflower oils in regards to nutrient/phytochemical concentration, and to correlate these factors with the colour and aroma of the oils. Design - This study investigated 13 oils in relation to their aroma, colour and nutritional qualities. The oils included extra virgin **olive oil**, light **olive oil** and sunflower oil. The phenolic compound, carotenoid, vitamin E and fatty acid composition was measured. These parameters were compared and correlated to the colour measures (L^*a^*b) and electronic nose responses for each oil. Outcomes - Two Australian extra virgin **olive oils** contained the highest concentration of phenolic compounds, including oleuropein aglycone ($P < 0.05$). Imported **olive oils** contained the highest beta- carotene concentration compared with local oils ($P = 0.002$). Chroma (b^*) was significantly related to lutein and zeaxanthin concentrations ($R(2) = 0.756$, $P = 0.003$). The responses of three electronic nose sensors (LY/LG, LY/G, LY/AA) significantly correlated with oleuropein aglycone concentrations ($P < 0.02$). Conclusions - These results have implications for food processors and consumers who wish to choose oils that have high phytonutrient content: Oils that are high in phenolic compounds and lutein/zeaxanthin can be readily identified, by using aroma and colour measurements.

Essential Fatty Acids Explained

Many people find it difficult to believe that fat can be essential to your health. Fatty acids are the "building blocks" of fat. Some of these fats are called "essential" because your body needs them; your body cannot make them; you must eat them.

Fats designated as essential (EFAs, see figure Naming the Fatty Acids) are all polyunsaturated fats. The two types of essential fatty acids are omega-3 fatty acids and omega-6 fatty acids. The short-chain omega-3 EFA is alpha-linolenic acid (LNA or ALA). Its elongated (made longer) derivatives include: eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA) and a few others, less well known and less studied.

The EFA short-chain omega-6 is linoleic acid (LA). Like LNA, it also has elongated derivatives, the main being arachidonic acid, necessary for prostaglandin formation and brain development and function.

The very long-chain omega-3 EFAs are connected with brain and visual development in infants. Deficiencies in adults can lead to impaired mental processes, including learning disorders, dementias and other neuronal diseases, impaired vision, and depression.

Studies suggest that prolonged deficiencies might lead to retinal and macular damage.^(289,320,321) In pregnant women low levels of the elongated omega-3 can actually reduce brain size in offspring.^(322,323)

What are realistic EFA daily intakes? There is no RDA yet, but many sources agree that Americans do not get nearly enough omega-3. Even worse, we get too much omega-6, which displaces omega-3 in cell membranes and neural membranes.

Researchers involved in the Workshop on the Essentiality of and Recommended Dietary Intakes for Omega-6 and Omega-3 Fatty Acids suggest "adequate intakes" of each EFA: Newer research suggests the value for omega-3 is too low, especially within the US food market. If we got only 4.4 grams of omega-6 it might work. We get much more, even when we try to intentionally avoid omega-6. Omega-6/Omega-3 is about ratio.

Suggested adequate intakes:	
Omega-3	0.65 grams (650 mg) of EPA and DHA combined (neither falling below 0.22 g)
Omega-6	4.44 grams (4,440 mg.)

A diet containing nuts and seeds or meat or even milk and eggs as a protein source has at least 12 grams of omega-6. That would mean that a minimum (not optimal) of omega-3 would be 1.95 grams. This is the amount in about 6 ounces of fatty fish daily (more would be needed if lean fish is used). This assumes you are eating wild caught, cold water fatty fish. Farmed fish is high in omega-3 but equally high in omega-6, canceling much of the benefit to balance ratios.

Sources looking at the dietary ratio of omega-6 to omega-3 fatty acids suggest that in early human history the ratio was about 1:1. Currently most Americans eat a dietary ratio that falls between 20:1 and 50:1. The optimal ratio is most likely 4:1 - 1:1. For most Americans this means greatly reducing the omega-6 fatty acids they consume and increasing the amount of omega-3 fatty acids.⁽³²⁴⁾

In perspective, there are 28 grams (28,000 mg) in one ounce. A tablespoon of safflower oil has 10 grams of omega-6 linoleic acid, twice the daily requirement. To balance omega-3 would require 1.5 grams combined DHA-EPA. One tablespoon of olive oil contains about 1,250 mg of EFA linoleic and 100 mg of EFA linolenic, a ratio of 12:1.

The concern about too much omega-6 is separate from concerns about omega-6 rancid fats, trans-fats or hydrogenated fats. These damaged, altered, omega-6 fats are not good for you. At issue here is over-consumption of omega-6, including the 'cold pressed' vegetable oils like canola, soy, safflower, sunflower or corn oils.

Even flax has a significant amount of omega-6. One tablespoon of flax seeds (not oil) contains 2,175 mg of omega-3 EFA linolenic acid and 500 mg of omega-6 EFA linoleic acid. If you are vegan or vegetarian you may consider using whole fresh organic flax seed as a source of omega-3 IF you convert. Many persons, genetically determined, convert the short omega-3 to the truly essential DHA poorly or not at all.⁽³²⁵⁾

Omega-3 Fatty Acid Food Sources

The best source of omega-3 fatty acids is cold-water fish, which is high in both EPA and DHA. You may need as little as three servings a week of very fatty fish (if you eat the skin and surrounding fat) to meet your genetic need.

Because of the possibility of mercury toxicity when consuming large amounts of fish, wild or farmed, most should consider a fish oil supplement. A standard fish oil concentrate soft gel weighing 1000 mg contains about 300 milligrams of omega-3. The suggested 'treatment' or 'replacement' dose is 300 mg of combined DHA-EPA for each 10 pounds of body weight for 3-4 weeks. Minimum suggested daily intake of combined DHA-EPA is 3,000 mg.

You may be tempted to eat foods or use supplements that contain LNA or ALA (linolenic acid- short chain omega-3) rather than EPA and DHA from fish or fish oil (particularly if you're a vegetarian). This may not satisfy your nutritional needs as many of us convert the short chain omega-3 to its long chain metabolites inefficiently. This conversion is further reduced in aging. In a number of studies even large doses of ALA (from flax or perilla) did not raise cell membrane DHA. Flaxseed, perilla oil and walnuts are common sources of LNA.

Recent studies suggest high amounts of ALA are associated with prostate cancer.^(326,327) Finding elevated levels of linolenic acid in the testes, where long-chain DHA is expected, may alter cell communication.

Vegetarians may consider using flax seeds (not the oil, not ever, rancidity is a huge issue with this oil in spite of advertising) and adding perilla oil (lower in omega-6) and buying the 'algae' DHA such as Neuromins from Solgar or Nature's Way, which contain 100 mg of DHA per each soft gel. To match the fish oil program you would need 1 or more tablespoons of perilla oil daily plus about 5-15 per day of the Neuromins providing 500-1,500 mg of DHA.

Table 8 Foods High in DHA/EPA

Food	g in 100-gram (3.5 oz.)	g in normal serving
Sardine oil	20.79	2.83 (1 tablespoon)
Cod liver oil	17.87	2.43 (1 tablespoon)
Herring oil	10.48	1.43 (1 tablespoon)
Salmon, Atlantic (farmed)***	2.15	3.89 (half fillet)
Mackerel, Pacific and jack***	1.85	3.25 (1 fillet)
Pickled herring	1.39	.42 (2 pieces)
Salmon, chinook***	1.74	2.68 (half fillet)
Salmon, pink***	1.28	1.6 (half fillet)
Mackerel, Atlantic***	1.20	1.07 (1 fillet)
Rainbow trout (farmed)***	1.15	.82 (1 fillet)
Bluefish***	.99	1.16 (1 fillet)
Sardines, canned in oil	.98	.90 (1 can, 92 g)
White tuna, canned in water	.86	.73 (3 oz., 85 g)
***cooked with dry heat		

Omega-6 Fatty Acids

Most of us get our excess omega-6 fatty acids from vegetable cooking oils, salad dressings, sauces, packaged foods, margarine, Crisco and mayonnaise. The popular evening primrose and borage supplements are also high in omega-6. As you can see from the chart below, simply changing the type of oil you use could greatly reduce your intake of LA.

Notice the difference between wild and farmed salmon as to omega-6 content. This pattern of higher omega-6 in farmed animals is repeated in wild compared to domestic game and grass-fed compared to grain-fed beef, poultry and pork. organic dairy, meat and poultry are products from animals fed organic grain so omega-3 content will not be favorably altered.

Table 9 Food Content Omega-6

Food	g in 100-gram (3.5 oz.)	g in normal serving
Sunflower oil, linoleic (60% and over)	65.70	8.94 (1 tablespoon)
Corn oil	58.00	7.89 (1 tablespoon)
Sunflower oil, linoleic (less than 60%)	39.80	5.41 (1 tablespoon)
Sunflower seeds, oil roasted	37.82	25.53 (half cup)
Sunflower oil, linoleic (hydrogenated)	35.30	4.80 (1 tablespoon)
Sunflower seeds, dry roasted	32.78	20.98 (half cup)
Canola oil	20.30	2.84 (1 tablespoon)
Peanuts	15.56	11.36 (half cup)
Safflower oil	14.35	1.95 (1 tablespoon)
Almonds, unblanched	12.21	8.67 (half cup)
Flax Seed	22.636	2.693 (1 tablespoon)
Pumpkin seeds	8.76	2.80 (half cup)
Hamburger	0.590	
Chicken Breast with skin, boneless	1.480	1.382(half breast)
Egg	1.36	0.686 (per egg)
Wild Salmon	0.562	0.866 (half filet)
Farmed Salmon	1.939	3.451 (half filet)
Butter (from grain-fed cows)	1.830	0.260 (1 tablespoon)
Cheese, cheddar white	0.577	0.164 (1 slice)
Milk, full fat	0.075	0.183 (1 cup)
Olive oil	7.90	1.07 (1 tablespoon)

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Table 10 Food Content Omega-6/Omega-3

Food Oils	Serving size	kcal	18-carbon		20- & 22-carbon	
			Short 6	Short 3	Long 6	Long 3
Oil, perilla	1 tbsp.	120	1680	8960	0	0
Oil, flaxseed	1 tbsp.	120	2240	7980	0	0
Fish oil, herring	1 tbsp.	123	156	417	39	1509
Fish oil, salmon	1 tbsp.	123	210	525	92	4657
Fish oil, sardine	1 tbsp.	123	274	592	239	3096
Fish oil, cod liver	1 tbsp.	123	127	254	127	2557
Fish oil, menhaden	1 tbsp.	123	293	575	159	3624
Butter oil, anhydrous	1 tbsp.	112	288	185	0	0
Oil, canola	1 tbsp.	124	2842	1302	0	0
Oil, mustard	1 tbsp.	124	2146	826	0	0
Oil, walnut	1 tbsp.	120	7194	1414	0	0
Oil, soybean	1 tbsp.	120	6936	925	0	0
Oil, soybean lecithin	1 tbsp.	104	5465	698	0	0
Oil, wheat germ	1 tbsp.	120	7453	938	0	0
Shortening, household, lard + vegetable oil	1 tbsp.	115	1242	141	0	0
Oil, olive	1 tbsp.	119	1067	81	0	0
Oil, soybean, (hydrogenated)	1 tbsp.	120	4746	354	0	0
Oil, sheanut	1 tbsp.	120	666	41	0	0
Mayonnaise, soybean and safflower oil	1 tbsp.	99	7176	414	0	0
Shortening, industrial, lard + vegetable oil	1 tbsp.	115	2317	128	0	0
Oil, sunflower, > 70% oleic	1 tbsp.	124	505	27	0	0
Oil, rice bran	1 tbsp.	120	4542	218	0	0
Margarine-butter blend	1 tbsp.	102	2162	103	0	0
Oil, cocoa butter	1 tbsp.	120	381	14	0	0
Oil, sunflower, linoleic, (hydrogenated)	1 tbsp.	120	4801	122	0	0
Oil, palm	1 tbsp.	120	1238	27	0	0
Oil, corn	1 tbsp.	120	7888	95	0	0
Oil, sesame	1 tbsp.	120	5617	41	0	0
Oil, sunflower, linoleic < 60%	1 tbsp.	120	5413	27	0	0
Oil, cottonseed	1 tbsp.	120	7004	27	14	0
Oil, grapeseed	1 tbsp.	120	9466	14	0	0
Oil, peanut	1 tbsp.	119	4320	0	0	0
Oil, coconut	1 tbsp.	117	245	0	0	0
Salad dressing, cottonseed, oil	1 tbsp.	88	5068	0	0	0
Oil, sunflower, linoleic >60%	1 tbsp.	120	8935	0	0	0
Oil, safflower, linoleic >70%	1 tbsp.	120	10149	0	0	0
Oil, safflower, oleic > 70%	1 tbsp.	120	1952	0	0	0
Oil, palm kernel	1 tbsp.	117	218	0	0	0

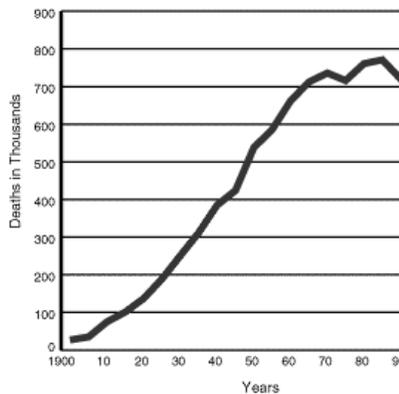
Avoid high Short 6 and get Long 3 Use Extra Virgin Olive, Butter and Coconut for cooking. You will get plenty of omega-6 without trying and if you feel you need omega-6, some is essential, simply eat nuts and seeds, raw, sprouted or lightly roasted.

Fatty Acid Table and Graph Explanations

The increase in cancer and heart disease clearly overlay the per capita increase in intake of vegetable oils, as salad dressings, margarine and shortening, all omega-6 fats. These increases in disease are not associated with natural unprocessed saturated fats.

Figure 5-8 Death from Heart Disease

Deaths From Diseases of the Heart*
United States: 1900-96



* See "Important Note" on page 1 for an explanation of "diseases of the heart." Total CVD data are not available for much of the time period covered by this chart.

Source: CDC/NCHS and the American Heart Association.

Figure 5-7 Per Capita Fat Consumption

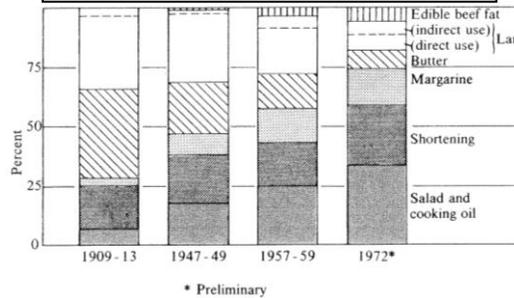


Figure 5-3: Sources of dietary fats and oils from 1909-1913 to 1972. From *Fat Content and Composition of Animal Products* (Washington, D.C.: National Research Council, 1976).

quality between wild game, surviving on grasses with small amounts of naturally occurring omega-3 fats and domesticated animals, which are fed high fat omega-6 containing grains.

In a page in the back of the binder, tables DI-D4 show the fat content of animals and other foods. You can clearly see the big difference in the fat quantity and

Table D-7 shows the varying types of fats that are found in seeds and their oils. Figure 41 shows types of fatty acids and food sources.

The human body requires fats for structural components, hormones, and for energy. Ideally, the largest part of daily fats will come from natural fats in the whole foods you eat. Omega-3 fats will be found in fish, omega-3 fortified eggs, and wild game or if you do not eat fish or wild game, fish oil supplements.

Flax provides omega-3 alpha-linolenic acid but conversion to the essential fats EPA and DHA is difficult with less than 1 in 5 Americans being able to produce adequate amounts.^(328,329) If using flax use seeds, not the oil. Fresh is best (and cheapest). Flax contains lectins and may not be suitable for everyone.

In countries using highly polyunsaturated oils traditionally, such as sesame in China, and sunflower in Russia, hand presses were used for pressing out the oil. These oils were not stored. They were purchased, pressed and used when needed, fresh.

High intakes of the omega-6 polyunsaturated seed oils are implicated in the development of all of the current degenerative diseases.

(289,330,331,332,333,334,335,336,337,338,339,340,341) It is the omega-6 fatty acids that sustain 'free radical' damage, which then creates the need to use anti-oxidants. Better to avoid the omega-6 fats, a problem in themselves when consumed in high quantity, as well as often rancid or containing trans fatty acids, than try to nullify their negative effects with

supplements that may or may not do the job. Omega-6 fats begin oxidation the minute the seed casing is broken and become rancid during manufacturing and storage, continuing to deteriorate in quality after you bring them home. Do not use these oils. Eat the nut or seed for your very small daily omega-6 requirement.

N-3 and n-6 fatty acids are VERY FRAGILE and are damaged by heat, light and air (oxygen). Processing of any kind easily damages them. For essential fatty acids eat fish, wild game, eggs from free-range chickens, and lightly roasted or sprouted nuts and seeds.

Nuts and seeds contain 'anti-digestive' enzymes and are more easily digested when cooked (flax in your oatmeal), lightly roasted or sprouted destroying these anti-enzymes without destroying the healthy nutrients.

Our natural source of omega-3 fats came from fish and shellfish and grass-fed or range fed animals. When beef are farm reared they are fed CORN or SOY, high in omega-6 fats, which alters the fat profile of the animal. When possible avoid these products. Look for sources of grass-fed beef, lamb, and chicken. Grass-fed beef and dairy, higher in omega-3 also contain CLA, conjugated linoleic acid, an important anti-cancer, anti-osteoporotic and anti-obesity fat.^(342,343,344,345,346)

Omega-3 fats from food benefit the brain and nervous system, primary targets of their action. If your ethnic heritage is from a coastal or island people your need for omega-3 fats is even more critical to health and higher amounts need to be consumed daily. Omega-3 fats are anti-inflammatory, anti-depressive and anti-cancer in their properties. If wild fish, sardines in fish oil, herring, mackerel or shellfish cannot be consumed regularly supplement with omega-3 fish oil.

Now Foods Super EPA, Costco Kirkland Fish Oil or the Trader Joe's omega-3 are good sources and reasonably priced. The minimum daily dose is about 6 soft gels. For some brands as many as 12 soft gels daily will be needed to alter fatty acid ratios in the body.

Omega-6 polyunsaturated essential fatty acids should be consumed in small quantities by eating the foods that contain them. All polyunsaturated oils lose much of their beneficial properties and gain negative properties such as rancidity when processed. This includes so called EFA supplements. Do not use them. EAT FOOD

PLEASE UNDERSTAND ALL VEGETABLE/SEED OILS ARE PROCESSED FOODS.

Fats are critically important in the maintenance of the strength and vitality of every cell membrane in your body. Nerve cells are 80% fat. As components of cell membranes they are important as regulators of neural transmission. That means fats profoundly affect your mood and energy. Cholesterol, also fat derived, is the basic element used to make all the steroid hormones and sex hormones in your body as well as vitamin D for healthy bones and teeth, fertility and longevity. 50% of the fat content of your brain is composed of cholesterol.

To get your daily allowance of omega-3 essential fatty acids (small amount, less than 5% of fats), eat a serving of fatty fish 3-4 days a week, making sure to consume the fat under the skin, at the fins and tail. It's the fat you're after not the flesh.

For omega-6 essential fatty acids regularly add small servings of lightly roasted or sprouted seeds or nuts to your daily diet.

For high heat cooking or baking use ghee or clarified butter or lard or natural coconut oil. Saturated fatty acids have a long history of safe use. Recently, saturated fatty acids have fallen into undeserved disrepute. These fats are natural, stable to heat and light and protect the cell membrane from free radical damage, including sun damage.

Coconut milk is an excellent source of medium chain fatty acids and potassium but should not be exposed to high heat.

To Summarize Fats

Consume naturally occurring fats found in the lean meat, fish, eggs or other protein source. Go ahead, eat the skin.

If you have an island or coastal heritage make fish, with skin and fat, and seafood your main protein/fat source but consider mercury toxicity. Poultry plus regular fish oil supplements may be a better modern choice.

Use butter (or ghee if dairy intolerant), natural unprocessed lard, natural palm oil, and/or coconut oil for cooking and baking.

Use extra virgin olive oil, cold pressed peanut oil or avocado oil for sauté or salad dressings.

Make your own mayonnaise from olive oil or other high oleic (omega-9) oil. Saffola is a national brand of mayonnaise from high oleic (n-9) safflower oil.

Get high quality omega-3 fats from wild caught fish, eggs and wild game

Buy grass-fed beef, lamb, pork and chickens whenever possible, 'grass-fed' is more important than 'organic'. Grass fed is leaner and contains natural omega-3 fatty acids.

Do not use processed (including cold processed) oils containing primarily omega-6 fats for any purpose. You won't be able to avoid them completely, eating out, visiting friends, so avoiding them at home helps you beat the odds.

Don't buy any foods for yourself or your pets that contain added omega-3.

Omega-3 fatty acids are quite fragile and are safe only when 'fresh'. Fish oil in soft gels will be fresher than fish oil in a liquid, less exposure to oxygen. Once you open the bottle of fish oil keep it in the refrigerator or freezer and use it up within a reasonable time. Like fish, fish oil won't keep. Manufacturers adding omega-3 to foods are just making food prematurely rancid which is NOT good. Do not use omega-3 eggs. They won't be fresh enough to assure non-oxidized fatty acids.

It has recently become popular to tell people they eat too much fat and protein without actually discovering if the person's genetics can deal with such a reduction. I have seen severe damage to the immune systems and structural proteins of persons who have

become unwise eaters, giving up too much protein or high quality fat for their genetic need and/or life style. Listen to your body and honor your ancestry.

Good fats are essential to health. As of July 2002 the American Heart Association reversed their position on low fat diets, now recommending fat as 30-40% of calories. They were forced into this position because low fat eating dramatically increased the intake of refined carbohydrates and has led to the incidence of diabetes more than doubling in the adult population between 1970 and 2002.

Real food has fat. Eat real food. Dairy has fat, there is no low fat milk or cheese in nature. Eggs and meat and fish have fat. Eat the fat that comes with the food unless it is artificially created fat as in grain fed beef. In that case avoid the excess fat by trimming or your choice of cut. Try to find pasture fed pork and chickens and grass fed beef. The Wise Traditions Journal available from <http://www.westonaprice.org> lists many sources.

Diets that lower glucose and fasting insulin are typically HIGH fat, moderate protein and low carbohydrate. They are healthy and they work.

Checklist and Notes:

- Do I allow myself normal amounts of naturally occurring fats (fats that naturally are present in food)?
- Have I cleared my cupboards and refrigerator of all products containing hydrogenated and partially-hydrogenated fats and all fake fats?
- Do I regularly consume raw walnuts or lightly roasted nuts and seeds in moderate amounts?
- Is dark, richly flavored, extra virgin olive oil in daily use in my kitchen?
- Fish store mercury in their bones and flesh. High intake of fish may lead to mercury toxicity but consuming fatty fish tails or fish with the skin and fat will increase my omega-3 without excess mercury. If I find it difficult to consume fish fat regularly do I use fish oil liquid or capsules a minimum of three times a week?

CHAPTER 6 MINERALS, STRUCTURAL AND FUNCTIONAL

Minerals should never be considered individually. The purpose of this chapter is to show some of the important things different minerals do we need a bit of all of them, calcium, magnesium, potassium, and all the trace elements, 72 of them.

MAGNESIUM- THE RELAXER

Magnesium is a critical element in 325+ biochemical reactions in the human body. It is found in bone broths, some waters, very dark green leafy vegetables and 'greens', nuts and seeds.

Research in France and several other European countries give a clue the role of magnesium in the transmission of hormones (such as insulin, thyroid, estrogen, testosterone, DHEA, etc.), neurotransmitters (such as dopamine, catecholamines, serotonin, melatonin, etc.), and minerals and mineral electrolytes.

This research concludes that it is magnesium, along with calcium and other electrolytes, that controls cell membrane potential (the electrical charge of the cell) and through this means controls uptake and release of all cell substances. Magnesium plays a primary role in regulation of cellular and extracellular potassium and calcium.

If magnesium is insufficient potassium and calcium may be lost in the urine or calcium may be deposited in the soft tissues (kidneys, arteries, joints, brain).

Magnesium and calcium protect the cell from aluminum, mercury, lead, cadmium, beryllium and nickel. Evidence is mounting that low levels of magnesium contribute to the heavy metal deposition in the brain that precedes Parkinson's, multiple sclerosis and Alzheimer's. It is probable that low magnesium contributes to heavy metal toxicity in children and is a participant in the etiology of learning disorders.

Magnesium is also important for lifelong hearing.

Cevette, M. J., Vormann, J., and Franz, K. 2003 J.Am.Acad.Audiol. 14 202-212

Magnesium and hearing

The last several decades have revealed clinical and experimental data regarding the importance of magnesium (Mg) in hearing. Increased susceptibility to noise damage, ototoxicity, and auditory hyperexcitability are linked to states of Mg deficiency. Evidence for

these processes has come slowly and direct effects have remained elusive because plasma Mg levels do not always correlate with its deficiency. Despite the major progress in the understanding of cochlear mechanical and auditory nerve function, the neurochemical and pharmacologic role of Mg is not clear. The putative mechanism suggests that Mg deficiency may contribute to a metabolic cellular cascade of events. Mg deficiency leads to an increased permeability of the calcium channel in the hair cells with a consequent over influx of calcium, an increased release of glutamate via exocytosis, and over stimulation of NMDA receptors on the auditory nerve. This paper provides a current overview of relevant Mg metabolism and deficiency and its influence on hearing

Formula To Calculate Magnesium Daily Requirement

For children the requirements are higher per kilo, not lower. They must be considered on an individual basis.

Standard Calculations: Using ideal body weight take a minimum of 3 mg. per pound per day of magnesium. .

If one or more of the symptoms or conditions listed below use 4-5 mg. per day per pound.

Table 11 You may need more magnesium-

Athlete in training
You take diuretics (any kind except magnesium sparing, make sure to check)
Diabetes, type 1 or 2
You have hypertension
You suffer from PMS
You suffer from chronic constipation with no obvious cause
You suffer from muscle stiffness or soreness without apparent cause
You are under large amounts of stress
You are dieting with or without medication
You consume large amounts of refined carbohydrates
The weather is very hot and/or you perspire profusely

EXAMPLE:

130 lb. Female, PMS, migraine headaches, and insomnia, muscle tension or soreness.

130 times 4 mg. equals total intake not less than 520 mg.

In a recent study analyzing the diet of 564 adult Americans, both male and female, the average intake of magnesium was less than two-thirds of the RDA for men and less than 50% of the RDA for women. This means that men are getting under 200 mg. and women under 150 mg. per day. When you take into consideration the current RDA may be less than half of the probable adequate amount of magnesium you begin to see the scope of the problem.

CALCIUM, MAGNESIUM AND VITAMIN D- METABOLIC FACTORS

While magnesium has been ignored as an element of importance, calcium has been considered of consequence primarily for women as a solitary nutrient to prevent bone loss. This is a grave underestimation of the importance of this alkaline earth metal. Calcium probably influences more body processes than any other mineral substance. Calcium composes 1.6% of the body composition (magnesium is 0.05%).

Calcium in its active form, ionized calcium, controls cell membrane potential, blood alkalinity and thereby stress response, allergic response and cell signaling. While these technical terms may not mean much to you, in your body calcium is a major controlling element of how you feel, your appetite, energy, strength, mood and more.

Ionized calcium, the active element, is the important determinant of the above-mentioned roles of calcium. Calcium ionization is regulated by Vitamin D. Please review the role and need for vitamin D before reading on.

Magnesium, calcium and D are keys to production of cellular energy. Many of the conditions that follow also respond to a reduction in omega-6 fats and an increase in omega-3 fats. Think of your overall program not singling out certain nutrients.

Table 12 Low Calcium, Vitamin D or Magnesium Related Conditions

ADD/ADHD	Allergies
ALS	Alzheimer's disease
Angina	Anxiety, panic disorders
Arrhythmia	Arthritis- rheumatoid and osteoarthritis
Asthma	Autism
Cavities	Cerebral Palsy
Chronic Fatigue Syndrome-	Congestive Heart Disease
Constipation	Crooked teeth, narrow jaw-
Dementia- all types	Depression
Diabetes Type I and II-	Eating disorders-
Fibromyalgia	Gut disorders- including peptic ulcer, Crohn's disease, colitis, food allergy
Heart Disease	High Blood Pressure
Hypoglycemia	Impaired Athletic Performance
Infantile Seizure	Insomnia
Kidney Stones	Migraines- cluster type especially
Mitral Valve Prolapse	Multiple sclerosis
Muscle cramps	Muscle weakness, fatigue- ATP production
Myopia	Obesity
Osteoporosis	Parkinson's disease
Premenstrual Syndrome	Primary Pulmonary Hypertension
Raynaud's Syndrome	SIDS- Sudden Infant Death Syndrome
Syndrome X, metabolic disorder	Thyroid disorders

Table 13 Substances/Conditions That Reduce Total Body Magnesium/Calcium

Alcohol-significant urinary losses	Amphetamines/cocaine/'uppers'
Burns- with large surface area	Refined carbohydrates
Chronic pain- any cause	Coffee- significant losses
Diabetes- magnesium spills with sugar in the urine, low D and calcium	Dieting- stress plus lowered intake
Diuretics-unless magnesium sparing	Extreme athletic conditioning/training
Injury- any physical trauma	Sodas- especially cola type sodas
Sodium- high salt intake	Stress- physical and mental
Surgery	Sweating profusely, night sweats, hot flashes

Table 14 Magnesium, Vitamin D or Calcium Deficiency Signs/Symptoms

Apathy, depression	Confusion and disorientation
Chronic Fatigue	Convulsions, epilepsy
Constipation (common) or diarrhea (rarely)	Eyes flick uncontrollably
Difficulty in swallowing	Heart rhythm problems
Fibromyalgia	Hypoglycemia, carbohydrate cravings
Hyperactivity	Chocolate cravings
Insomnia	Learning disability and memory impairment
Loss or increase of appetite	Muscle cramps, grimaces, jerks, tremors
Muscular in-coordination, weakness	Nausea
Numbness and tingling in extremities	Premenstrual symptoms
Tremor and jerks of the tongue	Vertigo
Weakness and tiredness	Hypertension

An added note regarding the above chart- many of those symptoms also occur when a condition called Hyperinsulinemia is present. (see chapter page 156)

To compensate for deficiencies and/or losses the new recommended DRI for magnesium is 450 mg. per day. Calcium DRI is from 800 mg – 1,300 mg. if bone loss has already occurred you may need 1,250-1,300 mg a day. If vitamin D levels are optimal, less calcium will be needed.

D₃ RDA values are 200 IU – 800 IU. However, ideal values must currently be based on blood testing for levels of 25(OH)D. Typically supplements of 800-2,000 IU are needed especially in winter months or if you avoid sunlight or use sunscreens.

Vitamin D- Test. Determination of optimal amounts must take into consideration body size and activity level and in the case of D, sunlight exposure and location (latitude and altitude). **We have been unable to determine the need for D without testing and follow-up.** Vitamin D alters the need for and use of both magnesium and calcium.

D, Magnesium, and Calcium - What and When

Vitamin D Guidelines

Have your physician test your 25(OH)D (25-hydroxyvitamin D) to determine how much D you need. Retest 6-8 weeks later to make sure you are getting the right amount, not too much or too little. Continue to retest until you get it right. After the initial adjustments, testing should be done every six months for the first 2 years and once a year thereafter. **Self-testing links may be found at <http://sunlightd.org>**

The vitamin D test: serum 25(OH)D also called 25-hydroxyvitamin D Test results may be given in ng/ml (nanograms per milliliter) or nmol/l (nanomoles per liter)

Ideal values: 40-60 ng/ml or 100-150 nmol/l

Acceptable values: 32-70 ng/ml or 75-175 nmol/l

Below 32 ng/ml or above 70 ng/ml there must be concern for clinical problems of deficiency or excess including bone loss and soft tissue calcification. For most problems will not occur unless values exceed 90 ng/ml for some period of time, a few may experience side effect between 70-90 ng/ml. Higher is not better.

Recently (May, 2013) researchers suggest optimal levels are 20-36 ng/ml. In their review persons with vitamin D levels above and below had a higher risk of mortality than those within this range. Nainggolan L. Safe upper limit of vitamin D identified for first time. *Medscape Medical News* [serial online]. May 1, 2013; Accessed May 8, 2013. Available at <http://www.medscape.com/viewarticle/803417>.

There are significant reasons why this range may be too narrow and may be complicated by confounding issues such as low vitamin A and/or low vitamin K. There is every reason to believe the 40-60 ng/ml is safe and adequate, especially when D is gotten from sunlight and not OVER supplementation..

If testing reveals you need more D make sure to retest after 8-12 weeks of supplementation or sun. Optimal levels of vitamin D are produced and maintained more easily by whole body sunning in the summer months. Supplementation may be necessary in the winter and in locations lacking UV-B sunlight.

Vitamin D sources are limited to sun exposure and supplements. Food provides little D unless it is added artificially. The only natural food source of vitamin D is cold water fatty fish and you need to eat the fat to get the D. Fish oil is processed molecular distillation and any vitamin D is removed. Vitamin D is not stored in the liver and fish liver oil contains little vitamin D, but significant amounts of vitamin A.

If you need more D:

Sun exposure guidelines are in the back pages, Exposure Guidelines. Typically, do not combine sun and supplements. Pick one or the other and begin testing for efficacy, does/did it work, keeping your D between 40-60 ng/ml summer and winter?

If you have tested to have an excess of vitamin A or are a vegetarian, dry vitamin D3 (often mixed with olive oil or other oil but still made from an extraction of lanosterol that has been irradiated with UV-B) is available. Do not use dry D3 or ergocalciferol, D2. Use oil based D3, cholecalciferol, when possible. The dry D, even when it is D3 seems to not absorb well and has not been as successful in normalizing 25(OH)D. If supplementing, take your vitamin D once a day either with fish oil or with the meal containing the largest amount of fat. Vitamin D, whatever the source, is fat soluble and to be absorbed requires bile. You do not need to split your dose.

Moderate supplementation over time is the best way to raise vitamin D. If you do that and your vitamin D levels do not reach optimal get the Fasting Insulin test. Problems will occur if your test result is above 8. Elevated insulin lowers magnesium AND vitamin D. Call to confer regarding elevated insulin levels.

Do not use 'water soluble' or 'emulsified' vitamin D as it has the greatest potential for vitamin D toxicity. Excess D harms and in high enough doses can kill. I realize many practitioners suggest the use of this product but if your child drank the bottle it would be fatal. One bottle of Bio-D-Mulsion contains 300,000 IU of highly absorbable D; one bottle of Bio-D-Mulsion Forte contains 1.5 million units of vitamin D which would be fatal to adults. Don't buy it or use it.

Magnesium and Calcium Guidelines:

If you need to add magnesium you may not want to take it after 5 PM. It can be energizing for some, not everyone, and may have a negative impact on getting to sleep and staying asleep when taken too late. The correct dose, taken early in the day, often helps to correct insomnia.

PLEASE NOTE: These supplement suggestions are totals. When counting up your numbers make sure to include your daily multiple vitamin and multiple mineral supplements and food sources high in magnesium such as blackstrap molasses or calcium from dairy products.

Basic Guidelines

1. Use the formula to work out your daily supplement goal for magnesium and add calcium in a ratio of 2:1 (2 parts calcium:1 part magnesium to) to as much as 1:1, equal calcium and magnesium.
2. When using calcium/magnesium supplements remember to split the dose. Minerals are absorbed more efficiently in smaller, more frequent, doses. For most, simply splitting in to two daily doses is fine.
3. Mineral sources include your multiple, a calcium and magnesium combination, a multi-mineral or regularly consumed dairy or homemade bone stock.
4. If extra magnesium is needed add Albion's chelated magnesium which is found in Douglas Labs AminoMag 200 or Carlson Labs Chelated Magnesium .Albion's chelate is much less likely to cause diarrhea, always a possibility with increased magnesium.
5. Simple calcium magnesium combinations may be taken in the evening or before bed but if your sleep is disturbed move supplements with magnesium to earlier in the day.
6. Get a minimum daily supplement level of 400-500 mg. magnesium from all sources. If magnesium seems to cause loose stool or diarrhea reduce your dose or stop completely and check with your health care practitioner.
7. If your bowel changes significantly, diarrhea common with some types of magnesium or constipation common when supplementing calcium, try a different type or brand or modify your dose.

You must decide what level of D, calcium and magnesium work for you. Listen to your body.

Table 15 Calcium Absorption, Typical Calcium Carbonate Supplement

500 mg. calcium in one dose	29% absorption (145 mg)
500 mg. calcium in two doses of 250 mg	36% absorption (180 mg)
500 mg. calcium in 3 doses of 165 mg	40% absorption (200 mg)
2,000 mg- one dose	14% absorption (280 mg)

Heaney, RP et.al. J of Bone and Mineral Research, 5:11; 1990 p.1135-1137

Be patient. Many systems (muscles, bone, immune system, and nervous system) will begin to change when you get adequate amounts of calcium, D and magnesium. Depending on your current condition it may take from several months to a year for you to see all of the positive changes.

When dealing with chronic pain and degenerative disease it may take 3-4 months for the calcium, D and magnesium and collagen to begin to regenerate damaged tissue. Taking a minimum of 2,000 mg ascorbic acid or 1,000 mg Liposomal Vitamin C twice a day in addition to the D and minerals is essential for bone and joint repair.

Using home-made bone stock daily or even twice a day can reduce healing time dramatically.

SPECIAL NOTE: Magnesium and calcium supplements and multi-minerals containing magnesium should not be taken when you have an infection, viral or bacterial. Virus and bacteria thrive on magnesium. Magnesium/calcium supplements should not be taken concurrently with any type of anti-biotic or sulfa drug. Many antibiotics work by chelating magnesium or calcium in the cells of invading bacteria and thereby causing cell death. The added magnesium or calcium may prevent the medication from working.

Magnesium Supplementation

The medical community repletes magnesium by giving 400 mg. of oxide, sulfate or gluconate 4--6 times a day. At this level diarrhea may become a serious problem. A loose stool depletes magnesium and other electrolytes quickly.

Albion Lab chelated magnesium sold by Solgar, Douglas Labs and Carlson Lab, is a well-absorbed source of magnesium that rarely alters the bowel. These products are Solgar Chelated Magnesium, Amino-Mag 200, and Carlson Chelated Magnesium. This form of magnesium is tightly bound to a protein and is carried across the gut wall as a protein, not as a mineral. Albion chelated magnesium is safe for children and adults.

Under certain conditions magnesium supplements may precipitate diarrhea. Please discontinue magnesium or any supplement (multiple) containing magnesium temporarily if your stool becomes soft or unformed.

Certain gut pathogens, that is pathogenic bacteria, certain parasites and/or candida, may flourish when given free access to ionized or chelated magnesium. Regular ionized magnesium frequently causes a loose stool or diarrhea. Albion chelates (glycinates) usually do not cause gut distress unless gut pathogens are present.

COMPLICATIONS- If you are only using the Albion chelated magnesium and you experience gas, bloating, diarrhea, alternating diarrhea and constipation or other unusual symptoms it is likely you have at some time in the past contracted a gut pathogen.

Refer to the Immune Restoration section. If that does not correct the problem you will need to request the Genova Diagnostics CDSA 2.0. When the results are returned using one of several lab defined programs to treat whatever pathogens or conditions are present will correct the problem. Albion magnesium may be taken at the end of the treatment program.

Continuing magnesium without treating a gut problem will not result in magnesium repletion. You will get worse, not better. This combination of magnesium deficit with gut pathogens is a common finding in many cases of chronic fatigue and fibromyalgia.

Try to keep all doses at not more than 100-200 mg. each. Experiment. Some clients cannot take magnesium in the evening. I have had reports of 'too much energy too late in the day' and disturbed sleep. Others sleep more deeply with magnesium and calcium before bed.

Is it worth the hassle? I am sorry if this seems difficult. Finding out what we need is hard in these times, lacking traditional sources for our food needs. Expending the time and energy to discover what works, for you and for your family members, is worth it.

WARNING: Restoring adequate total body ionized calcium (calcium + D), magnesium, or omega-3 fats may alter your need for supplemental l-tryptophan, melatonin, 5-HTP, St. John's Wort, anti-depressants, sleep medications, cholesterol lowering drugs, thyroid medications, insulin, diabetic drugs, anti-hypertensives, diuretics and other medications. If you are taking any of these substances please make sure to check with your physician as you will need to monitor and reduce or eliminate these medications if and when conditions warrant.

WESTERN DIET DEFICIENCY DISEASE

The Western Diet has been defined as a diet high in processed fats, omega-6 fats, hydrogenated fats and sugar and/or high fructose corn syrup, deficient in essential minerals, omega-3 fats and fat soluble vitamins. The first to identify, photograph, and write about these changes was Weston A. Price in Nutrition and Physical Degeneration, 1939. Price called this the 'modern diet'. Researchers refer to this as the Western Diet or SAD (Standard American Diet) and it has been shown to predispose to all degenerative diseases from cavities to osteoporosis to heart disease, diabetes and cancer. The key alterations in this diet are elevated levels of hydrogenated omega-6 fats and reduced levels of vitamins A, D and E and reduced minerals; magnesium, potassium and calcium as well as fewer micro-minerals and trace minerals.

Magnesium and trace minerals have been consistently depleted in our soils. Nutrients have further been depleted in plants by the use of potassium and phosphorus laden fertilizers which alter the plants ability to uptake magnesium and other trace elements. Historically water from deep wells supplied further levels of magnesium and calcium not found in food. Surface water, our common source of supply, is often low in magnesium and other minerals. Food processing removes minerals. Broiling, steaming and boiling remove minerals. High carbohydrate and high fat diets increase the need for all minerals, especially potassium, calcium and magnesium.

An example of the dramatic changes follows in the table comparing panela (traditional, unrefined, non-centrifugal whole sugar also sold as jaggery, muscovado dark, gur, chancaca, black sugar, panocha or piloncillo) to brown and white sugar. Panela can be found in small 'cones' at Mexican markets.

Table 16 Comparison of panela, brown sugar and white sugar

	100g of White and granulated sugar	100g of Brown Sugar	100g of Whole Sugar (panela)
Mineral salts	30 - 50 mg	330 - 740 mg	2850 mg
Phosphorus (P)	0.25 mg	3.0 - 3.9 mg	116 mg
Calcium (C)	14.0 mg	74 - 85 mg	118 mg
Magnesium (Mg)	0 mg	13 - 23 mg	136 mg
Potassium (K)	4.6 mg	40 - 100 mg	1056 mg
Iron (Fe)	0.1 mg	0.6 - 1.3 mg	3 mg

The large differences in mineral content of a commonly used substance such as sugar has the potential to alter our health in profound ways. The metabolism of carbohydrates requires potassium. If the potassium found in sugar (or whole grain) is removed, body stores will be depleted. In its natural state sugar is very healthy. See Sugar in the 'other contributors' section in the back.

Blood tests for mineral deficiencies are irrelevant and unusable. Serum levels of nutrients do not reflect total body magnesium (TBM), calcium in bone or trace elements

in cells. Magnesium levels of bone and intracellular levels of magnesium are what tell the true status of TBM. This is also true of other minerals including potassium.

Mineral health relates to many factors NOT just amount consumed. Once a mineral is in the blood stream it must be shunted to its 'place'. High or low serum (blood) levels of potassium or calcium or any other mineral are a marker for serious disease. However, serum levels of minerals can be normal and yet your cells, be they in the bone, muscle, artery or brain, may lack essential or be overwhelmed by minerals. Osteoporosis is common in persons with arterial calcification.⁽³⁴⁷⁾

Beef Bone Stock - building/maintaining bones and joints.

(for humans and their canine friends, this page is designed to be removed and copied)

There is one age-old remedy for keeping minerals in abundance and in balance in the human body, bone stock. Following is a recipe for our modern age still without match from any supplement available and worth the effort to make regularly and consume daily. When properly prepared it contains high amounts of calcium, magnesium, potassium, trace elements, whole collagen protein, and fat soluble vitamins including carotenes, A, D, K, and E.

Bone stock contains calcium, magnesium, trace minerals, fatty acids, essential fats, collagen protein, and other essential elements as well as 444 mg of potassium per cup (for beef stock before adding veggies). When properly prepared, allowed to simmer for 72 hours or longer, the available calcium, magnesium and trace minerals greatly increase. Poultry stock has the least amount of potassium and other nutrients, fish stock slightly greater and beef stock the highest values. Recipe yields 8 cups (2 qt.) of stock and is for a 6-quart pot. Adjust recipe to fit your pot. I prefer making this stock with ROASTED meat/bones. I find it enhances the flavor but make sure to add all drippings from roasting to the pot.

INGREDIENTS:

- 2 pounds beef soup bones (knuckle, feet, joint) important for collagen content (the gel)
- 2 pounds meaty bones (neck bones with meat or ribs with meat, other meaty bones, oxtails, or a mix)
- 2 pounds center cut marrow bones
- 1 large onion
- 3 large carrots
- 2-4 stalks celery, including some leaves
- 8 whole black peppercorns
- 1 bunch fresh parsley (optional)
- 1 bay leaf (optional)
- (optional) 1 tablespoon sea salt or potassium salt
- (optional) 2 teaspoons dried thyme or other herbs you like, such as tarragon
- (optional) 2 cloves garlic
- 12 cups water, approx.- enough to cover but leave one-inch clearance at top of pot
- (optional) use more vegetables to increase the potassium content of the stock

DIRECTIONS:

1. Preheat oven to 450 degrees F (230 degrees C). Slice onion. Chop scrubbed celery and carrots into 1-inch chunks. In a large shallow roasting pan place bones, onion, celery, and carrots. Bake, uncovered, about 30 minutes or until the bones are well browned, turning occasionally. You can buy larger quantities of bones, freeze the extras and take them directly from freezer to browning, about 80 minutes at 425-450 °. If using frozen bones add vegetables 30 minutes before the end. You may need a small amount of water in the roast pan.

Longer roasting at lower temperature may increase flavor so consider 'slow' roasting'. Set your oven to the 'done' temperature and cook for 18-24 hours, adding vegetables the last two hours.

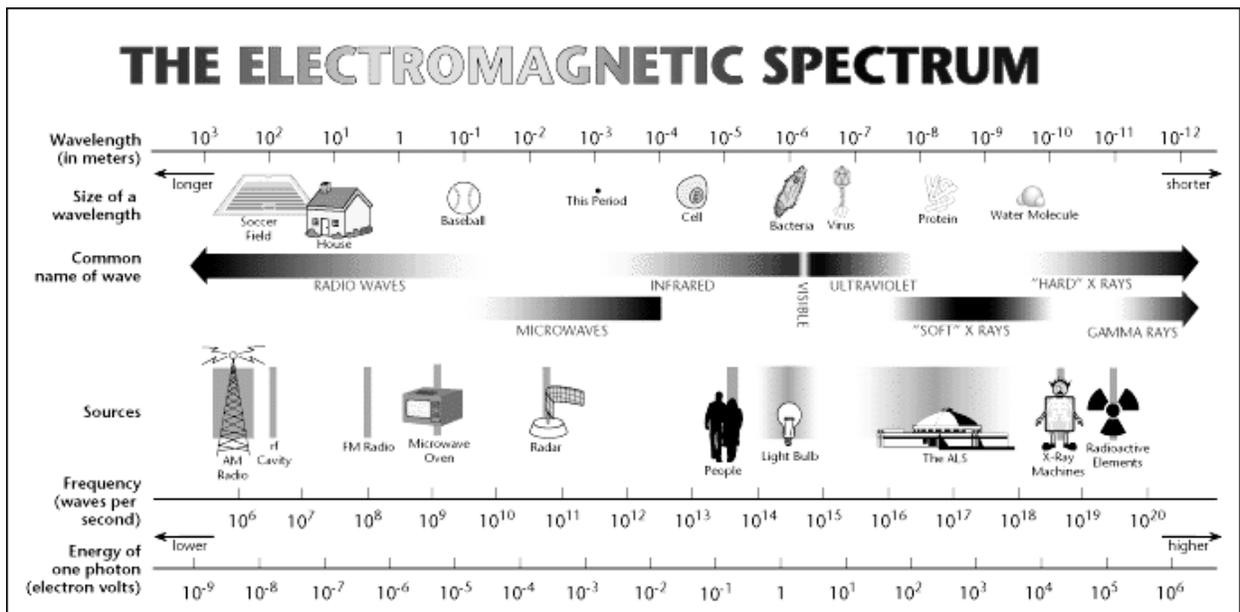
2. Pour off excess fat (not drippings). Place the browned bones, onion, and carrots in a large soup pot.
3. Pour 1/2 cup water into the roasting pan to loosen any drippings. Pour this liquid into the soup pot.
4. Add celery, peppercorns, parsley, bay leaf, salt, thyme, and garlic.
5. Add the 12 cups water, enough to cover but not higher than within one inch of top of pot.
6. Add ¼ cup vinegar, any you like.
7. Bring mixture to a boil. Reduce heat. Cover and simmer for 72 hours adding more vinegar, ¼ cup, once or twice on day one and day two to increase dissolution of bone. **Add water as needed so that you end up with not less than 10 cups of stock.** Take care not to burn when leaving on overnight. Very low heat is fine but think 'simmer' not 'warming'. *You may be able to use a slow cooker/crock pot for this step.*

- 8.** Strain stock. Discard (or give to your favorite pooch with some stock) meat, vegetables , and seasonings. For clear stock/broth use a mesh strainer or strain through cheesecloth.
- 9.** Cool and remove any fat which solidifies on the top; just the fat, leave the gel. If you keep your pot going all the time get and use a FoxRun Fat Mop, about \$8.00 at cooking supply stores such as Sur La Table. You can use it to remove fat without cooling the stock.
- 10. Divide into containers and freeze or keep the stockpot going continuously by ladling out stock as needed for broth, gravies, sauces, soups and stews and adding new veggies, bones and seasonings as needed.**
11. Other options that may be added to the soup pot and discarded before serving:
- 1 large tomato or some great chefs 'paint' bones with tomato paste near end of roasting
 - 1/2 cup chopped parsnip
 - 1/2 cup cubed potatoes with skin (or more or add just the potato peelings which greatly increase the potassium content of stock)

Other recipes, for fish stock, venison stock and chicken stock, are available in the Nourishing Traditions cookbook, authors Sally Fallon and Mary Enig, or online.

Checklist and Notes:

- Did I count my magnesium need? Do I get enough from the foods I eat? Is there an easy choice to add magnesium to my daily diet, nuts, dark greens, green drink (from whole fresh leaves not a powdered supplement), blackstrap molasses, legumes?
- What was my vitamin D that is my 25(OH)D test? _____ What should it be? _____ When should I test again? _____ Put this date in your tickler list.
- Do I regularly consume high calcium foods and if not supplement with calcium (multi-mineral preferred)?
- What are my sources for minerals and trace minerals? Dulse? Homemade bone stock? Homemade vegetable soups? Dairy products? Juicing using whole fruits and vegetables ?
- Do I make sure my children get adequate minerals and D or sunlight for quality bone and teeth development?
- When choosing a supplement do I make sure my mineral has calcium, magnesium, other essential minerals such as iron and zinc as well as trace minerals for healthy bone support?



CHAPTER 7 SUNLIGHT AND HEALTH

NOTE: Persons with active kidney disease or liver disease may need vitamin D and calcium and/or magnesium but they should not supplement without being monitored by a physician. This information is for persons with normal kidney and liver function only; that is, those free from medically diagnosed liver or kidney disease.

According to a paper published in the May, 1999 issue of the American Journal of Clinical Nutrition by Reinhold Vieth our current recommendation for vitamin D is woefully understated. 200-400 IU will prevent rickets in children but does not come close to optimum D sufficiency.

While more research is needed the minimal daily requirement of D will more likely be 800-1,000 IU instead of the 200-400 IU currently suggested. Much of the US does not have sufficient sunlight (UV-B) to provide adequate D during the winter months. Some locations have insufficient UV-B to provide optimal D in summer months.

Supplementation is critical when UV-B is not available.

Modern food and lifestyle choices are very poor sources of D. Our ancestors got D from sunlight, eggs from chickens naturally exposed to UV-B, fatty fish, meat, and organ meats, including intestinal linings, a rich source of D. The main D sources today are fortified milk, butter and cream from grass-fed summer milk, eggs from sunny chickens, and the fat of deep-sea cold-water fatty fish.

Ultraviolet Light

Ultraviolet (UV) light is divided into 3 bands or wavelength ranges, which are referred to as UV-A, UV-B and UV-C.

UV-A, known as the “tanning ray”, is primarily responsible for darkening the pigment in our skin. UV-A is less energetic than UV-B, so exposure to UV-A will not result in a burn, unless the skin is photo-sensitive or excessive dosages are used. UV-A penetrates more deeply into the skin than UV-B due to its longer wavelength. Most tanning bulbs have a high UV-A output, with a small percentage of UV-B. UV-A is not blocked by many sunscreens and is considered by some researchers to be a primary cause of non-melanoma skin cancers.^(348,349,350,351,352)

UV-B, sometimes called the “burning ray” is the primary cause of sunburn (erythema) when we are overexposed to sunlight. However, UV-B also initiates beneficial responses, such as stimulating the production of Vitamin D, which is necessary for numerous biological functions, and which (vitamin D) helps to repair damaged skin cells.^(353,354,355,356)

UV-B also stimulates special skin cells called melanocytes to produce melanin, which becomes additional protective pigmentation and increases the sun protection factor (SPF) in our skin. UV-B does not penetrate very deeply into the skin. The darker or more tanned the skin, the less UV-B penetrates.

The D Connection

- UV-B sunlight produces vitamin D on the skin. The amount produced depends on latitude and altitude of location, amount of skin exposed and season.
- Sunlight and vitamin D are critical to health in all cultures. Higher latitudes need D from sun and supplements. Our ancestors got extra D from fish and organ meats and consumption of the ‘whole’ animal and by spending significant time out of doors as well as living without glass.
- Glass (as in windows) allows only 5% of the UV-B light range that produces D to get into your home or car but 78% of UV-A, responsible for non-melanoma skin cancers, penetrates glass.
- A #8 sunscreen prevents 95% of UV-B from activating D. #15 prevents 99%.
- Sun exposure before 10AM or after 2PM will cause burning from UV-A before it will supply adequate D from UV-B.
- Sunning between 10AM and 2PM during summer months (or winter months in lower latitudes) for 10-120 minutes, depending on skin type (color), will form adequate D before burning occurs. Sun mid-day, expose lots of skin and stay only as long as you need. Never stay in the sun, mid-day or otherwise, long enough to see pinkening.
- The current suggested exposure of hands and face or arms to 10-20 minutes of sunlight three times a week during the summer would provide only 400 IU D each time (about 200 IU a day) and then only if exposure was during the time UV-B is present.
- 85% of body surface needs exposure to prime (summer) mid-day sun for 15 minutes (light skinned) to 120 minutes (dark skinned) to achieve optimal levels of D.
- Latitude and altitude determine the intensity of UV-B light.
- Latitudes higher than 30° (both north and south) have insufficient UV-B sunlight 4-6 months of the year (even mid-day).

- Latitudes higher than 40° have insufficient sunlight 8-9 months of the year or more.
- Large parts of the US are between 30° and 45°. In most parts of the US 6 months or more during each year have insufficient UV-B sunlight to produce optimal D levels.
- In far north or south locations, latitude 45° and higher, even summer sun is too weak to provide significant levels of D.
- High dietary levels of calcium, when D is insufficient, may contribute to calcification of the arteries, joints and kidney and perhaps even the brain.
- Vitamin D regulates vitamin D binding proteins (a whole family of these) that carry calcium to the 'right locations' and along with vitamin K and magnesium prevent precipitation of calcium in blood.

Calcium in the arteries equals heart disease and premature death. In the March 1995 issue of Analyst, Scottish researchers found hair calcium inversely correlated with arterial calcium, the more plaque (calcium) in the arteries, the less calcium in the hair. 90% of men experiencing myocardial infarction had low hair calcium. Vitamin D raised beard calcium and this rise continued as long as vitamin D was consumed. Almost immediately after stopping the D, beard calcium fell to pre-supplement levels.

Scotland, home of this study, has little UV-B sunlight. Northern countries have higher levels of cardiovascular disease and more heart attacks occur in winter months. However, there is an exception to this statistic. In India research suggests that light skinned Indians living in lower latitudes suffer from elevated vitamin 25(OH)D which contributes to deposition of calcium in soft tissues, predisposing to heart disease.

- Vitamin D and/or sunlight (UV-B, not UV-A or UV-C) have been shown to lower blood pressure, restore insulin sensitivity, and lower cholesterol.
- Sunlight as UV-B, and vitamin D normalize food intake and normalize blood sugar. Weight normalization is associated with higher levels of D and adequate calcium.
- When vitamin D levels are optimal less calcium is needed. (But a supplement is needed even when dietary calcium is high if bone loss has already occurred.)
- Vitamin D plays a role in regulation of both the 'infectious' immune system and the 'inflammatory' immune system.
- Low vitamin D is associated with several auto-immune diseases including Multiple Sclerosis, rheumatoid arthritis, thyroiditis and Crohn's disease.
- Levels of SIgA in the gut may be associated with D and thereby higher levels of D (and SIgA) may protect the gut from food allergy reactions and infections.
- Osteoporosis is strongly associated with low vitamin D. Post-menopausal women with osteoporosis respond favorably (and rapidly) to higher levels of D plus calcium and magnesium.
- Infertility is associated with low vitamin D.
- PMS has been eliminated by the addition of calcium, magnesium and vitamin D.
- Breast, prostate and colon cancer have a strong association with low levels of D and lack of sunlight.
- Activated vitamin D in the adrenal gland regulates tyrosine hydroxylase, the rate limiting enzyme necessary for the production of dopamine, epinephrine and norepinephrine.

- SAD- 1999 a research study compared high dose D (a onetime dose of 100,000 IU) and a full-spectrum light box in resolving Seasonal Affective Disorder (SAD). After 30 days patients given D had 75% higher levels of D and were found to be completely free from depression. 30 days of light box use did not resolve depression in any of the patients but did raise levels of D 25%.
- Low D or calcium and magnesium contribute to chronic fatigue and depression. High stress may increase the need for D or sunlight (UV-B) and calcium
- People with Parkinson's and Alzheimer's have been found to have lower levels of D.
- Hospitalized or immobilized patients may need more D. Immobilization may require active 1,24(OH)D as conversion of D3 seems to fail.

Low levels of D, and perhaps calcium, in a pregnant mother and/or later in the child may be the contributing cause of 'crooked teeth' and myopia. When these conditions are found in succeeding generations it means the genetics require higher levels than currently consumed of one or both nutrients to optimize health.

Behavior and learning disorders respond well to avoidance of junk foods and adequate protein, vitamin D, omega-3 and/or calcium, magnesium and zinc.

For many years the acceptable level of 25(OH)D has been >16 ng/ml (>40 nmol/l). Vieth believes that this is far from optimal and has collected a large amount of data to suggest he is right. Optimal levels are certainly >80 nmol/l (>32 ng/ml) and preferably >40 ng/ml (>100 nmol/l) but less than 70 ng/ml. Remember that the symbol > means 'greater than'.

Excess for some individuals may be >70 ng/ml (175 nmol/l) 25(OH)D.

Testing vitamin D

There are two vitamin D tests- 1,25(OH)D and 25(OH)D. The first is active D, which is usually normal even when the precursor D is insufficient. The precursor, 25(OH)D is the best marker of D status and it is this marker that is most strongly associated with overall health or disease. **Self-testing information: <http://sunlightd.org>**

Testing is critical as genetics vary and it is impossible to know your D status from symptoms. It is also impossible to determine the correct dose of D without testing. After testing you must retest one or more times each year over the next three years to make sure the level of D you are getting is working, whether from sunlight or supplements or some of both.

Once your need for D is determined, daily supplements will range from none to as much as 4,000 IU daily for a brief period of time. If using supplements of vitamin D STOP in summer months when you regularly sun mid-day. This does not mean take D on days you don't sun" it means in summer either sun or use D, not both, not a mix.

If you feel your situation is critical order from me the [Sunlight and D Preliminary Report with Physician Protocol](#) that contains more information, research references and physician guidelines for diagnosis and treatment.

Taking D or sunning, when you have optimal 25(OH)D levels, may raise your vitamin D levels above optimum. Do not supplement D without testing and do not suggest to anyone that they do so either. There are some experts who believe that 'natural' D as found in fish oil and cod liver oil is always safe. They are wrong. I have had to deal with the problems associated with overdose of vitamin D. Once vitamin D reaches excess values it may take months or even as long as a year to reduce levels within normal range. During this period of time significant bone loss may occur.

Cod liver oil intake (not lack of) was a risk factor for development of melanoma in Norwegian men and women.⁽³⁵⁷⁾

Do not supplement with D without testing to determine if you need a D supplement. For most the 400-800 IU found in your multiple is safe, actually because of the form, tablet or capsule, and therefore 'dry D' you are unlikely to be able to absorb it.

If it has been determined you need extra D, make sure to have adequate sources of vitamin C, calcium and magnesium. Total daily doses should be a minimum of 3,000 mg vitamin C taken twice a day, plus 600 mg calcium and 300 mg magnesium, preferably from food. Higher amounts are important for anyone diagnosed with bone-loss. 800-1,000 mg calcium and 400-500 mg magnesium a day is usual.

Split your daily doses up. Don't take all your calcium and magnesium once a day. More is absorbed if taken in smaller multiple doses. Three times a day is optimal but twice a day is better than once a day.



Enjoy the sun, just enough to get your D for your skin type. The best sunscreen is clothing. It's time to bring back large, wide-brimmed, hats.

Calcium, Insulin, Vitamin D and Obesity

Research done by Zemel at the University of Tennessee implicates low calcium and low vitamin D in obesity and Metabolic Syndrome (elevated fasting insulin) with all of its associated conditions- heart disease, hypertension and diabetes. Subjects given 1,000 mg of added calcium lost significantly more body weight on a restricted calorie diet than those given a placebo. The primary marker of Metabolic Syndrome is elevated fasting insulin. The low calorie diet lowers fasting insulin plus calcium compensated for lower levels of vitamin D.

Obese persons have been repeatedly shown to have lower vitamin D levels and the greater the BMI (body mass index) the more profound the deficiency. D regulates calcium absorption and serum calcium regulates the conversion of 25(OH)D to 1,25(OH)₂D. Higher levels of calcium lower 1,25(OH)₂D which that determines whether you will burn a calorie or store it as fat, any calorie from any source.^(358,359,360,361)

Wortsman et al showed that obese persons poorly convert the precursor D₃ to active 25(OH)D whether from sunlight or supplements.⁽³⁶²⁾ What we know now is that it is the elevated insulin found PRIOR to obesity that alters D conversion.⁽³⁶³⁾ That defect lowers

circulating D which lowers calcium absorption. Higher levels of calcium partially compensate for the ineffective conversion of vitamin D. Gallagher found women with higher BMI required much higher doses of vitamin D to elevated serum 25(OH)D.^(364,365,366)

Please work with a healthcare practitioner to lower fasting insulin AND optimize D and calcium. Adequate D and calcium reduce cravings, increase energy and combined with exercise and reducing fasting insulin, restore insulin sensitivity.^(362,367) Taking more D or calcium will not prevent the damage of elevated insulin.

United States Latitudes and Sunlight

The map shows US latitudes from 50°, 40° and 30°. Latitudes above 30° have insufficient UV sunlight to produce optimal vitamin D 4-6 months of the year. Latitudes near or above 40° have insufficient sunlight 6-9 months of the year. Latitudes above 50° rarely have enough UV sunlight any month of the year, including summer months. Please note that many of these areas may have enough sunlight to prevent rickets (if you go in the sun between 10:30AM and 1:30PM) but not enough to provide optimal levels of D.

Altitude may compensate for degrees of latitude during some portions of the year. Knowing your latitude and altitude can help you make wise decisions regarding vitamin D supplementation.

Figure 7-1 US Latitudes



Minimum vitamin D need is estimated to be 800- 2,000 IU daily. Sun exposed persons in latitudes below 30° have normal blood levels of 25(OH)D near or greater than 100 nmol/l or 40 ng/ml. Amounts lower than 80 nmol/l or 32 ng/ml mean sub-optimal D status and may contribute to the higher incidence of many degenerative and auto-

immune diseases found in more Northern locations or those more prevalent in winter months.

CHAPTER 8 VITAMINS, MINERALS AND MACRONUTRIENTS

How Vitamins and Minerals Are Measured

Water soluble vitamins and minerals are measured by microgram (mcg), milligram (mg) and gram (g) amounts. Vitamins are very 'small' in size and in weight and very rarely consumed in gram amounts with the exception of vitamin C. Macro-minerals such as potassium, calcium, phosphorus and sodium are often used in gram amounts. Magnesium and micro-minerals are listed in milligram amounts.

Table 17 Metric conversion

1000 mcg (microgram)	equals 1 mg. (milligram)
1000 mg (milligram)	equals 1 g. (gram)
1000 gram	equals one kilogram
28 grams	about one ounce

Macro-minerals such as calcium, magnesium and potassium, even in milligram amounts, are structurally very large (take up space) because the mineral must be attached to another molecule. Minerals do not occur in pure form. Depending on the size of the attached molecules (calcium carbonate=calcium+carbonic acid, calcium citrate=calcium+citric acid) you may need 4 or more tablets or capsules to get sufficient macro-minerals.

Trace minerals are in microgram amounts and are usually included in a good multi vitamin and mineral combination or can easily be added by using dulse (type of red seaweed) to season foods. So called colloidal minerals are not typically a good source of minerals or trace minerals being high in aluminum, a potentially toxic trace element, and expensive.

When reading the label on any supplement note how many tablets contain the stated amounts. Frequently a label will say 2 contain or 4 or 6 contain. To actually consume the amounts of nutrients listed on the label you must take the full dose.

Special Note: All of the values discussed in this workbook are for adults and not to be used with children.

Fat Digestion and Fat-soluble Vitamins

If you have difficulty digesting fats it is important to address this problem ASAP. Longevity and a strong immune system require adequate A, D, E and K, all fat soluble vitamins that cannot be absorbed/utilized without excellent fat digestion. Without normal fat digestion you will not get what you need, from supplements or from food.

If you have had your gallbladder removed you no longer make concentrated bile. You will need to take lecithin granules, 1-3 teaspoons per meal or triple strength lecithin, about 3-4 soft gels, or ox bile, or a concentrated fat-digesting enzyme (lipase) or concentrated pancreatin at every meal, especially meals containing your fat-soluble vitamins and omega-3 oils. I have listed fat digesting aids in order of preference.

If you have difficulty digesting fats but still have your gallbladder you likely need to increase your daily intake of vitamin C. The corrective and ongoing dose is 1,000 mg of ascorbic acid twice a day. Some persons with symptoms of subclinical scurvy may need a higher dose for several months.

Temporarily using the lecithin granules and increasing vitamin C and adding taurine, a conditionally essential amino acid, for a few weeks or months while making sure you have sufficient fat-soluble vitamins and omega-3 fats will most likely correct the problem. Use the digestive aids temporarily and see if your fat digestion improves.

Some persons find they need to continue taking taurine to maintain normal gallbladder function. Taurine is found in wild game, beef heart and shellfish (muscles) and is also good for your nerves and heart. Taurine increases GABA an anti-anxiety neurotransmitter/amino acid. A typical daily dose of taurine is 1,000-2,000 mg taken any time you like with or without food.

Fat digestive aids: Now Foods lecithin granules, about 1 rounded tablespoon per meal or Now Foods 8X Pancreatin taken with meals will digest fats for you. An alternative powdered vegetarian enzyme product, Absorb Aid powder is another possibility. You can tell if what you chose is working because fats won't reflux and your digestion will proceed normally.

Critical Nutrients, A, D, and Folacin

Three vitamins are showing up in the research literature with great frequency. All three are known to be protective against the most prevalent degenerative diseases and cancer. The FDA limits amounts of these nutrients allowed in supplements. For some these limits are insufficient to maintain optimum health. Because these nutrients are regulated it may be impossible to get sufficient amounts in a daily dose of any multi-vitamin supplement.

The limit, RDA, for vitamin A is 8,000 IU, for D, 400 IU and for folic acid (folacin) 800 mcg. Optimum amounts are likely closer to 10,000-15,000 IU for A, 1,000-2,000 IU for D. Excess folic acid in any form should be avoided.

A, as retinol, can be found in a separate fish-oil based A or A&D soft gel, cod liver oil, or regular consumption of beef liver (not calf or chicken liver, both are poor sources of A).

Vitamin D is produced in our skins from exposure to UV-B containing sunlight or found in the fat of deep-sea fish, eggs, and cod liver oil.

Folic acid is found in dark green leafy vegetables, fresh squeezed orange juice, liver and brewer's yeast.

You must make a concerted effort to get optimum amounts of these nutrients. You cannot depend on your multiple. Significant amounts of the food sources must be consumed to get adequate levels. If you use supplements you will need to purchase them separately and add them to your daily supplement intake.

Hypervitaminosis A may begin at extended intakes (more than a few weeks) of 15,000-50,000 IU daily. In rare individuals doses as low as 10,000 IU daily over many months/years combined with food sources of vitamin A may cause problems. Infrequent dosing with exceptionally high doses, 100,000 to a million international units, has not been found to cause toxicity. I have seen two cases of vitamin A excess, one caused by daily intake of half a pound of Foie Gras (goose liver pate) for more than three years, the other by chronic intake of 60,000+ IU of pre-formed vitamin A daily for more than 10 years.

Neither of these individuals had symptoms. Both had serum retinol values double the high normal value. Serum vitamin A is not a good indication of retinol sufficiency because liver stores of vitamin A may be seriously depleted and serum retinol normal. However, serum vitamin A is a way to check for excess. Serum values won't increase until the liver has all it can store.

Acute vitamin A toxicity may occur with extremely high intake, 200,000 IU for 10 days or more or higher amounts for just a few days resulting in dry skin, dry eyes, headache and nausea and loss of appetite. Symptoms resolve rapidly when the vitamin is discontinued.

Vitamin D toxicity may occur at intakes of 2,000-4,000 IU daily or more taken over weeks, months or years or when vitamin D supplementation is combined with high intake of calcium and/or enthusiastic sunning. With vitamin D, testing is imperative.

Folic acid is not toxic at suggested levels (unless you have the MTHFR gene, see below) but may increase the need for B-12 and other B vitamins. Ideally, higher doses of folic acid should be taken with additional B-12 and a multivitamin containing all of the B-complex vitamins. (Nutritional yeast and beef liver have folic acid, B-12 and the other B vitamins too.)

Vitamin A (Not Beta-Carotene)

Important for all body functions and all tissues, vitamin A is a controller of normal growth in the human body and therefore too little or too much can contribute to all diseases and degenerative conditions as well as birth defects. Vitamin A protects us from and helps us recover from viral and bacterial infections. Minimal dose is 8,000 IU (adult). Toxicity may begin at 40,000-50,000 IU daily for an extended (months or years) period of time. Vitamin A is a fat soluble vitamin whether it is pre-formed retinoic acid or beta-carotene. Doses up to 30,000 IU daily are considered safe for pregnant women.^(368,369,370)

Short courses of 100,000 IU for treatment of colds, flu and virus are not toxic even in children unless active liver or kidney disease is present. The World Health organization has been using 100,000 IU of A in infants and 200,000 IU daily in children 18 months or older for a brief course, 3-4 days, to treat measles (a virus), croup, and pneumonia.^(371,372,373,374)

Beta-carotene is not vitamin A (retinol), and must be converted to bioactive retinol. Persons of certain genetic origin (Northern European, Scandinavian and perhaps others), or persons with celiac-sprue, diabetes or hypothyroidism poorly convert or are unable to convert beta-carotene to vitamin A. Newer research suggests the rate of conversion is highly variable and there is growing concern that beta-carotene may not satisfy the body's need for vitamin A.^(375,376,377)

Any condition that involves disruption of gut function, pathogens such as bacteria, yeast or parasites, IBS, colitis or lectin intolerance, will also alter conversion. Vitamin B-12 deficiency prevents conversion of beta-carotene to retinol A as does elevated levels of homocysteine or low levels of zinc.

Higher levels of A can precipitate a vitamin D deficiency.⁽³⁷⁸⁾ In several studies men and women taking a supplement with as little as 5,000 IU of A had significant bone loss leading to osteoporosis and hip fractures.^(379,380,381,382) Vitamin A and vitamins D are not vitamins but rather pre-hormones. They are converted into their active hormone equivalents. Their 'end' action is in your genes. Having an excess or deficiency of either changes the message to your replicating cells. Hormones tell our cells when to grow, replicate and die. The wrong message/s may lead to early cell death, not enough new cells, too many cells (hyperplasia) or cells that don't die (cancer).

Things work together in our bodies. Too much of any nutrient, water or fat soluble, can cause a relative deficiency of another (known or unknown) nutrient. Do not supplement A or D without making sure both are sufficient. For vitamin D, only testing can tell you if you have enough.

Vitamin B complex

There are some 11 recognized B vitamins. All are essential, including PABA, choline and inositol. Liver is a good source as is brewer's yeast. Supplements should contain all 11 in amounts from 10 mg to 50 mg, with the exception of folic acid, biotin and B-12,

which are measured in microgram amounts. Higher amounts (more than 50 mg. per dose) should be taken with caution. If your urine is 'Day-Glo yellow or green' after taking a supplement containing B vitamins consider lowering your dose. More B is not better. Think enough but not too much. Also think- all together. There is no 1 B vitamins better or more necessary than another.

Two of the B complex are of special note. Folate and B-12 are limited in most multiples and in B-complex formulas. The doses needed are higher than typically found in most diets or supplements. There is some evidence the type of folic acid added to foods and in multi-vitamins may contribute to disease, especially if your ancestors have a gene that slows conversion to active folate.^(383,384,385,386,387,388,389)

Some persons for yet to be determined reasons, such as the MTHFR gene mutations, have difficulty converting some of the B vitamins into their active co-enzymes. Persons with CNS problems, learning disabilities, behavioral problems or autoimmune conditions may find the new co-enzyme B vitamins bring amazing and rapid results. To try them Life Extension Complete B-Complex or Swanson Vitamins Activated B-Complex High Bioavailability work well. To check your response take one on an empty stomach and check your brain/nerves/energy/mood in about 10 minutes. If you notice a difference you may need the co-enzyme Bs.

Folates Not Folic Acid

Folic Acid is one of the most deficient vitamins in the modern American diet. Current research shows that protective levels should be about 800 mcg daily. Many Americans get 200 mcg or less. Folates are found in dark green leafy vegetables, fresh whole vegetables and fruits, fresh squeezed orange juice, brewer's yeast and liver. If you eat enough potassium (from fruits and veggies) you will get more than enough folic acid.

Synthetic folic acid

Folates in very small amounts (micrograms) are critical for health in humans, animals and plants. Folates, as tetrahydrofolates, are found in whole foods. Folates are rapidly broken down, so as food ages folate levels drop. Folic acid (pteroylmonoglutamic acid, PGA) rarely exists in nature. It was first synthesized in the laboratory in 1943. Tetrahydrofolates, various versions of pteroylpolyglutamic acid are in fresh whole foods. These folates are unstable with poor 'shelf life'. Folic acid (PGA) is very stable, difficult to break down, and has a shelf life of 'years'. Most vitamin supplements, including all prenatal vitamins, and all fortified foods contain folic acid (PGA).

In July 2014 I began analyzing 23andme gene data to help clients with MTHFR mutations (see below) and other 'my genes are messing me up' issues. During my research/learning phase I was disturbed when it came to my attention (why did I not know this?) that supplements and fortified foods contain folic acid which is a SYNTHETIC substance, pteroylmonoglutamic acid (PGA). The rationale for using this substance was bioavailability and SHELF LIFE. The term 'folic acid' means pteroylmonoglutamic acid, not one of the natural tetrahydrofolates, though the FDA is trying to change terminology. Currently there is a plan to ban the use of alternate folate names on labels, requiring all to use the term folic acid, whether PGA or natural source. Confusing for consumers and problematic if issues occur as to source. The motivations for this change are yet to be determined.

Early in folic acid research some researchers warned of possible problems with PGA. They suggested it might not be as bioavailable as thought. They found high levels of unmetabolized PGA (which would have no function in the human body) and felt studies should be done to determine human safety, but no long term safety studies were done.⁽³⁹⁰⁾

Folic acid raised serum folate, it lowered rates of neural tube defects and corrected pernicious anemia. What could be wrong?

Natural folates are readily broken down. They do not have 'shelf life' and are found only in truly fresh foods. Synthetic folic acid is shelf stable for YEARS (should we not wonder?). It was/is believed this stability allows for higher availability and thereby greater serum folic acid levels leading to higher levels of health. Recent studies suggest two problems with PGA, it may NOT be broken down into active folate as easily as thought and unmetabolized PGA may cause problems, serious problems. Unfortunately a serum folic acid test does NOT show whether the folic acid is active l-5-methylfolate or inactive PGA. The test to determine unmetabolized folic acid is \$180 out of pocket (not covered by insurance).

We have been using folic acid in food and supplements since 1950 or so. In 1998 food fortification with folic acid (PGA) was mandated by law in the United States. This was considered wise because it has lowered the incidence of NTDs, neural tube defects, specifically anencephaly and spina bifida. These are devastating birth defects and finding a possible preventative was 'a miracle'. BUT

Am J Clin Nutr. 2007 Jan;85(1):285S-288S.

Folate and neural tube defects.

Pitkin RM1.

Abstract

A protective effect of folate against the development of neural tube defects (NTDs), specifically, anencephaly and spina bifida, is now well recognized, having been established by a chain of clinical research studies over the past half century. This article summarizes the more important of these studies, which have led to the current situation in which all women capable of becoming pregnant are urged to ingest folic acid regularly. The recommended intakes are 4 mg/d for those at high risk (by virtue of a previous NTD pregnancy outcome) and 0.4 mg/d for all others. However, a reduction in NTD births did not follow promulgation of these recommendations, and so folic acid fortification was mandated in the United States and some other countries. Although some controversy remains about the adequacy of fortification levels, the process was followed by significant improvement in folate indexes and a reduction of 25-30% in NTD frequency (about one-half of the proportion of cases assumed to be responsive to folate). The folate-NTD relation represents the only instance in which a congenital malformation can be prevented simply and consistently. Nevertheless, several research gaps remain: identification of the mechanism by which the defect occurs and how folate ameliorates it; characterization of the relative efficacy of food folate, folic acid added to foods, and folic acid by itself; delineation of the dose-response relations of folate and NTD prevention; and more precise quantification of the dose needed to prevent recurrences.

Researchers still don't know why folic acid prevents these birth defects, nor has fortification eliminated NTDs. Prenatal supplementation and mandated fortification of processed wheat and corn has led to a decrease, in NTDs CDC statistics show a post fortification reduction of annual cases per 10,000 live births from 4,177 to 2,851 in monitored states. This is a good thing but 'general' fortification has exposed millions, children and adults, to excess PGA which may not be safe. It is also possible that mothers of NTD babies that did not respond to fortification, the 2,821 per 10,000 live

births, may have MTHFR mutations that REQUIRE 5-MTHF NOT folic acid.^(391,392,393)
For them folic acid may be a very bad idea.⁽³⁹⁴⁾

Food folates are converted in the mucosa of the small intestine by folate conjugase producing primarily 5-methyltetrahydrofolate. Conversion is almost 100%. A small amount of 'folic acid' PGA is also converted in the mucosa but when ingested in amounts greater than 200 mcg PGA enters the body as unmetabolized folic acid. A serving of many cereals contains 400 mcg, double the amount a normal healthy body can convert. Kids consuming a large bowl of cereal could consume, just in their breakfast meal, 800 mcg or more, most of which will NOT be converted to methylfolate. Note I said healthy/normal. Some 50-60% of Americans have one or more MTHFR mutations that lower the ability to convert natural folates into methylfolate. It is highly probable they will have increased issues with PGA.

When researchers in 2013 tested natural and synthetic folic acid absorption they found-

... Fifteen minutes after a dose of folic acid, 80 +/- 12% of labeled folate in the hepatic portal vein was unmodified folic acid. In contrast, after a dose of labeled 5-FormylTHF, only 4 +/- 18% of labeled folate in the portal vein was unmodified 5-FormylTHF, and the rest had been converted to 5-MTHF after 15 min (postdose). Conclusions: The human gut appears to have a very efficient capacity to convert reduced dietary folates to 5-MTHF but limited ability to reduce folic acid. Therefore, large amounts of unmodified folic acid in the portal vein are probably attributable to an extremely limited mucosal cell dihydrofolate reductase (DHFR) capacity that is necessary to produce tetrahydrofolic acid before sequential methylation to 5-MTHF. This process would suggest that humans are reliant on the liver for folic acid reduction even though it has a low and highly variable DHFR activity. Therefore, chronic liver exposure to folic acid in humans may induce saturation, which would possibly explain reports of systemic circulation of unmetabolized folic acid.⁽³⁹⁵⁾

This means natural tetrahydrofolates from food are almost completely converted to active 5-MTHF in the small intestine before entering the general circulation in healthy humans. 80% of synthetic folic acid remains unconverted, entering the circulation as 'folic acid' an inactive folate. Because the human body was not designed to metabolize PGA (not found in quantity in nature), only small amounts of DHFR, the enzyme that converts folic acid (PGA) to tetrahydrofolates are available within the liver, resulting in high circulating amounts of unmetabolized (and unusable) folic acid (PGA).

The problem- ...

The extremely slow and variable activity of dihydrofolate reductase in human liver and its implications for high folic acid intake Bailey, S. W. and Ayling, J. E. 9-8-2009 Proc.Natl.Acad.Sci.U.S.A

Numerous clinical trials using folic acid for prevention of cardiovascular disease, stroke, cognitive decline, and neural tube defects have been completed or are underway. Yet, all functions of folate are performed by tetrahydrofolate and its one-carbon derivatives. Folic acid is a synthetic oxidized form not significantly found in fresh natural foods; to be used it must be converted to tetrahydrofolate by dihydrofolate reductase (DHFR). Increasing evidence suggests that this process may be slow in humans. Here we show, using a sensitive assay we developed, that the reduction of folic acid by DHFR per gram of human liver (n = 6) obtained from organ donors or directly from surgery is, on average, less than 2% of that in rat liver at physiological pH. Moreover, in contrast to rats, there was almost a 5-fold variation of DHFR activity among the human samples. This limited ability to activate the synthetic vitamer raises issues about clinical trials using high levels of folic acid. The extremely low rate of conversion of folic acid suggests that the benefit of its use in high doses will be limited by saturation of DHFR, especially in individuals possessing lower than

average activity. These results are also consistent with the reports of unmetabolized folic acid in plasma and urine.⁽³⁹⁶⁾

Folic acid added to fortified foods and found in almost all vitamin supplements is PGA, pteroylmonoglutamic acid. Foliates found in food are tetrahydrofolate derivatives. All forms of folate must be converted into 5-MTHF, the active USEABLE form of folate.

We may absorb the synthetic folate but we poorly convert it. Pteroylmonoglutamic acid (PGA, synthetic folic acid) in doses higher than 200 mcg results in high amounts of unmetabolized folic acid (PGA).⁽³⁹⁵⁾ In persons with the MTHFR gene mutation/s conversion/utilization may be even less resulting in even higher serum levels of PGA.

Unmetabolized PGA stays in our blood stream with nowhere to go, no function to perform, no natural metabolic pathway to follow. In several recent studies supplemental (synthetic) folic acid was associated with higher incidence of cancer⁽³⁹⁶⁾ Unmetabolized synthetic folic acid (PGA) has been shown to lower natural killer cells in postmenopausal woman.^(397,398) Natural killer cells are a part of our innate immunity, protecting us from viral infections and abnormal cell growth (cancer). Lower is not better.

Because of MANDATED folic acid fortification and because almost all supplement companies use synthetic folic acid (PGA) in their supplements, a large percentage of persons (70-99%) in countries with mandated folic acid fortification have high levels of unmetabolized folic acid (PGA).^(390,397,399,400,401,402,403) In Ireland, where mandatory fortification has been suspended, high levels of unmetabolized folic acid are viewed with great concern.

Unmetabolized folic acid prevalence is widespread in the older Irish population despite the lack of a mandatory fortification program Boilson, A., Staines, A., Kelleher, C. C., Daly, L., Shirley, I., Shrivastava, A., Bailey, S. W., Alverson, P. B., Ayling, J. E., McDermott, A. P., MacCooney, A., Scott, J. M., and Sweeney, M. R. 2012 *Am.J.Clin.Nutr.*

BACKGROUND: In 2006 the Food Safety Authority of Ireland recommended mandatory folic acid fortification of flour for the prevention of neural tube defects in addition to the existing extensive voluntary folic acid fortification culture in place there. This recommendation is now suspended until further scientific evidence surrounding safety becomes available. The safety issues include concerns about the masking of vitamin B-12 deficiency and potential cancer acceleration, both of which may be of concern for the elderly population. OBJECTIVE: The aim of this study was to measure the basal (fasted) concentrations of unmetabolized folic acid in the plasma of an elderly population group exposed to this liberal voluntary fortification of foodstuffs in Ireland. DESIGN: We invited participants aged 60-86 y from the Lifeways Cross-Generation Cohort Study to participate in this project. After providing informed consent, the participants were invited to provide fasting blood samples and to complete a standard food-frequency questionnaire and a questionnaire on recent and habitual intakes of folic acid. Samples were assayed for total plasma folate, red blood cell folate, homocysteine, and unmetabolized folic acid. RESULTS: A total of 137 subjects with a mean age of 67.4 y were studied. Unmetabolized folic acid was detected in 94.1% of the cohort with a mean concentration of 0.39 nmol/L (range: 0.07-1.59 nmol/L), accounting for 1.3% of total plasma folate. CONCLUSION: These results indicate unmetabolized folic acid in plasma in most of this elderly Irish cohort, even after an overnight fast. These results should be considered carefully by those legislating in this area

In the US a serving of fortified cereal may provide 400 mcg of PGA, double what may be tolerated and converted. Adding another 400-800 mcg found in many multi-vitamins or B-complex vitamins will raise serum PGA to even higher levels. Add a serving of fortified pasta or bread or a fortified protein bar or protein drink ???

High levels of synthetic folic acid during pregnancy have been linked to changes in glucose tolerance and insulin resistance in offspring, alteration of MTHFR genes in offspring, and in animal studies higher likelihood of seizures (lower seizure threshold) in offspring.^(404,405,406,407,408) High folic acid with low B-12 (imbalance) increases low birth weight of infants. Infants whose moms had high levels of folic acid (PGA) supplementation have higher incidence of allergy/asthma.^(409,410) There is also some indication of other brain changes when elevated PGA is present. Another study found high levels of folic acid (unmetabolized PGA) associated with thyroid issues in adolescence.⁽⁴⁰⁷⁾

Fortification and/or supplementation with a synthetic substance in supraphysiologic doses NOT FOUND IN NATURE is unwise on many levels, and if you are susceptible (your genes) you may pay a very high price.

It is true folates are required for healthy babies and low folate status prior to pregnancy may result in neural tube defects in some. What must be considered is dose, type of folic acid, and BALANCE with other key nutrients. If MTHFR mutations are present. It may be in our best interests to make use of a healthy diet and small amounts of methylfolate rather than relying on synthetic folic acid.^(411,412,413)

We all require a small amount of methyltetrahydrofolate (5-MTHF) which is normally produced in our small intestine from natural dietary folates. Because this conversion takes place in the gut wall persons with digestive issues, SIBO, IBS, Crohn's, colitis, may not be able to make enough. In some persons with healthy guts, having MTHFR mutations, conversion to active 5-MTHF may be limited.

Folates are important because without sufficient amounts we may develop-

- Fatigue
- Poor appetite
- Headache
- Pallor (pale skin)
- Grey hair
- Red, irritated, swollen, and sometimes shiny tongue
- Mouth ulcers
- Shortness of breath and lightheadedness
- Change in bowel patterns, usually diarrhea

Complications from folic acid deficiency include:

- Megaloblastic anemia—a blood disorder characterized by larger than normal red blood cells
- Elevated homocysteine levels in the blood—a risk factor for heart disease
- Neural tube defects that affect fetal spinal cord, brain, and skull development

Low folate status may also contribute to mood disorders, autism, ADHD, schizophrenia, cancers and autoimmune disorders.

...folate provides one-carbon unit for methylation of a wide variety of biological substances including DNA, proteins, phospholipids, and neurotransmitters, thereby regulating their function. Recent epidemiological-clinical and experimental studies suggest the association of folate deficiency with the risk of various cancers, birth defects, and cardiovascular diseases. Thus, it is important to consider the conditions that are associated with altered folate status and their consequences. The impairment in folate status has been found in number of pathophysiological conditions like inflammatory bowel disease, cancer, alcoholism, pregnancy, neonatal growth, and during administration of some drugs.⁽⁴¹⁴⁾

Folic acid (PGA) may be converted in the human gut BUT even in healthy adults (no MTHFR and not gut issues) doses exceeding 200 mcg enter the body as unmetabolized folic acid (PGA). There is some indication, yet to be confirmed, cancer increases in countries where folic acid fortification has been mandated.^(415,416,417,418,419,420,421,422,423,424)

This information suggests NO HUMAN should consume synthetic folic acid. Fully active 5-MTHF is available in a supplement as Metfolin or l-methylfolate or 5-MTHF. Life Extension multi-vitamins contain natural food folate from lemon peel. Some companies use other versions of natural tetrahydrofolates. OR try a supplement without folic acid and EAT your folates.

Also based on this information fortified foods (all cereals and breads and pasta, including organic) should not be consumed by children or adults. Read labels.

Methyl-folate is required in microgram amounts for health and longevity. Get your folate from food whenever possible and if supplementing use only natural folates, not PGA. With current information it is wise to not exceed 800 mcg (maybe as much as 1,000 mcg) daily even using natural folates. The human body does not need much folate, just enough.

As an added note do not supplement with folates unless you also supplement with vitamin B-12, (as methylcobalamin or hydroxycobalamin or adenosyl-cobalamin). Hydroxycobalamin is metabolized to either methylcobalamin (nerve and brain) and adenosyl-cobalamin (muscle and blood). You may need a good B-complex to keep things balanced. I like the Swanson Vitamins Activated B-Complex High Bioavailability as each B vitamin in the complex is in its coenzyme form. The dose per each capsule is a bit high for my liking but for now it is the best I have found. Life Extension also has a fully active B-complex but it is quite high dose and may not work for many.

Some persons with certain metabolic/health issues, including but not limited to MTHFR mutations, may need extra niacin or pyridoxal-5-phosphate (coenzyme B-6) or amino acids to reduce histamine. Do find a knowledgeable health care provider to get the answers you need.

Gene Testing and MTHFR- When Folate/B12/B6 Metabolism Doesn't Function

2014 brought about some significant changes in client analysis. I have been incorporating data from 23andme gene testing to help determine special nutrient needs. The most researched markers are related to MTHFR, vitamin D receptors, and MAO markers.

It has been clear over the 40+ years I have been consulting some persons eating 'right' and maintaining a healthy lifestyle still found 'health' just out of reach. Their struggles to avoid illness and enjoy life were exhausting and often they were unable to achieve their goals.

Turns out-

1. There is no one 'healthy' diet. (somewhat old news as eating like YOUR ancestors and restoring your microbiome does work)
2. Some persons have genetic mutations that may increase their chances of
 - a. Cancer
 - b. Heart disease
 - c. OCD, schizophrenia, bi-polar disorders
 - d. Mood disorders
 - e. Chronic anxiety
 - f. ADHD, learning disabilities
 - g. Autism
 - h. Autoimmune disorders
 - i. Down's Syndrome
 - j. Other genetic disorders
3. Some mutations may be modified by diet and/or supplements
4. Some mutations may be modified by your microbiota (gut microbes)

From Wikipedia- Methylene tetrahydrofolate reductase (MTHFR) is the rate-limiting enzyme in the methyl cycle, and it is encoded by the MTHFR gene. Methylene tetrahydrofolate reductase catalyzes the conversion of 5,10-methylene tetrahydrofolate to 5-methyltetrahydrofolate, a cosubstrate for homocysteine remethylation to methionine. Genetic variation in this gene may influence susceptibility to occlusive vascular disease, neural tube defects, Alzheimer's disease and other forms of dementia, colon cancer, and acute leukemia, because mutations in this gene are associated with methylene tetrahydrofolate reductase deficiency.

We need methylfolate. All 'folates' must be converted into methylfolate to be used by the human body. If you have an MTHFR mutation/s you may not efficiently convert natural folates into the active form, methylfolate, and synthetic folic acid may produce an even worse outcome, poor conversion and high serum unmetabolized folic acid.

Without sufficient amounts of methylfolate you may not make enough S-adenosylmethionine (SAM-e) or be unable to metabolize homocysteine or suffer impaired production of important neurotransmitters. These elements are essential for health and longevity. It is a BIG deal. Folate insufficiency, as well as other MTHFR mutation issues including problems with B-12, niacin, and/or B-6, contribute to cancers, infertility, heart disease, mood disorders, ADHD, depression, autism, schizophrenia, dementia, birth defects and more.

Whether we have gene mutations or not, I have come to believe we (all of us humans) cannot safely use synthetic folic acid. Consumption of more than 200 mcg of this man-made folic acid may increase the risk of developing several types of cancer.^(425,426,427) It may also alter gene expression leading to MTHFR mutations in offspring and contribute to other, yet discovered, metabolic problems.

1. Many persons (>50% in Europeans) have modified MTHFR genes.
2. The diseases mentioned above all strongly relate to folic acid/B12/B6 methylation sufficiency and metabolism.
3. Scientists created synthetic folic acid in the 1940's and in 1998 mandated its inclusion in most refined foods including 'organic' cereals and pasta. This was done without understanding how synthetic folic acid is metabolized in the human body and without understanding even greater problems for those with MTHFR issues.
4. There are three folate issues a) synthetic folic acid, avoid it, b) MTHFR mutations leading to health problems even when using natural folates and c) insufficient/excessive use of folates, synthetic or natural, creating imbalances with B-12 and other B vitamins and increasing the likelihood of potential health issues including mood disorders, autism, cancers, and heart disease.

Everyone with ongoing, unexplained health issues should be tested for MTHFR gene/s and if mutations are present find someone to help you modify the negative outcomes. An indicator you may need testing is elevated homocysteine on a yearly blood panel. Many with MTHFR issues will have elevated homocysteine but not all. There are other indicators of under or over methylation, including heart disease, depression, autism, ADHD and cancer.

Folate is important as noted above because (from Wikipedia)

...Vitamin B₉ (folic acid and folate) is essential for numerous bodily functions. Humans cannot synthesize folate de novo; therefore, folate has to be supplied through the diet to meet their daily requirements. The human body needs folate to synthesize DNA, repair DNA, and methylate DNA as well as to act as a cofactor in certain biological reactions.^[7] It is especially important in aiding rapid cell division and growth, such as in infancy and pregnancy. Children and adults both require folic acid to produce healthy red blood cells and prevent anemia.^[8] ...

Research suggests 25% of the world's population carry some version of the MTHFR gene mutation. Various mutations of this gene are associated with autism, varicose veins and surface thrombotic abnormalities, high homocysteine (and therefore heart disease), infertility, schizophrenia, susceptibility to several types of cancer, risk of Down's Syndrome in offspring, atrial fibrillation, mood disorders in children, congenital defects including cleft palate, and many more.

What the gene mutations do is alter conversion of folates into the active tetrahydromethylfolate and without the active co-enzyme the body's ability to perform methylation MANY body systems are impaired to a greater or lesser degree (detoxification is one role, production of neurotransmitters is another).

The most common MTHFR gene mutations are found at position 677 and/or position 1298 on the MTHFR gene.

At position 677 of the MTHFR gene, a Cytosine is what is supposed to be found there. When mutated, the Cytosine gets replaced with a Thymine.

At position 1298 of the MTHFR gene, an Adenine is what is supposed to be found there. When mutated, the Adenine gets replaced with a Cytosine.

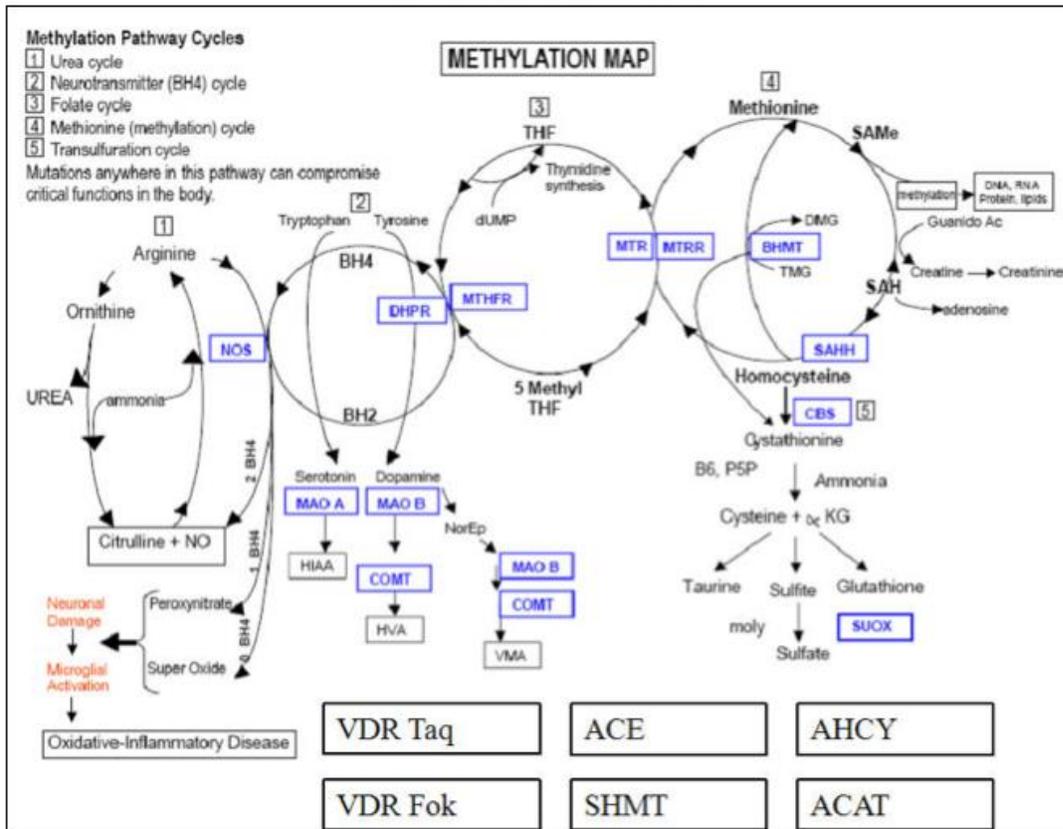
To order the test <http://mthfr.net/mthfr-testing-mthfr-test-kit/2012/01/25/>

Possible conditions/symptoms of the MTHFR 677 or 1298 gene mutation:

- Autism
- Addictions: smoking, drugs, alcohol
- Down's syndrome
- Miscarriages
- Pulmonary embolisms
- Depression in Post-Menopausal Women
- Schizophrenia
- Fibromyalgia
- Chronic Fatigue Syndrome
- Chemical Sensitivity
- Parkinson's
- Irritable Bowel Syndrome
- Pre-eclampsia
- Stroke
- Spina bifida
- Esophageal Squamous cell carcinoma
- Acute Lymphoblastic Leukemia
- Vascular Dementia
- Bipolar disorder
- Colorectal Adenoma
- Idiopathic male infertility
- Blood clots
- Rectal cancer
- Meningioma
- Glioma
- Congenital Heart Defects
- Infant depression via epigenetic processes caused by maternal depression
- Deficits in childhood cognitive development
- Gastric Cancer
- Migraines with aura
- Low HDL
- High homocysteine
- Post-menopausal breast cancer
- Atherosclerosis
- Oral Clefts
- Type 1 Diabetes
- Epilepsy
- Primary Closed Angle Glaucoma
- Alzheimer's
- Tetralogy of Fallot
- Decreased telomere length
- Potential drug toxicities: methotrexate, anti-epileptics
- Cervical dysplasia
- Increased bone fracture risk in post-menopausal women
- Multiple Sclerosis
- Essential Hypertension
- Differentiated Thyroid Carcinoma
- Prostate Cancer
- Premature Death
- Placental Abruptio
- Myocardial Infarction (Heart Attack)
- Methotrexate Toxicity
- Nitrous Oxide Toxicity
- Heart Murmurs
- Tight Anal Sphincters
- Tongue Tie
- Midline Defects (many are listed above)
- Behcet's Disease
- Ischemic Stroke in Children
- Unexplained Neurologic Disease
- Asthma
- Shortness of Breath
- Bladder Cancer
- Anecephaly

For information on the importance of methylation

Methyl Cycle Genomics



Possible symptoms associated with A1298C MTHFR mutations:

- hypertension
- delayed speech
- muscle pain
- insomnia
- irritable bowel syndrome
- fibromyalgia
- chronic fatigue syndrome
- hand tremor
- memory loss
- headaches
- brain fog

Possible signs associated with A1298C MTHFR Mutations:

- elevated ammonia levels
- decreased dopamine
- decrease serotonin
- decreased epinephrine and norepinephrine
- decreased nitric oxide

- elevated blood pressure
- muscle tenderness
- ulcers
- pre-eclampsia

Possible conditions associated with A1298C MTHFR mutations:

- fibromyalgia
- chronic fatigue syndrome
- autism
- depression
- insomnia
- ADD/ADHD
- irritable bowel syndrome
- inflammatory bowel syndrome
- erectile dysfunction
- migraine
- Raynaud's
- cancer
- Alzheimer's
- Parkinson's
- recurrent miscarriages

Vitamin B-12

B-12 supplementation is necessary if you have decided to supplement with folate.

Others who need to supplement include those with elevated homocysteine and those who have genetic pernicious anemia, typically because of an MTHFR mutation. Supplementation of these two Bs in addition to what is in any multi-vitamin will have long term benefits for those who need extra. The typical daily dose is 1,000 mcg. (1 mg)

There are three types of B-12 available, cyanocobalamin, adenosyl-cobalamin and methylcobalamin. Most supplements contain cyanocobalamin. Adenosyl-cobalamin is also called dibenzocozide and is used by athletes for muscle building.

Methylcobalamin is indicated for mood disorders including depression, elevated homocysteine, Bell's Palsy, nerve disorders and demyelinating conditions. Loading dose is 1-5 mg. (1,000-5,000 mcg.) daily for 1-2 weeks. Maintenance is probably 1 mg 2-3 times a week. High doses taken chronically are not needed and not supportive of long-term health.

Another Look at Vitamin C- Pauling Was Right

Vitamin C is used by every cell in the body. Only man, primates, the guinea pig and several species of bats lack the ability to make their own vitamin C. All other animals, reptiles, birds and even fish make vitamin C as needed. They have an enzyme (acronym- GLO) that converts glucose into vitamin C as needed. The amounts animals

make are significantly higher than the amounts recommended by the RDA or the DRI for human sufficiency.

Studying vitamin C in animals, who make their own, shows steady and significant production throughout the day and night and when any stress occurs, physical such as illness or injury or mental such as being caged, transported, abused, or chased, production of vitamin C dramatically increases. As an example goats make the human equivalent of 13,000 mg daily, and significantly more when under stress.

The pituitary and adrenal glands have one of the highest contents of vitamin C. In healthy vitamin C producing animals cortisol production rises, stimulated by ACTH from the pituitary, when stressed and immediately thereafter production and increase of serum vitamin C. A sufficiency of vitamin C enhances the production of ACTH, cortisol and adrenaline (epinephrine) so that the initial response to stress is improved.

Among other benefits, cortisol and epinephrine allow more powerful punches or faster running from danger (fight or flight) and less inflammation with illness or injury. Chronic stress may lead to exhaustion of epinephrine production and elevated cortisol, over time having great downsides. The production and release of large amounts of vitamin C immediately following cortisol release rapidly reduces cortisol and epinephrine to within normal range, the pre-stressed state.^(428,429,430,431)

Excess cortisol or inappropriately timed cortisol will slow healing and when dysregulated contributes to anxiety and mood disorders, insulin resistance, obesity, metabolic syndrome, insomnia and fatigue.^(428,429,430,432)

A primary reason animals don't suffer from these conditions is because they make their own vitamin C. The post stress production of abundant vitamin C returns cortisol levels to within unstressed ranges. Humans also release vitamin C during stress but as tissue levels of C are depleted the ability to recover from stress is reduced and eventually lost.

How it works- I am stressed, my cortisol and epinephrine rise, I deal successfully with the stress, as my vitamin C rises (in humans not produced but taken from serum and tissue stores) I return to my healthy, normal, state- unstressed.

When daily intake of vitamin C is too low to replenish body stores the system fails.

If we do not make C and we do not take C, over time we can use up all available body stores and find ourselves with inappropriately elevated cortisol and lower epinephrine production and eventually in full adrenal exhaustion, little cortisol production remaining. Vitamin C not only balances cortisol and epinephrine but given in appropriate doses restores normal epinephrine and cortisol production.

The current concept of adrenal supplements, ginseng, or even cortisol supplementation fails to replenish that one important key to long term health, vitamin C.

While 60 mg., the current RDA, may keep us from scurvy it is possible we need more daily to attain and maintain optimal health and it is CERTAIN we need more when under stress, whether illness, injury, or mental/emotional threat..

Regarding body parts, vitamin C is necessary for the formation of healthy collagen which is a part of skin, hair, nails, ligaments, joints, tendons, discs, teeth, and bones. Adequate vitamin C protects our skin from wrinkles and from sun damage.⁽⁴³³⁾ It is vitamin C in the skin that is responsible for the lipid barrier function of the stratum corneum, a key to healthy aging skin, keeping it moist and supple.^(434,435,436)

A note here that exfoliation destroys this barrier and further damages your skin. A better choice is to use oral and topical vitamin C (in the Topical Formulas section page 237) to improve the health, look and feel of your skin.

Low ascorbate status is associated with gallstones and gallbladder disease.^(437,438,439,440,441) Increasing vitamin C intake increases bile production and absorption of the fat soluble vitamins and essential fatty acids. Vitamin C also decreases cholesterol by improving hydroxylation of cholesterol into hormone production and into bile acids.

A report in the Lancet, March 2001, stated those with the highest serum levels of vitamin C in their blood had one half the risk of death from all causes, including heart disease.

Dr. Kay Tee Khaw found that there was a decreased risk of infection and heart disease for those with higher levels of C in their blood.^(442,443,444) Dr. Khaw also participated in studies showing the protective effect of vitamin C in preventing diabetes, stroke, hypertension, lung disease, degenerative disc disease, osteoporosis and cancer.^(445,446,447,448,449,450,451,452)

Significant research suggests ascorbate status regulates rates of 'secretion' from saliva to cortisol to gastric juices. Ascorbates alter insulin secretion and oxytocin. Vitamin C normalizes production and release of epinephrine and norepinephrine. Dry mouth and dry eyes, dry mucous membranes in general, may be a consequence of insufficient vitamin C.^(453,454,455,456,457,458,459,460,461,462,463,464,465)

Vitamin C plays a primary role in hydroxylation reactions including vitamin D3 hydroxylation to the active 1,25(OH)₂D and the conversion of l-tryptophan to 5-hydroxytryptophan, the precursor to serotonin. Another such key hydroxylation includes that of cholesterol to pregnenolone and then to other hormones including testosterone and progesterone.

Vitamin C reduces histamine and has been used to treat histamine induced mood disorders.⁽⁴⁶⁶⁾ Its actions regarding increasing epinephrine, increasing 5-HTP/serotonin, lowering histamine and optimizing levels of active vitamin D suggest an amazing variety of functions all related to feeling good. Abundant intake of Vitamin C and C rich foods might make our world much less stressed and happier.

Recommended daily doses of C range from the RDA of 60 mg to 2,000 mg. It is unlikely less than 1,000 mg daily would ever supply basic needs. Higher doses may be beneficial for everyone at certain times or situations but may have adverse consequences in some persons and should not be used without knowing your need. If you are ill, recovering from surgery, bruise easily, are pregnant or nursing or have been diagnosed with any of the following diseases/conditions you may need higher levels of vitamin C for a shorter or longer period of time.

You will need more C if you drink excessive amounts of coffee or alcohol, are under extreme stress, have an infection of any kind, jet lag, or you are sunning in the summer. Your skin needs extra C to protect from the dark side of sunlight. Exposure to intense UV (both A and B) reduces the skin's vitamin C content and it must be restored.

Conditions that may indicate a need for high dose (greater than 2,000 mg daily) vitamin C- Allergies, asthma, diarrheal diseases including colitis, Crohn's disease, and IBS^(467,468,469,470,471,472), cataract^(473,474,475,476,477), heart disease⁽⁴⁷⁸⁾, hypertension^(479,480,481,482), Type II diabetes^(483,484), anemia, cavities^(485,486,487), periodontal disease^(455,488,489), ligament, tendon and joint degeneration⁽⁴⁹⁰⁾, osteoporosis⁽⁴⁹¹⁾, autoimmune disorders^(492,493,494,495,496), thyroid disease both hypothyroid and hyperthyroid⁽⁴⁹⁷⁾, and acute infections^(455,498,499,500).

Use of high dose vitamin C in chronic infections such as Lyme's disease or mycoplasma or Cell Wall Deficient bacteria associated with Chronic Fatigue, Rheumatoid Arthritis, Multiple Sclerosis, Sarcoidosis, hepatitis, herpes, and other chronic diseases of unknown origin is more controversial however with the new liposomal vitamin C (see below) it is both safe and affordable and excellent results have been reported..

In rare cases bowel tolerance levels (doses high enough to cause diarrhea) of C, ascorbic acid, have caused serious allergic reactions. Stopping high doses of C abruptly may cause rebound scurvy. Vitamin C works better when combined with bioflavonoids such as quercetin or rutin (about 500 mg of either daily). C is water soluble and is rapidly used or excreted whatever the form.

There is no evidence taking higher doses (greater than 2,000 mg daily) when you have no apparent need will protect you from disease or improve your health. There is significant evidence taking more vitamin C WHEN NEEDED will profoundly improve your health. Example: High dose vitamin C may not prevent you from getting a cold or flu but once ill, high doses will rapidly reduce symptoms and significantly shorten the length of time you are ill.⁽⁵⁰¹⁾

When antibiotics are needed to treat diseases, such as helicobacter pylori, the stomach ulcer bug, or chlamydia, the addition of vitamin C shows clinical significance in improvement/success of treatment.^(502,503,504)

Liposomal Vitamin C

A new delivery system has been developed to make taking higher doses of vitamin C easier and more affordable with no digestive side-effects (diarrhea).

When vitamin C is ingested about 19% is actually absorbed so a capsule or tablet of 1,000 mg would provide about 190 mg to your body. Liposomal vitamin C has absorption percentages ranging from 70-93% providing 700-930 mg per 1,000 mg of liposomal C, an increase of 50-75% more per dose.

Liposomes are phospholipid nano-encapsulations. Liposomes are being used in the cosmetic industry in skin care products to enhance delivery of nutraceuticals into the

skin and in the pharmaceutical industry to increase absorption of drugs, particularly antibiotics and chemotherapeutic medications.

Phosphatidylcholine and phosphatidylinositol (think lecithin granules) are able to emulsify, mix fat and water together. In liposomal vitamin C the water soluble vitamin C, typically sodium ascorbate, is absorbed into the phospholipid and then the solution undergoes a process, either sonication (sound waves) or pressurized membrane straining (somewhat like the reverse osmosis membrane), that breaks the vitamin C saturated phospholipids into smaller and smaller phospholipid encapsulated nanoparticles. This process, liposomal encapsulation, does three important things,

1. The phospholipid water/lipid solubility allows rapid and direct absorption from the small intestine into the liver and then into your blood.
2. The small size and water/lipid encapsulation allows for rapid absorption and delivery to body tissues and not just blood, the ultimate bioavailability, intracellular delivery, including the mitochondria, endoplasmic reticulum, and even the nucleus of cells. This improved delivery system not only increases the amount absorbed, it allows for serum elevations of ascorbate equivalent to intravenous vitamin C.

Studies show serum levels reached using oral liposomal C may be as effective as intravenous vitamin C in cancer treatment.^(505,506,507,508) This is especially important if you have a chronic illness or degenerative disease whether heart disease^(444,509,510,511,512,513) or osteoporosis or degenerative disc⁽⁵¹⁴⁾ or joint issues.

It should be clear that humans need and benefit from vitamin C and the only way we get it is from FRESH fruits and vegetables (vitamin C is rapidly lost when the fruit is no longer intact or is liquefied as in juice) or by taking vitamin C.

The minimum daily dose in my opinion is 1,000 mg of ascorbic acid twice a day. The split dose is because of the short half-life of C in serum. If using liposomal C the dose is 500-1,000 mg twice daily; a likely (not yet verified by serum samples) 2,500- 4,000 mg twice daily ascorbic acid equivalent. 1,000 mg liposomal C twice a day is even better.

Tissue Levels of Vitamin C

Getting enough vitamin C is truly important. A New Zealand study⁽⁵¹⁵⁾ published in December 2010 looked at **tissue levels** of vitamin C in mice bred to lack the enzyme gulono-lactone oxidase (GLO) needed to produce their own vitamin C (just like humans). The tissues of these mice were compared with tissues of 'wild-type' mice that make their own vitamin C.

The researchers knew serum levels of C tend to stay within a certain range even with increasing doses of vitamin C. They sought to discover what happens within tissues.

When vitamin C was withheld dramatic losses of vitamin C occurred rapidly in all tissues except the brain. This is similar to humans where the brain is the last organ to deplete C before full blown scurvy occurs. Even brain levels will drop if vitamin C is deficient for just two weeks.

What they learned is highly important for humans. To keep tissues and organs saturated (equal to the 'wild-type' mice who make their own C) required 5 times the amount of vitamin C needed to keep serum C normal. Tissue levels did not 'fill up' until the mice were consistently and regularly given much higher levels of vitamin C.

Serum C must be chronically saturated for tissue levels of vitamin C to reach that of animals making their own C. To achieve this goal two or more doses of vitamin C must be taken throughout the day, ideally with meals containing additional C and bioflavonoids.

Serum C does not and will NOT reflect tissue levels. What tissues? Every tissue, every cell in your body, skin, muscle, bone, teeth, pituitary, adrenals, eyes, heart, kidney, liver, ovaries, testes, and brain contain and require vitamin C.

Persons with Parkinson's, Huntington's and Alzheimer's have low levels of vitamin C in the brain.⁽⁵¹⁶⁾ It is VERY important how much C you have in your cells/tissues, not just in your blood. How much C we have in our eyes, stomach lining, pituitary, adrenals, arteries, all tissues, makes a profound difference in our short and long term health.^(517,518,519,520) Lower tissue levels of C are found in aging and diabetes as well as other conditions/diseases.

As with ALL nutrients the blood is the LAST place you will see a deficiency, all organs and tissues being depleted prior to appearance of inadequate serum values. If vitamin C is low in your blood you are truly, cellularly deficient. Even if serum C is maintained at high normal levels you may still have low tissue/organ levels.

If you have been under stress, whatever the cause, for an extended period of time it will take high doses of vitamin C over a period of time, 3, 6 or even 12 months, to restore tissue vitamin C status. Our cells don't replace as fast as those of GLO-deficient mice. Even with high dose supplementation some tissues of the genetically altered mice still had lower values than their 'wild-type', C producing cousins at the end of the study.

For most 2,000 mg of ascorbic acid twice a day or 1,000 mg of liposomal vitamin C twice a day will suffice IF you take higher doses when your situation indicates. Many will need initial saturation doses if they have been sub-clinically C insufficient for some period of time or following serious illness or injury.

New evidence- Vitamin C May be One Key to Preventing and Reversing Osteoporosis and Alzheimer's

In 2010 researchers at Baylor School of Medicine found vitamin C deficiency in mice genetically bred to have only one of two C producing enzymes resulted in profound bone loss.

<http://www.bcm.edu/news/item.cfm?newsID=2218>

HOUSTON -- (May 11, 2010) -- Vitamin C, or ascorbate, plays an important role in maintaining bone mass – promoting the balance between old bone resorption and new bone formation, said researchers from Baylor College of Medicine and Lexicon Pharmaceuticals in a report that appears online in the Journal of Biological Chemistry.

"The assumption is that everyone gets enough vitamin C in their diet," said Dr. Kenneth Gabbay, professor of pediatrics – molecular diabetes and metabolism at BCM.

"However, multiple studies of large groups of people show that higher intakes of vitamin C are associated with higher bone mass and lower fracture rates. **Our study shows that vitamin C or ascorbate is critical to maintaining the homeostasis necessary for healthy bone mass.**"...

Gabbay and his colleagues built on the fact that mice can actually synthesize vitamin C, an ability that is lacking in humans. They identified two enzymes critical to this process by providing the building material for vitamin C – aldehyde reductase and aldose reductase. Aldehyde reductase is responsible for 85 percent of vitamin C production and aldose reductase, the remaining 15 percent. Mice bred to lack both enzymes cannot make any vitamin C and develop scurvy, a condition that affects many organ systems including bone.

However, if mice lack only aldehyde reductase, they and their skeletons develop and grow normally on the 15 percent ascorbate or vitamin X generated through aldose reductase **until they face a stressor that requires more vitamin C, such as pregnancy or the loss of sex hormones that accompany menopause and aging.**

"Then they fall off a cliff and develop early profound osteoporosis," said Gabbay.

His studies (in mice) show that ascorbate or vitamin C both suppresses osteoclasts, which promote bone resorption, and stimulates the development of osteoblasts that make new bone, thus enhancing new bone formation. The constant renewal of bone is crucial to healthy bone architecture.

Many treatments for osteoporosis, including bisphosphonates such as Fosamax and Actonel, suppress the function of osteoclasts, and hence blocks bone resorption and mechanisms of bone repair. Unfortunately, these treatments do not stimulate osteoblast formation and new bone is not made. Many anti-oxidants such as resveratrol (found in red wine) and pycnogenol do the same thing. Only vitamin C affects both sides of the equation – osteoclast suppression and osteoblast development, said Gabbay.

Important as vitamin D, calcium

Most experts recommend vitamin D, calcium, exercise and bisphosphonates to keep bones healthy, said Gabbay.

"Vitamin C is never mentioned, whereas it's likely an equally important element for maintaining strong healthy bones" he said. "Our studies necessitate formal studies in patients to evaluate the usefulness of vitamin C therapy in susceptible populations."

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Vitamin C found to reduce amyloid plaques in mice with Alzheimer's disease
http://alzheimers.org.uk/site/scripts/news_article.php?newsID=1040

Published 19 August 2011

New research has found vitamin C may help prevent the formation of amyloid-beta protein clumps that typically build up in the brains of those with Alzheimer's disease. Researchers at Lund University in Sweden found mice with Alzheimer's symptoms had reduced amyloid plaques when given vitamin C. Although present in all brains, a precursor to the protein amyloid-beta is broken down in a different way in the brains of people with Alzheimer's disease which can lead to clump formation. Researchers used specific antibodies to investigate very small amounts of chemicals associated with these plaques in thin slices of tissue. Vitamin C was found to influence the formation of the small clumps that can become plaques in the brain that lead to late onset Alzheimer's disease.

Make sure you get a minimum of 2,000 mg ascorbic acid twice a day every day, more if you need it or have any of the problems mentioned above.

Vitamin D

D is another fat soluble vitamin. Vitamin D, like folate and vitamin A, is a key player in DNA replication and repair, and is considered to be protective as regards degenerative diseases. D has shown anti-oxidant qualities superior to vitamin E. Vitamin D is now considered a pro-hormone rather than a vitamin. Made by the action of UV-B on your skin, it plays a role in the regulation of every tissue and organ in the human body. Recent valuation of American's D status seemed to show more than 60% of us may be at risk for diseases associated with clinical or sub-clinical D deficiency.

A review in the American Journal of Clinical Nutrition in May of 1999 found that 4,000 IU of vitamin D daily **from all sources, sun, food and supplements**, was necessary before optimum levels of D appeared in the blood. Current accepted serum D values are outdated and may mark sub-clinical deficiency of D associated with osteoporosis, hypertension, diabetes, and obesity.

The ability of the sun to form vitamin D on our skin is based on season and latitude as well as skin type. The higher latitudes, 30^o and above, require supplementation from food or supplements to achieve optimal levels. Putting your face and arms in the sun for 20 minutes between 10AM and 2PM will not produce optimal levels and before 10AM and 2PM none at all. See the end of this workbook for sunning guidelines.

Most persons can safely supplement with 800-2,000 IU but test to make sure this is enough and not too much. Too much D is toxic (building over time so check every year) and precipitates bone loss and deposition of calcium in soft tissues such as arteries.

Vitamin D and vitamin A as retinoic acid moderate DNA gene transcription along with thyroid and the sex hormones. The balance between D and A is critical. Unfortunately little research is available to help determine what the balance is likely to be. Currently the best guess is for each 10,000 IU of vitamin A (food or supplements) about 1,000-3,000 IU of D is needed, from supplements or sunlight.

It is better to have too little of both A and D or too much of both than high amounts of just one. Elevated vitamin A may cause a relative vitamin D deficiency and elevated vitamin D may cause a relative vitamin A deficiency.

Vitamin E

E is fat-soluble and must have fat and adequate bile for absorption. Vitamin E is an excellent anti-oxidant but **not much is needed if you avoid rancid and processed oils**. Read the section on fats and oils carefully. The usual dose is 100-200 IU. Some sources suggest 400 IU or more but excess vitamin E is NOT beneficial.

Doses of 900-1,000 IU and higher have been implicated in fatigue syndromes and respiratory insufficiency. Do not use a total, combined, supplemental dose higher than 400 IU. High doses of vitamin E lower vitamin K, not a good thing.

A typical dose is 100-200 IU d'alpha plus mixed tocopherols and is usually adequate. Vitamin E works with vitamin C.^(521,522,523)

Vitamin K, Anti-oxidant Extraordinaire

Needed to protect Omega-3, your heart and your bones.

A typical breakfast in Tokyo, Japan contains natto, fish, rice and pickles. Natto is high in vitamin K. The fish contains vitamin K, vitamin D, omega-3, minerals and amino acids. The pickle improves digestion. In all traditional cultures the daily diet contains protein, dark greens and some fermented food from natto to yogurt to fermented cabbage. This wide variety assures adequate nutrition from fresh whole foods. Without this natural balance nutritional deficiencies are inevitable.

Vitamin K is a fat-soluble vitamin found in dark green leafy foods and naturally fermented foods. The symbol K is used for potassium on the periodic chart. We are not talking about potassium here, but a vitamin. Vitamin K1 is phylloquinone, found in plants. Vitamin K2, menaquinone, is found in animals and made in the human gut by 'good' bacteria. Antibiotics destroy our ability to make K in the gut. Probiotics like acidophilus restore gut K production. There is some evidence that natural gut production is not enough to support artery and bone health. Dietary sources are critical.

Vitamin K reverses postmenopausal bone loss by keeping calcium in the bone where it belongs, working better than Fosamax. Low levels of vitamin K lead to under-carboxylated calcium forming plaque in the arteries in heart disease. K is necessary for the formation of osteocalcin a bone builder. It is intimately related to the functions and actions of vitamin D. Vitamin K is an effective anti-oxidant in the cell membrane and necessary for normal blood clotting.

Large doses of the naturally occurring K1 and K2, up to 45 mg daily, have been given with few side effects. Vitamin K, found in dark green leafy vegetables, seaweeds and animal livers, does not 'over' coagulate the blood. Adequate vitamin K normalizes fragile membranes. It has proven useful preventing or correcting easy bruising, varicose veins and 'spider' veins. Vitamin K does not make blood thicker or 'stickier'. K toxicity has occurred in infants given vitamin K3 (not a natural form of K) by injection. In research only the analog 'man-made' K3 has shown toxicity.

If you are on a blood thinning medication, such as Coumadin or aspirin or other non-steroidal anti-inflammatory, you must discuss K supplementation or consumption from foods with your physician.

Research demonstrates a high intake of fat, whether omega-3, omega-6, omega-9 or saturated fat, dramatically increases the need for vitamins E and K. In animals given diets high in omega-3, omega-6, omega-9 or saturated fat, liver content of vitamin K was reduced to 1/5 of controls (normal chow diet).

The tendency of blood to coagulate more slowly or a reduction in blood platelets is often a side effect of using omega-3 fatty acids and may occur when eating a diet high in fatty fish. Normalizing levels of vitamin K with high vitamin K foods or a vitamin K supplement reverses both of these tendencies.

In the US vitamin E supplementation is common. Most health food store multiples contain 200-400 IU per daily dose. Higher levels of E have a reverse effect. In fact, high levels of E actually reduce levels of vitamin K, not a good idea for postmenopausal women needing to keep or rebuild bone or heart patients using omega-3 and vitamin K to prevent or reverse arteriosclerosis.

Finding vitamin K is much harder, whether in foods or in a supplement. The DRI is 90 mcg. but just 1 mg (1,000 mcg) has reversed bone loss in post-menopausal women, reducing urinary calcium loss by 25% within a few days of starting supplementation.

10 mg (10,000 mcg) of vitamin K daily has been used by our space program to prevent bone loss in astronauts during weightlessness.

A study published April 2001 in *Kardiologie* correlated low levels of vitamin K to under-carboxylated MGP (a protein that reflect artery health). The conclusion? Low levels of K allow calcium to leave the bone, not be delivered to the bone, and promote the deposition of calcium in soft tissues. They suggest a minimum of 900 mcg, almost 1 mg., to prevent deposition of calcium in arteries.

More recently studies suggest vitamin K may normalize insulin response and prevent metabolic disease.^(524,525,526,527,528)

Vitamin K works **with** vitamin D (both are equally important) to prevent bone loss and build new bone. It also influences blood sugar levels and adult onset diabetes. **Low vitamin K contributes to post meal hyperinsulinemia (high insulin) and insulin resistance.**

We do make some, but unlikely enough, vitamin K in our guts if we have normal bowel flora (the 'good' gut bugs, they make the K for us) and normal bowel function. Constipation, diarrhea, IBS or Crohn's would all indicate a problem with vitamin K, either making it or absorbing it. Dietary fiber (soluble fiber) helps the 'good' gut bacteria thrive so soluble fibers, found in high fiber foods like berries, figs and some legumes, will increase vitamin K if the gut bugs are right.

Vitamin K is found in very dark green leafy vegetables like chard, spinach, bok choy and seaweeds such as dulse. It is also found in cod liver oil, beef and poultry livers. To

be absorbed it must be consumed with fat. Fat-free vegetables for dinner, no K absorbed, but with a little added butter or olive oil on your greens, the K is very well absorbed. Wrapping seafood based sushi in seaweed gives a meal high in vitamin K and omega-3, both well absorbed. This rule, regarding the need for fats to absorb, is also true of 'green drinks or carrot juice'. Unless you add fat to your drink, such as coconut milk, or have some with it (not later) the important fat-soluble nutrients will pass you by.

Vitamins A, D and E also need fat for absorption. Since they are usually found in a fat containing supplement (cod liver oil) or in fats found in animal or poultry livers, butter, full-fat dairy and such, absorption is usually not a problem. Our modified 'low-fat' or 'no fat' diets are un-natural and rob us of the very important fat-soluble vitamins, A, D, E and K. Absorption of calcium, A and D from non-fat milk is poor.

Who Needs Supplemental Vitamin K?

- Anyone taking the suggested amounts of omega-3 ⁽⁵²⁹⁾
- Anyone on a high fatty fish diet
- Anyone with osteoporosis or beginning bone loss (vitamin K works as well or better than Fosamax to retain bone) ^(530,531,532,533)
- Anyone with diabetes, Type I or Type II ^(534,535,536)
- Anyone with Hyperinsulinemia/Metabolic Syndrome (Syndrome X, obesity, hypertension, heart) ^(524,525,526,527,528)
- Anyone with gut problems, IBS, celiac or Crohn's or other malabsorption condition including removal of their gallbladder ^(537,538,539)
- Anyone with heart disease or a family history of heart disease ^(540,541)
- Anyone with calcification of joints, arteries or kidney. ^(542,543)
- Post-menopausal women ^(532,544,545,546)

While the DRI for vitamin K is 90 micrograms (0.090 milligrams) there is no UL (upper limit of safety) and up to 45 mg have been given daily to treat osteoporosis. 1 mg. of vitamin K is a physiologic amount, meaning you could get this much from food if using dark greens and naturally fermented products. There is no reason to take higher doses. More is not better.

A minimum dose of 1 mg. daily is protective for both bone and heart. ^(533,542,547,548,549,550)
Remember to take your fat-soluble vitamins, A, D, E and K, with the meal highest in fat or with your daily dose of fish oil or cod liver oil.

Few supplement companies make a vitamin K supplement in a useful 'dose'. Most are too high or too low for daily use or contain the wrong type of K.

Complementary Prescriptions makes a 1.5 mg vitamin K complex at a reasonable cost. This dose is both safe and effective, just one small capsule daily. Order from <http://cpmedical.net> or call 888-401-1105 and use my pin number 230288. The product code is CP1091. Make sure you get the right product, 1.5 mg NOT the 15 mg product. Life Extension Foundation also makes a mixed vitamin K called Super K. Dose is 1 per day taken with a meal containing fat (for absorption).

Other vitamin K supplements, such as Solgar and Solaray, contain 100 mcg (0.100 mg). To get the bare minimum, 1 mg, the smallest amount shown successful in the studies, would require a minimum of 10 pills per day.

2005 studies support earlier studies showing benefit for children's bones, post-menopausal bones, and reduction in heart disease. Recent studies also show that dietary intake in the US is not adequate. ^(551,552,553,554,555,556,557,558,559,560,561,562,563,564,565,566)

Vitamin K Studies

Adams, J. and Pepping, J. 8-1-2005 *Am.J.Health Syst.Pharm.* 62 1574-1581 **Vitamin K in the treatment and prevention of osteoporosis and arterial calcification**

*PURPOSE: The role of vitamin K in the prevention and treatment of osteoporosis and arterial calcification is examined. SUMMARY: Vitamin K is essential for the activation of vitamin K-dependent proteins, which are involved not only in blood coagulation but in bone metabolism and the inhibition of arterial calcification. In humans, vitamin K is primarily a cofactor in the enzymatic reaction that converts glutamate residues into gamma-carboxyglutamate residues in vitamin K-dependent proteins. Numerous studies have demonstrated the importance of vitamin K in bone health. The results of recent studies have suggested that concurrent use of menaquinone and vitamin D may substantially reduce bone loss. Menaquinone was also found to have a synergistic effect when administered with hormone therapy. Several epidemiologic and intervention studies have found that vitamin K deficiency causes reductions in bone mineral density and increases the risk of fractures. Arterial calcification is an active, cell-controlled process that shares many similarities with bone metabolism. Concurrent arterial calcification and osteoporosis have been called the "calcification paradox" and occur frequently in postmenopausal women. **The results of two dose-response studies have indicated that the amount of vitamin K needed for optimal gamma-carboxylation of osteocalcin is significantly higher than what is provided through diet alone** and that current dosage recommendations should be increased to optimize bone mineralization. Few adverse effects have been reported from oral vitamin K. CONCLUSION: Phytonadione and menaquinone may be effective for the prevention and treatment of osteoporosis and arterial calcification*

Amizuka, N., Li, M., and Maeda, T. 2005 *Clin.Calcium* 15 57-61 **[The interplay of magnesium and vitamin K2 on bone mineralization]**

Magnesium (Mg) is most likely restored in bone matrix, implicating a pivotal role in bone mineralization. Mg-insufficient bone reveals fragility to mechanical loading despite normal or higher levels of bone mineral content, permitting stimulated osteoclastic bone resorption. In contrast, vitamin K(2) (MK-4:menatetrenone) inhibited osteoclastic bone resorption stimulated by the Mg-insufficiency, thereby normalizing bone remodeling. The Mg-insufficiency caused an increased concentration of calcium, which resulted in an extremely-high purity of hydroxyapatite (HA) crystal [Ca(10)(PO(4))(6)(OH)(2)] and accelerated mineralization in bone. In contrast, MK-4 did not affect the calcium-concentration nor HA-purity, but repressed mineralization accelerated by Mg-insufficiency. Thus, MK-4 appears to recover the "bone quality" lessened by the Mg-insufficiency by two mechanisms; controlling bone turnover and mineralization

Nutr Rev 1998 Aug;56(8):223-30 **The vitamin K-dependent proteins: an update. Ferland G.** Universite de Montreal, Department of Nutrition, Quebec, Canada.

Historically known for its role in blood coagulation, vitamin K also has been shown to be required for the physiologic activation of numerous proteins that are not involved in hemostasis. Over the

last 20 years, vitamin K-dependent proteins have been isolated in bone, cartilage, kidney, atheromatous plaque, and numerous soft tissues. Although the precise mechanism of action of many of these proteins remains to be determined, their discovery has proven important from a physiologic point of view.

Zeitschrift für Kardiologie **Abstract Volume 90 Issue 15 (2001) pp III57-III63 Role of vitamin K and vitamin K-dependent proteins in vascular calcification** L.J. Schurgers, P.E.P. Dissel, H.M.H. Spronk, B.A.M. Soute, C.R. Dhore, J.P.M. Cleutjens, C. Vermeer Department of Biochemistry, Maastricht University, P. O. Box 616, 6200 MD Maastricht, The Netherlands, E-mail: c.vermeer@bioch.unimaas.nl

Summary Objectives. To provide a rational basis for recommended daily allowances (RDA) of dietary phylloquinone (**vitamin K₁**) and menaquinone (**vitamin K₂**) intake that adequately supply extrahepatic (notably **vascular**) tissue requirements. **Background.** **Vitamin K** has a key function in the synthesis of at least two proteins involved in calcium and bone metabolism, namely osteocalcin and matrix Gla-protein (MGP). MGP was shown to be a strong inhibitor of **vascular** calcification. Present RDA values for **vitamin K** are based on the hepatic phylloquinone requirement for coagulation factor synthesis. Accumulating data suggest that extrahepatic tissues such as bone and vessel wall require higher dietary intakes and have a preference for menaquinone rather than for phylloquinone. **Methods.** Tissue-specific **vitamin K** consumption under controlled intake was determined in warfarin-treated rats using the **vitamin K**-quinone/epoxide ratio as a measure for **vitamin K** consumption. Immunohistochemical analysis of human **vascular** material was performed using a monoclonal antibody against MGP. The same antibody was used for quantification of MGP levels in serum. **Results.** At least some extrahepatic tissues including the arterial vessel wall have a high preference for accumulating and using menaquinone rather than phylloquinone. Both intima and media sclerosis are associated with high tissue concentrations of MGP, with the most prominent accumulation at the interface between **vascular** tissue and calcified material. This was consistent with increased concentrations of circulating MGP in subjects with atherosclerosis and diabetes mellitus. **Conclusions.** This is the first report demonstrating the association between MGP and **vascular** calcification. **The hypothesis is put forward that undercarboxylation of MGP is a risk factor for vascular calcification and that the present RDA values are too low to ensure full carboxylation of MGP.**

Journal of orthopaedic Science **Abstract Volume 5 Issue 6 (2000) pp 546-551 Effect of combined administration of vitamin D₃ and vitamin K₂ on bone mineral density of the lumbar spine in postmenopausal women with osteoporosis** Jun Iwamoto (1), Tsuyoshi Takeda (1), Shoichi Ichimura (2)(1) Department of Sports Clinic, Keio University School of Medicine, 35 Shinanomachi, Shinjuku-ku, Tokyo 160-8582, Japan (2) Department of orthopaedic Surgery, National Defense Medical College, 3-2 Namiki, Tokorozawa, Saitama 359-8513, Japan Received: January 13, 2000 / Accepted: June 5, 2000

Abstract The effect of the combined administration of **vitamin D₃** and **vitamin K₂** on bone mineral density (BMD) of the lumbar spine was examined in postmenopausal women with **osteoporosis**. Ninety-two osteoporotic women who were more than 5 years after menopause, aged 55-81 years, were randomly divided into four administration groups: **vitamin D₃** (1α-hydroxyvitamin D₃, 0.75 μ g/day) (D group; n = 29), **vitamin K₂** (menatetrenone, 45 mg/day) (K group; n = 22), **vitamin D₃** plus **vitamin K₂** (DK group, n = 21), and calcium (calcium lactate, 2 g/day) (C group; n = 20). BMD of the lumbar spine (L2-L4) was measured by dual energy X-ray absorptiometry at 0, 1, and 2 years after the treatment started. There were no significant differences in age, body mass index, years since menopause, and initial BMD among the four groups. One-way analysis of variance (ANOVA) with repeated measurements showed a significant decrease in BMD in the C group ($P < 0.001$). Two-way ANOVA with repeated measurements showed a significant increase in BMD in the D and K groups compared with that in the C group ($P < 0.05$ and $P < 0.001$, respectively), and a significant increase in BMD in the DK group compared with that in the C, D, and K groups ($P < 0.0001$, $P < 0.05$ and $P < 0.01$,

respectively). These findings indicate that combined administration of **vitamin D₃** and **vitamin K₂**, compared with calcium administration, appears to be useful in increasing the BMD of the lumbar spine in postmenopausal women with **osteoporosis**.

Osteoporosis International **Abstract Volume 12 Issue 8 (2001) pp 680-687 1,25-Dihydroxyvitamin D₃ Promotes Vitamin K₂ Metabolism in Human Osteoblasts** N. Miyake (1), K. Hoshi (1), Y. Sano (2), K. Kikuchi (2), K. Tadano (2), Y. Koshihara (1) (1) Department of Nutrition, Tokyo Metropolitan Institute of Gerontology, Tokyo, Japan (2) Tsukuba Research Laboratories, Eisai Co. Ltd., Tsukuba, Japan Received: 20 September 2000 / Accepted: 19 February 2001

Abstract. It has been reported that **vitamin K₂** (menaquinone-4) promoted 1,25-dihydroxyvitamin D₃ (1,25(OH)₂D₃)-induced mineralization and enhanced γ -carboxyglutamic acid (Gla)-containing osteocalcin accumulation in cultured human osteoblasts. In the present study, we investigated whether menaquinone-4 (MK-4) was metabolized in human osteoblasts to act as a cofactor of γ -glutamyl carboxylase. Both conversions of MK-4 to MK-4 2,3-epoxide (epoxide) and epoxide to MK-4 were observed in cell extracts of cultured human osteoblasts. The effect of 1,25(OH)₂D₃ and warfarin on the **vitamin K** cycle in cultured osteoblasts was examined. With the addition of 1 nM 1,25(OH)₂D₃ or 25 μ M warfarin in cultured osteoblasts, the yield of epoxide from MK-4 increased. However, the conversion of epoxide to MK-4 was strongly inhibited by the addition of warfarin (2.5-25 μ M), whereas it was almost not inhibited by 1,25(OH)₂D₃ (0.1-10 nM). To clarify the mechanism for this phenomenon, a cell-free assay system was studied. Osteoblast microsomes were incubated with 10 μ M epoxide in the presence or absence of warfarin and 1,25(OH)₂D₃. Epoxide reductase, one of the enzymes in the **vitamin K** cycle was strongly inhibited by warfarin (2.5-25 μ M), whereas it was not affected by 1,25(OH)₂D₃ (0.1-1 nM). Moreover, there was no effect of pretreatment of osteoblasts with 1 nM 1,25(OH)₂D₃ on the activity of epoxide reductase. However, the activity of epoxidase, that is the γ -glutamyl carboxylase was induced by the pretreatment of osteoblasts with 1 nM 1,25(OH)₂D₃. In the present study, it was demonstrated that the **vitamin K** metabolic cycle functions in human osteoblasts as well as in the liver, the post-translational mechanism, by which 1,25(OH)₂D₃ caused mineralization in cooperation with **vitamin K₂** was clarified.

Calcif Tissue Int 59:352-356 (1996) © Springer-Verlag New York, Inc. 1996 **Vitamin K Status and Bone Mass in Women With and Without Aortic Atherosclerosis: A Population-Based Study** K.-S. G. Jie, M. L. Bots, C. Vermeer, J. C. M. Witteman, D. E. Grobbee

Abstract γ -Carboxyglutamate (Gla) is an uncommon amino acid formed by **vitamin K** action. Increasing evidence indicates that Gla-proteins are involved in the regulation of calcification processes in both bone tissue and atherosclerotic vessel wall. In a population-based study we have previously shown that in a group of 113 postmenopausal women the presence of abdominal aortic calcifications is associated with a reduced **vitamin K** status. In the present study we investigated whether this reduced **vitamin K** status was also associated with differences in bone mass or circulating calciotropic hormone levels. Serum immunoreactive osteocalcin with low affinity for hydroxyapatite (irOC_{free}) was used as a marker for **vitamin K** status. After correction for age it was found that women with atherosclerotic calcifications had a 7% lower bone mass as measured by metacarpal radiogrammetry (mean difference: 3.2 mm², 95% CI: -0.2-6.5, P = 0.06). No differences between both groups of women were observed for serum intact parathyroid hormone (PTH) and serum 25-hydroxyvitamin D levels. In the atherosclerotic women (n = 34), markers for **vitamin K** status were inversely associated with bone mass (r = -0.47, P = 0.013), whereas no such association was found in the nonatherosclerotic women (n = 79). It is concluded that the atherosclerotic women in this study may be at higher risk for osteoporotic fractures as evidenced by their lower bone mass and higher serum irOC_{free} levels. The finding that in atherosclerotic women **vitamin K** status is

associated with bone mass supports our hypothesis that **vitamin K** status affects the mineralization processes in both bone and in atherosclerotic plaques.

Calcif Tissue Int 65:285-289 (1999) © 1999 by Springer-Verlag New York, Inc. **The Effect of Vitamin K and D Supplementation on Ovariectomy-Induced Bone Loss** S. Matsunaga, H. Ito, T. Sakou

Abstract This study was designed to assess the effect of **vitamin K** and D supplementation on ovariectomy-induced bone loss. Female Sprague-Dawley rats aged 8-9 months were ovariectomized (OVX) or sham operated and divided into five experimental groups: (1) ovariectomy (OVX), (2) OVX plus **vitamin K** supplementation, (3) OVX plus **vitamin D** supplementation, (4) OVX plus **vitamin K** and **vitamin D** supplementation, and (5) sham operation. The trabecular bone area was estimated by bone histomorphometry by microradiography and histological examination. Bone loss in OVX plus **vitamin K** and **vitamin D** group was significantly reduced at both 7 and 14 weeks compared with the OVX group. No significant bone loss in OVX plus **vitamin K** or OVX plus **vitamin D** groups was found. A similar effect of **vitamin K** and D supplementation on ovariectomy-induced bone loss was recognized in histological examination. Our findings indicate that vitamins **K** and **D** may have a synergistic effect on reducing bone loss. This is valuable information for the treatment of bone loss in postmenopausal women with osteoporosis.

Calcif Tissue Int 59:466-473 (1996) © Springer-Verlag New York, Inc. 1996 **Vitamin K₂ Promotes 1 α ,25(OH)₂ Vitamin D₃-Induced Mineralization in Human Periosteal Osteoblasts** Y. Koshihara, K. Hoshi, H. Ishibashi, M. Shiraki

Abstract The effect of **vitamin K** on mineralization by human periosteal osteoblasts was investigated in the absence and presence of 1 α ,25 dihydroxyvitamin D₃ (1,25(OH)₂D₃). **Vitamin K₁** and **K₂**, but not **K₃**, at 2.5 μ M enhanced *in vitro* mineralization when cells were cultured with **vitamin K** for 20 days after reaching confluence *in vitro*. **Vitamin K₂** (2-methyl-3-all-trans-tetraphenyl-1,4-naphthoquinone : menatetrenone) was the most potent of these **vitamin K** analogs; it slightly inhibited alkaline phosphatase (ALP) activity. Human osteoblasts were mineralized and showed the enhanced ALP activity on treatment with 10⁻⁹ M of 1,25(OH)₂D₃ for 20 or 25 days after confluence. **Vitamin K₂** promoted the 1,25(OH)₂D₃-induced mineralization, but slightly inhibited the 1,25(OH)₂D₃-induced ALP activity. Moreover, **vitamin K₂** enhanced the 1,25(OH)₂D₃-induced osteocalcin accumulation in the cells and the extracellular matrix (cell layer), but inhibited the osteocalcin content in the medium produced by the 1,25(OH)₂D₃ treatment. However, **vitamin K₂** alone did not induce osteocalcin production in the human osteoblasts. On Northern blot analysis, osteocalcin mRNA expression on 1,25(OH)₂D₃-treated cells was enhanced by **vitamin K₂** treatment, but **vitamin K₂** alone did not induce osteocalcin mRNA expression. Warfarin blocked both the 1,25(OH)₂D₃-induced osteocalcin production and the accumulation in the cell layer, and also blocked the 1,25(OH)₂D₃ plus **vitamin K₂**-induced osteocalcin production and the accumulation in the cell layer. The 1,25(OH)₂D₃-induced mineralization promoted by **vitamin K₂** was probably due to the enhanced accumulation of osteocalcin induced by **vitamin K₂** in the cell layer. However, we concluded that the mineralization induced by **vitamin K₂** alone was due to the accumulation of osteocalcin in bovine serum on the cell layer, since osteocalcin extracted from the cell layer was not identified by specific antiserum against human osteocalcin, which does not cross-react with bovine osteocalcin. These results suggest that the mechanism underlying the mineralization induced by **vitamin K₂** in the presence of 1,25(OH)₂D₃ was different from that of **vitamin K₂** alone, and that osteocalcin plays an important role in mineralization by osteoblasts *in vitro*.

Crit Rev Food Sci Nutr 2001 May;41(4):225-49 **Delay of natural bone loss by higher intakes of specific minerals and vitamins.** Schaafsma A, de Vries PJ, Saris WH. Friesland Coberco

Dairy Foods, Dep. of Research & Development Leeuwarden, The Netherlands.
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For early prevention or inhibition of postmenopausal and age-related bone loss, nutritional interventions might be a first choice. For some vitamins and minerals an important role in bone metabolism is known or suggested. Calcium and vitamin D support bone mineral density and are basic components in most preventive strategies. Magnesium is involved in a number of activities supporting bone strength, preservation, and remodeling. Fluorine and strontium have bone-forming effects. However, high amounts of both elements may reduce bone strength. Boron is especially effective in case of vitamin D, magnesium, and potassium deficiency. Vitamin K is essential for the activation of osteocalcin. Vitamin C is an important stimulus for osteoblast-derived proteins. Increasing the recommended amounts (US RDA 1989), adequate intakes (US DRI 1997), or assumed normal intakes of mentioned food components may lead to a considerable reduction or even prevention of bone loss, especially in late postmenopausal women and the elderly.

Clin Endocrinol (Oxf) 2001 Feb;54(2):219-24 **Effect of vitamin K and/or D on undercarboxylated and intact osteocalcin in osteoporotic patients with vertebral or hip fractures.** Takahashi M, Naitou K, Ohishi T, Kushida K, Miura M. Department of orthopaedic Surgery, Hamamatsu University School of Medicine, Hamamatsu, Japan. taka1m@hama-med.ac.jp

OBJECTIVE: To examine serum undercarboxylated osteocalcin (OC) with application of an ELISA in normal women and in osteoporotic patients with vertebral fractures or hip fractures, and to investigate the effects of vitamin K and/or D treatment on undercarboxylated OC and intact OC in vertebral fractures. **PATIENTS:** They were 43 premenopausal (PRE) and 48 postmenopausal healthy females (POST), 89 osteoporotic patients with vertebral fractures (VX) and, 24 patients with hip fracture (HX). **MEASUREMENTS:** Intact OC was measured by an IRMA and undercarboxylated OC was measured by an ELISA. **RESULTS:** Intact osteocalcin was significantly higher in POST and VX than in PRE, and was significantly lower in HX than in POST and VX. Undercarboxylated OC tended to be higher in POST, VX and HX than in PRE, but not significantly. The ratio of undercarboxylated OC to intact OC was significantly higher in HX than in POST and in VX. After 4 weeks treatment with K, D, and K + D to 56 VX, undercarboxylated OC decreased significantly in the groups with K and K + D. Intact OC tended to increase slightly in the groups given K, D, K + D, but not significantly so. Vitamin K and vitamin K + D markedly decreased the ratio of undercarboxylated/intact OC to approximately 80%. On the other hand, vitamin D did not decrease that ratio. **CONCLUSIONS:** There was a disproportion of undercarboxylated osteocalcin to intact osteocalcin between postmenopausal women and osteoporotic patients with vertebral fractures or hip fractures. Vitamin K did decrease undercarboxylated osteocalcin, vitamin D did not change undercarboxylated osteocalcin, and vitamin D did not enhance the effect of vitamin K on undercarboxylated osteocalcin.

J orthop Sci 2000;5(6):546-51 **Effect of combined administration of vitamin D3 and vitamin K2 on bone mineral density of the lumbar spine in postmenopausal women with osteoporosis.** Iwamoto J, Takeda T, Ichimura S. Department of Sports Clinic, Keio University School of Medicine, 35 Shinanomachi, Shinjuku-ku, Tokyo 160-8582, Japan.

The effect of the combined administration of vitamin D3 and vitamin K2 on bone mineral density (BMD) of the lumbar spine was examined in postmenopausal women with osteoporosis. Ninety-two osteoporotic women who were more than 5 years after menopause, aged 55-81 years, were randomly divided into four administration groups: vitamin D3 (1alpha hydroxyvitamin D3, 0.75 microg/day) (D group; n = 29), vitamin K2 (menatetrenone, 45 mg/day) (K group; n = 22), vitamin

D3 plus vitamin K2 (DK group, n = 21), and calcium (calcium lactate, 2 g/day) (C group; n = 20). BMD of the lumbar spine (L2-L4) was measured by dual energy X-ray absorptiometry at 0, 1, and 2 years after the treatment started. There were no significant differences in age, body mass index, years since menopause, and initial BMD among the four groups. One-way analysis of variance (ANOVA) with repeated measurements showed a significant decrease in BMD in the C group ($P < 0.001$). Two-way ANOVA with repeated measurements showed a significant increase in BMD in the D and K groups compared with that in the C group ($P < 0.05$ and $P < 0.001$, respectively), and a significant increase in BMD in the DK group compared with that in the C, D, and K groups ($P < 0.0001$, $P < 0.05$ and $P < 0.01$, respectively). These findings indicate that combined administration of vitamin D3 and vitamin K2, compared with calcium administration, appears to be useful in increasing the BMD of the lumbar spine in postmenopausal women with osteoporosis.

Maturitas 1999 Jan 4;31(2):161-4 **A longitudinal study of the effect of vitamin K2 on bone mineral density in postmenopausal women a comparative study with vitamin D3 and estrogen-progestin therapy.** Iwamoto I, Kosha S, Noguchi S, Murakami M, Fujino T, Douchi T, Nagata Y. Department of Obstetrics and Gynecology, Faculty of Medicine, Kagoshima University, Japan.

OBJECTIVES: To investigate the effect of vitamin K2 treatment for a year on spinal bone mineral density (BMD) in postmenopausal women, comparing with vitamin D3 hormone replacement therapy and to determine the factors which affect the efficacy of vitamin K2 therapy. **SUBJECTS and METHODS:** Seventy-two postmenopausal women were randomized into four groups and treated with respective agents. Before the therapy, 6 and 12 months after the treatment, their lumbar spine BMD were measured by dual energy X-ray absorptiometry. The rates of change in BMD (delta BMD) were calculated. Correlations of BMD with age, year since menopause and the initial BMD were determined. **RESULTS:** Vitamin K2 suppressed the decrease in spinal BMD as compared with no treatment group. BMD in women treated with vitamin K2 was inversely correlated with their age ($r = -0.54$; $P < 0.05$). **CONCLUSIONS:** Vitamin K2 therapy may be a useful method for preventing postmenopausal spinal bone mineral loss. In addition, the therapy should be started early in postmenopausal period.

Nippon Ronen Igakkai Zasshi 1996 Apr;33(4):240-4 **[Recent progress in treatment of osteoporosis]** Hosoi T. Department of Geriatrics, Faculty of Medicine, University of Tokyo, Japan.

Osteoporosis is a multifactorial disease. Understanding the genetic and environmental background of this disease is essential for prevention and treatment. We examined the relationship between polymorphisms of the estrogen receptor gene, bone mineral density, and markers of bone metabolism in postmenopausal women. Restriction fragment length polymorphisms of the estrogen receptor (ER) gene and its relation to bone mineral density were examined in 238 postmenopausal healthy women (66.7 +/- 0.9 yr, mean +/- standard error of the mean) in Japan. In those with the PPxx genotype, Z score values of bone mineral density were significantly lower than those for other genotypes (lumbar spine; $p = 0.005$, total body; $p = 0.013$). Dinucleotide repeat polymorphisms in the upstream region of ER gene were related to bone mineral density and to bone metabolic markers. These data suggest that some variation of the ER gene linked to these genetic markers is associated with the pathogenesis of postmenopausal osteoporosis. In addition, we focused on the role of vitamin K as a nutritional factor for bone metabolism. Japanese fermented beans, Natto, contain large amounts of vitamin K2. We found a significant positive correlation between the level of vitamin K2 in serum and the habit of eating Natto in postmenopausal women in the Toyo area. Natto may contribute to the prevention of osteoporosis.

J Nutr 1996 Apr;126(4 Suppl):1187S-91S **Effects of vitamin K on bone mass and bone metabolism.** Vermeer C, Gijsbers BL, Craciun AM, Groenen-van Dooren MM, Knapen

MH.Department of Biochemistry and Cardiovascular Research Institute Maastricht, University of Limburg, The Netherlands.

Vitamin K is involved in blood coagulation and in bone metabolism via the carboxylation of glutamate residues in (hepatic) blood coagulation factors and (osteoblastic) bone proteins. The bioavailability of nutritional vitamin K depends on the type of food, the dietary fat content, the length of the aliphatic side chain in the K-vitamer and probably also the genetically determined polymorphism of apolipoprotein E. Although undercarboxylation of blood coagulation factors is very rare, undercarboxylated osteocalcin (bone Gla-protein) is frequently found in postmenopausal women. Supplementation of these women with extra vitamin K causes the markers for bone formation to increase. In parallel, a decrease of the markers for bone resorption is frequently seen. Insufficient data are available to conclude that the regular administration of vitamin K concentrates will reduce the loss of bone mass in white women at risk for developing postmenopausal osteoporosis.

Bone 1995 Jul;17(1):15-20 **Carboxylation of osteocalcin in post-menopausal osteoporotic women following vitamin K and D supplementation.** Douglas AS, Robins SP, Hutchison JD, Porter RW, Stewart A, Reid DM. University Department of Medicine & Therapeutics, Medical School, Aberdeen, UK.

The effect of vitamin supplements on bone metabolism indices in patients with osteoporosis has received scant attention in the literature. Over a 2-week period, vitamin supplements of K and K+D were given to 20 post-menopausal osteoporotic women with previous Colles fractures. Osteoporosis was confirmed by bone mass measurements that demonstrated that broadband ultrasound attenuation (os calcis) was almost as discriminatory as dual energy X-ray absorptiometry (spine and hip) in Colles fracture patients compared with matched controls. Vitamin K corrected the carboxylation defect in osteocalcin and while less marked 4 weeks later, the improvement was still detectable. The result after K+D was similar. The level of carboxylation became the same as in premenopausal women. Total osteocalcin level (bound osteocalcin). While there was vitamin K correctable undercarboxylation of osteocalcin, simultaneously there was no evidence of undercarboxylation of prothrombin.

Nippon Ronen Igakkai Zasshi 1995 Mar;32(3):195-200 **[Serum concentration of vitamin K in elderly women with involutional osteoporosis]** Kaneki M, Mizuno Y, Hosoi T, Inoue S, Hoshino S, Akishita M, Akedo Y, Horiki K, Nakamura T, Shiraki M, et al. Department of Geriatrics, Faculty of Medicine, University of Tokyo.

Oral administration of vitamin K was reported to increase bone mineral density. However, the possible role of vitamin K in the pathogenesis of osteoporosis still remains unclear. Therefore, we measured the serum concentration of vitamin K1 and K2 (menaquinone-4, 7, 8) in 24 elderly women with osteoporotic vertebral compression fracture and in 36 elderly women without fracture. Major forms of vitamin K present in sera in this study were vitamin K1 and menaquinone-7. On the other hand, serum menaquinone-4 and -8 were undetectable in most women. Serum concentration of menaquinone-7 was significantly lower in women with fracture than in those without fracture (3.29 +/- 3.63 ng/ml vs 6.26 +/- 5.62, mean +/- SD, respectively), while no difference was found in serum vitamin K1 concentration (0.837 +/- 0.620 ng/ml vs 0.820 +/- 0.686, respectively). There was no difference between both groups in background data such as age, body height, body weight, and body mass index, as well as serum level of calcium, inorganic phosphate, creatinine, albumin, and alkaline phosphatase. These results suggest the possibility that deficiency of vitamin K, particularly that of menaquinone-7, is one of the risk factors for developing osteoporosis.

Cas Lek Cesk 1990 Dec 14;129(50):1569-73 **[Osteocalcin]** Neradilova M. Vyzkumny ustav endokrinologicky, Praha.

Osteocalcin, non-collagenous vitamin K dependent bone protein is as a biochemical indicator of osteoblastic activity and metabolic turnover in bone, valuable in the diagnosis of several diseases and in investigations of the dynamics of osseous changes (processes) during treatment of osteopathies. Elevated osteocalcin levels are normal in childhood and adolescence. In the diurnal rhythm the peak is recorded in the early hours. Pathologically elevated values are associated with primary hyperparathyroidism, Paget's disease, chronic renal failure, acromegaly and some malignities. A rise in women during the early postmenopausal period signals an enhanced metabolic turnover of bone in those women who are candidates of postmenopausal osteoporosis. Low levels are as a rule recorded in advanced age, in nanism, hypoparathyroidism, type 1 diabetes, rheumatoid arthritis, vitamin D deficiency, vitamin K deficiency, hypercorticalism and glucocorticoid treatment.

Ann Intern Med 1989 Dec 15;111(12):1001-5 **The effect of vitamin K supplementation on circulating osteocalcin (bone Gla protein) and urinary calcium excretion.** Knapen MH, Hamulyak K, Vermeer C. University of Limburg, Maastricht, The Netherlands.

STUDY OBJECTIVE: To determine whether vitamin K administration affects urinary calcium excretion in postmenopausal women. **DESIGN:** Before- and after-trials with a 2-week treatment period. **SUBJECTS:** Healthy postmenopausal women (55 to 75 years old) were recruited from the convents in and around Maastricht. Controls (25 to 40 years old) were healthy premenopausal volunteers. **INTERVENTION:** Daily administration of 1 mg of vitamin K for 2 weeks. **MEASUREMENTS:** Serum immunoreactive osteocalcin: hydroxylapatite binding (HAB) capacity of serum immunoreactive osteocalcin; excretion of calcium, hydroxyproline, and creatinine in the urine during the last 2 h of a 16-h fasting period. **RESULTS:** In premenopausal women, no effect of vitamin K administration was seen. In the postmenopausal group, vitamin K induced increased serum immunoreactive osteocalcin concentration; normalization of the HAB capacity of serum immunoreactive osteocalcin (this marker was less than 50% that of the controls in the pretreatment samples); a decrease in urinary calcium excretion, notably in the "fast losers" of calcium; and a parallel decrease in urinary hydroxyproline excretion in the fast losers of calcium. **CONCLUSIONS:** The serum immunoreactive osteocalcin level may vary with vitamin K status. This variance should be taken into consideration if osteocalcin is used as a marker for osteoblast activity. Vitamin K is one factor that may play a role in the loss of bone mass in postmenopausal osteoporosis.

Med Res Rev 2001 Jul;21(4):274-301 **Arterial calcification: a review of mechanisms, animal models, and the prospects for therapy.** Wallin R, Wajih N, Greenwood GT, Sane DC. Section of Rheumatology, Department of Internal Medicine, Wake Forest University School of Medicine, Winston-Salem, North Carolina, USA.

The causes of arterial calcification are beginning to be elucidated. Macrophages, mast cells, and smooth muscle cells are the primary cells implicated in this process. The roles of a variety of bone-related proteins including bone morphogenetic protein-2 (BMP-2), matrix Gla protein (MGP), osteoprotegerin (OPG), osteopontin, and osteonectin in regulating arterial calcification are reviewed. Animals lacking MGP, OPG, *smad6*, carbonic anhydrase isoenzyme II, *fibrillin-1*, and *klotho* gene product develop varying extents of arterial calcification. **Hyperlipidemia, vitamin D, nicotine, and warfarin, alone or in various combinations, produce arterial calcification in animal models.** MGP has recently been discovered to be an inhibitor of bone morphogenetic protein-2, the principal osteogenic growth factor. Many of the forces that induce arterial calcification may act by disrupting the essential post-translational modification of MGP, allowing BMP-2 to induce mineralization. MGP requires gamma-carboxylation before it is functional, and this process uses vitamin K as an essential cofactor. Vitamin K deficiency, drugs that act as vitamin K antagonists, and oxidant stress are forces that could prevent the formation of GLA residues on MGP. The potential role of arterial apoptosis in calcification is discussed. Potential therapeutic options to limit the rate of arterial calcification are summarized. Copyright 2001 John Wiley & Sons, Inc.

Gut 2001 Apr;48(4):473-7 Comment in: *Gut*. 2001 Apr;48(4):448. UI: 21145537 **Low serum and bone vitamin K status in patients with longstanding Crohn's disease: another pathogenetic factor of osteoporosis in Crohn's disease?** Schoon EJ, Muller MC, Vermeer C, Schurgers LJ, Brummer RJ, Stockbrugger RW. Department of Gastroenterology and Hepatology, University Hospital Maastricht, Maastricht, the Netherlands. ESCH@sint.azm.nl

BACKGROUND: A high prevalence of osteoporosis is reported in Crohn's disease. The pathogenesis is not completely understood but is probably multifactorial. Longstanding Crohn's disease is associated with a deficiency of fat soluble vitamins, among them vitamin K. Vitamin K is a cofactor in the carboxylation of osteocalcin, a protein essential for calcium binding to bone. A high level of circulating uncarboxylated osteocalcin is a sensitive marker of vitamin K deficiency. **AIMS:** To determine serum and bone vitamin K status in patients with Crohn's disease and to elucidate its relationship with bone mineral density. **METHODS:** Bone mineral density was measured in 32 patients with longstanding Crohn's disease and small bowel involvement, currently in remission, and receiving less than 5 mg of prednisolone daily. Serum levels of vitamins D and K, triglycerides, and total immunoreactive osteocalcin, as well as uncarboxylated osteocalcin ("free" osteocalcin) were determined. The hydroxyapatite binding capacity of osteocalcin was calculated. Data were compared with an age and sex matched control population. **RESULTS:** Serum vitamin K levels of CD patients were significantly decreased compared with normal controls ($p < 0.01$). "Free" osteocalcin was higher and hydroxyapatite binding capacity of circulating osteocalcin was lower than in matched controls ($p < 0.05$ and $p < 0.001$, respectively), indicating a low bone vitamin K status in Crohn's disease. In patients, an inverse correlation was found between "free" osteocalcin and lumbar spine bone mineral density ($r = -0.375$, $p < 0.05$) and between "free" osteocalcin and the z score of the lumbar spine ($r = -0.381$, $p < 0.05$). Multiple linear regression analysis showed that "free" osteocalcin was an independent risk factor for low bone mineral density of the lumbar spine whereas serum vitamin D was not. **CONCLUSIONS:** The finding that a poor vitamin K status is associated with low bone mineral density in longstanding Crohn's disease may have implications for the prevention and treatment of osteoporosis in this disorder.

Micro-Minerals

Iron, zinc and manganese are needed in milligram amounts.

Iron

Iron deficiency is the most common deficiency in the world. Blood loss, such as may occur with a heavy menstrual cycle or with use of NSAIDs, a diet low in red meat and liver, malabsorption as in IBS or gluten intolerance or Crohn's, and chemotherapy require extra iron. Infection and heavy perspiration, hot climates or exercise, can also increase the need for iron.

Iron is found in brewer's yeast, blackstrap molasses, red meat, bone marrow, liver and supplements. The RDA is 18 mg for women. Men or postmenopausal women, who often avoid supplements containing iron, can become iron deficient on cholesterol lowering diets that avoid red meat and organ meats.

Iron supplementation with Albion Ferrochel is safe for adults and children. It does not upset the stomach or contribute to constipation. Ferrochel is found in a number of supplements on the market.

My favorite iron supplement is Solgar Hematinic Formula. When anemic, pregnant, menstruating or dieting the dose is 3 tablets once a day. Maintenance is 1 tablet once a day or 3 tablets daily one week out of each month. **Supplementation of three once or twice a day also works during chemotherapy or radiation to prevent or rapidly recover from treatment induced anemia.**

The best test to determine your iron sufficiency is Ferritin. Less than 50 ng/ml is a deficiency, strongly associated with behavioral and/or learning disorders and/or fatigue, though your lab may not agree. Optimal is 70-90 ng/ml and if yours is lower get and take an iron supplement. Greater than 110 ng/ml means avoid supplemental iron.

Too much ferritin, greater than 150 ng/ml, is a potential concern.

Iron Overload Disease- Hemochromatosis

For a certain group of genetically susceptible individuals there is a possibility of iron overload.

From the Iron Overload Association: Diagnosis - How Do You Find Out

To diagnose hemochromatosis is an easy affair. Basically there are three tests that confirm an iron overload. First there is Transferrin Saturation (TS) or as it is called in some labs Percentage of Saturation:

Test # 1

After a 12 hour fast, measure Total Iron Binding Capacity (TIBC) and the Serum Iron (SI). To achieve the percentage of Saturation you divide the TIBC into SI..

TIBC Safe range = 12-44%

Any values above this range must be considered diagnostic for hemochromatosis and should cause immediate protocol treatment. Any values far below this range may be a sign of bleeding ulcers, chronic infection or cancer. Physicians should look for the cause of anemia.

Test # 2

Using the blood from the first draw, next check the amount of storage iron

Serum Ferritin (SF) Safe range = 5-150

A hemochromatosis patient needs to be at the lowest end of this range, below 10. This needs to be the treatment goal.

Test # 3

This next test is given less frequently. It is initialized as UIBC. It stands for unbound iron binding capacity. Safe range is above = 146

If a patient checks below this test value, then he or she needs to be treated for their hemochromatosis or their other iron overload condition.

If these tests measure out of safe ranges then aggressive treatment is indicated. Diagnosis without treatment is useless. The patient must be motivated to off load the iron as fast as possible. The physician should not watch these values over time or ignore them thinking they will improve on their own. Once iron is absorbed in excess it will not correct itself. Iron is not excreted. Its only exit from the body is by frequent bleeding or chelation.

Some iron overloaded patients will present with a normal saturation and still have an overload of iron. If there is family history or symptoms or elevated ferritin over time, the patient may be involved with this problem.

Minority Populations:

The Irish are reporting a 33% carrier rate in Ireland. That is that one Irishman is three has at least partial genetics for too much iron. In the U.S. we are reporting a carrier rate of 20% for Irish Americans. The carrier rate is also known as heterozygosity or being a heterozygote. We have information that these people with partial genetics can also express excess iron especially if they take over the counter vitamin C or multi vitamins.

African Americans too have a 20% carrier rate in the U.S. This population has a special problem in that the main screening lab value - transferrin saturation (TS) - sometimes seems normal. This one group may need to depend on family history, symptoms or elevated serum ferritin as a diagnostic device to determine hemochromatosis.

Zinc

Zinc is necessary for the production of and is a part of many critical enzymes including digestive enzymes. Vitamin A will not work, that is reach tissues and organs, without zinc. Zinc is critical for absorption of vitamin A in the gut and for production of retinol binding proteins to carry vitamin A to your tissues and glands. If zinc is marginally low vitamin A, if present, will sit in the liver rather than being delivered to cells in other parts of the body where it is needed.

Often symptoms of zinc or vitamin A deficiency are similar because of this relationship. One example is acne, at any age. Both A and zinc treat and prevent this condition.^(567,568,569,570)

Zinc is important for men because they tend to have lower than optimal tissue levels (not serum). Sexual activity depletes zinc rapidly as seminal fluid has high zinc content. Some symptoms of zinc deficiency include smelly feet and body odor (think teenage male with a high need for zinc for sexual development). Without sufficient body stores of zinc, perspiration lacks the zinc needed to prevent bacterial growth on the surface of the skin (armpits, feet, body) causing odor. Zinc in our sweat and saliva is a primary defense against pathogenic bacteria that assault us daily.^(571,572,573,574,575,576)

Grumpiness or depression may also be associated with low levels of zinc.
(577,578,579,580,581)

A number of studies have found additional zinc seems to prevent migraines. Do monitor your zinc with the Zinc Test.

Zinc is found in shellfish, ocean fish and red meat and liver. There are few sources of zinc in the vegetarian diet. Supplementation of 15-60mg is safe and adequate unless a deficiency is present. Doses over 90 mg may needed for short periods of time to replete zinc. Over time excess zinc will be toxic and can significantly suppress the immune system. Test, test and retest. As levels change change your dose. The preferred type of zinc for supplementation is zinc monomethionine but any zinc supplement will work.

Higher doses of zinc can and should be used for brief periods of time when infection is present or following surgery. Both of these situations rapidly deplete body stores of zinc.

Zinc Test

Zinc deficiency is difficult to detect in a laboratory (blood test) since most of the body's zinc is found in the cells. Gustin is a zinc dependent polypeptide, which is required for normal development of taste buds. Adequate gustin indicates adequate body stores of zinc.

Zinc Status is one in several zinc solutions designed for testing zinc deficiency in the body (tissues). The product was accepted in the British 1988 Pharmacopoeia as a good way of testing one's zinc status.

You can test your tissue levels of zinc. Use Design for Health Zinc Challenge or Ethical Nutrients Zinc Status (same product, different labels). Instructions for testing are on the bottle and in the chart below. Check your local health food store or online at <http://amazon.com> or <http://iherb.com> Cost is about \$16 plus shipping. The test material should last several years.

Do not use the liquid as a zinc supplement. My favorite supplemental zinc, keeps a long time and each small pill is 50 mg, is Now Foods Zinc 50mg tablets. They are easy to use when extra zinc is needed, when ill, injured, before/after surgery, after sunburn, or if you test low in zinc. If you find they upset your stomach (rare but it happens) switch to Jarrow Zinc Balance which contains zinc monomethionine, very absorbable.

The Zinc Taste Test

Directions: Rinse your mouth with water. Place 2 teaspoons of the prepared liquid in your mouth, swish it around and hold for 10 seconds. Count it out. Spit out the zinc liquid or swallow it. Check your response.
Category 1: A strong, immediate, identifiable zinc taste. Means you have an adequate intake of zinc. No extra is needed. You can still take zinc if you become ill but in moderate amounts. If you can 'smell' the zinc test or it has an intensely unpleasant taste that grows stronger even after you spit out the liquid, stop zinc supplements for a few weeks and retest.
Category 2: A definite, though not strongly unpleasant, taste is noted almost immediately (6 to 10 seconds), and tends to intensify with time. This means that levels are good but if you pick up an infection you will need extra zinc to get well.

Category 3: Taste develops within 10 seconds described as “dry”, “mineral”, “furry”, or sweet”. Means you are zinc deficient and need to supplement with extra zinc.

Category 4: No specific taste or other sensation of zinc. This means that you have little or no zinc in your diet or do not metabolize zinc efficiently and must supplement individual zinc to stay strong and healthy.

Retest MONTHLY until you know you have enough (a definite taste develops rapidly and intensifies with time) and determine how much you need to supplement daily. **Do not retest sooner than 3 weeks as you may get a false positive.**

If you need extra zinc: You may need a daily dose of 90-100 mg to raise tissue zinc. If you are low Category 3 or 4 above, add 90-100 mg zinc daily and retest every 3 weeks. When you reach Category 1 drop your dose to ½ of what you used to raise it and again test every 3 weeks to determine if that dose will keep your zinc optimal.

Typical doses of zinc are 15-50 mg daily. Zinc monomethionine, zinc gluconate, zinc aspartate or zinc glycinate are acceptable. Do not use zinc picolinate. Doses higher than 100 mg daily are never recommended. Excess zinc suppresses the immune system. If the taste test is so strong you are repulsed stop all zinc for a few weeks and test again.

Infections, surgery, and injury rapidly deplete zinc body stores and you'll need to replace zinc by doubling or tripling your daily dose for a few days to a few weeks. Chronic doses of zinc exceeding 90 mg a day taken over many months have been associated with immune system suppression and failure. Think balance and moderation, just enough but not too much. Test to make sure. Do not test more than once a month.

Manganese for Disc Regeneration

Manganese is critical to the formation of collagen, especially disc collagen. Manganese plays a role in disc regeneration. Multi-mineral supplementation with additional manganese has clinically demonstrated the ability to restore disc health. Response is superior to surgery.

Combining Source Naturals Athred (bovine collagen), and Solgar chelated manganese 20 mg once a day may be effective in restoring joint and disc health in humans and dogs. ^(492,582) Adding 1,000 mg liposomal vitamin C makes this an even better combo. Continue for 6-9 months.

Trace Minerals

Trace minerals are critical to overall health. Trace minerals are found in whole foods, bone stock, edible bone meal, alfalfa tablets, blue green algae, dulse and other seaweeds.

Most good multi-vitamin/mineral combos contain trace amounts of essential chromium, selenium, boron, iodine, vanadium and molybdenum. These amounts are usually

sufficient. Recommended amounts are 200 mcg, 50 mcg, 1-3 mg, 225-1,000 mcg, 1 mg and 50 mcg respectively. Note most are micrograms (mcg) a very small amount.

Trace minerals are needed in trace amounts. More is NOT better. Most trace elements, including iodine, are toxic in high doses. A common cause of autoimmune thyroiditis is excess iodine. The rule, enough but not too much, is mandatory with trace minerals.

Colloidal minerals are not a good source of essential trace minerals as these formulas all contain aluminum and other heavy metals. Consider using bone broth or dulse or alfalfa tablets.

Iodine

Iodine, like all essential trace elements, is needed in minute quantities. Popular use of iodine load tests and high doses of iodine are unlikely to correct thyroid function and may actually precipitate autoimmune thyroid disease (Hashimoto's Thyroiditis).
(583,584,585,586)

If you have determined you need more iodine in your diet consider regular use of dulse or other seaweed, as a condiment or seasoning. Large doses of iodine have long been used in medicine to suppress thyroid function. The latest 'fad' of high dose iodine WILL cause many new cases of thyroid autoimmune disease.
(584,585,586,587) While some persons using high dose iodine may initially 'feel better' autoimmune thyroid disease is a devastating, slow progressing, irreversible condition. More than 1 mg (1,000 mcg, the upper limit of safety) of iodine daily is not advisable unless you have been clinically diagnosed with an iodine deficiency. I like the Life Extension Sea-Iodine 3-7 times a week depending on need.

Certain specific conditions may increase need temporarily. Pregnancy increases the need for iodine and insufficient iodine during pregnancy may lead to lower cognitive function in offspring.
(588,589,590) Using 2% Lugol's Solution, just make sure it is the 2%, 1 drop mixed with 8 ounces of water or juice 2 times a week will ensure iodine sufficiency without excess or if that is too complicated use the Life Extension Sea-Iodine 3 times a week..

Selenium

Selenium is an often neglected trace element. It is of special importance to thyroid function and normal immune function. Higher selenium intake protects from the effects of iodine overdose, is key to several anti-oxidant enzymes, protects the heart and brain, protects cells from cancer, and improves resistance to infectious illness.
(587,591,592,592,593,594,595,596,597,598,599,600,601,602,603)

Selenium enzymes are important for the health of your good bacteria and protect the digestive tract. Glutathione depends on selenium and keeps your toxic burden low. Glutathione protects all your tissues from oxidative stress. Getting sufficient selenium every day will keep your glutathione levels optimal.
(604,605,606,607,608,609,610,611,612,613,614)

Persons on thyroid hormone may need extra selenium and anyone using iodine or consuming quantities of seaweed should consider extra selenium.
(591,594) A selenium

dependent enzyme converts T4 into the active T3. Selenium is also important if you suffer from chronic illness, virus, mycoplasma, herpes, hepatitis or HIV. Increasing selenium intake often dramatically lowers incidence of colds and flu as well as chronic viral infections.^(615,616,617,618,619,620,621,622,623)

Excessively high dose selenium and inorganic selenium exposure is toxic. The preferred source of selenium is methyl-selenocysteine or selenomethionine available from <http://cpmedical.net> (use my pin 230288 to order) or from <http://iherb.com> Excess selenium may contribute to a number of serious conditions including adult onset diabetes. Balance and moderation in all things is important.

The requirement is 70 mcg but studies using 200 mcg per day have shown benefit. Selenium 200 mcg. is not found in most multiples or multi-minerals. Check with your healthcare provider.

Electrolytes

Electrolytes are critical for a functioning heart as well as general muscle strength and energy. Electrolytes include sodium, chlorine, calcium, bicarbonate, potassium, magnesium, and sulfur.

Salt is healthy and should be used as desired to taste. Vegetarians often avoid salt yet the high level of potassium in the vegetarian diet may increase the need for sodium chloride. It provides electrolytes critical for many functions including the production of hydrochloric acid. Celtic salt provides additional trace elements.

During pregnancy low levels of electrolytes, including sodium or chloride (salt), may contribute to low stomach acid and may cause or increase nausea.

Other possible symptoms of low electrolytes include abnormally low blood pressure or an inability to perspire even when the weather is warm or your activity level is high. Perspiration is important not only to regulate body temperature but also to remove toxins from the body. Perspiration removes heavy metals, fat soluble and water soluble chemicals and drugs, and other harmful substances from your tissues. Sweating (from exercise or even a low heat sauna) is the safest way to detoxify, avoiding damage to the liver or kidney.

If you need to restore electrolytes because of vomiting, diarrhea, sweating, hot weather or extended exercise use Trace Mineral Research Electrolyte Stamina Tablets. The typical dose is 2-4 tablets as need with water or juice. Under some conditions it is appropriate to use up to 16 a day for brief periods of time.

Bulimia, an eating disorder involving self-induced vomiting and laxative use causing diarrhea, rapidly depletes electrolytes leading to great stress on the body, especially the heart. Recovering from this condition may be complicated by lack of electrolytes and consequent difficult digestion with chronic constipation.

Use of the Trace Mineral Research Electrolyte Stamina Tablets 300 tablets per bottle (this product only, careful what you buy, there is no substitute, <http://amazon.com> or

<http://vitaminshoppe.com>) can restore the missing elements in a short period of time, under 15 minutes when used according to instructions.

Checklist and Notes:

- Am I balancing my vitamin A and D intake (or sun exposure) so that I have enough but not too much of both?
- If I don't daily consume natto or other fermented fatty food am I supplementing with vitamin K complex?
- If I don't regularly consume wild game, dark meat, organ meats such as liver and beef heart, and shellfish do I supplement with the amino acid taurine and essential minerals iron, zinc and manganese?
- Do I test zinc monthly? Am I adding extra zinc when injured/ill or preparing for surgery?
- Does my supplement contain selenium? Of the right kind? The right amount?
- Do I regularly consume sufficient iodine (seaweed or Lugol's) and if pregnant have I increased my intake to 1,000 mcg daily (2,000 mcg every other day)?
- Iron deficiency- Do I sigh or yawn frequently, inappropriately? Have pale gums and/or pale fingernail beds? Am I cold even when it's warm? Is my ferritin below 70 ng/ml?
- Iron overload symptoms are many and varied. If I have unresolved health issues with no apparent cause have I had my ferritin checked to exclude iron overload (or insufficiency)?

CHAPTER 9 BASIC FOOD PLAN- EASY WAY OR HARD WAY

For slackers, math impaired and the wise who have better things to do-

I have found that if you forgo the more difficult method below and just count protein and potassium (the formulas prior), drink plenty of water, and eat mostly/only whole foods in their natural state you will have the perfect diet.

High potassium foods contain simple and complex carbohydrates and proteins naturally contain plenty of fat. Avoid processed 'low-fat' or 'non-fat' foods. It is easier to use the two numbers (your two numbers) for potassium and protein and trust your taste for good, real food. With adequate protein and potassium, water and a decent basic multi-vitamin and mineral supplement, food cravings and binge eating are rare.

As not just what we eat but when and how much we eat counts do read the section How Food Destroys page 156

For those who like to make life complicated:

Once you have decided to eat real food, the next step is to determine the balance of carbohydrates, fats and proteins. After careful consideration during my 30 years of working with nutrition and health it is my decided opinion that Americans have great variables in their nutrient needs. Some do best on 60% carbohydrates, 20% fat and 20% protein (expressed as percent of calories) and others may need as much as 30% protein, 60% fat and 10% carbohydrate.

The type of protein you choose also makes a difference. Refer to the section on lectins page 40. Not all proteins are created equal.

Because there are no exact numbers, you need to listen to your body and determine what is right for you. Most clients need at least 20% protein and 20-30% fat. Women tend to need more protein per pound of body weight than men. Many early aging symptoms may be caused by low protein and/or low potassium intake.

Formula for Determining Your Daily Nutrient Need

Paleo, No Need to Count

The Western Diet has truly damaged us and processed foods continue to contribute to increasing disease including Metabolic Syndrome, cancer and dementia. Clinical evidence suggests some version of the paleolithic diet may rapidly restore health and reverse disease process.^(624,625,626,627,628,629,630) If you suffer from chronic illness please consider this option. A good book to use is It Starts with Food, Hartwig and Hartwig. You won't need to count protein but should count potassium as higher potassium (more fruits and vegetables) is associated with a longer and healthier life span. You're your minimum daily intake of fruits/veggies no less than 5 servings, whatever diet plan you pick.

AS A PERCENT OF CALORIES The complex calculation, you don't have to do this-

[Desired body weight] x 15-18 calories for women or 17-22 calories for men = total required calories per day. Use lower figure for inactivity, higher for regular exercise, add more (25+) if you are an athlete.

My Daily Caloric Need Is _____

Multiply total calories per day x

Percent divided by 4.5 for carbohydrate grams

Percent (see below) divided by 4.5 for protein grams

Percent divided by 9 for fat grams

Example: 130-lb. woman exercises 3 hours per week. $130 \times 18 = 2,340$ calories per day.

Sample results on varied %--

40/30/30 208 grams of carbohydrate/156 grams of protein/75 grams of fat (Zone Diet)

20/20/60 100 grams of carbohydrate/100 grams of protein/162 grams of fat (Jaminet)

10/20/70 50 grams of carbohydrate/100 grams of protein/189 grams of fat (Rosedale)

Dietary Recommendation for Americans 2010 were 45-65% carbohydrate/10-35% protein/20-35% fat. These ratios however you put them together almost guarantee elevated fasting insulin and development of Metobolic Syndrome or dementia. Sample
↓

50/20/30 270 grams of carbohydrates/108 grams of protein/80 grams of fat

60/20/20 108 312 grams of carbohydrate/grams of protein/50 grams of fat

Low carbohydrate diets typically include not more than 40-60 grams of complex carbohydrates or about 20% of total calories a day from mostly non-starchy vegetables. Jaminet allows 100 grams of carbohydrate daily. It is possible up to 200 grams of carbohydrate may be acceptable if fasting insulin is below 6 uU/ml and blood work normal. The lower carbohydrate numbers may be needed during disease recovery.

Variation in low carbohydrate plans center around either protein or fat being higher. The diets that are low carbohydrate, moderate protein and high fat seem to have the greatest long term health benefits reducing fasting insulin and preventing/reversing

Metabolic Syndrome. Check out authors Hartwig, Eades, Rosedale, Jaminet, or any of the Paleo diets but COUNT YOUR POTASSIUM. You won't need to count protein, fat or carbs.

As far as I am able to tell many of the high protein or low carb diets limit fruit. You absolutely must get a minimum of 5 servings of fruits or vegetables every day. This ensures your potassium goal and studies show this is key to longevity.^(631,632,633)

MY DAILY NEEDS ARE:

PROTEIN _____ FAT _____ CARBOHYDRATE _____

CARBOHYDRATES

CARBOHYDRATES—Your primary source should be fresh, whole fruits and vegetables. Get 5 or MORE servings every day.

Whenever we eat refined carbohydrates, that is, white flour or white sugar, high fructose corn syrup containing foods, we alter the body's ability to handle glucose, elevate post meal and/or fasting insulin, and predispose the body to insulin resistance.

Natural sugar, called panela, has 2 mg. of potassium for each calorie whereas white sugar has none. If you ate 600 calories of panela you would get 1200 mg. of potassium and other associated minerals, trace minerals and vitamins. As you have read, potassium strongly influences the way our bodies handle all types of carbohydrates. When empty calories and salt are increased and potassium decreased we feel a significant loss of energy often followed by elevated fasting insulin, insulin resistance, cravings and weight gain.

America's favorite complex carbohydrates include, but are not limited to, cookies, crackers, bread, muffins, croissants, pretzels and the like. Many of these foods contain added sugar and processed (rancid) fat. Do not choose these foods as a source of carbohydrate.

Please remember that pasta is made from white, refined flour. While it is a source of complex carbohydrates it does not contain many of the nutrients that would be found in the whole grain. The potassium content has been greatly reduced. Make sure to read the section on sugar in the Addendum page 334.

Refined carbohydrates, whether simple or complex, do not contain vitamins and minerals that promote health and their consumption depletes the body of certain minerals, vitamins and trace elements. Chronic over consumption of refined foods as carbohydrates - starches, sugars and alcohol - is strongly implicated in the development of hyperinsulinemia and cellular insulin resistance that we can now clinically document as being the cause of obesity and adult onset diabetes.

A study at State University of New York, Buffalo, suggests that overzealous consumption of carbohydrates can backfire. Researchers put six highly trained runners on one of three dietary regimens for a week at a time: a high-carbohydrate diet (73% carbohydrates, 15 % fat), a high-fat diet (50 % carbohydrates, 38% fat) and their normal diet (61% carbohydrates, 24% fat), They then measured aerobic power, how efficiently the body uses oxygen, and the time it took the athletes to reach exhaustion running laps on the track.

Surprisingly, **the high fat--not the high carbohydrate--diet correlated with the best performances.** The runners' maximum aerobic capacity was higher, and they lasted longer. It took them 91 minutes to reach exhaustion compared with 76 and 69 minutes, respectively, for those on the high carbohydrate and normal regimes. American Health 6/94

Best Sources Of Carbohydrates

Vegetables - 4 or more servings per day. All vegetables are high in potassium. Eat in soup or extract the juice as well as eating the vegetables whole. Serving size is 1 cup. If you are following a low carbohydrate plan, starchy vegetables (like potatoes) are not allowed.

- Sprouts, alfalfa and other small seeds (sprouted legumes have more carb)
- Greens – lettuce, spinach, chard, etc.
- Hearty Greens - collards, mustard greens, kale, etc.
- Radicchio and endive count as greens
- Herbs - parsley, cilantro, basil, rosemary, thyme, etc.
- Bok Choy
- Bamboo Shoots
- Celery
- Radishes
- Sea Vegetables (Nori, etc)
- Mushrooms
- Cabbage (or sauerkraut)
- Jicama
- Asparagus
- Okra
- Cucumbers (or pickles without added sugars)
- Green Beans and Wax Beans
- Fennel
- Cauliflower
- Broccoli
- Peppers
- Green Bell Peppers
- Red Bell Peppers
- Jalapeno Peppers
- Summer Squash
- Zucchini
- Brussels Sprouts
- Scallions or green onions
- Snow Peas/Snap Peas/Pea Pods
- Tomatoes
- Eggplant
- Tomatillos
- Artichokes
- Turnips
- Pumpkin
- Rutabagas
- Spaghetti Squash
- Celery Root (Celeriac)
- Carrots
- Onions
- Leeks
- Water Chestnuts (note: water chestnuts are starchy root vegetables, but usually used in smaller quantities than other root vegetables)

Legumes – 0-2 Includes peanuts and peanut butter. High in lectins. Some will tolerate and find they provide protein, complex carbohydrates and fiber. Many will not tolerate them and should avoid them. Typically are not included in Paleo diets but you are an individual, see how your body responds.

Fruits -- 2 or more servings per day. These are your high potassium choice. If you have high or low blood sugar and feel the sugar in the fruit is a problem use whole berries. Best GI (glycemic index) fruits include berries, cherries, apples, pears, grapefruit, apricots, peaches and figs. The high fiber content makes them safe even for diabetics. Serving size is one medium fruit or 1 cup fruit (less if using small berries).

During low carbohydrate dieting only avocados and olives are suitable. Low carbohydrate is fine for weight loss or reversing elevated insulin at any weight but when goals are achieved add back whole fruits and/or fresh pressed or squeezed vegetable (not fruit) juices in moderation. NO bottled, canned or reconstituted juices.

Whole Grains- 0-2 servings per day. Grains are not necessary for health. If you have tested your fasting insulin and it is above 8 uU/ml eliminate grains. If you are grain intolerant do not eat them. Serving size is 2 slices sprouted whole grain bread or 1 sprouted whole grain bun, 1 cup cooked grain (oatmeal, rice), or 2 corn tortillas.

If you are gluten intolerant you cannot eat wheat, rye, or barley and it will be necessary for you to eliminate grains or find substitutes that you can enjoy and can tolerate. Rice or corn products are usually tolerated. Watch out for hidden grains.

Because grains contain the germ which is high in polyunsaturated fatty acids it is important to use fresh ground flours (hard to find) or breads like Alvarado or Ezekiel Bread that use no flour or added oil. These breads are made from sprouted whole grains.

Wheat germ, corn germ, rice germ and the like have a very short period of freshness before the by-products of oxidation appear and they become rancid. Rancid polyunsaturated fatty acids are major contributors to degenerative diseases, including heart disease, arthritis, and all forms of cancer.

PROTEINS

PROTEINS 3-6 servings per day. Serving size is 3 oz. lean meat, fish or poultry, . cheese, ½ cup low or nonfat cottage cheese, 16 oz. whole organic milk or buttermilk or yogurt so 8 ounces would be a half serving, 1/2 cup nuts or seeds, 6 ounces tofu, 1 cup of cooked legumes (beans), 2 eggs.

If you are over 180 pounds (healthy body weight), recovering from illness or surgery or are pregnant or nursing, you will need 5-8 servings per day. Most natural whole foods contain a healthy mix of fat, protein and carbohydrate.

The Protein Rule- Three palms full a day, your palm, no one else's. Raise this to 4 palms full if pregnant, nursing, or recovering from illness or injury. Palm should be covered, about 1-2 inch high if using animal protein, 3-4 inches high if using legumes, 2 inches if consuming nuts or seeds as your protein source.

Sources include nuts, seeds, legumes (unless you have an intolerance to legume lectins), meat, fish, shellfish, poultry, eggs and dairy.

FATS

Eat the fats that occur naturally in foods. Do not eat processed low-fat and non-fat products. Since the introduction of low fat foods including non-fat and low-fat dairy the incidence of type II adult onset diabetes has doubled. Reduction in fat intake led to a dramatic increase in carbohydrate intake and consequent hyperinsulinemia and insulin resistance. The American Heart Association recommends 30-40% of calories be from fat. Low carbohydrate plans such as those used by Dr. Rosedale or Paul Jaminet, PhD Perfect Health Diet recommend 50-70% fat.

Add fats to taste. Healthy fats include organic cultured butter (clarified or ghee if you are dairy intolerant), non-hydrogenated coconut oil and extra virgin olive oil. Non-hydrogenated lard and nut butters are also acceptable.

If not using fatty wild fish or shellfish 3 or more times a week supplement with omega-3.

Never eat foods containing hydrogenated, partially hydrogenated fat or oil or shortening or margarine. Avoid omega-6 fats except as they occur in food such as whole nuts and seeds. See below and the article in the 'other contributors' section near the back on the Oiling of America.

Make your own mayonnaise. Recipes can be found in [Lets Cook It Right](#) by Adelle Davis or [Nourishing Traditions](#) by Fallon, Connolley and Enig.

FOOD, HOW MUCH AND WHEN

Vegetarians must eat more frequently to get an adequate amount of nutrients. The vegetarian diet is very 'bulky' and not nutrient dense. Vegetarian animals spend the entire day eating/grazing, unlike their carnivorous relatives who may eat just once a day.

Breakfast in the morning is an important meal for infants and growing children. Adults do not need to eat on arising. We also do not need to eat 'frequently throughout the day'.

Do eat a mid-day meal, ideally make it the largest meal of the day. Do eat a moderate dinner. This type of eating stabilizes insulin and prevents impaired glucose-insulin response.

For long term health if you are an adult, limit your eating to 10 hours or less daily. Allow your digestive tract to rest (zero calories) 14-16 hours a day.

As sleep allows regeneration during 'off' time so does resting your digestive tract. Fasting (no food) triggers autophagy, a natural process that clears dead and dying cells and promotes regeneration. Prior to the development of refrigeration, grocery stores, all night restaurants and 'processed snacks' food was not available for consumption day and night.

Processed snacks include protein bars and granola and smoothies and chips and the like. The word organic or natural does NOT mean 'fresh' or 'real'.

Persons with elevated fasting insulin (9 uU/ml or above) need to follow a plan to rapidly reduce insulin levels. Time Restricted Feeding/Intermittent Fasting combined with an acceptable low carbohydrate or Paleo diet may be a preferred meal plan choice until fasting insulin reaches <6 ng/ml. Please see information on 'hyperinsulinemia page 156

SAMPLE MEALS

BREAKFAST/BRUNCH- 1-3 servings protein, 2++ vegetable and/or 1 fruit

- 2-4 eggs , bacon or cheese or cottage cheese and fruit
- A vegetable rich 2-4 egg omelet with or without cheese
- Leftovers from dinner with butter or coconut milk or added cheese
- Anytime Smoothie from the potassium list with full fat coconut milk and added fiber
- Breakfast tortilla (use corn not wheat) with beans, salsa, eggs and cheese and corn (if bean/tortilla lectins are tolerated)

LUNCH(or dinner for two meal a day eaters)- 1-3 proteins, 3-4 vegetables, and fruit optional.

- Large salad with extra virgin olive oil dressing, use lots of vegetables, sprouts, add eggs or tuna or turkey or ham, and/or soup with veggies/chicken and fruit for dessert.
- One or two pita bread sandwiches with lettuce, tomatoes, cucumbers, sprouts and any other vegetables you desire plus meat/poultry or water pack tuna w/homemade mayo or mustard and fruit.

DINNER- Try to keep dinner light. Use soup, salad or a high protein casserole or leftovers from lunch. Ideally dinner should be the smallest meal of the day. 1-2 protein, 1-2 vegetables , and optional fruit.

- Meat, fish or poultry, rice or potato (if fasting insulin is below 6). 2 cups or more vegetables and a salad with olive oil dressing (home-made).
- Home-made soup using bone stock, with added protein (meat/poultry/eggs) and lots of veggies
- Leftovers with coconut milk or broth (make a soup)
- Fish, rice, vegetables and fruit.

SNACKS- Snacks should be infrequent for most adults. If you participate in high intensity training or have a very physical job (firefighter, construction) snack should ideally contain some protein, fat and unrefined carbohydrate. They are not likely needed unless you are engaged in intense physical activity or are under 20 years of age.

- Sprouted whole grain bread (check fasting insulin) with nut butter (fresh) or leftover turkey or chicken pieces
- Cheese and fruit

- Fresh peanut or almond butter and fruit (if not allergic or intolerant)
- Homemade yogurt (not frozen, sweetened only with honey, maple syrup or fruit)
- Glass of buttermilk or kefir
- Boiled egg/s with homemade mayonnaise
- Rye or rice cracker with cream cheese or smoked salmon
- Smoothie or potassium drink
- Cup of soup with coconut milk, vegetables and fish or chicken

Use this space to list your favorite foods and see how you might combine them into a high protein/potassium feast. Simply adding avocado or tomato or eating potato with skin can dramatically raise your potassium intake. Boiled eggs or canned tuna (not too often as tuna contains mercury) can be a quick no prep protein addition. Dump either on your salad.

CHAPTER 10 PUTTING IT ALL TOGETHER

The Checklist

- ✓ Eat real, fresh whole foods. Avoid processed and refined including those found in the health food store. Wash your food before preparing with water or spray with regular 3% hydrogen peroxide, let sit and then rinse to remove any bacteria or chemicals.
- ✓ Count your protein, minimum 1 gram per each two pounds of body weight, more when stressed whether mental or physical.
- ✓ Count your daily fluid intake and drink at least 1 ounce for each 2 lbs body weight, ideally water.
- ✓ Count your potassium, minimum 4,000 mg from food every day
- ✓ Count your vegetables and fruits (for potassium and fiber) and get 3 or more pounds of vegetables and whole fruits (berries) a day, really.
- ✓ Check your ferritin, optimal 70-90 ng/ml Add Ferrochel iron if needed.
- ✓ Check your vitamin D, optimal 40-60 ng/ml Add D or sunlight if needed and keep it balanced with vitamin A in your supplement or 50,000 IU A once a week.
- ✓ Check your thyroid, TSH less than 2
- ✓ Check your fasting insulin keep it less than 6 uU/ml. If it is higher get fasting glucose and hemoglobin A1C tests. Do what it takes to lower them all.
- ✓ Super load liposomal C 3,000 mg twice daily for several months, then lower to 1,000 mg twice daily, more when stressed, and more if it seems you need it.
- ✓ Take a broad spectrum multi-vitamin and mineral every day
- ✓ Make sure you get a minimum of 1 mg (1,000 mcg) vitamin K daily
- ✓ Make sure you get 200 mcg selenium daily, more is not better, from food or a supplement
- ✓ Check your zinc with the Zinc Status test and keep your levels at category 1-2, add extra zinc as needed
- ✓ Restore gut flora with the Immune Restoration Protocol and then keep it healthy by intermittent use of appropriate fibers and VSL#3 or homemade kefir or yogurt
- ✓ Exercise regularly. High Intensity Intermittent Training (HIIT) is best.
- ✓ Sleep in a dark room and make sleep regular and important
- ✓ Avoid mold, airborne toxins, chlorinated/fluoridated water, vaccines, antibiotics, heavy metals (such as mercury in fish), chemical cleaners, toxic cosmetics and hair dyes, chemical perfumes, air fresheners, any and all chemicals on you, in you or around you absolutely don't need. (Some may need a rare vaccination or antibiotic, keep it rare.)
- ✓ If you have any lingering health issues complete 30 days of the Immune Restoration Protocol page 180

If you have done everything above and you still have health issues check with me for more targeted solutions.

The Concepts

The foods you eat must be 'your' foods. Make sure that you tolerate common lectins (see Lectin chapter) and do not have related food intolerances. If you do not tolerate a group of lectins or other protein source foods do not consume these foods as they will do you harm, either in the short term or long term.

Harm is done when persons consume foods they do not tolerate because they have been told these foods 'are good for them'. Dairy is implicated in juvenile onset diabetes because of an autoimmune reaction caused by undigested proteins crossing the semi-permeable infant gut. Other lectins may play a role in autoimmune thyroiditis and rheumatoid arthritis.

With both protein and fat there is a margin of healthy variance. Too much and too little have significant consequences. While it is possible to go for relatively long periods of time with either element being out of healthy range, eventually effects to the body will be felt and it will take a long time to regain health. Both high quality proteins and high quality fats and oils are essential to maintain a healthy immune system and appropriate cell regeneration.

Water is essential. Determine and consume your optimum every day.

Make sure to get the essential vitamins and minerals, in your food or with wise supplementation. Get the basics. Save the expensive, 'high tech' supplements for elite athletes or others who have money to burn.

Many highly marketed supplements treat the symptoms of deficiencies of the essential nutrients but do not take care of the base deficiency. One example of this is SAME. Methyltetrahydrofolate is necessary for the production of SAME in the human body. Foliates are often ignored in the diet. Go for the folates in food, dark green leafy vegetables, liver, fresh oranges, other fruits and veggies, fresh, and you'll most likely make your own SAME UNLESS you carry the MTHFR gene. If you do, supplementing with Folacin or methylfolate may boost your production.

Be creative. The key is quantity, quality, frequency and composition (% fat, carbohydrate or protein). Some current nutrition gurus suggest lower amounts of fat and protein. Not only are these diets unpalatable, hard to find when eating out and obsessive, they also do not support long-term health. Eat fresh, whole, foods that appeal to you and that fit your genetics.

Research indicates, and humans who have tried it agree a successful system for health maintenance and/or weight loss should consist of plenty of good tasting, fresh, whole foods that you like eaten within an 8-10 hour window (intermittent fasting) ^(634,635,636,637,638,639,640) and exercise that is challenging, fun and safe.

Limiting calories leads to a significant decline in metabolic rate that cannot be overcome by exercise. Without supplementation, low calorie dieting impairs all aspects of health including lowering immunity. Time Restricted Feeding does not require calorie

restriction and has the same anti-aging benefits as low calorie diets. Worldwide we eat too often and/or too much. Consider the chapter How Food Destroys page 156. Limit your feeding time to not more than 10 hours daily; allow your digestive tract to rest for a minimum of 14 hours. Your mind and body will benefit greatly.^(641,642,643,644,645,646,647,648,649)

Limiting healthy fats for an extended period of time can lead to immune system deficiency and changes in mood as well as degenerative symptoms in brain, nerves, skin, hair and nails. Eat natural fats found in fresh foods. You don't need omega-3 supplements unless you are unable to consume fatty fish (with the fat and skin) and seafood a minimum of three times a week. The key is to eat enough of the right foods for you and exercise moderately! PLEASE-Start any change in diet or exercise slowly.

STRESS REDUCTION, relaxation techniques. meditation or prayer, IS IMPORTANT!

Exercise (and read the chapter on exercise page 170)-

Regular, intermittently intense, enjoyable exercise is necessary to maintain health at any age. Begin exercising 10-15 minutes twice a day 3 days a week. Add one day each week until you are exercising 5-6 days a week. Begin adding 5 minutes to each workout until you reach the goal of 60-90 minutes a day (all at once or split in to many small breaks) 5-6 days per week. Type of exercise is not important. Look to duration (30 minutes 3 times a day, 45 minutes twice a day, or 90 minutes or more once a day) and intensity.

A day of rest, from everything including exercise (and even food if you can do it), is very important.

The most efficient form of exercise to prevent or reverse osteoporosis and/or lose weight is weight lifting. (Yes, it's true.) If you are unfamiliar with this type of exercise get someone to help you. Find a personal trainer or join a gym and get a staff member to help you learn the best way to train. Mountain biking or walking hills once a day for 60+ minutes and lifting free weights another 30 minutes will keep you in shape and ready for fun year round well into old age. Ideally train using High Intensity Intermittent Training. See the exercise section page 170.

For an easy, fun, non-impact aerobic workout nothing beats regular use of a mini-trampoline. The forces involved are weight bearing just like weight lifting. Once you have the knowledge you can get equipment and train at home. Yoga is also excellent but should be combined with some sort of aerobic exercise and weight-bearing exercise.

For getting lean consider HIIT, High Intensity Intermittent Training. Lot's of free resources on the web.

Listen to your body. Go at your own pace. It will take you about one or two weeks to get used to thinking in terms of protein and potassium. Get a good nutrient content guide, such as Food Values of Portions Commonly Used edited by Bowes and Church and use it. It will not be long before you understand the principles of healthy eating and are able to find the types of food you like and that are healthy for you anywhere, at home or abroad.

If you are serious about gaining and maintaining your health you need to read labels and then eliminate the foods in this list from your kitchen and shopping list.

Table 18 Non-Foods: Do Not Consume

Added omega-6 fats	Hydrogenated peanut butter
American cheese food	Low calorie, chemically filled frozen or boxed food
Artificial colors	Margarine
Artificial flavors	Non-dairy creamers
Aspartame	Non-dairy toppings
Candy, cookies, or pastries containing any of the above	Non-fat anything unless nature made it that way
Cheese puffs	NutraSweet
Cheese spread	Partially hydrogenated or hydrogenated fat/oil
Commercial mayonnaise	Pork rinds
Concentrated fruit juice sweetener	Potato chips including health food store brands
Corn chips, make your own by baking corn tortillas	Preservatives other than vitamin C or E
Crisco	Processed meats including baloney , hot dogs
Equal	Processed cheese
Fructose	Saccharine
High fructose corn sweetener	Shortening
Hydrogenated coconut oil	Sweet and Low

PROCESSED FOODS refined, canned, frozen, etc.-- if used regularly make it impossible to attain or maintain an optimum level of health. Some processed foods are better than others and have had wiser handling but-- Real food must be the basis of any truly healthy food plan. Food processing, and more recently genetic engineering, has a dramatic effect on the nutrient content , value and safety of ALL foods.

FROZEN VEGETABLES or FRUITS better than canned foods but even in their natural state often have added salt or sugar. Read the label carefully. Whole frozen berries with nothing added are an excellent source for making smoothies or mixing with yogurt for a treat.

COFFEE and ALCOHOL in moderate amounts will not contribute to poor health in most persons. If there is a history of substance abuse, diabetes, obesity, or heart disease it may not be in your best interest to consume these substances.

If you decide to use coffee the same rule applies as with any other food. Coffee beans should be purchased as fresh roasted beans, and ground the day you use them. These beans contain oils, which do become rancid.

DEBUNKING MEDIA NUTRITION MYTHS

Certain foods have fallen into disrepute because of their cholesterol content and/or suspected chemical residues content. Based on current research, the following guidelines are considered prudent and sufficient.

RED MEAT: Red meat is a good source of l-carnitine, iron, copper, zinc and B₁₂ as well as other nutrients and protein. These nutritional substances are important, especially for children, premenopausal women and athletes. If you have been told to avoid red meat by your health care practitioner or physician, or have chosen to do so on your own, please make sure you have an adequate source of these nutrients in other foods or supplements. Red meat should be avoided only by persons with diagnosed iron storage disease. If you can afford it and find it grass-fed beef is high in CLA an important anti-cancer nutrient. Grass-fed beef can be ordered from several ranches with websites on the Internet.

DO NOT AVOID EGGS. They are an exceptional food buy, high in lecithin and one of the few food sources of vitamin D. Eggs are an important source of D, essential fats, lecithin for brain function and high quality proteins. organic, fertile or even better 'local' (from your neighbor) eggs are best. Like beef, grass-fed, free-range chickens produce eggs with more natural and beneficial fats.

Cooking methods include vegetable omelet, poaching, baking or light scramble use olive oil, butter or coconut oil.

WARNING: DO NOT USE OMEGA-3 EGGS or OTHER OMEGA-3 ADDED PRODUCTS. THESE ITEMS RAPIDLY TURN RANCID and ARE NOT POSITIVE ADDITIONS TO YOUR HEALTH. USE FISH OIL or COD LIVER OIL TO SATISFY YOUR NEED FOR OMEGA-3

The food value of organ meats, such as sweet breads, heart, liver and kidney, is such that 2-3 servings of organ meats are desirable each week.

The notion held by many that liver contains toxins has not been validated by random analysis of beef, pork and chicken livers purchased in the US. Toxins are removed by the liver and are stored in fat (such as found in your steak). If the animal has had toxic chemicals you will see visible damage to the organ. Avoid organs that appear damaged.

- Technology works well with inanimate, non-living things. It does not work well with food.
- Artificial fertilizers do not provide the nutrients and cofactors needed in the soil for optimal plant nutrition. Genetically altered seeds and plants, genetically altered animals, artificial flavors and colors and chemical preservatives do not provide us with the nutrients we require.
- Food grown locally with natural fertilization and restored trace minerals, eaten fresh, in season, will always be best for you.
- Food that meets your body's genetic needs is necessary for health.
- Vitamins and other supplements do not alter your need for real food.

- Processed foods from the health food store are still processed foods.
- Eat real food.
- Real food is food that is currently alive or was recently alive and is identifiable as such. It is found around the edges of your supermarket, at farmers' markets or in your garden.

NOTES/QUESTIONS:

SPECIAL SITUATIONS

Dairy or Grain or Legume (LECTIN) Intolerant

If you are dairy intolerant make sure you have a source of calcium from other foods or supplements. Without dairy, calcium and protein can be compromised, especially if this occurs with a vegetarian diet. Dairy intolerance can take the form of gas, diarrhea, and bloating or over-production of mucous, ear infections in children and unusual allergic reactions to the environment. Sometimes the Immune Restoration Protocol will allow you to consume dairy safely. If the condition is hereditary, it is not reversible and dairy should be avoided.

Grain or legume intolerance may be hereditary or caused by gut pathogens or post-infective sensitization. Hereditary intolerance is called Gluten Intolerance or Celiac-Sprue disease or more currently Lectin Intolerance. It is particularly common in the Irish and Scot ancestry and somewhat common in other northern European races. It is likely all humans are intolerant to some family of lectins. Ancestral foods are safest.

If you are genetically gluten-lectin-grain Intolerant it cannot be changed and you must learn to avoid all wheat, rye, buckwheat, oats and quinoa and perhaps other grains as well including corn. You must also avoid products that contain derivatives of these grains.

Legume intolerance (lectins found in legumes) requires the elimination of all legumes including soy (and all products containing soy), peanuts and peanut products, kidney, garbanzo, navy and all other beans.

Possible non-genetic (and therefore modifiable) reasons for reactions to dairy and/or grains and/or legumes may include candida overgrowth in the bowel, parasites, imbalanced intestinal flora, low stomach acid, or a zinc deficiency. You will need a modified program and/or a treatment program to correct these problems before adding back suspect lectins to your diet.

Vegetarian/Vegan

If you are a vegetarian or vegan, please make sure you are getting enough iron, B12, zinc and copper. Some of these can be found in vegetarian foods. Others may need to be supplemented. Do get the Zinc Test and monitor zinc status. Vegetarian diets contain little zinc. Check your ferritin yearly and keep it between 70-90 ng/ml. Iron is also difficult to access in vegan or vegetarian diets. Especially watch zinc and iron if you are considering pregnancy/nursing.

There is no food source for vitamin D in the vegetarian or vegan diet so sunlight or a supplement is a requirement. Vegetarian mothers seem to have an increased incidence of rickets in their children.^(650,651,652,653,654) Make sure to get enough sun and at the right time of day. If you are in an area lacking UV-B you will need to supplement D. Make sure to test.

Make sure your daily totals of protein are adequate. The vegetarian diet requires large quantities of food to get the necessary protein.

Vegetarian/vegans frequently need to add salt, especially if they do not use dairy products or eggs. Soy sauce is naturally high in sodium.

It is important to consider the need for iron and vitamin B-12 as well as zinc. Check.

Action list-

- Test zinc (oral Zinc Status test)
- Test ferritin
- Test vitamin D
- Test fasting insulin, glucose and hemoglobin A1C
- Count your protein, get enough and more when pregnant
- NEVER take a supplement with folic acid. Make sure it has natural (food) folate or methylfolate.
- Do not eat foods fortified with folic acid. Check labels.
- If you carry the MTHFR gene use methylfolate only.
- Take an iron supplement if not consuming high iron foods
- Make sure your protein is adequate, even if using only vegan foods, it is possible.

CHAPTER 11 HOW FOOD DESTROYS- ELEVATED FASTING INSULIN

For several decades it had been believed insulin resistance and elevated insulin were caused by obesity. There have been researchers since the 1990's who have wondered if that was true. They found elevated fasting insulin and insulin resistance in many different conditions and diseases in persons who were not obese or overweight.

December 2012 Cell Metabolism has changed the way we need to think about fasting insulin, obesity and all the consequent diseases and conditions. Researchers confirmed elevated insulin precedes obesity and insulin resistance. With that bit of information it is possible to suggest, based on prior research, elevated fasting insulin precedes a lot of other conditions, from hypertension to elevated PSA , many types of cancer and even Alzheimer's Disease. Elevated fasting insulin makes autoimmune diseases worse as it increases inflammation.^(655,656,657)

In many studies regarding conditions which include Metabolic Syndrome, cancer, and dementia you will see the issue stated as 'insulin resistance'. It turns out a common cause of insulin resistance is too much insulin. It was hypothesized insulin resistance elevated insulin production but it looks more like the reverse is true in many situations. Elevated insulin over time leads to insulin resistance. Every time a cell is exposed to insulin, the production of GLUT4 (type four glucose receptors) on the cell's membrane is decreased. This leads to a greater need for insulin, which again leads to fewer glucose receptors. Lowering fasting insulin reverses insulin resistance and Metabolic Syndrome.

In 2011 researchers published the results a 5 year study of weight normal adults with no known medical conditions which showed elevated fasting insulin predicted who would develop Metabolic Syndrome within 5 years.⁽⁶⁵⁸⁾ Fasting insulin is currently a little used test that when understood and utilized will provide you with a tool to keep you healthy and prevent disease.

If you know your fasting insulin is elevated you can, with a number of dietary choices, lower it rapidly without need for medications or even supplements. The 5 year metabolic study put the fasting insulin cut-off for development of disease at 8.5. uUnits/ml. While not currently consider high, normal 5-15 uUnits/ml, we need to reconsider because 8.5 uUnits/ml was the number above which problems occurred over time.

Hyperinsulinemia is defined as higher insulin in relation to glucose however I use the term to describe elevated fasting insulin. This indicates excess insulin in your bloodstream day and night (still there when fasted in the AM). In early stages, even if fasting insulin is only slightly elevated, it may reflect abnormal post-meal elevation (higher than normal) of insulin, so that some part of everyday your body is dealing with insulin removal and beginning to develop insulin resistance. As serum (fasting and basal) insulin rises cells become less responsive. While all obesity is preceded by elevated insulin, thin people may have elevated fasting and insulin resistance too.

We need to test fasting insulin yearly. Normal fasting insulin in the United States is considered to be 5-15 uUnits/ml, going higher as we age. In traditional lean, healthy cultures fasting insulin is estimated to be 3-6 uUnits/ml with no increase during aging. These cultures rarely suffer from heart disease, hypertension, obesity or stroke. Rates of dementia and cancer are lower too.

If fasting insulin is 5 or greater consider also testing fasting glucose and hemoglobin A1C. The values you want are-

- Fasting insulin less than 5
- Fasting glucose less than 84
- Hemoglobin A1C less than 5

We really need a new goal here. Clinicians have good reason to believe fasting insulin \Rightarrow 9 uUnits/ml indicates Metabolic Syndrome or other complications of elevated insulin may be in your future.⁽⁶⁵⁸⁾ The ideal value is \leq 5 uUnits/ml and should be everyone's goal. Serious measures should be taken if fasting insulin is \Rightarrow 8.5. uUnits/ml

Elevated fasting insulin precedes (important, because insulin rises months or years before any symptoms develop):

- Insulin resistance
- Metabolic syndrome (obesity, hypertension, heart disease, type ii diabetes)
- Alzheimer's disease^(659,660,661)
- Benign prostatic hypertrophy^(662,663,664)
- Elevated PSA⁽⁶⁶⁵⁾
- Many types of cancer including prostate and breast^(666,667,668,669,670,671,672,673,674,675)
- Polycystic ovarian syndrome (PCOS)^(676,677,678,679,680,681,682,683,684)
- Essential hypertension⁽⁶⁸⁵⁾
- Thyroid reverse T3 syndrome
- Low bone mass in children and young adults⁽⁶⁸⁶⁾
- Heart disease⁽⁶⁸⁷⁾
- Low vitamin D⁽³⁶³⁾

Some symptoms of elevated fasting insulin may include:

- Weight gain
- Pre-hypertension
- Food cravings (sugar/fat)

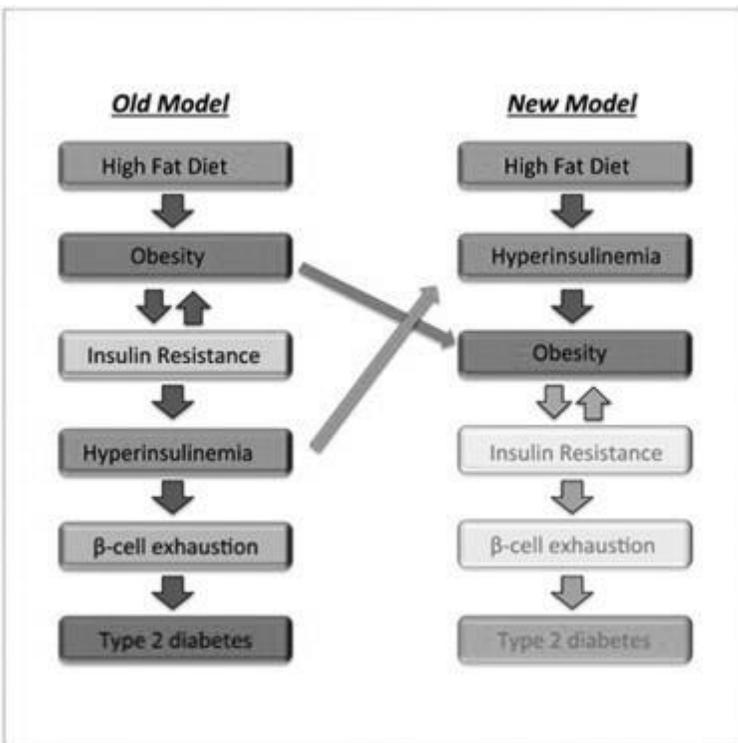
- Intense hunger or feeling frequently hungry or feeling hungry after eating
- Difficulty concentrating
- Feeling anxious or panicky
- Lacking focus or motivation
- Brain fog
- Fatigue
- Hypoglycemia (low blood sugar because of elevated/excess insulin)

As mentioned elevated insulin has traditionally been seen as a result of obesity but the study below determined elevated insulin precedes weight gain (and because of certain hormonal and metabolic changes all of the other diseases on the list above). In this model 'high fat diet' is used as the 'cause' but high carbohydrate diets or even 'chronic eating' may have the same effect in susceptible persons.^(688,689)

Hyperinsulinemia drives diet-induced obesity independently of brain insulin production

Mehran, A. E., Templeman, N. M., Brigidi, G. S., Lim, G. E., Chu, K. Y., Hu, X., Botezelli, J. D., Asadi, A., Hoffman, B. G., Kieffer, T. J., Bamji, S. X., Clee, S. M., and Johnson, J. D. 12-5-2012 Cell Metab

Hyperinsulinemia is associated with obesity and pancreatic islet hyperplasia, but whether insulin causes these phenomena or is a compensatory response has remained unsettled for decades. We examined the role of insulin hypersecretion in diet-induced obesity by varying the pancreas-specific Ins1 gene dosage in mice lacking Ins2 gene expression in the pancreas, thymus, and brain. Age-dependent increases in fasting insulin and beta cell mass were absent in Ins1(+/-):Ins2(-/-) mice fed a high-fat diet when compared to Ins1(+/+):Ins2(-/-) littermate controls. Remarkably, Ins1(+/-):Ins2(-/-) mice were completely protected from diet-induced obesity. Genetic prevention of chronic **hyperinsulinemia** in this model reprogrammed white adipose tissue to express uncoupling protein 1 and increase energy expenditure. Normalization of adipocyte size and activation of energy expenditure genes in white adipose tissue was associated with reduced inflammation, reduced fatty acid spillover, and reduced hepatic steatosis. Thus, we provide genetic evidence that pathological circulating **hyperinsulinemia** drives diet-induced obesity and its complications



Possible Causes of Hyperinsulinemia

Hyperinsulinemia may be precipitated by thyroid disease, gut pathogens, drugs- such as amphetamines, serious infections, extreme stress, certain antidepressants, heart medications, diuretics, hormones- including estrogens and corticosteroids, chronic dieting or a diet high in calories or refined fats or simple carbohydrates and/or alcohol, lack of

physical activity or just eating too much too often.

Research suggests the mothers' insulin status, obesity, early delivery, and even cesarean delivery may predispose offspring to hyperinsulinemia later in life.^(690,691,692,693,694,695,696,697,698)

Insulin and What We Eat

Many studies suggest high fat diets cause elevated insulin, disregarding the fact we have seen a dramatic increase in Metabolic Syndrome during the AHA push for low fat dieting.^(699,700,701) The greatest success long term in reversing Metabolic Syndrome has been seen with any of the versions of low carbohydrate dieting. Authors with workable plans include Hartwig, Rosedale, Eades, Volek, Jaminet, or any of the Paleo and Caveman diets. Processed and refined carbohydrates are unnecessary and will contribute to disease. Excess omega-6 fats or trans fats or hydrogenated fats will also increase insulin and insulin resistance.^(702,703,704)

The basic food plan, counting protein with its natural fats and potassium in whole fruits and vegetables is a good starting place. If insulin is elevated a more rigid carbohydrate restriction may be needed until fasting insulin levels drop.

Insulin and When We Eat

Our ancestors did not have a refrigerator, grocery stores, or all night restaurants. Consuming food 12-16 hours a day may just be 'too much' when we are done growing. While lack of certain nutrients or overabundance of calories may contribute to elevated insulin and insulin resistance it may really be about eating frequency. A healthy diet is required but we also need to stop stimulating the digestive tract and pancreas day and night.

My concerns with elevated fasting insulin go well beyond Metabolic Syndrome which in itself is widespread. Elevated fasting insulin and metabolic disease are NOT just an American issue. Prevalence of Metabolic Syndrome is 40 % in Saudi Arabia. Worldwide statistics show a low of 19% in Brazil to a high of 50% in urban Southern India. US statistics suggest currently 35% of Americans have some indicators of Metabolic Syndrome. If fasting insulin is considered, which it should be, the numbers are likely much higher.

The newest research indicates the connection between elevated fasting insulin and insulin resistance in both cancer

^(666,672,675,705,706,707,708,709,710,711,712,713,714,715,716,717,718,719,720,721)

and

Alzheimer's.^(659,660,722,723,724,725,726,727,728,729,730,731,732,733,734,735,736) The mechanisms involved are still being studied but in the case of cancer and Benign Prostatic Hypertrophy elevated insulin stimulates IGF-1 which is a growth promoter. In Alzheimer's an early theory recognizes the enzyme IDE (Insulin Degrading Enzyme) that degrades insulin is also responsible for degrading (removing) amyloid beta. The thought is that excess insulin redirects the IDE to insulin destruction and there is not enough left to remove amyloid beta plaque.

**Keeping fasting insulin low does CHANGE EVERYTHING
in a good way.**

Eating frequency and timing alter metabolism and fasting insulin

When mice were fed three diets⁽⁶³⁷⁾, mice chow ad libitum (eat when you want, 24 hours a day), high fat mice chow ad libitum, and high fat mice chow using Time Restricted Feeding, 8 hours feeding, 16 hours fasting, there were very interesting and unexpected results.

- Ad libitum mice chow mice were normal weight/healthy but had some markers of inflammation.
- Ad libitum high fat mice chow mice had inflammation, elevated lipids, increased body fat and liver damage, a model for Metabolic Syndrome/insulin resistance.
- Time Restricted Feeding high fat mice chow mice, consuming the exact same amount of calories as the ad libitum high fat mice, were normal weight, had normal livers, normal lipids, had no inflammation AND performed better at exercise than either the ad libitum regular or high fat mice.
- Ad libitum mice chow mice (not high fat) had inflammatory markers which reversed when they were fed the same standard mice chow using Time Restricted Feeding.

The 'high fat mice chow' mice consumed exactly the same amount of calories/food spread over 24 hours or within the 8 hour feeding window with very different health outcomes.

The study suggests, and those who have been using Time Restricted Feeding would concur, it may not be the calories, or the fat content. We just eat too often for our own good. Ad libitum feeding is not suitable for long term health in adult humans or animals.

One study note, the 8 hours of feeding occurred at night which fits normal mouse circadian rhythms. For humans Time Restricted Feeding is appropriate in daylight hours. Get your rhythm back 😊

Macro-nutrients that are critical in determining the way your body handles insulin are vitamin D, calcium, potassium, magnesium, zinc, fatty acids and protein. Supplements can help you recover your insulin response, but only changing your eating, what you eat, when you eat, and how often you eat, can reverse elevated insulin and abnormal glucose-insulin response.

Low tissue levels of vitamin D, calcium, zinc, chromium, potassium or magnesium enhance insulin resistance. ^(358,359,361,737,738) Note I wrote 'tissue levels' not blood levels. Tissue levels can be significantly depleted while blood levels remain normal.

An example: A woman may lose up to or more than 30% of her bone mass yet blood (serum) calcium will remain normal.

Tissue sufficiency of vitamin C is a marker of a better waist to hip ratio and improved insulin sensitivity (and lower fasting insulin). Vitamin C actually alters genes expressing whether food is stored as fat or used for energy.^(479,739,740,741)

From one of the studies- ... Dietary ascorbic acid was able to protect against high fat diet effects, reducing the increase of body weight, total body fat and enlargement of different adipose depots induced by the Cafeteria diet without affecting food intake. An association analysis accurately and differentially allowed the detection of gene expression changes related with adiposity and insulin resistance. The genes that more strongly correlated with body fat and HOMA insulin resistance index were involved in adipocyte differentiation, lipid and glucocorticoid metabolism, cell cycle regulation, as well as in several insulin-induced processes. Some other transcripts are regulated by the vitamin C-mediated reduction of adiposity, such as genes that participate in glucocorticoid metabolism, adipogenesis, pentose phosphate pathway, or tricarboxylic acid cycle⁽⁷⁴⁰⁾

Vitamin C changes GENES and keeps us thinner and younger longer.

Omega-3 is important when reversing elevated insulin. In a research study using one fish meal (not cooked with omega-6 fats) per day weight loss was greater in the fish group than in the control group of equal calories.^(742,743,744,745)

Stress, because it raises cortisol levels can increase insulin resistance.⁽⁷⁴⁶⁾ High cortisol levels further reduce magnesium, calcium, and potassium through urinary loss.

If stress, whether from food intolerances, illness, or life stress, played a role in your weight gain consider adding L-theanine 200 mg twice a day, every day, for about 3 months. Take it 20 minutes before a meal, twice a day. L-theanine normalizes cortisol levels to block the elevated blood sugar and insulin response. It also normalizes dopamine, important for mood and exercise. L-theanine, an extract from green tea (no caffeine), works rapidly, taking only 30 minutes to show results.

Lack of exercise contributes to insulin resistance. Calories are primarily burned in muscle. The more muscle, the more calories burned 24 hours a day (resting metabolic rate). Moderate exercise for 30 or more minutes twice a day, is the fastest way to increase fat burning. Hill walking, running or weight lifting or a combination make the kind of muscle that burns fat. High intensity intermittent training increases exercise effectiveness.^(747,748,749,750,751,752,753)

As one paper concluded **what is important is not that we know why hyperinsulinemia occurs but that we rapidly reverse it.**^(754,755)

REVERSING HYPERINSULINEMIA (AND INSULIN RESISTANCE)

When insulin is overproduced, whether all day and night or just after meals, calories may be quickly removed from circulation and stored as fat. The person so afflicted feels generally fatigued, hungry, and frequently unable to think clearly. Eating actually makes them hungrier, and more tired. These are two of the symptoms of hyperinsulinemia.

Other symptoms may not be as obvious, hypertension, muscle weakness or no symptoms at all. The fasting insulin test is very important because five years before health issues are recognized fasting insulin may already be elevated.⁽⁶⁵⁸⁾

There are specific steps to normalize insulin and the glucose-insulin response. These changes in diet must be adhered to faithfully until hyperinsulinemia is reversed. If the client does not take the necessary steps to correct inappropriately elevated insulin, the next stage may be hypertension, Metabolic Syndrome, or elevated PSA, or even cancer.

Things that reverse elevated insulin and insulin resistance

- High fat, moderate protein, low carbohydrate diet (Protein Power, Perfect Health Diet, Rosedale)
- Restoring the microbiome (see Immune Restoration Protocol)
- Berberine 500 mg with each meal
- High Intensity Intermittent Exercise (HIIT)
- Fasted exercise
- Time Restricted Feeding-Intermittent Fasting (TRF-IF)

Time Restricted Feeding (i.e. Intermittent Fasting, the real deal)-

Numerous studies have found Time Restricted Feeding/Intermittent Fasting reverses hyperinsulinemia/elevated fasting insulin and thereby metabolic syndrome, heart disease and type II diabetes and may prevent Alzheimer's and other age related dementias. It may be the most profoundly anti-aging diet since the discovery of 'calorie restriction'. (646,756,757,758,759,760,761,762,763,764,765,766,767,768,769,770,771)

Time Restricted Feeding allows an eating window of 8-10 hours followed by no food or drink, other than water, for the remaining 14-16 hours.

- Men- 8 hour 'eating window' and 16 hour ZERO calories
- Women (pre-menopause)- 10 hour eating window and 14 hours ZERO calories

It isn't just that we eat too much, we eat too often. Constantly stimulating the pancreas to produce insulin is NOT a good thing. Not 'resting' from eating is also not a good thing.

When our digestive tract rests for a significant period as in intermittent fasting, insulin declines and a process called autophagy increases.

Autophagy, signaling and obesity Lavallard, V. J., Meijer, A. J., Codogno, P., and Gual, P. 2012 *Pharmacol.Res.*

*Autophagy is a cellular pathway crucial for development, differentiation, survival and homeostasis. **Autophagy can provide protection against aging and a number of pathologies such as cancer, neurodegeneration, cardiac disease and infection. Recent studies have reported new functions of autophagy in the regulation of cellular processes such as lipid metabolism and insulin sensitivity.** Important links between the regulation of autophagy and obesity including food intake, adipose tissue development, beta cell function, insulin sensitivity and hepatic steatosis exist. This review will provide insight into the current*

understanding of autophagy, its regulation, and its role in the complications associated with obesity

...Autophagy (auto - self, phagy - eating) is defined as a fundamental lysosomal catabolic pathway responsible for degrading long-lived proteins, protein aggregates, oxidised lipids, damaged organelles, and even microbial invaders...

Reduced autophagy, which occurs with elevated insulin-chronic feeding whether you are overweight or THIN, turns your body into a cellular hoarder, keeping your JUNK, dead and damaged cells, debris that needs to be removed for regeneration and healing to occur.

Reducing fasting insulin is critical to long term health. In addition to lowering our chances of early disease and death, lowering insulin enhances autophagy. Without ample autophagy we live in bodies overburdened with damaged cells and toxic cellular waste. Time Restricted Feeding-Intermittent Fasting lowers fasting insulin to return health to the pancreas, restores balance so that food produces energy instead of being stored, and maintains autophagy to rid the body of daily debris.

There are three basic types of Intermittent Fasting; 24/24 feed one day and fast then next; 5/2 feed 5 days and fast 2 days (in this group would also be the longer intermittent fasts of 7-10 days every few months); the 8/16 feeding for 8 hours and fasting for 16 (also includes the 10/14).

The advantage of the 8/16 is that you may do it every day, or just 5-6 days a week, still with great benefit. It increases autophagy on a daily basis and is really quite easy to do. If you have elevated insulin, 9 or above, I suggest starting with 7 days a week and continuing until your fasting insulin is ≤ 6 uUnits/ml. Maintain this level by continuing the 8/16, but for fewer days a week.

I don't think of this as a weight loss diet. I think of it as 'the way we all should eat to live long and healthy lives'. If you are overweight, you will lose those excess pounds but the long term benefit FAR exceeds improved body mass index. Remember, you may have elevated insulin even if you are at weight normal. TEST your fasting insulin once a year.

The Time Restricted Feeding Food Plan

- Pick your 8-10 hour feeding window. Common time frames 11-7; 12-8; 1-9 For pre-menopausal women add TWO hours as the 8 hour frame may contribute to menstrual irregularities. 9-7; 10-8; 11-9
- Within those hours eat healthy whole foods, typically split into 2-3 meals
- Outside those hours consume ZERO calories, which may include coffee, tea, bouillon, water, or (not my favorite) zero calorie soft drinks. Zero calorie sweeteners may be used, such as Trader Joe's Stevia Extract BUT some persons react to these zero calorie sweeteners so if you have any unusual symptoms including water retention or rashes, STOP.

- High fat, moderate protein & vegetable intake: During the 8-hour eating window, eat protein with fat (meat, poultry, fish) and vegetables (think green growing things). You cannot eat too much of these. Add fruits as desired but NO fruit juice. Use good fats freely.
- Fasted exercise. Do intense exercise (running, lifting, biking, using High Intensity Intermittent Training) 3 times a week, right before you eat your first meal. When exercising on an empty stomach you may take 10 grams of BCAA, branched chain amino acids. They come in powders or capsules. They help burn fat for energy and don't count as calories.

THIS PLAN IS NEVER SUITABLE FOR PERSONS UNDER 18 YEARS OF AGE OR PREGNANT/NURSING WOMEN.

Supplements:

- Use a high quality multivitamin and multi-mineral every day.
- Make sure you take a minimum of 2,000 mg ascorbic acid or 1,000 mg liposomal vitamin C twice a day, at the beginning and end of your fasting period. Don't miss. .
- Minimum intake of calcium from supplements should reach 600-900 mg daily with balanced magnesium and other minerals ie. multi-mineral.
- Take extra magnesium if indicated. Use (1-3) AminoMag 200 daily
- Fish oil omega-3 helps reverse insulin resistance, get yours daily, at least 3,000 mg combined EPA and DHA
- Vitamin D 2,000-4,000 IU depending on serum 25(OH)D test
- Extra zinc if needed (Zinc Test)
- Extra iron if ferritin is less than 70 ng/ml

If 'Time Restricted Feeding' is difficult or not possible due to your schedule

Berberine lowers fasting and basal insulin when taken on a regular basis. It should be taken before the first and last meal of the day, whatever the time. If your values are very high you will need to take it three times a day. Do not miss for it to be effective. **This does not work as well as Time Restricted Feeding and will not increase autophagy but is likely better than doing nothing.**

GlycoX 500 mg (berberine) 2-3 times a day with/before a meal.

Food Guidelines:

- Eat a minimum of 3-4 palms full of protein, especially fish and seafood, with whole fruits and vegetables. Use dairy products if tolerated to add quality protein and absorbable calcium. Use full fat dairy NOT non-fat or reduced fat.
- Homemade soups or stews will make getting potassium easy.
- During your 'eating hours' vegetable juices may add more potassium. Avoid fruit juices. When weight and insulin are problematic all fruit juices and some vegetable juices are too high in carbohydrates to use regularly.

- Yogurt, kefir, or whey protein powder blended with fresh or frozen whole unsweetened blueberries or blackberries makes a delightful quick meal with protein, potassium, calcium and fiber.
- IF YOU LIKE IT- Use non-hydrogenated coconut oil as the primary added fat in your diet. Coconut oil can increase metabolic rate by 25% and stabilize blood sugar levels. Coconut oil also contributes to normalizing adrenal function and cortisol production to reverse insulin resistance. Omega-6 fats, from vegetable oils, contribute to lowered thyroid function. The fatty acids found in coconut oil help to restore thyroid function. Be careful in purchasing coconut oil. As with any fat rancidity is a possible issue. **If it tastes 'funny' it is rancid, throw it out.** Buy in small quantities and use it up. Refrigerate after opening.

If stress is a factor in your elevated insulin and/or weight gain:

- Make sure to take your vitamin C every day. Do the loading dose of liposomal C if it is determined you have been long insufficient.
- Make sure your multivitamin has sufficient B-complex vitamins and if needed add (1) Swanson Vitamins Activated B-Complex High Bioavailability (NOT high potency).
- Take 200 mg of L-theanine twice a day on an empty stomach. L-theanine alters brain waves within 20 minutes reducing the load of stress chemicals and increasing dopamine, an amino acid associated with reward. Read labels carefully to determine how much theanine is actually in each pill or capsule.
- Take (1) capsule of Seriphos (no substitute for this) mid-afternoon and/or before bed to reduce afternoon/evening cortisol which contributes to stress related obesity and impaired sleep..
- Use melatonin 3 mg every night at the same time, whether you go to bed or not.
- Omega-3 fats are critical to weight loss. Make sure you get a minimum of 3,000 mg of omega-3 (combined EPA and DHA) daily. Remember you must total the DHA/EPA in each capsule to determine how much you are getting in each one. Read the label carefully.
- Exercise is critical. Refer to the section on muscle and exercise page 170 to see how to burn calories 24 hours a day. Exercise reduces stress.
- Get the Ubiome test <http://ubiome.refr.cc/XL3MGSK> (link gives 10% discount) and rebalance your microbiome using the Immune Restoration Protocol.

KRISPIN'S NOTE: In industrialized societies fasting insulin rises as we age. Check once a year. Any value above 7 uUnits/ml is an issue, ideal is under 5 uUnits/ml. Exercise can help but diet (food and food frequency) plays the largest role keeping insulin low.

In the section below we see the relationship of insulin and inflammation but it is also suggested obesity is required. In the Time Restricted Feeding study mice on an ad libitum regular diet were weight normal but had inflammation and this was reversed by Time Restricted Feeding which lowers fasting insulin.

Insulin, Obesity, Inflammation and Hypoxia

White fat cells, these are the kind that store in all the places you don't want them, actually produce chemicals that cause general inflammation. Researchers are now considering these cells to be an endocrine organ as adipocytokines produced in white fat increase production of inflammatory chemicals throughout the body. **Reducing fasting and basal insulin reduces the inflammatory chemicals produced in fat cells and reduces the number of fat cells.**

Obesity is also associated with changes in breathing and tissue oxygenation, which increase insulin resistance and impair fat burning. Sleep apnea, when you briefly stop breathing while asleep, common in obesity, further contributes to oxygen desaturation in your blood, hypoxemia, insulin resistance, fat storage, and inflammation. Iron deficiency (check your ferritin) increases inflammation, and lowers body oxygen as well as preventing the production of carnitine making 'fat burning' difficult.

Reducing fasting and basal insulin reduces body fat, improves body oxygen levels, reverses insulin resistance and reverses abnormal inflammation. The way to recovery is finding the food plan that will lower your insulin while continuing to eat fresh, real food, making sure both C and iron are sufficient.

Obesity: More Than 30 Pounds over Ideal Body Weight

Make sure your thyroid is functioning normally. Thyroid disease may be a cause of elevated insulin and insulin resistance.^(772,773,774,775,776,777)

Get the 25(OH)D test as low D contributes to insulin resistance and calorie storage. Make sure your 25(OH)D is between 40-60 ng/ml. If vitamin D is less than 39 ng/ml and/or any of the thyroid values are abnormal, or fasting insulin above 8 call for help.

If your physician won't order or your insurance doesn't cover these tests all are available at reasonable prices from Life Extension <http://lef.org> You need not become a member to purchase the tests.

The tests to take are

1. TSH (normal is less than 2)
2. Free T3
3. Free T4
4. Fasting insulin (never higher than 8 and less than 5 is ideal)
5. Homocysteine
6. Hemoglobin A1C (should be normal, less than 5)
7. Fasting glucose (should be under 85)
8. Vitamin D 25(OH)D (ideal 40-60 ng/ml)
9. Ferritin (ideal 70-90, greater than 200 is an issue)
10. Ubiome microbiota test <http://ubiome.refr.cc/XL3MGSK> Your microbiome has a huge role in insulin resistance, overweight and metabolic syndrome. After testing start the Immune Restoration Protocol.

These are not all standard tests so make sure your physician is clear about what tests you want.

To Normalize BMI

1. Commit to the Time Restricted Feeding plan
2. Get the protein, potassium and good fats that you need. This must be first. Make sure you actually count potassium so that you confirm your intake.
3. Make sure you have the RIGHT microbes. Complete the Immune Restoration Protocol (10 days)
4. Get your tissues loaded with vitamin C. Higher levels of vitamin C are associated with a lower waist-hip ratio.⁽⁷⁷⁸⁾ Vitamin C also reduces total body inflammation.⁽⁵²³⁾
5. Have your thyroid checked (TSH, free T3, free T4, reverse T3) before you begin and make sure you take selenium (as 200 mcg. selenomethionine) every day. If there is a thyroid issue, call in.
6. Test fasting insulin, glucose and A1C (above), retest every 3 months as your begin
7. Make sure you pass the Zinc Status test.
8. Make sure your serum 25(OH)D is 40-60 ng/ml
9. Make sure your serum ferritin is 70-110 ng/ml

There are answers. Call if you need help.

In response to this information on Time Restricted Feeding a client wrote-

Why is it that everyone (healthcare professionals, dietitians, nutritionists, etc.) recommends small and frequent meals to stabilize blood sugar and lose weight? I've been questioning this for a while, because if you eat every two hours how do you ever get the chance to burn your fat reserves? But everyone seems to promote that, for both blood sugar stability and weight loss. That's all I hear from all my teachers in my Nutrition program.

My response: Rather than rewrite what has already been written let the answer come from one of the earliest adopters of Time Restricted Feeding Martin Berkhan <http://leangains.com> who has successfully been using TRF since 2009. I do not have permission to publish his full article, so it is heavily edited but I think he does a good job at addressing the issues for those who have come to believe they must eat all the time to be healthy.

Martin's language is sometimes a bit raw and his version of Time Restricted Feeding-Intermittent Fasting is specifically designed for body builders, to be as lean as possible with the largest muscles possible. While the specifics of his training plan are not necessary for non-body builders, he is very good at what he does and I am grateful to him for working with the concept early on, even before the science could catch up-

I have heavily edited this to the key points. For the full explanation, IF you need it, please visit Martin's site <http://www.leangains.com/2010/10/top-ten-fasting-myths-debunked.html>

Top Ten Fasting Myths Debunked (Major Update Nov 4th) Posted by Martin Berkhan ...The myths I'll debunk today are being kept alive by:

- 1. Repetition. Repeat something often enough and it becomes the truth...*
- 2. Commercial forces. For example, the supplement industry benefits greatly from people believing that frequent feedings provide a metabolic advantage. People don't have time to eat six cooked meals a day. Instead, they turn to meal replacement powders, shakes and protein bars. The cereal and grain industry benefits by preaching about the virtues of breakfast for weight control, health and fat loss. There's no commercial incentive in telling people that they would do just fine with three squares a day.*
- 3. Few people have the knowledge or interest needed to interpret the scientific evidence and draw their own conclusions. ...However, an academic background, or an extensive education in nutrition or physiology, seems to correlate very poorly with truthfulness and objectivity in the field of dietetics in my experience. The advice and claims I have seen made by many RDs (Registered Dietitians) has been so shamelessly wrong that I put little stock in anything they have to say. The same goes for many "diet gurus" and so-called health experts with a solid list of academic credentials...*

The top ten fasting myths debunked (Krispin's note, see leangains.com for all 10, just the basic 4 here)

The dietary recommendations and advice given in mainstream media and most forums will have you believe that fasting is a hazardous practice. On top of wrecking your metabolism, you should expect ravenous hunger, fat gain, muscle loss, and severe mental impairment. Or so you are told.

1. Myth: Eat frequently to "stoke the metabolic fire".

Truth Each time you eat, metabolic rate increases slightly for a few hours. Paradoxically, it takes energy to break down and absorb energy. This is the Thermic Effect of Food (TEF). The amount of energy expended is directly proportional to the amount of calories and nutrients consumed in the meal.

Origin Seeing how conclusive and clear research is on the topic of meal frequency, you might wonder why it is that some people, quite often RDs in fact, keep repeating the myth of "stoking the metabolic fire" by eating small meals on a frequent basis. My best guess is that they've somehow misunderstood TEF. After all, they're technically right to say you keep your metabolism humming along by eating frequently. They just missed that critical part where it was explained that TEF is proportional to the calories consumed in each meal...

There's a saying that goes "correlation does not imply causation" and this warrants further explanation since it explains many other dietary myths and fallacies. Just because there's a connection between low meal frequencies and higher body weights, doesn't mean that low meal frequencies cause weight gain. Those studies likely show that people who tend to eat less frequently have:

** Dysregulated eating patterns; the personality type that skips breakfast in favor of a donut in the car on the way to work, undereat during the day, and overeat in the evening. They tend to be less concerned with health and diet than those who eat more frequently.*

** Another feasible explanation for the association between low meal frequencies and higher body weight is that meal skipping is often used as a weight loss strategy. People who are overweight are more likely to be on a diet and eat fewer meals.*

The connection between lower meal frequency and higher body weight in the general population, and vice versa, is connected to behavioral patterns - not metabolism.

2. Myth: Eat smaller meals more often for hunger control.

Truth Given the importance of finding the most favorable meal pattern for hunger and appetite

control, there's a surprising scarcity of studies on the topic.

The latest research, performed under conditions that more closely resemble a real-world scenario, shows the opposite result. In this study, three high-protein meals lead to greater fullness and appetite control when compared to six high-protein meals...Origin This myth might have originated from the limited data from studies on meal frequencies and appetite control. It's also likely that it's another case of mistaking correlation for causation from studies and meal frequencies and higher body weights; if people who eat more often weigh less, then it must mean they can control their hunger better, etc.

3. Myth: Eat small meals to keep blood sugar levels under control.

Truth According to legions of diet and health "experts," eating small meals every so often will help you avoid hunger pangs, provide you with stable energy throughout the day and keep you mentally sharp. Contrary to what many people seem to believe, blood sugar is extremely well-regulated and maintained within a tight range in healthy people. It does not swing wildly up and down like a chimpanzee on meth and it doesn't plummet from going a few hours without food. Or even a full day without food; or a week without food for that matter.

Origin Not sure how people came to believe that skipping a meal would dumb them down. There is some truth to blood sugar and hunger, but this is often taken out of context. There's no need to eat regularly to "maintain" blood sugar as it maintains itself just fine and adapts to whatever meal pattern you choose.

4. Myth: Fasting tricks the body into "starvation mode".

Truth Efficient adaptation to famine was important for survival during rough times in our evolution. Lowering metabolic rate during starvation allowed us to live longer, increasing the possibility that we might come across something to eat. Starvation literally means starvation. It doesn't mean skipping a meal not eating for 24 hours. Or not eating for three days even. The belief that meal skipping or short-term fasting causes "starvation mode" is so completely ridiculous and absurd that it makes me want to jump out the window...

Origin- I guess some genius read that fasting or starvation causes metabolic rate to drop and took that to mean that meal skipping, or not eating for a day or two, would cause starvation mode.

CHAPTER 12 EXERCISE FOR LIFE AND HEALTH

Understanding the importance of exercise to health is critical. 90% of all energy is produced in muscle. Used (exercised) muscles have a high metabolic rate, readily burning fatty acids and glycogen.

Unused muscles metabolize energy poorly, especially fatty acid derived energy. In real terms this means unexercised muscles lose the capacity to burn fat (which also means they produce less heat, been feeling cold lately?).

Figures 11-1 and 11-2 show the profound differences in exercised and unexercised muscle cells. Mitochondria are prevalent in the exercised muscle and all but missing in the unexercised muscle cell. Whatever you eat it will have little benefit if you don't exercise regularly. The mitochondria are the squiggly ovals labeled M.

*mitochondria: A small intracellular organelle which is responsible for **energy production and cellular respiration**.*

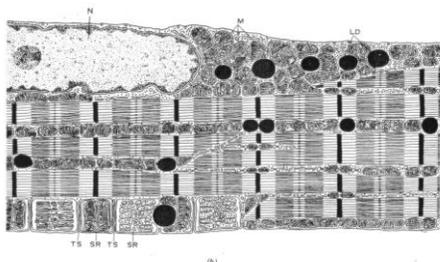


Figure 18.3b
Muscle with high metabolic activity. N, nucleus; M, mitochondria; LD, lipid droplets; TS, tubular system; SR, sarcoplasmic reticulum. (From T. L. Lentz, *Cell Fine Structure*, W. B. Saunders Co., Philadelphia, 1971, p. 89.)

Figure 12-1 Used Muscle Cell, Readily burns fat. to produce energy.

The mighty mitochondria are the secret of 'vitality'. The more you have the better you feel, all the time. Mitochondria control the metabolic processes of every cell. Mitochondria supply cells with oxygen and the furnace

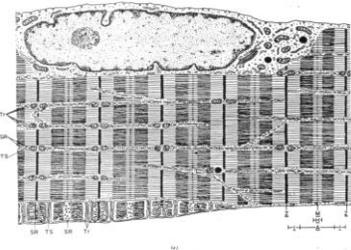


Figure 18.3a
Muscle with low metabolic activity. N, nucleus; SR, sarcoplasmic reticulum; TS, tubular system. (From T. L. Lentz, *Cell Fine Structure*, W. B. Saunders Co., Philadelphia, 1971, p. 87.)

Figure 12-2 Unused Muscle Cell burns fat poorly, few mitochondria.

The small black dots are brown fat used for cellular energy. They are a good thing. Brown fat means energy. The squiggly cells within the cell are the mitochondria. The used muscle has many mitochondria and burnable fat. The unused muscle cell has few mitochondria and little fat.

The fat we don't like is white fat found outside of cells and very difficult to burn for energy.

Acta Physiol Scand. 2000 Apr; 168(4): 445-56. **Structural and functional limits for oxygen supply to muscle.** Hoppeler H, Weibel ER. Department of Anatomy, University of Berne, Buhlstrasse 26, CH-3000 Berne 9, Switzerland.

Environmental oxygen is transported by the respiratory cascade to the site of oxidation in active tissues. Under conditions of heavy exercise it is ultimately the working skeletal muscle cells that determine the aerobic demand as over 90% of energy is spent in muscle cells. Oxygen is transported in the circulation bound to haemoglobin of erythrocytes while substrates are transported in the plasma. The supply of oxygen must be continuous because there are only minimal oxygen stores in the body of most mammalian species while substrates are stored in significant quantities both within muscle cells as also in organismic substrate stores. **The pathways for oxygen and substrates ultimately converge in muscle mitochondria.** In mammals, a structural limitation of carbohydrate and lipid transfer from the microvascular system to muscle cells is reached at a moderate work intensity (i.e. at less than 50% of VO₂max). At higher work rates intracellular substrate stores must be used for oxidation. It is therefore not surprising to find larger intramyocellular carbohydrate and lipid stores in 'athletic' species as well as in endurance-trained human athletes. The transfer limitations for carbohydrates and lipids presumably occur on the level of the sarcolemma. These findings imply that the design of the respiratory cascade from lungs to muscle mitochondria has to be analyzed with regard to satisfying the demand for oxygen of the working muscle cells. Substrate stores are replenished at low flux rates during periods of rest and are stored intracellularly. They are therefore locally available to mitochondria for aerobic work at high intensities.

ONLY exercise builds muscle cells that burn calories 24 hours a day (resting metabolic rate). Eating enough protein, quality fats and foods high in potassium improves exercise capacity and enhances the cells ability to respond to stress **as long as fasting and basal insulin remain stable/low..**

How do we get more mitochondria? Mitochondria are a component of every muscle cell but how many we have in each cell depends. Mitochondria come into being when we 'ask' them. Exercise is 'asking'. Life is plastic. We are plastic. We move and life responds.

plastic

1. Having the power to give form or fashion to a mass of matter; as, the plastic hand of the Creator. "See plastic Nature working to his end." (Pope)
 2. Capable of being molded, formed, or modeled, as clay or plaster; used also figuratively; as, the plastic mind of a child.
 3. Pertaining or appropriate to, or characteristic of, molding or modeling; produced by, or appearing as if produced by, molding or modeling; said of sculpture and the kindred arts, in distinction from painting and the graphic arts. "Medallions . . . Fraught with the plastic beauty and grace of the palmy days of Italian art." (J. S.)
- Origin: L. *Plasticus*, Gr, fr. To form, mold: cf. F. *Plastique*.
Source: Websters Dictionary

Molecular and cellular biologists are learning that 'genes' don't always act the way we expect. Genes change in response to their environment. We mold and we are molded by all that lives around us and by the things we do, how and when we eat, sleep, exercise. Just as melanin is produced in response to sunlight mitochondria are produced within the cell in response to exercise.

Exerc Sport Sci Rev. 2000 Apr; 28(2): 68-73. **Assembly of the cellular powerhouse: current issues in muscle mitochondrial biogenesis.** Hood DA, Takahashi M, Connor MK, Freyssenet D. Department of Kinesiology and Health Science, York University, Toronto, Ontario, Canada. dhoo@yorku.ca

Mitochondrial biogenesis occurs in muscle in response to chronic exercise, resulting in fatigue resistance. The assembly of the organelle is initiated by contraction-induced signals, which lead to the transcriptional activation of nuclear genes. This is accompanied by alterations in mRNA stability, as well as increases in protein import and mitochondrial DNA copy number, leading to a greater muscle mitochondrial content.

People who exercise regularly don't just feel better when they exercise, they feel better all of the time and they burn calories (and fat) 24 hours a day. Their cells actually contain more oxygen and mitochondria for energy production.

Recent data suggest that mitochondria may function as O₂ sensors by increasing their generation of ROS during hypoxia. These oxidant signals appear to act as second messengers in the adaptive responses to hypoxia in a variety of cell types. Such observations contribute to a growing awareness that mitochondria do more than just generate ATP, in that they initiate signaling cascades involved in adaptive responses to hypoxia and that they participate in the control of cell death pathways.

As hypoxia is a common finding in obesity it is likely the increase in body fat and reduction in used (exercised) muscle alters oxygen sensing and recovery from hypoxia.

J Appl Physiol. 2001 Mar; 90(3): 1137-57. **Invited Review: contractile activity-induced mitochondrial biogenesis in skeletal muscle.** Hood DA. Department of Kinesiology and Health Science, York University, Toronto, Ontario, Canada M3J 1P3. dhood@yorku.ca

Chronic contractile activity produces mitochondrial biogenesis in muscle. This adaptation results in a significant shift in adenine nucleotide metabolism, with **attendant improvements in fatigue resistance**. The vast majority of mitochondrial proteins are derived from the nuclear genome, necessitating the transcription of genes, the translation of mRNA into protein, the targeting of the protein to a mitochondrial compartment via the import machinery, and the assembly of multisubunit enzyme complexes in the respiratory chain or matrix. Putative signals involved in initiating this pathway of gene expression in response to contractile activity likely arise from combinations of accelerations in ATP turnover or imbalances between mitochondrial ATP synthesis and cellular ATP demand, and Ca(2+) fluxes. These rapid events are followed by the activation of exercise-responsive kinases, which phosphorylate proteins such as transcription factors, which subsequently bind to upstream regulatory regions in DNA, to alter transcription rates. Contractile activity increases the mRNA levels of nuclear-encoded proteins such as cytochrome c and mitochondrial transcription factor A (Tfam) and mRNA levels of upstream transcription factors like c-jun and nuclear respiratory factor-1 (NRF-1). mRNA level changes are often most evident during the post exercise recovery period, and they can occur as a result of contractile activity-induced increases in transcription or mRNA stability. Tfam is imported into mitochondria and controls the expression of mitochondrial DNA (mtDNA). mtDNA contributes only 13 protein products to the respiratory chain, but they are vital for electron transport and ATP synthesis. Contractile activity increases Tfam expression and accelerates its import into mitochondria, resulting in increased mtDNA transcription and replication. The result of this coordinated expression of the nuclear and the mitochondrial genomes, along with poorly understood changes in phospholipid synthesis, is an expansion of the muscle mitochondrial reticulum. Further understanding of 1) regulation of mtDNA expression, 2) upstream activators of NRF-1 and other transcription factors, 3) the identity of mRNA stabilizing proteins, and 4) potential of contractile activity-induced changes in apoptotic signals are warranted.

In the drawing of the exercised muscle cell the dark spots labeled LP are fats readily available to be burned for muscle energy. The unexercised muscle cell with few fats and few mitochondria has a hard time burning fatty acids for energy and will burn glycogen instead but very inefficiently. This is the type of cell that will eventually

develop insulin resistance. EXERCISE. Whatever your age or condition exercise will change things, in a very good way.

Think of used muscle as dark meat and unused muscle as white meat. Desk sitters and couch potatoes have lots of white meat, athletes mostly dark (like wild game). Only dark meat produces energy (burns calories and produces heat) 24 hours a day. The endpoint of eating well is providing energy to the muscles and providing nutrients to rebuild the body as old parts fall away.

If you don't use your muscles, vigorously, every day, you will lose your mitochondria and your body will change from energy burning muscle to energy deficient muscle and finally to fat with little muscle to produce energy.

As we age our ability to respond to exercise was thought to be diminished but much of that is simply lifestyle, meaning too many calories/carbohydrates, too little protein, and too little physical activity. With the new knowledge concerning the role of insulin, that it tends to increase with age, the article below states the symptoms but misses the cause. Now 13 years later we can safely conclude rising fasting insulin is the cause of reduced exercise capacity in aging and we can reverse it.

Ann Med. 2000 Sep; 32(6): 380-2. *Adrenergically stimulated fat utilization and ageing.* Blaak EE.

Ageing is associated with a diminished ability to use fat as a fuel during exercise. Also, middle-aged subjects have a blunted ability to mobilize fatty acids and to increase skeletal muscle fatty acid uptake and oxidation during intravenous beta-adrenergic stimulation, indicating that the sympathetic nervous system may play a role in the disturbed fat utilization. The blunted lipolytic response may be related to disturbances at the receptor level, eg a diminished number or agonist affinity of beta-adrenoceptors, or at the postreceptor level, eg a diminished activity of the hormone-sensitive lipase complex. As the rates of fatty acid availability are not limiting during exercise or beta-adrenergic stimulation in the elderly, the lowered skeletal muscle fat oxidation is probably related to an age-related decline in the capacity of skeletal muscle to oxidize fatty acids. Factors responsible for this decline may be a diminished content of oxidative enzymes, an increased glycolytic flux inhibiting fatty acid transport into the mitochondria, or a diminished (possibly beta-adrenergically-mediated) activation of fatty acid transport. It remains to be determined to what extent disturbances of fat metabolism may be related to the ageing process per se or whether they are secondary to age-related changes in body fat distribution and level of physical activity. Nevertheless, the impairments in sympathetically mediated lipolysis and fat oxidation may be of importance in the age-related increase in adiposity and insulin resistance and may thus be one of the links between ageing and increased prevalence of chronic diseases, such as obesity, type 2 diabetes mellitus, and cardiovascular disease.

Very obese persons have great difficulty exercising because what little muscle they retain is very low in mitochondria and particularly inefficient at burning fat, preferentially burning glycogen BUT due to elevated insulin muscle cells become insulin and therefore glycogen resistant. Reversing elevated insulin will allow muscles to use energy normally.

Reducing fasting insulin through diet AND exercising, preferentially High Intensity Intermittant Training (HIIT), throughout the day for 10-30 minutes will change your energy deficient body to an energy efficient body at any age.^(779,780)

Exercising for 1.5-2 minutes every 30 minutes during a 9 hour sedentary time period lowered plasma glucose 39% and plasma insulin 26%. **Eighteen intermittent short activity breaks, walking at 45% maximum output, had a better, more rapid effect on glucose and insulin than a 30 minute exercise period at 60% maximum output.** Take a break and walk, jump on a trampoline or get on a stationary bicycle. It will make a difference.^(781,782,783)

Fat is stored energy. The secret of accessing stored energy (fat) and producing new energy from food rather than storing it as fat is reducing post meal and fasting insulin and reversing insulin resistance and thereby increasing muscle mitochondria through exercise.

Diets that reverse fasting insulin will shift your body from fat storing to fat burning and exercise will enhance the process.

Anthropologists have studied the physical activity levels of our ancestors. Until quite recently an average minimum of 90 minutes a day was spent in intermittent intense activity in all cultures. Whether 45 minutes twice a day, 30 minutes 3 times a day, 10 minutes 9 times a day, or one long stretch of 90 minutes this does seem to be a minimum for health and longevity. Brisk walking counts, as does tennis, weights, jogging, swimming or hiking. Kick it up a notch and go full out intermittently.

Muscles and their myokines Pedersen, B. K. 1-15-2011 J.Exp.Biol.

*In the past, the role of physical activity as a life-style modulating factor has been considered as that of a tool to balance energy intake. Although it is important to avoid obesity, physical inactivity should be discussed in a much broader context. **There is accumulating epidemiological evidence that a physically active life plays an independent role in the protection against type 2 diabetes, cardiovascular diseases, cancer, dementia and even depression.** For most of the last century, researchers sought a link between muscle contraction and humoral changes in the form of an 'exercise factor', which could be released from skeletal muscle during contraction and mediate some of the exercise-induced metabolic changes in other organs such as the liver and the adipose tissue. We have suggested that cytokines or other peptides that are produced, expressed and released by muscle fibres and exert autocrine, paracrine or endocrine effects should be classified as 'myokines'. **Given that skeletal muscle is the largest organ in the human body, our discovery that contracting skeletal muscle secretes proteins sets a novel paradigm: skeletal muscle is an endocrine organ producing and releasing myokines, which work in a hormone-like fashion, exerting specific endocrine effects on other organs.** Other myokines work via paracrine mechanisms, exerting local effects on signaling pathways involved in muscle metabolism. It has been suggested that myokines may contribute to exercise-induced protection against several chronic diseases.*

High Intensity Intermittent Training (HIIT)

Research studies support the use of high intensity intermittent training.^(747,748,749,750,751,752,753)

High-intensity intermittent training is a form of interval training consisting of short bouts of all-out activity separated by rest periods of between 20 s and 5 min. It is a low-volume strategy for producing gains in aerobic power and endurance normally associated with longer training bouts. Christian Finn Learn Fitness, Middlesex HA3 7EQ, United Kingdom.

For each 5 minutes of whatever you do, running, walking, rebounding, biking, lifting, 30 seconds should be 'full out' with 4.5 minutes of recovery at a steady moderate (50% of full out) pace. Like Time Restricted Feeding you may choose intervals, 1 minute full intensity 9 minutes moderate. Starting with 30 seconds and 4.5 minutes makes it easy for most fitness levels. Increase the cycle 30 s 4.5 min up to 6 cycles (total 30 minutes) or 5 minutes full out 10 minutes moderate X 2 total 30 minutes.

Sessions never last longer than 30 minutes. The advantage of interval training is that you progress much faster in repleting mitochondria and improving muscle endurance while exercising for a shorter period of time. Wikipedia has an excellent article on HIIT. It is important to modify the technique to keep you exercised and happy.

Exercise should be fun, but also hard work. Intensity is important. Walking on the flats, unless you're race walking, won't change your muscle cells into fat burning powerhouses. To build mitochondria in your upper body you'll need to do push-ups, lift weights or climb ropes or rocks. Intense walking on hills or steep inclines or stairs, running, and/or weight lifting, heavy weight (have a buddy) with few lifts, will all produce muscle cells that readily consume fatty acids and oxygen 24 hours a day, not just when you're exercising. These cells don't become insulin resistant and don't force the body to store calories, instead they readily burn available fuel.

Take a hike.... ride a bike... lift a load... take a chance and dance... get moving.

CHAPTER 13 HEALTH, IMMUNITY AND AGING

A functioning immune system is one of the keys to health and longevity. Immune function is all about walls, walls that divide 'self' from 'not-self'. It is true good walls make good neighbors.

The human body is very much like the description of a cell

From chapter 9, The Plasma Membrane, Nutrition an Integrated Approach, Pike and Brown, 1986

All cells are units separated from their environment by a membrane. This is a barrier whose presence determine the shape and encloses the substance of the cell. Despite the variability and potential hostility of the outside environment, it is the membrane on which the constancy of the internal chemistry of the cell is dependent. The discharge of this responsibility is made possible by the ability of the membrane to discriminate among those organic and inorganic molecules in the surrounding medium, permitting the entrance to some and rebuffing others. This is a truly vital task since either mass invasion of potentially toxic material or rejection of essential nutrients can lead to cellular death by asphyxiation, hydration, desiccation, poisoning, starvation, or other equally effective means. The cell, thus dependent on the external environment for all the raw materials from which it is made and with which it operates, by means of the membrane barrier and its fastidious selectivity, can enjoy a distinct and separate existence.

A cell in equilibrium with its environment is a dead cell. (emphasis is mine)

For survival, selectivity, that is **discrimination**, is the only choice. It is necessary that the cell selects and allows those things that are needed and avoids those things that are unnecessary or toxic. This is equally true throughout your body as a whole. Your body must remain vigilant to accept that which is able to maintain life and become 'self' and to avoid or destroy that which is 'not self'. Tolerance of 'not self' brings dissolution of the cell and death.

Inflamm Res. 2000 Nov;49(11):561-70. Unregulated inflammation shortens human functional longevity. Rod SA. University of Texas Health Science Center at Houston, Department of Neurology, 77225, USA. Staley.a.brod@uth.tmc.edu

Systemic inflammation, represented in large part by the production of pro-inflammatory cytokines, is the response of humans to the assault of the non-self on the organism. Three distinct types of human ailments - namely autoimmunity, presenile dementia (Alzheimer's disease), or atherosclerosis - are initiated or worsened by systemic inflammation. Autoimmunity is unregulated hyperimmunity to organ-

specific proteins, inducing rapid turnover of antigen-specific T cells of the acquired immune system with ultimate exhaustion and loss of acquired immunity IL-2 and IFN-gamma production and proliferative decline, conforming to the limited capacity of clonal division (Hayflick phenomenon). In Alzheimer's disease (AD), the primary degenerative process of amyloid-beta (A β) protein precedes a cascade of events that ultimately leads to a local "brain inflammatory response". Unregulated systemic immune processes are secondary but important as a driving-force role in AD pathogenesis. Atherosclerosis, an underlying cause of myocardial infarction, stroke, and other cardiovascular diseases, consists of focal plaques characterized by cholesterol deposition, fibrosis, and inflammation. The presence of activated T lymphocytes and macrophages indicate a local immunologic activation in the atherosclerotic plaque that may be secondary to unregulated pro-inflammatory cytokines too. The premature hyperimmunity of autoimmunity, the local "brain inflammatory response" to A β protein in AD, and the immune response to fatty changes in vessels in atherosclerosis all signal the critical importance of unregulated systemic inflammation to common neurological and cardiovascular disease that shortens the nominal longevity of humans.

Over a lifetime assaults include inflammation from elevated post meal or fasting insulin, over-exposure to infectious pathogens including bacteria, virus, spirochetes, and mycoplasmas; damage to healthy gut microflora from pathogens or antibiotics resulting in immune failure of the gut wall; and consumption of lectins, glycoproteins such as gluten or casein, that are not genetically appropriate resulting in immune dysfunction and damage to the gut wall. These assaults can be intensified, meaning immune response does not result in full recovery, if sources of nutrients needed by the immune system, such as protein, zinc, selenium, iron, vitamin A, vitamin D, vitamin E, and others, are missing or insufficient.

The immune system exists to protect our bodies from invasion by toxins (xenobiotics, chemicals, drugs, heavy metals, poisons), pathogens (infectious agents including virus, bacteria, parasites and fungi), allergens (injected, including vaccines, inhaled or ingested) and other environmental assaults.

Lack of exposure to 'other/not me' assaults (living in a bubble) prevents the development of critical parts of the immune system, hence the advice to allow children to have pets at an early age. BUT over stressing the immune system also shortens life expectancy.

The immune system is keyed to all 'surfaces', the skin, the gut from mouth to anus, the cell walls and cell membranes. In infants the gut wall is semi-permeable at birth but rapidly develops closure in breast fed infants. Feeding of formula, even 'hypo-allergenic formula' seems to delay development of gut barrier function.⁽⁷⁸⁴⁾

The bacteria we all carry on our mucous membranes, when 'friendly', are an essential part of our 'walls' composing more than 60% of the barrier function. Without the right bacterial balance walls rapidly fail. NO supplement will fix dysbiosis, only restoration of the good bacteria will restore our immunity, our walls.

Early introduction of inappropriate proteins can irreversibly alter immune function with dire results.^(785,786,787) Evidence indicates breast feeding, even for a few months, feeding genetically appropriate foods, and early introduction of probiotics help to lower immune assaults early in life and reduce lifetime immune burden.⁽⁷⁸⁸⁾

Vaccinations prevent a number of life-threatening diseases but over-vaccination, becoming more likely with the new policies of yearly flu vaccines and increasing insistence on vaccines for other viral diseases, are likely to lead to increases in autoimmune diseases. Some researchers suggest this may already be happening. Evidence from veterinary medicine shows a steep

increase in auto-antibodies (autoimmune disease) in vaccinated versus unvaccinated dogs.^(789,790,791)

Our immune system has been most recently classified by stimulation of T cells, T helper cells, T Suppressor cells and T Killer cells. Assaults stimulate expression of T Helper cells 1 and/or T Helper cells 2 (TH1 and TH2).

Th1 function regulates the cellular or cell-mediated immune system designed to destroy, digest and expel foreign antigens out of the body via the lymph system. This is your body's 'acute inflammatory response' and is often accompanied by inflammation, fever, pain, malaise and discharge of mucus, pus, rash or diarrhea.

Th2 functions as your humoral immune system regulating the production of antibodies which recognize foreign antigens in your blood.

The two types of T-helper cells are defined by the cytokines they produce. Th1 cells, involved in cellular immunity, produce IL-2, TNF-beta and IFN-gamma, while Th2 cells, with roles in humoral immunity, produce IL-4, IL-5 and IL-10. The cytokines produced by Th2 cells enhance Th2 development and inhibit Th1 development, while Th1 cytokines stimulate development of Th1 and inhibit development of Th2.

These two functions work together to protect us from 'not us'. Th2 functions act as a sense organ, 'tasting', identifying and remembering foreign invaders (not-self). Th1 functions digest and eliminate foreign invaders from the body. While cellular immunity (Th1) directs Natural Killer T-cells and macrophages to attack abnormal cells and microorganisms at sites of infection inside the cells, humoral immunity (Th2) results in the production of antibodies used to neutralize foreign invaders and substances outside of the cells.

We are daily assaulted by virus, bacteria, parasites, fungus and antigenic proteins.

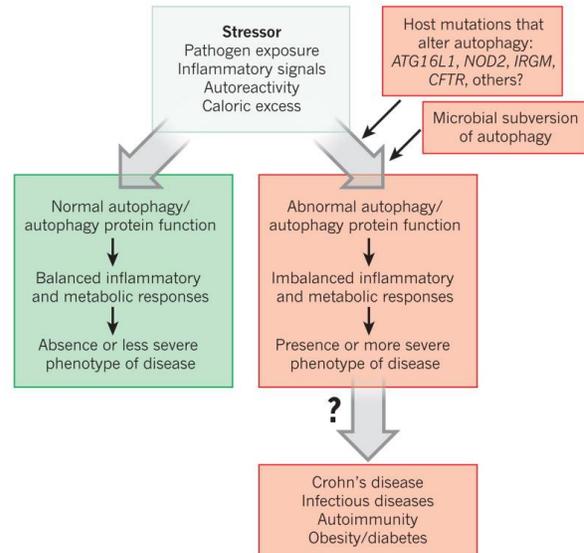
Our first line of defense is the 100+ trillion bacteria populating our mucous membranes killing pathogens, keeping fungus and parasites from invading the mucous lining and binding antigenic proteins. If our 'first line' defense is compromised, degeneration and disease are not far off. Without this friendly army our immune system is under constant direct assault.

In many cases, an infection is fought with both arms of the immune system. At other times predominantly one is needed to control an infection. A healthy immune system is balanced and dynamic, Th1 and Th2 activity switching back and forth as needed. This allows for a quick eradication of a threat and then a return to balance before responding to the next threat.

The inability to respond adequately with a Th1 response can result in chronic infection and cancer; an overactive Th2 response can contribute to allergies, and play a role in the development of autoimmune diseases. In end stage illnesses, both arms of the immune system fail. Introduction of high potency probiotics has been clinically demonstrated to reverse the aging or insufficiency of both side of our immune defense.^(792,793,794,795,796,797,798,799)

Substances that have shown themselves to be critical to keeping the Th1 and Th2 system balanced include FIRST and FOREMOST probiotics, prebiotics (dietary fibers) and also selenium, zinc, and omega-3 fatty acids.^(800,801)

A primary, yet to be fully understood, component of healthy aging and immunity is autophagy. Autophagy (self-eating) is a process whereby the body removes (digests) dead and dying cells, bacteria, virus, and other damaged and/or potentially harmful proteins. Autophagy is a primary component of both innate and adaptive immunity. When autophagy is able to function normally our bodies are able to remove damaged DNA and useless cell components and better fight bacterial and viral loads. Elevated fasting insulin precedes chronic inflammation and suppresses autophagy.



Nature. 2011 January 20; 469(7330): 323–335. doi: 10.1038/nature09782 **Autophagy in immunity and inflammation** Beth Levine, 1,2,3 Noboru Mizushima, 4 and Herbert W. Virgin 55

...Perturbations in autophagy-protein-dependent functions in immunity may contribute not only to increased susceptibility to infection, but also to chronic inflammatory diseases and autoimmune diseases.

For autophagy to function optimally the body requires:

- adequate vitamin D (40-60 ng/ml)
- normal thyroid function (TSH less than 2)
- rest (with adequate melatonin production)
- fasting insulin <6 uU/ml (elevated insulin suppresses autophagy)
- time restricted feeding or intermittent fasting

The food we eat, the drugs we use, the infectious and toxic agents we are intentionally or unintentionally exposed to and the health of our symbiotic bacteria all potentially contribute to immune load. Enough but not too much is the rule. We need a certain amount of exposure to 'foreign invaders' to stimulate immune function but chronic over stimulation results in acute or chronic illness and aging of the immune system.

An example of 'stress but not too much' would be using 'exfoliation' to stimulate regeneration of sun-damaged skin. Infrequent use in some persons will produce the desired results but chronic use or even light use in susceptible persons will damage underlying structures in the skin and increase the risk of skin cancer. In all cases exfoliation renders the skin more vulnerable to chemical and sun damage for 7-10 days following treatment.

As we age there is a shift from Th1 to Th2 dominance resulting in less ability to resist and recover from infectious disease, a generalized increase in inflammation and an increased likelihood of autoimmune disease.^(802,803,804) This change increases the risk of altered cell-cell communication resulting in higher rates of cell hyperplasia (over production of cells as found in breast calcifications, benign prostatic hyperplasia or skin 'tags').

Some of this change may be modulated by excess insulin. While insulin is necessary for life, excess insulin increases inflammation (increased cell destruction) and reduces autophagy

(removal of damaged cells). Americans tend to have increasingly elevated insulin and reduced autophagy as they age.

Much of this aging of the immune system is modifiable. Researchers have shown balancing gut bacteria can restore even aging immune system and improve an already healthy one.^(35,43,75,132,801) A covering of friendly microbes reduces general inflammation, not just in your gut. Chronic inflammation is recognized as a promoter in heart disease, hypertension, diabetes, osteoporosis, obesity, and cancer.

Our Living Shield (why microbes ARE our immune system)

The human body is designed to be, and is, covered by microbes. Before you say yuck read on to find out why this is a very good thing. The science behind what I will be discussing is found in numerous studies on PubMed and in the Cambridge University Press textbook, *Microbial Inhabitants of Humans*, 2005. The research is new, exciting, and the implications won't truly be known or understood for some years. One reason for the delay in knowledge and understanding is that there are many more microbes than science is able to culture. The total count of types of just 'friendly' microbes exceeds 500 types, most of which cannot survive outside a living organism so trying to understand them is quite expensive and often impossible.

Some microbes are considered friendly, others pathogenic, the rest, neutral (but likely we just don't know what they are supposed to do yet).

The premise: The human body is designed to be covered (outside and inside, all 'surfaces') by microbes, human friendly living organisms, actually performing services for our bodies. Most of these organisms are anaerobic, cannot be 'taken' but are grown by using specific fibers. Some are aerobic (<10%) and can be replenished or enhanced through use of probiotics such as kefir, yogurt, VSL#3 and similar supplements.

The proof: Taking high potency probiotics in clinically effective types and amounts and using fibers known to feed healthy anaerobic bacteria and reporting your results.

We have (or should have) this covering because friendly microbes:

1. Maintain the health (rapidly forming barrier function) of our mucous membranes and skin.
2. Metabolize (breakdown and remove) proteinous and/or toxic substances which include but are not limited to pathogenic bacteria and their endotoxins, virus, fungus, chemicals, pesticides, herbicides, other potential exotoxins, pollen and other inhaled potential allergens, consumed potential allergens, and excreted hormones and cholesterol found in bile.
3. Increase the size and capacity of the duodenal villi increasing digestive and absorptive capacity
4. Heal, strengthen and protect the rapidly forming mucous membrane immune barrier.
5. Interact with the body through the mucous membrane to lower total body burden of chemicals, toxins and waste; increase secretory IgA and NK (natural killer) cells; improve the immune function of the spleen and other immune markers to reduce both allergic and autoimmune disease and decrease total body inflammation;

When the total number of friendly microbes is reduced because we didn't get the right microbes from our parents in the beginning, or lost them because of antibiotics, flu, or because we got a dose of pathogenic microbes, bad things happen.

The bad things that may happen:

1. We may become easily susceptible to infection.
2. We may become allergic to our environment.
3. We may become allergic to the food we eat.
4. We may develop asthma.
5. We may become chronically fatigued from 'bearing the burdens of the world'.
6. We may be unable to fully benefit from the food we eat, our digestion is impaired.
7. We may develop metabolic disease and/or obesity.
8. We may become carriers of infection to others.
9. We may suffer from chronic constipation.
10. We may suffer from IBS, Crohn's Disease, or colitis.
11. Our mucous membranes may become permeable from chemical or pathogenic microbial or microbial endotoxin damage.
12. Proteinous substances in our environment (bacteria, virus, pollen, dust mite, peanut, soy, chemical, insecticide, etc.) may directly contact or even cross our mucous membranes and result in allergic or autoimmune reactions/disease.
13. Substances meant to be metabolized by our friendly microbes aren't and our bodies bear the burden with high loads of exotoxins, chemicals, internal and external waste products, and endotoxins breaching the inner barrier and circulating throughout our bodies putting undue burdens on our liver and kidney and other organs.
14. When 'good' bacteria are in short supply the 'neutral' or so called 'normal' bacteria may become pathogenic, including klebsiella and others. The lack of good bacteria promotes growth of some microbes and when a certain microbial threshold is reached non-pathogenic bacteria actually becoming pathogenic bacteria.
15. Breaching our failed microbial and mucous barrier the overwhelming burden of 'junk' may create an inner condition of chronic inflammation supporting the progression of both degenerative and malignant disease.

This is NOT about taking vitamin or mineral supplements. This is not about avoiding foods or environments or chemicals. This is about restoring your 'walls'. Having the right microbes keeps out those things that should not enter your body proper, helps metabolize needed elements for absorption, and feeds and protects the mucous membranes (your inside walls).

Unfortunately the 90% of your gut microbes are anaerobic (they cannot live with oxygen) so they cannot be 'replaced' by using probiotics (good aerobic bacteria, kefir, yogurt). In a few years it is likely anaerobes will be commercially available but at great cost. Honor your anaerobes, feed them and do not destroy them with antibiotics unless your disease is more life-threatening than loss of your anaerobes. Gut bacteria are primarily anaerobic so MORE important than probiotics are the types of fiber in your diet. Anaerobic bacteria thrive on soluble fibers. Most whole foods contain these fibers so eat 'whole' (apple with peel, potato with peel, etc)

The most clinically relevant probiotic to improve and support aerobic bacteria and suppress pathogenic anaerobic bacteria is VSL#3. It has the best balance of microbes designed to repair and restore the entire length of the digestive tract and nasal passages, urethra, and vaginal vault. We are all 'crawling' with microbes. Make sure yours are the right ones.

If you currently have digestive issues of any kind complete repair of your 'walls' takes a minimum of four weeks and longer in those with current pathogens, long term dysbiosis, or chronic disease. Co-infections with burgdorferi (Lyme Disease) or other pathogens requires additional treatment.

Why should you make this investment? Because, immunity starts with our microbial walls (our living shield).

Oral administration of live *Bifidobacterium* substrains isolated from healthy centenarians enhanced immune function in BALB/c mice. Hai-ying Yang a, Song-ling Liu a, Salam A. Ibrahim, Liang Zhaoa, Jing-li Jiangc, Wen-feng Sund, Fa-zheng Rena,. College of Food Science and Nutritional Engineering, China Agricultural University, PO Box 303, Beijing 100083, China Food Microbiology and Biotechnology Laboratory, North Carolina A & T State University, Greensboro, NC 27411-1064, USA Meng Niu Dairy (Beijing) Company, Beijing 101107, China Food Science College, Xinjiang Agricultural University, Urumchi 830052, China Received 8 January 2009; revised 22 March 2009; accepted 26 March 2009

*Study conclusions on the effects of bacteria isolated from centenarians- After 4 weeks, the immune parameters including cellular immunity (delayed-type hypersensitivity [DTH], and splenic lymphocyte proliferation), humoral immunity (serum hemolytic activity in immunized animals), and nonspecific immunity (peritoneal macrophages phagocytosis natural killer [NK] cell activity) were measured. We report that both Bifidobacterium strains independently increased the DTH response. Delayed type hypersensitivity (DTH) reactions are antigen-specific, cell-mediated immune responses which, depending on the antigen involved, mediate beneficial (resistance to viruses, bacteria, fungi, and tumors) or harmful (allergic dermatitis, autoimmunity) aspects of immune function. Macrophage phagocytosis (macrophage phagocytosis of micro-organisms is important in host immunity and activated macrophages kill ingested pathogens by production of reactive oxygen and nitrogen metabolites) was also enhanced, while activities of the NK cells (Natural Killer cells are a type of cytotoxic lymphocyte that constitute a major component of the innate immune system. NK cells play a major role in the rejection of tumors and cells infected by viruses. The cells kill by releasing small cytoplasmic granules of proteins called perforin and granzyme that cause the target cell to die by apoptosis) and levels of the serum hemolysin also were significantly higher than in the control group. There was a significant increase in splenic lymphocyte proliferation (our ability to bind and remove antigens) in bifidobacteria treatment animals compared to controls. In conclusion, ingestion of *B. adolescentis* BBMN23 and *B. longum* BBMN68 can enhance both innate and acquired immunity*

What research shows is an adequate balanced diet, low normal fasting insulin, adequate gut flora, normal thyroid function and adequate serum vitamin D levels support immune health even in centenarians.^(805,806,807,808) Exercise reduces overall inflammation.^(809,810,811)

Consumption of whole, fresh foods, genetically appropriate, (Did your ancestors eat it?) including fish, shell fish, poultry, meat and organ meats supports immune health at any age. organ meats, especially livers, provide the important fat soluble vitamins and key minerals required for immune function.^(812,813,814) Fresh whole foods provide abundant anti-oxidants, protein, fiber, minerals and vitamins.

Intense intermittent exercise stimulates immune functions, both Th1 and Th2 in a positive way.^(815,816,817,818,819) Regular exercise also enhances autophagy.^(820,821,822,823,824) Regular moderate sun exposure strengthens immunity at any age. Lack of sunlight or overexposure to sunlight suppresses immune response.⁽⁸²⁵⁾

Vitamin C and Immunity

Humans are one of the few living organism that do not make their own vitamin C. Since vitamin C is a primary component of both types of immunity, innate and adaptive, making sure you have enough is important. (496,826,827,828,829,830,831,832,833,834,835,836,837,838,839,840)

Components of the immune system (from Wikipedia)

Innate immune system	Adaptive immune system
Response is non-specific	Pathogen and antigen specific response
Exposure leads to immediate maximal response	Lag time between exposure and maximal response
Cell-mediated and humoral components	Cell-mediated and humoral components
No immunological memory	Exposure leads to immunological memory
Found in nearly all forms of life	Found only in jawed vertebrates

Both innate and adaptive immunity depend on the ability of the immune system to distinguish between self and non-self-molecules. In immunology, *self*-molecules are those components of an organism's body that can be distinguished from foreign substances by the immune system. Conversely, *non-self* molecules are those recognized as foreign molecules. One class of non-self molecules are called antigens (short for *antibody generators*) and are defined as substances that bind to specific immune receptors and elicit an immune response.

Vitamin C is necessary for the body's response to infection and infection depletes vitamin C. (innate immunity). Since vitamin C regulates cortisol and histamine it also plays a role in adaptive immunity allowing exposures without serious allergic responses. Adequate tissue levels of vitamin C may also lower the potential for the development of autoimmune disease. (461,494,495)

Minimum daily intake of vitamin C in children and adults is likely 500-2,000 mg and may be higher as research on this issue continues. Minimum daily intake does NOT take into account the amounts needed when ill, injured or otherwise stressed.

Vaccinate?

Vaccination may be important in areas where exposure to the disease is likely, but vaccination when exposure is unlikely may increase immune load without long-term benefit. Yearly flu vaccines will more rapidly push the immune system into Th2 response found in aged individuals. Why? Here is the hypothesis from Gary Null.

http://www.garynull.com/Documents/niin/how_vaccinations_work.htm

...A vaccination consists of introducing a disease agent or disease antigen into an individual's body without causing the disease. If the disease agent provoked the whole immune system into action it would cause all the symptoms of the disease! The symptoms of a disease are primarily the symptoms (fever, pain, malaise, loss of function) of the acute inflammatory response to the disease.

So the trick of a vaccination is to stimulate the immune system just enough so that it makes antibodies and "remembers" the disease antigen but not so much that it provokes an acute inflammatory response by the cellular immune system and makes us sick with the disease we're trying to prevent! Thus a vaccination works by stimulating very much the antibody production (Th2) and by stimulating very little or not at all the digesting and discharging function of the cellular immune system (Th1).

Vaccine antigens are designed to be "unprovocative" or "indigestible" for the cellular immune system (Th1) and highly stimulating for the antibody-mediated humoral immune system (Th2).

Perhaps it is not difficult to see then why the repeated use of vaccinations would tend to shift the functional balance of the immune system toward the antibody-producing side (Th2) and away from the acute inflammatory discharging side (the cell-mediated side or Th1). This has been confirmed by observation especially in the case of Gulf War Illness: most vaccinations cause a shift in immune function from the Th1 side (acute inflammatory discharging response) to the Th2 side (chronic auto-immune or allergic response).

... There is no system of the human being, from mind to muscles to immune system, which gets stronger through avoiding challenges, but only through overcoming challenges. The wise use of vaccinations would be to use them selectively, and not on a mass scale. In order for vaccinations to be helpful and not harmful, we must know beforehand in each individual to be vaccinated whether the Th1 function or the Th2 function of the immune system predominates.

In individuals in whom the Th1 function predominates, causing many acute inflammations because the cellular immune system is over reactive, a vaccination could have a balancing effect on the immune system and be helpful for that individual.

In individuals in whom the Th2 function predominates, causing few acute inflammations but rather the tendency to chronic allergic or autoimmune inflammations, a vaccination would cause the Th2 function to predominate even more, aggravating the imbalance of the immune system and harming the health of that individual.

Aging, the Thyroid, Vitamin D, Fasting Insulin, and Probiotics

In a significant study of nonagenarians and centenarians the most consistent remarkable values were thyroid hormone levels and vitamin D. These two substances ensured normal NK cells, which protect against cancer and other abnormal cell growth. Vitamin D normalized muscle strength in seniors of any age and reduced falls. Vitamin D along with vitamin K places calcium in the blood and bone where it belongs, not in the joints or arteries. Vitamin D can be taken as a supplement but sun exposure is preferred.

Both thyroid and vitamin D are strongly influenced by fasting insulin. Elevated fasting insulin contributes to thyroid dysfunction and lowers vitamin D by reducing conversion of D3 or sunlight to the active 25(OH)D. Test fasting insulin and if yours is above 6 uU/ml immediately institute diet and exercise changes to reduce it. ^(841,842,843,844,845,846,847)

Testing of fasting insulin, 25(OH)D and thyroid should be yearly and mandatory for everyone over 45. Make sure your fasting insulin is less than 6, D levels are normal (100-150 nmol/l or 40-60 ng/ml) and your TSH is less than 2. If your TSH is greater than 2 ask your physician for further testing, including free T3, free T4 and reverse T3. You'll be glad you did.

Our microbes play a big role in health and longevity. Make sure you have completed the Immune Restoration Protocol and continue to use high potency probiotics and anaerobic promoting fiber regularly.

When the bacteria found in centenarians from Bama longevity villages in China were placed in healthy mice both innate and acquired immunity were significantly improved in just four weeks.⁽⁴¹⁾ Longevity and immunity are intimately linked. We aren't just what we eat but the sum total of what we eat, the life we live, and the microbes we carry.

Final Words on Immunity

Sleep plays an important role in immune health.^(848,849,850,851,852,853,854) Studies show sleep deprivation decreases production of NK and NKT cells. Sleep, quality and quantity, regulates melatonin production. Melatonin enhances autophagy.

Like autophagy, Natural Killer cells destroy cells that have become infected with a virus or cells that are replicating abnormally including pre-cancerous or cancerous cells. Natural Killer T cells secrete cytokines of both the Th1 and Th2 family and destroy infectious agents as well as protecting against autoimmune disease. Both of these sleep and probiotic modifiable cell types are critical players in immune maintenance.

New research in autophagy shows how important 'house keeping' is to human health. With impaired autophagy, caused by chronic eating (no rest), impaired sleep, illness, or nutritional insufficiencies, virus, bacteria, old cells, and damaged DNA, are HOARDED. The consequences of this hoarding are premature aging, disease reactivation, plaque build up in arteries or brain, or even cancer.^(160,161,820,855,856,857,858,859,860,861,862,863,864) A healthy body is self-cleaning.

Our environment, those around us, family, friends and co-workers, and even the thoughts we think alter immune function. Positive thinking, a positive human support system, and faith in God improve immune health.^(865,866,867,868,869,870)

To remain healthy into advanced age we need a lifetime of good friends, including friendly microbes, genetically appropriate fresh, real, whole food, faith, exposure to and full recovery from common pathogens and infectious agents, quality and quantity of good sleep, intermittent doses of high potency broad spectrum probiotics and naturally fermented foods, a regular dose of sunlight, and regular exercise.

Things to avoid for long-term health: Excessive exercise, avoidance of exercise, excessive food, dead fake food, processed food, genetically inappropriate food, refined carbohydrates, antibiotics unless needed for life-threatening illness, vaccinations unless life-threatening disease exposure is impossible to avoid, excessive alcohol, chronically depressed or angry friends or family, chronically angry or paranoid politics, a bad attitude, and sleep deprivation.

CHAPTER 14 SPECIAL PROTOCOLS FOR SPECIAL SITUATIONS

These protocols are not prescriptive but suggestive and may be safely used by most people. If you have a reaction to any program or supplement or medication stop and seek professional advice. These formulas are to be used on a temporary basis for temporary conditions, not long term. They are not a substitute for medical care when needed.

Staying Well

The human immune system takes time to develop. Your lifetime exposure to immune assaults tells your real age. The more vaccines you get, the more infections you get, the more exposures you have whether to bacteria, virus or vaccine the greater the stress on your immune system. One vaccine may boost your system to conquer a virus. Six vaccines may overload your system and cause it to over respond with an autoimmune disease. ^(871,872,873,874,875,876)

Make sure you get enough iodine (small amount of dulse or seaweed regularly or a drop of 2% Lugol's Solution three times a week) or Life Extension Sea-Iodine one a day and selenium (methylselenocysteine or selenomethionine, in a supplement or found in garlic or brewer's yeast) daily. Both are critical for a healthy thyroid and for fighting off virus and bacteria. So is zinc, so regularly take the zinc test page 136 and make sure you have enough.

Avoid illness when possible. Stay home when you are sick. If you must go out wear a mask to prevent spreading your condition to others. If you are out where many inconsiderate people who are ill gather, wear a mask to protect yourself. Do not ask your immune system to be endlessly stressed and expect no cost. If you become ill consume easily digested foods like chicken soup with vegetables, fruit or vegetable juices, hardy stews slow cooked. If you do this you will get well quickly, recover fully and all of your energy will be available to your immune system for your recovery.

If you insist on continuing to expend energy in keeping warm, going out, eating more complex foods, expect to be ill for some time and to pass on your illness to others. Shame on you! Stay home and get well. Keep your kids home too.

Diseases are contagious and continuing to get them (whether we then treat them with drugs, herbs, or vitamins) has led to immune compromise and increased autoimmune disease, drug

resistant strains of bacteria, and mutated virus and super virus. Because of international travel, increased population, increased consumption of foods grown or prepared in unsanitary conditions, over use of antibiotics, failure to maintain gut probiotics, and rejection of basic principles of contagious disease control we are in one lifetime exposed to more pathogenic organisms (or vaccines derived from them) than any population in the history of man.

For Colds and Flu With or Without Fever Including H1N1

Day one (as soon as you even think you might be ill):

100,000 IU Vitamin A (must be fish liver oil source, read the label) 50,000 IU for infants/children ONCE A DAY Never continue beyond suggested use.

AND

SIPPY C (see formula below)* as needed for comfort (cough, tickle, sore throat) throughout the day/night. DO NOT MAKE THIS TOO STRONG. It should taste like water with something slightly tart/sweet' in it. If it is really tart you used too much C. ALL DAY AND NIGHT, KEEP IN WATER BOTTLE OR SPORT BOTTLE AND TAKE ALONG

And

30-50 mg zinc ONCE A DAY

And

Vitacost Olive Leaf Extract 500 mg (2) twice a day. Excellent anti-viral. TWICE A DAY

Days two and three:

100,000 IU vitamin A (50,000 IU for infants/children)

Sippy C Drink* as needed for comfort, taken continuously day and night.

And

30-60 mg zinc

And Vitacost Olive Leaf Extract (2) twice a day.

Day four until fully well (all symptoms resolved):

50,000 IU vitamin A, 25,000 IU for infants/children

Sip Sippy C* DAY AND NIGHT until fully well

And

30-60 mg zinc

Continue Olive Leaf Extract (2) twice daily

Usually symptoms resolve in 2-3 days. Continue the suggestions from day four until you feel perfectly well. If you do not start immediately you will have to 'survive' symptoms. Just continue 'day four' until perfectly well and next time start immediately when even a slight symptom occurs. The faster you respond the sooner you will be well again.

Remember to always take 100,000 IU vitamin A before boarding a plane. Having elevated levels of vitamins A in your blood when on a plane will kill bacterial and viral infections before you get them. No more post flight colds or flu.

If you have only Olive Leaf Extract, A or C or zinc lozenges use them. Any part of the program will help your immune system fight the infection.

Make sure to eat enough protein even when ill. Chicken soup, eggs and the like are easy on the stomach. Salt is needed by your adrenals during illness and you can balance the salt with potassium from a veggie broth or even hot or cold V-8 juice. Add hot spices for a treat.

If no significant improvement is noticed by day 4-5 please contact your health care practitioner. If you have seen improvement but are not yet well continue 'day four' until completely well.

Sippy C Drink- Use only ascorbic acid powder U.S.P. other types of C won't work. Add enough C powder to allow you to taste a **slight, barely there taste**, sort of sweet-tart, like a dash of lemon in water. Stronger is NOT better. Too much concentration will cause diarrhea. Drink this throughout the day and keep it near your bed at night. Vitamin C does not prevent colds but vitamin C does reduce the severity and duration of viral infections.
(877,878,879,880,881)

This drink will STOP your cough and allow you to sleep. Really. This formula must be made 'to taste' (by the person who will be drinking it). When you are seriously ill you will find that you will need to add more C to get the same taste. As you improve you will need to add less C. By diluting C in water you can take as much as you need to get well without causing intestinal distress. Don't 'drink' it, sip it. Using a 'sport' bottle helps slow consumption.

Olive Leaf Extract

Olive leaf extract has been available since about 1995. It has been used to combat virus, bacteria, fungus and parasites. Historically olive leaf tea was used with some success in treating malaria and other difficult diseases.

Oleuropein is a natural component of olive oil. The amount of this and other bioactive elements in the oil depends on the type of olive oil. Darker, more deeply flavored olive oils contain the highest levels of these bioactive elements.^(306,882,883,884,885) (Remember- Look, smell, taste, swallow?)

Regular use of bioactive extra virgin olive oil may prevent inflammation induced post-menopausal bone loss,⁽³¹⁸⁾ reduce free radical damage and inflammation associated with the development of cancer and heart disease^(305,319,886,887,888,889,890,891,892,893)

Extra virgin olive oil applied topically after exposure to UV-B sunlight helps restore skin immune function and in studies with mice reduced the number of tumors from sun exposure⁽²⁸¹⁾

Recent studies suggest oleuropein and its metabolites hydroxytyrosol and tyrosol to be the most bioactive components of olives, olive oil and olive leaf. In the lab oleuropein or its metabolites have been effective in killing many types of virus including herpes, CMV, common flu virus, common cold virus, pathogenic bacteria, salmonella, enterotoxin and others.^(307,894,895,896,897,898,899) Oleuropein has also shown bactericidal activity against all tested species of mycoplasma.⁽⁹⁰⁰⁾

As noted in the chapter on immunity and aging, pathogenic organisms including chlamydia, herpes, hepatitis, gut pathogens such as helicobacter and mycoplasmas have all been implicated as potential causative agents in cancer, degenerative and autoimmune diseases. Regular use of olives, black or green, or dark, deeply flavored extra virgin olive oil seems an excellent immune support strategy.

Periodic use of olive leaf extract may also be protective or even curative. There are numerous reports of immune improvement in regular users of olive leaf extract. Of particular interest are those suffering from fibromyalgia, Epstein-Barre, chronic fatigue, Gulf War Syndrome and Post-Polio Syndrome. In such cases it is likely higher doses are necessary and any 'treatment' should be monitored by your health care provider.

Oleuropein and its metabolites have anti-inflammatory, anti-atherogenic and anti-oxidant properties.^(314,887,890,891,892,901,902,903) These qualities may partly explain the dramatically lower incidence of cancer and heart disease in populations consuming large amounts of fresh, dark, flavorful extra virgin olive oil. Other olive oil components are also bioactive.^(317,887)

Of great interest is the use of olive leaf extract to treat early stage hypertension. In a recent (2011) study 500 mg of olive leaf extract taken twice a day lowered blood pressure as well as medication and NO side effects.^(904,905)

Currently oleuropein is being tested as a chemotherapeutic agent in mice who spontaneously develop tumors. Early results are positive and startling.⁽³¹¹⁾

Olive leaf extract supplements may contain as little as 30 mg of oleuropein per pill or capsule or as much as 110 mg per each. Used for viral elimination, doses range from 120 mg of the active oleuropein three times a day to 220 mg three times a day. Used to reverse abnormal cell growth doses may be as high as 550-1,000 mg of the active oleuropein twice a day.

As oleuropein may alter blood sugar, cell cytoskeleton and liver P450 enzymes higher doses should only be used under close supervision by your health care practitioner.^(308,311,906,907) Lower doses seem to enhance health and general immunity but high doses may lead to cellular DNA changes in normal cells as well as malignant cells.⁽⁹⁰⁸⁾

A Caution: Olive leaf extract in high concentrations may rapidly and dramatically lower blood sugar leading to light-headedness, dizziness, mood changes, fatigue and extreme hunger. If high doses are necessary, olive leaf extract should be taken after eating, never when you are 'hungry'.

Two excellent choices are Vitacost Olive Leaf Extract (best buy) and Planetary Herbals Full Spectrum Olive Leaf Extract. Dose is 1-2 twice a day or check with your physician.

As with any supplement stop if negative side effects occur.

Antibiotics, When and How?

First choice in any infection, viral or bacterial, is the cold/flu protocol with Vitamin A, zinc and high dose liposomal vitamin C 2,000 mg up to four times a day or in serious illness 1,000 mg liposomal C every waking hour. Adding Olive Leaf Extract may make antibiotics unnecessary

Antibiotics do not work on flu or viruses. They are only effective for bacterial infections. Overuse of antibiotics has led to antibiotic resistant bacteria. Do not use an antibiotic unless you are sure you need it. When you do take an antibiotic make sure you take the full dose and that you take the full prescription. Taking less may not fully destroy the bacteria and may lead to the development, in you, of antibiotic resistant super bugs.

Taking vitamin C with your antibiotic will make it work better so don't forget to take extra vitamin C whether liposomal or ascorbic acid. The addition of vitamin C and a probiotic, as below, will protect you from the worst negative effects of antibiotics. ^(502,504,909,910,911,912,913)

If you have a bacterial infection and must take antibiotics do not take extra calcium or magnesium while using the antibiotic. Many antibiotics, particularly the tetracycline derivatives, work by chelating magnesium and preventing its use by the bacteria. Magnesium can bind the antibiotic and prevent it from working. Resume calcium and magnesium after your course of antibiotic is finished.

If your infection does not respond to natural remedies and you must take antibiotics complete a short course of the Immune Restoration Protocol. Continue as long as you are taking the antibiotic and for one week following. This practice ensures that your good gut flora will have the best chance of survival while using the antibiotic and in women will prevent yeast infection.

A Healthy Gut May Resist Allergies, Asthma

Keeping Helpful Bacteria and Fungi in Balance Is Key, Say Researchers By Miranda Hitti WebMD Medical News Reviewed By Brunilda Nazario, MD on Thursday, December 23, 2004

Dec. 23, 2004 -- Allergies and asthma may start in your gut. Upset the gut's natural mix of helpful bacteria and fungi, and allergies and asthma may develop.

According to researchers, the rates of allergies and asthma have increased. They say this correlates with increasing antibiotic use and possibly relates to the hygiene theory. This may mean that modern practices of sanitation could deprive people of defenses needed to prevent asthma and allergies.

That theory was recently tested on lab mice. First, the mice drank water laced with antibiotics for a few days. This disrupted their microflora -- healthy bacteria and fungi found naturally in the gastrointestinal tract. The mice

got increasing numbers of fungal inhabitants. Specifically, they had increased amounts of the yeast called *Candida*, which is commonly seen after taking antibiotics.

Candida, like many other yeast, secrete molecules that affect the immune system's response to allergens.

With their microflora out of whack, the mice were then exposed to allergens. They promptly showed signs of allergic airway disease similar to asthma.

But another group of mice weren't bothered by the mold. Their microflora had been left alone. That suggests that allergies and related breathing problems could start in the gut.

The study didn't stop there. The researchers pushed a bit further to see if genetics or other allergens mattered.

They found that the genes of the mice made no difference, and they saw the same effect with several other allergens (pollens, dander, dust mites, and cockroach feces).

Change the microflora in the gut and you upset the immune system's balance between being exposed to allergens and having a severe reaction to them, says researcher Gary Huffnagle, PhD, in a news release.

Huffnagle is an associate professor of internal medicine, microbiology, and immunology at the University of Michigan's medical school. He worked on the study with Mairi Noverr, PhD, a postdoctoral fellow at the University of Michigan, as well as British colleagues.

The findings could apply to humans. (my note- they DO apply to humans) People need a mix of healthy bacteria and fungi in their guts. Microflora in humans can be thrown off by antibiotics and a sugary, high-fat, low-fiber diet. Swallowing also brings potential allergens to the gut.

The researchers aren't against antibiotics. Instead, they want people to know that eating a healthy diet with lots of fruits and vegetables is important after taking antibiotics to restore microflora as quickly as possible.

SOURCES: Noverr, M. *Infection and Immunity*, January 2005. News release, University of Michigan.

For Allergies Caused By Pollen, Dust, Animals, Etc.

Make sure you have loaded with Liposomal C, 3,000 mg twice a day for 2-3 months. If you still have allergies use Source Natural's Activated Quercitin (4) and then (2) as often as needed, which may be every few hours. Usually you will get relief in less than 20 minutes. This is a temporary aid to stop the immediate allergic response.

Gut dysbiosis or gut permeability are common causes of immune reactions. Probiotics are now commonly used to treat and prevent all types of allergy including food allergy.

(914,915,916,917,918,919,920,921,922,923,924,925,926,927,928,929,930) Make sure you complete the Immune Restoration Protocol and the mix to maintain healthy microbes.

To prevent future allergic response and quiet an overactive immune system, after you have completed the Immune Restoration Protocol make sure you are getting daily-

- Vitamin A 8,000 I.U. retinol (safe if pregnant) May be difficult to find in multi-vitamins today as formulators have shifted to beta-carotene. Taking fish liver derived A, 50,000 IU once a week is a substitute for daily intake.

- Liposomal C 1,000-3,000 mg twice daily with 500 mg of rutin or quercitin.
- Zinc 50-60 mg. Take the zinc test. Too much zinc suppresses the immune system
- Taurine 1,000-2,000 mg.
- L-glutamine powder ½ level teaspoon dissolved in your mouth twice a day

Potassium, calcium, D and magnesium as in your program; remove added omega-6 fats from your diet; Increase omega-3 by taking 8-10 fish oil capsules daily (not cod liver oil)

If you continue to suffer from allergies to food or the environment after you have been on your program for several months there is a probability that you suffer from lectin or food intolerance or gut dysbiosis and/or gut permeability. (924,931,932,933,934,935,936,937,938,939,940,941)

Dysbiosis may be caused by antibiotics, lack of probiotics, parasites or pathogenic bacteria or fungal overgrowth or a genetic or induced lectin intolerance. Dysbiosis may be progressive and must be corrected. Do not ignore this. Complete the Immune Restoration Protocol and if this does not change your immune response request a Genova Diagnostics CDSA 2.0. See Tests at the back of this workbook.

For Asthma, Cold or Flu Night Time Relief

In a cool mist humidifier add 1 pint hydrogen peroxide 3%, (may be purchased from any drug store), to each gallon (minus 1 pint) of water. Hydrogen peroxide is H₂O₂. When used in a cool mist humidifier the H₂O₂ is broken down into H₂O (water) and the free O₁ combine to make O₂ (oxygen). This is not ozone (O₃) and is not harmful to humans, animals or plants. It just makes breathing easier when you are sleeping (or trying to sleep)

Run the humidifier throughout the night (and day if you are home). Increasing the oxygen content of the air improves breathing capacity. It will reduce the need for medication and hasten recovery. Because it does super-oxygenate the air it may cause restless sleep or vivid dreaming for those not ill.

Low Blood Sugar or Following Sugar or Alcohol Bingeing

1,000-2,000 mg of l-glutamine powder under your tongue (directly fuels the brain) or

<p>YEAST DRINK 2-3 heaped tablespoons yeast flakes 6-8 ounces of V-8 or grapefruit juice Optional- ½ -1 level teas. ascorbic acid powder ½ -1 level teas. Kal dolomite powder</p>	<p>MOLASSES DRINK 1 T. unsulfured blackstrap molasses 8 oz. warm milk or hot water</p>
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Depression-Mild

IMPORTANT NOTE: If depression is serious you will need hands on guidance to make the switch from medication to natural treatment. Do not try 5-HTP or any natural therapy on your own if your depression is chronic or seriously acute or you use any medications.

WARNING: Melatonin, L-tryptophan or St. John's Wort (Hypericum) are not recommended to treat depression unless you are working directly with a knowledgeable health care practitioner. There may be unexpected side-effects.

Underlying deficiencies that contribute to depression include insufficient protein, incorrect types of fats (too much omega-6, not enough omega-3) and/or low magnesium, zinc, folate, B-12 or B-6 and especially low intake of vitamin C (see information on vitamin C in the vitamin section of this workbook). Deficient vitamin D and calcium have also been implicated in depression. Check the section on vitamin D and calcium. Thyroid disorders are a common cause of depression, especially around puberty, pregnancy, and menopause. Have your physician test your TSH. It should be between 0.4 and 2.0. If you have adequate vitamin D and take 'lots' of calcium you may also experience depression, more is not better. The rule to follow with all nutrients is enough and not too much.

Make sure you get sufficient protein; a minimum of 3 palms full (your palm) daily. Taurine and tyrosine, free form amino acids, may help relieve depression. Taurine is especially good at relieving anxiety. The trial dose is 1,000 mg of one or both twice a day. Amino acids work faster if taken on an empty stomach but may be taken with food.

In research adding omega-3 is often used as a monotherapy for depression with good results. ^(292,293,295,330,942) The dose is a minimum of 3,000 mg of combined EPA and DHA every day. Read the label carefully to make sure you get enough.

Under methylation, your body's inability to methylate certain essential elements may be a cause of mood disorders. Adding a coenzyme B-complex such as Swanson Vitamins Activated B-Complex High Bioavailability (NOT the high dose version) may rapidly correct this condition. SAME is being sold for mood but if you take a well made B-complex containing 5-MTHF (methylfolate) and B-12 as well as B-6, pyridoxal-5-phosphate you will make your own SAME. Synthetic folic acid found in fortified foods and most multi-vitamins is NOT a good idea. B-12 and folate are major players in depressive disorders. ^(943,944,945,946,947,948) B-6 plays a large role also. ^(949,950,951,952)

In some cases you will need to work with a health care provider to carefully adjust levels of B vitamins to suit your genomic type. More is not better and using higher doses than needed may make your depression or anxiety worse.

Make sure you get enough zinc in food, such as wild game, red meat, shellfish and fish, or in a supplement (30-50mg a day). One large oyster has 50 mg of zinc, 3.5 ounces of oysters contain 77 mg. Zinc is critical for production of enzymes controlling many processes in body and brain. Don't exceed 90 mg of zinc daily, Excess zinc is toxic over time, it suppresses the immune system. High daily doses may also unfavorably alter cholesterol. ^(953,954,955,956,957,958,959) Take the Zinc Test (page 136) to make sure you have enough but not too much.

If adding zinc also add 1,000 mg of taurine, as they work well together. Taurine is found in lean red meat, wild game and shellfish. It stabilizes cell membranes important for neurotransmitter function. Doses as high as 2,000 mg twice a day may protect and heal the heart.^(960,961)

Make sure you get 200-400 mcg selenium daily, such as methylselenocysteine or selenomethionine. Selenium balances iodine protecting from autoimmune thyroid diseases and is an important element in the immune system.^(962,963,964,965,966,967,968) More is not better so check you multi-vitamin and mineral.

Often persons who have low levels of neurotransmitters do not consume enough protein to supply the amino acid precursors needed for neurotransmitter production. If they do consume adequate protein and depression continues they may respond to increased sunlight or vitamin D and/or calcium with magnesium.^(969,970)

If stress preceded your depression get L-theanine and take 200 mg twice a day mid-morning and mid-afternoon. Take 2,000-3,000 mg of Liposomal Vitamin C twice a day for 2-3 months. Altered cortisol and insulin can contribute to depression, especially depression with anxiety and insomnia. L-theanine works in 20 minutes and the vitamin C over time. Continue as long as needed. L-theanine is an extract from green tea, caffeine free, and has no known downside. L-theanine has been called Zen in a bottle.^(971,972,973)

Sometimes adding a special supplement, Seriphos, (Interplexus or Neesby, the products are exactly the same) is useful to lower chronically elevated cortisol. Seriphos may be taken once or twice daily. For anxiety take (1) before lunch and (1) before dinner. If cortisol rhythm causes insomnia (1) mid-afternoon and (1) before bed. Only use if needed, it works immediately. Discontinue after a month or so to see if your rhythm is corrected. NEVER take Seriphos in the AM.

The two necessary steps to chemical 'happiness' (a good mood day) are adequate levels of neurotransmitters (from proteins) and the cell being able to release or uptake the appropriate neurotransmitter which requires enzymes and carriers made from protein, vitamins and minerals.

Vitamin D, vitamin C, calcium, magnesium and omega-3 fatty acids regulate cellular response to serotonin, dopamine and other neurotransmitters so make sure your intakes are adequate. Have your vitamin D tested.

Calcium and magnesium levels inside and outside of the cell decide what substances move in or out. Fatty acids in the cell membrane regulate membrane permeability. Omega-6 fats block vitamin D receptors and prevent the omega-3 fats from doing their job. Make sure you avoid excess omega-6 fats and supplement omega-3 fats using fish oil, not flax.

Vitamin D, calcium, magnesium and cell membrane fatty acids don't just regulate neurotransmitter movement, they also play a key role in the regulation of the movement of hormones, vitamins, minerals and electrolytes across cell membranes.

Magnesium, in particular, plays a key role in your body's response to thyroid hormone, estrogen, testosterone, DHEA, insulin and other hormones. Amino Mag 200, bottled by

several different companies, may give excellent results. The dose is one tablet one to three times a day. Experiment. Especially important if you have muscle tension and sleep issues.

Often depression is associated with low gonadal function (sex based hormones) or obesity with cravings (hyperinsulinemia, metabolic syndrome) low thyroid or fatigue. In all of these cases the first choice is to maximize protein, potassium, good fats, and vitamin C. Check your vitamin D, zinc, calcium and magnesium.

Give your body a chance to heal before adding herbs, exogenous hormones, or allopathic drugs.

Don't forget to EXERCISE. Exercise has been shown to reduce depression, anxiety, insomnia, and anger ^(974,975,976,977,978) better than any medications.

Anxiety

Chronic anxiety is rarely a problem with good diet but may be a factor if particular high genetic needs exist. One amino acid that is currently considered conditional but may be essential for some is taurine. Taurine has demonstrated anti-anxiety effects in animal studies and humans report mood stabilization (grounding, a sense of solidity). It makes sense because taurine is both a component and regulator of all cell membranes.

Another supplement that may help chronic anxiety is niacinamide (in addition to a good B-complex that does not contain synthetic folic acid).⁽⁹⁷⁹⁾

If your anxiety is situational try this:

I-theanine 200 mg twice a day on an empty stomach, works in 40 minutes, safe
--

Amino Mag 200 (any brand but must be this name) twice a day with or without food.

And if anxiety includes difficulty sleeping add

Country Life GABA Relaxer (2) before bed and if you wake up during the night, make sure you get only this brand.
--

Optimize your vitamin C with 3,000 mg Liposomal C twice daily.

Exercise daily. Exercise rapidly lowers all of the stress hormones. Ideally daily exercise should be 60-90 minutes. You may split it into smaller segments. Research supports regular exercise as being BETTER THAN antidepressant medications in the short and long term.

Don't underestimate the power of prayer or meditation. Consider the Forgiveness page at <http://krispin.com> or learn and use EFT (Emotional Freedom Technique) look for sites

online offering free instructions and other free materials. Remember to practice Gratitude. It is impossible to be anxious when feeling grateful.

5-HTP, kava or other aids are not always a good answer. If all else fails and you decide to use them watch for side-effects. L-tryptophan is a safer choice than 5-HTP but is rarely needed if protein is adequate. Stress and anxiety increase your need for protein.

Pain and Inflammation- Acute or Chronic

Acute pain/injury: When injuries occur using bromelain, 1,000-1,500 mg of the 2,000 GDU (or stronger) every two to three hours immediately after injury on an EMPTY STOMACH dramatically reduces swelling and speeds recovery. Continue every 4 hours after the first day/night. Bromelain is safe as it does not thin the blood. It is one of the few anti-inflammatories that can be used safely at any time. Excess intake may result in a looser stool but no other side-effects.

Surgery: When undergoing elective surgery, including gum surgery, take 1,000-1,500 mg of high potency bromelain every four hours the day before surgery and every three or four hours (daytime only) the following 2-3 days.

Chronic inflammation/pain: FIRST COMPLETE 30 DAYS OF THE IMMUNE RESTORATION PROTOCOL and check your fasting insulin.

For chronic inflammation AFTER YOU HAVE COMPLETED THE RESTORATION PROGRAM, lowered fasting insulin if needed, and MAXIMIZED CELLULAR VITAMIN C consider curcumin extract. This can also be used pre and post-surgery safely. Theracurmin has significant research showing bioavailability. Swanson Vitamins carries it. Give it a month long trial. For chronic pain the dose is 1-2 capsule three times a day. In cases of severe pain it may be combined with the bromelain (above) or dl-phenylalanine. For acute pain 900 mg. followed by 300-600 mg three times a day. Theracurmin is useful for any type of pain; injury, headache, joint pain, or muscle pain. It is protective of the liver and kidneys unlike NSAIDs.

The combination of curcumin extract and d-phenylalanine has been used to effectively treat cancer pain. Curcumin has been shown to have anti-inflammatory action protective against heart disease, osteoporosis and arthritis, and documented anti-cancer potential as well as effective pain relief. (980,981,982,983,984,985,986,987,988,989,990,991,992,993,994,995)

Degenerative Arthritis- Pain and Inflammation

As we age knees and backs and shoulders seem to fail us. One cause may be chronically low vitamin C levels in actively regenerating tissue such as discs, ligaments, joints and tendons. The body does repair but may need more than just a good diet to fix joint degeneration. Minimum daily dose is likely 2,000 mg twice a day of ascorbic acid or 1,000-2,000 mg Liposomal Vitamin C.

Kaufman, in 1949, designed an arthritic treatment protocol using adequate levels of vitamins A and D plus niacinamide. His protocol used 150 mg. niacinamide every three waking hours. OR 250 mg four times a day. Higher doses taken less frequently did NOT seem to help. Results were greatly improved range of motion within 30 days and continuing improvement over the next year (or two). There is some indication that Souce Naturals Time Release Niacinamide 1500 mg may work. Test for one month. If no improvement increase dose for another 30 days.

From THE COMMON FORM OF JOINT DYSFUNCTION

by William Kaufman, M.D., Ph.D.

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...The vitamins were administered orally, usually in equal doses at equal intervals during the day, and, in severe and extremely severe joint dysfunction, during the night when the patient would spontaneously awaken from sleep. In slight grades of joint dysfunction, the daily continuous ingestion of 100 mg of niacinamide after meals and at bedtime sufficed for treatment (400 mg/24 hours). Usually adequate in moderate joint dysfunction was the continuous ingestion of 150 mg niacinamide administered every 3 hours for 6 daily doses (900 mg/24 hours). In extremely severe and severe grades of joint dysfunction, 100-150 mg niacinamide were prescribed every hour (1500-2250 mg/24 hours), every hour and a half (1110-1650 mg./24 hours), or every two hours (800-1200 mg/24 hours), depending on the severity of the joint dysfunction, the more frequent schedule being used in more severe cases (97) (51).

Please remember, in above dosing, smaller more frequent doses worked better than higher doses less frequently. As you improve find the lowest daily multiple dosing that maintains your improvements.

As water is critical to lubricate joints read and follow the information on hydration. Dehydration, even slight, increases joint pain and inflammation.

Bovine or chicken collagen has shown great promise to both reduce pain and even promote recovery from disk and joint injury. When combined with Manganese 5 mg and 2,000 mg or more of vitamin C it has shown promise in regenerating cartilage including disc cartilage. Try Jarrow Collagen Type II from iherb.com or if you prefer Arthred by Source Naturals 1 scoop daily. It works for dogs too. If you prefer collagen from grass fed beef use Bulletproof Collagen from <http://www.bulletproofexec.com>

Collagen ingredient better than glucosamine for joint health? By Stephen Daniells, 29-Oct-2009

A patented collagen ingredient may be twice as effective as glucosamine and chondroitin for joint health, according to results of randomized, double-blind study.

...The new study compared a daily dose of UC-II (40 mg) with a combination of glucosamine (1500mg of glucosamine HCl, USP Grade) and chondroitin (1200mg, USP Grade), the big hitters in the joint health supplements world.

Looking at markers of joint health in 52 volunteers experiencing joint pain and stiffness in the knees from osteoarthritis, researchers led by Siba Raychaudhuri, MD, from the University of California Davis report that the effects were superior to those recorded in previous clinical investigations for glucosamine and chondroitin.

... "The clinical benefits we saw in osteoarthritic patients taking UC-II, showing significant overall improvement in conventional osteoarthritis efficacy measures, are positive clinical indicators that UC-II is highly effective at

supporting joint health,” said Raychaudhuri. “While the overall benefits were impressive, it is important to note that reduction in pain and stiffness were seen as early as 30 days after taking UC-II.”

... the UC-II type II collagen product was found to reduce pain during exercise by 20 per cent, compared to 6.0 per cent for glucosamine and chondroitin, state the researchers.

...Commenting on the mechanism, the researchers stated that the precise biochemical mechanism “is not clearly established”. They note, however, that the primary form of collagen in cartilage is type II collagen, and the amino acids it contains are “required for the synthesis and repair of connective tissue throughout the body. Source: International Journal of Medical Sciences 2009; Volume 6, Pages 312-321 “Safety and efficacy of undenatured type II collagen in the treatment of osteoarthritis of the knee: a clinical trial” Authors: D.C. Crowley, F.C. Lau, P. Sharma, M. Evans, N. Guthrie, M. Bagchi, D. Bagchi, D.K. Dey, S.P. Raychaudhuri

Available online here <http://www.medsci.org/v06p0312.htm>

Headaches

Tension Headaches First check hydration. The most common cause of headaches in all age groups is dehydration. If you are fully hydrated some respond to Country Life Amino Relaxer (1-2) tablets, taken immediately and repeated as needed. If aspirin is used see the section on safe use of aspirin. If caused by low blood sugar take ½-1 teaspoon of L-glutamine and let it dissolve in your mouth.

Willow Bark, the original source of salicylic acid is also available and does less gut damage than aspirin. Try Planetary Herbals Willow Aid or Christopher’s Original Formula Stop Ache.

Peroxy Gel (see formula) applied to the back of the neck may help all types of headaches almost instantaneously. If Peroxy Gel isn't handy soak, wet but not drippy, a paper towel or old piece of toweling in hydrogen peroxide (from the drugstore) and lay it across the back of your neck. It provides direct oxygen to the bloodstream through your skin.

Pre-Menstrual Headaches caused by an estrogen/progesterone imbalance may be helped by:

Silymarin (3) capsules two times a day
Vitamin A, 8,000-10,000 IU retinol ongoing, daily or 100,000 IU Vitamin A once a week (from fish liver oil not beta-carotene). Vitamin A is critical for hormone balance (it normalizes progesterone rapidly ^(996,997,998)) Read your vitamin labels and subtract any preformed A in your daily multiple from your daily/weekly vitamin A dose. Higher dosing is not needed.
Vitamin D3, 2,000-4,000 IU (test to make sure you need D) once a day
Calcium 500-800mg + 400-600 mg magnesium in divided doses daily

Do not supplement vitamin D3 without testing first. Get in the sun if possible.

Migraine Headaches are more problematic.

Migraine sufferers have chronically elevated histamine levels which make them more susceptible to migraine and allergic response. ⁽⁹⁹⁹⁾ Daily vitamin C intake lowers histamine. ^(1000,1001,1002) Lowering histamine is important in other diseases, such as allergy, asthma and atherosclerosis as well as migraine. ^(511,1003,1004) Increasing your daily intake of vitamin C using ascorbic acid or liposomal C or a supplement such as Emergen-C may reduce or stop migraine attacks. Do not take so much C you have a loose stool or diarrhea. Just one gram of C daily decreased histamine in all study participants. ⁽¹⁰⁰⁵⁾ 1,000 mg once a day of Liposomal C or 500 mg ascorbic acid twice a day should be more than adequate.

You may want to test to see if you are histadelic (high histamine all the time). If you are there are special diets and/or supplements to help. The test may be purchased from <https://pyroluriatesting.com/shop/histamine/> There is a protocol but you need to be monitored. You might also consider gene testing from 23andme.com. Once you have your raw data, let me know.

Migraines are often associated with allergies or trigger foods. ⁽¹⁰⁰⁶⁾ Elevated histamine and Nitric Oxide (NO) are found in all migraines. Keep a diary of your food, mood and the weather to help discover your triggers. Consider the association between low vitamin C and allergies. You might try increasing C before considering allergy testing. Repleting vitamin C may take 4-6 months.

Magnesium has clinically reduced migraine attacks and in many studies has been found to be low in serum in migraineurs. Amino Mag 200 (a specific form of magnesium sold by several different companies) is very effective. The dose to try is one tablet two or three times a day. May be taken with or without food. Amazon Prime has it. There is some indication persons with migraine absorb magnesium poorly from the diet or have a higher genetic need for magnesium.

Why all migraine patients should be treated with magnesium Mauskop, A. and Varughese, J. 2012 J.Neural Transm.

Magnesium, the second most abundant intracellular cation, is essential in many intracellular processes and appears to play an important role in migraine pathogenesis. Routine blood tests do not reflect true body magnesium stores since <2% is in the measurable, extracellular space, 67% is in the bone and 31% is located intracellularly. Lack of magnesium may promote cortical spreading depression, hyperaggregation of platelets, affect serotonin receptor function, and influence synthesis and release of a variety of neurotransmitters. Migraine sufferers may develop magnesium deficiency due to genetic inability to absorb magnesium, inherited renal magnesium wasting, excretion of excessive amounts of magnesium due to stress, low nutritional intake, and several other reasons. There is strong evidence that magnesium deficiency is much more prevalent in migraine sufferers than in healthy controls. Double-blind, placebo-controlled trials have produced mixed results, most likely because both magnesium deficient and non-deficient patients were included in these trials. This is akin to giving cyanocobalamin in a blinded fashion to a group of people with peripheral neuropathy without regard to their cyanocobalamin levels. Both oral and intravenous magnesium are widely available, extremely safe, very inexpensive and for patients who are magnesium deficient can be highly effective. Considering these features of magnesium, the fact that magnesium deficiency may be present in up to half of migraine patients, and that routine blood tests are not indicative of magnesium status, empiric treatment with at least oral magnesium is warranted in all migraine sufferers

Read the section on lectins. Test for and remove offending lectins in your diet. Also consider the association of allergies to gut dysbiosis and if appropriate begin the Immune Restoration Protocol.

Daily intake of adequate vitamin D, magnesium, vitamin B-complex vitamins including B-6 (pyridoxal-5-phosphate) and B-12 (methylcobalamin), and vitamin C with bioflavonoids, especially quercetin, may reduce or eliminate migraine occurrence.

Zinc lowers nitric oxide so take the zinc test and add zinc glycinate TRAAC if you need it. Other important supplements that may help include omega-3 fatty acids and taurine.
(1007,1008,1009,1010,1011,1012,1013)

Migraines may respond favorably to a nightly dose of melatonin, typically 3 mg taken between 8 and 9 PM nightly whether you go to bed on time or not. The nightly rhythm is important. Never take melatonin more than once a night and if you miss your dose- wait until the next night. Keep the rhythm.^(1014,1015,1016,1017,1018,1019)

Hypertension

The most common cause of hypertension is hyperinsulinemia.^(843,1020,1021,1022,1023,1024) Test fasting insulin. If it is above 5 uUnits/ml immediately begin a program to reduce it. If insulin elevation is mild Time Restricted Feeding may lower blood pressure to normal within the first 3 weeks.

PSA- Prostate Specific Antigen-Prostate Cancer

First, make sure your fasting insulin is under 5 uUnits/ml. Recent studies have confirmed as fasting insulin rises so does PSA.⁽⁶⁶⁵⁾

Natural folates seem to prevent and reverse markers of prostate cancer.^(1025,1026,1027,1028,1029,1030) but NOT synthetic folic acid which should be avoided in all supplements and fortified foods. Higher levels of unmetabolized synthetic folic acid are associated with an increased risk of prostate cancer and a faster cancer progression.

Diet alone may be effective but if you need more consider pomegranate juice^(1031,1032) in addition to a dietary plan to reduce insulin (Time Restricted Feeding). Drink 100% pomegranate juice and/or consume the whole fruit daily.

*Cell Cycle. 2006 Feb;5(4):371-3. Epub 2006 Feb 15. **Prostate cancer prevention through pomegranate fruit.** Malik A, Mukhtar H. Department of Dermatology, University of Wisconsin, Madison 53706, USA.*

Abstract Prostate cancer (CaP) is the second leading cause of cancer-related deaths among U.S. males with a similar trend in many Western countries. CaP is an ideal candidate disease for chemoprevention because it is typically diagnosed in men over 50 years of age, and thus even a modest delay in disease progression achieved through pharmacological or nutritional intervention could significantly impact the quality of life of these patients. In this regard we and others have proposed the use of dietary antioxidants as candidate CaP chemopreventive agents. The fruit pomegranate derived from the tree Punica granatum has been shown to possess strong antioxidant

and anti-inflammatory properties. In a recent study, we showed that pomegranate fruit extract (PFE), through modulations in the cyclin kinase inhibitor-cyclin-dependent kinase machinery, resulted in inhibition of cell growth followed by apoptosis of highly aggressive human prostate carcinoma PC3 cells. These events were associated with alterations in the levels of Bax and Bcl-2 shifting the Bax:Bcl-2 ratio in favor of apoptosis. Further, we showed that oral administration of a human acceptable dose of PFE to athymic nude mice implanted with CWR22Rnu1 cells resulted in significant inhibition of tumor growth with concomitant reduction in secretion of prostate-specific antigen (PSA) in the serum. The outcome of this study could have a direct practical implication and translational relevance to CaP patients, because it suggests that pomegranate consumption may retard CaP progression, which may prolong the survival and quality of life of the patients.

Healthy Teeth and Gums

Check your salivary pH. Weston Price, DDS was able to 'heal' cavities by increasing the amounts of vitamin A (not beta-carotene), vitamin D, vitamin C, calcium and magnesium, which shifted the salivary pH to an AM reading of 6.8-7.0. At this pH cavities do not progress, plaque-forming bacteria do not survive and the dentin hardens to 'heal' the lesion. No new cavities will form when ionized calcium (D + calcium) and vitamin C remains adequate.

Research shows a strong connection between cavities and mouth bacteria. Probiotics protect teeth and gums,^(9,11,12,917,1033,1034) as does vitamin C and zinc in your saliva. Mouthwash destroys both good and bad bacteria, do NOT use it. Brush with Ecodent powder and replace mouth bacteria eating some probiotics whether VSL3 in yogurt or applesauce or kefir or add fermented foods like home made sauerkraut or buttermilk.

Bone loss is first present in the jaw. Gum disease is often a result of this bone loss, creating pockets for bacteria. Gum surgery will not correct bone loss nor rebuild bone. In addition to using hydrogen peroxide on your tooth brush make sure to have your D tested and use a good multi-mineral daily and a minimum of 1 mg vitamin K every day. In addition take 2,000-4,000 mg ascorbic acid twice daily or 2,000 mg of Liposomal Vitamin C twice a day.

Gum disease may be a consequence of folate deficiency. Folate as found in foods or 5-MTHF will protect and reverse gum disease in many.^(1035,1036,1037,1038,1039,1040,1041) Make sure you do not consume synthetic folic acid.

Keep your toothbrushes in a glass jar containing hydrogen peroxide 3%, don't dilute. Change the hydrogen peroxide every 3-5 days. You can safely keep all of your family's toothbrushes in the same container. It will not breed bacteria or transmit virus.

Brush with Ecodent tooth powder and hydrogen peroxide (on your brush from storage method above). Ecodent Tooth Powder has been shown clinically to re-mineralize enamel. The hydrogen peroxide kills some bacteria, in the mouth and on the brush, helping to prevent plaque. (Do not soak the brush if you use the Sonicare. Dip the brush in H₂O₂ and Ecodent before use and rinse in H₂O₂ when done.)

Use the Sonicare toothbrush. This brush uses sound waves to thoroughly clean the tooth surface and between the teeth. This is the same technology used to clean very expensive jewelry. It works. The impulses from the sound waves also help to rebuild any bone loss that has occurred in the mouth by stimulating bone regeneration.

Follow the instructions that come with the brush. In my experience persons using this brush and the hydrogen peroxide plus Ecodent and maintain adequate vitamins C and D plus calcium never need to have their teeth cleaned again. No flossing necessary.

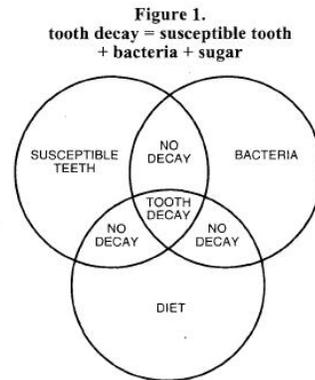
If you 'whiten' your teeth using a peroxide derivative remember to restore mouth flora with VSL3 or other high dose multi-bacteria probiotic.

Below is a paper showing higher levels of serum vitamin C result in fewer cavities, whether you brush or floss or NOT.

The Case of the Invisible Toothbrush: Why Some People Can Brush Less

by E. Cheraskin, M.D., D.M.D. Park Tower 904/906, 2717 Highland Avenue South, Birmingham, AL 35205-1725.

(Reprinted with permission from the Journal of Orthomolecular Medicine Vol. 8, No. 3, 1993)



U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service, National Institutes of Health
NIH Publication No. 80-1146

Abstract A long time ago, President Harry S. Truman was asked the question, "What's new?" His response, "If you never heard it before, regardless of how old it is, it's new!" Utilizing the Truman benchmark, several points are obvious. First, the present notion that dental accumulations contribute to dental diseases and that these collections can be mechanically removed is not only old but generally conceded. What is also not new, as far as the published literature is concerned, is that there are nonmechanical contributions to the common dental diseases. Many of the reports are 30 to 40 years old. Some of them are quite recent, particularly the innovative discussions by Nigel Clarke and his associate in Australia. However, what is really new and emphasized in this report, is that the accumulations in themselves may be due to the absence of an invisible toothbrush. The whodunit may well be hypoascorbemia! Obviously, this is a relatively new thought and requires further study. And, by the way, vitamin C serves many functions. It is well-documented as an electron donor, impressive scavenger, important in capillary fragility and permeability, extraordinary for wound healing, and much, much more. So, providing the ascorbates may add a bonus to improved oral health ... by contributing to general well-being!

Introduction Apropos, there are three inescapable facts:

** The principal site for chronic disease is the mouth ... even in this day and age, 95% of the civilized population suffers with tooth decay and/or periodontal disease.*

** Judged by our current successes/failures, the present explanations and solutions are filled with contradictions (i.e. more brushing and flossing doesn't necessarily guarantee less disease).*

** Maybe ... just maybe ... this is all because we haven't heeded the counsel of the experts.*

The National Institutes of Health (NIH) (1) and other authorities, as we shall learn, argue that oral pathosis is a multifactorial problem. They identify three essential ingredients: (1) a critical microbial population, (2) an appropriate diet, and (3) a susceptible state (Figure 1). (Incidentally, other buzzwords are available such as resistance, tissue tolerance, internal milieu, coping systems, immunity, and homeostasis). And, by the way, this same chart is just as applicable to the periodontal

tissues by simply substituting "periodontal disease" for "tooth decay". More importantly, in their pictorial portrayal, they underline the product relationship. If any of these three variables is absent, then oral disease does not occur. Parenthetically, this has not been translated into their arithmetic formula which suggests that the phenomenon is additive!

...Be that as it may, principal attention has been devoted to the role of diet and microorganisms; only scant attention has been accorded the resistance/susceptibility factor. And, when it is considered, susceptibility and genetics become synonyms. This report is one in a series on Medical Ignorance: Myths and Magics in Modern Medicine. It will remind us of the role and emphasize the measurability of tissue tolerance in oral pathosis. Specifically, we shall devote our attention to the question, "Can you get away with brushing your teeth less?"

A Different Look at Mr. and Mrs. America Two hundred presumably healthy middle income Caucasians (with the usual mouth problems of dental caries and/or periodontal disease) participated in this study. (2) To quantitate tooth cleansing, we choose the most simple measurable system. Each subject was questioned regarding the frequency of toothbrushing. It was convenient to divide the group into those with less than twice (n 71), the 95 who brushed twice per day, and the 34 more than two times daily. To assess tooth cleanliness, a simple, popular, and easy grading of foreign material, the debris score, was utilized. Finally, as one measure of susceptibility, the fasting plasma ascorbic acid concentration was obtained in each of the subjects. Our reason for using the ascorbates is based on the observation that in some subsets of the general population suboptimal vitamin C state is as high as 100%. (3) Additionally, we have studied vitamin C deficiency in dental patients and discovered that up to 72% may be hypoascorbemic. (4) By this trinity of information, it was then possible to construct, and hopefully respond, to three questions.

The Traditional Confirmation The most often asked question is, "How effective is toothbrushing?" In other words, "What's the connection between debris (oral cleanliness) and toothbrushing habits?"

Figure 2 shows the frequency of daily toothbrushing on the horizontal axis and the mean debris scores on the vertical. Three points warrant special emphasis. First, those brushing least (black column) represent the greatest accumulations. Second, in the group with the most toothbrushing (white column), there is the least amount of debris. Finally, while the correlation coefficient is statistically significant ($r = -0.265$, $p < 0.01$), it is not perfect. This suggests the possibility that other factors may be operative.

Hence, in answer to the first question, there does indeed appear to be a convincing relationship between tooth cleansing (tooth-brushing frequency) and tooth cleanliness (debris score). These observations are not surprising and support the current dental philosophy of the importance of local and mechanical factors in periodontal health and sickness.

(Comparing Figure 2 "Relationship of daily toothbrushing frequency and debris index" with Figure 3 "Relationship of plasma ascorbic acid and debris index" shows that vitamin C reduces tooth debris to a similar extent that brushing does.)

A Second Opinion Turn on the television and we will guarantee within minutes news about a new-fangled vitamin-stuffed cereal. Tune in the radio and

Figure 2. Relationship of daily toothbrushing frequency and debris index

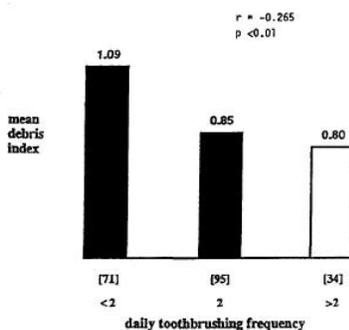
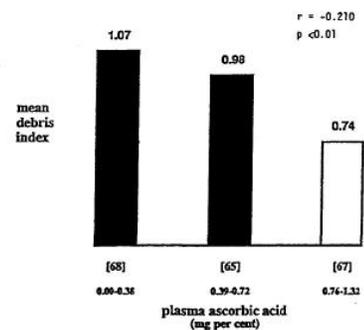


Figure 3. Relationship of plasma ascorbic acid and debris index



discover that we now have fiber in finger foods. All of this stems from the well-established fact that vitamins and minerals influence every cell, tissue, organ and site in the human system. It figures, therefore, that the mouth should also be part of the story. What is the connection between diet/nutrition and susceptibility to oral disease?

In other words, the query now to be posed is, "Can we alter oral debris by changing vitamin state?" Our personal experience has been quite extensive with ascorbic acid ("AA").(5-7). So, for purposes of this experiment, "What is the correlation of the ascorbates and oral cleanliness without altering the usual oral cleansing habits?"

Figure 3 (above next to Figure 2) pictorially portrays the plasma ascorbic acid levels on the x-axis. The 200 subjects were divided into three near equal subsets. There were 68 with the poorest ascorbate levels (black column) ranging from 0.0 to 0.4. Sixty-seven showed the best (white column) vitamin C levels (0.8 to 1.3). The average debris scores are shown on the ordinate. Three items deserve special note. First, those with the poorest AA demonstrate the most debris (black column). Second, the group with the best ascorbate level (white column) is characterized by the least accumulations. Finally, the correlation is statistically significant ($r -0.210$, $p < 0.01$), very much like that shown in Figure 2 and also not perfect.

Therefore, within the limits of these data, there appears to be a very real correlation between vitamin C state (as a possible nonmechanical contributor) and debris irrespective of tooth cleansing habits.

The Current Ecologic Thinking What we have witnessed thus far (Figures 2 and 3) is actually an analysis of a series of surreal events. In the real world, people who do or don't clean their mouth also do or don't ingest ascorbates. And so, are the accumulations totally the result of how much one brushes or how much vitamin C is ingested?

Viewing brushing frequency-debris score relationships as influenced by ascorbic acid status (Figure 4) provides additional insights into plaque prevention and control. At all levels of brushing frequency, those with the better plasma AA levels exhibit cleaner teeth. In fact, the average debris score (0.92) for those who brush less than twice daily but have better vitamin C levels compares favorably with that of the poorer C subjects who brush twice or more daily (0.90 and 0.87).

The key fact underscored in this investigation is not the existence of a particular nutrient-plaque relationship, but the need to completely reevaluate existing concepts of oral hygiene (tooth cleanliness).

The philosophic considerations and the practical implications of the ecology of oral health and sickness not only continues but seems to intensify. This is superbly borne out in the citations by Nigel Clarke and his co-worker. (19) "... Some individuals experience severe inflammation to minimal plaque, whereas others have minimal inflammation to heavy plaque ... Whether these variations occur as a result of differences in host response or in virulence of the microbes is undetermined; however, the probabilities point to host factors rather than to microbes ... Periodontal disease has long been recognized as a chronic disease, but the literature describes a disease that is derived entirely from the effects of a microbial colonization of the gingival crevice. If this were so, it would mean that periodontal disease is unique among chronic diseases, all of which represent the long-term cumulative effects of interaction between a host biologic system and the surrounding environment ... Perhaps dentistry has lost the perspective between the oral tissues and the entire organism ..."

Additionally, we note from the work of these Australian investigators of their interest in the relationship of ecologic principles to the specifics of oral disease. This is emphasized in the following quotation:

"... (There is a possible) causal role for the host factors and (there is the suggestion) that the type and severity of periodontal disease(s) are reflections of the competence of the host defense rather than of the virulence of commensal oral organisms ... (It can be) postulated that chronic periodontal

disease results when environmental factors, specifically those that compromise the peripheral blood supply, disturb the delicate balance between host and parasite in favor of the parasite ..."

Finally, the importance of ascorbates is also emphasized as one of a number of contributing factors to the genesis of periodontal pathosis.

"... It has been established that 20% of gingival collagen is turned over daily Fibroblasts require ascorbate to produce collagen. Hence, the high turnover of gingival collagen probably renders gingival remodeling and repair particularly vulnerable to ascorbate deficiency. Vitamin C is also required by polymorphs in their vital defense role. The phagocytic and chemotactic functions of the white cells require vitamin C concentration within the cell ... Although debate continues concerning the required plasma ascorbate levels, it appears likely that the demand for ascorbates and essential metabolites for defense and repair of gingival tissue may be met in the presence of chronic inflammation, smoking, stress, inadequate diet, aging, or any other vaso-constrictive factors

References

1. National Institutes of Health. Brochure No. 80-1146, Bethesda, U.S. Department of Health and Human Services.
2. Clark JW, Cheraskin E and Ringsdorf WM Jr: An Ecologic Study of Oral Hygiene. *Journal of Periodontology/Periodontics* 40: #8, 476-480, August 1969.
3. Schorah CJ: Vitamin C Status in Population Groups. In: Counsell JN and Hornig DH. *Vitamin C (Ascorbic Acid)*, 1981. Englewood, Applied Science Publishers.
4. Cheraskin E and Ringsdorf WM Jr: Vitamin C State in a Dental School Patient Population. *Journal of the Southern California State Dental Association* 32: #10, 375-378, October 1964.
5. Cheraskin E, Ringsdorf WM Jr and Sisley EL: *The Vitamin C Connection*. 1983, New York, Harper and Row Publishers, Inc. (hardback). 1984, New York, Bantam Books, Inc. (paperback).
6. Cheraskin E: *The Vitamin C Controversy: Questions and Answers*, 1988. Wichita, BioCommunications Press.
7. Cheraskin E: *Vitamin C... Who Needs It?*, 1993. Birmingham, Arlington Press.
8. Amim SS: Thoughts Concerning Cause, Pathogenesis, Treatment and Prevention of Periodontal Disease. *Journal of Periodontology* 29: #3, 217-223, July 1958.
9. Amim SS: Microcosms of the Mouth - Role in Periodontal Disease. *Texas Dental Journal* 82: #3, 4-10, March 1964.
10. Coven EM: Relationship of Vitamin C State and Oral Health of a Pedodontic Group in a Prepayment Program. *Industrial Medicine and Surgery* 24: #5, 410-412, May 1965.
11. Holmes CB and Collier D: Periodontal Disease, Dental Caries, Oral Hygiene and Diet in Adventist and Other Teenagers. *Journal of Periodontology* 37: #2, 100-107, March-April 1966.
12. Mandel ID: Histochemical and Biochemical Aspects of Calculus Formation. *Periodontics* 1: #2, 43-52, March-April 1963.
13. Cohen MM: The Effect of Large Doses of Ascorbic Acid on Gingival Tissues at Puberty. *Journal of Dental Research* 34: #5, 750-751, October 1955.
14. Dusterwinkle S, Cheraskin E and Ringsdorf WM Jr: Tissue Tolerance to Orthodontic Banding: A Study in Multivitamin-Trace Mineral Supplementation. *Journal of Periodontology* 37: #2, 132-145, March-April 1966.
15. Lane WB: Nutrition and Oral Response to Orthodontic Banding. University of Alabama School of Dentistry Thesis, August 1968.
16. Waerhaug J: Current Basis for Prevention of Periodontal Disease. *International Dental Journal* 17: #2, 267-281, June 1967.
17. Greene JC: Oral Health Care for the Prevention and Control of Periodontal Disease - Review of the Literature. *World Workshop in Periodontics* 1966. Ann Arbor, University of Michigan Press, pp. 397-455.
18. Waerhaug, J: Epidemiology of Periodontal Disease - Review of the Literature. *World Workshop in Periodontics* 1966. Ann Arbor, University of Michigan Press, pp. 181-222.
19. Clarke NG and Carey SE: Etiology of Chronic Periodontal Disease: An Alternative Perspective. *Journal of the American Dental Association* 110: #5, 689-691, May 1985.

Testing pH

Complementary Prescriptions <http://cpmedical.net> and other online sites have pH testing paper. If you are not online order pH testing paper in the 5.5-8.0 range from Micro Essential Laboratory, Inc, The catalog order number is 067. The price is \$5.50 per roll. The minimum order is three (3) rolls plus shipping and handling charges. Minimum Credit Card orders are US\$30.00. To place your order for three (3) rolls of item #067, please send a check or

money order in US funds in the amount US \$20.00 (for shipment to the U.S.; US \$30.00 for Canada) addressed to:

Micro Essential Laboratory Inc.
P.O. Box 100824
Brooklyn, N.Y. 11210

Phone: 1-718-338-3618

Normal morning saliva, for healthy teeth and bones: 6.8-7.0

If you take your saliva pH at other times of day it may shift radically. It is the fasting AM pH that best reflects serum (blood) pH and alkaline reserve. Do not use pH to diagnose disease. It is useful to determine if you are getting adequate calcium, magnesium, potassium and vitamin D BUT does not indicate D deficiency or excess.

Insomnia Chronic

Chronic sleep issues almost always relate to a cortisol rhythm disturbance. If this is your problem, more awake later in the day, foggy in the AM, difficulty 'getting going', wired but tired, please make an appointment for consultation. An individual program to address your specific needs and follow-up will be provided. 775-831-0292 or email krispin@krispin.com

Insomnia-Intermittent

Energizing substances (for some, not all) DO NOT take before bed if you notice they cause you a problem. Test individually. Vitamin E, fish oil, large amounts of the B vitamins, especially B-1, or foods high in potassium, extra magnesium.

Likely the most common cause of insomnia is inappropriate cortisol rhythm. The treatment is 1,000 mg Liposomal Vitamin C twice a day for one month PLUS Interplexus Seriphos (1) before dinner on an empty stomach and (1) before bed. Empty stomach is 30 minutes before or 2 hours after a meal. Once your cortisol is corrected stop the Seriphos but continue with 1,000 mg liposomal vitamin C twice a day.

Extra calcium and/or magnesium before bed such as calcium carbonate or calcium lactate and magnesium carbonate or gluconate, may increase the depth of sleep. If you have a tight jaw or grind your teeth this is especially important. Make sure you use calcium carbonate or lactate. Other types of calcium may not help. Some find ¼ - ½ teaspoon of lead free dolomite powder (Kal brand) in a small amount of juice works well. Now Foods Calcium Magnesium soft gels (1-2) may be more convenient.

A small amount of carbohydrate before bed or milk products are usually well tolerated. Whole grain cereal (if tolerated) with milk (if tolerated) is a great bedtime snack raising I-tryptophan and bringing on sleep, funny we eat this in the AM. This is not appropriate for anyone with grain or dairy intolerance. Don't eat a large amount of carbohydrates before

bed as high amounts of insulin will be excreted and your meal will be converted to fat and stored.

If stress or anxiety is a factor take L-theanine 200 mg twice a day on an empty stomach. Now Foods offers it, best buy, as well as other companies. It has been called Zen in a bottle because it actually changes brain waves to those found during meditation. L-theanine works rapidly, 20 minutes, and only need be taken as long as the stress continues. L-theanine is very safe, even during pregnancy. Though you want the nighttime result, take the theanine in the day, to prepare.

Temporary Aid: Before retiring use Country Life GABA Relaxer (2) on an empty stomach. Country Life GABA Relaxer is also useful to easily return to sleep if you wake during the night. The dose is always (2) tablets.

If the Relaxer is not enough add a simple calcium and magnesium such as ½ teaspoon of dolomite powder in water or juice or a soft gel containing 500 mg of calcium carbonate and 250 mg of magnesium oxide. (Now Foods has a soft gel cal-mag)

If you fall asleep but wake up and cannot go back to sleep take two (2) Country Life GABA Relaxer when you wake. Keep the bottle near your bed.

If this doesn't help add 1 tablespoon of lecithin granules (not the soft gels) to your daily diet or two or more eggs daily for the inositol. Lecithin is best taken plain, just put it in your mouth and use water or juice to swallow it. Don't chew the granules. They stick to your teeth, really, for days. Inositol, especially as phosphatidylinositol as found in lecithin, is very calming.

To Prevent Viral Infections Which Frequently Occur After Flying

100,000 I.U. Vitamin A (retinol- from fish oil concentrate) before boarding the plane. Do not forget to do this. My clients do not get sick during or after travel because they do this. **Do not take high dose vitamin A if you are or may be pregnant. The vitamin A safe range during pregnancy is less than 35,000 IU daily ongoing or 50,000 IU for a few days.**

For Jet Lag

During the flight Now Foods GliSODin or Vitaline Superoxide Dismutase. (4) every 4 hours with 10 ounces of water.

Before bed: Country Life GABA Relaxer (2) before bed (2) more Relaxers if you wake during the night.

Melatonin 6-9 mg. 1 hour before desired bedtime for 3 nights only to acclimate to the new time zone.

For PMS

For immediate relief- 1,000 mg taurine + 1,000 mg l-tyrosine + 1,000 mg l-glutamine + 500 mg vitamin C + Swanson Vitamins Activated B-Complex High Bioavailability(1).

To correct and prevent PMS

EAT MORE PROTEIN.
Multi-vitamin plus Swanson Vitamins Activated B-Complex High Bioavailability one or two per day.
Vitamin D- a total daily intake from food, sunlight and supplements of 2,000 IU Make sure to test D levels. You may need more D. D test should be 40-60 ng/ml
Vitamin A 10,000 IU total daily of retinol A (not beta-carotene) safe for pregnancy
800-1,000 mg. calcium / 400-800 mg. magnesium
Liposomal Vitamin C 1,000 mg twice a day or 2,000 mg ascorbic acid twice a day.

Vitamin A regulates progesterone levels which are important to normal cycling and pregnancy. ^(996,998,1042) Daily doses of vitamin A up to 30,000 IU are considered safe even during pregnancy. ⁽³⁷⁰⁾ Vitamin B-complex, especially vitamin B-6, Vitamin D and calcium with magnesium help reduce inflammatory response and stabilize mood. ^(997,1043,1044,1045)

MELATONIN, NOT JUST FOR SLEEP

As cortisol is our wake up hormone melatonin is our rest and repair hormone. Light at night, stress, illness and injury, shift work and even aging can lower your melatonin production. Impaired sleep is no fun but impaired repair (what happens when melatonin is produced) is worse. Without sufficient melatonin regeneration will fail and degeneration will thrive.

Melatonin production is disturbed by excess levels of cortisol (too much cortisol at the wrong time of day). If you are more awake later in the day you may need additional help to normalize cortisol rhythm. Call if you need help.

To assure your own melatonin production requires regular bedtime in a completely darkened room. It is darkness (no visible light) that stimulates melatonin production. Too much light at night can alter your circadian rhythm and lower melatonin leading to issues from insomnia to hyperinsulinemia to cancer.

Aging, injury, surgery, or shift work will alter melatonin production and melatonin supplementation, temporary or long term, may greatly improve health. The actions of melatonin are anti-aging and neuroprotective. While melatonin may NOT improve sleep for some it may benefit greatly for depression, avoidance or recovery from cancer, cognitive function, and optimal autophagy.

Melatonin doses range from ½ mg -10 mg 1-½ hour before bed on an empty stomach. Melatonin is best taken by itself, not in combination with other 'sleep aids'. Lower doses may work better to improve sleep. A few are very sensitive to this hormone and will feel hung-over in the morning. Others may actually have disturbed sleep during the first week. Before deciding if your dose is correct, trial a dose for 7 days.

Persons with cancer may use doses as high as 20-50 mg nightly before bed as melatonin lowers risk of metastasis and improves the outcome of chemotherapy. ^(1046,1047,1048,1049,1050)

Aging shifts melatonin production and additional melatonin has reversed symptoms of andropause and menopause. ^(1051,1052,1053,1054,1055,1056,1057,1058,1059,1060,1061,1062,1063,1064,1065,1066,1067,1068,1069,1070,1071) In addition melatonin protects from breast cancer, benign prostatic disease and prostate cancer. ^(1072,1073,1074,1075,1076,1077,1078,1079,1080,1081,1082,1083) Melatonin has shown some success in reversing macular degeneration when added to a zinc sufficient diet. ^(1084,1085,1086,1087)

The Life Extension Foundation suggests supplementing melatonin nightly after age 55. Experience with clients suggests melatonin has many regenerative benefits besides sleep. One of many important roles melatonin regulates the process of autophagy, which removes virus and bacteria, toxins, and damaged DNA helping keep us cancer free. ^(1088,1089,1090,1091,1092)

CAUTIONS: Children should never be given melatonin, unless specific testing determines melatonin insufficiency. Excess (very high dose) melatonin has been implicated in lowered testosterone and sperm count in men.

The greatest amount of melatonin, 100 times pineal output, is produced in the human gut. In IBS and other gastrointestinal disorders the normal balance between serotonin and melatonin may be disrupted and serotonin will predominate. Melatonin producing cells may actually disappear. ^(800,1093,1094,1095) Serotonin contributes to inflammation and irritability of the gut leading to chronic and often explosive diarrhea. Restoring the gut with probiotics will help restore the balance of serotonin and melatonin, important to keep the bowel normal, and gut melatonin protects cells from cancer producing substances.

Unfortunately taking melatonin does not restore the gut's production however in some cases 6-9 mg melatonin nightly has helped reverse some of the mental and physical symptoms of IBS and combined with the Immune Restoration Protocol improves gut function.

If you decide to try melatonin-

- Take your dose at the same time every night, whether you go to bed on time or not
- If you miss your nightly dose WAIT, do not take it late, begin again the next night. You are establishing a rhythm.
- Use only regular melatonin NOT timed-release and not a formula with other elements (vitamins, herbs, etc.).
- Never take more (a second dose) melatonin during the night (or day) as you will further damage your circadian rhythm.

DIGESTIVE DISTURBANCES

NOTE: It is my experience completing the Immune Restoration Protocol will resolve MOST digestive problems. Get serious and follow the program for 30 days, faithfully. Call me with questions or concerns.

Heart Burn After Eating or GERD (Gastrointestinal Reflux Disease)

Eat slowly. Do not consume alcohol with your meals. Relax and learn diaphragmatic breathing. You can learn this type of breathing from a book by Pam Grout, Jumpstart Your Metabolism, How to Lose Weight By Changing the Way You Breathe or if you prefer any book on Yoga breathing or breathing for singers. All use similar techniques that strengthen the diaphragm and improve the function of the esophageal sphincter.

This pain is not caused by over production of stomach acid. Using an anti-acid will make you more susceptible to food poisoning and will impair digestion often causing bloating and gas, constipation or diarrhea. It will also contribute to further imbalance of your gut bacteria, the development of food allergies and possible overgrowth of bacteria in the small bowel leading to nutrient malabsorption. ^(1096,1097,1098,1099,1100)

In some persons taking probiotics, VSL#3 capsules (1) *Jarro-dophilus (Original Formula or EPS)* (8) capsules or Jarro-dophilus Ultra (2) capsules mixed with food or liquid, not hot, at each meal (or each large meal) will help correct the condition. In others drinking a small amount of *George's Aloe Juice* with or after the meal will help.

If low stomach acid is the cause make sure you are fully hydrated. If that does not help try *Trace Mineral Research Electrolyte Stamina Tablets and Vitamin C* as a first line protocol. Take (2-3) Electrolyte Stamina Tablets and 1,000-2,000 mg ascorbic acid powder with each meal for 5-7 days and see if digestion improves. The electrolyte supplement contains elements necessary for HCl production and vitamin C ascorbic acid increases acidity and stimulates digestive secretions. It is fine to take the electrolytes with the probiotic.

If the condition is long standing consider using ½ -1 teaspoon of Absorb Aid powder (not capsules) with every meal for 1-3 weeks. Take as directed on the bottle. If it doesn't help don't continue to use it. If it does help, try stopping after a week or so to see if your gut has improved.

If you still cannot find relief consider melatonin 3-6 mg nightly for several months. Melatonin has been shown as effective as Proton Pump Inhibitors in healing GERD. ^(65,66,67,68,69,70,71,72,73)

Start with 6 mg nightly, exactly the same time each night, whether you actually go to bed or not. Continue the dose for a minimum of one week before you decide if the dose is excessive. If you find, after one week, you are loggy in the AM reduce to 3 mg for the duration. Give it a minimum of two months to heal the gut. If you stop and symptoms return, start again. Melatonin has a high safety profile when taken correctly, so continue your nightly dose.

Never take melatonin more than once per night; never take melatonin 'late', if you miss your dose take it the next night. You are establishing a rhythm. Timing is important.

Gallbladder Pain After Eating

You need more vitamin C.^(1101,1102,1103,1104,1105,1106,1107) Take 2,000 mg ascorbic acid or 1,000 mg Liposomal C twice daily ongoing. Higher doses may be needed for the first few months to improve gallbladder function. For immediate help use plain lecithin granules 1 rounded teaspoon with each meal plus 1,000 mg of the amino acid taurine twice daily until there are no more symptoms.

If the pain is severe:

Now Foods LipoTrim (3) with each meal

Taurine, 1,000 mg twice daily.

Do not use any type of 'gallbladder flush'. It could be life threatening. In the process of expelling a stone the bile duct can become blocked and necessitate immediate surgery.

Gallbladder problems are associated with low body stores of vitamins C and D, high intakes of vegetable fats/oils and/or low intake of taurine and calcium. Use extra virgin olive oil, coconut oil and butter (from grass fed cows if you can get it) as your primary added fats. Read and re-read the section on fats.

Healthy bile is taurocholic acid as it more readily stays soluble in the gallbladder. As the name implies taurine is key to its production. If taurine is unavailable your body will make glycocholic acid which may precipitate and contribute to gallbladder 'sludge' and stones.

Diarrhea

Diarrhea may be caused by lectin intolerance, infection from bacteria, virus or fungus, post-infectious IBS or by certain foods or supplements. Common supplements that cause diarrhea include excesses of magnesium or vitamin C, ascorbic acid. However, chronic diarrhea has been stopped by taking appropriate levels of vitamin C. Read the section on Immune Restoration carefully to fully restore and normalize bowel function.

If you are using a new supplement and experience a loose bowel STOP all supplements and determine which is causing the problem. **Diarrhea is never acceptable for any length of time.** Loss of electrolytes, and rapid transit time in the small bowel quickly leads to nutrient deficiencies and fatigue.

Should you experience diarrhea (or vomiting), whatever the reason, please keep on hand Trace Mineral Research Electrolyte Stamina Tablets. Make sure you get this exact product. The dose is 2-4 tablets with 4-10 ounces of water or juice as often as needed throughout the day and night. The tablets work more quickly on an empty stomach but will work regardless. Amount of water depends on how much

fluid you have 'lost'. There is no substitute for this product as most electrolyte formulas contain other substances that will make your diarrhea worse. Online available from Amazon or Vitamin Shoppe.

To Prevent Traveler's Diarrhea

Use the Japanese product Miyarisan STRONG. Dose is (3) with each of two or three meals daily. It will prevent food issues and it does not have to be refrigerated. Make sure to get the STRONG. Available from Japan on ebay.com.

If you are traveling to particularly hazardous locations use Freeda Hydrochloric Acid tablets or Source Naturals Betaine HCl just after your first bite at each meal to prevent infection followed later in the meal with the Jarro-dophilus EFS capsules.

To Treat Infectious Diarrhea- Traveler's Diarrhea, Food Poisoning, Stomach 'Flu'

Pepto-Bismol is an excellent treatment. Use it if necessary to stop diarrhea. In addition to slowing the bowel it also has bismuth which kills a number of pathogens. Also use the Immune Restoration Protocol for a few days.

If your symptoms don't rapidly resolve use the following program as long as needed, a minimum of 10 days. May be needed as long as 21 days.

(3) Allergy Research Tricycline (same as Nutricology Tribiotic) twice a day before breakfast and dinner, in serious attacks you may increase to (3) three times a day.
2,000 mg Liposomal Vitamin C twice a day, ascorbic acid won't work
Immune Restoration Protocol (absolutely required)

Constipation

The most common causes of constipation are a processed foods lacking essential fibers to feed your microbiota, antibiotics causing dysbiosis, lack of electrolytes, low protein leading to low levels of hydrochloric acid or dehydration. Hydrate and complete the Immune Restoration Protocol.

Lack of sufficient hydrochloric acid may result in constipation. *Trace Mineral Research Electrolyte Stamina Tablets* plus hydration may correct constipation rapidly. The dose is (3) with each meal. Usually you need do this for about a week or two, not longer.

If you have dry mucous membranes, dry mouth, dry eyes, this may be reflected in lack of digestive juices and be a result of chronic dehydration. Carefully read and follow the section on water. Consume enough fluids with your meals. Contrary to what some believe it is good to drink with your meal as fluids, including water, stimulate hydrochloric acid production.

Make sure your body stores of vitamin C are more than adequate.

Constipation may indicate you are not consuming enough fiber to allow your microbes to multiply. Make sure to include berries, figs, dates or prunes regularly. These are all easy to take sources of natural fiber. So are apples (with the skin) or any foods with 'tough' outer skins that you consume. Bran is fiber, but not soluble and not tolerated by many. Berries, dates and figs are better for you, providing potassium and other minerals and vitamins, and more fun to eat.

Rarely constipation may be caused by overenthusiastic consumption of fibers such as psyllium. When using a commercial fiber you need a minimum of 8 oz. of liquid for each rounded teaspoon of fiber. You may even need more fluid. When using fiber products you must take all of the fluid at the same time you take the fiber. Without enough fluid at the time you take it fiber will bulk on your stomach contents and may cause serious constipation or even bowel blockage.

One other common cause of constipation is thyroid disease estimated to afflict 12% of the US population, more than 60 million people, predominately women. A serum TSH greater than 2 should be followed by complete thyroid testing. Even if your TSH is within range if you still find constipation is an ongoing issue, have your physician check your TSH, free T3 and free T4.

In IBS-C (irritable bowel with constipation) a bug, a methane producing bacteria, *Methanobrevibacter smithii*, is the predominant bacteria.^(1108,1109,1110,1111,1112,1113) The Tribiotic protocol used for gut pathogens seems to destroy this bug so the protocol should be considered as a first line treatment. If symptoms do not improve the drug Rifaxin is useful but should be combined with the full gut protocol.

Many medications may cause or contribute to diarrhea or constipation. If you are taking ANY medications, check the possible side-effects and discuss with your prescribing physician. Nutrition cannot correct drug side-effects.

Ulcer or Dyspepsia caused by Helicobacter Pylori

Treatment Protocol

- Allergy Research/Nutricology Tribiotic/Tricycline (2-3) before each meal or prescribed antibiotic for 10 days
- Pepto Bismol three times a day for 10 days (take with the Tribiotic)
- Now Foods Ulcetrol (1) or PepZin GI twice a day for 8 weeks
- Now Foods DGL with L-Glycine (instructions on the bottle)
- L-glutamine powder 1 teaspoon twice a day
- George's Aloe Juice 4-6 oz. as needed for pain, discomfort; Sip it as needed.
- Immune Restoration Protocol for 30 days
- Vitamin C 1,000 mg twice a day
- OPTIONAL: Now Foods Acid Comfort (as per instructions on the bottle)

Parasite Treatment Protocol

Protocol should be completed for a minimum of 10 days, more typically 21 days. On rare occasions you may need to continue for 28 days.

20-30 minutes before breakfast and dinner (twice daily). Must be on an empty stomach, not with food:

- (4) Vaxa Paracidin twice a day
- (3) Allergy Research – Nutricology Tribiotic/Tricycline
- 2,000 mg Liposomal Vitamin C three times a day, though this may already be in your daily program.
- Immune Restoration Protocol

It is possible to have parasites, a pathogenic bacteria (such as salmonella), and candida all at the same time. This protocol covers them all except candida. Call for help. Sometimes when killing pathogens a reaction, called Herxheimer's Reaction, may occur. This condition feels like 'flu' or like a hangover or you just feel 'toxic'. It will resolve in 24-72 hours and may be reduced or relieved by taking Now Foods Silymarin Extract 2X (1) twice a day.

Irritable Bowel (IBS), Diarrhea and Constipation

First step is to complete the Immune Restoration Protocol for 30 days. Some may need modification so call for help.

In addition make sure you are regularly consuming omega-3 fatty acids. Omega-3 fatty acids increase the binding of probiotics to the gut, an important effect for immune health.⁽¹¹¹⁴⁾ Make sure you are NOT consuming lectins you don't tolerate. (Lectin chapter page 40)

When stool testing is done more than 90% of persons diagnosed with IBS or colitis or Crohn's have current or past gut pathogens and/or food intolerances. It is impossible to recover from these conditions if existing pathogens are not discovered and treated or offending foods eliminated. Gut pathogens and lectin intolerance may occur together. Try the lectin restricted diet (or Paleo diet). Also consider the Specific Carbohydrate Diet, info on the internet.

The SCD 24 hour yogurt is excellent for everyone, much better than store bought yogurt of any brand. You'll find a recipe on the SCD website You may also make VSL#3 SCD yogurt by using 1 capsule of VSL#3 per 2 quarts of milk substituting the VSL#3 for the suggested bacteria in the recipe. <http://breakingtheviciouscycle.org>

Severe IBS, Ulcerative Colitis, Mucous Colitis, Crohn's

You need to call in for a more specific protocol requiring monitoring.

In addition to the Immune Restoration add-

- Add MSM powder ½ -1 teaspoon 2-3 times a day mixed in V-8 or other liquid to tolerate taste.

Eliminate all grains and legumes (beans, including soy and peanut).

Overgrowth Of Candida In The Bowel

Eliminate possible offending lectins. That means a diet free of all grains and legumes. You must reverse the gut damage to prevent regrowth. Blood tests are not a good diagnostic for this condition. A stool sample is the best indicator of yeast overgrowth. A stool test for candida costs about \$30.

Treatment: for 30 days
T.E. Neesby Mycophryl 680 (2) with each meal, three times a day.
Once a day with yogurt or applesauce 1 packet of VSL#3 (If your symptoms increase do the Immune Restoration Protocol).

Continue 30 days. During the treatment if you do have overgrowth of candida in the bowel you may experience a condition known as die-off. You will begin to feel as if you have a hangover or the flu and it will last 24-48 hours. This is caused by the body having to deal with large quantities of dead yeast cells. Just keep going. The symptoms will pass rapidly.

YOUR DIGESTIVE TRACT- A REVIEW

Health begins with the digestive tract. As explained in the beginning of this workbook if the digestive tract does not function NOTHING else will work. The digestive tract cannot be bypassed. Injections, IV nutrients, sublingual supplements, may be used in emergencies but for actual, daily living our source is FOOD and it must be digested. The entire process exists for a reason.

Chewing (teeth) breaks food into digestible particles and alerts the digestive system to 'wake up' and produce hydrochloric acid and all of the digestive enzymes secreted by the mucous membranes lining the mouth, esophagus, stomach, duodenum, and ilium, as well as expressing digestive enzymes and bile from the pancreas. The colon furthers digestion by mixing food particles, typically indigestible fibers, with various healthy bacteria.

When problems occur in the upper digestive tract, reflux disease caused by a weakened lower esophageal sphincter muscle or a hiatal hernia, stomach acid is lowered and food is poorly digested. Lower stomach acid encourages gut pathogens in the stomach (helicobacter pylori) or small and large bowel.

Hiatal hernia or reflux must be addressed by breathing exercises to strengthen the lower esophageal sphincter and/or by manipulation or by surgery in severe cases. If anti-acids, over the counter or prescription, become the treatment choice more gut pathogens will be present in the lower digestive tract and more damage from gut permeability (see below) will occur over time.

The stool (or bowel movement) consists of the shed lining of the digestive tract, bacteria (more than 60% of total stool volume), and undigested (insoluble) fiber. The best sources of fiber are nuts, figs, dates, strawberries, blueberries, or other berries, and apples with the skin. Bran is a poor source of fiber to promote gut health but better than no fiber at all. To get most fiber from fruit you must eat the skin or if using citrus the white parts of the inside of the skin, the 'pulp'.

The health of the digestive system may be determined by testing when needed but on a day to day basis if you have one bowel movement daily, more frequently if you have a high intake of fruits, vegetables and whole grains, that is fully formed, medium to dark brown in color with little odor, and do not have gas with odor, your gut is working.

Any deviation from the above description is a problem that must be fixed before any other health issues are addressed.

If actual food is present in the stool or the stool is beige or yellow in color maldigestion is apparent. If food is not present in the stool, digestion has completed, but symptoms may be present because of overgrowth of bacteria in the small bowel or a condition called 'leaky gut' or "gut permeability" which is not maldigestion or malabsorption but the presence of partially digested proteins within the body (the lymph and blood) that do not belong there.

The gut is designed to be SEMI-permeable; to allow digested amino acids, bound minerals and other nutrients to be absorbed into the lymph and serum (blood) but NOT allow partially digested foods to cross the barrier. **It is not a condition of poor digestion but one of 'gut permeability'**; failure of the gut wall barrier.

Gut Permeability

There are only two causes of this condition.

1.) Eating lectins to which you are genetically intolerant. Please read carefully the information on lectins in the workbook. ALL FOODS contain lectins. Likely suspect lectin families: milk (casein), egg, legumes, wheat or gluten, soy (legume), potato (deadly nightshade) or others. Few persons have more than one or two lectin family intolerances BUT their gut will be damaged and stay damaged as long as they eat foods containing the offending lectins.

If offending foods are present the gut will not be restored to full health until complete removal of offending foods from the diet and completion of the Immune Restoration Protocol.

2.) Lack of friendly microbiota (dysbiosis) because of current or past overgrowth of gut pathogens which may include parasites, pathogenic bacteria, and yeasts or overuse of antibiotics. Not all bacteria are good for the human gut nor are all yeasts harmful. There are probiotics (good bacteria) and harmful bacteria which may cause serious damage to the gut including klebsiella, h. pylori, staph aureus, salmonella, Giardia, and citrobacter. Parasites are both visible, some worms like tapeworm and pinworm, and invisible such as amoeba cryptosporidium, microsporidia, and isospora.

If you suffer from dysbiosis or gut pathogens are present and have damaged your gut wall you may also find that certain foods make you worse because the gut now reacts to many foods and substances due to gut immunity impairment, promotion of pathogens by food choices, or other immune interactions with proteins and lectins in the foods. This is not primary lectin intolerance but a side-effect of pathogen presence or damage. Foods may be tolerated again following complete eradication of pathogens and gut immune system restoration.

From the American Gastroenterological Association: Each year an estimated 76 million cases of food borne illness occur in the United States, according to figures from the Centers for Disease Control and Prevention (CDC). These food borne pathogens, such as Campylobacter, E.coli O157:H7 and Salmonella enter the body through the gastrointestinal tract and often cause nausea, vomiting, abdominal cramps and diarrhea. Over 325,000 hospitalizations and 9,000 deaths are associated with food borne diseases each year.

If gut pathogens are present the gut will not and cannot be restored to health. Without complete removal of the pathogens and restoration of normal gut flora there is no healing. Gut pathogens may cause diarrhea, constipation, or alternating constipation and diarrhea often mis-diagnosed as irritable bowel syndrome.

There really isn't anything as important to health and longevity as restoring our 'living shield', our friendly microbiota. I have called it 'one's spacesuit' or, personally, 'my blankey'. Walking in the world without our barrier microbes inevitably leads to degeneration and disease. The great news is there is a way to restore the microbial balance for us all.

The Immune Restoration Protocol assumes that you are eating significant amounts of protein, one gram for each two pounds of body weight, every day from foods that do not contain offending lectins. It also assumes you are consuming adequate potassium found in whole fruits and vegetables, a minimum of 4,000 mg daily. If you do not do this your body cannot heal. Supplements do not support long term health. Appropriate food (for you and your microbiota) heals, restores and maintains the human body.

YOUR MICROBIOME

Microbiota are the organisms and microbiome is the collective genomes of all the organisms. Having the right microbes living on your 'walls', your skin and your mucous membranes from mouth to anus, really is your body's 'first defense'. Without these friendly helpers we are all at risk. There are no supplements or foods that can make up for not having or having lost our 'living shield'.

The largest influence on the health of your microbiome is DIVERSITY. As your GIT contains some 100 TRILLION bacteria it requires significant and repeated doses of high potency multi-strain microbial probiotics and prebiotic fiber to alter your immunity and restore balance.

While the probiotics suggested are the best available, 90% of your gut microbes are anaerobic. Very few probiotics are anaerobic; most tolerate oxygen, so trying to replace with probiotics alone won't increase your natural anaerobic defense system.

RE-Building Your Ancestral Microbiome

There are two ways to restore anaerobes, feed them appropriate microbe food (prebiotic fibers), or get a Fecal Transplant. Fecal transplants, however gross sounding, save lives. If your gut has lost most of its healthy anaerobes a fecal transplant may be the only way to restore balance.

Fecal transplants from live donors are difficult and expensive. The problem of finding someone, anyone, antibiotic free with a perfectly healthy gut having a diverse microbiome is huge.

From the NIH-

Prevalence: 60 to 70 million people affected by all digestive diseases

Hospitalizations: 21.7 million (2010)

Mortality: 245,921 deaths (2009)

Diagnostic and therapeutic inpatient procedures: 5.4 million

Ambulatory surgical procedures: 20.4 million

Costs: \$141.8 billion (2004)

A researcher in Canada, Elaine Petrof, has built Robogut, an anaerobic environment to grow anaerobic bacteria. They are using 33 strains of anaerobes to 'RePOOPulate' patient's healthy flora. It will be some time before the technique is available to the millions of humans suffering from anaerobe imbalance throughout the world. Even if production is able to replicate these organisms the healthy human gut contains 500-1,000 species.

If existing anaerobes can be 'repopulated' the gut may recover. The protocol is designed to enhance aerobic bacteria (probiotics) and regrow anaerobes.

We are covered, inside and out, in living bacteria. The creatures living in/on us may be friends, neutral microbes or serious enemies. Antibiotics, caesarean births, formula-fed infants and overall 'sanitation' has dramatically altered our gut and body flora removing

many of our friendlies and allowing our enemies to thrive or leaving us depleted of species we desperately need.

There is strong evidence our 'living shield' effects mood, energy, immunity, and whether we are fat or thin. In 2009 when I began writing about the microbiome ideas were plentiful but understanding was limited. Since that time 4,681 papers have been published just on the human gut microbiome.

In the past we analyzed for gut bacteria with a stool test. This test uses 'cultured' (petri dish) bacteria and is only able to show aerobic bacteria as anaerobic bacteria would not make it to the lab. As only 10% of your organisms are aerobic it was a very small window to your living shield.

In the US, two universities have begun sequencing the human microbiome, collected from all surfaces, not just the gut. The projects are being run from the University of San Francisco- <http://ubiome.com> and from the University of Colorado- <http://americangut.org> Both provide kits to sample organisms living in and on your body.

The data is being analyzed (DNA profiles of all organisms, aerobic and anaerobic) and then correlated with both diet and lifestyles (exercise changes your microbiome^(1115,1116,1117,1118)). These projects will tell us a great deal about our own microbiomes AND those of our friends, families and neighbors. The ongoing collection of data will also contribute to finding the healthiest microbial balance, what might disrupt this balance, and what might restore our ancestral microbial heritage. At the present time estimates from data collected suggest we may have lost as much as 50% of our microbiome diversity.

Extending Our View of Self: the Human Gut Microbiome Initiative (HGMI) Jeffrey I. Gordon, Ruth E. Ley, Center for Genome Sciences, Washington University, St. Louis, MO, Richard Wilson, Elaine Mardis, Jian Xu, Genome Sequencing Center, Washington University, St. Louis MO, Claire M. Fraser, The Institute for Genome Research, Rockville, MD, David A. Relman, Department of Medicine, Stanford University, Palo Alto, CA

The human GI tract is predominantly a bacterial ecosystem. Cell densities in the colon are the highest recorded for any known ecosystem. The vast majority of phylotypes belong to two divisions (superkingdoms) of Bacteria — the Bacteroidetes (48%) and the Firmicutes (51%). The remaining phylotypes are distributed among the Proteobacteria, Verrucomicrobia, Fusobacteria, Cyanobacteria, Spirochaetes and VadinBE97.

Antibiotics, even one 10 day course, caesarian births, lack of breast feeding, antibacterials (in mouthwashes and hand soaps and vaginal wipes), chlorine in the water supply, NSAIDs, PPI (proton pump inhibitors) all damage your natural living bacterial covering (microbiome).

Probiotics (so called friendly bacteria) are sold in every health food store and health food department of drugstores and grocery stores across the US. While many of these products may contain friendly bacteria there are BIG problems.

- Most probiotics found in health food stores or purchased online are very low potency, unable to have much influence on microbial balance. 1 billion organisms have little effect on the 100 TRILLION microbes in your gut.
- Most of these probiotics are aerobic, that is, oxygen tolerant .

- Aerobic probiotics have a short shelf life, the living bacteria often dying before you buy or take them. Most must be refrigerated to stay 'active'.
- Probiotic aerobic bacteria compose about 10% of the human microbiome.
- 90% of your microbial milieu are anaerobic, oxygen intolerant. They cannot survive in a normal oxygen containing environment. They cannot be cultured outside the human gut. So the majority of your healthy microbes cannot be purchased, they must be passed from human (or animal) to human and 'farmed' by specific foods needed for their health and growth.
- Dysbiosis, an imbalance of the microbiome, is common in most developed countries, caused by use of antibiotics, an overuse of antibacterial cleaning products, caesarian births, lack of breast feeding, stress, lack of exercise, and an imbalanced diet that lacks necessary elements to support microbial growth.
- Lack of diversity, that is, a great reduction in number of species, impacts health and longevity in all studies.

We need to restore our ancestral microbiome to attain health and longevity. This is a big deal because your microbes control:

- Your neurotransmitters and your mood ^(1119,1120,1121,1122)
- Your susceptibility to cancer and recovery from cancer treatments ^(1123,1124,1125,1126,1127,1128,1129,1130,1131,1132,1133,1134)
- Your heart and your metabolism, including whether you are fat or thin ^(1135,1136,1137,1138,1139,1140,1141,1142,1143,1144,1145,1146)
- Your cognitive ability including your susceptibility to dementia ^(1121,1147,1148,1149,1150,1151,1152,1153,1154)
- Your gut. Dysbiosis is the root cause of IBS (irritable bowel syndrome), IBD (ulcerative colitis and Crohn's disease), ulcers, SIBO (small intestine bacterial overgrowth) and post infectious IBS. Almost 16 million Americans have diagnosed ulcers (h. pylori) and 45 million suffer from IBS. 1.6 million are diagnosed with IBD which shortens life span by at least 10 years.

We are not healthy unless our microbes are abundant and diverse. There it is. You have a choice. Ignore your microbial self and no matter what diet or supplement or drug or lifestyle you choose health will elude you OR put in the effort to restore and maintain your ancestral microbiome.

Your microbiome is implicated in your mood, your weight, your immunity (allergy, asthma), and your longevity. It counts. It also alters your response to your environment. Some of your microbes actually change your genes. ^(1124,1135,1136,1155,1156)

Your living shield makes life on planet earth wonderful ☺ or miserable☹. The microbes you carry alter and are altered by your body and brain. Even your mood (or your dreams) may be a result of the microbes you carry.

Our microbiome is supported by fibrous foods. Instead of thinking 'grains' or 'bran' think vegetables, lots of vegetables. Think fibrous parts of fruits. Think berries. Think nuts and seeds. Think legumes (beans). Once your microbiome is restored a diet of whole fruits and LOTS of vegetables with adequate protein and fat will support you and your 'living shield'

but the restoration process requires supplementation as indicated in the Immune Protocol below.

There are many types of prebiotic fiber. A prebiotic is a substance that grows beneficial bacteria in the gut. Those chosen for the protocol have been clinically tested to increase the specific bacteria need to replenish and rebalance the microbiome.

Why Do I Need A Protocol?

Antibiotics destroy the microbiota balance. One 10 day exposure may be corrected with some probiotics, fiber and time. A second round may so imbalance the gut flora restoration becomes very difficult or even impossible. Serious infections destroy the microbiome. Stress damages the microbiome. Chemotherapy and radiation destroy the microbiome. NSAIDs damage the microbiome. PPI (protein pump inhibitors) destroy the microbiome. A lifetime of bacterial disruption damages the gut and the bacterial balance so that health is elusive.

Recent research suggests the specific items in the protocol have the best chance of restoring even a very dysbiotic gut. There are cases when this won't work and a fecal transplant will be the only chance for microbiome balance.

The original protocol designed in 2009 was a good base but not broad enough for full restoration for many clients. The new protocol covers the broadest possible choices currently available. It seems complicated and 'lots of stuff'. That is because it gives us the best chance of BROAD microbial support. Diversity is key. There is NO ONE BACTERIA that restores and maintains health. It is the 'ALL together NOT the same' that maintains life.

Who Should Attempt the Protocol

If you-

- have taken more than one course of antibiotics at any time in your life
- are overweight/obese (elevated glucose/insulin)
- have Type II diabetes or pre-diabetes (elevated HgA1c)
- have elevated cholesterol or LDL or insulin or glucose
- have been diagnosed with a mood disorder, autism spectrum disorder, ADHD
- have any type of gut disease, ulcers, colitis, IBS, SIBO, constipation, diarrhea
- have allergies or asthma
- have an autoimmune disease

Before beginning the protocol consider testing your microbiome.

<http://ubiome.refr.cc/XL3MGSK> Link gives a 10% discount. At this time I am mostly interested in the gut microbiome but test away. They offer gut, mouth, nose, genital, and skin. If you have 'issues' with any area add that test to your gut test. Your test/s will show what you grow now.

In as little as 30 days you will have a whole new 'self'.

For more information on the human microbiome <http://en.wikipedia.org/wiki/Microbiome>
When you have completed the protocol and note positive changes retest your 'living shield'. See what changed. You must continue to feed your biome or it will revert.

The protocol supports all bacteria currently seen as most beneficial including bifidobacteria, roseburia, eubacteria, f. Prausnitzii, and akkermansia. Do not buy a product that suggests it is the 'one' that fixes your microbiome. Remember always, DIVERSITY.

IMMUNE RESTORATION PROTOCOL-

Useful to correct IBD (ulcerative colitis and Crohn's Disease), IBS, SIBO, obesity (really), insulin resistance/diabetes, low energy, cognitive decline, chronic pain, mood disorders, sleep disorders, immune disorders. ***This protocol must be modified (call for help) if your immune system is compromised (HIV, hepatitis, under treatment for cancer, etc.).***

If you start and have symptoms, odiferous gas, cramping, bloating, call for help. You will need to remove possible pathogens before feeding your 'good bugs'.

In addition to the basic protocol consider eating some RS2 (see below) daily as GREEN bananas and/or RS3 roasted (creates highest RS value) and cooled potatoes or boiled and cooled rice. Cooking and cooling results in RS (resistant starch) to feed your gut bugs, the good ones. If you reheat, the RS goes away. Think potato salad or sushi.

Perhaps start with HALF a recipe for a few days. It is powerful. If SIBO is present lower amounts of fiber but double amounts of the SBO probiotics for a week or so, then do as written below.

In 18-24 ounces of fluid (juice, smoothie, water if you can handle the taste, I prefer V-8 diluted with water)-

1. 1 teaspoon Now Foods FOS Powder (prebiotic/fiber) use up to 2 teaspoons if overweight or insulin resistant
2. 1 tablespoon psyllium (fiber)
3. 1 tablespoon inulin (prebiotic/fiber)
4. 1 tablespoon acacia fiber, such as Heather's Tummy Fiber (fiber)
5. 1 tablespoon plantain flour RS2 (resistant starch, prebiotic)
<http://www.barryfarm.com> (see contraindications below)
6. 1 tablespoon potato STARCH (not flour) RS2 (resistant starch, prebiotic) Bob's Red Mill (see temporary contraindications below)
7. 1 level teaspoon chlorella powder (broken cell) GREEN grows anaerobic bacteria
8. 1 level teaspoon spirulina powder GREEN grows anaerobic bacteria
9. Primal Defense Powder (1 scoop) SBO probiotic
10. AOR Probiotic-3 (1) open in drink SBO probiotic
11. Prescript Assist (1) open in drink SBO probiotic
12. 1 packet unflavored VSL#3 (aerobic probiotic) <http://vsl3.com>

Batch Recipe-

- ❖ 1 cup each acacia fiber, psyllium, inulin, plantain flour and potato starch
- ❖ 1/3 cup each FOS, chlorella, spirulina

Dose is 6 level tablespoons in 18-24 ounces of fluid, your choice. Add probiotics directly to the drink, do NOT pre-mix with fibers.

It's a lot of 'stuff'. **All items need to be present for it to work.** The more food choices your microbiome has the more diversity and balance is possible. Each probiotic and fiber support different bacteria and different locations in your digestive tract.

After 30 days on the full program drop the three SBO probiotics to just one (pick one of the types and open one capsule or put one scoop into the drink) three-five days a week, alternate probiotics. The VSL#3, 1 packet, may be added just twice a week.

Fiber/prebiotics (FOS, acacia, inulin, psyllium, potato starch, plantain flour) are ONGOING at least 3 days a week as are the two GREEN supplements. They are needed to continue growing the good microbes. Each fiber type supports a different set of microbes in varying locations along your digestive tract. All are needed for a healthy gut.

Call if you have symptoms. You may bloat or have some digestive distress or gas when beginning, push through. If you have 'odiferous' gas please call. You likely need to take a course of Tribiotic.

TEMPORARY CONTRAINDICATIONS FOR POTATO STARCH/PLANTAIN FLOUR (RS2, RAW STARCH):

Don't take resistant starch alone; rs2 needs to be taken with other fiber to spread fermentation completely across the entire colon

Real food resistant starch (rs3) is superior to high-dose potato starch to expand the lean and immunoprotective core microbiota (roseburia, eubacteria, f. Prausnitzii, bifidobacteria)

If you have IBS or SIBO start the probiotics before adding resistant starch

Not all resistant starches are the same. At the current time the best long term support for microbes appears to come from RS1 and RS3. RS2 is useful for rebalancing the microbes.

RS1 is found in seeds and legumes and resists digestion because it is bound within the fibrous cell walls.

RS2 is found in some starchy foods, including raw potatoes and green (unripe) bananas.

RS3 is formed when certain starchy foods, such as potatoes and rice, are cooked and then cooled. The cooling turns some of the digestible starches into resistant starches via a process called retrogradation. (potato salad, sushi)

Reference List

1. Diet and exercise orthogonally alter the gut microbiome and reveal independent associations with anxiety and cognition Kang, S. S., Jeraldo, P. R., Kurti, A., Miller, M. E., Cook, M. D., Whitlock, K., Goldenfeld, N., Woods, J. A., White, B. A., Chia, N., and Fryer, J. D. 2014 Mol. Neurodegener.

2. Exercise and associated dietary extremes impact on gut microbial diversity Clarke, S. F., Murphy, E. F., O'Sullivan, O., Lucey, A. J., Humphreys, M., Hogan, A., Hayes, P., O'Reilly, M., Jeffery, I. B., Wood-Martin, R., Kerins, D. M., Quigley, E., Ross, R. P., O'Toole, P. W., Molloy, M. G., Falvey, E., Shanahan, F., and Cotter, P. D. 2014 Gut
3. The gut microbiota, dietary extremes and exercise Hold, G. L. 2014 Gut
4. Gut microbiota. Tackling the effects of diet and exercise on the gut microbiota Ray, K. 2014 Nat.Rev.Gastroenterol.Hepatol.
5. Neural networks in intestinal immunoregulation Costes, L. M., Boeckxstaens, G. E., de Jonge, W. J., and Cailotto, C. 2013 Organogenesis.
6. Absence of the gut microbiota enhances anxiety-like behavior and neuroendocrine response to acute stress in rats Crumeyrolle-Arias, M., Jaglin, M., Bruneau, A., Vancassel, S., Cardona, A., Dauge, V., Naudon, L., and Rabot, S. 2014 Psychoneuroendocrinology
7. The gut microbiome and the brain Galland, L. 2014 J.Med.Food
8. Neuropeptides and the microbiota-gut-brain axis Holzer, P. and Farzi, A. 2014 Adv.Exp.Med.Biol.
9. Microbiota dysbiosis is associated with colorectal cancer Gao, Z., Guo, B., Gao, R., Zhu, Q., and Qin, H. 2015 Front Microbiol.
10. Exploring gut microbes in human health and disease: Pushing the envelope Sun, J. and Chang, E. B. 2014 Genes Dis.
11. [Obesity and cancer] Ungefahren, H., Gieseler, F., and Lehnert, H. 2015 Internist (Berl)
12. Cancer and the gut microbiota: An unexpected link Zitvogel, L., Galluzzi, L., Viaud, S., Vetzizou, M., Daillere, R., Merad, M., and Kroemer, G. 1-21-2015 Sci.Transl.Med.
13. Uncovering Microbes' Role in Tumor Progression 1-21-2015 Cancer Discov.
14. Gut microbial metabolism and colon cancer: Can manipulations of the microbiota be useful in the management of gastrointestinal health? Belcheva, A., Irrazabal, T., and Martin, A. 1-20-2015 Bioessays
15. The microbiome of the urinary tract-a role beyond infection Whiteside, S. A., Razvi, H., Dave, S., Reid, G., and Burton, J. P. 2015 Nat.Rev.Urol.
16. Galacto-oligosaccharides and Colorectal Cancer: Feeding our Intestinal Probiome Bruno-Barcena, J. M. and Azcarate-Peril, M. A. 2015 J.Funct.Foods
17. Microbiota-Mediated Inflammation and Antimicrobial Defense in the Intestine Caballero, S. and Pamer, E. G. 1-2-2015 Annu.Rev.Immunol.
18. Microbiome: the bacterial tightrope Bourzac, K. 12-4-2014 Nature
19. Microbiome and cancer Ohtani, N. 2015 Semin.Immunopathol.
20. Substantial decreases in the number and diversity of microbiota during chemotherapy-induced gastrointestinal mucositis in a rat model Fijlstra, M., Ferdous, M., Koning, A. M., Rings, E. H., Harmsen, H. J., and Tissing, W. J. 11-8-2014 Support.Care Cancer
21. The immunity-diet-microbiota axis in the development of metabolic syndrome Brandsma, E., Houben, T., Fu, J., Shiri-Sverdlov, R., and Hofker, M. H. 2-16-2015 Curr.Opin.Lipidol.
22. Does our gut microbiome predict cardiovascular risk? A review of the evidence from metabolomics Griffin, J. L., Wang, X., and Stanley, E. 2015 Circ.Cardiovasc.Genet.
23. Dysbiosis of the gut microbiota in disease Carding, S., Verbeke, K., Vipond, D. T., Corfe, B. M., and Owen, L. J. 2015 Microb.Ecol.Health Dis.
24. Gut microbiota composition correlates with changes in body fat content due to weight loss Remely, M., Tesar, I., Hippe, B., Gnauer, S., Rust, P., and Haslberger, A. G. 1-21-2015 Benef.Microbes.
25. Intestinal Microbiota: a Regulator of Intestinal Inflammation and Cardiac Ischemia? Bashashati, M., Habibi, H. R., Keshavarzian, A., Schmulson, M., and Sharkey, K. A. 1-19-2015 Curr.Drug Targets.
26. Fecal microbiota transplantation broadening its application beyond intestinal disorders Xu, M. Q., Cao, H. L., Wang, W. Q., Wang, S., Cao, X. C., Yan, F., and Wang, B. M. 1-7-2015 World J.Gastroenterol.
27. The intestinal microbiota: its role in health and disease Biedermann, L. and Rogler, G. 2015 Eur.J.Pediatr.
28. Insights into the role of the microbiome in obesity and type 2 diabetes Hartstra, A. V., Bouter, K. E., Backhed, F., and Nieuwdorp, M. 2015 Diabetes Care
29. Gut microbiota and metabolic syndrome Festi, D., Schiumerini, R., Eusebi, L. H., Marasco, G., Taddia, M., and Colecchia, A. 11-21-2014 World J.Gastroenterol.
30. Fecal microbiota transplantation: a new old kid on the block for the management of gut microbiota-related disease Cammarota, G., Ianiro, G., Bibbo, S., and Gasbarrini, A. 2014 J.Clin.Gastroenterol.
31. Dynamic interplay between metabolic syndrome and immunity Paragh, G., Seres, I., Harangi, M., and Fulop, P. 2014 Adv.Exp.Med.Biol.
32. Microbiota and diabetes: an evolving relationship Tilg, H. and Moschen, A. R. 2014 Gut
33. The gut microbiota and its correlations with the central nervous system disorders Catanzaro, R., Anzalone, M. G., Calabrese, F., Milazzo, M., Capuana, M. L., Italia, A., Occhipinti, S., and Marotta, F. 11-12-2014 Panminerva Med.
34. Dealing with ability of the microbiota to influence the brain, and ultimately cognition and behavioral Lyte, M. and Cryan, J. F. 2014 Adv.Exp.Med.Biol.
35. The impact of microbiota on brain and behavior: mechanisms & therapeutic potential Borre, Y. E., Moloney, R. D., Clarke, G., Dinan, T. G., and Cryan, J. F. 2014 Adv.Exp.Med.Biol.
36. Microbiota-gut-brain axis and cognitive function Gareau, M. G. 2014 Adv.Exp.Med.Biol.
37. The effects of inflammation, infection and antibiotics on the microbiota-gut-brain axis Bercik, P. and Collins, S. M. 2014 Adv.Exp.Med.Biol.
38. The effects of gut microbiota on CNS function in humans Tillisch, K. 2014 Gut Microbes.
39. Cognitive decline, dietary factors and gut-brain interactions Caracciolo, B., Xu, W., Collins, S., and Fratiglioni, L. 2014 Mech.Ageing Dev.
40. Microbial genes, brain & behaviour - epigenetic regulation of the gut-brain axis Stilling, R. M., Dinan, T. G., and Cryan, J. F. 2014 Genes Brain Behav.

41. The human microbiome in autoimmune diseases Cojocaru, M. and Chicos, B. 2014 Rom.J.Intern.Med.
42. Application of metagenomics in the human gut microbiome Wang, W. L., Xu, S. Y., Ren, Z. G., Tao, L., Jiang, J. W., and Zheng, S. S. 1-21-2015 World J.Gastroenterol.
43. Effects of age and region on fecal microflora in elderly subjects living in Bama, Guangxi, China Zhao, L., Xu, W., Ibrahim, S. A., Jin, J., Feng, J., Jiang, J., Meng, J., and Ren, F. 2011 Curr.Microbiol.
44. Oral administration of live Bifidobacterium substrains isolated from healthy centenarians enhanced immune function in BALB/c mice Yang, H. Y., Liu, S. L., Ibrahim, S. A., Zhao, L., Jiang, J. L., Sun, W. F., and Ren, F. Z. 2009 Nutr.Res.
45. Probiotic properties of lactic acid bacteria isolated from stool samples of longevous people in regions of Hotan, Xinjiang and Bama, Guangxi, China Gu, R. X., Yang, Z. Q., Li, Z. H., Chen, S. L., and Luo, Z. L. 2008 Anaerobe.

To restore body microbiota you will need a minimum of 30 days. Repeat the program for a few days after any bout with food poisoning; during and/or after any antibiotic or antifungal treatment for yeast, parasites, pathogenic bacteria, or if you contract a gut virus (stomach flu). You may decide to make your own 24 hour yogurt to provide the friendly microbes. Email for the recipe.

Special note: If the probiotics are being used with any form of antibiotic, prescription or natural, take your probiotic 1-2 hours after any such 'medication', otherwise take it any time. After your gut is restored and you begin to experience the energy part of probiotics taking this before bed may make for a less restful sleep so pay attention to your body and adjust.

What you will need:

1. Now Foods FOS Powder (psyllium (fiber)
 2. inulin (prebiotic/fiber)
 3. acacia fiber, such as Heather's Tummy Fiber (fiber)
 4. plantain flour RS2 (resistant starch, prebiotic) <http://www.barryfarm.com>
 5. potato STARCH (not flour) RS2 (resistant starch, prebiotic) Bob's Red Mill
 6. chlorella powder (broken cell) GREEN grows anaerobic bacteria
 7. spirulina powder GREEN grows anaerobic bacteria
 8. Primal Defense Powder
 9. AOR Probiotic-3
 10. Prescript Assist
 11. unflavored VSL#3 (aerobic probiotic) <http://vsl3.com>
- Optional, use only if gut pathogens are present- Allergy Research Tribiotic (also called Nutricology Tricycline)
 - Optional- if immune system is impaired: EpiCor 500 mg for 30 days.
 - Optional – use if you think you have any gut pathogens, will improve 'kill'. Lactoferrin 250-300 mg (1-2) twice a day (any brand, Jarrow or Life Extension or Symbiotics, just make sure it is JUST lactoferrin, nothing added) Open the capsules into the applesauce or other food (see below). The amount of lactoferrin found in protein powders and colostrum is small, about 4-6 mg. 300-500 mg of pure lactoferrin is the treatment dose. Use of lactoferrin is explained below.
 - Optional- SeaCure, a special protein. If your gut is seriously damaged it will speed healing time. Helpful for ulcerative colitis. The dose is 6 capsules once a day for a minimum of one month. Available from <http://iherb.com> use my PIN for a discount RIS664

- Optional- if severe long term damage has occurred the addition of zinc-l-carnosine such as found in PepZin GI helps heal damaged intestinal cells. The dose is one twice a day for 8 weeks.

After the protocol is completed to maintain anaerobes take the mix below two to three times a week. These items may be mixed in a fruit/protein smoothie if you like.

VSL#3 must be refrigerated at all times. Available for \$87 for the 30 packet box, <http://vsl3.com> or Costco or Wal-Mart Pharmacy. Costco codes are VSL#3 flavored packs 1650233 (McKesson); unflavored packs 1944339 (McKesson) and for making yogurt the capsules 1767516 (McKesson). If buying from Costco order ahead from the Costco pharmacy by phone for pick up the next day.

It will be necessary to continue to take the high potency probiotics and fiber ongoing, several times a week, to keep your immune system healthy. Please email or call for information on making the VSL#3 yogurt.

Immune Restoration in SIBO (Small Intestine Bacterial Overgrowth)

If you have or think you might have dysbiosis- an imbalance of gut bacteria, use the protocol plus the Tribiotic to lower bacterial count in the small intestine. Tribiotic dose is (2) before each meal for 10 days concurrent with the Restoration Protocol. Give the protocol a full 30 days.

Symptoms are bloating and sometimes gas pain (but without gas) soon after meals and constipation. It is caused by translocation of bacteria from the large intestine to the small intestine. The most common cause is insufficient gastric acid. A secondary cause is the presence of methane producing bacteria. Because oral hydrochloric acid is problematic you need to seek help from a knowledgeable healthcare provider.

Immune Restoration in Allergy and Asthma

Restoration of friendly bacteria has been found to reduce both food allergy reactions and inhalant allergies.^(25,122) Use the protocol for a minimum of 60 days. Also make sure to use the Liposomal C, 2,000-3,000 mg twice a day as in the protocol..

Immune Restoration and Children

Children and infants benefit from added probiotics. If gut issues are a problem in your family please call for a program. Use of probiotics in children and infants should be monitored. They will not be able to do the drink. Probiotics may be added to food and the Tummy Fiber may also be added to food. Psyllium, spirulina and chlorella are not suitable for children.

Immune Restoration and Autism

Several recent research papers have suggested gut dysbiosis as a factor in autism. Since the gut provides the major source of both serotonin and melatonin and has a powerful effect on immunity it makes some sense. ^(35,126,128,129,130,1157)

PROBIOTICS FOR AUTISM

Medical study proved 'too effective' A medical study on probiotics for autism has proven so successful that the study 'failed', according to a New Scientist report on September 9, 2006.

*The study, by Prof Glenn Gibson at Reading University, UK, found that autistic children vastly improved their concentration and behavior when given probiotics, or 'friendly bacteria'. It involved 40 autistic children, aged 4 to 8, half of whom were given the probiotic bacteria *L. Plantanum* while the other half received a dummy 'probiotic'.*

It was supposed to have been a blind study, where the participants were not told who were taking the actual probiotics and who were taking placebos or dummy medicine. As part of this probiotics for autism study, parents were asked to record their children's mood and behaviour in a diary.

The results were too obvious. Parents whose autistic children were taking the actual probiotics saw such great improvements in their children's behaviour that they knew their children were taking the real thing. Thus, problems arose during the 'crossover' point of this probiotics for autism study, where the two groups were supposed to switch medicines. Many of the parents whose children were taking the actual probiotics refused to make the switch as they wanted their autistic children to continue their improvement.

Due to the high drop-out rate, Prof Gibson was not able to draw any firm, 'scientific' conclusion from his probiotics for autism study. Prof Gibson noted, however, that autistic children often suffer bowel conditions and a previous study had found high levels of a "bad" bacteria called clostridia in their gut.

The probiotics for autism study was designed to reduce the levels of clostridia and promote "friendly" bacteria instead, to see what effect this would have. Prof Gibson said the children appeared to show fewer signs of autistic behaviour when taking the probiotics supplement, which was given in a powder once a day.

Very subjectively, we asked the parents to fill in diaries about the mood of the children. We got very positive feedback generally," he said. Prof Gibson said that certain kinds of clostridia produced neuro-toxins, which potentially could be the cause of autism or a contributory factor. However, he said this was speculation. The apparent improvement which the parents observed could also simply be because the children had felt better.

"If your gut is not behaving yourself, you feel rough," Prof Gibson said. Many parents of autistic children have reported vast improvements in their children's behaviour with the use of probiotic supplements. The Autism Clinic recommends a special, ultra-high potency probiotics supplement specially formulated for children with autism.

The probiotic currently being used in the autism community is Doctor's Formula which contains 5 strains of good bacteria. The VSL#3 contains 8 specifically tested strains. So far the VSL3 is the best formulated and the least expensive per 'dose'.

Balanced microbes- Key to a healthy immune system

The key to success in restoring your immune system is to provide your body with its natural 'living shield' of microbiota. These living organisms do the work for you fighting pathogens, normalizing bowel function, restoring both the innate and acquired immune system, and

healing gut permeability. You must use a broad-spectrum probiotic (many kinds of bacteria) and in large quantity, a minimum dose of 400-500 billion in children and adults, daily, up to 3+ trillion in serious gut disease. High dose probiotics should always be taken on/in food or drink (not hot as it will kill the bacteria). Also incorporate soluble fiber. It may easily be added to food. Soluble fibers include grapefruit pectin, apple pectin, and Heather's Tummy Fiber (gum arabic).

Lactoferrin

Once your microbes are healthy and happy and your gut restored you will make your own lactoferrin. In the meantime the addition of lactoferrin supplementation to anti-bacterial and anti-fungal treatments increases destruction of pathogens by greater than 70%.

Lactoferrin: Lactoferrin (LF) is a globular multifunctional protein with antimicrobial activity (bactericide, fungicide), is part of the innate defense, mainly at mucosae. Lactoferrin is found in milk and many mucosal secretions such as tears and saliva. Lactoferrin is also present in secondary granules of PMN and also is secreted by some acinar cells. Lactoferrin can be purified from milk or produced recombinantly. Human colostrum has the highest concentration, followed by human milk, then cow milk.

Lactoferrin belongs to the iron transporter or transferrin family of glycoproteins. Lactoferrin is also found in exocrine secretions from mammals and is released from neutrophil granules during inflammation. The lactoferrin concentration in bovine (cows) milk is only 0.5% to 1.0% while human breast milk can contain as much as 15% lactoferrin.

Lactoferrin appears to have antibacterial, antiviral, antifungal, anti-inflammatory, antioxidant and immunomodulatory activities.

How Lactoferrin Works

Receptors for lactoferrin are found in monocytes, lymphocytes, neutrophils, intestinal tissue and on certain bacteria. Lactoferrin's ability to bind iron may account for some of its anti-bacterial activity. Iron is essential to support the growth of pathogenic bacteria. Lactoferrin may also inhibit the attachment of bacteria to the intestinal wall.

The possible antiviral activity of supplemental lactoferrin may be due to its inhibition of virus-cell fusion and viral entry into cells. It is believed that Lactoferrin may promote the growth and differentiation of T lymphocytes. Lactoferrin appears to bind uniquely to sites on the T4 (helper) and T8 (suppressor) lymphocytes. Lactoferrin also appears to play a role in the regulation of cytokines and lymphokines, such as tumor necrosis (TNF)-alpha and interleukin (IL)-6.

Lactoferrin's possible antioxidant activity may also contribute to its possible immunomodulatory activity. Antioxidants are getting increasing attention as possible therapeutic agents in infections and a variety of other diseases. Lactoferrin's ability to bind iron probably contributes to both its antioxidant properties and its antibacterial action. Free iron is a contributor in the generation of free radicals.

Lactoferrin Contraindications, Interactions & Precautions

Some individuals may have a hypersensitivity or allergy to lactoferrin. It is contraindicated for those individuals. It is generally recommended that pregnant women and nursing mothers avoid using lactoferrin because it has not been tested in these conditions. Some *in vitro* studies suggest that lactoferrin acts synergistically with antifungal agents, making them more potent.

Lactoferrin References

- Adamik B, Zimecki M, Wlaszczyk A, et al. Lactoferrin effects on the *in vitro* immune response in critically ill patients. *Arch Immunol Ther Exp (Warsz)*. 1998; 46:169-176.
- Baveye S, Ellass E, Mazurier J, et al. Lactoferrin: a multifunctional glycoprotein involved in the modulation of the inflammatory process. *Clin Chem Lab Med*. 1999; 37:281-286.
- Bhimani RS, Vendrov Y, Furmanski P. Influence of lactoferrin feeding and injection against systemic staphylococcal infections in mice. *J Appl Microbiol* 1999 Jan;86(1):135-44.
- Britigan BE, Serody JS, Cohen MS. The role of lactoferrin as an anti-inflammatory molecule. *Adv Exp Med Biol*. 1994; 357:143-156. Defer MC, Dugas B, Picard O, Damais C. Impairment of circulating lactoferrin in HIV-1 infection. *Cell Mol Biol (Noisy-le-grand)* 1995 May;41(3):417-21.
- Dial EJ, Hall LR, Serna H, Romero JJ, Fox JG, Lichtenberger LM. Antibiotic properties of bovine lactoferrin on *Helicobacter pylori*. *Dig Dis Sci* 1998 Dec;43(12):2750-6.
- Harmsen MC, Swart PJ, de Bethune MP, Pauwels R, De Clercq E, The TH, Meijer DK. Antiviral effects of plasma and milk proteins: lactoferrin shows potent activity against both human immunodeficiency virus and human cytomegalovirus replication *in vitro*. *J Infect Dis* 1995 Aug;172(2):380-8.
- Ikeda M, Nozak A, Sugiyama K, et al. Characterization of antiviral activity of lactoferrin against hepatitis C virus infection in human cultured cells. *Virus Res*. 2000; 66:51-63.
- Kruzel ML, Harari Y, Chen CY, Castro GA. The gut. A key metabolic organ protected by lactoferrin during experimental systemic inflammation in mice. *Adv Exp Med Biol* 1998;443:167-73.
- Kuwata H, Yip TT, Tomita M, Hutchens TW. Direct evidence of the generation in human stomach of an antimicrobial peptide domain (lactoferricin) from ingested lactoferrin. *Biochim Biophys Acta* 1998 Dec 8;1429(1):129-41.
- Lee WJ, Farmer JL, Hilty M, Kim YB. The Protective Effects of Lactoferrin Feeding against Endotoxin Lethal Shock in Germfree Piglets. *Infect Immun* Apr. 1999; Vol 66 No 4, 1421-1426.
- Levy PF, Viljoen M. Lactoferrin: a general review. *Haemologica*. 1995; 80:252-267.
- Lonnerdal B, Iyer S. Lactoferrin: molecular structure and biological function. *Annu Rev Nutr*. 1995; 15:93-110. Muller F, Holberg-Petersen M, Rollag H, Degre M, Brandtzaeg P, Froland SS. Nonspecific oral immunity in individuals with HIV infection. *J Acquir Immune Defic Syndr* 1992;5(1):46-51.
- Percival M. Intestinal Health. *Clin. Nutri. Insights*. 1997, Vol 5. No 5, 1-6.
- Puddu P, Borghi P, Gessani S, Valenti P, Belardelli F, Seganti L. Antiviral effect of bovine lactoferrin saturated with metal ions on early steps of human immunodeficiency virus type 1 infection. *Int J Biochem Cell Biol* 1998 Sep;30(9):1055-62.
- Sakamoto N. Antitumor effect of human lactoferrin against newly established human pancreatic cancer cell line SPA. *Gan To Kagaku Ryoho* 1998 Aug;25(10):1557-63.
- Stella V, Postaire E. Evaluation of the antiradical protector effect of multifermented milk serum with reiterated dosage in rats. *C R Seances Soc Biol Fil* 1995;189(6):1191-7.
- Superti F, Ammendolia MG, Valenti P, Seganti L. Antitrotaviral activity of milk proteins: lactoferrin prevents rotavirus infection in the enterocyte-like cell line HT-29. *Med Microbiol Immunol (Berl)* 1997 Oct;186(2-3):83-91.
- Swart PJ, Kuipers EM, Smit C, et al. Lactoferrin. Antiviral activity of lactoferrin. *Adv Exp Med Biol*. 1998; 443:205-213.
- Trumpler U, Straub PW, Rosenmund A. Antibacterial prophylaxis with lactoferrin in neutropenic patients. *Eur J Clin Microbiol Infect Dis*. 1989; 8:310-313.
- Tsuda H, Sekine K, Nakamura J, Ushida Y, Kuhara T, Takasuka N, Kim DJ, Asamoto M, Baba-Toriyama H, Moore MA, Nishino H, Kakizoe T. Inhibition of azoxymethane initiated colon tumor and aberrant crypt foci development by bovine lactoferrin administration in F344 rats. *Adv Exp Med Biol* 1998;443:273-84.
- Ushida Y, Sekine K, Kuhara T, Takasuka N, Iigo M, Tsuda H. Inhibitory effects of bovine lactoferrin on intestinal polyposis in the Apc(Min) mouse. *Cancer Lett* 1998 Dec 25;134(2):141-5.
- Vorland LH. Lactoferrin: a multifunctional glycoprotein. *APMIS*. 1999; 107:971-981.
- Vorland LH, Ulvatne H, andersen J, et al. Antibacterial effects of lactoferricin B. *Scand J Infect Dis*. 1999; 31:179-184.
- Vorland LH, Ulvatne H, andersen J, Haukland H, Rekdal O, Svendsen JS, Gutteberg TJ. Lactoferricin of bovine origin is more active than lactoferricins of human, murine and caprine origin. *Scand J Infect Dis* 1998;30(5):513-7.
- Yamauchi K, Wakabayashi H, Hashimoto S, Teraguchi S, Hayasawa H, Tomita M. Effects of orally administered bovine lactoferrin on the immune system of healthy volunteers. *Adv Exp Med Biol* 1998;443:261-5.
- Yoo YC, Watanabe S, Watanabe R, Hata K, Shimazaki K, Azuma I. Bovine lactoferrin and lactoferricin, a peptide derived from bovine lactoferrin, inhibit tumor metastasis in mice. *Jpn J Cancer Res* 1997 Feb;88(2):184-90.
- Zhang GH, Mann DM, Tsai CM. Neutralization of endotoxin *in vitro* and *in vivo* by a human lactoferrin-derived peptide. *Infect Immun* 1999 Mar;67(3):1353-8.

ASPIRIN, ADVIL, MOTRIN AND OTHER NSAIDS, SAFE USE OF PAIN MEDS

If you need to take aspirin, or any other non-steroidal anti-inflammatory, please take lecithin granules 1 rounded teaspoon with each dose of NSAID. NSAIDs including Aspirin, Motrin, Advil, Aleve, and similar medications work by combining with phospholipids to create anti-inflammatory prostaglandins that reduce pain and inflammation.

Aspirin, Motrin, Advil and other NSAIDS strip phospholipids from the gut wall. Lecithin naturally contains these phospholipids. When lecithin is combined with aspirin or other non-steroidals not only is there no damage to the intestine, according to a study at the University of Texas, the medication is 80% more effective in reducing pain and inflammation. ^(1158,1159)

Taking an anti-inflammatory with lecithin allows the medication to use the phospholipids in the lecithin rather than stripping them from the gut wall. Because the lecithin provides significant amounts of the anti-inflammatory raw material the medication is more effective.

With each dose of medication use 1 rounded teaspoon lecithin granules. The granules, while less convenient than lecithin soft gels, have a MUCH higher content of phospholipids so are the best choice. Egg yolk also contains significant lecithin and could be taken as a substitute, one cooked egg yolk with each dose. **Lecithin must be taken immediately before or with the medication to protect the gut and increase effectiveness.**

You will need to periodically use the Immune Restoration Protocol as NSAIDs cause dysbiosis over time. ^(61,1160,1161,1162)

If NSAIDS or aspirin must be taken regularly in addition to lecithin buy PepZin GI and take one twice a day ongoing. Studies found the ingredient in PepZin GI, zinc-l-carnosine protects from and heals any damage from the medication. ^(1163,1164,1165,1166,1167) **Zinc-l-carnosine does NOT improve the anti-inflammatory effect so keep up the lecithin.**

TOPICAL OINTMENT RECIPES AND APPLICATIONS

For all skin conditions the use of topical C, zinc, A and D have a long and safe history. Vitamin E is used for tissue regeneration and to prevent or reverse scars. These supplements can be mixed with a coconut or lanolin based cream or lotion or mix with water or glycerin or aloe. Do not use omega-6 based lotions or creams as omega-6 fatty acids rapidly oxidize and are absorbed by your skin. Creams and lotions with omega-6 will make your skin more sensitive to sunlight, increase inflammatory response and contribute to skin aging over time. Read labels.

Your Skin

As I have suggested using sunlight to get vitamin D I want to give you information on skin cancer. Skin cancer may be melanoma, the most deadly and difficult to treat, or basal or squamous cell carcinoma, common and usually easily treated.

It has been suggested that skin cancer is on the rise because of

1. Loss of the ozone layer
2. Excess sun exposure

Number one does not hold true for most of the world. There is an ozone hole at the South Pole but essentially no change in ozone coverage over Michigan or Florida or Hawaii or Europe or other global locations. Even with loss of 10% of the ozone the increase in UV-B would be equivalent to moving 100 miles closer to the equator, not much change in UV-B exposure.

If increased exposure to UV-B sunlight is the cause of skin cancer we should find increased levels of vitamin D (produced in the skin exposed to UV-B) in persons with skin cancer but overall levels of vitamin D have decreased in the past 20 years.

There is a combination of factors that play a role in skin cancer. The outer layer of human skin is called the stratum corneum. This layer was long thought to be simply excess dead skin cells. New research has found this 'horny' layer to be responsible for maintaining moisture in the skin, protecting underlying cells from UV damage and protecting us from varying infectious agents.

The health of the stratum corneum depends on and generally healthy diet and adequate vitamin C. If you have any history of skin cancers please use the Liposomal C 2,000 mg twice a day ongoing until you have a checkup with no abnormal cells and then reduce to 1,000 mg twice daily. If using ascorbic acid the dose is 2,000-3,000 mg three times a day and then 2,000-3,000 mg twice daily.

If you decide (and I hope you do) to use sunlight to get your D DONOT use chemically based cleansers to wash your face and body. Sun sensitivity, the result of damage to the stratum corneum, is a side-effect of some common skin treatments and cleansers.

A primary destroyer of the integrity of the stratum corneum is 'sodium lauryl sulfate' and its derivatives as well as other chemicals found in cleansers commonly used on our skins daily. Modern cleansers and shampoos are not 'cancer causing' as is sometimes claimed by alarmists and overzealous websites, but they do damage the body's protective layer making it more susceptible to environmental assaults, including UV damage.

Avoid topical chemicals. These chemicals, including detergents, cleansers, skin peels and hydroxy acids, damage the stratum corneum leaving newly developing cells open to lipid or water loss, radiation damage and infection. **When using a product such as 'fruit acids' to peel the skin it takes a minimum of 7 days to restore the stratum corneum to provide protection from the outside environment, including UV light. .**

If you wish to have beautiful skin all your life and/or you are using the sun to get your vitamin D avoid products containing Retin-A; Alcohol (Isopropyl); Fluoride; Parabens; Sodium Lauryl Sulfate (SLS); DEA; Fragrance; Polyethylene Glycol (PEG); TEA; DMDM; Hydantoin; MEA; Propylene Glycol (PG); Triclosan; FD&C Color; Mineral Oil; Sodium Laureth Sulfate (SLES); Urea; or Hydantoin. Never use products containing alpha hydroxy acid (AHA) or other strong exfoliants.

Read labels, including labels on your sunscreen and your shampoo and conditioner. The use of lotions, cosmetics and soaps containing sun sensitizing chemicals and other lipid dissolving chemicals damage the skin's barrier function and make your skin more susceptible to sun damage, water loss and infection.

For a list of chemicals and reasons to avoid them visit <http://www.lindachae.com> or read Beauty To Die For by Judi Vance or Dying to Look Good by Christine H Farlow.

Aubrey organics and Zia have a number of safe shampoos, conditioners and other creams and lotions, some especially for babies.

Chlorine and Your Skin

Chlorine wreaks havoc with the stratum corneum and with the surface cells of your hair. In the past chlorine was able to be removed by some filters or dissipated after standing (for your fish tank). Currently most municipal water treatment plants use chloramines, a chemical difficult to remove. The good news is that plain ascorbic acid powder dissipates chlorine and chloramines in seconds. While this won't work in your shower (below) it will work in your bath (or fish tank).

Just one heaping teaspoon will remove all chlorine from the largest bathtub before you step in. I use a tablespoon to allow for the benefits of topical C in my bath.

Don't buy vitamin C shower filters. They will work for about two showers. Vitamin C is inherently unstable when wet and rapidly oxidizes which means it loses its capacity to break down chloramines or chlorine.

Vitamin C and Your Skin

Vitamins A and D and the mineral zinc improve skin health but one of the most important vitamins for your skin is vitamin C. Vitamin C is essential for skin health protecting from UV radiation, improving the lipid composition of your stratum corneum, not dead skin but a living barrier, keeping moisture in and chemicals and toxins out.^(434,435) Whether from diet, supplements or topical application optimal vitamin C keeps skin younger, longer.
(1168,1169,1170,1171,1172,1173,1174,1175,1176,1177,1178,1179)

The minimum daily dose is 1,000 mg ascorbic acid twice a day. Higher doses may be needed if you are injured, ill, stressed or sun-exposed. If you want to use topical vitamin C make your own (recipe section) as once vitamin C is mixed it rapidly loses its potency.

Soaks

Straight hydrogen peroxide, 3%. For fungus, plantar warts, cuts or burns. If this is too strong dilute with water, rose water, and/or glycerin. (If you soak your nails they will turn white.) If fungus or warts are problematic also take Planetary Formulas Full Spectrum Olive Leaf Extract (2) tablets twice a day for one month.

Vitamin C as ascorbic acid powder U.S.P. mixed in very warm water approximately 1 heaping tablespoon per cup. For skin infections, fungus, scars or warts. Soak for 20 or more minutes.

MSM soak- 2 cups MSM powder in bath (add a tablespoon of ascorbic acid powder to boost this). For any skin problems.

Soaks should last 15-30 minutes. The hydrogen peroxide can be put on a cloth and placed over the injured area. If the foot or hand is soaked in hydrogen peroxide the nails may turn white and they will not turn back to normal until they grow out. Maximum time for H₂O₂ is 15 minutes. The C soak should be as warm (hot) as is allowable.

Ointments, Sprays and Lotions

Burns, Rashes, Wounds:

Desitin Ointment- (drug store, usually the generic version is OK) contains zinc oxide, A and D from cod liver oil. Rashes, skin irritation (anywhere on the body), floor burns, burns, wounds, infections (wounds should be disinfected and infections should be soaked in either of the above soaks first).

Homemade Desitin (sort of, but stronger concentration)- Two fish oil based A&D capsules (about 5,000 I.U. A and 400 I.U. D each- total 10,000 IU A and 800-1,000 IU D) and one 400 I.U. d-alpha E capsule and a pinch of ascorbic acid mixed with about 1 teaspoon zinc oxide U.S.P. (drug store). Apply several times a day, small amount, rubbed in.

Skin Cancer, Basal Cell, and Plantar Warts:

Ointment for minor pre-cancerous skin sites and for all warts including Plantar warts: Often minor skin cancers, the so called Basal-Cell cancers can be treated topically with this ointment. PLEASE NOTE: If the spot(s) does not clear rapidly, is large or is advanced, do not use this ointment, see your physician for standard therapies.

Ingredients:

- ½-1 teaspoon ascorbic acid U.S.P.
- 3 teaspoons 100% Shark Cartilage Powder by Lane Labs
- 10,000 IU D3 (soft gel) 10,000 IU Vitamin A (soft gel fish liver oil extract)
- Enough 70% DMSO gel to make a paste. (<http://myvitanet.com>)

Do not make more than a two day supply. Keep in a closed container. Apply once or twice a day. Use with the zinc ointment combo above. Usually, use the DMSO combo in the PM and the zinc combo in the AM.

Athlete's foot fungus

Lavilin foot deodorant will eliminate athlete's foot (it's zinc oxide paste). Low levels of zinc allow bacteria to grow on the skin (and between your toes). Test with the Zinc Test page 136 and improve your zinc nutrition.

If warts or chronic skin infections are a chronic problem (including acne and athlete's foot) make sure the diet is adequate in zinc (test), A (minimum 50,000 IU total from all supplements per week), C (2,000-4,000 mg daily), D (test), and protein as well as short and medium chain fatty acids found in whole raw milk, unprocessed coconut oil or coconut milk.

Topicals for Joint or Muscle Pain

DMSO 70% gel with aloe. May dry your skin. Do not use on open sores or burned or abraded skin. Make sure your hands and the application surface are clean. DMSO stronger than 70% will burn the skin. Don't use it. DMSO is used on animals for muscle and joint injuries to reduce inflammation and speed healing.

Table 19 Peroxy Gel Recipe

Peroxy Gel (6% Hydrogen Peroxide) One Pint Formula (external use only)
Ingredients:
1 1/3 cups pure, very thick Aloe Vera gel (Best to use is Fruit of the Earth Aloe Vera Gel 100% No Color Added, available from Target or Long's Drugs. Not as good, Aloe Vera 80 Gel by Naturade)
1/3 cup of glycerin U.S.P (from health food store or drug store)
1/3 cup of 35% food grade H ₂ O ₂ (Very strong. May be available online or from your health food store)
Recipe:
Mix together the 1/3 cup of glycerin and the 1/3 cup of 35% food grade hydrogen peroxide with a plastic or rubber spatula. Be very careful mixing the hydrogen peroxide as it is very strong, don't splash. Any spills can be cleaned up with plain water to dilute the concentration.
Add the 1 1/3 cups of Aloe Vera gel to the mix.
Carefully blend ingredients together with a spatula. This will look soupy at first. Keep stirring gently until it thickens.
Store: Use the spatula to put this mixture into a mayonnaise jar or other wide mouth jar. A used large size empty face cream/scrub container is great. Do not put in a metal container. Hydrogen peroxide is safe in plastic or glass. It will oxidize metals. The cap of the jar may be metal as the gel won't really touch it. If you don't use the gel regularly use only plastic as it will 'expand' as the oxygen is released and may burst a sealed glass container (unlikely but possible). Do not get near your jewelry as it will oxidize the metals (rinse quickly with plain water).
Store this mixture in the refrigerator (If kept at room temperature it will oxidize more rapidly and turn to liquid rapidly. It is still ok to use but very runny and not as strong)
Clearly mark the container: "Peroxy Gel 6% Hydrogen Peroxide, External Use Only!"

Use on sore muscles, arthritic joints, insect bites, sprains. On open wounds it will promote healing but will burn. It can be used on the skin around a burn or wound rather than directly on it. It dramatically increases oxygen to area where it is applied.

Peroxy Gel has been used on the inner arms of asthmatics to abort an asthma attack by increasing blood oxygen. It works. It also works well on simple basal cell skin cancers and pre-cancerous tissues. Use for sinus infection, apply on skin near sinus pain or headache by applying to the skin on the sides of your neck. Do not get it in your eyes, it will burn.

Peroxy Gel is very effective to stop the pain of shingles.

It can be streaked through hair in summer while sunning to give 'natural' sun bleached highlights. Some hair colors will turn ORANGE so use with care.

WARNING: It is advisable to keep this and all other hydrogen peroxide out of the reach of children. The 35% food grade hydrogen peroxide in its pure state can be harmful if not fatal if accidentally consumed undiluted. Keep it in a cool dark place safely out of reach. One teaspoon of undiluted 35% food grade H₂O₂ swallowed accidentally can plunge a person's blood sugar and cause their blood to become too alkaline. Typically vomiting occurs before damage. If it is accidentally ingested undiluted, immediately give one pint water or fruit juice to dilute the peroxide in the stomach and help raise the blood sugar back up. Follow with a second pint of juice and get the person to a hospital or doctor immediately!

Arthritis, Bursitis, Tendonitis

Adequate body stores of vitamin C have shown promise in reducing primary cause and promoting healing all three conditions.^(1168,1180,1181,1182,1183) It will work over time as you increase and maintain your levels. Vitamin B12, 1-2 mg (1,000-2,000 mcg) taken daily has relieved bursitis in a few weeks.^(1184,1185,1186)

Use Peroxy Gel. It works to reduce pain and inflammation rapidly.

Try Source Naturals Arthred (bovine collagen) or Doctors Best Collagen. Take 1 scoop twice a day for one month plus 2,000 mg of Liposomal C twice a day and if you find relief continue, ongoing. Also works for dogs. Maintenance dose of the Athred may be once a day. Collagen requires you also have enough D and C and protein to make a difference long term. If you prefer collagen from grass-fed beef look here.

<https://www.bulletproofexec.com/bulletproof-upgraded-collagen/>

You may benefit from the addition of 1500 mg glucosamine and 1500 mg chondroitin twice a day plus Solgar Manganese 20 mg and Boron 3 mg. once a day. It may stabilize early arthritis.

Exercise every day. <http://www.mayoclinic.org/diseases-conditions/arthritis/in-depth/arthritis/art-20047971>

Vitamin K Topical Treatment- Bruises, Varicose Veins, Spider Veins

Get Life Extension Super Vitamin K. Use the capsule directly for full strength, small areas or mix the formula below. Always make small amounts as it won't keep fresh long. Check the label and use the # of soft gels to equal about 10 mg.

Table 20 Vitamin K Oil

Life Extension Super K vitamin K soft gels to equal about 10 mg vitamin K squeezed into
1 teaspoon (approximate) warmed coconut oil mix well
Optional additions:
1 5,000 IU vitamin A / 400 IU vitamin D soft gel squeezed
1 400 IU d'alpha vitamin E soft gel squeezed
pinch of ascorbic acid (you may grind the ascorbic acid finer with a mortar before adding)
Mix well and store in closed container in the refrigerator.

All ingredients except the K and coconut are optional. Do not make more than will be used in 3-5 days. The coconut oil will harden in the fridge. Just scrape out the amount you need and let it soften in your hand.

C Spray or Lotion to Prevent and Reverse Sun Damage

Table 21 Skin C Recipes

<p>10% SKIN SPRAY FORMULA-</p> <p>4 ounces distilled water OR 4 oz. Home Health Rose Water 10 grams (about 2.5 level teaspoons) ascorbic acid powder USP (optional: add essential rose oil fragrance)</p> <p>Put in 4 ounce spray bottle Shake and use one or two times a day. Put make-up or other creams or lotions over the top Always re-spray AFTER sunning. Do not keep if solution is not clear. Store in refrigerator to slow oxidation.</p>	<p>10% SERUM FORMULA-</p> <p>Small amber bottle with eyedropper 1 ¼ teaspoons. Home Health Rose Water or distilled water 1 teaspoon anhydrous glycerin USP. ¼ level teaspoon ascorbic acid powder USP</p> <p>Mix first with rose water/distilled water to dissolve and then add glycerin. Put in small amber bottle (use small funnel). Keep in refrigerator. Use a few drops on your fingers to apply. If too concentrated add a drop of water to your fingers and massage in. Toss after 5-7 days. Smooth on your face before bed as a nighttime serum. If you use other facial products make sure this one goes on first.</p>
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MAKE FRESH, DO NOT KEEP LONGER THAN 5-7 DAYS. DO NOT USE if your solution has turned orange, it is oxidized.- Do not apply this spray/serum immediately before sunning. It will oxidize and turn orange on your skin and it will not protect you. The C-spray/serum must be absorbed into the skin to be effective which means daily use at least 3-7 days before you are protected from sun exposure damage.

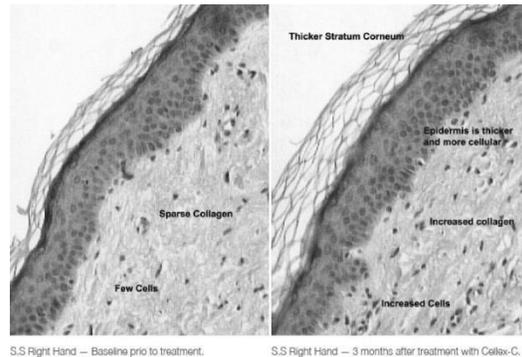
In 1992 research showed that topical application of a 10% solution of ascorbic acid (a common type of vitamin C) prevented and reversed sun damage to skin. Further studies have confirmed this.^(434,521,1173,1175,1177,1179,1187,1188,1189,1190,1191,1192,1193,1194,1195,1196,1197,1198) It may also help rosacea. There is research showing that 10% ascorbic acid will reverse past sun damage and IT HAS NO SIDE EFFECTS. UNLIKE RETIN A, you may continue to expose your skin to moderate sun according to your skin type.

If applied 1 or more times per day, in the morning after your shower and before bed at night, no sunscreen is necessary but do sun sensibly. It won't protect you from 8 hours of tropical sun or general 'over' sunning. This is not a block. The vitamin C is incorporated into the skins cells to prevent ultraviolet damage to DNA. It does not wash off. You will still tan and be able to make vitamin D.

Do not apply immediately before sunning. This solution is applied after sunning to restore levels of C in the skin that are depleted by sun exposure.

Use once a day and after sunning to protect your skin. To reverse prior skin aging use the spray or lotion two times a day and after sunning.

DO NOT MAKE MORE THAN 4 OUNCES AT A TIME unless you are using it for your entire body. LIQUIDS and LOTIONS containing antioxidants DO NOT KEEP WELL. Vitamin C is readily destroyed in any solution so probable keep time is only 4-5 days. The glycerin formula lasts somewhat longer. Products advertised to contain C or other antioxidants have a very short shelf life once they are opened, not more than 4-5 days. To slow oxidation keep in refrigerator.



Picture show changes after several months of daily use of topical vitamin C. Vitamin C rebuilds the important stratum corneum. Studies confirm 82% reduction in wrinkles when used daily. The spray you make yourself will work as well as or better than expensive lotions or creams. The key is freshness. Vitamin C in solution does not keep.

After sunning use unprocessed coconut oil or extra virgin olive oil to restore moisture with or without the C spray. If using oil and vitamin C, spray C on your skin first.

For your body's moisture and skin elasticity extra virgin olive oil is the best skin restorer available.⁽²⁸¹⁾ Make sure the oil is extra virgin and fresh. Don't expose olive oil to direct sunlight. If you aren't ready to smell like a salad, consider pure coconut oil.

Avoid lotions or creams containing omega-6 fatty acids (seed oils like safflower or sunflower or canola). Omega-6 fats are incorporated into your skin making you more susceptible to sun damage and aging. Eating omega-6 promotes sun damage too.^(333,1199,1200)

If your skin has lost collagen and you have increased facial hair consider using Bezewekin OstaDerm 1-1-8. This is a hormonal cream that when used topically in addition to oral intake of Liposomal Vitamin C, may restore skin thickness, reduce facial hair and remove fine lines. It contains natural plant-based estrogens and progesterone. One tube will last many (6-9) months. It is available online. Use sparingly only on problem areas NOT the entire face.

Recent research suggests topical collagen formulas work well to rejuvenate facial skin. ^(1194,1201,1202,1203) Collagen production (joints, skin, bone, hair and nails) depends on vitamin C so adequate C in your diet and supplements as well as the spray will help keep your skin younger from the inside and outside. ^(1178,1179,1204,1205,1206,1207)

Do not be tempted to buy and use premixed creams or lotions containing vitamin C, which oxidizes readily, or those containing ascorbyl palmitate. In studies this form of vitamin C INCREASED skin damage from UV light. ⁽¹²⁰⁸⁾

For extra skin regeneration consider 100% pure hyaluronic acid available on amazon.com Put on a small amount over the C spray or serum.

SUPPLEMENT FORMULA FOR ANIMALS

Includes cats, dogs, rats (and other rodents) and birds. Make sure to give cats and dogs a bi-weekly dose of high quality cod liver oil, 1 teaspoon (cat) to 1 tablespoon (large dog). Birds and reptiles need the addition of a UV-B light to their cages to insure healthy bones and other vitamin D dependent body parts.

1. 2 cups nutritional yeast flakes (or one cup yeast powder). This contains amino acids, potassium, B vitamins and trace minerals.
2. 2-4 level teaspoons of ascorbic acid or sodium ascorbate powder- For collagen formation and coat, skin, eyes and nerve.
3. 4 level tablespoons of Doctors Best Collagen
4. The contents of ten 500 mg. capsules (5,000 mg) of taurine- For the heart, eyes, nervous system and digestion, especially important for cats.
5. The contents of ten 500 mg. capsules (5,000 mg) of tyrosine. For coat and nerve. Especially important for cats.
6. The contents of four 400 IU. dry E capsules- Antioxidant, preservative and anti-aging nutrient

Options you can add--

- 1/4 cup lecithin granules- For the nervous system, skin and coat.
- 1/4 cup Schiff or Solgar Desiccated Liver Powder- It contains vitamins, minerals and trace minerals and animals like the taste.
- 6 level teaspoons Schiff or Solgar bone meal- For bone, joint and beak, a must if you don't regularly give raw meaty bones like turkey necks and chicken wings.
- Boron to equal 0.5 mg per 10 pounds per daily dose (calculate for your animal/s) to relieve arthritis pain
- 1/2 level teaspoon dulse (not kelp, too high in iodine)- for iodine and other trace elements, don't add much.

Directions: Sprinkle powder over wet or dry food daily to lightly cover the surface of the food. Approximate serving size is one rounded teaspoon of the mix per each 20 pounds. If using powdered instead of flake yeast use 1/2 teaspoon per 20 pounds. Your animals may not like it at first. Persist.

For Dogs- Degenerative bone or joint or post injury: 1,000 mg sodium ascorbate or ascorbic acid and 1 scoop Source Naturals Arthred daily. Add to food. Double the Vitamin C and collagen II if your dog weighs more than 80 lbs.; give 1/2 dose if you dog weighs less than 15 lbs.

Add fish oil daily- about 1 capsule of omega-3 fatty acids per 20 pounds of body weight. For cats one a day will do, or once a week give some tuna and squeeze the week's dose of omega-3 on the tuna. Some pets will eat the soft gels, no squeezing necessary. Some animals prefer FRESH ground flax seed. Buy seeds and grind before use as pre-ground flax rapidly becomes rancid. Cod liver oil may be used but SMALL amounts. Do not overdose your pet with A and D found in cod liver oil.

Avoid pet foods containing omega-3 or omega-6 fats. Processing and storage will have contributed to rancidity. Don't feed your animals rancid fats which contribute to immune disorders and cancer. If they need essential fatty acids use fresh ground flax seeds, olive oil, cod liver oil or fish oil. ALWAYS refrigerate cod liver oil or fish oil including soft gels.

You can purchase all of the ingredients at any health food store or iherb.com. Now Foods packages the yeast flakes, lecithin granules, and ascorbic acid (C) or sodium ascorbate powder. Everything in the mix must be dry. Store your mix in a closed container that is not exposed to moisture, heat or sunlight.

Cod liver oil is a good source of A, omega-3 and D. Cats and dogs do not produce their own D and get D from the organs and flesh of the animals they consume. Keep the cod liver oil in the refrigerator and give from 1 teaspoon to 1 tablespoon 3 times a week. Dose according to the size of the animal. If you give beef liver regularly it is best to avoid cod liver oil as you don't want to give your pet too much vitamin A. You'll need another source of vitamin D3,

Once a week give all cats and dogs a small serving of mixed organ meats such as beef heart, tripe, kidney or liver. You may serve it raw or cooked depending on your animal's bowel and personal preference. Liver typically must be cooked or diarrhea may occur. If you do not regularly serve meat or fish (the BARF or PREY diet) give 1-4 or more raw or lightly cooked egg yolks per week.

Pet Dysbiosis (Gut bugs including Giardia)

Treatment for common gut bugs in dogs and cats:

- Nutricology/Allergy Research Tricycline (also called Tribiotic) (1) per each 30 pounds of body weight, once a day for 3-7 days. One capsule for 2-30 lbs, two capsules 30-60 lbs and 3 capsules 60 lbs and above (even if your dog is HUGE). Give directly, without food.

- Probiotic such as VSL#3, Jarro-dophilus Ultra or Nature's Way Primadophilus Optima PLUS Swanson Vitamins SBO (soil based organisms) on food. 1-3 capsules (based on size of animal) Mixed with food once a day for each day of treatment plus 3 days.

If the problem persists see your vet. (It won't, this really does work)

Note: Some bugs will respond better to Planetary Formulas Full Spectrum Olive Leaf Extract. Dose is (1) for each 50 pounds of body weight, once a day.

SANITATION OF FOOD AND FOOD AREAS

Use wood cutting boards. Wood boards and surfaces naturally destroy bacteria. Season your board regularly with cutting board oil (mineral oil plus a little lemon juice).

Spray cutting surfaces, and foods such as lettuce, meat, fruits, anything you want to disinfect, with a straight 3% hydrogen peroxide. Let it sit for 1-3 minutes and rinse (or not, you do not have to rinse this off).

Buy 3% hydrogen peroxide at your local drug or variety store. Keep in the original bottle but add a spray top (safer, you won't forget what it is). Hydrogen peroxide is the safest and most nontoxic disinfectant you can use. It leaves no toxic residue in the environment.

For serious contamination including mold issues or c. difficile or other environmental pathogens use Accelerated Hydrogen Peroxide. This product kills pathogens in under 5 minutes instead of 10-15 minutes using regular 3% hydrogen peroxide. It is available from <http://amazon.com> as Anvac Accel TB.

Per the CDC- Hydrogen peroxide is active against a wide range of microorganisms, including bacteria, yeasts, fungi, viruses, and spores. A 0.5% accelerated hydrogen peroxide demonstrated bactericidal and virucidal activity in 1 minute and mycobactericidal and fungicidal activity in 5 minutes ...Other studies demonstrated the antiviral activity of hydrogen peroxide against rhinovirus. The time required for inactivating three serotypes of rhinovirus using a 3% hydrogen peroxide solution was 6–8 minutes

Do not use anti-bacterial wipes, soaps or cleaners. These cleaners contribute to the growing problem of anti-biotic resistant strains of bacteria.

Sterilize sponges daily in your dishwasher or by soaking in hydrogen peroxide for 15 minutes.

Cleaning fruits and vegetables

A three-year study by Dr. Walter J. Krol from the Department of Analytical Chemistry at the Connecticut Agricultural Experiment Station showed that rinsing under tap water significantly reduced residues of nine of the twelve pesticides examined across fourteen commodities. Four fruit and vegetable wash products were found to be no more effective at removing eight of nine pesticide residues from produce than either a 1% solution of dishwashing liquid or rinsing under tap water alone for three commodities studied.

CHAPTER 15 SPECIAL CONSIDERATIONS

Healthy Brain and Aging

A good diet, exercise and several specialty nutrients may be key to keeping brains youthful.

1. Test your fasting insulin (insulin not glucose). If it is above 5 immediately begin the 'Time Restricted Feeding' protocol. Retest in 3 months. Hyperinsulinemia and insulin resistance precede all forms of dementia including Alzheimer's as well as many other degenerative diseases..
2. Make sure every cell, including your brain cells, are loaded with ascorbic acid. Take liposomal vitamin C 3,000 mg twice a day for a minimum of 2 months and then 1,000-4,000 mg of liposomal or regular C twice a day ongoing..
(515,1209,1210,1211,1212,1213,1214,1215,1216,1217,1218)
3. Make sure you get enough zinc (use the Zinc Status test) and 200 mcg selenomethionine or equivalent every day ongoing
(1219,1220,1221,1222,1223,1224,1225,1226,1227,1228,1229,1230,1231,1232,1233,1234,1235,1236,1237,1238)
4. Eat a minimum of 1 gram of quality protein every day for each two pounds of ideal or actual body weight. As we age we need MORE protein, not less.⁽¹⁸⁵⁾
5. Take your 3,000 mg DHA/EPA every day ongoing
(1239,1240,1241,1242,1243,1244,1245,1246,1247,1248,1249,1250,1251,1252)
6. If you are over 60 or have had a serious head injury or stroke, consider taking vinpocetine 20 mg in the morning every day.
(1253,1254,1255,1256,1257,1258,1259,1260,1261,1262,1263)
7. If you are over 60 consider nightly melatonin 3-9 mg
(1089,1264,1265,1266,1267,1268,1269,1270,1271,1272,1273) See section on melatonin in this workbook.
8. if your brain seems a bit off, take PQQ (pyrroloquinoline quinone) 10-20 mg daily to begin to regenerate your mitochondria in 72 hours, minimum two to three months for healing
(1274,1275,1276,1277,1278)
9. Exercise is key to healthy aging, including your brain. Exercise a minimum of 45 minutes every day, try for 90 minutes. It's ok to exercise 5-15 minutes at a time.
(1279,1280,1281,1282,1283,1284,1285,1286,1287,1288,1289,1290,1291,1292,1293,1294,1295,1296,1297,1298)

Hidden Enemies- Mycoplasmas, Chlamydia and the Dreaded Viruses

Heart disease, autoimmune disorders including multiple sclerosis, thyroiditis, rheumatoid arthritis, sarcoidosis and myasthenia gravis, Gulf War Syndrome, Post-Polio Syndrome, Chronic Fatigue, Epstein Barre, Fibromyalgia and even cancer may be caused or complicated by chronic mutating infections.

All of the common viruses, Chlamydia, common pathogenic gut bacteria like helicobacter, and the cell wall deficient mycoplasmas may cause or contribute to chronic inflammation associated with aging and degenerative diseases and autoimmune diseases.

Recently many of these conditions have been or are being treated with long-term antibiotics with great success. This includes sarcoidosis, rheumatoid arthritis, multiple sclerosis and even hypertension, associated with a gut infection. (1299,1300,1301,1302,1303,1304,1305,1306,1306)

If you have a history of an acute infection that seemed to be followed by very slow recovery and you never 'felt quite like yourself again', consider a chronic infectious agent. First complete the Immune Restoration Protocol. If this does not resolve your 'dis-ease' testing is available and includes serum, urine and stool testing. Most insurance companies will not pay for this testing. Costs may be as high as \$500-1,000.

These conditions may also respond to higher doses of vitamin C, that is Liposomal Vitamin C, 2,000 mg up to 6 or 8 times daily. (12,000-16,000 mg Liposomal C) For some using Planetary Herbals Full Spectrum Olive Leaf Extract (2) three times a day, alone or with the Liposomal C for 1-3 months PLUS the Immune Restoration protocol dramatically resolves long standing illness.

Olive Leaf Extract, hydroxytyrosol, oleuropein and its derivatives to be exact, kill many virus, mycoplasmas, many pathogenic bacteria and some spirochetes. Dose is critical. Best results may need support from your healthcare practitioner. Always remember to complete the Immune Restoration Protocol no matter what your other treatment choices.

For a few, use of antibiotics may be necessary for full recovery. Always use Liposomal Vitamin C in any program with or without antibiotics.

Fibromyalgia/Chronic Fatigue

First make sure you have PERFECT thyroid function, TSH between 0.4 and 2.0 and normal Free T4 and Free T3. If not get treatment, preferably with desiccated thyroid not thyroxine.

Consider the issue discussed immediately preceding this. Seek diagnosis and treatment if the profile seems to fit you. Make sure you have optimum gut function with no gut pathogens. Read the protein, potassium, calcium, magnesium and vitamin D sections of this workbook first. Make sure you have adequate nutrition as a base and have completed 30 days of the Immune Restoration protocol. Do not avoid salt. Both conditions are

associated with adrenal exhaustion and sodium, magnesium, B vitamins, vitamins C and D, and potassium are critical to adrenal function.

Check fasting insulin. Chronic fatigue is strongly associated with Metabolic Syndrome. (1307,1308,1309,1310,1311,1312) Lowering fasting insulin with diet and exercise makes a difference. In fibromyalgia lowering insulin and increasing melatonin improve outcome. (1060,1313,1314)

A common treatment for this condition in the past was intravenous vitamin C. Now that we have Liposomal C the protocol is much easier. Again, you may need doses of liposomal C that are higher than listed in the Immune Protocol.

Methylcobalamin may help with this condition. The dose is 1,000 mcg. (1 mg.) daily and should be combined with excellent nutrition, a Coenzyme B-complex such as Swanson Vitamins Activated B-Complex High Bioavailability and extra folic acid as methylfolate, about 400-800 mcg.

Scand J Rheumatol. 1997;26(4):301-7. Increased concentrations of homocysteine in the cerebrospinal fluid in patients with fibromyalgia and chronic fatigue syndrome. Regland B, andersson M, Abrahamsson L, Bagby J, Dyrehag LE, Gottfries CG. Institute of Clinical Neuroscience, Goteborg University, Sweden.

Twelve outpatients, all women, who fulfilled the criteria for both fibromyalgia and chronic fatigue syndrome were rated on 15 items of the Comprehensive Psychopathological Rating Scale (CPRS-15). These items were chosen to constitute a proper neurasthenic subscale. Blood laboratory levels were generally normal. The most obvious finding was that, in all the patients, the homocysteine (HCY) levels were increased in the cerebrospinal fluid (CSF). There was a significant positive correlation between CSF-HCY levels and fatigability, and the levels of CSF-B12 correlated significantly with the item of fatigability and with CPRS-15. The correlations between vitamin B12 and clinical variables of the CPRS-scale in this study indicate that low CSF-B12 values are of clinical importance. Vitamin B12 deficiency causes a deficient re-methylation of HCY and is therefore probably contributing to the increased homocysteine levels found in our patient group. We conclude that increased homocysteine levels in the central nervous system characterize patients fulfilling the criteria for both fibromyalgia and chronic fatigue syndrome.

Chronic fatigue may also be associated with dysbiosis. (120,1315) Do complete the Immune Restoration Protocol.

Take a look at the latest research concerning optimal vitamin D. Test to determine your current level of D and consider taking, with the monitoring of your healthcare practitioner, sufficient supplementation to bring your test level to optimum.

Maintenance dose is determined by retesting. After the initial loading dose a minimum daily intake to maintain optimal D should be continued indefinitely. Monitor serum 25(OH)D for summer and winter values. Retest if you move to a different latitude or altitude and when the seasons change.

Sun can contribute significantly or replace the daily dose if you live in lower than 30 degree latitudes. Blacks need 6 times the sun exposure to maintain normal blood levels of D. Above 30 degrees (San Francisco and the bay area are 38°) or darker skins will need some level of supplementation.

Summer sun works only if you spend adequate time in the sun with large areas of skin exposed without sunscreen. Reread the sections on D and calcium and sunlight found throughout this workbook and, if needed, request the D and Sunlight research packet and Physician Protocol.

Winter sun is not sufficient to restore or maintain optimum levels. To achieve optimal D status a dose of as much as 4,000 IU daily may be required for a brief period of time. Testing is essential to efficacy and safety.

*Arch Intern Med 2000 Apr 24;160(8):1199-203 **Severe myopathy associated with vitamin D deficiency in western New York.** Prabhala A, Garg R, Dandona P Division of Endocrinology, Diabetes and Metabolism, State University of New York at Buffalo, 14209, USA.*

Five cases of severe myopathy associated with vitamin D deficiency are described. Each patient was confined to a wheelchair because of weakness and immobility. Two were elderly, 1 was a 37-year-old African American with type 1 diabetes mellitus, 1 was being treated for carcinoid syndrome, and 1 was severely malnourished due to poor oral intake. In each, weakness had previously been attributed to other causes, including old age, concomitant diabetic neuropathy, or general debility. Correct diagnosis was made initially by a high index of suspicion, following the demonstration of clinical proximal myopathy; confirmation was made by the demonstration of low 25-hydroxyvitamin D and elevated parathyroid hormone concentrations. **Treatment with vitamin D caused a resolution of body aches and pains and a restoration of normal muscle strength in 4 to 6 weeks.** Four patients became fully mobile and had normal 25-hydroxyvitamin D concentrations, and the fifth also became mobile. In the 4 fully recovered cases, parathyroid hormone levels on follow-up were lower but still elevated. This finding suggests a degree of autonomy of parathyroid secretion known to occur in cases of long-standing vitamin D deficiency. Myopathy, due to chronic vitamin D deficiency, probably contributes to immobility and ill health in a significant number of patients in the northern United States. An awareness of this condition may significantly improve mobility and quality of life in patient populations vulnerable to vitamin D deficiency.

Polycystic Ovarian Syndrome- PCOS

If you have PCOS you suffer from hyperinsulinemia. There may be a predisposition in your 'genes'. Reducing fasting insulin will correct the condition within several months. Please refer to the section on Time Restricted Feeding page 163 for the diet plan you need. In addition you will need calcium, magnesium, vitamin A and vitamin D. Call for personal support.

Vitamin D and Calcium Dysregulation In The Polycystic Ovarian Syndrome. Thys-Jacobs S ; Donovan D ; Papadopoulos A ; Sarrel P ; Bilezikian JP Department of Medicine, St. Lukes-Roosevelt Hospital Center, Columbia University, College of Physicians & Surgeons, New York, NY 10019, USA. Steroids, 64(6):430-5 1999 Jun

Over the past 30 years, numerous studies in invertebrates and vertebrates have established a role of calcium in oocyte maturation as well as in the resumption and progression of follicular development. Polycystic ovarian syndrome (PCO) is characterized by hyperandrogenic chronic anovulation, theca cell hyperplasia, and arrested follicular development. The aim of this observational study was to determine whether vitamin D and calcium dysregulation contribute to the development of follicular arrest in women with PCO, resulting in reproductive and menstrual dysfunction. Thirteen premenopausal women (mean age 31 +/- 7.9 years) with documented chronic

anovulation and hyperandrogenism were evaluated. Four women were amenorrheic and nine had a history of oligomenorrhea, two of whom had dysfunctional bleeding. Nine had abnormal pelvic sonograms with multiple ovarian follicular cysts. All were hirsute, two had alopecia, and five had acanthosis nigricans. The mean 25 hydroxyvitamin D was 11.2 +/- 6.9 ng/ml [normal (nl): 9-52], and the mean 1,25 dihydroxyvitamin D was 45.8 +/- 18 pg/ml. with one woman with a 1,25 dihydroxyvitamin D <5 pg/ml (nl: 15-60). The mean intact parathyroid hormone level was 47 +/- 19 pg/ml (nl: 10-65), with five women with abnormally elevated parathyroid hormone levels. All were normocalcemic (9.3 +/- 0.4 mg/dl). Vitamin D repletion with calcium therapy resulted in normalized menstrual cycles within 2 months for seven women, with two experiencing resolution of their dysfunctional bleeding. Two became pregnant, and the other four patients maintained normal menstrual cycles. These data suggest that abnormalities in calcium homeostasis may be responsible, in part, for the arrested follicular development in women with PCO and may contribute to the pathogenesis of PCO.

Pregnancy- Creating New Life

You are not eating for two but eating to provide all the nutrients to build a brand new life. You need more protein, 4 or more palms full daily and great amounts of potassium containing fresh foods, meaning soups and salads, daily fruits and veggies.

Make sure to use a food plan that keeps fasting insulin low. Check your fasting insulin as soon as you know you are pregnant. If needed (fasting insulin 9 uU/ml or greater) switch to Protein Power or Paleo plus daily exercise to rapidly reduce fasting insulin. Elevated fasting insulin can precede 'gestational diabetes', elevate blood pressure and contribute to other health issues during pregnancy and delivery. **KEEP YOUR FASTING INSULIN LOW.**

Eat only the best fats, unprocessed coconut oil, butter, and dressings made with extra virgin olive oil.

If you are pregnant or nursing fish is **not** a good source of protein or omega-3 due to the presence of mercury. You will need to supplement with fish oil or cod liver oil. They are not the same. One contains just the omega-3 fats, the other contains vitamins A and D and omega-3.

Fish oil does not contain mercury as mercury is water soluble not fat soluble. Mercury is a problem in high or low fat fish, because it is found in the muscle (flesh).

Other contaminants are found in fish fat (but not fish oil capsules) including pesticides. High quality fish oils are molecularly distilled and free of major contaminants. This includes those sold at Trader Joes and Costco.

Your fish oil intake should include a total omega-3 DHA/EPA intake of not less than 3,000 mg daily, more is better. Fish oil soft gels are not 100% omega-3 so you have to read the label carefully. The omega-3 content is the combined total of DHA and EPA. Most contain 300-500 mg total per each no matter the size of the soft gel.

See below for using cod liver oil as your source of omega-3.

If indigestion occurs (nausea) first check to make sure you are fully hydrated. Also make sure to get plenty of the B vitamins. Source Naturals makes a sublingual CoEnzyme B-

Complex you don't even have to swallow and it works rapidly, helping with cravings, nausea and mood.

Also consider more vinegar on foods with your meals or drinking lemon juice with your meal to stimulate/increase hydrochloric acid. Don't avoid salt. If you experience bloating check in. There are reasons and answers.

Digestive enzymes such as Twinlab Super Enzymes or Chewable Papaya Enzymes or Jarro-dophilus Original Formula taken with the meal may rapidly improve digestion and help you avoid nausea.

Pregnancy demands a minimum of 800 mcg folate daily to protect against birth defects. Okra, spinach, orange juice, broccoli, beets and asparagus contain 100-300 mcg per serving. You may need more in a supplement if you don't regularly consume these foods. Look for a prenatal that contains methylfolate if you carry the MTHFR gene.

B-12 goes with folate, about 400-800 mcg of hydroxycobalamin or a combination B-12. Read the label carefully to make sure you got the right one.

Vitamin K (a fat soluble vitamin not potassium) is important for you and your baby, about 1 mg daily. It is found in dark greens and fermented foods like fermented cabbage, natto, natural yogurts and buttermilk but won't absorb without fat, so add butter to your greens or virgin olive oil on your dark green salad. It is likely a separate supplement containing a minimum of 1,000 mcg (1 mg) is necessary to protect both mom and babe. See information on ordering vitamin K in the Fat Soluble Vitamins section.

Minerals are critical for brain and bone. Iron, the Ferrochel by Albion is safe and not constipating. You will likely need to supplement. Solgar Gentle Iron one a day should suffice.

Recently many pregnant women in the US have been found to be iodine deficient resulting in lower cognitive function in their offspring.^(1316,1317,1318,1319,1320) The safest way to ensure iodine sufficiency is Life Extension Sea Iodine one per day.

Calcium should range from 800-1,000 mg daily with all other minerals and trace minerals. This is in addition to any dairy you might consume. Consider the long term health of your baby's bones and teeth.

Vitamin A is important. Beef liver once a week provides a safe and adequate source of vitamin A, and provides additional iron, vitamin K, folate, B-12 and other essential nutrients. Beta-carotene is NOT vitamin A.

Both too much A and too little A cause birth abnormalities and too little A reduces progesterone and can lead to spontaneous abortion. A good average daily amount is between 5,000-10,000 IU of vitamin A, retinol (not beta-carotene). Research has shown these levels to be safe and adequate. Some symptoms of too little A include abnormal menstrual cycles, overly dry or oily skin, poor night vision, permanent 'goosebumps' on the back of upper arms, or frequent infections.

If you don't or won't eat liver you might consider cod liver oil during pregnancy for omega-3 fats, vitamin A and vitamin D. Carlson Norwegian Cod Liver Oil is well tolerated, no fishy smell or odor. The dose is 1 tablespoon once a day and no, it does not come in capsules. If you are sunning in summer cod liver oil is not a good choice as you would be more than doubling your D.

Vitamin D is critical for you and your baby and should be tested regularly. Moms with adequate D have breast milk with adequate D. A major concern currently is a reappearance of rickets in breast fed babies.^(1321,1322,1323,1324,1325) Partly this is due to lack of sun and partly to the low levels of D in most pregnant US females. Don't rely on guessing. Test.

A good prenatal contains most of the things you need (but not all). Acceptable brands include Country Life, Natrol, or Twinlab. There are others. Look for one that is easy to take and that you digest well. Some need tablets, others capsules, others may even need a powdered or liquid supplement.

At some time during your pregnancy make sure to complete a minimum of two weeks of the Immune Restoration. This will make sure both you and the babe have optimal microbiota during and after birth.^(800,801,1326,1327,1328,1329,1330,1331,1332,1333,1334,1335,1336,1337,1338,1339)

While it is an older out of print book Adelle Davis' Let's Have Healthy Children is still one of the best guides to healthy babies. Find a copy at your used book store or online at <http://bookfinders.com> Check daily totals of all nutrients and supplement with the missing elements. Happy Baby.

New Life, Infants and Children, What to Feed

First, it starts with mom. Food counts, real foods, lots of veggies and fresh fruits and protein plus more protein. See section above.

And then the babe. Nurse as long as possible. Your baby will be smarter. Whatever the hassle you will not regret the benefits. Breastfeeding increases intelligence, improves bonding between mother and child, and is associated with lower body weight as your child grows up. Breastfeeding increases brain matter, prevents many allergies, and improves the balance of gut bacteria.^(1340,1341,1342,1343,1344,1345,1346,1347,1348,1349,1350,1351)

For a healthy babe there must be a healthy mom. Feed your babe the same foods you eat. Use a grinder or food processor. Introduce new foods slowly but over time include eggs and RED meat and poultry. Cooked veggies are fruits are a good beginning. Oatmeal is a whole food. Bread is not necessary. Small bits of organ meats may be mixed in, liver, kidney, beef heart and even tripe. Get and use Sally Fallon's Nourishing Traditions.

Infants and children benefit from simple supplementation. Call if you need help. Food is first. They should be allowed to eat when they are hungry BUT only real, whole, fresh foods. There are NO advantages in feeding snacks, sodas, desserts, candies. They simply set you child up for a lifetime of illness. Children raised on processed foods, junk foods, low protein fare, few fresh fruits and veggies never know what it is to feel well. They have chronic infections, allergies, cavities, difficulty in school, sleep disorders and more.

Healthy children are a delight, their whole lives. They do know the difference between feeling good and not so good and will tend over a lifetime to make excellent food choices.

Eat real. Feed real.

Feldenkrais for Healing Bodily Injury and Chronic Pain

When we are injured pain suggests we should not use the injured part and another process, armoring, alters the way our entire body functions. This is not a process of nutrition and what you eat or do not eat will not heal the injury. Having adequate nutrition will enhance the healing process and reduce or prevent scar tissue. Taking bromelain when injured can reduce damage and speed healing but some injuries become chronic.

If you have chronic pain from any cause including an injury to bone, muscle or joint, I strongly recommend Feldenkrais. My favorite resource is Anat Baniel. You'll find her at <http://anatbanielmethod.com> or by calling 1-800-386-1441. If you are unable to see her locally in San Rafael, CA her office will refer you to an experienced practitioner in your area.

You may buy Feldenkrais MP3 exercises on several online websites. Feldenkrais practitioners gain skill with experience, so do work with someone who has been practicing for 10 or more years.

Anat Baniel Method- Feldenkrais for ADD, ADHD, Learning Disorders, Cerebral Palsy, Post-surgical Injury Recovery and More

There are amazing stories, true stories, about the effectiveness of Feldenkrais and especially Anat's version of the work, dramatically altering brain and body function in infants and children. I have seen the results and highly recommend at least an evaluation if you want the very best chance for yourself or your child.

When we experience limited movement our brain patterns change. These changes are actually viewable with a PET scan. The work of Moshe Feldenkrais, continued after his passing by Anat and others, has proven successful in ending chronic pain and in restoring freedom of movement at any age. Most exciting to me is the increase in well-being and mental function that accompanies the increase in strength and flexibility when working with a practitioner, attending an Awareness Through Movement class, or doing the simple exercises in your home.

For serious conditions do consider hands on help from Anat or another qualified Feldenkrais practitioner. If you are just interested in anti-aging flexibility consider any of the audio or video lessons or Feldenkrais books.

I rarely refer because much of what we need to do to get and remain healthy must be done by us. But when injury occurs we need help and Feldenkrais is the only method of body work I have consistently found to actually heal injury. It is something you learn to do, not something that is done to you.

THE RESEARCH REFERENCES

1. Urinary potassium excretion and sodium sensitivity in blacks Aviv, A., Hollenberg, N. K., and Weder, A. 2004 Hypertension
2. [Monogenic hypertension] Bahr, V., Oelkers, W., and Diederich, S. 4-15-2003 Med.Klin.(Munich)
3. Identification and chromosomal localization of ecogenetic components of electrolyte excretion Dumas, P., Kren, V., Krenova, D., Pravenec, M., Hamet, P., and Tremblay, J. 2002 J.Hypertens.
4. Altered renal handling of sodium in human hypertension: short review of the evidence Strazzullo, P., Galletti, F., and Barba, G. 2003 Hypertension
5. Probiotics for preventive health Minocha, A. 2009 Nutr.Clin.Pract.
6. Novel anti-microbial therapies for dental plaque-related diseases Allaker, R. P. and Douglas, C. W. 2009 Int.J.Antimicrob.Agents
7. Probiotics and oral healthcare Teughels, W., Van, Essche M., Sliepen, I., and Quirynen, M. 2008 Periodontol.2000.
8. Probiotics and oral health effects in children Twetman, S. and Steckslen-Blicks, C. 2008 Int.J.Paediatr.Dent.
9. Dental caries: from infection to prevention Islam, B., Khan, S. N., and Khan, A. U. 2007 Med.Sci.Monit.
10. Probiotics: contributions to oral health Meurman, J. H. and Stamatova, I. 2007 Oral Dis.
11. Molecular and biochemical characterizations of human oral lactobacilli as putative probiotic candidates Strahinic, I., Busarcevic, M., Pavlica, D., Milasin, J., Golic, N., and Topisirovic, L. 2007 Oral Microbiol.Immunol.
12. A probiotic approach to caries management Anderson, M. H. and Shi, W. 2006 Pediatr.Dent.
13. Bacteriotherapy and probiotics' role on oral health Caglar, E., Kargul, B., and Tanboga, I. 2005 Oral Dis.
14. Effect of probiotic supplementation on immunoglobulins, isoagglutinins and antibody response in children of low socio-economic status Perez, N., Iannicelli, J. C., Girard-Bosch, C., Gonzalez, S., Varea, A., Disalvo, L., Apezteguia, M., Pernas, J., Vicentin, D., and Cravero, R. 10-17-2009 Eur.J.Nutr.
15. Pro- and synbiotics to control inflammation and infection in patients with multiple injuries Giamarellos-Bourboulis, E. J., Bengmark, S., Kanellakopoulou, K., and Kotzampassi, K. 2009 J.Trauma
16. Lactoferrin supplementation to prevent nosocomial infections in preterm infants Kaufman, D. A. 10-7-2009 JAMA
17. Probiotic Lactobacillus rhamnosus GR-1 and Lactobacillus reuteri RC-14 May Help Downregulate TNF-Alpha, IL-6, IL-8, IL-10 and IL-12 (p70) in the Neurogenic Bladder of Spinal Cord Injured Patient with Urinary Tract Infections: A Two-Case Study Anukam, K. C., Hayes, K., Summers, K., and Reid, G. 2009 Adv.Urol.
18. Targeting the vaginal microbiota with probiotics as a means to counteract infections Reid, G., Dols, J., and Miller, W. 2009 Curr.Opin.Clin.Nutr.Metab Care
19. Antagonistic activity of spent culture supernatants of lactic acid bacteria against Helicobacter pylori growth and infection in human gastric epithelial AGS cells Lin, W. H., Lin, C. K., Sheu, S. J., Hwang, C. F., Ye, W. T., Hwang, W. Z., and Tsen, H. Y. 2009 J.Food Sci.
20. Probiotic preparation VSL#3 alters the distribution and phenotypes of dendritic cells within the intestinal mucosa in C57BL/10J mice Wang, X., O'Gorman, M. R., Bu, H. F., Koti, V., Zuo, X. L., and Tan, X. D. 2009 J.Nutr.
21. Protective efficacy of probiotic alone or in conjunction with a prebiotic in Salmonella-induced liver damage Rishi, P., Mavi, S. K., Bharrhan, S., Shukla, G., and Tewari, R. 2009 FEMS Microbiol.Ecol.
22. [Choice of probiotic for rational therapy of infection caused by Klebsiella in children] Gonchar, N. V., Berezina, L. V., Tikhomirova, O. V., Dobrolezh, O. V., Verbitskaia, N. B., Petrov, L. N., and Bondarenko, V. M. 2009 Zh.Mikrobiol.Epidemiol.Immunobiol.
23. Probiotic yogurt in the elderly with intestinal bacterial overgrowth: endotoxaemia and innate immune functions Schiffrin, E. J., Parlesak, A., Bode, C., Bode, J. C., van't Hof, M. A., Grathwohl, D., and Guigoz, Y. 2009 Br.J.Nutr.
24. Probiotic acidified formula in an animal model reduces pulmonary and gastric bacterial load Boneti, C., Habib, C. M., Keller, J. E., Diaz, J. A., Kokoska, E. R., Jackson, R. J., and Smith, S. D. 2009 J.Pediatr.Surg.
25. Obesity - extending the hygiene hypothesis Isolauri, E., Kalliomaki, M., Rautava, S., Salminen, S., and Laitinen, K. 2009 Nestle.Nutr.Workshop Ser.Pediatr.Program.
26. The microbiome and obesity: is obesity linked to our gut flora? Tsai, F. and Coyle, W. J. 2009 Curr.Gastroenterol.Rep.
27. The gut microbiota ecology: a new opportunity for the treatment of metabolic diseases? Burcelin, R., Luche, E., Serino, M., and Amar, J. 2009 Front Biosci.
28. [Gut microbiota, responsible for our body weight?] Pataky, Z., Bobbioni-Harsch, E., Hadengue, A., Carpentier, A., and Golay, A. 3-25-2009 Rev.Med.Suisse
29. The role of the gut microbiota in energy metabolism and metabolic disease Cani, P. D. and Delzenne, N. M. 2009 Curr.Pharm.Des
30. Microecology, obesity, and probiotics Tennyson, C. A. and Friedman, G. 2008 Curr.Opin.Endocrinol.Diabetes Obes.
31. Natural products for chemopreventive and adjunctive therapy in oncologic disease Dennis, T., Fanous, M., and Mousa, S. 2009 Nutr.Cancer
32. Probiotic-induced changes in the intestinal epithelium: implications in gastrointestinal disease Ramakrishna, B. S. 2009 Trop.Gastroenterol.
33. Gastrointestinal microflora, food components and colon cancer prevention Davis, C. D. and Milner, J. A. 2009 J.Nutr.Biochem.
34. A human, double-blind, placebo-controlled, crossover trial of prebiotic, probiotic, and synbiotic supplementation: effects on luminal, inflammatory, epigenetic, and epithelial biomarkers of colorectal cancer Worthley, D. L., Le Leu, R. K., Whitehall, V. L., Conlon, M., Christophersen, C., Belobrajdic, D., Mallitt, K. A., Hu, Y., Irahara, N., Ogino, S., Leggett, B. A., and Young, G. P. 2009 Am.J.Clin.Nutr.
35. Probiotics: delineation of prophylactic and therapeutic benefits Kaur, I. P., Kuhad, A., Garg, A., and Chopra, K. 2009 J.Med.Food

36. Roles of Probiotics and Prebiotics in Colon Cancer Prevention: Postulated Mechanisms and In-vivo Evidence Liang, M. T. 2008 *Int.J.Mol.Sci.*
37. Probiotics regulate the expression of COX-2 in intestinal epithelial cells Otte, J. M., Mahjirian-Namari, R., Brand, S., Werner, I., Schmidt, W. E., and Schmitz, F. 2009 *Nutr.Cancer*
38. Probiotic potential of lactic acid bacteria isolated from fermented dairy milks on antiproliferation of colon cancer cells Thirabunyanon, M., Boonprasom, P., and Niamsup, P. 2009 *Biotechnol.Lett.*
39. Recent advances and remaining gaps in our knowledge of associations between gut microbiota and human health Mai, V. and Draganov, P. V. 1-7-2009 *World J.Gastroenterol.*
40. The pathogenic role of intestinal flora in IBD and colon cancer Rescigno, M. 2008 *Curr.Drug Targets.*
41. Oral administration of live Bifidobacterium strains isolated from healthy centenarians enhanced immune function in BALB/c mice Yang, H. Y., Liu, S. L., Ibrahim, S. A., Zhao, L., Jiang, J. L., Sun, W. F., and Ren, F. Z. 2009 *Nutr.Res.*
42. Boosting the immune system Short, R. 2006 *Nurs.Older.People.*
43. Impact of nutrition on ageing and disease Bengmark, S. 2006 *Curr.Opin.Clin.Nutr.Metab Care*
44. The Probiotic Preparation, VSL#3 Induces Remission in Patients With Mild-to-Moderately Active Ulcerative Colitis Sood, A., Midha, V., Makharia, G. K., Ahuja, V., Singal, D., Goswami, P., and Tandon, R. K. 7-22-2009 *Clin.Gastroenterol.Hepatol.*
45. Effects of live and inactivated VSL#3 probiotic preparations in the modulation of in vitro and in vivo allergen-induced Th2 responses Mastrangeli, G., Corinti, S., Butteroni, C., Afferni, C., Bonura, A., Boirivant, M., Colombo, P., and Di Felice G. 2009 *Int.Arch.Allergy Immunol.*
46. [Update on the treatment of ulcerative colitis] Nos, Mateu P. 2008 *Gastroenterol.Hepatol.*
47. Probiotic mixture VSL#3 protects the epithelial barrier by maintaining tight junction protein expression and preventing apoptosis in a murine model of colitis Mennigen, R., Nolte, K., Rijcken, E., Utech, M., Loeffler, B., Senninger, N., and Bruewer, M. 2009 *Am.J.Physiol Gastrointest.Liver Physiol*
48. Effect of a probiotic preparation (VSL#3) on induction and maintenance of remission in children with ulcerative colitis Miele, E., Pascarella, F., Giannetti, E., Quaglietta, L., Baldassano, R. N., and Staiano, A. 2009 *Am.J.Gastroenterol.*
49. Gastric juice: a barrier against infectious diseases Martinsen, T. C., Bergh, K., and Waldum, H. L. 2005 *Basic Clin.Pharmacol.Toxicol.*
50. [Gastric function in patients with skin diseases. Analysis of electrogastrographical findings in 1282 dermatologic patients] Zaun, H. 1-7-1972 *Munch.Med.Wochenschr.*
51. Gastrointestinal findings in autoimmune thyroiditis and non-goitrous juvenile hypothyroidism in children Kuitunen, P., Maenpaa, J., Krohn, K., and Visakorpi, J. K. 1971 *Scand.J.Gastroenterol.*
52. Gastric secretion Schubert, M. L. 2003 *Curr.Opin.Gastroenterol.*
53. Alteration in digestion and absorption of nutrients during profound acid suppression Evenepoel, P. 2001 *Best.Pract.Res.Clin.Gastroenterol.*
54. Effect of omeprazole on plasma zinc levels after oral zinc administration Ozutemiz, A. O., Aydin, H. H., Isler, M., Celik, H. A., and Batur, Y. 2002 *Indian J.Gastroenterol.*
55. Proton pump inhibitors as a risk factor for Clostridium difficile diarrhoea Cunningham, R., Dale, B., Undy, B., and Gaunt, N. 2003 *J.Hosp.Infect.*
56. Helicobacter pylori in cathartic stools of subjects with and without cimetidine-induced hypochlorhydria Haggerty, T., Shmueli, H., and Parsonnet, J. 2003 *J.Med.Microbiol.*
57. Effects of proton pump inhibitors and electrolyte disturbances on arrhythmias El-Charabaty, E., Saifan, C., Abdallah, M., Naboush, A., Glass, D., Azzi, G., Azzi, Y., Khan, A., Baydoun, H., Rondla, C., Parekh, N., and El-Sayegh, S. 2013 *Int.J.Gen.Med.*
58. Subacute cutaneous lupus erythematosus induced and exacerbated by proton pump inhibitors Almeyad, M., Regnier-Rosencher, E., Carlotti, A., Goulvestre, C., Le, Guern, V., Mouthon, L., Avril, M. F., and Dupin, N. 2013 *Dermatology*
59. Effects of different proton pump inhibitors on cardiac contractility in isolated human failing myocardium Sossalla, S., Schotola, H., Schmitto, J., Toischer, K., Sohns, C., Schworer, H., Hasenfuss, G., Maier, L., and Schillinger, W. 2011 *J.Cardiovasc.Surg.(Torino)*
60. Proton-pump inhibitors are associated with increased cardiovascular risk independent of clopidogrel use: a nationwide cohort study Charlot, M., Ahlehoff, O., Norgaard, M. L., Jorgensen, C. H., Sorensen, R., Abildstrom, S. Z., Hansen, P. R., Madsen, J. K., Kober, L., Torp-Pedersen, C., and Gislason, G. 9-21-2010 *Ann.Intern.Med.*
61. Nonsteroidal anti-inflammatory drugs, proton pump inhibitors, and gastrointestinal injury: contrasting interactions in the stomach and small intestine Marlicz, W., Loniewski, I., Grimes, D. S., and Quigley, E. M. 2014 *Mayo Clin.Proc.*
62. Systems biology analysis of omeprazole therapy in cirrhosis demonstrates significant shifts in gut microbiota composition and function Bajaj, J. S., Cox, I. J., Betrapally, N. S., Heuman, D. M., Schubert, M. L., Ratneswaran, M., Hylemon, P. B., White, M. B., Daita, K., Noble, N. A., Sikaroodi, M., Williams, R., Crossey, M. M., Taylor-Robinson, S. D., and Gillevet, P. M. 11-15-2014 *Am.J.Physiol Gastrointest.Liver Physiol*
63. The effect of proton pump inhibitors on the human microbiota Vesper, B. J., Jawdi, A., Altman, K. W., Haines, G. K., III, Tao, L., and Radosevich, J. A. 2009 *Curr.Drug Metab*
64. Hypochlorhydria induced by a proton pump inhibitor leads to intragastric microbial production of acetaldehyde from ethanol Vakevainen, S., Tillonen, J., Salaspuro, M., Jousimies-Somer, H., Nuutinen, H., and Farkkila, M. 2000 *Aliment.Pharmacol.Ther.*
65. Stress and the gut: pathophysiology, clinical consequences, diagnostic approach and treatment options Konturek, P. C., Brzozowski, T., and Konturek, S. J. 2011 *J.Physiol Pharmacol.*
66. Does a melatonin supplement alter the course of gastro-esophageal reflux disease? Madalinski, M. H. 12-6-2011 *World J.Gastrointest.Pharmacol.Ther.*
67. Gut clock: implication of circadian rhythms in the gastrointestinal tract Konturek, P. C., Brzozowski, T., and Konturek, S. J. 2011 *J.Physiol Pharmacol.*

68. Gastroesophageal reflux disease (GERD): a review of conventional and alternative treatments Patrick, L. 2011 *Altern.Med.Rev.*
69. Which is the best choice for gastroesophageal disorders: Melatonin or proton pump inhibitors? de Oliveira Torres, J. D. and de Souza, Pereira R. 10-6-2010 *World J.Gastrointest.Pharmacol.Ther.*
70. Melatonin for the treatment of gastroesophageal reflux disease Werbach, M. R. 2008 *Altern.Ther.Health Med.*
71. Nocturnal secretion of melatonin in patients with upper digestive tract disorders Klupinska, G., Wisniewska-Jarosinska, M., Harasiuk, A., Chojnacki, C., Stec-Michalska, K., Blasiak, J., Reiter, R. J., and Chojnacki, J. 2006 *J.Physiol Pharmacol.*
72. Regression of gastroesophageal reflux disease symptoms using dietary supplementation with melatonin, vitamins and aminoacids: comparison with omeprazole Pereira, Rde S. 2006 *J.Pineal Res.*
73. The potential therapeutic effect of melatonin in Gastro-Esophageal Reflux Disease Kandil, T. S., Mousa, A. A., El-Gendy, A. A., and Abbas, A. M. 2010 *BMC.Gastroenterol.*
74. Protective influence of melatonin against acute esophageal lesions involves prostaglandins, nitric oxide and sensory nerves Konturek, S. J., Zayachkivska, O., Havryluk, X. O., Brzozowski, T., Sliwowski, Z., Pawlik, M., Konturek, P. C., Czesnikiewicz-Guzik, M., Gzhegotsky, M. R., and Pawlik, W. W. 2007 *J.Physiol Pharmacol.*
75. The clinical significance of gastrointestinal changes with aging Bhutto, A. and Morley, J. E. 2008 *Curr.Opin.Clin.Nutr.Metab Care*
76. Influence of gastric acid on susceptibility to infection with ingested bacterial pathogens Tennant, S. M., Hartland, E. L., Phumoonna, T., Lyras, D., Rood, J. I., Robins-Browne, R. M., and van, Driel, I 2008 *Infect.Immun.*
77. Immunologic control of soluble protein absorption from the small intestine: a gut-surface phenomenon Walker, W. A., Isselbacher, K. J., and Bloch, K. J. 1974 *Am.J.Clin.Nutr.*
78. Uptake and transport of macromolecules by the intestine. Possible role in clinical disorders Walker, W. A. and Isselbacher, K. J. 1974 *Gastroenterology*
79. Vitamin B12 deficiency in the elderly Baik, H. W. and Russell, R. M. 1999 *Annu.Rev.Nutr.*
80. Cobalamin, the stomach, and aging Carmel, R. 1997 *Am.J.Clin.Nutr.*
81. [Efficacy of tea blends in the treatment of dyspeptic disorders--an application observation] Iten, F., Meier, B., and Saller, R. 2002 *Forsch.Komplementarmed.Klass.Naturheilkd.*
82. [Iberogast: a modern phytotherapeutic combined herbal drug for the treatment of functional disorders of the gastrointestinal tract (dyspepsia, irritable bowel syndrome)--from phytomedicine to "evidence based phytotherapy." A systematic review] Saller, R., Pfister-Hotz, G., Iten, F., Melzer, J., and Reichling, J. 2002 *Forsch.Komplementarmed.Klass.Naturheilkd.*
83. Small Intestinal Bacterial Overgrowth and Orocecal Transit Time in Patients of Inflammatory Bowel Disease Rana, S. V., Sharma, S., Malik, A., Kaur, J., Prasad, K. K., Sinha, S. K., and Singh, K. 5-7-2013 *Dig.Dis.Sci.*
84. Microscopic colitis and small intestinal bacterial overgrowth--diagnosis behind the irritable bowel syndrome? Stoicescu, A., Andrei, M., Becheanu, G., Stoicescu, M., Nicolaie, T., and Diculescu, M. 2012 *Rev.Med.Chir Soc.Med.Nat.Iasi*
85. Proton Pump Inhibitor Use and the Risk of Small Intestinal Bacterial Overgrowth: A Meta-analysis Lo, W. K. and Chan, W. W. 2013 *Clin.Gastroenterol.Hepatol.*
86. Effect of probiotic or prebiotic supplementation on antibiotic therapy in the small intestinal bacterial overgrowth: a comparative evaluation Rosania, R., Giorgio, F., Principi, M., Amoroso, A., Monno, R., Di, Leo A., and Ierardi, E. 5-1-2013 *Curr.Clin.Pharmacol.*
87. Erosive esophagitis may be related to small intestinal bacterial overgrowth Kim, K. M., Kim, B. T., Lee, D. J., Park, S. B., Joo, N. S., Kim, Y. S., and Kim, K. N. 2012 *Scand.J.Gastroenterol.*
88. The prevalence of overgrowth by aerobic bacteria in the small intestine by small bowel culture: relationship with irritable bowel syndrome Pylaris, E., Giamarellos-Bourboulis, E. J., Tzivras, D., Koussoulas, V., Barbatzas, C., and Pimentel, M. 2012 *Dig.Dis.Sci.*
89. Small intestinal bacterial overgrowth and lactose intolerance contribute to irritable bowel syndrome symptomatology in Pakistan Yakooob, J., Abbas, Z., Khan, R., Hamid, S., Awan, S., and Jafri, W. 2011 *Saudi.J.Gastroenterol.*
90. Gastrointestinal host defence: importance of gut closure in control of macromolecular transport Walker, W. A. 1-16-1979 *Ciba Found.Symp.*
91. Macromolecular absorption of food antigens in health and disease Reinhardt, M. C. 1984 *Ann.Allergy*
92. New aspects of the functionalities of probiotics Bourlioux, P., Bouley, C., and Ashwell, M. 2003 *Forum Nutr.*
93. Immunobiology of the gastrointestinal tract Galant, S. P. 1976 *Compr.Ther.*
94. The intestine and its microflora are partners for the protection of the host: report on the Danone Symposium "The Intelligent Intestine," held in Paris, June 14, 2002 Bourlioux, P., Koletzko, B., Guarner, F., and Braesco, V. 2003 *Am.J.Clin.Nutr.*
95. Role of intestinal flora in the development of allergy Kalliomaki, M. and Isolauri, E. 2003 *Curr.Opin.Allergy Clin.Immunol.*
96. The improvement of hypertension by probiotics: effects on cholesterol, diabetes, Renin, and phytoestrogens Lye, H. S., Kuan, C. Y., Ewe, J. A., Fung, W. Y., and Liong, M. T. 2009 *Int.J.Mol.Sci.*
97. The probiotic *Lactobacillus acidophilus* reduces cholesterol absorption through the down-regulation of Niemann-Pick C1-like 1 in Caco-2 cells Huang, Y. and Zheng, Y. 10-9-2009 *Br.J.Nutr.*
98. Orally delivered microencapsulated live probiotic formulation lowers serum lipids in hypercholesterolemic hamsters Bhatena, J., Martoni, C., Kulamarva, A., Urbanska, A. M., Malhotra, M., and Prakash, S. 2009 *J.Med.Food.*
99. Cholesterol-lowering effect of probiotic yogurt in comparison with ordinary yogurt in mildly to moderately hypercholesterolemic subjects taie-Jafari, A., Larijani, B., Alavi, Majd H., and Tahbaz, F. 2009 *Ann.Nutr.Metab.*
100. Effects of probiotic bacteria, isoflavones and simvastatin on lipid profile and atherosclerosis in cholesterol-fed rabbits: a randomized double-blind study Cavallini, D. C., Bedani, R., Bomdespacho, L. Q., Vendramini, R. C., and Rossi, E. A. 2009 *Lipids Health Dis.*

101. Four-week short chain fructo-oligosaccharides ingestion leads to increasing fecal bifidobacteria and cholesterol excretion in healthy elderly volunteers Bouhnik, Y., Achour, L., Paineau, D., Riottot, M., Attar, A., and Bornet, F. 2007 *Nutr.J.*
102. [An in vitro study of cholesterol-lowering properties of probiotics isolated from the human feces] Zhao, J. R., Fan, X. B., Hang, X. M., Wang, Y. M., and Yang, H. 2005 *Wei Sheng Wu Xue.Bao.*
103. Probiotics as functional foods Lin, D. C. 2003 *Nutr.Clin.Pract.*
104. The potential mechanisms involved in the anti-carcinogenic action of probiotics Commane, D., Hughes, R., Shortt, C., and Rowland, I. 12-11-2005 *Mutat.Res.*
105. Effects of consumption of probiotics and prebiotics on serum lipid levels in humans Pereira, D. I. and Gibson, G. R. 2002 *Crit Rev.Biochem.Mol.Biol.*
106. Long-term consumption of fermented dairy products over 6 months increases HDL cholesterol Kiessling, G., Schneider, J., and Jahreis, G. 2002 *Eur.J.Clin.Nutr.*
107. Cholesterol assimilation by lactic acid bacteria and bifidobacteria isolated from the human gut Pereira, D. I. and Gibson, G. R. 2002 *Appl.Environ.Microbiol.*
108. Hypocholesterolemic effect of *Lactobacillus gasseri* SBT0270 in rats fed a cholesterol-enriched diet Usman and Hosono, A. 2001 *J.Dairy Res.*
109. Effects of probiotic bacteria on diarrhea, lipid metabolism, and carcinogenesis: a review of papers published between 1988 and 1998 de Roos, N. M. and Katan, M. B. 2000 *Am.J.Clin.Nutr.*
110. [Probiotics: history, definition, requirements and possible therapeutic applications] Montalto, M., Arancio, F., Izzi, D., Cuoco, L., Curigliano, V., Manna, R., and Gasbarrini, G. 2002 *Ann.Ital.Med.Int.*
111. Short-chain fatty acids in the human colon: relation to gastrointestinal health and disease Mortensen, P. B. and Clausen, M. R. 1996 *Scand.J.Gastroenterol.Suppl*
112. Health benefits of non-digestible oligosaccharides Roberfroid, M. B. 1997 *Adv.Exp.Med.Biol.*
113. The metabolic importance of unabsorbed dietary lipids in the colon Vonk, R. J., Kalivianakis, M., Minich, D. M., Bijleveld, C. M., and Verkade, H. J. 1997 *Scand.J.Gastroenterol.Suppl*
114. Gut flora in health and disease Guarner, F. and Malagelada, J. R. 2-8-2003 *Lancet*
115. Molecular crosstalk of probiotic bacteria with the intestinal immune system: Clinical relevance in the context of inflammatory bowel disease Homannspurger, G. and Haller, D. 10-12-2009 *Int.J.Med.Microbiol.*
116. Mechanisms of probiotic actions - A review Oelschlaeger, T. A. 9-22-2009 *Int.J.Med.Microbiol.*
117. Mechanisms involved in the immunostimulation by probiotic fermented milk Galdeano, C. M., de Leblanc, Ade M., Carmuega, E., Weill, R., and Perdigon, G. 2009 *J.Dairy Res.*
118. Probiotics, immune function, infection and inflammation: a review of the evidence from studies conducted in humans Lomax, A. R. and Calder, P. C. 2009 *Curr.Pharm.Des*
119. Clinical evidence for immunomodulatory effects of probiotic bacteria Ruemmele, F. M., Bier, D., Marteau, P., Rechkemmer, G., Bourdet-Sicard, R., Walker, W. A., and Goulet, O. 2009 *J.Pediatr.Gastroenterol.Nutr.*
120. Effect of supplement with lactic-acid producing bacteria on fatigue and physical activity in patients with chronic fatigue syndrome Sullivan, A., Nord, C. E., and Evengard, B. 2009 *Nutr.J.*
121. The impact of probiotic on gut health Collado, M. C., Isolauri, E., Salminen, S., and Sanz, Y. 2009 *Curr.Drug Metab*
122. Health, probiotics, and inflammation Mengheri, E. 2008 *J.Clin.Gastroenterol.*
123. Probiotics: a novel approach in the management of food allergy Majamaa, H. and Isolauri, E. 1997 *J.Allergy Clin.Immunol.*
124. The role of probiotics in the clinical management of food allergy and atopic dermatitis Miraglia del Giudice M. and De Luca, M. G. 2004 *J.Clin.Gastroenterol.*
125. Nonsteroidal anti-inflammatory drugs, short-chain fatty acids, and reactive oxygen metabolism in human colorectal cancer cells Giardina, C. and Inan, M. S. 3-5-1998 *Biochim.Biophys.Acta*
126. Complementary alternative medicine for children with autism: a physician survey Golnik, A. E. and Ireland, M. 2009 *J.Autism Dev.Disord.*
127. Autism Parr, J. 2008 *Clin.Evid.(Online.)*
128. Novel treatments for autistic spectrum disorders Levy, S. E. and Hyman, S. L. 2005 *Ment.Retard.Dev.Disabil.Res.Rev.*
129. Diet in autism and associated disorders Garvey, J. 2002 *J.Fam.Health Care*
130. Probiotics as an adjuvant to detoxification protocols Brudnak, M. A. 2002 *Med.Hypotheses*
131. *Saccharomyces boulardii*: potential adjunctive treatment for children with autism and diarrhea Linday, L. A. 2001 *J.Child Neurol.*
132. Inflammatory disease processes and interactions with nutrition Calder, P. C., Albers, R., Antoine, J. M., Blum, S., Bourdet-Sicard, R., Ferns, G. A., Folkerts, G., Friedmann, P. S., Frost, G. S., Guarner, F., Lovik, M., Macfarlane, S., Meyer, P. D., M'Rabet, L., Serafini, M., van, Eden W., van, Loo J., Vas, Dias W., Vidry, S., Winkhofer-Roob, B. M., and Zhao, J. 2009 *Br.J.Nutr.*
133. Probiotic carbohydrates reduce intestinal permeability and inflammation in metabolic diseases Strowski, M. Z. and Wiedenmann, B. 2009 *Gut*
134. Control of mucosal polymicrobial populations by innate immunity Mason, K. L. and Huffnagle, G. B. 2009 *Cell Microbiol.*
135. Chronic pancreatitis: maldigestion, intestinal ecology and intestinal inflammation Pezzilli, R. 4-14-2009 *World J.Gastroenterol.*
136. Oral probiotic control skin inflammation by acting on both effector and regulatory T cells Hacini-Rachinel, F., Gheit, H., Le Ludec, J. B., Dif, F., Nancey, S., and Kaiserlian, D. 2009 *PLoS.One.*
137. Changes in gut microbiota control inflammation in obese mice through a mechanism involving GLP-2-driven improvement of gut permeability Cani, P. D., Possemiers, S., Van de Wiele T., Guiot, Y., Everard, A., Rottier, O., Geurts, L., Naslain, D., Neyrinck, A., Lambert, D. M., Muccioli, G. G., and Delzenne, N. M. 2009 *Gut*

138. The role of gastrin in ulcer pathogenesis McColl, K. E., Gillen, D., and El-Omar, E. 2000 *Baillieres Best.Pract.Res.Clin.Gastroenterol.*
139. Post-diarrhea chronic intestinal symptoms and irritable bowel syndrome in North American travelers to Mexico Okhuysen, P. C., Jiang, Z. D., Carlin, L., Forbes, C., and DuPont, H. L. 2004 *Am.J.Gastroenterol.*
140. Significantly increased IgG2 subclass antibody levels to *Blastocystis hominis* in patients with irritable bowel syndrome Hussain, R., Jaferi, W., Zuberi, S., Baqai, R., Abrar, N., Ahmed, A., and Zaman, V. 1997 *Am.J.Trop.Med.Hyg.*
141. Infection, inflammation, and the irritable bowel syndrome Spiller, R. and Garsed, K. 8-27-2009 *Dig.Liver Dis.*
142. Irritable bowel syndrome: current review on pathophysiology and diagnostic aspects Abdullah, M. 2008 *Acta Med.Indones.*
143. Prognosis in post-infective irritable bowel syndrome: a six year follow up study Neal, K. R., Barker, L., and Spiller, R. C. 2002 *Gut*
144. Antinutritional properties of plant lectins Vasconcelos, I. M. and Oliveira, J. T. 9-15-2004 *Toxicon*
145. Autophagy - An Emerging Anti-Aging Mechanism Gelino, S. and Hansen, M. 7-12-2012 *J.Clin.Exp.Pathol.*
146. Autophagy protects from liver injury He, Z. and Simon, H. U. 2013 *Cell Death.Differ.*
147. Autophagy in epithelial homeostasis and defense Sukseere, S., Eckhart, L., Tschachler, E., and Watanapokasin, R. 2013 *Front Biosci.(Elite.Ed)*
148. The Relationship between Metabolism and the Autophagy Machinery during the Innate Immune Response Martinez, J., Verbist, K., Wang, R., and Green, D. R. 6-4-2013 *Cell Metab*
149. Inhibition of human immunodeficiency virus type-1 through autophagy Campbell, G. R. and Spector, S. A. 6-5-2013 *Curr.Opin.Microbiol.*
150. The significance of macroautophagy in health and disease Tukaj, C. 2013 *Folia Morphol.(Warsz.)*
151. Autophagy: A critical regulator of cellular metabolism and homeostasis Ryter, S. W., Cloonan, S. M., and Choi, A. M. 2013 *Mol.Cells*
152. Autophagy in obesity and atherosclerosis: Interrelationships between cholesterol homeostasis, lipoprotein metabolism and autophagy in macrophages and other systems Ouimet, M. 2013 *Biochim.Biophys.Acta*
153. Autophagy: Emerging roles in lipid homeostasis and metabolic control Christian, P., Sacco, J., and Adeli, K. 2013 *Biochim.Biophys.Acta*
154. Is reactivation of autophagy a possible therapeutic solution for obesity and metabolic syndrome? Sciarretta, S., Volpe, M., and Sadoshima, J. 2012 *Autophagy.*
155. Transition from obesity to metabolic syndrome is associated with altered myocardial autophagy and apoptosis Li, Z. L., Woollard, J. R., Ebrahimi, B., Crane, J. A., Jordan, K. L., Lerman, A., Wang, S. M., and Lerman, L. O. 2012 *Arterioscler.Thromb.Vasc.Biol.*
156. Autophagy and regulation of lipid metabolism Singh, R. 2010 *Results Probl.Cell Differ.*
157. The LIR motif - crucial for selective autophagy Birgisdotir, A. B., Lamark, T., and Johansen, T. 8-1-2013 *J.Cell Sci.*
158. A ginseng metabolite, compound K, induces autophagy and apoptosis via generation of reactive oxygen species and activation of JNK in human colon cancer cells Kim, A. D., Kang, K. A., Kim, H. S., Kim, D. H., Choi, Y. H., Lee, S. J., Kim, H. S., and Hyun, J. W. 2013 *Cell Death.Dis.*
159. Autophagy in cancer 2013 *Anticancer Res.*
160. Autophagy in breast cancer and its implications for therapy Jain, K., Paranandi, K. S., Sridharan, S., and Basu, A. 2013 *Am.J.Cancer Res.*
161. Role of the Crosstalk between Autophagy and Apoptosis in Cancer Su, M., Mei, Y., and Sinha, S. 2013 *J.Oncol.*
162. Targeting autophagy as a potential therapeutic approach for melanoma therapy Liu, H., He, Z., and Simon, H. U. 7-2-2013 *Semin.Cancer Biol.*
163. Probing the depths of cellular senescence Baker, D. J. and Sedivy, J. M. 7-8-2013 *J.Cell Biol.*
164. Ubiquitin at the crossroad of cell death and survival Chen, Y. S. and Qiu, X. B. 7-2-2013 *Chin J.Cancer*
165. Autophagy regulation and its role in cancer Lorin, S., Hamai, A., Mehrpour, M., and Codogno, P. 6-27-2013 *Semin.Cancer Biol.*
166. Impairment of autophagy: From hereditary disorder to drug intoxication Aki, T., Funakoshi, T., Unuma, K., and Uemura, K. 7-10-2013 *Toxicology*
167. Rapamycin, Autophagy, and Alzheimer's Disease Cai, Z. and Yan, L. J. 2013 *J.Biochem.Pharmacol.Res.*
168. Autophagy in physiological and pathological processes--selected aspects Niedzwiedzka-Rystwej, P., Tokarz-Dept, and Deptula, W. 2013 *Pol.J.Vet.Sci.*
169. Autophagy Modulation for Alzheimer's Disease Therapy Zhu, X. C., Yu, J. T., Jiang, T., and Tan, L. 4-27-2013 *Mol.Neurobiol.*
170. Tau degradation: the ubiquitin-proteasome system versus the autophagy-lysosome system Lee, M. J., Lee, J. H., and Rubinsztein, D. C. 2013 *Prog.Neurobiol.*
171. The role of lipids in the control of autophagy Dall'Armi, C., Devereaux, K. A., and Di, Paolo G. 1-7-2013 *Curr.Biol.*
172. Autophagy enhancer carbamazepine alleviates memory deficits and cerebral amyloid-beta pathology in a mouse model of Alzheimer's disease Li, L., Zhang, S., Zhang, X., Li, T., Tang, Y., Liu, H., Yang, W., and Le, W. 5-1-2013 *Curr.Alzheimer Res.*
173. Hypovitaminosis D and hyperparathyroidism in physically inactive elderly Japanese living in nursing homes: relationship with age, sunlight exposure and activities of daily living Nashimoto, M., Nakamura, K., Matsuyama, S., Hatakeyama, M., and Yamamoto, M. 2002 *Aging Clin Exp.Res.*
174. Correlation between breakfast tryptophan content and morning-evening in Japanese infants and students aged 0-15 yrs Harada, T., Hirotsu, M., Maeda, M., Nomura, H., and Takeuchi, H. 2007 *J.Physiol Anthropol.*
175. An integrated effect of protein intake at breakfast and morning exposure to sunlight on the circadian typology in Japanese infants aged 2-6 years Nakade, M., Takeuchi, H., Taniwaki, N., Noji, T., and Harada, T. 2009 *J.Physiol Anthropol.*
176. Dietary influences on neurotransmission Zeisel, S. H. 1986 *Adv.Pediatr.*

177. Evaluation of erythrocyte deformability in experimentally induced osteoporosis in female rats and the effects of vitamin C supplementation on erythrocyte deformability Arslan, A., Aydin, G., Keles, I., Fm, C., and Arslan, M. 2011 Bratisl.Lek.Listy
178. Cytoplasmic superoxide causes bone fragility owing to low-turnover osteoporosis and impaired collagen cross-linking Nojiri, H., Saita, Y., Morikawa, D., Kobayashi, K., Tsuda, C., Miyazaki, T., Saito, M., Marumo, K., Yonezawa, I., Kaneko, K., Shirasawa, T., and Shimizu, T. 2011 J.Bone Miner.Res.
179. Effects of ovariectomy and ascorbic acid supplement on oxidative stress parameters and bone mineral density in rats Arslan, A., Orkun, S., Aydin, G., Keles, I., Tosun, A., Arslan, M., and Caglayan, O. 2011 Libyan.J.Med.
180. Exploiting the antioxidant potential of a common vitamin: Could vitamin C prevent postmenopausal osteoporosis? Talaulikar, V. S., Chambers, T., and Manyonda, I. 2012 J.Obstet.Gynaecol.Res.
181. [Anti-aging studies on the senescence accelerated mouse (SAM) strains] Takahashi, R. 2010 Yakugaku Zasshi
182. Protective effect of total and supplemental vitamin C intake on the risk of hip fracture--a 17-year follow-up from the Framingham Osteoporosis Study Sahni, S., Hannan, M. T., Gagnon, D., Blumberg, J., Cupples, L. A., Kiel, D. P., and Tucker, K. L. 2009 Osteoporos.Int.
183. High vitamin C intake is associated with lower 4-year bone loss in elderly men Sahni, S., Hannan, M. T., Gagnon, D., Blumberg, J., Cupples, L. A., Kiel, D. P., and Tucker, K. L. 2008 J.Nutr.
184. Effects of whey and fortified collagen hydrolysate protein supplements on nitrogen balance and body composition in older women Hays, N. P., Kim, H., Wells, A. M., Kajkenova, O., and Evans, W. J. 2009 J.Am.Diet.Assoc.
185. Increased protein requirements in elderly people: new data and retrospective reassessments Campbell, W. W., Crim, M. C., Dallal, G. E., Young, V. R., and Evans, W. J. 1994 Am.J.Clin.Nutr.
186. Human protein requirements: assessment of the adequacy of the current Recommended Dietary Allowance for dietary protein in elderly men and women Gersovitz, M., Motil, K., Munro, H. N., Scrimshaw, N. S., and Young, V. R. 1982 Am.J.Clin.Nutr.
187. The problem of human protein requirements: some kinetic and metabolic considerations Flodin, N. W., Morgan, P. H., and Mercer, L. P. 1977 Med.Hypotheses
188. Protective effects of high dietary potassium: nutritional and metabolic aspects Demigne, C., Sabboh, H., Remesy, C., and Meneton, P. 2004 J.Nutr.
189. Dietary instead of pharmacological management to counter the adverse effects of physiological adaptations to space flight Fettman, M. J. 2000 Pflugers Arch.
190. Diet, evolution and aging--the pathophysiologic effects of the post-agricultural inversion of the potassium-to-sodium and base-to-chloride ratios in the human diet Frassetto, L., Morris, R. C., Jr., Sellmeyer, D. E., Todd, K., and Sebastian, A. 2001 Eur.J.Nutr.
191. Dietary protein, phosphorus and potassium are beneficial to bone mineral density in adult men consuming adequate dietary calcium Whiting, S. J., Boyle, J. L., Thompson, A., Mirwald, R. L., and Faulkner, R. A. 2002 J.Am.Coll.Nutr.
192. Vegetable and fruit intake and pancreatic cancer in a population-based case-control study in the San Francisco bay area Chan, J. M., Wang, F., and Holly, E. A. 2005 Cancer Epidemiol.Biomarkers Prev.
193. Phytochemicals: guardians of our health Craig, W. J. 1997 J.Am.Diet.Assoc.
194. Prevention and therapy of cancer by dietary monoterpenes Crowell, P. L. 1999 J.Nutr.
195. [Cancer preventive value of natural, non-nutritive food constituents] Frohlich, R. H., Kunze, M., and Kiefer, I. 1997 Acta Med.Austriaca
196. The citrus flavonoid naringenin stimulates DNA repair in prostate cancer cells Gao, K., Henning, S. M., Niu, Y., Youssefian, A. A., Seeram, N. P., Xu, A., and Heber, D. 8-17-2005 J.Nutr.Biochem.
197. Inhibition of mammary cancer by citrus flavonoids Guthrie, N. and Carroll, K. K. 1998 Adv.Exp.Med.Biol.
198. Plant foods, antioxidants, and prostate cancer risk: findings from case-control studies in Canada Jain, M. G., Hislop, G. T., Howe, G. R., and Ghadirian, P. 1999 Nutr.Cancer
199. Do dietary lycopene and other carotenoids protect against prostate cancer? Jian, L., Du, C. J., Lee, A. H., and Binns, C. W. 3-1-2005 Int.J.Cancer
200. Botanicals in cancer chemoprevention Park, E. J. and Pezzuto, J. M. 2002 Cancer Metastasis Rev.
201. Citrus limonoids induce apoptosis in human neuroblastoma cells and have radical scavenging activity Poulouse, S. M., Harris, E. D., and Patil, B. S. 2005 J.Nutr.
202. Anticancer and health protective properties of citrus fruit components Silalahi, J. 2002 Asia Pac.J.Clin.Nutr.
203. Antioxidant and antiproliferative activities of common fruits Sun, J., Chu, Y. F., Wu, X., and Liu, R. H. 12-4-2002 J.Agric.Food Chem.
204. Citrus peel use is associated with reduced risk of squamous cell carcinoma of the skin Hakim, I. A., Harris, R. B., and Ritenbaugh, C. 2000 Nutr.Cancer
205. Joint effects of citrus peel use and black tea intake on the risk of squamous cell carcinoma of the skin Hakim, I. A. and Harris, R. B. 2001 BMC.Dermatol.
206. Antioxidant Activity of Limonene on Normal Murine Lymphocytes: Relation to HO Modulation and Cell Proliferation Roberto, D., Micucci, P., Sebastian, T., Graciela, F., and Anesini, C. 10-1-2009 Basic Clin.Pharmacol.Toxicol.
207. D-Limonene: safety and clinical applications Sun, J. 2007 Altern.Med.Rev.
208. Induction of apoptosis by d-limonene is mediated by a caspase-dependent mitochondrial death pathway in human leukemia cells Ji, J., Zhang, L., Wu, Y. Y., Zhu, X. Y., Lv, S. Q., and Sun, X. Z. 2006 Leuk.Lymphoma
209. The synthesis of L-carvone and limonene derivatives with increased antiproliferative effect and activation of ERK pathway in prostate cancer cells Chen, J., Lu, M., Jing, Y., and Dong, J. 10-1-2006 Bioorg.Med.Chem.
210. Cancer prevention by natural compounds Tsuda, H., Ohshima, Y., Nomoto, H., Fujita, K., Matsuda, E., Iigo, M., Takasuka, N., and Moore, M. A. 2004 Drug Metab Pharmacokin.
211. Inhibition of growth and metastasis of human gastric cancer implanted in nude mice by d-limonene Lu, X. G., Zhan, L. B., Feng, B. A., Qu, M. Y., Yu, L. H., and Xie, J. H. 7-15-2004 World J.Gastroenterol.

212. [D-limonene induces apoptosis of gastric cancer cells] Lu, X. G., Feng, B. A., Zhan, L. B., and Yu, Z. H. 2003 *Zhonghua Zhong.Liu Za Zhi*.
213. Monoterpenes in breast cancer chemoprevention Crowell, P. L. 1997 *Breast Cancer Res.Treat*.
214. d-Limonene inhibits N-nitrosobis(2-oxopropyl)amine induced hamster pancreatic carcinogenesis Nakaizumi, A., Baba, M., Uehara, H., Iishi, H., and Tatsuta, M. 7-15-1997 *Cancer Lett*.
215. Potassium intake and the calcium economy Rafferty, K., Davies, K. M., and Heaney, R. P. 2005 *J.Am.Coll.Nutr*.
216. Dietary macro- and micronutrient intakes of nonsupplemented pre- and postmenopausal women with a perspective on menopause-associated diseases Masse, P. G., Dossy, J., Tranchant, C. C., and Dallaire, R. 2004 *J.Hum.Nutr.Diet*.
217. Blood pressure response to dietary modifications in free-living individuals Nowson, C. A., Worsley, A., Margerison, C., Jorna, M. K., Frame, A. G., Torres, S. J., and Godfrey, S. J. 2004 *J.Nutr*.
218. Serum potassium level and dietary potassium intake as risk factors for stroke Di, Legge S., Spence, J. D., Tamayo, A., and Hachinski, V. 6-10-2003 *Neurology*
219. Serum potassium level and dietary potassium intake as risk factors for stroke Hart, R. G. and Pearce, L. A. 6-10-2003 *Neurology*
220. Potassium: more beneficial effects He, F. J. and MacGregor, G. A. 2003 *Climacteric*.
221. Dietary minerals and modification of cardiovascular risk factors Vaskonen, T. 2003 *J.Nutr.Biochem*.
222. Dietary magnesium, potassium, sodium, and children's lung function Gilliland, F. D., Berhane, K. T., Li, Y. F., Kim, D. H., and Margolis, H. G. 1-15-2002 *Am.J.Epidemiol*.
223. Serum potassium level and dietary potassium intake as risk factors for stroke Green, D. M., Ropper, A. H., Kronmal, R. A., Psaty, B. M., and Burke, G. L. 8-13-2002 *Neurology*
224. Importance of potassium in cardiovascular disease Sica, D. A., Struthers, A. D., Cushman, W. C., Wood, M., Banas, J. S., Jr., and Epstein, M. 2002 *J.Clin.Hypertens.(Greenwich.)*
225. Dietary potassium intake and risk of stroke in US men and women: National Health and Nutrition Examination Survey I epidemiologic follow-up study Bazzano, L. A., He, J., Ogden, L. G., Loria, C., Vupputuri, S., Myers, L., and Whelton, P. K. 2001 *Stroke*
226. Are low intakes of calcium and potassium important causes of cardiovascular disease? McCarron, D. A. and Reusser, M. E. 2001 *Am.J.Hypertens*.
227. Nutrition and blood pressure MacGregor, G. A. 1999 *Nutr.Metab Cardiovasc.Dis*.
228. Vascular protective effects of potassium Young, D. B. and Ma, G. 1999 *Semin.Nephrol*.
229. Dietary sodium and potassium intake and colorectal cancer risk Kune, G. A., Kune, S., and Watson, L. F. 1989 *Nutr.Cancer*
230. Dietary potassium and stroke-associated mortality. A 12-year prospective population study Khaw, K. T. and Barrett-Connor, E. 1-29-1987 *N.Engl.J.Med*.
231. Dietary potassium intake and grip strength in older people Judge, T. G. and Cowan, N. R. 1971 *Gerontol.Clin.(Basel)*
232. Potassium's cardiovascular protective mechanisms Young, D. B., Lin, H., and McCabe, R. D. 1995 *Am.J.Physiol*
233. Changes in adrenal responsiveness and potassium balance with shifts in sodium intake Adler, G. K., Moore, T. J., Hollenberg, N. K., and Williams, G. H. 1987 *Endocr.Res*.
234. [Intake of dietary fiber, sodium, potassium, and calcium and its relation with arterial blood pressure in normotensive adult men] Ballesteros-Vasquez, M. N., Cabrera-Pacheco, R. M., Saucedo-Tamayo, M. S., and Grijalva-Haro, M. I. 1998 *Salud Publica Mex*.
235. Blood pressure response to changes in sodium and potassium intake: a metaregression analysis of randomised trials Geleijnse, J. M., Kok, F. J., and Grobbee, D. E. 2003 *J.Hum.Hypertens*.
236. Dietary sodium and potassium in the genesis, therapy, and prevention of hypertension Haddy, F. J. 1987 *J.Am.Coll.Nutr*.
237. Effect of dietary electrolytes upon calcium excretion: the Yi People Study He, J., Tell, G. S., Tang, Y. C., Mo, P. S., and He, G. Q. 1992 *J.Hypertens*.
238. Regression analysis of cancer incidence rates and water fluoride in the U.S.A. based on IACR/IARC (WHO) data (1978-1992). International Agency for Research on Cancer Takahashi, K., Akiniwa, K., and Narita, K. 2001 *J.Epidemiol*.
239. Effects of hydration on cognitive function of pilots Lindseth, P. D., Lindseth, G. N., Petros, T. V., Jensen, W. C., and Caspers, J. 2013 *Mil.Med*.
240. Cognitive performance and dehydration Adan, A. 2012 *J.Am.Coll.Nutr*.
241. Effects of drinking supplementary water at school on cognitive performance in children Fadda, R., Rapinett, G., Grathwohl, D., Parisi, M., Fanari, R., Calo, C. M., and Schmitt, J. 2012 *Appetite*
242. Hydration and cognitive performance Secher, M. and Ritz, P. 2012 *J.Nutr.Health Aging*
243. Dehydration influences mood and cognition: a plausible hypothesis? Benton, D. 2011 *Nutrients*.
244. Dehydration during sleep affects cognitive performance Thornton, S. N. and Trabalon, M. 2012 *Sleep Med*.
245. The effects of exercise, heat, cooling and rehydration strategies on cognitive function in football players Bandelow, S., Maughan, R., Shirreffs, S., Ozgunen, K., Kurdak, S., Ersoz, G., Binnet, M., and Dvorak, J. 2010 *Scand.J.Med.Sci.Sports*
246. Dehydration affects brain structure and function in healthy adolescents Kempton, M. J., Ettinger, U., Foster, R., Williams, S. C., Calvert, G. A., Hampshire, A., Zelaya, F. O., O'Gorman, R. L., McMorris, T., Owen, A. M., and Smith, M. S. 2011 *Hum.Brain Mapp*.
247. Does having a drink help you think? 6-7-Year-old children show improvements in cognitive performance from baseline to test after having a drink of water Edmonds, C. J. and Jeffes, B. 2009 *Appetite*
248. Voluntary dehydration and cognitive performance in trained college athletes D'anci, K. E., Vibhakar, A., Kanter, J. H., Mahoney, C. R., and Taylor, H. A. 2009 *Percept.Mot.Skills*
249. Should children drink more water?: the effects of drinking water on cognition in children Edmonds, C. J. and Burford, D. 2009 *Appetite*

250. Carbohydrate expression in the intestinal mucosa Sharma, R. and Schumacher, U. 2001 *Adv.Anat.Embryol.Cell Biol.*
251. Homing of intestinal immune cells Uhlig, H. H., Mottet, C., and Powrie, F. 2004 *Novartis.Found.Symp.*
252. Type I (insulin-dependent) diabetes mellitus and cow milk: casein variant consumption Elliott, R. B., Harris, D. P., Hill, J. P., Bibby, N. J., and Wasmuth, H. E. 1999 *Diabetologia*
253. Relationship between dairy product consumption and incidence of IDDM in childhood in Italy Fava, D., Leslie, R. D., and Pozzilli, P. 1994 *Diabetes Care*
254. Early introduction of dairy products associated with increased risk of IDDM in Finnish children. The Childhood in Diabetes in Finland Study Group Virtanen, S. M., Rasanen, L., Ylonen, K., Aro, A., Clayton, D., Langholz, B., Pitkaniemi, J., Savilahti, E., Lounamaa, R., Tuomilehto, J., and . 1993 *Diabetes*
255. Diet, cow's milk protein antibodies and the risk of IDDM in Finnish children. Childhood Diabetes in Finland Study Group Virtanen, S. M., Saukkonen, T., Savilahti, E., Ylonen, K., Rasanen, L., Aro, A., Knip, M., Tuomilehto, J., and Akerblom, H. K. 1994 *Diabetologia*
256. Effects of a gluten-free diet in primary IgA nephropathy Coppo, R., Roccatello, D., Amore, A., Quattrocchio, G., Molino, A., Gianoglio, B., Amoroso, A., Bajardi, P., and Piccoli, G. 1990 *Clin.Nephrol.*
257. Dietary antigens and primary immunoglobulin A nephropathy Coppo, R., Amore, A., and Roccatello, D. 1992 *J.Am.Soc.Nephrol.*
258. Macromolecular IgA and abnormal IgA reactivity in sera from children with IgA nephropathy. Italian Collaborative Paediatric IgA Nephropathy Study Coppo, R., Amore, A., Gianoglio, B., Porcellini, M. G., Peruzzi, L., Gusmano, R., Giani, M., Sereni, F., Gianviti, A., and Rizzoni, G. 1995 *Clin.Nephrol.*
259. [Significance of IGA antigliadin antibodies during primary glomerulonephritis with mesangial IGA deposits] Rostoker, G., Delprato, S., Benmaadi, A., Petit-Phar, M., Andre, C., Laurent, J., Lang, P., Weil, B., and Lagrue, G. 1989 *Ann.Med.Interne (Paris)*
260. Proteins that bind high-mannose sugars of the HIV envelope Botos, I. and Wlodawer, A. 2005 *Prog.Biophys.Mol.Biol.*
261. Microdomains of the C-type lectin DC-SIGN are portals for virus entry into dendritic cells Cambi, A., de Lange F., van Maarseveen, N. M., Nijhuis, M., Joosten, B., van Dijk, E. M., de Bakker, B. I., Franssen, J. A., Bovee-Geurts, P. H., van Leeuwen, F. N., Van Hulst, N. F., and Figdor, C. G. 1-5-2004 *J.Cell Biol.*
262. Role of intestinal flora in the development of allergy Kalliomaki, M. and Isolauri, E. 2003 *Curr.Opin.Allergy Clin.Immunol.*
263. [Probiotics: history, definition, requirements and possible therapeutic applications] Montalto, M., Arancio, F., Izzi, D., Cuoco, L., Curigliano, V., Manna, R., and Gasbarrini, G. 2002 *Ann.Ital.Med.Int.*
264. Novel probiotics for the management of allergic inflammation von der Weid T., Ibnou-Zekri, N., and Pfeifer, A. 2002 *Dig.Liver Dis.*
265. Milk-induced eczema is associated with the expansion of T cells expressing cutaneous lymphocyte antigen bernathy-Carver, K. J., Sampson, H. A., Picker, L. J., and Leung, D. Y. 1995 *J.Clin.Invest*
266. Peanut lectin binding sites in colons of patients with ulcerative colitis Cooper, H. S., Farano, P., and Coapman, R. A. 1987 *Arch.Pathol.Lab Med.*
267. Major dietary patterns are related to plasma concentrations of markers of inflammation and endothelial dysfunction Lopez-Garcia, E., Schulze, M. B., Fung, T. T., Meigs, J. B., Rifai, N., Manson, J. E., and Hu, F. B. 2004 *Am.J.Clin.Nutr.*
268. Altered lectin binding by colonic epithelial glycoconjugates in ulcerative colitis and Crohn's disease Rhodes, J. M., Black, R. R., and Savage, A. 1988 *Dig.Dis.Sci.*
269. Trans fatty acids in hydrogenated fat inhibited the synthesis of the polyunsaturated fatty acids in the phospholipid of arterial cells Kummerow, F. A., Zhou, Q., Mahfouz, M. M., Smiricky, M. R., Grieshop, C. M., and Schaeffer, D. J. 4-16-2004 *Life Sci.*
270. Dietary intake of trans fatty acids and systemic inflammation in women Mozaffarian, D., Pischon, T., Hankinson, S. E., Rifai, N., Joshipura, K., Willett, W. C., and Rimm, E. B. 2004 *Am.J.Clin.Nutr.*
271. Dietary fatty acids and coronary heart disease Wolfram, G. 8-20-2003 *Eur.J.Med.Res.*
272. Influence of palm oil (*Elaeis guineensis*) on health Ebong, P. E., Owu, D. U., and Isong, E. U. 1999 *Plant Foods Hum.Nutr*
273. Choice of cooking oils--myths and realities Sircar, S. and Kansra, U. 1998 *J.Indian Med.Assoc.*
274. Optimization of physiological lipid mixtures for barrier repair Man, MQ M., Feingold, K. R., Thornfeldt, C. R., and Elias, P. M. 1996 *J Invest Dermatol.*
275. Essential fatty acids and epidermal integrity Wertz, P. W., Swartzendruber, D. C., Abraham, W., Madison, K. C., and Downing, D. T. 1987 *Arch.Dermatol.*
276. Covalently bound lipids of human stratum corneum Wertz, P. W., Madison, K. C., and Downing, D. T. 1989 *J Invest Dermatol.*
277. Eicosapentaenoic acid and docosahexaenoic acid reduce UVB- and TNF-alpha-induced IL-8 secretion in keratinocytes and UVB-induced IL-8 in fibroblasts Storey, A., McArdle, F., Friedmann, P. S., Jackson, M. J., and Rhodes, L. E. 2005 *J.Invest Dermatol.*
278. Nutritional protection against skin damage from sunlight Sies, H. and Stahl, W. 2004 *Annu.Rev.Nutr.*
279. Effect of sunlight exposure and aging on skin surface lipids and urate Hayashi, N., Togawa, K., Yanagisawa, M., Hosogi, J., Mimura, D., and Yamamoto, Y. 2003 *Exp.Dermatol.*
280. Structural and biochemical basis for the UVB-induced alterations in epidermal barrier function Holleran, W. M., Uchida, Y., Halkier-Sorensen, L., Haratake, A., Hara, M., Epstein, J. H., and Elias, P. M. 1997 *Photodermatol.Photoimmunol.Photomed.*
281. Protective effect of topically applied olive oil against photocarcinogenesis following UVB exposure of mice Budiyoanto, A., Ahmed, N. U., Wu, A., Bito, T., Nikaido, O., Osawa, T., Ueda, M., and Ichihashi, M. 2000 *Carcinogenesis*
282. The possible role of long-chain, omega-3 fatty acids in human brain phylogeny Chamberlain, J. G. 1996 *Perspect.Biol.Med.*

283. Dietary lean red meat and human evolution Mann, N. 2000 *Eur.J.Nutr.*
284. Overview of evolutionary aspects of omega 3 fatty acids in the diet Simopoulos, A. P. 1998 *World Rev.Nutr.Diet.*
285. Evolutionary aspects of omega-3 fatty acids in the food supply Simopoulos, A. P. 1999 *Prostaglandins Leukot.Essent.Fatty Acids*
286. Evolutionary aspects of diet and essential fatty acids Simopoulos, A. P. 2001 *World Rev.Nutr.Diet.*
287. Importance of the ratio of omega-6/omega-3 essential fatty acids: evolutionary aspects Simopoulos, A. P. 2003 *World Rev.Nutr.Diet.*
288. Significantly reduced docosahexaenoic and docosapentaenoic acid concentrations in erythrocyte membranes from schizophrenic patients compared with a carefully matched control group Assies, J., Lieverse, R., Vreken, P., Wanders, R. J., Dingemans, P. M., and Linszen, D. H. 3-15-2001 *Biol.Psychiatry*
289. Roles of unsaturated fatty acids (especially omega-3 fatty acids) in the brain at various ages and during ageing Bourre, J. M. 2004 *J.Nutr.Health Aging*
290. Novel treatments for bipolar disorder Bowden, C. L. 2001 *Expert.Opin.Investig.Drugs*
291. Major depression is associated with lower omega-3 fatty acid levels in patients with recent acute coronary syndromes Frasure-Smith, N., Lesperance, F., and Julien, P. 5-1-2004 *Biol.Psychiatry*
292. Omega-3 fatty acids in psychiatry: a review Freeman, M. P. 2000 *Ann.Clin.Psychiatry*
293. Dietary supplements and natural products as psychotherapeutic agents Fugh-Berman, A. and Cott, J. M. 1999 *Psychosom.Med.*
294. Treatment-resistant bipolar disorder Gitlin, M. J. 2001 *Bull.Menninger Clin.*
295. Essential fatty acids and the brain Haag, M. 2003 *Can.J.Psychiatry*
296. Ethanol, essential fatty acids and prostaglandins Anggard, E. 1983 *Pharmacol.Biochem.Behav.*
297. Effects of omega-3 fatty acids on cognitive function with aging, dementia, and neurological diseases Maclean, C. H., Issa, A. M., Newberry, S. J., Mojica, W. A., Morton, S. C., Garland, R. H., Hilton, L. G., Traina, S. B., and Shekelle, P. G. 2005 *Evid.Rep.Technol.Assess.(Summ.)*
298. Chronic administration of docosahexaenoic acid ameliorates the impairment of spatial cognition learning ability in amyloid beta-infused rats Hashimoto, M., Tanabe, Y., Fujii, Y., Kikuta, T., Shibata, H., and Shido, O. 2005 *J.Nutr.*
299. Good fats prevent dendritic damage in mouse model of AD Love, R. 2004 *Lancet Neurol.*
300. Food for thought: essential fatty acid protects against neuronal deficits in transgenic mouse model of AD Mucke, L. and Pitas, R. E. 9-2-2004 *Neuron*
301. [Importance of "health foods", EPA and DHA, for preventive medicine] Yazawa, K. 2004 *Rinsho Byori*
302. Omega-3 fatty acids and risk of cognitive impairment and dementia Laurin, D., Verreault, R., Lindsay, J., Dewailly, E., and Holub, B. J. 2003 *J.Alzheimers.Dis.*
303. Sunflower, virgin-olive and fish oils differentially affect the progression of aortic lesions in rabbits with experimental atherosclerosis Aguilera, C. M., Ramirez-Tortosa, M. C., Mesa, M. D., Ramirez-Tortosa, C. L., and Gil, A. 2002 *Atherosclerosis*
304. Comparative antibacterial and antifungal effects of some phenolic compounds Aziz, N. H., Farag, S. E., Mousa, L. A., and bo-Zaid, M. A. 1998 *Microbios*
305. Effects of virgin olive oil phenolic compounds on LDL oxidation and vasorelaxation activity Benkhalti, F., Legssyer, A., Gomez, P., Paz, E., Lopez-Miranda, J., Perez-Jimenez, F., and el Boustani, E. S. 2003 *Therapie*
306. Bioactive derivatives of oleuropein from olive fruits Bianco, A. D., Muzzalupo, I., Piperno, A., Romeo, G., and Uccella, N. 1999 *J.Agric.Food Chem.*
307. On the in-vitro antimicrobial activity of oleuropein and hydroxytyrosol Bisignano, G., Tomaino, A., Lo, Cascio R., Crisafi, G., Uccella, N., and Saija, A. 1999 *J.Pharm.Pharmacol.*
308. Differential effects of oleuropein, a biophenol from *Olea europaea*, on anionic and zwitterionic phospholipid model membranes Caturla, N., Perez-Fons, L., Estepa, A., and Micol, V. 2005 *Chem.Phys.Lipids*
309. Microbiological activity in stored olive oil Ciafardini, G. and Zullo, B. A. 5-5-2002 *Int.J.Food Microbiol.*
310. Chemopreventive n-3 polyunsaturated fatty acids reprogram genetic signatures during colon cancer initiation and progression in the rat Davidson, L. A., Nguyen, D. V., Hokanson, R. M., Callaway, E. S., Isett, R. B., Turner, N. D., Dougherty, E. R., Wang, N., Lupton, J. R., Carroll, R. J., and Chapkin, R. S. 9-15-2004 *Cancer Res.*
311. Oleuropein, a non-toxic olive iridoid, is an anti-tumor agent and cytoskeleton disruptor Hamdi, H. K. and Castellon, R. 9-2-2005 *Biochem.Biophys.Res.Commun.*
312. Preventive effect of antioxidant on ultraviolet-induced skin cancer in mice Ichihashi, M., Ahmed, N. U., Budiyo, A., Wu, A., Bito, T., Ueda, M., and Osawa, T. 2000 *J.Dermatol.Sci*
313. Secoiridoids, tocopherols, and antioxidant activity of monovarietal extra virgin olive oils extracted from destoned fruits Lavelli, V. and Bondesan, L. 2-23-2005 *J.Agric.Food Chem.*
314. Supplementation of plasma with olive oil phenols and extracts: influence on LDL oxidation Leenen, R., Roodenburg, A. J., Vissers, M. N., Schuurbiens, J. A., van Putte, K. P., Wiseman, S. A., and van de Put, F. H. 2-27-2002 *J.Agric.Food Chem.*
315. Direct vascular antiatherogenic effects of oleic acid: a clue to the cardioprotective effects of the Mediterranean diet Massaro, M., Carluccio, M. A., and De Caterina, R. 1999 *Cardiologia*
316. Antioxidant effect of phenolic compounds, alpha-tocopherol, and other minor components in virgin olive oil Mateos, R., Dominguez, M. M., Espartero, J. L., and Cert, A. 11-19-2003 *J.Agric.Food Chem.*
317. Olive-oil consumption and health: the possible role of antioxidants Owen, R. W., Giacosa, A., Hull, W. E., Haubner, R., Wurtele, G., Spiegelhalder, B., and Bartsch, H. 2000 *Lancet Oncol.*
318. Olive oil and its main phenolic micronutrient (oleuropein) prevent inflammation-induced bone loss in the ovariectomised rat Puel, C., Quintin, A., Agalias, A., Mathey, J., Obled, C., Mazur, A., Davicco, M. J., Lebecque, P., Skaltsounis, A. L., and Coxam, V. 2004 *Br.J.Nutr.*

319. Olive oil and red wine antioxidant polyphenols inhibit endothelial activation: antiatherogenic properties of Mediterranean diet phytochemicals Carluccio, M. A., Siculella, L., Ancora, M. A., Massaro, M., Scoditti, E., Storelli, C., Visioli, F., D'Amico, A., and De Caterina R. 4-1-2003 *Arterioscler.Thromb.Vasc.Biol.*
320. Nutrition supplements and the eye Brown, N. A., Bron, A. J., Harding, J. J., and Dewar, H. M. 1998 *Eye*
321. Dietary fat and risk for advanced age-related macular degeneration Seddon, J. M., Rosner, B., Sperduto, R. D., Yannuzzi, L., Haller, J. A., Blair, N. P., and Willett, W. 2001 *Arch.Ophthalmol.*
322. Fish and healthy pregnancy: more than just a red herring! Rice, R. 1996 *Prof.Care Mother.Child*
323. Omega-3 fatty acids in health and disease and in growth and development Simopoulos, A. P. 1991 *Am.J.Clin.Nutr.*
324. Essential fatty acids in health and chronic disease Simopoulos, A. P. 1999 *Am.J.Clin.Nutr.*
325. [Vegetarian diets of breastfeeding women in the light of dietary recommendations] Strucinska, M. 2002 *Rocz.Panstw.Zakl.Hig.*
326. Dietary intake of n-3 and n-6 fatty acids and the risk of prostate cancer Leitzmann, M. F., Stampfer, M. J., Michaud, D. S., Augustsson, K., Colditz, G. C., Willett, W. C., and Giovannucci, E. L. 2004 *Am.J.Clin.Nutr.*
327. Dietary alpha-linolenic acid is associated with reduced risk of fatal coronary heart disease, but increased prostate cancer risk: a meta-analysis Brouwer, I. A., Katan, M. B., and Zock, P. L. 2004 *J.Nutr.*
328. The use of n-3 PUFAs (fish oil) in enteral nutrition Gerster, H. 1995 *Int.J.Vitam.Nutr.Res.*
329. Health benefits of docosahexaenoic acid (DHA) [see comments] Horrocks, L. A. and Yeo, Y. K. 1999 *Pharmacol.Res.*
330. Fatty acids and homocysteine levels in patients with recurrent depression: an explorative pilot study Assies, J., Lok, A., Bockting, C. L., Weverling, G. J., Lieveise, R., Visser, I., Abeling, N. G., Duran, M., and Schene, A. H. 2004 *Prostaglandins Leukot.Essent.Fatty Acids*
331. Dietary polyunsaturated fatty acids and cancers of the breast and colorectum: emerging evidence for their role as risk modifiers Bartsch, H., Nair, J., and Owen, R. W. 1999 *Carcinogenesis*
332. Omega-3 fatty acids: their role in the prevention and treatment of atherosclerosis related risk factors and complications Bhatnagar, D. and Durrington, P. N. 2003 *Int.J.Clin.Pract.*
333. Influence of dietary omega-6, -3 fatty acid sources on the initiation and promotion stages of photocarcinogenesis Black, H. S., Thornby, J. I., Gerguis, J., and Lenger, W. 1992 *Photochem.Photobiol.*
334. Dietary fat and asthma: is there a connection? Black, P. N. and Sharpe, S. 1997 *Eur.Respir.J.*
335. Dietary treatment of familial hypercholesterolemia Connor, W. E. and Connor, S. L. 1989 *Arteriosclerosis*
336. Diet, atherosclerosis, and fish oil Connor, W. E. and Connor, S. L. 1990 *Adv.Intern.Med.*
337. Perinatal supplementation of long-chain polyunsaturated fatty acids, immune response and adult diseases Das, U. N. 2004 *Med.Sci.Monit.*
338. Dietary lipids and risk of autoimmune disease Fernandes, G. 1994 *Clin.Immunol.Immunopathol.*
339. Insulin resistance, inflammation, and serum fatty acid composition Fernandez-Real, J. M., Broch, M., Vendrell, J., and Ricart, W. 2003 *Diabetes Care*
340. Dietary fatty acids and allergy Kankaanpaa, P., Sutas, Y., Salminen, S., Lichtenstein, A., and Isolauri, E. 1999 *Ann Med.*
341. Gastrointestinal disorders and rheumatic diseases Parke, A. L. 1993 *Curr.Opin.Rheumatol.*
342. Consumer acceptability of conjugated linoleic Acid-enriched milk and cheddar cheese from cows grazing on pasture Khanal, R. C., Dhiman, T. R., Ure, A. L., Brennard, C. P., Boman, R. L., and McMahon, D. J. 2005 *J.Dairy Sci.*
343. The effect of conjugated linoleic acid on calcium absorption and bone metabolism and composition in adult ovariectomised rats Kelly, O. and Cashman, K. D. 2004 *Prostaglandins Leukot.Essent.Fatty Acids*
344. Conjugated linoleic acid prevents the development of essential hypertension in spontaneously hypertensive rats Inoue, N., Nagao, K., Hirata, J., Wang, Y. M., and Yanagita, T. 10-15-2004 *Biochem.Biophys.Res.Commun.*
345. Immunomodulatory properties of conjugated linoleic acid O'Shea, M., Bassaganya-Riera, J., and Mohede, I. C. 2004 *Am.J.Clin.Nutr.*
346. A test of Ockham's razor: implications of conjugated linoleic acid in bone biology Watkins, B. A., Li, Y., Lippman, H. E., Reinwald, S., and Seifert, M. F. 2004 *Am.J.Clin.Nutr.*
347. [Arteriosclerosis and osteoporosis (editorial)] Laroche, M. 1-20-1996 *Presse Med.*
348. UV-A irradiation induces transcription of IL-6 and TNF alpha genes in human keratinocytes and dermal fibroblasts Avalos-Diaz, E., Alvarado-Flores, E., and Herrera-Esparza, R. 1999 *Rev.Rhum.Engl.Ed*
349. The acute effects of long-wave ultraviolet radiation on human skin Kaidbey, K. H. and Kligman, A. M. 1979 *J Invest Dermatol.*
350. [The effect of UV-A and UV-B irradiation on the skin barrier. Skin physiologic, electron microscopy and lipid biochemistry studies] Lehmann, P., Melnik, B., Holzle, E., Neumann, N., and Plewig, G. 1992 *Hautarzt*
351. UV-A induces persistent genomic instability in human keratinocytes through an oxidative stress mechanism Phillipson, R. P., Tobi, S. E., Morris, J. A., and McMillan, T. J. 3-1-2002 *Free Radic.Biol.Med.*
352. [Effect of long-wave ultraviolet light (UV-A) and medium-wave ultraviolet rays (UV-B) on human skin. Critical comparison] Raab, W. 4-15-1980 *Z.Hautkr.*
353. Vitamin D and genomic stability Chatterjee, M. 4-18-2001 *Mutat Res*
354. Vitamin D: balancing cutaneous and systemic considerations Fuller, K. E. and Casparian, J. M. 2001 *South.Med.J*
355. Effects of ultraviolet exposure on the immune system Garssen, J. and van Loveren, H. 2001 *Crit Rev.Immunol.*
356. A novel pathway for hormonally active calcitriol Lehmann, B., Knuschke, P., and Meurer, M. 2000 *Horm.Res.*
357. Diet and risk of cutaneous malignant melanoma: a prospective study of 50,757 Norwegian men and women Veierod, M. B., Thelle, D. S., and Laake, P. 5-16-1997 *Int.J.Cancer*
358. Body fat content and 25-hydroxyvitamin d levels in healthy women Arunabh, S., Pollack, S., Yeh, J., and Aloia, J. F. 2003 *J Clin Endocrinol.Metab*
359. Evidence for alteration of the vitamin D-endocrine system in obese subjects Bell, N. H., Epstein, S., Greene, A., Shary, J., Oexmann, M. J., and Shaw, S. 1985 *J.Clin.Invest*

360. Vitamin D Deficiency in the Morbidly Obese Buffington, C., Walker, B., Cowan, G. S., Jr., and Scruggs, D. 1993 *Obes.Surg.*
361. Low circulating vitamin D in obesity Liel, Y., Ulmer, E., Shary, J., Hollis, B. W., and Bell, N. H. 1988 *Calcif.Tissue Int.*
362. Decreased bioavailability of vitamin D in obesity Wortsman, J., Matsuoka, L. Y., Chen, T. C., Lu, Z., and Holick, M. F. 2000 *Am.J.Clin.Nutr.*
363. Possible role of hyperinsulinemia and insulin resistance in lower vitamin D levels in overweight and obese patients De, Pergola G., Nitti, A., Bartolomeo, N., Gesuita, A., Giagulli, V. A., Triggiani, V., Guastamacchia, E., and Silvestris, F. 2013 *Biomed.Res.Int.*
364. Relation of obesity with serum 25 hydroxy vitamin D3 levels in type 2 diabetic patients Cimbek, A., Gursoy, G., Kirnap, N. G., Acar, Y., Kilic, Z., Gungor, F., and Ozasik, I. 2012 *J.Res.Med.Sci.*
365. Dose response to vitamin D supplementation in postmenopausal women: a randomized trial Gallagher, J. C., Sai, A., Templin, T., and Smith, L. 3-20-2012 *Ann.Intern.Med.*
366. The effect of vitamin D supplementation on serum 25OHD in thin and obese women Gallagher, J. C., Yalamanchili, V., and Smith, L. M. 2013 *J.Steroid Biochem.Mol.Biol.*
367. Relation of body fat indexes to vitamin D status and deficiency among obese adolescents Lenders, C. M., Feldman, H. A., Von, Scheven E., Merewood, A., Sweeney, C., Wilson, D. M., Lee, P. D., Abrams, S. H., Gitelman, S. E., Wertz, M. S., Klish, W. J., Taylor, G. A., Chen, T. C., and Holick, M. F. 2009 *Am.J.Clin.Nutr.*
368. Safety of vitamin A Bendich, A. and Langseth, L. 1989 *Am.J Clin Nutr*
369. Periconceptional vitamin A use: how much is teratogenic? Miller, R. K., Hendrickx, A. G., Mills, J. L., Hummler, H., and Wiegand, U. W. 1998 *Reprod.Toxicol.*
370. Safety of vitamin A: recent results Wiegand, U. W., Hartmann, S., and Hummler, H. 1998 *Int.J Vitam.Nutr Res.*
371. Effect of vitamin A supplementation on childhood morbidity and mortality Chowdhury, S., Kumar, R., Ganguly, N. K., Kumar, L., and Walia, B. N. 2002 *Indian J Med.Sci*
372. Vitamin A for the treatment of children with measles--a systematic review D'Souza, R. M. and D'Souza, R. 2002 *J Trop.Pediatr.*
373. Multiple high dose vitamin A supplementation. A report on five cases Rosales, F. J. and Kjolhede, C. L. 1993 *Trop.Geogr.Med.*
374. Recommendations for vitamin A supplementation Ross, D. A. 2002 *J Nutr*
375. The vitamin A spectrum: from deficiency to toxicity Russell, R. M. 2000 *Am.J Clin Nutr*
376. Plant sources of provitamin A and human nutriture Solomons, N. W. and Bulux, J. 1993 *Nutr Rev.*
377. Consequences of revised estimates of carotenoid bioefficacy for dietary control of vitamin A deficiency in developing countries West, C. E., Eilander, A., and van Lieshout, M. 2002 *J Nutr*
378. Vitamin A antagonizes calcium response to vitamin D in man Johansson, S. and Melhus, H. 2001 *J Bone Miner.Res.*
379. Serum retinol levels and the risk of fracture Michaelsson, K., Lithell, H., Vessby, B., and Melhus, H. 1-23-2003 *N Engl.J Med.*
380. Vitamin A intake and hip fractures among postmenopausal women Feskanich, D., Singh, V., Willett, W. C., and Colditz, G. A. 1-2-2002 *JAMA*
381. Retinol intake and bone mineral density in the elderly: the Rancho Bernardo Study Promislow, J. H., Goodman-Gruen, D., Slymen, D. J., and Barrett-Connor, E. 2002 *J Bone Miner.Res.*
382. Hypervitaminosis A and bone Binkley, N. and Krueger, D. 2000 *Nutr Rev.*
383. Plasma folate concentrations and colorectal cancer risk: A case-control study nested within the Shanghai Men's Health Study Takata, Y., Shrubsole, M. J., Li, H., Cai, Q., Gao, J., Wagner, C., Wu, J., Zheng, W., Xiang, Y. B., and Shu, X. O. 4-2-2014 *Int.J.Cancer*
384. The failure of cancer chemoprevention Potter, J. D. 4-12-2014 *Carcinogenesis*
385. Folic acid fortification and colorectal cancer risk Keum, N. and Giovannucci, E. L. 2014 *Am.J.Prev.Med.*
386. [Dietary supplements as a treatment for cervical cancer: a systematic review] Arellano Ortiz, A. L., Jimenez, Vega F., and Salcedo, Vargas M. 2013 *Nutr.Hosp.*
387. Folic acid supplementation promotes mammary tumor progression in a rat model Deghan, Manshadi S., Ishiguro, L., Sohn, K. J., Medline, A., Renlund, R., Croxford, R., and Kim, Y. I. 2014 *PLoS.One.*
388. The importance of the blood levels of homocysteine, folic acid and vitamin B12 in children with malignant diseases Aleksic, D., Djokic, D., Golubicic, I., Jakovljevic, V., and Djuric, D. 2013 *J.BUON.*
389. Folate intake and the risk of upper gastrointestinal cancers: a systematic review and meta-analysis Tio, M., Andrici, J., Cox, M. R., and Eslick, G. D. 2014 *J.Gastroenterol.Hepatol.*
390. Unmetabolized folic acid in serum: acute studies in subjects consuming fortified food and supplements Kelly, P., McPartlin, J., Goggins, M., Weir, D. G., and Scott, J. M. 1997 *Am.J.Clin.Nutr.*
391. Folate Metabolism and Human Reproduction Thaler, C. J. 2014 *Geburtshilfe Frauenheilkd.*
392. C677T mutation in methylenetetrahydrofolate reductase gene and neural tube defects: should Japanese women undergo gene screening before pregnancy? Kondo, A., Fukuda, H., Matsuo, T., Shinozaki, K., and Okai, I. 2014 *Congenit.Anom.(Kyoto)*
393. Epigenetic profiles in children with a neural tube defect; a case-control study in two populations Stolk, L., Bouwland-Both, M. I., van Mil, N. H., Verbiest, M. M., Eilers, P. H., Zhu, H., Suarez, L., Uitterlinden, A. G., and Steegers-Theunissen, R. P. 2013 *PLoS.One.*
394. [Metafolin--alternative for folate deficiency supplementation in pregnant women] Seremak-Mrozikiewicz, A. 2013 *Ginekol.Pol.*
395. Folic acid handling by the human gut: implications for food fortification and supplementation Patanwala, I., King, M. J., Barrett, D. A., Rose, J., Jackson, R., Hudson, M., Philo, M., Dainty, J. R., Wright, A. J., Finglas, P. M., and Jones, D. E. 6-18-2014 *Am.J.Clin.Nutr.*
396. The extremely slow and variable activity of dihydrofolate reductase in human liver and its implications for high folic acid intake Bailey, S. W. and Ayling, J. E. 9-8-2009 *Proc.Natl.Acad.Sci.U.S.A*

397. Is folic acid good for everyone? Smith, A. D., Kim, Y. I., and Refsum, H. 2008 *Am.J.Clin.Nutr.*
398. Unmetabolized folic acid in plasma is associated with reduced natural killer cell cytotoxicity among postmenopausal women Troen, A. M., Mitchell, B., Sorensen, B., Wener, M. H., Johnston, A., Wood, B., Selhub, J., McTiernan, A., Yasui, Y., Oral, E., Potter, J. D., and Ulrich, C. M. 2006 *J.Nutr.*
399. Unmetabolized folic acid prevalence is widespread in the older Irish population despite the lack of a mandatory fortification program Boilson, A., Staines, A., Kelleher, C. C., Daly, L., Shirley, I., Shrivastava, A., Bailey, S. W., Alverson, P. B., Ayling, J. E., McDermott, A. P., MacCooey, A., Scott, J. M., and Sweeney, M. R. 2012 *Am.J.Clin.Nutr.*
400. Circulating unmetabolized folic Acid: relationship to folate status and effect of supplementation Tam, C., O'Connor, D., and Koren, G. 2012 *Obstet.Gynecol.Int.*
401. Serum unmetabolized folic acid in a nationally representative sample of adults ≥ 60 years in the United States, 2001-2002 Bailey, R. L., Mills, J. L., Yetley, E. A., Gahche, J. J., Pfeiffer, C. M., Dwyer, J. T., Dodd, K. W., Sempos, C. T., Betz, J. M., and Picciano, M. F. 2012 *Food Nutr.Res.*
402. Concentrations of unmetabolized folic acid and primary folate forms in pregnant women at delivery and in umbilical cord blood Obeid, R., Kasoha, M., Kirsch, S. H., Munz, W., and Herrmann, W. 2010 *Am.J.Clin.Nutr.*
403. Concentrations of unmetabolized folic acid and primary folate forms in plasma after folic acid treatment in older adults Obeid, R., Kirsch, S. H., Kasoha, M., Eckert, R., and Herrmann, W. 2011 *Metabolism*
404. Maternal high folic acid supplement promotes glucose intolerance and insulin resistance in male mouse offspring fed a high-fat diet Huang, Y., He, Y., Sun, X., He, Y., Li, Y., and Sun, C. 2014 *Int.J.Mol.Sci.*
405. Vitamin D, folate, and potential early lifecycle environmental origin of significant adult phenotypes Lucock, M., Yates, Z., Martin, C., Choi, J. H., Boyd, L., Tang, S., Naumovski, N., Furst, J., Roach, P., Jablonski, N., Chaplin, G., and Veysey, M. 2014 *Evol.Med.Public Health*
406. Folic acid supplementation in pregnancy: Are there devils in the detail? Burdge, G. C. and Lillycrop, K. A. 12-14-2012 *Br.J.Nutr.*
407. Excess folate during adolescence suppresses thyroid function with permanent deficits in motivation and spatial memory Sittig, L. J., Herzing, L. B., Xie, H., Batra, K. K., Shukla, P. K., and Redei, E. E. 2012 *Genes Brain Behav.*
408. High dose folic acid supplementation of rats alters synaptic transmission and seizure susceptibility in offspring Giroto, F., Scott, L., Avchalumov, Y., Harris, J., Iannatone, S., Drummond-Main, C., Tobias, R., Bello-Espinosa, L., Rho, J. M., Davidsen, J., Teskey, G. C., and Colicos, M. A. 2013 *Sci.Rep.*
409. High folate and low vitamin B-12 intakes during pregnancy are associated with small-for-gestational age infants in South Indian women: a prospective observational cohort study Dwarkanath, P., Barzilay, J. R., Thomas, T., Thomas, A., Bhat, S., and Kurpad, A. V. 2013 *Am.J.Clin.Nutr.*
410. Prenatal folic acid and risk of asthma in children: a systematic review and meta-analysis Crider, K. S., Cordero, A. M., Qi, Y. P., Mulinare, J., Dowling, N. F., and Berry, R. J. 2013 *Am.J.Clin.Nutr.*
411. Folic Acid supplementation and pregnancy: more than just neural tube defect prevention Greenberg, J. A., Bell, S. J., Guan, Y., and Yu, Y. H. 2011 *Rev.Obstet.Gynecol.*
412. Multivitamin Supplementation During Pregnancy: Emphasis on Folic Acid and L-Methylfolate Greenberg, J. A. and Bell, S. J. 2011 *Rev.Obstet.Gynecol.*
413. The methylfolate axis in neural tube defects: in vitro characterisation and clinical investigation Lucock, M. D., Wild, J., Schorah, C. J., Levene, M. I., and Hartley, R. 1994 *Biochem.Med.Metab Biol.*
414. Folate status in various pathophysiological conditions Wani, N. A., Hamid, A., and Kaur, J. 2008 *IUBMB.Life*
415. How folate metabolism affects colorectal cancer development and treatment; a story of heterogeneity and pleiotropy Jennings, B. A. and Willis, G. 1-28-2015 *Cancer Lett.*
416. Folic acid supplementation promotes mammary tumor progression in a rat model Deghan, Manshadi S., Ishiguro, L., Sohn, K. J., Medline, A., Renlund, R., Croxford, R., and Kim, Y. I. 2014 *PLoS.One.*
417. Cancer risk with folic acid supplements: a systematic review and meta-analysis Wien, T. N., Pike, E., Wisloff, T., Staff, A., Smeland, S., and Klemp, M. 2012 *BMJ Open.*
418. Effect of maternal and postweaning folic acid supplementation on mammary tumor risk in the offspring Ly, A., Lee, H., Chen, J., Sie, K. K., Renlund, R., Medline, A., Sohn, K. J., Croxford, R., Thompson, L. U., and Kim, Y. I. 2-1-2011 *Cancer Res.*
419. Mandatory fortification with folic acid in the United States appears to have adverse effects on histone methylation in women with pre-cancer but not in women free of pre-cancer Piyathilake, C. J., Macaluso, M., Celedonio, J. E., Badiga, S., Bell, W. C., and Grizzle, W. E. 2010 *Int.J.Womens Health*
420. Cancer incidence and mortality after treatment with folic acid and vitamin B12 Ebbing, M., Bonna, K. H., Nygard, O., Arnesen, E., Ueland, P. M., Nordrehaug, J. E., Rasmussen, K., Njolstad, I., Refsum, H., Nilsen, D. W., Tverdal, A., Meyer, K., and Vollset, S. E. 11-18-2009 *JAMA*
421. Folic acid fortification: a double-edged sword Lucock, M. and Yates, Z. 2009 *Curr.Opin.Clin.Nutr.Metab Care*
422. Folate intake and bowel cancer risk Mathers, J. C. 2009 *Genes Nutr.*
423. Control of mucosal polymicrobial populations by innate immunity Mason, K. L. and Huffnagle, G. B. 2009 *Cell Microbiol.*
424. [Folic acid fortification: prevention as well as promotion of cancer] Kloosterman, J., de Jong N., Rempelberg, C. J., van Kranen, H. J., Kampman, E., and Ocke, M. C. 7-1-2006 *Ned.Tijdschr.Geneeskd.*
425. Dietary folate and related micronutrients, folate-metabolising genes, and ovarian cancer survival Dixon, S. C., Ibiebele, T. I., Protani, M. M., Beesley, J., deFazio, A., Crandon, A. J., Gard, G. B., Rome, R. M., Webb, P. M., and Nagle, C. M. 2014 *Gynecol.Oncol.*
426. Altered folate availability modifies the molecular environment of the human colorectum: implications for colorectal carcinogenesis Protiva, P., Mason, J. B., Liu, Z., Hopkins, M. E., Nelson, C., Marshall, J. R., Lambrecht, R. W., Pendyala, S., Kopelovich, L., Kim, M., Kleinstein, S. H., Laird, P. W., Lipkin, M., and Holt, P. R. 2011 *Cancer Prev.Res.(Phila)*

427. Folate intake, alcohol use, and postmenopausal breast cancer risk in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial Stolzenberg-Solomon, R. Z., Chang, S. C., Leitzmann, M. F., Johnson, K. A., Johnson, C., Buys, S. S., Hoover, R. N., and Ziegler, R. G. 2006 *Am.J.Clin.Nutr.*
428. Effect of marginal ascorbic acid deficiency on saliva level of cortisol in the guinea pig Enwonwu, C. O., Sawiris, P., and Chanaud, N. 1995 *Arch.Oral Biol.*
429. The role of ascorbic acid in the function of the adrenal cortex: studies in adrenocortical cells in culture Hornsby, P. J., Harris, S. E., and Aldern, K. A. 1985 *Endocrinology*
430. Influence of vitamin C status on the urinary excretion of catecholamines in stress Kallner, A. 1983 *Hum.Nutr.Clin.Nutr.*
431. Effects of ascorbic acid deficiency on adrenal mitochondrial hydroxylations in guinea pigs Bjorkhem, I., Kallner, A., and Karlmar, K. E. 1978 *J.Lipid Res.*
432. Evidence for an in vivo role of insulin-like growth factor-binding protein-1 and -2 as inhibitors of collagen gene expression in vitamin C-deficient and fasted guinea pigs Gosiewska, A., Wilson, S., Kwon, D., and Peterkofsky, B. 1994 *Endocrinology*
433. [Vitamin C: structure-activity correlation and cytoprotective actions through free radical scavenging and extracellular matrix construction] Kaneko, K., Nagao, N., and Miwa, N. 1999 *Nippon Rinsho*
434. Further investigations on the role of ascorbic acid in stratum corneum lipid models after UV exposure Trommer, H., Bottcher, R., Huschka, C., Wohlrab, W., and Neubert, R. H. 2005 *J.Pharm.Pharmacol.*
435. Vitamin C enhances differentiation of a continuous keratinocyte cell line (REK) into epidermis with normal stratum corneum ultrastructure and functional permeability barrier Pasonen-Seppanen, S., Suhonen, T. M., Kirjavainen, M., Suihko, E., Urtti, A., Miettinen, M., Hyttinen, M., Tammi, M., and Tammi, R. 2001 *Histochem.Cell Biol.*
436. The formation of competent barrier lipids in reconstructed human epidermis requires the presence of vitamin C Ponec, M., Weerheim, A., Kempenaar, J., Mulder, A., Gooris, G. S., Bouwstra, J., and Mommaas, A. M. 1997 *J.Invest Dermatol.*
437. Long-term effects of inadequate and excessive dietary ascorbate on bile acid metabolism in the guinea pig Holloway, D. E. and Rivers, J. M. 1984 *J.Nutr.*
438. Vitamin C in the control of hypercholesterolemia in man Ginter, E., Bobek, P., Kubec, F., Vozar, J., and Urbanova, D. 1982 *Int.J.Vitam.Nutr.Res.Suppl*
439. Influence of chronic ascorbic acid deficiency and excessive ascorbic acid intake on bile acid metabolism and bile composition in the guinea pig Holloway, D. E. and Rivers, J. M. 1981 *J.Nutr.*
440. Hypocholesterolemic effect of ascorbic acid in maturity-onset diabetes mellitus Ginter, E., Zdichynec, B., Holzerova, O., Ticha, E., Kobza, R., Koziakova, M., Cerna, O., Ozdin, L., Hruba, F., Novakova, V., Sasko, E., and Gaher, M. 1978 *Int.J.Vitam.Nutr.Res.*
441. Serum bile acids in man during vitamin C supplementation and restriction Kallner, A. 1977 *Acta Med.Scand.*
442. Seasonal variation of risk factors for cardiovascular disease and diet in older adults Woodhouse, P. R. and Khaw, K. T. 2000 *Int.J.Circumpolar.Health*
443. Plasminogen activator inhibitor-1, the acute phase response and vitamin C Woodhouse, P. R., Meade, T. W., and Khaw, K. T. 1997 *Atherosclerosis*
444. Interrelation of vitamin C, infection, haemostatic factors, and cardiovascular disease Khaw, K. T. and Woodhouse, P. 6-17-1995 *BMJ*
445. Plasma vitamin C level, fruit and vegetable consumption, and the risk of new-onset type 2 diabetes mellitus: the European prospective investigation of cancer--Norfolk prospective study Harding, A. H., Wareham, N. J., Bingham, S. A., Khaw, K., Luben, R., Welch, A., and Forouhi, N. G. 7-28-2008 *Arch.Intern.Med.*
446. Plasma vitamin C concentrations predict risk of incident stroke over 10 y in 20 649 participants of the European Prospective Investigation into Cancer Norfolk prospective population study Myint, P. K., Luben, R. N., Welch, A. A., Bingham, S. A., Wareham, N. J., and Khaw, K. T. 2008 *Am.J.Clin.Nutr.*
447. Plasma concentrations of ascorbic acid and C-reactive protein, and risk of future coronary artery disease, in apparently healthy men and women: the EPIC-Norfolk prospective population study Boekholdt, S. M., Meuwese, M. C., Day, N. E., Luben, R., Welch, A., Wareham, N. J., and Khaw, K. T. 2006 *Br.J.Nutr.*
448. Dietary antioxidants and asthma in adults Patel, B. D., Welch, A. A., Bingham, S. A., Luben, R. N., Day, N. E., Khaw, K. T., Lomas, D. A., and Wareham, N. J. 2006 *Thorax*
449. Plasma ascorbic acid concentrations and fat distribution in 19,068 British men and women in the European Prospective Investigation into Cancer and Nutrition Norfolk cohort study Canoy, D., Wareham, N., Welch, A., Bingham, S., Luben, R., Day, N., and Khaw, K. T. 2005 *Am.J.Clin.Nutr.*
450. Plasma vitamin C, cancer mortality and incidence in men and women: a prospective study Luben, R., Khaw, K. T., Welch, A., Bingham, S., Wareham, N., Oakes, S., and Day, N. E. 2002 *IARC Sci.Publ.*
451. Relation between plasma ascorbic acid and mortality in men and women in EPIC-Norfolk prospective study: a prospective population study. European Prospective Investigation into Cancer and Nutrition Khaw, K. T., Bingham, S., Welch, A., Luben, R., Wareham, N., Oakes, S., and Day, N. 3-3-2001 *Lancet*
452. Vitamin C and hyperglycemia in the European Prospective Investigation into Cancer--Norfolk (EPIC-Norfolk) study: a population-based study Sargeant, L. A., Wareham, N. J., Bingham, S., Day, N. E., Luben, R. N., Oakes, S., Welch, A., and Khaw, K. T. 2000 *Diabetes Care*
453. Is ascorbate in human tears from corneal leakage or from lacrimal secretion? Choy, C. K., Benzie, I. F., and Cho, P. 2004 *Clin.Exp.Optom.*
454. Antioxidants in tears and plasma: Inter-relationships and effect of vitamin C supplementation Choy, C., Benzie, I., and Cho, P. 2003 *Curr.Eye Res.*
455. Salivary antioxidants and periodontal disease status Sculley, D. V. and Langley-Evans, S. C. 2002 *Proc.Nutr.Soc.*
456. Ascorbate deficiency impairs the muscarinic-cholinergic and ss-adrenergic receptor signaling systems in the guinea pig submandibular salivary gland Sawiris, P. G. and Enwonwu, C. O. 2000 *J.Nutr.*

457. [Inhibitory effects of serotonin and sodium ascorbate on the oxidative aggregation of lipoproteins] Petrenko, IuM, Titov, V. I., and Vladimirov, IuA 2000 Eksp.Klin.Farmakol.
458. Do iron and vitamin C co-supplementation influence platelet function or LDL oxidizability in healthy volunteers? Yang, M., Collis, C. S., Kelly, M., Diplock, A. T., and Rice-Evans, C. 1999 Eur.J.Clin.Nutr.
459. Ascorbic acid and total vitamin C concentrations in plasma, gastric juice, and gastrointestinal mucosa: effects of gastritis and oral supplementation Waring, A. J., Drake, I. M., Schorah, C. J., White, K. L., Lynch, D. A., Axon, A. T., and Dixon, M. F. 1996 Gut
460. Ascorbate on cell growth and differentiation Alcain, F. J. and Buron, M. I. 1994 J.Bioenerg.Biomembr.
461. Ascorbate status and xerostomia Enwonwu, C. O. 1992 Med.Hypotheses
462. Ascorbic acid requirement for optimal flexor tendon repair in vitro Russell, J. E. and Manske, P. R. 1991 J.Orthop.Res.
463. The time-course of oxytocin secretion from cultured bovine granulosa cells, stimulated by ascorbate and catecholamines Luck, M. R. and Jungclas, B. 1988 J.Endocrinol.
464. Induction of collagen synthesis by ascorbic acid. A possible mechanism Pinnel, S. R., Murad, S., and Darr, D. 1987 Arch.Dermatol.
465. Ascorbic acid enhances the release of luteinizing hormone-releasing hormone from the mediobasal hypothalamus in vitro Miller, B. T. and Cicero, T. J. 12-22-1986 Life Sci.
466. The Role of Histamine in Mental Illness and its Attenuation with Vitamin C Jensen, R 2005
467. Dietary risk factors for inflammatory bowel disease: a multicenter case-control study in Japan Sakamoto, N., Kono, S., Wakai, K., Fukuda, Y., Satomi, M., Shimoyama, T., Inaba, Y., Miyake, Y., Sasaki, S., Okamoto, K., Kobashi, G., Washio, M., Yokoyama, T., Date, C., and Tanaka, H. 2005 Inflamm.Bowel.Dis.
468. Effects of free radicals and leukocytes on increases in blood-brain barrier permeability during colitis Hathaway, C. A., Percy, W. H., and Williams, J. L. 2000 Dig.Dis.Sci.
469. Depleted mucosal antioxidant defences in inflammatory bowel disease Buffinton, G. D. and Doe, W. F. 1995 Free Radic.Biol.Med.
470. Altered ascorbic acid status in the mucosa from inflammatory bowel disease patients Buffinton, G. D. and Doe, W. F. 1995 Free Radic.Res.
471. Vitamin C status, glutathione and histamine in gastric carcinoma, tuberculous enteritis and non-specific ulcerative colitis Dubey, S. S., Sinha, K. K., and Gupta, J. P. 1985 Indian J.Physiol Pharmacol.
472. Vitamin C and gastroduodenal disorders Esposito, R. and Valentini, R. 4-13-1968 Br.Med.J.
473. Effect of oral administration of vitamin C on human aqueous humor ascorbate concentration Iqbal, Z., Midgley, J. M., Watson, D. G., Karditsas, S. D., Dutton, G. N., and Wilson, W. S. 1999 Zhongguo Yao Li Xue.Bao.
474. A physiological level of ascorbate inhibits galactose cataract in guinea pigs by decreasing polyol accumulation in the lens epithelium: a dehydroascorbate-linked mechanism Yokoyama, T., Sasaki, H., Giblin, F. J., and Reddy, V. N. 1994 Exp.Eye Res.
475. Associations between nutrition and cataract Taylor, A. 1989 Nutr.Rev.
476. Ascorbic acid and the eye lens Varma, S. D. and Richards, R. D. 1988 Ophthalmic Res.
477. Vitamin C in the human aqueous humor and cataracts Chandra, D. B., Varma, R., Ahmad, S., and Varma, S. D. 1986 Int.J.Vitam.Nutr.Res.
478. Inflammation in the vascular bed: importance of vitamin C Aguirre, R. and May, J. M. 2008 Pharmacol.Ther.
479. The planetary biology of ascorbate and uric acid and their relationship with the epidemic of obesity and cardiovascular disease Johnson, R. J., Gaucher, E. A., Sautin, Y. Y., Henderson, G. N., Angerhofer, A. J., and Benner, S. A. 2008 Med.Hypotheses
480. How does ascorbic acid prevent endothelial dysfunction? May, J. M. 5-1-2000 Free Radic.Biol.Med.
481. Effect of vitamin C on ambulatory blood pressure and plasma lipids in older persons Fotherby, M. D., Williams, J. C., Forster, L. A., Craner, P., and Ferns, G. A. 2000 J.Hypertens.
482. Does vitamin C reduce blood pressure? Results of a large study of people aged 65 or older Bates, C. J., Walmsley, C. M., Prentice, A., and Finch, S. 1998 J.Hypertens.
483. Are diabetic neuropathy, retinopathy and nephropathy caused by hyperglycemic exclusion of dehydroascorbate uptake by glucose transporters? Root-Bernstein, R., Busik, J. V., and Henry, D. N. 6-7-2002 J.Theor.Biol.
484. Inhibition of aldose reductase in human erythrocytes by vitamin C Vincent, T. E., Mendiratta, S., and May, J. M. 1999 Diabetes Res.Clin.Pract.
485. Effect of ascorbic acid deficiency on primary and reparative dentinogenesis in non-ascorbate-synthesizing ODS rats Ogawara, M., Aoki, K., Okiji, T., and Suda, H. 1997 Arch.Oral Biol.
486. Effects of ascorbate-deficiency on collagen secretion and resorption in cultured mouse incisor germs Amar, S., Fabre, M., and Ruch, J. V. 1992 Connect.Tissue Res.
487. The role of ascorbic acid on the structural integrity of developing tooth germs Levenson, G. E. and Schiltz, J. R. 1979 J.Biol.Buccale
488. Periodontal disease is associated with lower antioxidant capacity in whole saliva and evidence of increased protein oxidation Sculley, D. V. and Langley-Evans, S. C. 2003 Clin.Sci.(Lond)
489. Diabetes and periodontal diseases. Possible role of vitamin c deficiency: an hypothesis Aleo, J. J. 1981 J.Periodontol.
490. High-dose vitamin C supplementation accelerates the Achilles tendon healing in healthy rats Omeroglu, S., Peker, T., Turkozkan, N., and Omeroglu, H. 2009 Arch.Orthop.Trauma Surg.
491. Ascorbate synthesis pathway: dual role of ascorbate in bone homeostasis Gabbay, K. H., Bohren, K. M., Morello, R., Bertin, T., Liu, J., and Vogel, P. 6-18-2010 J.Biol.Chem.
492. Effect of pre-loading oral glucosamine HCl/chondroitin sulfate/manganese ascorbate combination on experimental arthritis in rats Beren, J., Hill, S. L., ener-West, M., and Rose, N. R. 2001 Exp.Biol.Med.(Maywood.)
493. Ascorbate availability and neurodegeneration in amyotrophic lateral sclerosis Kok, A. B. 1997 Med.Hypotheses

494. Treatment of chronic autoimmune thrombocytopenic purpura with ascorbate Godeau, B. and Bierling, P. 1990 Br.J.Haematol.
495. The vitamin C treatment of allergy and the normally unprimed state of antibodies Cathcart, R. F., III 1986 Med.Hypotheses
496. Vitamin C and immunity: natural killer (NK) cell factor Siegel, B. V. and Morton, J. I. 1983 Int.J.Vitam.Nutr.Res.
497. The effect of hypothyroidism, hyperthyroidism, and their treatment on parameters of oxidative stress and antioxidant status Erdamar, H., Demirci, H., Yaman, H., Erbil, M. K., Yakar, T., Sancak, B., Elbeg, S., Biberoglu, G., and Yetkin, I. 2008 Clin.Chem.Lab Med.
498. Mechanism of action of vitamin C in sepsis: ascorbate modulates redox signaling in endothelium Wilson, J. X. 2009 Biofactors
499. Vitamin C: from popular food supplement to specific drug Goldenberg, H. 2003 Forum Nutr.
500. Serum ascorbic acid concentration in patients with acute Falciparum malaria infection: possible significance Hassan, G. I., Gregory, U., and Maryam, H. 2004 Braz.J.Infect.Dis.
501. Vitamin C for preventing and treating the common cold Douglas, R. M., Hemila, H., Chalker, E., and Treacy, B. 2007 Cochrane.Database.Syst.Rev.
502. Randomised double-blind trial of the effect of vitamin C on dyspareunia and vaginal discharge in women receiving doxycycline and triple sulfa for chlamydial cervicitis Khajehei, M., Keshavarz, T., and Tabatabaee, H. R. 2009 Aust.N.Z.J.Obstet.Gynaecol.
503. Oxidative stress in Helicobacter pylori infection: does supplementation with vitamins C and E increase the eradication rate? Sezikli, M., Cetinkaya, Z. A., Sezikli, H., Guzelbulut, F., Tiftikci, A., Ince, A. T., Gokden, Y., Yasar, B., Atalay, S., and Kurdas, O. O. 2009 Helicobacter.
504. Effect of addition of vitamin C to clarithromycin-amoxicillin-omeprazol triple regimen on Helicobacter pylori eradication Kaboli, S. A., Zojaji, H., Mirsattari, D., Talaie, R., Derakhshan, F., Zali, M. R., and Sheikhvatan, M. 2009 Acta Gastroenterol.Belg.
505. High dose of ascorbic acid induces cell death in mesothelioma cells Takemura, Y., Satoh, M., Satoh, K., Hamada, H., Sekido, Y., and Kubota, S. 4-2-2010 Biochem.Biophys.Res.Comm.
506. Pharmacologic concentrations of ascorbate are achieved by parenteral administration and exhibit antitumoral effects Verrax, J. and Calderon, P. B. 7-1-2009 Free Radic.Biol.Med.
507. Pharmacokinetics of vitamin C: insights into the oral and intravenous administration of ascorbate Duconge, J., Miranda-Massari, J. R., Gonzalez, M. J., Jackson, J. A., Warnock, W., and Riordan, N. H. 2008 P.R.Health Sci.J.
508. Pharmacokinetics of oral vitamin C Hickey, Stephen, Roberts, Hilary J., and Miller, Nicholas J. 1-1-2008 Journal of Nutritional and Environmental Medicine
509. [Lipid peroxidation as a common pathomechanism in coronary heart disease and Alzheimer disease] Artl, S., Kontush, A., Muller-Thomsen, T., and Beisiegel, U. 2001 Z.Gerontol.Geriatr.
510. Interaction of dietary antioxidants in vivo: how fruit and vegetables prevent disease? Eastwood, M. A. 1999 QJM.
511. The key role of histamine in the development of atherosclerosis and coronary heart disease Clemetson, C. A. 1999 Med.Hypotheses
512. Vitamin C deficiency and risk of myocardial infarction: prospective population study of men from eastern Finland Nyyssonen, K., Parviainen, M. T., Salonen, R., Tuomilehto, J., and Salonen, J. T. 3-1-1997 BMJ
513. Oxidants, antioxidants, and the degenerative diseases of aging Ames, B. N., Shigenaga, M. K., and Hagen, T. M. 9-1-1993 Proc.Natl.Acad.Sci.U.S.A
514. Vitamin C deficiency is an under-diagnosed contributor to degenerative disc disease in the elderly Smith, V. H. 2010 Med.Hypotheses
515. Dietary ascorbate intake affects steady state tissue concentrations in vitamin C-deficient mice: tissue deficiency after suboptimal intake and superior bioavailability from a food source (kiwifruit) Vissers, M. C., Bozonet, S. M., Pearson, J. F., and Braithwaite, L. J. 2011 Am.J.Clin.Nutr.
516. [Free radicals in the central nervous system] Rokyta, R., Racek, J., and Holecek, V. 1996 Cesk.Fysiol.
517. Decreased plasma and tissue levels of vitamin C in a rat model of aging: implications for antioxidative defense van der Loo, B., Bachschmid, M., Spitzer, V., Brey, L., Ullrich, V., and Luscher, T. F. 4-4-2003 Biochem.Biophys.Res.Comm.
518. Vitamin C in human and guinea pig aqueous, lens and plasma in relation to intake Taylor, A., Jacques, P. F., Nowell, T., Perrone, G., Blumberg, J., Handelman, G., Jozwiak, B., and Nadler, D. 1997 Curr.Eye Res.
519. Effect of vitamin C upon gastric mucosal O6-alkyltransferase activity and on gastric vitamin C levels Dyke, G. W., Craven, J. L., Hall, R., and Garner, R. C. 11-11-1994 Cancer Lett.
520. Tissue levels and optimum dosage of vitamin C in guinea pigs Ginter, E., Bobek, P., and Vargova, D. 1979 Nutr.Metab
521. Effectiveness of antioxidants (vitamin C and E) with and without sunscreens as topical photoprotectants Darr, D., Dunston, S., Faust, H., and Pinnell, S. 1996 Acta Derm.Venereol.
522. Ascorbic acid and atherosclerotic cardiovascular disease Lynch, S. M., Gaziano, J. M., and Frei, B. 1996 Subcell.Biochem.
523. Vitamin C status is related to proinflammatory responses and impaired vascular endothelial function in healthy, college-aged lean and obese men Mah, E., Matos, M. D., Kawiecki, D., Ballard, K., Guo, Y., Volek, J. S., and Bruno, R. S. 2011 J.Am.Diet.Assoc.
524. Effect of phyloquinone supplementation on glucose homeostasis in humans Kumar, R., Binkley, N., and Vella, A. 2010 Am.J.Clin.Nutr.
525. Is vitamin K consumption associated with cardio-metabolic disorders? A systematic review Rees, K., Guraewal, S., Wong, Y. L., Majanbu, D. L., Mavrodaris, A., Stranges, S., Kandala, N. B., Clarke, A., and Franco, O. H. 2010 Maturitas

526. Dietary phyloquinone intakes and metabolic syndrome in US young adults Pan, Y. and Jackson, R. T. 2009 *J.Am.Coll.Nutr.*
527. Effect of vitamin K supplementation on insulin resistance in older men and women Yoshida, M., Jacques, P. F., Meigs, J. B., Saltzman, E., Shea, M. K., Gundberg, C., Dawson-Hughes, B., Dallal, G., and Booth, S. L. 2008 *Diabetes Care*
528. Phyloquinone intake, insulin sensitivity, and glycemic status in men and women Yoshida, M., Booth, S. L., Meigs, J. B., Saltzman, E., and Jacques, P. F. 2008 *Am.J.Clin.Nutr.*
529. Long-chain n-3 fatty acids specifically affect rat coagulation factors dependent on vitamin K: relation to peroxidative stress Leray, C., Wiesel, M. L., Freund, M., Cazenave, J. P., and Gachet, C. 2001 *Arterioscler.Thromb.Vasc.Biol.*
530. Vitamin K nutrition and osteoporosis Binkley, N. C. and Suttie, J. W. 1995 *J.Nutr.*
531. Vitamin K intake and hip fractures in women: a prospective study Feskanich, D., Weber, P., Willett, W. C., Rockett, H., Booth, S. L., and Colditz, G. A. 1999 *Am.J.Clin.Nutr.*
532. Effect of combined administration of vitamin D3 and vitamin K2 on bone mineral density of the lumbar spine in postmenopausal women with osteoporosis Iwamoto, J., Takeda, T., and Ichimura, S. 2000 *J Orthop.Sci.*
533. Effects of vitamin K on bone mass and bone metabolism Vermeer, C., Gijssbers, B. L., Craciun, A. M., Groenen-van Dooren, M. M., and Knapen, M. H. 1996 *J Nutr*
534. [Antithrombotic agents and diabetes. Benefits and recommendations for use] Guillausseau, P. J. and Dupuy, E. 1996 *Arch.Mal Coeur Vaiss.*
535. Red blood cell deformability in diabetes mellitus: effect of phytomenadione Sabo, A., Jakovljevic, V., Stanulovic, M., Lepsanovic, L., and Pejin, D. 1993 *Int.J.Clin.Pharmacol.Ther.Toxicol.*
536. Comparative effects of vitamin K2 and estradiol on experimental arteriosclerosis with diabetes mellitus Seyama, Y., Kimoto, S., Marukawa, Y., Horiuchi, M., Hayashi, M., and Usami, E. 2000 *Int.J.Vitam.Nutr.Res.*
537. Fat-soluble vitamin deficiency in infants and children Argao, E. A. and Heubi, J. E. 1993 *Curr.Opin.Pediatr.*
538. Bones and Crohn's: problems and solutions Buchman, A. L. 1999 *Inflamm.Bowel.Dis.*
539. [Vitamin K: biochemistry, function, and deficiency. Review] Mijares, M. E., Nagy, E., Guerrero, B., and Arocha-Pinango, C. L. 1998 *Invest Clin.*
540. Corn oil-induced decrease in arterial thrombosis tendency may be related to altered plasma vitamin K transport Schurgers, L. J. and Vermeer, C. 2001 *J Lipid Res.*
541. The role of Gla proteins in vascular calcification Shanahan, C. M., Proudfoot, D., Farzaneh-Far, A., and Weissberg, P. L. 1998 *Crit Rev.Eukaryot.Gene Expr.*
542. Skeletal functions of vitamin K-dependent proteins: not just for clotting anymore Booth, S. L. 1997 *Nutr.Rev.*
543. Effect of vitamin K2 (menaquinone-7) on bone metabolism in the femoral-metaphyseal tissues of normal and skeletal-unloaded rats: enhancement with zinc Ehara, Y., Takahashi, H., Hanahisa, Y., and Yamaguchi, M. 1996 *Res.Exp.Med.(Berl)*
544. Serum vitamin K level and bone mineral density in post-menopausal women Kanai, T., Takagi, T., Masuhiro, K., Nakamura, M., Iwata, M., and Saji, F. 1997 *Int.J.Gynaecol.Obstet.*
545. Bone health: the role of micronutrients New, S. A. 1999 *Br.Med.Bull.*
546. Impairment of gamma carboxylation of circulating osteocalcin (bone gla protein) in elderly women Plantalech, L., Guillaumont, M., Vergnaud, P., Leclercq, M., and Delmas, P. D. 1991 *J.Bone Miner.Res.*
547. Matrix Gla protein accumulates at the border of regions of calcification and normal tissue in the media of the arterial vessel wall Spronk, H. M., Soute, B. A., Schurgers, L. J., Cleutjens, J. P., Thijssen, H. H., De Mey, J. G., and Vermeer, C. 11-30-2001 *Biochem.Biophys.Res.Commun.*
548. Role of vitamin K and vitamin K-dependent proteins in vascular calcification Schurgers, L. J., Dissel, P. E., Spronk, H. M., Soute, B. A., Dhore, C. R., Cleutjens, J. P., and Vermeer, C. 2001 *Z.Kardiol.*
549. Vitamin K intake and osteocalcin levels in women with and without aortic atherosclerosis: a population-based study Jie, K. S., Bots, M. L., Vermeer, C., Witteman, J. C., and Grobbee, D. E. 1995 *Atherosclerosis*
550. Vitamin K status and bone mass in women with and without aortic atherosclerosis: a population-based study Jie, K. G., Bots, M. L., Vermeer, C., Witteman, J. C., and Grobbee, D. E. 1996 *Calcif.Tissue Int.*
551. Vitamin K status may be an important determinant of childhood bone health Cashman, K. D. 2005 *Nutr.Rev.*
552. Vitamin K deficiency mimicking child abuse Brousseau, T. J., Kisson, N., and McIntosh, B. 2005 *J.Emerg.Med.*
553. [Influence of nutrients intake on bone turnover markers] Katsuyama, H., Sunami, S., and Fukunaga, M. 2005 *Clin.Calcium*
554. [Vitamin D, K and bone mineral density] Okano, T. 2005 *Clin.Calcium*
555. Vitamin K in the treatment and prevention of osteoporosis and arterial calcification Adams, J. and Pepping, J. 8-1-2005 *Am.J.Health Syst.Pharm.*
556. The vitamin K-dependent carboxylase Berkner, K. L. 2005 *Annu.Rev.Nutr.*
557. Calcium and vitamin D in preventing fractures: vitamin K supplementation has powerful effect Radecki, T. E. 7-9-2005 *BMJ*
558. [The interplay of magnesium and vitamin K2 on bone mineralization] Amizuka, N., Li, M., and Maeda, T. 2005 *Clin.Calcium*
559. [Vitamin K2 and bone quality] Kobayashi, M., Hara, K., and Akiyama, Y. 2005 *Clin.Calcium*
560. [Osteoporosis and supplements] Kido, M. 2005 *Clin.Calcium*
561. [Vitamin K2 (menatetrenone) and bone quality] Iinuma, N. 2005 *Clin.Calcium*
562. [Molecular mechanisms of vitamin K action in the bone homeostasis] Ichikawa, T. and Inoue, S. 2005 *Clin.Calcium*
563. Vitamin K2 in bone metabolism and osteoporosis Plaza, S. M. and Lamson, D. W. 2005 *Altern.Med.Rev.*
564. Vitamin K2 inhibits glucocorticoid-induced bone loss partly by preventing the reduction of osteoprotegerin (OPG) Sasaki, N., Kusano, E., Takahashi, H., Ando, Y., Yano, K., Tsuda, E., and Asano, Y. 2005 *J.Bone Miner.Metab*
565. Phyloquinone intake as a marker for coronary heart disease risk but not stroke in women Erkkila, A. T., Booth, S. L., Hu, F. B., Jacques, P. F., Manson, J. E., Rexrode, K. M., Stampfer, M. J., and Lichtenstein, A. H. 2005 *Eur.J.Clin.Nutr.*

566. Ethnic differences in osteocalcin gamma-carboxylation, plasma phyloquinone (vitamin K1) and apolipoprotein E genotype Beavan, S. R., Prentice, A., Stirling, D. M., Dibba, B., Yan, L., Harrington, D. J., and Shearer, M. J. 2005 *Eur.J.Clin.Nutr.*
567. Low doses of zinc gluconate for inflammatory acne Dreno, B., Amblard, P., Agache, P., Sirot, S., and Litoux, P. 1989 *Acta Derm.Venerol.*
568. Efficacy and safety study of two zinc gluconate regimens in the treatment of inflammatory acne Meynadier, J. 2000 *Eur.J.Dermatol.*
569. Oral vitamin A in acne vulgaris. Preliminary report Kligman, A. M., Mills, O. H., Jr., Leyden, J. J., Gross, P. R., Allen, H. B., and Rudolph, R. I. 1981 *Int.J Dermatol.*
570. Vitamin A as an anti-inflammatory agent Reifen, R. 2002 *Proc.Nutr Soc.*
571. The excretion of trace metals in human sweat Cohn, J. R. and Emmett, E. A. 1978 *Ann.Clin.Lab Sci.*
572. Sweat iron and zinc losses during prolonged exercise DeRuisseau, K. C., Chevront, S. N., Haymes, E. M., and Sharp, R. G. 2002 *Int.J.Sport Nutr.Exerc.Metab*
573. Effect of dietary zinc on whole body surface loss of zinc: impact on estimation of zinc retention by balance method Milne, D. B., Canfield, W. K., Mahalko, J. R., and Sandstead, H. H. 1983 *Am.J.Clin.Nutr.*
574. Trace elements in the sweat of acclimatized persons Omokhodion, F. O. and Howard, J. M. 1994 *Clin.Chim.Acta*
575. Zinc retention and losses of zinc in sweat by preadolescent girls Ritchey, S. J., Korslund, M. K., Gilbert, L. M., Fay, D. C., and Robinson, M. F. 1979 *Am.J.Clin.Nutr.*
576. Zinc loss in sweat of athletes exercising in hot and neutral temperatures Tipton, K., Green, N. R., Haymes, E. M., and Waller, M. 1993 *Int.J.Sport Nutr.*
577. Altered zinc metabolism in mood disorder patients Little, K. Y., Castellanos, X., Humphries, L. L., and Austin, J. 1989 *Biol.Psychiatry*
578. Affective illness and zinc deficiency Innes, C. 3-16-1985 *Lancet*
579. Serum zinc in psychiatric patients Hullin, R. P. 1983 *Prog.Clin.Biol.Res.*
580. [Role of calcium, magnesium, copper and zinc in mental diseases] Castillo, A. and Ordenez, L. A. 1981 *Acta Cient.Venez.*
581. Letter: Zinc deficiency and disturbances of mood and visual behaviour Moynahan, E. J. 1-10-1976 *Lancet*
582. Effects on bone loss of manganese alone or with copper supplement in ovariectomized rats. A morphometric and densitometric study Rico, H., Gomez-Raso, N., Revilla, M., Hernandez, E. R., Seco, C., Paez, E., and Crespo, E. 2000 *Eur.J.Obstet.Gynecol.Reprod.Biol.*
583. The role of iodine in the evolution of thyroid disease in Greece: from endemic goiter to thyroid autoimmunity Fountoulakis, S., Philippou, G., and Tsatsoulis, A. 2007 *Hormones.(Athens.)*
584. High prevalence of thyroid dysfunction and autoimmune thyroiditis in adolescents after elimination of iodine deficiency in the Eastern Black Sea Region of Turkey Bastemir, M., Emral, R., Erdogan, G., and Gullu, S. 2006 *Thyroid*
585. Effect of iodine intake on thyroid diseases in China Teng, W., Shan, Z., Teng, X., Guan, H., Li, Y., Teng, D., Jin, Y., Yu, X., Fan, C., Chong, W., Yang, F., Dai, H., Yu, Y., Li, J., Chen, Y., Zhao, D., Shi, X., Hu, F., Mao, J., Gu, X., Yang, R., Tong, Y., Wang, W., Gao, T., and Li, C. 6-29-2006 *N.Engl.J.Med.*
586. [Effects of chronic administration of high doses of potassium iodide on iodine metabolism in the rat thyroid gland] Lupachik, S. V., Nadol'nik, L. I., Netsetskaia, Z. V., and Vinogradov, V. V. 2006 *Biomed.Khim.*
587. Autoimmune thyroid diseases Caturegli, P., Kimura, H., Rocchi, R., and Rose, N. R. 2007 *Curr.Opin.Rheumatol.*
588. Iodine and pregnancy: a call to action Stagnaro-Green, A. and Pearce, E. N. 5-21-2013 *Lancet*
589. Effect of inadequate iodine status in UK pregnant women on cognitive outcomes in their children: results from the Avon Longitudinal Study of Parents and Children (ALSPAC) Bath, S. C., Steer, C. D., Golding, J., Emmett, P., and Rayman, M. P. 5-21-2013 *Lancet*
590. Study links iodine deficiency in pregnancy with poor cognitive outcomes in children Loewenthal, L. 2013 *BMJ*
591. [Effects of iodine excess and selenium supplement on the levels of thyroid hormone and its receptor expression in filial cerebrum of mice] Guo, H., Feng, J., Yang, X., and Xu, J. 2007 *Wei Sheng Yan.Jiu.*
592. From selenium to selenoproteins: synthesis, identity, and their role in human health Papp, L. V., Lu, J., Holmgren, A., and Khanna, K. K. 2007 *Antioxid.Redox.Signal.*
593. The influence of selenium supplementation on postpartum thyroid status in pregnant women with thyroid peroxidase autoantibodies Negro, R., Greco, G., Mangieri, T., Pezzarossa, A., Dazzi, D., and Hassan, H. 2007 *J.Clin.Endocrinol.Metab*
594. Selenium supplement alleviated the toxic effects of excessive iodine in mice Xu, J., Yang, X. F., Guo, H. L., Hou, X. H., Liu, L. G., and Sun, X. F. 2006 *Biol.Trace Elem.Res.*
595. Selenium treatment in autoimmune thyroiditis: 9-month follow-up with variable doses Turker, O., Kumanlioglu, K., Karapolat, I., and Dogan, I. 2006 *J.Endocrinol.*
596. Selenium and antioxidant defenses as major mediators in the development of chronic heart failure de Lorgeril M. and Salen, P. 2006 *Heart Fail.Rev.*
597. The role of selenium in thyroid autoimmunity and cancer Duntas, L. H. 2006 *Thyroid*
598. Selenoprotein synthesis: UGA does not end the story Allmang, C. and Krol, A. 2006 *Biochimie*
599. Selenocysteine, soluble liver antigen/liver-pancreas, and autoimmune hepatitis Herkel, J., Manns, M. P., and Lohse, A. W. 2007 *Hepatology*
600. Myocardial ischemia-reperfusion injury, antioxidant enzyme systems, and selenium: a review Venardos, K. M. and Kaye, D. M. 2007 *Curr.Med.Chem.*
601. Decreased selenoprotein expression alters the immune response during influenza virus infection in mice Sheridan, P. A., Zhong, N., Carlson, B. A., Perella, C. M., Hatfield, D. L., and Beck, M. A. 2007 *J.Nutr.*
602. Seleno-independent glutathione peroxidases. More than simple antioxidant scavengers Herbertte, S., Roeckel-Drevet, P., and Drevet, J. R. 2007 *FEBS J.*

603. Selenium: from cancer prevention to DNA damage Letavayova, L., Vlckova, V., and Brozmanova, J. 10-3-2006 Toxicology
604. Selenium and its' role in the maintenance of genomic stability Ferguson, L. R., Karunasinghe, N., Zhu, S., and Wang, A. H. 1-5-2012 Mutat.Res.
605. Effect of selenium supplementation on glutathione peroxidase and catalase activities in senescent cultured human fibroblasts Ghneim, H. K. and Al-Sheikh, Y. A. 2011 Ann.Nutr.Metab
606. Serum selenium and single-nucleotide polymorphisms in genes for selenoproteins: relationship to markers of oxidative stress in men from Auckland, New Zealand Karunasinghe, N., Han, D. Y., Zhu, S., Yu, J., Lange, K., Duan, H., Medhora, R., Singh, N., Kan, J., Alzaher, W., Chen, B., Ko, S., Triggs, C. M., and Ferguson, L. R. 12-3-2011 Genes Nutr.
607. Effect of zinc supplementation on glutathione peroxidase activity and selenium concentration in the serum, liver and kidney of rats chronically exposed to cadmium Galazyn-Sidorczuk, M., Brzoska, M. M., Rogalska, J., Roszczenko, A., and Jurczuk, M. 11-17-2011 J.Trace Elem.Med.Biol.
608. Chromium, Selenium, and Zinc Multimineral Enriched Yeast Supplementation Ameliorates Diabetes Symptom in Streptozocin-Induced Mice Liu, J., Bao, W., Jiang, M., Zhang, Y., Zhang, X., and Liu, L. 11-12-2011 Biol.Trace Elem.Res.
609. Selenium, selenoproteins and the thyroid gland: interactions in health and disease Schomburg, L. 10-18-2011 Nat.Rev.Endocrinol.
610. Impact of Intensive Physical Activity on Selenium Status Pograjc, L., Stibilj, V., and Falnoga, I. 9-29-2011 Biol.Trace Elem.Res.
611. Determinants of selenium status in healthy adults Combs, G. F., Jr., Watts, J. C., Jackson, M. I., Johnson, L. K., Zeng, H., Scheett, A. J., Uthus, E. O., Schomburg, L., Hoeg, A., Hoefig, C. S., Davis, C. D., and Milner, J. A. 2011 Nutr.J.
612. Dietary selenomethionine increases exon-specific DNA methylation of the p53 gene in rat liver and colon mucosa Zeng, H., Yan, L., Cheng, W. H., and Uthus, E. O. 2011 J.Nutr.
613. Dietary selenium affects host selenoproteome expression by influencing the gut microbiota Kasaikina, M. V., Kravtsova, M. A., Lee, B. C., Seravalli, J., Peterson, D. A., Walter, J., Legge, R., Benson, A. K., Hatfield, D. L., and Gladyshev, V. N. 2011 FASEB J.
614. Relative and combined effects of selenium, protein deficiency and ethanol on bone Gonzalez-Perez, J. M., Gonzalez-Reimers, E., Duran-Castellon, Mdel C., Santolaria-Fernandez, F., Galindo-Martin, L., RosVilamajo, R., de la Vega-Prieto MJ, Vina-Rodriguez, J., and Abreu-Gonzalez, P. 2011 J.Trace Elem.Med.Biol.
615. Selenium Alexander, J. 2007 Novartis.Found.Symp.
616. A nutritional supplement formula for influenza A (H5N1) infection in humans Friel, H. and Lederman, H. 2006 Med.Hypotheses
617. The relevance of selenium to immunity, cancer, and infectious/inflammatory diseases Ryan-Harshman, M. and Aldoori, W. 2005 Can.J.Diet.Pract.Res.
618. Are there functional consequences of a reduction in selenium intake in UK subjects? Jackson, M. J., Dillon, S. A., Broome, C. S., McArdle, A., Hart, C. A., and McArdle, F. 2004 Proc.Nutr.Soc.
619. An increase in selenium intake improves immune function and poliovirus handling in adults with marginal selenium status Broome, C. S., McArdle, F., Kyle, J. A., Andrews, F., Lowe, N. M., Hart, C. A., Arthur, J. R., and Jackson, M. J. 2004 Am.J.Clin.Nutr.
620. [Selenium and the immune system] Zagrodzki, P. 3-18-2004 Postepy Hig.Med.Dosw.(Online.)
621. Skeletal muscle disorders associated with selenium deficiency in humans Chariot, P. and Bignani, O. 2003 Muscle Nerve
622. Marginal dietary selenium intakes in the UK: are there functional consequences? Jackson, M. J., Broome, C. S., and McArdle, F. 2003 J.Nutr.
623. Selenium deficiency and viral infection Beck, M. A., Levander, O. A., and Handy, J. 2003 J.Nutr.
624. Comparison with ancestral diets suggests dense acellular carbohydrates promote an inflammatory microbiota, and may be the primary dietary cause of leptin resistance and obesity Spreadbury, I. 2012 Diabetes Metab Syndr.Obes.
625. [Evaluation of biological and clinical potential of paleolithic diet] Kowalski, L. M. and Bujko, J. 2012 Rocz.Panstw.Zakl.Hig.
626. Over-stimulation of insulin/IGF-1 signaling by western diet may promote diseases of civilization: lessons learnt from laron syndrome Melnik, B. C., John, S. M., and Schmitz, G. 2011 Nutr.Metab (Lond)
627. A paleolithic diet is more satiating per calorie than a mediterranean-like diet in individuals with ischemic heart disease Jonsson, T., Granfeldt, Y., Erlanson-Albertsson, C., Ahren, B., and Lindeberg, S. 2010 Nutr.Metab (Lond)
628. The beneficial effects of a Paleolithic diet on type 2 diabetes and other risk factors for cardiovascular disease Klonoff, D. C. 2009 J.Diabetes Sci.Technol.
629. Evolution of the human diet: linking our ancestral diet to modern functional foods as a means of chronic disease prevention Jew, S., AbuMweis, S. S., and Jones, P. J. 2009 J.Med.Food
630. A Paleolithic diet confers higher insulin sensitivity, lower C-reactive protein and lower blood pressure than a cereal-based diet in domestic pigs Jonsson, T., Ahren, B., Pacini, G., Sundler, F., Wierup, N., Steen, S., Sjoberg, T., Ugander, M., Frostegard, J., Goransson, L., and Lindeberg, S. 2006 Nutr.Metab (Lond)
631. Fruit and vegetable consumption and all-cause mortality: a dose-response analysis Bellavia, A., Larsson, S. C., Bottai, M., Wolk, A., and Orsini, N. 2013 Am.J.Clin.Nutr.
632. Fruit and Vegetable Consumption and Mortality: European Prospective Investigation Into Cancer and Nutrition Leenders, M., Sluijs, I., Ros, M. M., Boshuizen, H. C., Siersema, P. D., Ferrari, P., Weikert, C., Tjonneland, A., Olsen, A., Boutron-Ruault, M. C., Clavel-Chapelon, F., Nailler, L., Teucher, B., Li, K., Boeing, H., Bergmann, M. M., Trichopoulou, A., Lagiou, P., Trichopoulos, D., Palli, D., Pala, V., Panico, S., Tumino, R., Sacerdote, C., Peeters, P. H., van Gils, C. H., Lund, E., Engeset, D., Redondo, M. L., Agudo, A., Sanchez, M. J., Navarro, C., Ardanaz, E.,

- Sonestedt, E., Ericson, U., Nilsson, L. M., Khaw, K. T., Wareham, N. J., Key, T. J., Crowe, F. L., Romieu, I., Gunter, M. J., Gallo, V., Overvad, K., Riboli, E., and Bueno-de-Mesquita, H. B. 4-18-2013 *Am.J.Epidemiol.*
633. Fruit and vegetable intake and mortality from ischaemic heart disease: results from the European Prospective Investigation into Cancer and Nutrition (EPIC)-Heart study Crowe, F. L., Roddam, A. W., Key, T. J., Appleby, P. N., Overvad, K., Jakobsen, M. U., Tjonneland, A., Hansen, L., Boeing, H., Weikert, C., Linseisen, J., Kaaks, R., Trichopoulou, A., Misirli, G., Lagiou, P., Sacerdote, C., Pala, V., Palli, D., Tumino, R., Panico, S., Bueno-de-Mesquita, H. B., Boer, J., van Gils, C. H., Beulens, J. W., Barricarte, A., Rodriguez, L., Larranaga, N., Sanchez, M. J., Tormo, M. J., Buckland, G., Lund, E., Hedblad, B., Melander, O., Jansson, J. H., Wennberg, P., Wareham, N. J., Slimani, N., Romieu, I., Jenab, M., Danesh, J., Gallo, V., Norat, T., and Riboli, E. 2011 *Eur.Heart J.*
634. Time-restricted feeding and risk of metabolic disease: a review of human and animal studies Rothschild, J., Hoddy, K. K., Jambazian, P., and Varady, K. A. 4-16-2014 *Nutr.Rev.*
635. Time-restricted feeding and the realignment of biological rhythms: translational opportunities and challenges Sunderram, J., Sofou, S., Kamisoglu, K., Karantza, V., and Androulakis, I. P. 2014 *J.Transl.Med.*
636. Genome-wide analysis of SREBP1 activity around the clock reveals its combined dependency on nutrient and circadian signals Gilardi, F., Migliavacca, E., Naldi, A., Baruchet, M., Canella, D., Le, Martelot G., Guex, N., and Desvergne, B. 2014 *PLoS.Genet.*
637. Time-restricted feeding without reducing caloric intake prevents metabolic diseases in mice fed a high-fat diet Hatori, M., Vollmers, C., Zarrinpar, A., DiTacchio, L., Bushong, E. A., Gill, S., Leblanc, M., Chaix, A., Joens, M., Fitzpatrick, J. A., Ellisman, M. H., and Panda, S. 6-6-2012 *Cell Metab*
638. Influence of a time-restricted feeding schedule on the daily rhythm of abcb1a gene expression and its function in rat intestine Hayashi, Y., Ushijima, K., Ando, H., Yanagihara, H., Ishikawa, E., Tsuruoka, S., Sugimoto, K., and Fujimura, A. 2010 *J.Pharmacol.Exp.Ther.*
639. Time-restricted feeding entrains daily rhythms of energy metabolism in mice Satoh, Y., Kawai, H., Kudo, N., Kawashima, Y., and Mitsumoto, A. 2006 *Am.J.Physiol Regul.Integr.Comp Physiol*
640. Scheduled feeding caused activation of dopamine metabolism in the striatum of rats Inoue, K., Kiriike, N., Okuno, M., Ito, H., Fujisaki, Y., Matsui, T., and Kawakita, Y. 1993 *Physiol Behav.*
641. Selectively starving cancer cells through dietary manipulation: methods and clinical implications Simone, B. A., Champ, C. E., Rosenberg, A. L., Berger, A. C., Monti, D. A., Dicker, A. P., and Simone, N. L. 2013 *Future.Oncol.*
642. Chronic intermittent fasting improves cognitive functions and brain structures in mice Li, L., Wang, Z., and Zuo, Z. 2013 *PLoS.One.*
643. Fasting or caloric restriction for Healthy Aging Anton, S. and Leeuwenburgh, C. 4-29-2013 *Exp.Gerontol.*
644. Effects of intermittent fasting on metabolism in men de Azevedo, F. R., Ikeoka, D., and Caramelli, B. 2013 *Rev.Assoc.Med.Bras.*
645. Intermittent fasting: the science of going without Collier, R. 6-11-2013 *CMAJ.*
646. Dietary restriction supports peripheral nerve health by enhancing endogenous protein quality control mechanisms Lee, S. and Notterpek, L. 12-23-2012 *Exp.Gerontol.*
647. Energy restriction and the prevention of breast cancer Harvie, M. and Howell, A. 2012 *Proc.Nutr.Soc.*
648. Annual fasting; the early calories restriction for cancer prevention Eslami, S., Barzegari, Z., Saliyani, N., Saeedi, N., and Barzegari, A. 2012 *Bioimpacts.*
649. Late-onset intermittent fasting dietary restriction as a potential intervention to retard age-associated brain function impairments in male rats Singh, R., Lakhanpal, D., Kumar, S., Sharma, S., Kataria, H., Kaur, M., and Kaur, G. 2012 *Age (Dordr.)*
650. Vitamin D intake: a global perspective of current status Calvo, M. S., Whiting, S. J., and Barton, C. N. 2005 *J.Nutr.*
651. Vegetarian diets and children Sanders, T. A. 1995 *Pediatr.Clin.North Am.*
652. High prevalence of rickets in infants on macrobiotic diets Dagnelie, P. C., Vergote, F. J., van Staveren, W. A., van den, Berg H., Dingjan, P. G., and Hautvast, J. G. 1990 *Am.J.Clin.Nutr.*
653. Vitamin D deficiency rickets and vitamin B12 deficiency in vegetarian children Hellebostad, M., Markestad, T., and Seeger, Halvorsen K. 1985 *Acta Paediatr.Scand.*
654. Nutritional rickets in vegetarian children Curtis, J. A., Kooh, S. W., Fraser, D., and Greenberg, M. L. 1-15-1983 *Can.Med.Assoc.J.*
655. Inflammation-associated insulin resistance: differential effects in rheumatoid arthritis and systemic lupus erythematosus define potential mechanisms Chung, C. P., Oeser, A., Solus, J. F., Gebretsadik, T., Shintani, A., Avalos, I., Sokka, T., Raggi, P., Pincus, T., and Stein, C. M. 2008 *Arthritis Rheum.*
656. Hyperinsulinemia, insulin resistance, and circulating oxidized low density lipoprotein in women with systemic lupus erythematosus El, Magadmi M., Ahmad, Y., Turkie, W., Yates, A. P., Sheikh, N., Bernstein, R. M., Durrington, P. N., Laing, I., and Bruce, I. N. 2006 *J.Rheumatol.*
657. High insulin levels and increased low-density lipoprotein oxidizability in pediatric patients with systemic lupus erythematosus Posadas-Romero, C., Torres-Tamayo, M., Zamora-Gonzalez, J., Aguilar-Herrera, B. E., Posadas-Sanchez, R., Cardoso-Saldana, G., Ladron de Guevara G., Solis-Vallejo, E., and El, Hafidi M. 2004 *Arthritis Rheum.*
658. Elevated fasting insulin predicts the future incidence of metabolic syndrome: a 5-year follow-up study Sung, K. C., Seo, M. H., Rhee, E. J., and Wilson, A. M. 2011 *Cardiovasc.Diabetol.*
659. Hyperinsulinemia, insulin resistance and cognitive decline in older cohort Zhong, Y., Miao, Y., Jia, W. P., Yan, H., Wang, B. Y., and Jin, J. 2012 *Biomed.Enviro.Sci.*
660. Insulin resistance in the nervous system Kim, B. and Feldman, E. L. 2012 *Trends Endocrinol.Metab*
661. A common pathogenic mechanism linking type-2 diabetes and Alzheimer's disease: evidence from animal models Park, S. A. 2011 *J.Clin.Neurol.*
662. [Etiology and pathophysiology of benign prostate hyperplasia] Roosen, A., Gratzke, C., Herlemann, A., Magistro, G., Strittmatter, F., Weinhold, P., Tritschler, S., and Stief, C. G. 2013 *Urologe A*

663. [Correlation between metabolic syndrome and clinical progression in patients with benign prostatic hyperplasia] Cao, B., Sun, H. B., Su, J. H., Shen, M. S., Cao, Z. G., Jia, R. P., and Liu, J. 11-2-2010 *Zhonghua Yi.Xue.Za Zhi*.
664. Insulin-resistance and benign prostatic hyperplasia: the connection Vikram, A., Jena, G., and Ramarao, P. 9-1-2010 *Eur.J.Pharmacol*.
665. Altered insulin sensitivity, insulin secretion and lipid profile in non-diabetic prostate carcinoma Nandeeshha, H., Koner, B. C., and Dorairajan, L. N. 2008 *Acta Physiol Hung*.
666. Diabetes And Cancer: Two Diseases With Obesity As A Common Risk Factor Garg, S. K., Maurer, H., Reed, K., and Selagamsetty, R. 5-13-2013 *Diabetes Obes.Metab*
667. A molecular rheostat at the interface of cancer and diabetes Osman, M. A., Sarkar, F. H., and Rodriguez-Boulan, E. 2013 *Biochim.Biophys.Acta*
668. New players for advanced prostate cancer and the rationalisation of insulin-sensitising medication Gunter, J. H., Sarkar, P. L., Lubik, A. A., and Nelson, C. C. 2013 *Int.J.Cell Biol*.
669. Hyperinsulinemia promotes metastasis to the lung in a mouse model of Her2-mediated breast cancer Ferguson, R. D., Gallagher, E. J., Cohen, D., Tobin-Hess, A., Alikhani, N., Novosyadlyy, R., Haddad, N., Yakar, S., and Leroith, D. 2013 *Endocr.Relat Cancer*
670. The key role of growth hormone-insulin-IGF-1 signaling in aging and cancer Anisimov, V. N. and Bartke, A. 2-21-2013 *Crit Rev.Oncol.Hematol*.
671. Insulin resistance: a risk marker for disease and disability in the older person Krentz, A. J., Viljoen, A., and Sinclair, A. 2013 *Diabet.Med*.
672. [Insulin, IGF-I and cancer] Ogawa, W. 2012 *Nihon Rinsho*
673. Metabolic correlates of menopause: an update Ross, L. A. and Polotsky, A. J. 2012 *Curr.Opin.Obstet.Gynecol*.
674. Elevated insulin and insulin resistance are associated with the advanced pathological stage of prostate cancer in Korean population Yun, S. J., Min, B. D., Kang, H. W., Shin, K. S., Kim, T. H., Kim, W. T., Lee, S. C., and Kim, W. J. 2012 *J.Korean Med.Sci*.
675. Insulin resistance and cancer: epidemiological evidence Inoue, M. and Tsugane, S. 2012 *Endocr.Relat Cancer*
676. Glucose-induced inhibition of the appetitive brain response to visual food cues in polycystic ovary syndrome patients Van Vugt, D. A., Krzemien, A., Alsaadi, H., Frank, T. C., and Reid, R. L. 4-16-2014 *Brain Res*.
677. Polycystic ovary syndrome Nandi, A., Chen, Z., Patel, R., and Poretsky, L. 2014 *Endocrinol.Metab Clin.North Am*.
678. PCOS and obesity: insulin resistance might be a common etiology for the development of type I endometrial carcinoma Li, X. and Shao, R. 2014 *Am.J.Cancer Res*.
679. Metabolomics in polycystic ovary syndrome Murri, M., Insenser, M., and Escobar-Morreale, H. F. 2-15-2014 *Clin.Chim.Acta*
680. Adiponectin and its receptors in the ovary: further evidence for a link between obesity and hyperandrogenism in polycystic ovary syndrome Comim, F. V., Hardy, K., and Franks, S. 2013 *PLoS.One*.
681. [Polycystic ovary syndrome: physiopathology review] Fux, Otta C., Fiol de, Cuneo M., and Szafryk de, Mereshian P. 2013 *Rev.Fac.Cien.Med.Univ Nac.Cordoba*
682. Serum leptin level in women with polycystic ovary syndrome: correlation with adiposity, insulin, and circulating testosterone Chakrabarti, J. 2013 *Ann.Med.Health Sci.Res*.
683. [Chronic inflammation and metabolic syndrome in comparison with other signs belonging to the image of polycystic ovary syndrome] Marciniak, A., Nawrocka-Rutkowska, J., Wisniewska, B., Brodowska, A., and Starczewski, A. 2013 *Pol.Merkur Lekarski*.
684. Cardiometabolic aspects of the polycystic ovary syndrome Randeve, H. S., Tan, B. K., Weickert, M. O., Lois, K., Nestler, J. E., Sattar, N., and Lehnert, H. 2012 *Endocr.Rev*.
685. Fasting insulin level is positively associated with incidence of hypertension among American young adults: a 20-year follow-up study Xun, P., Liu, K., Cao, W., Sidney, S., Williams, O. D., and He, K. 2012 *Diabetes Care*
686. The association of fasting insulin, glucose, and lipids with bone mass in adolescents: findings from a cross-sectional study Lawlor, D. A., Sattar, N., Sayers, A., and Tobias, J. H. 2012 *J.Clin.Endocrinol.Metab*
687. Fasting insulin has a stronger association with an adverse cardiometabolic risk profile than insulin resistance: the RISC study de Rooij, S. R., Dekker, J. M., Kozakova, M., Mitrakou, A., Melander, O., Gabriel, R., Guidone, C., Hojlund, K., Murphy, M. S., and Nijpels, G. 2009 *Eur.J.Endocrinol*.
688. Hyperinsulinemia drives diet-induced obesity independently of brain insulin production Mehran, A. E., Templeman, N. M., Brigidi, G. S., Lim, G. E., Chu, K. Y., Hu, X., Botezzelli, J. D., Asadi, A., Hoffman, B. G., Kieffer, T. J., Bamji, S. X., Clee, S. M., and Johnson, J. D. 12-5-2012 *Cell Metab*
689. Is hyperinsulinemia required to develop overeating-induced obesity? Buettner, C. 12-5-2012 *Cell Metab*
690. Preterm birth and the metabolic syndrome in adult life: a systematic review and meta-analysis Parkinson, J. R., Hyde, M. J., Gale, C., Santhakumaran, S., and Modi, N. 2013 *Pediatrics*
691. Current thoughts on maternal nutrition and fetal programming of the metabolic syndrome Brenseke, B., Prater, M. R., Bahamonde, J., and Gutierrez, J. C. 2013 *J.Pregnancy*.
692. Maternal hyperinsulinism and glycaemic status in the first trimester of pregnancy are associated with the development of pregnancy-induced hypertension and gestational diabetes Kayemba-Kay's, S., Peters, C., Geary, M. P., Hill, N. R., Mathews, D. R., and Hindmarsh, P. C. 2013 *Eur.J.Endocrinol*.
693. The impact of recurrent gestational diabetes on maternal metabolic and cardiovascular risk factors Winhofer, Y., Tura, A., Prikoszovich, T., Winzer, C., Schneider, B., Pacini, G., Luger, A., and Kautzky-Willer, A. 2013 *Eur.J.Clin.Invest*
694. Impact of maternal diabetes on epigenetic modifications leading to diseases in the offspring Vrachnis, N., Antonakopoulos, N., Iliodromiti, Z., Dafopoulos, K., Siristatidis, C., Pappa, K. I., Deligeoroglou, E., and Vitoratos, N. 2012 *Exp.Diabetes Res*.
695. Dietary glycemic index and the risk of birth defects Parker, S. E., Werler, M. M., Shaw, G. M., Anderka, M., and Yazdy, M. M. 12-15-2012 *Am.J.Epidemiol*.

696. The long-term effects of birth by caesarean section: the case for a randomised controlled trial Hyde, M. J. and Modi, N. 2012 *Early Hum.Dev.*
697. The fetal origins of the metabolic syndrome: can we intervene? Ma, N. and Hardy, D. B. 2012 *J.Pregnancy.*
698. The risk of maternal obesity to the long-term health of the offspring O'Reilly, J. R. and Reynolds, R. M. 2013 *Clin.Endocrinol.(Oxf)*
699. Effects of dietary carbohydrate restriction versus low-fat diet on flow-mediated dilation Volek, J. S., Ballard, K. D., Silvestre, R., Judelson, D. A., Quann, E. E., Forsythe, C. E., Fernandez, M. L., and Kraemer, W. J. 2009 *Metabolism*
700. Carbohydrate restriction has a more favorable impact on the metabolic syndrome than a low fat diet Volek, J. S., Phinney, S. D., Forsythe, C. E., Quann, E. E., Wood, R. J., Puglisi, M. J., Kraemer, W. J., Bibus, D. M., Fernandez, M. L., and Feinman, R. D. 2009 *Lipids*
701. A moderate-fat diet for combined hyperlipidemia and metabolic syndrome Knopp, R. H., Fish, B., Dowdy, A., Retzlaff, B., Walden, C., Rusanu, I., and Paramsothy, P. 2006 *Curr.Atheroscler.Rep.*
702. [Trans fatty acids: consumption effect on human health and regulation challenges] Ballesteros-Vasquez, M. N., Valenzuela-Calvillo, L. S., Artalejo-Ochoa, E., and Robles-Sardin, A. E. 2012 *Nutr.Hosp.*
703. Toward a unifying hypothesis of metabolic syndrome Bremer, A. A., Mietus-Snyder, M., and Lustig, R. H. 2012 *Pediatrics*
704. Trans fat feeding results in higher serum alanine aminotransferase and increased insulin resistance compared with a standard murine high-fat diet Koppe, S. W., Elias, M., Moseley, R. H., and Green, R. M. 2009 *Am.J.Physiol Gastrointest.Liver Physiol*
705. Associations of adipokines & insulin resistance with sex steroids in patients with breast cancer Al Awadhi, S. A., Al Khaldi, R. M., Al Rammah T., Kapila, K., and Mojiminiyi, O. A. 2012 *Indian J.Med.Res.*
706. Metabolic syndrome in patients with hematological diseases Annaloro, C., Airaghi, L., Saporiti, G., Onida, F., Cortelezzi, A., and Delilliers, G. L. 2012 *Expert.Rev.Hematol.*
707. Insulin resistance and cancer risk: an overview of the pathogenetic mechanisms Arcidiacono, B., Iritano, S., Nocera, A., Possidente, K., Nevolo, M. T., Ventura, V., Foti, D., Chiefari, E., and Brunetti, A. 2012 *Exp.Diabetes Res.*
708. Diet-induced metabolic change induces estrogen-independent allometric mammary growth Berryhill, G. E., Gloviczki, J. M., Trott, J. F., Aimo, L., Kraft, J., Cardiff, R. D., Paul, C. T., Petrie, W. K., Lock, A. L., and Hovey, R. C. 10-2-2012 *Proc.Natl.Acad.Sci.U.S.A*
709. Endocrine metabolic disorders in patients with breast cancer, carriers of BRCA1 gene mutations Berstein, L. M., Boyarkina, M. P., Vasilyev, D. A., Poroshina, T. E., Kovalenko, I. G., Imyanitov, E. N., and Semiglazov, V. F. 2012 *Bull.Exp.Biol.Med.*
710. Obesity, type 2 diabetes, and cancer: the insulin and IGF connection Cohen, D. H. and Leroith, D. 2012 *Endocr.Relat Cancer*
711. Metformin enhances the antiproliferative and apoptotic effect of bicalutamide in prostate cancer Colquhoun, A. J., Venier, N. A., Vandersluis, A. D., Besla, R., Sugar, L. M., Kiss, A., Fleshner, N. E., Pollak, M., Klotz, L. H., and Venkateswaran, V. 2012 *Prostate Cancer Prostatic.Dis.*
712. Metabolic syndrome and risk of cancer: a systematic review and meta-analysis Esposito, K., Chiodini, P., Colao, A., Lenzi, A., and Giugliano, D. 2012 *Diabetes Care*
713. Metabolic syndrome and breast cancer: an overview Gezgen, G., Roach, E. C., Kizilarslanoglu, M. C., Petekkaya, I., and Altundag, K. 2012 *J.BUON.*
714. Effects of short-term high-fat overfeeding on genome-wide DNA methylation in the skeletal muscle of healthy young men Jacobsen, S. C., Brons, C., Bork-Jensen, J., Ribel-Madsen, R., Yang, B., Lara, E., Hall, E., Calvanese, V., Nilsson, E., Jorgensen, S. W., Mandrup, S., Ling, C., Fernandez, A. F., Fraga, M. F., Poulsen, P., and Vaag, A. 2012 *Diabetologia*
715. What do magnetic resonance-based measurements of Pi-->ATP flux tell us about skeletal muscle metabolism? Kemp, G. J. and Brindle, K. M. 2012 *Diabetes*
716. Autophagy, signaling and obesity Lavallard, V. J., Meijer, A. J., Codogno, P., and Gual, P. 2012 *Pharmacol.Res.*
717. The cellular and molecular mechanisms by which insulin influences breast cancer risk and progression Rose, D. P. and Vona-Davis, L. 2012 *Endocr.Relat Cancer*
718. A liver full of JNK: signaling in regulation of cell function and disease pathogenesis, and clinical approaches Seki, E., Brenner, D. A., and Karin, M. 2012 *Gastroenterology*
719. Colorectal cancer and its association with the metabolic syndrome: a Malaysian multi-centric case-control study Ulaganathan, V., Kandiah, M., Zaliyah, M. S., Faizal, J. A., Fijeraid, H., Normayah, K., Gooi, B. H., and Othman, R. 2012 *Asian Pac.J.Cancer Prev.*
720. Obesity-driven inflammation and colorectal cancer Vazzana, N., Riondino, S., Toto, V., Guadagni, F., Roselli, M., Davi, G., and Ferroni, P. 2012 *Curr.Med.Chem.*
721. A novel role for insulin resistance in the connection between obesity and postmenopausal breast cancer Weichhaus, M., Broom, J., Wahle, K., and Bermano, G. 2012 *Int.J.Oncol.*
722. Astrogliosis in the brain of obese Zucker rat: A model of metabolic syndrome Tomassoni, D., Nwankwo, I. E., Gabrielli, M. G., Bhatt, S., Muhammad, A. B., Lokhandwala, M. F., Tayebati, S. K., and Amenta, F. 5-24-2013 *Neurosci.Lett.*
723. Alzheimer's disease and insulin resistance: translating basic science into clinical applications De Felice, F. G. 2-1-2013 *J.Clin.Invest*
724. The impairment of insulin signaling in Alzheimer's disease Candeias, E., Duarte, A. I., Carvalho, C., Correia, S. C., Cardoso, S., Santos, R. X., Placido, A. I., Perry, G., and Moreira, P. I. 2012 *IUBMB.Life*
725. Brain insulin resistance may exacerbate Alzheimer's progression. Researchers call it "Type III" diabetes 2012 *Duke.Med.Health News*
726. Insulin and Alzheimer's disease: untangling the web Craft, S., Cholerton, B., and Baker, L. D. 2013 *J.Alzheimers.Dis.*
727. [Mechanisms of neurodegeneration in Alzheimer's disease] Jovanovic, Z. 2012 *Med.Pregl.*

728. Metabolic derangements mediate cognitive impairment and Alzheimer's disease: role of peripheral insulin-resistance diseases De La Monte, S. M. 2012 *Panminerva Med.*
729. Fasting plasma insulin and the default mode network in women at risk for Alzheimer's disease Kenna, H., Hoeft, F., Kelley, R., Wroolie, T., DeMuth, B., Reiss, A., and Rasgon, N. 2013 *Neurobiol.Aging*
730. Insulin resistance in the brain: an old-age or new-age problem? Williamson, R., McNeilly, A., and Sutherland, C. 9-15-2012 *Biochem.Pharmacol.*
731. Exercise is more effective than diet control in preventing high fat diet-induced beta-amyloid deposition and memory deficit in amyloid precursor protein transgenic mice Maesako, M., Uemura, K., Kubota, M., Kuzuya, A., Sasaki, K., Hayashida, N., Asada-Utsugi, M., Watanabe, K., Uemura, M., Kihara, T., Takahashi, R., Shimohama, S., and Kinoshita, A. 6-29-2012 *J.Biol.Chem.*
732. Can Alzheimer disease be a form of type 3 diabetes? Accardi, G., Caruso, C., Colonna-Romano, G., Camarda, C., Monastero, R., and Candore, G. 2012 *Rejuvenation.Res.*
733. Neurodegeneration in diabetes mellitus Umegaki, H. 2012 *Adv.Exp.Med.Biol.*
734. Brain insulin signaling and Alzheimer's disease: current evidence and future directions Schioth, H. B., Craft, S., Brooks, S. J., Frey, W. H., and Benedict, C. 2012 *Mol.Neurobiol.*
735. Metabolic syndrome as a risk factor for neurological disorders Farooqui, A. A., Farooqui, T., Panza, F., and Frisardi, V. 2012 *Cell Mol.Life Sci.*
736. Insulin resistance and pathological brain ageing Cholerton, B., Baker, L. D., and Craft, S. 2011 *Diabet.Med.*
737. Insulin resistance, inflammation, and serum fatty acid composition Fernandez-Real, J. M., Broch, M., Vendrell, J., and Ricart, W. 2003 *Diabetes Care*
738. Magnesium, insulin resistance and body composition in healthy postmenopausal women Laires, M. J., Moreira, H., Monteiro, C. P., Sardinha, L., Limao, F., Veiga, L., Goncalves, A., Ferreira, A., and Bicho, M. 2004 *J.Am.Coll.Nutr.*
739. Lessons from comparative physiology: could uric acid represent a physiologic alarm signal gone awry in western society? Johnson, R. J., Sautin, Y. Y., Oliver, W. J., Roncal, C., Mu, W., Gabriela Sanchez-Lozada, L., Rodriguez-Iturbe, B., Nakagawa, T., and Benner, S. A. 2009 *J.Comp Physiol B*
740. Differential gene expression and adiposity reduction induced by ascorbic acid supplementation in a cafeteria model of obesity Campion, J., Milagro, F. I., Fernandez, D., and Martinez, J. A. 2006 *J.Physiol Biochem.*
741. Possible connections between stress, diabetes, obesity, hypertension and altered lipoprotein metabolism that may result in atherosclerosis Brindley, D. N. and Rolland, Y. 1989 *Clin.Sci.(Lond)*
742. Randomized trial of weight-loss-diets for young adults varying in fish and fish oil content Thorsdottir, I., Tomasson, H., Gunnarsdottir, I., Gisladdottir, E., Kiely, M., Parra, M. D., Bandarra, N. M., Schaafsma, G., and Martinez, J. A. 5-15-2007 *Int.J.Obes.(Lond)*
743. Dietary intervention increases n-3 long-chain polyunsaturated fatty acids in skeletal muscle membrane phospholipids of obese subjects. Implications for insulin sensitivity Haugaard, S. B., Madsbad, S., Hoy, C. E., and Vaag, A. 2006 *Clin.Endocrinol.(Oxf)*
744. Fish-seafood consumption, obesity, and risk of type 2 diabetes: an ecological study Nkondjock, A. and Receveur, O. 2003 *Diabetes Metab*
745. Dietary fish as a major component of a weight-loss diet: effect on serum lipids, glucose, and insulin metabolism in overweight hypertensive subjects Mori, T. A., Bao, D. Q., Burke, V., Puddey, I. B., Watts, G. F., and Beilin, L. J. 1999 *Am.J.Clin.Nutr.*
746. Cortisol-induced insulin resistance in man: impaired suppression of glucose production and stimulation of glucose utilization due to a postreceptor defect of insulin action Rizza, R. A., Mandarino, L. J., and Gerich, J. E. 1982 *J.Clin.Endocrinol.Metab*
747. The Yo-Yo intermittent recovery test level 1 as a high intensity training tool: aerobic and anaerobic responses Delahunt, E., Callan, L., Donohoe, J., Melican, R., and Holden, S. 2013 *Prev.Med.*
748. Small-sided games versus interval training in amateur soccer players: effects on the aerobic capacity and the ability to perform intermittent exercises with changes of direction Dellal, A., Varliette, C., Owen, A., Chirico, E. N., and Pialoux, V. 2012 *J.Strength.Cond.Res.*
749. Effects of nonexhaustive bouts of high-intensity intermittent swimming training on GLUT-4 expression in rat skeletal muscle Fujimoto, E., Machida, S., Higuchi, M., and Tabata, I. 2010 *J.Physiol Sci.*
750. Impressive anaerobic adaptations in elite karate athletes due to few intensive intermittent sessions added to regular karate training Ravier, G., Dugue, B., Grappe, F., and Rouillon, J. D. 2009 *Scand.J.Med.Sci.Sports*
751. Effects of high-intensity intermittent training on potassium kinetics and performance in human skeletal muscle Nielsen, J. J., Mohr, M., Klarskov, C., Kristensen, M., Krstrup, P., Juel, C., and Bangsbo, J. 2-1-2004 *J.Physiol*
752. Effects of moderate-intensity endurance and high-intensity intermittent training on anaerobic capacity and VO₂max Tabata, I., Nishimura, K., Kouzaki, M., Hirai, Y., Ogita, F., Miyachi, M., and Yamamoto, K. 1996 *Med.Sci.Sports Exerc.*
753. Impact of exercise intensity on body fatness and skeletal muscle metabolism Tremblay, A., Simoneau, J. A., and Bouchard, C. 1994 *Metabolism*
754. Hyperinsulinemia: an innocent bystander? Muralledharan, M. V. and Jayakumar, R. V. 1997 *J.Assoc.Physicians India*
755. Hyperinsulinemia--how innocent a bystander? Zimmet, P. Z. 1993 *Diabetes Care*
756. Effects of intermittent fasting on metabolism in men Azevedo, F. R., Ikeoka, D., and Caramelli, B. 2013 *Rev.Assoc.Med.Bras.*
757. Intermittent fasting: A "new" historical strategy for controlling seizures? Hartman, A. L., Rubenstein, J. E., and Kossoff, E. H. 2013 *Epilepsy Res.*
758. Intermittent fasting combined with calorie restriction is effective for weight loss and cardio-protection in obese women Klempel, M. C., Kroeger, C. M., Bhutani, S., Trepanowski, J. F., and Varady, K. A. 2012 *Nutr.J.*

759. Improvement in coronary heart disease risk factors during an intermittent fasting/calorie restriction regimen: Relationship to adipokine modulations Kroeger, C. M., Klempel, M. C., Bhutani, S., Trepanowski, J. F., Tangney, C. C., and Varady, K. A. 2012 *Nutr.Metab* (Lond)
760. Intermittent fasting modulation of the diabetic syndrome in streptozotocin-injected rats Belkacemi, L., Selselet-Attou, G., Hupkens, E., Nguidjoe, E., Louchami, K., Sener, A., and Malaisse, W. J. 2012 *Int.J.Endocrinol*.
761. Neuroprotective role of intermittent fasting in senescence-accelerated mice P8 (SAMP8) Tajes, M., Gutierrez-Cuesta, J., Folch, J., Ortuno-Sahagun, D., Verdaguer, E., Jimenez, A., Junyent, F., Lau, A., Camins, A., and Pallas, M. 2010 *Exp.Gerontol*.
762. Effect of feeding regimens on circadian rhythms: implications for aging and longevity Froy, O. and Miskin, R. 2010 *Aging* (Albany.NY)
763. Cardioprotective effect of intermittent fasting is associated with an elevation of adiponectin levels in rats Wan, R., Ahmet, I., Brown, M., Cheng, A., Kamimura, N., Talan, M., and Mattson, M. P. 2010 *J.Nutr.Biochem*.
764. Chronic intermittent fasting improves the survival following large myocardial ischemia by activation of BDNF/VEGF/PI3K signaling pathway Katare, R. G., Kakinuma, Y., Arikawa, M., Yamasaki, F., and Sato, T. 2009 *J.Mol.Cell Cardiol*.
765. Intermittent fasting prevents the progression of type I diabetic nephropathy in rats and changes the expression of Sir2 and p53 Tikoo, K., Tripathi, D. N., Kabra, D. G., Sharma, V., and Gaikwad, A. B. 3-6-2007 *FEBS Lett*.
766. Intermittent fasting and caloric restriction ameliorate age-related behavioral deficits in the triple-transgenic mouse model of Alzheimer's disease Halagappa, V. K., Guo, Z., Pearson, M., Matsuoka, Y., Cutler, R. G., Laferla, F. M., and Mattson, M. P. 2007 *Neurobiol.Dis*.
767. Caloric restriction and intermittent fasting: two potential diets for successful brain aging Martin, B., Mattson, M. P., and Maudsley, S. 2006 *Ageing Res.Rev*.
768. Cardioprotection by intermittent fasting in rats Ahmet, I., Wan, R., Mattson, M. P., Lakatta, E. G., and Talan, M. 11-15-2005 *Circulation*
769. Energy intake, meal frequency, and health: a neurobiological perspective Mattson, M. P. 2005 *Annu.Rev.Nutr*.
770. Meal size and frequency affect neuronal plasticity and vulnerability to disease: cellular and molecular mechanisms Mattson, M. P., Duan, W., and Guo, Z. 2003 *J.Neurochem*.
771. [Insulin resistance and evolution] Fernandez-Real Lemos, J. M. 2002 *Nutr.Hosp*.
772. Insulin resistance and thyroid disorders Gierach, M., Gierach, J., and Junik, R. 2014 *Endokrynol.Pol*.
773. The effect of L-thyroxine substitution on lipid profile, glucose homeostasis, inflammation and coagulation in patients with subclinical hypothyroidism Anagnostis, P., Efstathiadou, Z. A., Slavakis, A., Selalmatzidou, D., Poulasouchidou, M., Katergari, S., Karathanasi, E., Dogramatzi, F., and Kita, M. 2-18-2014 *Int.J.Clin.Pract*.
774. Effect of treatment of overt hypothyroidism on insulin resistance Nada, A. M. 8-15-2013 *World J.Diabetes*
775. Relationship between thyroid-stimulating hormone and blood pressure in the middle-aged and elderly population Jian, W. X., Jin, J., Qin, L., Fang, W. J., Chen, X. R., Chen, H. B., Su, Q., and Xing, H. L. 2013 *Singapore Med.J*.
776. Insulin resistance and lipid alterations in subclinical hypothyroidism Sridevi, A., Vivekanand, B., Giridhar, G., Mythili, A., and Subrahmanyam, K. A. 2012 *Indian J.Endocrinol.Metab*
777. Hypothyroidism in metabolic syndrome Kota, S. K., Meher, L. K., Krishna, S., and Modi, K. 2012 *Indian J.Endocrinol.Metab*
778. Plasma vitamin C is inversely related to body mass index and waist circumference but not to plasma adiponectin in nonsmoking adults Johnston, C. S., Beezhold, B. L., Mostow, B., and Swan, P. D. 2007 *J.Nutr*.
779. Abundant daily non-sedentary activity is associated with reduced prevalence of metabolic syndrome and insulin resistance Uemura, H., Katsuura-Kamano, S., Yamaguchi, M., Nakamoto, M., Hiyoshi, M., and Arisawa, K. 7-26-2013 *J.Endocrinol.Invest*
780. A Single Session of Low-Intensity Exercise Is Sufficient to Enhance Insulin Sensitivity Into the Next Day in Obese Adults Newsom, S. A., Everett, A. C., Hinko, A., and Horowitz, J. F. 6-11-2013 *Diabetes Care*
781. [Sitting and cardiovascular morbidity and mortality] Shiyovich, A., Shlyakhover, V., and Katz, A. 2013 *Harefuah*
782. Breaking prolonged sitting reduces postprandial glycemia in healthy, normal-weight adults: a randomized crossover trial Peddie, M. C., Bone, J. L., Rehner, N. J., Skeaff, C. M., Gray, A. R., and Perry, T. L. 2013 *Am.J.Clin.Nutr*.
783. Effects of breaking up prolonged sitting on skeletal muscle gene expression Latouche, C., Jowett, J. B., Carey, A. L., Bertovic, D. A., Owen, N., Dunstan, D. W., and Kingwell, B. A. 2-15-2013 *J.Appl.Physiol*
784. Intestinal permeability changes during the first month: effect of natural versus artificial feeding Catassi, C., Bonucci, A., Coppa, G. V., Carlucci, A., and Giorgi, P. L. 1995 *J.Pediatr.Gastroenterol.Nutr*.
785. Allergenicity of food proteins and its possible modification Coombs, R. R. and McLaughlan, P. 1984 *Ann.Allergy*
786. Food protein-induced enterocolitis syndrome: laboratory perspectives Dupont, C. and Heyman, M. 2000 *J.Pediatr.Gastroenterol.Nutr*.
787. Dietary antigens: uptake and humoral immunity in man Husby, S. 1988 *APMIS Suppl*
788. Probiotics: a novel approach in the management of food allergy Majamaa, H. and Isolauri, E. 1997 *J.Allergy Clin.Immunol*.
789. Vaccination and autoimmunity-'vaccinosis': a dangerous liaison? Shoenfeld, Y. and ron-Maor, A. 2000 *J.Autoimmun*.
790. Vaccine-induced autoimmunity in the dog HogenEsch, H., zcona-Olivera, J., Scott-Moncrieff, C., Snyder, P. W., and Glickman, L. T. 1999 *Adv.Vet.Med*.
791. Autoimmunity in spontaneous myasthenia gravis in dogs Garlepp, M. J., Kay, P. H., Farrow, B. R., and Dawkins, R. L. 1984 *Clin.Immunol.Immunopathol*.
792. Probiotic *Lactobacillus rhamnosus* GG Enhanced Th1 Cellular Immunity but Did Not Affect Antibody Responses in a Human Gut Microbiota Transplanted Neonatal Gnotobiotic Pig Model Wen, K., Tin, C., Wang, H., Yang, X., Li, G., Giri-Rachman, E., Kocher, J., Bui, T., Clark-Deener, S., and Yuan, L. 2014 *PLoS.One*.
793. Faecal transplantation for the treatment of *Clostridium difficile* infection: a review McCune, V. L., Struthers, J. K., and Hawkey, P. M. 2014 *Int.J.Antimicrob.Agents*

794. Are There Any Different Effects of Bifidobacterium, Lactobacillus and Streptococcus on Intestinal Sensation, Barrier Function and Intestinal Immunity in PI-IBS Mouse Model? Wang, H., Gong, J., Wang, W., Long, Y., Fu, X., Fu, Y., Qian, W., and Hou, X. 2014 PLoS.One.
795. Ageing, immunity and influenza: a role for probiotics? Yaqoob, P. 2014 Proc.Nutr.Soc.
796. Clinical efficacy and mechanism of probiotics in allergic diseases Kim, H. J., Kim, H. Y., Lee, S. Y., Seo, J. H., Lee, E., and Hong, S. J. 2013 Korean J.Pediatr.
797. Understanding immunomodulatory effects of probiotics Pot, B., Foligne, B., Daniel, C., and Grangette, C. 2013 Nestle.Nutr.Inst.Workshop Ser.
798. Effects of oral administration of probiotics from Mongolian dairy products on the Th1 immune response in mice Takeda, S., Kawahara, S., Hidaka, M., Yoshida, H., Watanabe, W., Takeshita, M., Kikuchi, Y., Bumbein, D., Muguruma, M., and Kurokawa, M. 2013 Biosci.Biotechnol.Biochem.
799. Feeding the immune system Calder, P. C. 2013 Proc.Nutr.Soc.
800. Th1/Th2 balance: the hypothesis, its limitations, and implications for health and disease Kidd, P. 2003 Altern.Med.Rev.
801. Disease outcomes as a consequence of environmental influences on the development of the immune system Bjorksten, B. 2009 Curr.Opin.Allergy Clin.Immunol.
802. Age-related changes in Type 1 and Type 2 cytokine production in humans Gardner, E. M. and Murasko, D. M. 2002 Biogerontology.
803. Impaired apoptosis and immune senescence - cause or effect? Hsu, H. C., Scott, D. K., and Mountz, J. D. 2005 Immunol.Rev.
804. [The immune system in aging] Ibs, K. H. and Rink, L. 2001 Z.Gerontol.Geriatr.
805. Natural killer activity and thyroid hormone levels in young and elderly persons Kmiec, Z., Mysliwska, J., Rachon, D., Kotlarz, G., Sworzczak, K., and Mysliwski, A. 2001 Gerontology
806. Vitamin D, thyroid hormones and muscle mass influence natural killer (NK) innate immunity in healthy nonagenarians and centenarians Mariani, E., Ravaglia, G., Forti, P., Meneghetti, A., Tarozzi, A., Maioli, F., Boschi, F., Pratelli, L., Pizzoferrato, A., Piras, F., and Facchini, A. 1999 Clin.Exp.Immunol.
807. Reversibility of age associated NK defect by endocrinological and/or nutritional intervention Provinciali, M., Pieri, C., and Fabris, N. 1991 Ann.Ist.Super.Sanita
808. [Vitamin D and the immune system] Thomasset, M. 1994 Pathol.Biol.(Paris)
809. Is the anti-inflammatory effect of regular exercise responsible for reduced cardiovascular disease? Wilund, K. R. 2007 Clin.Sci.(Lond)
810. Immune function in sport and exercise Gleeson, M. 2-15-2007 J.Appl.Physiol
811. Changes in inflammatory biomarkers following one-year of moderate resistance training in overweight women Olson, T. P., Dengel, D. R., Leon, A. S., and Schmitz, K. H. 2007 Int.J.Obes.(Lond)
812. Nutrition and the immune system from birth to old age Chandra, R. K. 2002 Eur.J.Clin.Nutr.
813. Carotenoid action on the immune response Chew, B. P. and Park, J. S. 2004 J.Nutr.
814. Dietary folate improves age-related decreases in lymphocyte function Field, C. J., Van, Aerde A., Drager, K. L., Goruk, S., and Basu, T. 8-9-2005 J.Nutr.Biochem.
815. Acute and "chronic" phase reaction-a mother of disease Bengmark, S. 2004 Clin.Nutr.
816. Aging and the endothelium d'Alessio, P. 2004 Exp.Gerontol.
817. The immune system in the oxidative stress conditions of aging and hypertension: favorable effects of antioxidants and physical exercise De la, Fuente M., Hernanz, A., and Vallejo, M. C. 2005 Antioxid.Redox.Signal.
818. Moderate exercise improves antibody response to influenza immunization in older adults Kohut, M. L., Arntson, B. A., Lee, W., Rozeboom, K., Yoon, K. J., Cunnick, J. E., and McElhaney, J. 6-2-2004 Vaccine
819. Reversing age-associated immunosenescence via exercise Kohut, M. L. and Senchina, D. S. 2004 Exerc.Immunol.Rev.
820. Autophagy is required for exercise training-induced skeletal muscle adaptation and improvement of physical performance Lira, V. A., Okutsu, M., Zhang, M., Greene, N. P., Laker, R. C., Breen, D. S., Hoehn, K. L., and Yan, Z. 6-27-2013 FASEB J.
821. Chronic Caloric Restriction and Exercise Improve Metabolic Conditions of Dietary-Induced Obese Mice in Autophagy Correlated Manner without Involving AMPK Cui, M., Yu, H., Wang, J., Gao, J., and Li, J. 2013 J.Diabetes Res.
822. Exercise restores decreased physical activity levels and increases markers of autophagy and oxidative capacity in myostatin/activin-blocked mdx mice Hulmi, J. J., Oliveira, B. M., Silvennoinen, M., Hoogaars, W. M., Pasternack, A., Kainulainen, H., and Ritvos, O. 2013 Am.J.Physiol Endocrinol.Metab
823. Autophagic response to exercise training in skeletal muscle with age Kim, Y. A., Kim, Y. S., Oh, S. L., Kim, H. J., and Song, W. 3-8-2013 J.Physiol Biochem.
824. Chronic resistance training activates autophagy and reduces apoptosis of muscle cells by modulating IGF-1 and its receptors, Akt/mTOR and Akt/FOXO3a signaling in aged rats Luo, L., Lu, A. M., Wang, Y., Hong, A., Chen, Y., Hu, J., Li, X., and Qin, Z. H. 2013 Exp.Gerontol.
825. Solar ultraviolet radiation as a trigger of cell signal transduction Heck, D. E., Gerecke, D. R., Vetrano, A. M., and Laskin, J. D. 3-15-2004 Toxicol.Appl.Pharmacol.
826. Ascorbate deficiency results in impaired neutrophil apoptosis and clearance and is associated with up-regulation of hypoxia-inducible factor 1alpha Vissers, M. C. and Wilkie, R. P. 2007 J.Leukoc.Biol.
827. Sodium ascorbate (vitamin C) induces apoptosis in melanoma cells via the down-regulation of transferrin receptor dependent iron uptake Kang, J. S., Cho, D., Kim, Y. I., Hahm, E., Kim, Y. S., Jin, S. N., Kim, H. N., Kim, D., Hur, D., Park, H., Hwang, Y. I., and Lee, W. J. 2005 J.Cell Physiol
828. L-ascorbic acid (vitamin C) induces the apoptosis of B16 murine melanoma cells via a caspase-8-independent pathway Kang, J. S., Cho, D., Kim, Y. I., Hahm, E., Yang, Y., Kim, D., Hur, D., Park, H., Bang, S., Hwang, Y. I., and Lee, W. J. 2003 Cancer Immunol.Immunother.

829. Vitamin C and cellular immune functions. Protection against hypochlorous acid-mediated inactivation of glyceraldehyde-3-phosphate dehydrogenase and ATP generation in human leukocytes as a possible mechanism of ascorbate-mediated immunostimulation Anderson, R., Smit, M. J., Joone, G. K., and Van Staden, A. M. 1990 *Ann.N.Y.Acad.Sci.*
830. Severe hypovitaminosis C occurring as the result of adoptive immunotherapy with high-dose interleukin 2 and lymphokine-activated killer cells Marcus, S. L., Dutcher, J. P., Paietta, E., Ciobanu, N., Strauman, J., Wiernik, P. H., Hutner, S. H., Frank, O., and Baker, H. 8-1-1987 *Cancer Res.*
831. A biological role for ascorbate in the selective neutralization of extracellular phagocyte-derived oxidants Anderson, R. and Lukey, P. T. 1987 *Ann.N.Y.Acad.Sci.*
832. Activated polymorphonuclear leucocytes consume vitamin C Hemila, H., Roberts, P., and Wikstrom, M. 12-3-1984 *FEBS Lett.*
833. Vitamin C and immunity: influence of ascorbate on prostaglandin E2 synthesis and implications for natural killer cell activity Siegel, B. V. and Morton, J. I. 1984 *Int.J.Vitam.Nutr.Res.*
834. Cell-mediated immunity in nutritional deficiency McMurray, D. N. 1984 *Prog.Food Nutr.Sci.*
835. The immunostimulatory, antiinflammatory and anti-allergic properties of ascorbate Anderson, R. 1984 *Adv.Nutr.Res.*
836. The effect of ascorbate on cellular humoral immunity in asthmatic children Anderson, R., Hay, I., van, Wyk H., Oosthuizen, R., and Theron, A. 12-13-1980 *S.Afr.Med.J.*
837. The effect of variations in vitamin C intake on the cellular immune response of guinea pigs Fraser, R. C., Pavlovic, S., Kurahara, C. G., Murata, A., Peterson, N. S., Taylor, K. B., and Feigen, G. A. 1980 *Am.J.Clin.Nutr.*
838. The effects of increasing weekly doses of ascorbate on certain cellular and humoral immune functions in normal volunteers Anderson, R., Oosthuizen, R., Maritz, R., Theron, A., and van Rensburg, A. J. 1980 *Am.J.Clin.Nutr.*
839. Effects of ascorbic acid and sodium ascorbate on cyclic nucleotide metabolism in human lymphocytes Atkinson, J. P., Weiss, A., Ito, M., Kelly, J., and Parker, C. W. 1979 *J.Cyclic.Nucleotide.Res.*
840. Vitamin C and immunity: an assessment of the evidence Thomas, W. R. and Holt, P. G. 1978 *Clin.Exp.Immunol.*
841. Calorie restriction in overweight males ameliorates obesity-related metabolic alterations and cellular adaptations through anti-aging effects, possibly including AMPK and SIRT1 activation Kitada, M., Kume, S., Takeda-Watanabe, A., S T, Kanasaki, K., and Koya, D. 6-23-2013 *Biochim.Biophys.Acta*
842. Long-Chain Omega-3 Fatty Acids Improve Brain Function and Structure in Older Adults Witte, A. V., Kerti, L., Hermannstadter, H. M., Fiebach, J. B., Schreiber, S. J., Schuchardt, J. P., Hahn, A., and Floel, A. 6-24-2013 *Cereb.Cortex*
843. Impact of hyperinsulinemia on the development of hypertension in normotensive, nondiabetic adults: a 4-year follow-up study Park, S. E., Rhee, E. J., Park, C. Y., Oh, K. W., Park, S. W., Kim, S. W., and Lee, W. Y. 2013 *Metabolism*
844. Dietary patterns, insulin sensitivity and inflammation in older adults Anderson, A. L., Harris, T. B., Tyllavsky, F. A., Perry, S. E., Houston, D. K., Lee, J. S., Kanaya, A. M., and Sahyoun, N. R. 2012 *Eur.J.Clin.Nutr.*
845. Frailty status and altered glucose-insulin dynamics Kalyani, R. R., Varadhan, R., Weiss, C. O., Fried, L. P., and Cappola, A. R. 2012 *J.Gerontol.A Biol.Sci.Med.Sci.*
846. Glucose and insulin measurements from the oral glucose tolerance test and relationship to muscle mass Kalyani, R. R., Metter, E. J., Ramachandran, R., Chia, C. W., Saudek, C. D., and Ferrucci, L. 2012 *J.Gerontol.A Biol.Sci.Med.Sci.*
847. Fasting plasma insulin, C-peptide and cognitive change in older men without diabetes: results from the Physicians' Health Study II Okereke, O. I., Kurth, T., Pollak, M. N., Gaziano, J. M., and Grodstein, F. 2010 *Neuroepidemiology*
848. Cytokines, stress, and depressive illness Anisman, H. and Merali, Z. 2002 *Brain Behav.Immun.*
849. Sleep, cytokines and immune function Dickstein, J. B. and Moldofsky, H. 1999 *Sleep Med.Rev.*
850. Sleep disruption in the intensive care unit Gabor, J. Y., Cooper, A. B., and Hanly, P. J. 2001 *Curr.Opin.Crit Care*
851. Increased dietary fat prevents sleep deprivation-induced immune suppression in rats Horohov, D. W., Pourciau, S. S., Mistic, L., Chapman, A., and Ryan, D. H. 2001 *Comp Med.*
852. Effects of sleep and sleep loss on immunity and cytokines Irwin, M. 2002 *Brain Behav.Immun.*
853. Sleep deprivation Malik, S. W. and Kaplan, J. 2005 *Prim.Care*
854. Effects of 48 hours sleep deprivation on human immune profile Ozturk, L., Pelin, Z., Karadeniz, D., Kaynak, H., Cakar, L., and Gozukirmizi, E. 1999 *Sleep Res.Online.*
855. The variability of autophagy and cell death susceptibility: Unanswered questions Loos, B., Engelbrecht, A. M., Lockshin, R. A., Klionsky, D. J., and Zakeri, Z. 7-10-2013 *Autophagy.*
856. Deconstructing mitochondrial dysfunction in Alzheimer disease Garcia-Escudero, V., Martin-Maestro, P., Perry, G., and Avila, J. 2013 *Oxid.Med.Cell Longev.*
857. Targeting autophagy as a potential therapeutic approach for melanoma therapy Liu, H., He, Z., and Simon, H. U. 7-2-2013 *Semin.Cancer Biol.*
858. Silibinin protects murine fibroblast L929 cells from UVB-induced apoptosis through the simultaneous inhibition of ATM-p53 pathway and autophagy Liu, W., Otkur, W., Zhang, Y., Li, Q., Ye, Y., Zang, L., He, H., Hayashi, T., Tashiro, S. I., Onodera, S., and Ikejima, T. 7-5-2013 *FEBS J.*
859. Impaired autophagy and APP processing in Alzheimer's disease: The potential role of Beclin 1 interactome Salminen, A., Kaarniranta, K., Kauppinen, A., Ojala, J., Haapasalo, A., Soininen, H., and Hiltunen, M. 7-1-2013 *Prog.Neurobiol.*
860. Inhibition of androgen induces autophagy in benign prostate epithelial cells Li, M., Yang, X., Wang, H., Xu, E., and Xi, Z. 7-2-2013 *Int.J.Urol.*
861. Emerging regulation and functions of autophagy Boya, P., Reggiori, F., and Codogno, P. 7-1-2013 *Nat.Cell Biol.*
862. The Amazing Odontoblast: Activity, Autophagy, and Aging Couve, E., Osorio, R., and Schmachtenberg, O. 6-26-2013 *J.Dent.Res.*
863. Autophagy as an immune effector against tuberculosis Bradfute, S. B., Castillo, E. F., Arko-Mensah, J., Chauhan, S., Jiang, S., Mandell, M., and Deretic, V. 6-18-2013 *Curr.Opin.Microbiol.*
864. Management of multicellular senescence and oxidative stress Haines, D. D., Juhasz, B., and Tosaki, A. 6-22-2013 *J.Cell Mol.Med.*

865. Psychoneuroimmunology in critically ill patients DeKeyser, F. 2003 AACN.Clin.Issues
866. Stress-induced immune dysfunction: implications for health Glaser, R. and Kiecolt-Glaser, J. K. 2005 Nat.Rev.Immunol.
867. Effects of stress on the immune system Khansari, D. N., Murgo, A. J., and Faith, R. E. 1990 Immunol.Today
868. Psychoneuroimmunology: psychological influences on immune function and health Kiecolt-Glaser, J. K., McGuire, L., Robles, T. F., and Glaser, R. 2002 J.Consult Clin.Psychol.
869. Psychoneuroimmunology and the faith factor Koenig, H. G. 2000 J.Gend.Specif.Med.
870. Psychoneuroimmunology: new avenues of research for the twenty-first century Prolo, P., Chiappelli, F., Fiorucci, A., Dovio, A., Sartori, M. L., and Angeli, A. 2002 Ann.N.Y.Acad.Sci.
871. Unraveling the soul of autoimmune diseases: pathogenesis, diagnosis and treatment adding dowels to the puzzle Colafrancesco, S., Agmon-Levin, N., Perricone, C., and Shoenfeld, Y. 2013 Immunol.Res.
872. Human papillomavirus vaccine and systemic lupus erythematosus Gatto, M., Agmon-Levin, N., Soriano, A., Manna, R., Maoz-Segal, R., Kivity, S., Doria, A., and Shoenfeld, Y. 4-28-2013 Clin.Rheumatol.
873. AUTOIMMUNE THYROID DISEASE ELICITED BY NY-ESO-1 VACCINATION Vita, R., Guarneri, F., Agah, R., and Benvenga, S. 4-16-2013 Thyroid
874. Adverse events following immunization with vaccines containing adjuvants Cerpa-Cruz, S., Paredes-Casillas, P., Landeros, Navarro E., Bernard-Medina, A. G., Martinez-Bonilla, G., and Gutierrez-Urena, S. 2013 Immunol.Res.
875. [Drugs that trigger or exacerbate myasthenia gravis] Elsais, A., Popperud, T. H., Melien, O., and Kerty, E. 2-5-2013 Tidsskr.Nor Laegeforen.
876. [Vaccines and autoimmunity: a strange association under debate] Batista-Duharte, A. 2012 Rev.Peru Med.Exp.Salud Publica
877. Vitamin C for preventing and treating the common cold Douglas, R. M., Hemila, H., D'Souza, R., Chalker, E. B., and Treacy, B. 2004 Cochrane.Database.Syst.Rev.
878. Vitamin C supplementation and respiratory infections: a systematic review Hemila, H. 2004 Mil.Med.
879. Vitamin C and acute respiratory infections Hemila, H. and Douglas, R. M. 1999 Int.J.Tuberc.Lung Dis.
880. Vitamin C supplementation and common cold symptoms: factors affecting the magnitude of the benefit Hemila, H. 1999 Med.Hypotheses
881. Vitamin C intake and susceptibility to the common cold Hemila, H. 1997 Br.J.Nutr.
882. Relationship between colour and aroma of olive oil and nutritional content Fielding, J. M., Sinclair, A. J., DiGregorio, G., Joveski, M., and Stockmann, R. 2003 Asia Pac.J.Clin.Nutr.
883. Sensory properties of virgin olive oil polyphenols: identification of deacetoxy-ligstroside aglycon as a key contributor to pungency Andrewes, P., Busch, J. L., de Joode T., Groenewegen, A., and Alexandre, H. 2-26-2003 J.Agric.Food Chem.
884. Comparison of the antioxidant activities of extra virgin olive oils Lavelli, V. 12-18-2002 J.Agric.Food Chem.
885. Oleuropein, the bitter principle of olives, enhances nitric oxide production by mouse macrophages Visioli, F., Bellosta, S., and Galli, C. 1998 Life Sci.
886. Inhibitory activity of minor polyphenolic and nonpolyphenolic constituents of olive oil against in vitro low-density lipoprotein oxidation Andrikopoulos, N. K., Kaliora, A. C., Assimopoulou, A. N., and Papageorgiou, V. P. 2002 J.Med.Food
887. Effect of minor components of virgin olive oil on topical antiinflammatory assays de la, Puerta R., Martinez-Dominguez, E., and Ruiz-Gutierrez, V. 2000 Z.Naturforsch.[C.]
888. Effects of virgin olive oil phenolics on scavenging of reactive nitrogen species and upon nitrenergic neurotransmission de la, Puerta R., Martinez Dominguez, M. E., Ruiz-Gutierrez, V., Flavill, J. A., and Hault, J. R. 7-27-2001 Life Sci.
889. Oleuropein prevents oxidative myocardial injury induced by ischemia and reperfusion Manna, C., Migliardi, V., Golino, P., Scognamiglio, A., Galletti, P., Chiariello, M., and Zappia, V. 2004 J.Nutr.Biochem.
890. Differential anti-inflammatory effects of phenolic compounds from extra virgin olive oil identified in human whole blood cultures Miles, E. A., Zoubouli, P., and Calder, P. C. 2005 Nutrition
891. Antioxidant and anti-atherogenic activities of olive oil phenolics Turner, R., Etienne, N., Alonso, M. G., de Pascual-Teresa, S., Minihane, A. M., Weinberg, P. D., and Rimbach, G. 2005 Int.J.Vitam.Nutr.Res.
892. Antiatherogenic components of olive oil Visioli, F. and Galli, C. 2001 Curr.Atheroscler.Rep.
893. Olive oil and modulation of cell signaling in disease prevention Wahle, K. W., Caruso, D., Ochoa, J. J., and Quiles, J. L. 2004 Lipids
894. Inhibition of Staphylococcus aureus by oleuropein is mediated by hydrogen peroxide Zanichelli, D., Baker, T. A., Clifford, M. N., and Adams, M. R. 2005 J.Food Prot.
895. The olive leaf extract exhibits antiviral activity against viral haemorrhagic septicaemia rhabdovirus (VHSV) Micol, V., Caturla, N., Perez-Fons, L., Mas, V., Perez, L., and Estepa, A. 2005 Antiviral Res.
896. Inhibition of Salmonella enteritidis by oleuropein in broth and in a model food system Tassou, C. C. and Nychas, G. J. 1995 Lett.Appl.Microbiol.
897. The effect of the olive phenolic compound, oleuropein, on growth and enterotoxin B production by Staphylococcus aureus Tranter, H. S., Tassou, S. C., and Nychas, G. J. 1993 J.Appl.Bacteriol.
898. Antimicrobial properties of oleuropein and products of its hydrolysis from green olives Fleming, H. P., Walter, W. M., Jr., and Etchells, J. L. 1973 Appl.Microbiol.
899. Studies on the mechanism of the antimicrobial action of oleuropein Juven, B., Henis, Y., and Jacoby, B. 1972 J.Appl.Bacteriol.
900. In vitro antimycoplasmal activity of oleuropein Furneri, P. M., Marino, A., Saija, A., Uccella, N., and Bisignano, G. 2002 Int.J.Antimicrob.Agents
901. The antioxidant/anticancer potential of phenolic compounds isolated from olive oil Owen, R. W., Giacosa, A., Hull, W. E., Haubner, R., Spiegelhalder, B., and Bartsch, H. 2000 Eur.J.Cancer

902. Antioxidant and other biological activities of phenols from olives and olive oil Visioli, F., Poli, A., and Gall, C. 2002 *Med.Res.Rev.*
903. Free radical-scavenging properties of olive oil polyphenols Visioli, F., Bellomo, G., and Galli, C. 6-9-1998 *Biochem.Biophys.Res.Comm.*
904. Olive (*Olea europaea*) leaf extract effective in patients with stage-1 hypertension: comparison with Captopril Susalit, E., Agus, N., Effendi, I., Tjandrawinata, R. R., Nofiarny, D., Perrinjaquet-Mocchetti, T., and Verbruggen, M. 2-15-2011 *Phytomedicine.*
905. Olive leaf extract attenuates cardiac, hepatic, and metabolic changes in high carbohydrate-, high fat-fed rats Poudyal, H., Campbell, F., and Brown, L. 2010 *J.Nutr.*
906. Hypoglycemic and antioxidant effect of oleuropein in alloxan-diabetic rabbits Al-Azzawie, H. F. and Alhamdani, M. S. 10-15-2005 *Life Sci.*
907. Inactivation of cytochrome P450 by the food-derived complex phenol oleuropein Stupans, I., Murray, M., Kirlich, A., Tuck, K. L., and Hayball, P. J. 2001 *Food Chem.Toxicol.*
908. DNA protecting and genotoxic effects of olive oil related components in cells exposed to hydrogen peroxide Nousis, L., Doulias, P. T., Aligiannis, N., Bazios, D., Agalias, A., Galaris, D., and Mitakou, S. 2005 *Free Radic.Res.*
909. Tetracycline-induced reproductive toxicity in male rats: effects of vitamin C and N-acetylcysteine Farombi, E. O., Ugwuezunmba, M. C., Ezenwadu, T. T., Oyeyemi, M. O., and Ekor, M. 2008 *Exp.Toxicol.Pathol.*
910. Protective effects of caffeic acid phenethyl ester, vitamin C, vitamin E and N-acetylcysteine on vancomycin-induced nephrotoxicity in rats Ocak, S., Gorur, S., Hakverdi, S., Celik, S., and Erdogan, S. 2007 *Basic Clin.Pharmacol.Toxicol.*
911. Antimicrobial effects of antioxidants with and without clarithromycin on *Helicobacter pylori* Chatterjee, A., Bagchi, D., Yasmin, T., and Stohs, S. J. 2005 *Mol.Cell Biochem.*
912. Effects of co-supplementation of vitamins E and C on gentamicin-induced nephrotoxicity in rat Kadkhodae, M., Khastar, H., Faghihi, M., Ghaznavi, R., and Zahmatkesh, M. 2005 *Exp.Physiol*
913. Protection against minocycline pigment formation by ascorbic acid (vitamin C) Bowles, W. H. 1998 *J.Esthet.Dent.*
914. Evidence of probiotics in prevention of allergy and asthma Bjorksten, B. 2005 *Curr.Drug Targets.Inflamm.Allergy*
915. Probiotics as mainstream allergy therapy? Murch, S. H. 2005 *Arch.Dis.Child*
916. Probiotics: the benefits of bacterial cultures Macintyre, A. and Cymet, T. C. 2005 *Compr.Ther.*
917. Probiotics: do they have a role in oral medicine and dentistry? Meurman, J. H. 2005 *Eur.J.Oral Sci.*
918. *Bacillus clausii* exerts immuno-modulatory activity in allergic subjects: a pilot study Ciprandi, G., Vizzaccaro, A., Cirillo, I., and Tosca, M. A. 2005 *Allerg.Immunol.(Paris)*
919. Preventive and curative effects of probiotics in atopic patients Bongaerts, G. P. and Severijnen, R. S. 2005 *Med.Hypotheses*
920. Probiotics: a complementary approach in the treatment and prevention of pediatric atopic disease Ogden, N. S. and Bielory, L. 2005 *Curr.Opin.Allergy Clin.Immunol.*
921. Atopic dermatitis and the 'hygiene hypothesis': too clean to be true? Flohr, C., Pascoe, D., and Williams, H. C. 2005 *Br.J.Dermatol.*
922. Food allergy and the gastrointestinal tract Bischoff, S. and Crowe, S. E. 2004 *Curr.Opin.Gastroenterol.*
923. Mucosae, allergy and probiotics Munoz-Lopez, F. 2004 *Allergol.Immunopathol.(Madr.)*
924. Does the microbiota regulate immune responses outside the gut? Noverr, M. C. and Huffnagle, G. B. 2004 *Trends Microbiol.*
925. Probiotics and human health: a clinical perspective Gill, H. S. and Guarner, F. 2004 *Postgrad.Med.J.*
926. Probiotics in primary prevention of atopic disease: a randomised placebo-controlled trial Kalliomaki, M., Salminen, S., Arvilommi, H., Kero, P., Koskinen, P., and Isolauri, E. 4-7-2001 *Lancet*
927. Prophylactic and therapeutic uses of probiotics: a review Kopp-Hoolihan, L. 2001 *J.Am.Diet.Assoc.*
928. Probiotics: effects on immunity Isolauri, E., Sutas, Y., Kankaanpaa, P., Arvilommi, H., and Salminen, S. 2001 *Am.J.Clin.Nutr.*
929. Healthy gut microflora and allergy: factors influencing development of the microbiota Kirjavainen, P. V. and Gibson, G. R. 1999 *Ann.Med.*
930. Clinical uses of probiotics for stabilizing the gut mucosal barrier: successful strains and future challenges Salminen, S., Isolauri, E., and Salminen, E. 1996 *Antonie Van Leeuwenhoek*
931. The pathogenetic significance of intestinal *Candida* colonization--a systematic review from an interdisciplinary and environmental medical point of view Lacour, M., Zunder, T., Huber, R., Sander, A., Daschner, F., and Frank, U. 2002 *Int.J.Hyg. Environ.Health*
932. [Dysbioses of the oral cavity and intestines and immune reactivity in of adolescent bronchial asthma patients] Gavrish, T. V. 2001 *Zh.Mikrobiol.Epidemiol.Immunobiol.*
933. Gut barrier dysfunction in food allergy Heyman, M. 2005 *Eur.J.Gastroenterol.Hepatol.*
934. The mast cell and gut nematodes: damage and defence Pennock, J. L. and Grecis, R. K. 2006 *Chem.Immunol.Allergy*
935. Tight junctions, leaky intestines, and pediatric diseases Liu, Z., Li, N., and Neu, J. 2005 *Acta Paediatr.*
936. Preventing intolerance: the induction of nonresponsiveness to dietary and microbial antigens in the intestinal mucosa Smith, D. W. and Nagler-Anderson, C. 4-1-2005 *J.Immunol.*
937. Helminth infections: protection from atopic disorders Smits, H. H., Hartgers, F. C., and Yazdanbakhsh, M. 2005 *Curr.Allergy Asthma Rep.*
938. The role of probiotics in the clinical management of food allergy and atopic dermatitis Miraglia del Giudice M. and De Luca, M. G. 2004 *J.Clin.Gastroenterol.*
939. Dietary modification of atopic disease: Use of probiotics in the prevention of atopic dermatitis Isolauri, E. 2004 *Curr.Allergy Asthma Rep.*
940. Probiotics, prebiotics and child health: where are we going? Salvini, F., Granieri, L., Gemmellaro, L., and Giovannini, M. 2004 *J.Int.Med.Res.*

941. Treatment of perennial allergic rhinitis with lactic acid bacteria Wang, M. F., Lin, H. C., Wang, Y. Y., and Hsu, C. H. 2004 *Pediatr.Allergy Immunol.*
942. Are fish oils an effective therapy in mental illness--an analysis of the data Maidment, I. D. 2000 *Acta Psychiatr.Scand.*
943. The neurology of folic acid deficiency Reynolds, E. H. 2014 *Handb.Clin.Neurol.*
944. The periconceptual period, reproduction and long-term health of offspring: the importance of one-carbon metabolism Steegers-Theunissen, R. P., Twigt, J., Pestinger, V., and Sinclair, K. D. 2013 *Hum.Reprod.Update.*
945. Genetic defects in folate and cobalamin pathways affecting the brain Kirsch, S. H., Herrmann, W., and Obeid, R. 2013 *Clin.Chem.Lab Med.*
946. Mood disorder with mixed, psychotic features due to vitamin b12 deficiency in an adolescent: case report Tufan, A. E., Bilici, R., Usta, G., and Erdogan, A. 2012 *Child Adolesc.Psychiatry Ment.Health*
947. B vitamins and n-3 fatty acids for brain development and function: review of human studies van de Rest, O., van Hooijdonk, L. W., Doets, E., Schiepers, O. J., Eilander, A., and de Groot, L. C. 2012 *Ann.Nutr.Metab*
948. Elevated plasma homocysteine in association with decreased vitamin B(12), folate, serotonin, lipids and lipoproteins in depressed patients Ebesunun, M. O., Eruvulobi, H. U., Olagunju, T., and Owoeye, O. A. 2012 *Afr.J.Psychiatry (Johannesbg.)*
949. A synergistic effect of a daily supplement for 1 month of 200 mg magnesium plus 50 mg vitamin B6 for the relief of anxiety-related premenstrual symptoms: a randomized, double-blind, crossover study De Souza, M. C., Walker, A. F., Robinson, P. A., and Bolland, K. 2000 *J.Womens Health GenD.Based.Med.*
950. Plasma pyridoxine deficiency is related to increased psychological distress in recently bereaved homosexual men Baldewicz, T., Goodkin, K., Feaster, D. J., Blaney, N. T., Kumar, M., Kumar, A., Shor-Posner, G., and Baum, M. 1998 *Psychosom.Med.*
951. Decreased vitamin B-6 status of submariners during prolonged patrol Reynolds, R. D., Styer, D. J., and Schlichting, C. L. 1988 *Am.J.Clin.Nutr.*
952. Oral contraceptives and depression: impact, prevalence and cause Slap, G. B. 1981 *J.Adolesc.Health Care*
953. Chronic zinc toxicity in an infant who received zinc therapy for atopic dermatitis Sugiura, T., Goto, K., Ito, K., Ueta, A., Fujimoto, S., and Togari, H. 2005 *Acta Paediatr.*
954. Subacute toxic effects of zinc on various tissues and organs of rats Piao, F., Yokoyama, K., Ma, N., and Yamauchi, T. 11-1-2003 *Toxicol.Lett.*
955. Copper deficiency anemia and nephrosis in zinc-toxicity: a case report Hein, M. S. 2003 *S.D.J.Med.*
956. Zinc inhibition of cellular energy production: implications for mitochondria and neurodegeneration Dineley, K. E., Votyakova, T. V., and Reynolds, I. J. 2003 *J.Neurochem.*
957. [Zinc: concepts on an essential micronutrient] Salgueiro, J., Zubillaga, M., Lysionek, A., Sarabia, M. I., Calmanovici, G., Caro, R., De, Paoli T., Hager, A., Weill, R., and Boccio, J. 1999 *Acta Physiol Pharmacol.Ther.Latinoam.*
958. Zinc toxicity Fosmire, G. J. 1990 *Am.J.Clin.Nutr.*
959. Cytotoxicity of zinc in vitro Borovansky, J. and Riley, P. A. 1989 *Chem.Biol.Interact.*
960. Effect of taurine supplementation on exercise capacity of patients with heart failure Beyranvand, M. R., Khalafi, M. K., Roshan, V. D., Choobineh, S., Parsa, S. A., and Piranfar, M. A. 2011 *J.Cardiol.*
961. Hypotensive effect of taurine. Possible involvement of the sympathetic nervous system and endogenous opiates Fujita, T. and Sato, Y. 1988 *J.Clin.Invest*
962. Strong induction of iodothyronine deiodinases by chemotherapeutic selenocompounds Stoedter, M., Renko, K., Ibanez, E., Plano, D., Becker, N. P., Martitz, J., Palop, J. A., Calvo, A., Sanmartin, C., and Schomburg, L. 1-12-2015 *Metallomics.*
963. Effect of low-dose selenium on thyroid autoimmunity and thyroid function in UK pregnant women with mild-to-moderate iodine deficiency Mao, J., Pop, V. J., Bath, S. C., Vader, H. L., Redman, C. W., and Rayman, M. P. 12-19-2014 *Eur.J.Nutr.*
964. Selenium: an element for life Duntas, L. H. and Benvenga, S. 12-18-2014 *Endocrine.*
965. [The importance of selenium in Hashimoto's disease] Zagrodzki, P. and Kryczyk, J. 2014 *Postepy Hig.Med.Dosw.(Online.)*
966. Metabolic changes associated with selenium deficiency in mice Mickiewicz, B., Villemaire, M. L., Sandercock, L. E., Jirik, F. R., and Vogel, H. J. 7-11-2014 *Biometals*
967. Selenoproteins in nervous system development and function Pitts, M. W., Byrns, C. N., Ogawa-Wong, A. N., Kremer, P., and Berry, M. J. 2014 *Biol.Trace Elem.Res.*
968. Selenium supplementation alleviates autoimmune thyroiditis by regulating expression of TH1/TH2 cytokines Tan, L., Sang, Z. N., Shen, J., Wu, Y. T., Yao, Z. X., Zhang, J. X., Zhao, N., and Zhang, W. Q. 2013 *Biomed.Enviro.Sci.*
969. Vitamin D vs broad spectrum phototherapy in the treatment of seasonal affective disorder Gloth, F. M., III, Alam, W., and Hollis, B. 1999 *J.Nutr.Health Aging*
970. Bone mineral density in women with depression Michelson, D., Stratakis, C., Hill, L., Reynolds, J., Galliven, E., Chrousos, G., and Gold, P. 10-17-1996 *N.Engl.J.Med.*
971. The acute effects of L-theanine in comparison with alprazolam on anticipatory anxiety in humans Lu, K., Gray, M. A., Oliver, C., Liley, D. T., Harrison, B. J., Bartholomeusz, C. F., Phan, K. L., and Nathan, P. J. 2004 *Hum.Psychopharmacol.*
972. Possible involvement of group I mGluRs in neuroprotective effect of theanine Nagasawa, K., Aoki, H., Yasuda, E., Nagai, K., Shimohama, S., and Fujimoto, S. 7-16-2004 *Biochem.Biophys.Res.Comm.*
973. Effect of theanine, r-glutamylethylamide, on brain monoamines and striatal dopamine release in conscious rats Yokogoshi, H., Kobayashi, M., Mochizuki, M., and Terashima, T. 1998 *Neurochem.Res.*
974. [Value of sports in treatment of psychiatric illness] Broocks, A., Meyer, T. F., George, A., Pekrun, G., Hillmer-Vogel, U., Hajak, G., Bandelow, B., and Ruther, E. 1997 *Psychother.Psychosom.Med.Psychol.*
975. Mood alterations in older adults following acute exercise Pierce, E. F. and Pate, D. W. 1994 *Percept.Mot.Skills*

976. Exercise training: significance of regional alterations in serotonin metabolism of rat brain in relation to antidepressant effect of exercise Dey, S., Singh, R. H., and Dey, P. K. 1992 *Physiol Behav*.
977. Physical exercise and brain monoamines: a review Chaouloff, F. 1989 *Acta Physiol Scand*.
978. Changes in heart rate, noradrenaline, cortisol and mood during Tai Chi Jin, P. 1989 *J.Psychosom.Res*.
979. [Psychoregulating role of nicotinamide] Akhundov, R. A., Sultanov, A. A., Gadzhily, R. A., and Sadykhov, R. V. 1993 *Biull.Eksp.Biol.Med*.
980. The influence of curcumin and manganese complex of curcumin on cadmium-induced oxidative damage and trace elements status in tissues of mice Eybl, V., Kotyzova, D., Leseticky, L., Bludovska, M., and Koutensky, J. 12-12-2005 *J.Appl.Toxicol*.
981. Curcuma longa extract protects against gastric ulcers by blocking H2 histamine receptors Kim, D. C., Kim, S. H., Choi, B. H., Baek, N. I., Kim, D., Kim, M. J., and Kim, K. T. 2005 *Biol.Pharm.Bull*.
982. Inflammation, pain, and chronic disease: an integrative approach to treatment and prevention Edwards, T. 2005 *Altern.Ther.Health Med*.
983. Prevention of Alzheimer's disease: Omega-3 fatty acid and phenolic anti-oxidant interventions Cole, G. M., Lim, G. P., Yang, F., Teter, B., Begum, A., Ma, Q., Harris-White, M. E., and Frautschy, S. A. 2005 *Neurobiol.Aging*
984. Curcumin Inhibits Platelet-Derived Growth Factor-Stimulated Vascular Smooth Muscle Cell Function and Injury-Induced Neointima Formation Yang, X., Thomas, D. P., Zhang, X., Culver, B. W., Alexander, B. M., Murdoch, W. J., Rao, M. N., Tulis, D. A., Ren, J., and Sreejayan, N. 10-20-2005 *Arterioscler.Thromb.Vasc.Biol*.
985. Immunomodulatory effects of curcumin Yadav, V. S., Mishra, K. P., Singh, D. P., Mehrotra, S., and Singh, V. K. 2005 *Immunopharmacol.Immunotoxicol*.
986. Inhibition of lipid peroxidation and protein oxidation in rat liver mitochondria by curcumin and its analogues Wei, Q. Y., Chen, W. F., Zhou, B., Yang, L., and Liu, Z. L. 2006 *Biochim.Biophys.Acta*
987. Curcumin (Diferuloylmethane) Downregulates Expression of Cell Proliferation, Antiapoptotic and Metastatic Gene Products Through Suppression of κ B α Kinase and AKT Activation Aggarwal, S., Ichikawa, H., Takada, Y., Sandur, S. K., Shishodia, S., and Aggarwal, B. B. 10-11-2005 *Mol.Pharmacol*.
988. Curcumin is a potent broad spectrum inhibitor of matrix metalloproteinase gene expression in human astrogloma cells Kim, S. Y., Jung, S. H., and Kim, H. S. 11-18-2005 *Biochem.Biophys.Res.Commun*.
989. Antiangiogenic activity of curcumin in hepatocellular carcinoma cells implanted nude mice Yoysungnoen, P., Wirachwong, P., Bhattarakosol, P., Niimi, H., and Patumraj, S. 2005 *Clin.Hemorheol.Microcirc*.
990. Comparative effects of curcumin and its analog on alcohol- and polyunsaturated fatty acid-induced alterations in circulatory lipid profiles Rukkumani, R., Aruna, K., Varma, P. S., Rajasekaran, K. N., and Menon, V. P. 2005 *J.Med.Food*
991. Curcumin: the story so far Sharma, R. A., Gescher, A. J., and Steward, W. P. 2005 *Eur.J.Cancer*
992. Curcumin suppresses growth and induces apoptosis in primary effusion lymphoma Uddin, S., Hussain, A. R., Manogaran, P. S., Al-Hussein, K., Platanius, L. C., Gutierrez, M. I., and Bhatia, K. G. 10-27-2005 *Oncogene*
993. Curcumin has a palliative action on gentamicin-induced nephrotoxicity in rats Ali, B. H., Al-Wabel, N., Mahmoud, O., Mousa, H. M., and Hashad, M. 2005 *Fundam.Clin.Pharmacol*.
994. The effect of turmeric extracts on inflammatory mediator production Lantz, R. C., Chen, G. J., Solyom, A. M., Jolad, S. D., and Timmermann, B. N. 2005 *Phytomedicine*.
995. Curcumin-induced antiproliferative and proapoptotic effects in melanoma cells are associated with suppression of κ B kinase and nuclear factor κ B activity and are independent of the B-Raf/mitogen-activated/extracellular signal-regulated protein kinase pathway and the Akt pathway Siwak, D. R., Shishodia, S., Aggarwal, B. B., and Kurzrock, R. 8-15-2005 *Cancer*
996. Effect of vitamin A supplementation of plasma progesterone and estradiol levels during pregnancy Panth, M., Raman, L., Ravinder, P., and Sivakumar, B. 1991 *Int.J Vitam.Nutr Res*.
997. Treatment strategies for premenstrual syndrome Daugherty, J. E. 1998 *Am.Fam.Physician*
998. Sex hormone patterns and serum retinol concentrations in adolescent girls Brabin, L., Roberts, C., Barr, F., Agbaje, S., Harper, G., and Briggs, N. 2004 *J.Reprod.Med*.
999. A correlation between migraine, histamine and immunoglobulin e Gazerani, P., Pourpak, Z., Ahmadiani, A., Hemmati, A., and Kazemnejad, A. 2003 *Scand.J.Immunol*.
1000. Vitamin C depletion is associated with alterations in blood histamine and plasma free carnitine in adults Johnston, C. S., Solomon, R. E., and Corte, C. 1996 *J.Am.Coll.Nutr*.
1001. Antihistamine effect of supplemental ascorbic acid and neutrophil chemotaxis Johnston, C. S., Martin, L. J., and Cai, X. 1992 *J.Am.Coll.Nutr*.
1002. The antihistamine action of ascorbic acid Johnston, C. S. 1996 *Subcell.Biochem*.
1003. Blood histamine is associated with coronary artery disease, cardiac events and severity of inflammation and atherosclerosis Clejan, S., Japa, S., Clemetson, C., Hasabnis, S. S., David, O., and Talano, J. V. 2002 *J.Cell Mol.Med*.
1004. Asthma and vitamin C Bielory, L. and Gandhi, R. 1994 *Ann.Allergy*
1005. Histamine and ascorbic acid in human blood Clemetson, C. A. 1980 *J.Nutr*.
1006. [Migraine as one of the symptoms of food allergy] Mylek, D. 1-20-1992 *Pol.Tyg.Lek*.
1007. Intravenous nutrient therapy: the "Myers' cocktail" Gaby, A. R. 2002 *Altern.Med.Rev*.
1008. Role of individual free fatty acids in migraine Anthony, M. 1978 *Res.Clin.Stud.Headache*
1009. Role of magnesium, coenzyme Q10, riboflavin, and vitamin B12 in migraine prophylaxis Bianchi, A., Salomone, S., Caraci, F., Pizza, V., Bernardini, R., and D'Amato, C. C. 2004 *Vitam.Horm*.
1010. The multifaceted and widespread pathology of magnesium deficiency Johnson, S. 2001 *Med.Hypotheses*
1011. Serum and erythrocyte magnesium concentrations and migraine Thomas, J., Thomas, E., and Tomb, E. 1992 *Magnes.Res*.

1012. Free and total magnesium in lymphocytes of migraine patients - effect of magnesium-rich mineral water intake Thomas, J., Millot, J. M., Sebillé, S., Delabroise, A. M., Thomas, E., Manfait, M., and Arnaud, M. J. 2000 *Clin.Chim.Acta*
1013. Vitamin D and calcium in menstrual migraine Thys-Jacobs, S. 1994 *Headache*
1014. A possible new option for migraine management: agomelatine Guglielmo, R., Martinotti, G., Di, Giannantonio M., and Janiri, L. 2013 *Clin.Neuropharmacol.*
1015. Melatonin in antinociception: its therapeutic applications Srinivasan, V., Lauterbach, E. C., Ho, K. Y., Acuna-Castroviejo, D., Zakaria, R., and Brzezinski, A. 2012 *Curr.Neuropharmacol.*
1016. Melatonin for migraine prevention Peres, M. F. 2011 *Curr.Pain Headache Rep.*
1017. Analgesic effects of melatonin: a review of current evidence from experimental and clinical studies Wilhelmsen, M., Amirian, I., Reiter, R. J., Rosenberg, J., and Gogenur, I. 2011 *J.Pineal Res.*
1018. Melatonin to prevent migraine or tension-type headache in children Miano, S., Parisi, P., Pelliccia, A., Luchetti, A., Paolino, M. C., and Villa, M. P. 2008 *Neurol.Sci.*
1019. "Natural" or alternative medications for migraine prevention Evans, R. W. and Taylor, F. R. 2006 *Headache*
1020. Hypertension association with serum lipoproteins, insulin, insulin resistance and C-Peptide: unexplored forte of cardiovascular risk in hypothyroidism Purohit, P. and Mathur, R. 2013 *N.Am.J.Med.Sci.*
1021. [Metabolic syndrome components in arterial hypertension] Marchi-Alves, L. M., Rigotti, A. R., Nogueira, M. S., Cesarino, C. B., and de, Godoy S. 2012 *Rev.Esc Enferm.USP.*
1022. Hypertension and vascular dynamics in men and women with metabolic syndrome Safar, M. E., Balkau, B., Lange, C., Protogerou, A. D., Czernichow, S., Blacher, J., Levy, B. I., and Smulyan, H. 1-8-2013 *J.Am.Coll.Cardiol.*
1023. One-hour post-load plasma glucose and IGF-1 in hypertensive patients Perticone, F., Sciacqua, A., Tassone, E. J., Miceli, S., Maio, R., Addesi, D., Falbo, T., Arturi, F., and Sesti, G. 2012 *Eur.J.Clin.Invest*
1024. White coat hypertension may be an initial sign of the metabolic syndrome Helvacı, M. R., Kaya, H., and Gundogdu, M. 2012 *Acta Med.Indones.*
1025. Nutrition, dietary interventions and prostate cancer: the latest evidence Lin, P. H., Aronson, W., and Freedland, S. J. 2015 *BMC.Med.*
1026. Folate intake, serum folate levels, and prostate cancer risk: a meta-analysis of prospective studies Wang, R., Zheng, Y., Huang, J. Y., Zhang, A. Q., Zhou, Y. H., and Wang, J. N. 2014 *BMC.Public Health*
1027. Folate intake and the risk of prostate cancer: a systematic review and meta-analysis Tio, M., Andrici, J., Cox, M. R., and Eslick, G. D. 2014 *Prostate Cancer Prostatic.Dis.*
1028. Opposing roles of folate in prostate cancer Rycyna, K. J., Bacich, D. J., and O'Keefe, D. S. 2013 *Urology*
1029. Folate and B12 in prostate cancer Collin, S. M. 2013 *Adv.Clin.Chem.*
1030. Serum folate and prostate-specific antigen in the United States Han, Y. Y., Song, J. Y., and Talbott, E. O. 2013 *Cancer Causes Control*
1031. Pomegranate and its components as alternative treatment for prostate cancer Wang, L. and Martins-Green, M. 2014 *Int.J.Mol.Sci.*
1032. A double-blind, placebo-controlled randomised trial evaluating the effect of a polyphenol-rich whole food supplement on PSA progression in men with prostate cancer--the U.K. NCRN Pomi-T study Thomas, R., Williams, M., Sharma, H., Chaudry, A., and Bellamy, P. 2014 *Prostate Cancer Prostatic.Dis.*
1033. Novel preventive treatment options Longbottom, C., Ekstrand, K., Zero, D., and Kambara, M. 2009 *Monogr Oral Sci.*
1034. [Probiotics: from Metchnikoff to the current preventive and therapeutic possibilities] Caramia, G. 2004 *Pediatr.Med.Chir*
1035. Micronutrients decrease incidence of common infections in type 2 diabetic outpatients Liu, Y., Jing, H., Wang, J., Zhang, R., Zhang, Y., Zhang, Y., Xu, Q., Yu, X., and Xue, C. 2011 *Asia Pac.J.Clin.Nutr.*
1036. Relationship between folic acid intake and gingival health in non-smoking adults in Japan Esaki, M., Morita, M., Akhter, R., Akino, K., and Honda, O. 2010 *Oral Dis.*
1037. Effects of a nutritional supplement on periodontal status Munoz, C. A., Kiger, R. D., Stephens, J. A., Kim, J., and Wilson, A. C. 2001 *Compend.Contin.Educ.Dent.*
1038. Folate mouthwash: effects on established gingivitis in periodontal patients Pack, A. R. 1984 *J.Clin.Periodontol.*
1039. The effect of topical application of folic acid on gingival health Vogel, R. I., Fink, R. A., Frank, O., and Baker, H. 1978 *J.Oral Med.*
1040. The effect of folic acid on gingival health Vogel, R. I., Fink, R. A., Schneider, L. C., Frank, O., and Baker, H. 1976 *J.Periodontol.*
1041. Oral indications of the deficiency states Dreizen, S. 1971 *Postgrad.Med.*
1042. [Correlations between vitamins A and E and steroid hormones] Audisio, M., Fidanza, A., Mastroiacovo, P., Suraci, C., Strollo, F., Torella, G., and Di, Pietro S. 3-31-1987 *Boll.Soc.Ital.Biol.Sper.*
1043. Calcium and vitamin D intake and risk of incident premenstrual syndrome Bertone-Johnson, E. R., Hankinson, S. E., Bendich, A., Johnson, S. R., Willett, W. C., and Manson, J. E. 6-13-2005 *Arch.Intern.Med.*
1044. Pyridoxine in the treatment of premenstrual syndrome: a retrospective survey in 630 patients Brush, M. G., Bennett, T., and Hansen, K. 1988 *Br.J.Clin.Pract.*
1045. Platelet serotonin uptake and effects of vitamin B6-treatment in premenstrual tension Malmgren, R., Collins, A., and Nilsson, C. G. 1987 *Neuropsychobiology*
1046. Basic mechanisms involved in the anti-cancer effects of melatonin Mediavilla, M. D., Sanchez-Barcelo, E. J., Tan, D. X., Manchester, L., and Reiter, R. J. 2010 *Curr.Med.Chem.*
1047. Molecular mechanisms of melatonin anticancer effects Hill, S. M., Frasch, T., Xiang, S., Yuan, L., Duplessis, T., and Mao, L. 2009 *Integr.Cancer Ther.*
1048. Melanocyte receptors: clinical implications and therapeutic relevance Carlson, J. A., Linette, G. P., Aplin, A., Ng, B., and Slominski, A. 2007 *Dermatol.Clin.*

1049. Five years survival in metastatic non-small cell lung cancer patients treated with chemotherapy alone or chemotherapy and melatonin: a randomized trial Lissoni, P., Chillelli, M., Villa, S., Cerizza, L., and Tancini, G. 2003 *J.Pineal Res.*
1050. Direct antiproliferative effects of melatonin on two metastatic cell sublines of mouse melanoma (B16BL6 and PG19) Cos, S., Garcia-Bolado, A., and Sanchez-Barcelo, E. J. 2001 *Melanoma Res.*
1051. Urinary melatonin levels and postmenopausal breast cancer risk in the Nurses' Health Study cohort Schernhammer, E. S. and Hankinson, S. E. 2009 *Cancer Epidemiol.Biomarkers Prev.*
1052. Endocrine regulation of the course of menopause by oral melatonin: first case report Diaz, B. L. and Llana, P. C. 2008 *Menopause.*
1053. Melatonin treatment in peri- and postmenopausal women elevates serum high-density lipoprotein cholesterol levels without influencing total cholesterol levels Tamura, H., Nakamura, Y., Narimatsu, A., Yamagata, Y., Takasaki, A., Reiter, R. J., and Sugino, N. 2008 *J.Pineal Res.*
1054. Effects of melatonin supplementary on the sciatic nerve conduction velocity in the ovariectomized-aged rat Ek, R. O., Zencirci, S. G., Dost, T., Birincioglu, M., and Bilgin, M. D. 2007 *Neuro.Endocrinol.Lett.*
1055. [Menopause--a key aspect of aging: role of the pineal gland] Ivanov, S. V. 2007 *Adv.Gerontol.*
1056. [The role of melatonin in regulation of gonadal function and its use in the treatment of pathological climax symptoms] Mal'tseva, L. I., Gafarova, E. A., and Garipova, G. K. 2007 *Adv.Gerontol.*
1057. Effects of melatonin in perimenopausal and menopausal women: our personal experience Bellipanni, G., Di, Marzo F., Blasi, F., and Di, Marzo A. 2005 *Ann.N.Y.Acad.Sci.*
1058. Menopause related sleep disorders Eichling, P. S. and Sahni, J. 7-15-2005 *J.Clin.Sleep Med.*
1059. Long-term effects of melatonin or 17 beta-estradiol on improving spatial memory performance in cognitively impaired, ovariectomized adult rats Feng, Z., Cheng, Y., and Zhang, J. T. 2004 *J.Pineal Res.*
1060. Melatonin deficiencies in women Rohr, U. D. and Herold, J. 4-15-2002 *Maturitas*
1061. Effects of melatonin in perimenopausal and menopausal women: a randomized and placebo controlled study Bellipanni, G., Bianchi, P., Pierpaoli, W., Bulian, D., and Ilyia, E. 2001 *Exp.Gerontol.*
1062. Influence of melatonin administration on glucose tolerance and insulin sensitivity of postmenopausal women Cagnacci, A., Arangino, S., Renzi, A., Paoletti, A. M., Melis, G. B., Cagnacci, P., and Volpe, A. 2001 *Clin.Endocrinol.(Oxf)*
1063. A role for melatonin in breast disease and the menopause Oosthuizen, G. M., Joubert, G., and du Toit, R. S. 2001 *S.Afr.Med.J.*
1064. Chronobiological basis of female-specific mood disorders Parry, B. L. and Newton, R. P. 2001 *Neuropsychopharmacology*
1065. Melatonin in postmenopausal females Blaicher, W., Speck, E., Imhof, M. H., Gruber, D. M., Schneeberger, C., Sator, M. O., and Huber, J. C. 2000 *Arch.Gynecol.Obstet.*
1066. Andropause: a misnomer for a true clinical entity Morales, A., Heaton, J. P., and Carson, C. C., III 2000 *J.Urol.*
1067. Changes in nocturnal melatonin secretion in perimenopausal women: correlation with endogenous estrogen concentrations Okatani, Y., Morioka, N., and Wakatsuki, A. 2000 *J.Pineal Res.*
1068. [Rejuvenating hormones] Sternon, J. 1999 *Rev.Med.Brux.*
1069. Melatonin enhances cortisol levels in aged women: reversible by estrogens Cagnacci, A., Soldani, R., and Yen, S. S. 1997 *J.Pineal Res.*
1070. Melatonin enhances cortisol levels in aged but not young women Cagnacci, A., Soldani, R., and Yen, S. S. 1995 *Eur.J.Endocrinol.*
1071. Melatonin levels are decreased in rheumatoid arthritis West, S. K. and Oosthuizen, J. M. 1992 *J.Basic Clin.Physiol Pharmacol.*
1072. Melatonin as a negative mitogenic hormonal regulator of human prostate epithelial cell growth: potential mechanisms and clinical significance Tam, C. W., Chan, K. W., Liu, V. W., Pang, B., Yao, K. M., and Shiu, S. Y. 2008 *J.Pineal Res.*
1073. Physiological effects of melatonin: role of melatonin receptors and signal transduction pathways Pandi-Perumal, S. R., Trakht, I., Srinivasan, V., Spence, D. W., Maestroni, G. J., Zisapel, N., and Cardinali, D. P. 2008 *Prog.Neurobiol.*
1074. [Pineal gland and extrapineal melatonin in visceral organs during natural human aging] Kniaz'kin, I. V. 2008 *Adv.Gerontol.*
1075. [Melatonin, aging and tumors of the prostate] Kniaz'kin, I. V. 2008 *Adv.Gerontol.*
1076. Towards rational and evidence-based use of melatonin in prostate cancer prevention and treatment Shiu, S. Y. 2007 *J.Pineal Res.*
1077. Effects of melatonin administration on the clinical course of adrenocortical disease in domestic ferrets Ramer, J. C., Benson, K. G., Morrissey, J. K., O'Brien, R. T., and Paul-Murphy, J. 12-1-2006 *J.Am.Vet.Med.Assoc.*
1078. Long-term melatonin or 17beta-estradiol supplementation alleviates oxidative stress in ovariectomized adult rats Feng, Z. and Zhang, J. T. 7-15-2005 *Free Radic.Biol.Med.*
1079. Melatonin pharmacotherapy for nocturia in men with benign prostatic enlargement Drake, M. J., Mills, I. W., and Noble, J. G. 2004 *J.Urol.*
1080. Mindfulness-based stress reduction in relation to quality of life, mood, symptoms of stress and levels of cortisol, dehydroepiandrosterone sulfate (DHEAS) and melatonin in breast and prostate cancer outpatients Carlson, L. E., Speca, M., Patel, K. D., and Goodey, E. 2004 *Psychoneuroendocrinology*
1081. The ageing male Schulman, C. and Lunenfeld, B. 2002 *World J.Urol.*
1082. Melatonin elicits nuclear exclusion of the human androgen receptor and attenuates its activity Rimler, A., Culig, Z., Levy-Rimler, G., Lupowitz, Z., Klocker, H., Matzkin, H., Bartsch, G., and Zisapel, N. 10-1-2001 *Prostate*
1083. Antiproliferative action of melatonin on human prostate cancer LNCaP cells Moretti, R. M., Marelli, M. M., Maggi, R., Dondi, D., Motta, M., and Limonta, P. 2000 *Oncol.Rep.*

1084. Urinary 6-sulfatoxymelatonin level in age-related macular degeneration patients Rosen, R., Hu, D. N., Perez, V., Tai, K., Yu, G. P., Chen, M., Tone, P., McCormick, S. A., and Walsh, J. 2009 *Mol.Vis.*
1085. Daytime levels of melatonin in patients with age-related macular degeneration Schmid-Kubista, K. E., Glittenberg, C. G., Cezanne, M., Holzmann, K., Neumaier-Ammerer, B., and Binder, S. 2009 *Acta Ophthalmol.*
1086. Effects of melatonin in age-related macular degeneration Yi, C., Pan, X., Yan, H., Guo, M., and Pierpaoli, W. 2005 *Ann.N.Y.Acad.Sci.*
1087. Melatonin protects human retinal pigment epithelial (RPE) cells against oxidative stress Liang, F. Q., Green, L., Wang, C., Alssadi, R., and Godley, B. F. 2004 *Exp.Eye Res.*
1088. Melatonin induces autophagy via an mTOR-dependent pathway and enhances clearance of mutant-TGFB1p Choi, S. I., Kim, K. S., Oh, J. Y., Jin, J. Y., Lee, G. H., and Kim, E. K. 12-27-2012 *J.Pineal Res.*
1089. Role of melatonin in the regulation of autophagy and mitophagy: a review Coto-Montes, A., Boga, J. A., Rosales-Corral, S., Fuentes-Broto, L., Tan, D. X., and Reiter, R. J. 9-25-2012 *Mol.Cell Endocrinol.*
1090. Melatonin-induced autophagy protects against human prion protein-mediated neurotoxicity Jeong, J. K., Moon, M. H., Lee, Y. J., Seol, J. W., and Park, S. Y. 2012 *J.Pineal Res.*
1091. Beneficial effects of endogenous and exogenous melatonin on neural reconstruction and functional recovery in an animal model of spinal cord injury Park, S., Lee, S. K., Park, K., Lee, Y., Hong, Y., Lee, S., Jeon, J. C., Kim, J. H., Lee, S. R., Chang, K. T., and Hong, Y. 2012 *J.Pineal Res.*
1092. New paradigms in chronic intestinal inflammation and colon cancer: role of melatonin Motilva, V., Garcia-Maurino, S., Talero, E., and Illanes, M. 2011 *J.Pineal Res.*
1093. [Irritable bowel syndrome: dietary and pharmacological therapeutic options] Ducrotte, P. 2009 *Gastroenterol.Clin.Biol.*
1094. Treatment approaches to irritable bowel syndrome Sood, M. R. 2009 *Pediatr. Ann.*
1095. Inflammatory bowel disease Part 1: ulcerative colitis--pathophysiology and conventional and alternative treatment options Head, K. A. and Jurenka, J. S. 2003 *Altern.Med.Rev.*
1096. [Mechanisms and risk factors for type 1 food allergies: the role of gastric digestion] Diesner, S. C., Pali-Scholl, I., Jensen-Jarolim, E., and Untersmayr, E. 2012 *Wien.Med.Wochenschr.*
1097. Antacids and dietary supplements with an influence on the gastric pH increase the risk for food sensitization Pali-Scholl, I., Herzog, R., Wallmann, J., Szalai, K., Brunner, R., Lukschal, A., Karagiannis, P., Diesner, S. C., and Jensen-Jarolim, E. 2010 *Clin.Exp.Allergy*
1098. Suppression of gastric acid increases the risk of developing immunoglobulin E-mediated drug hypersensitivity: human diclofenac sensitization and a murine sensitization model Riemer, A. B., Gruber, S., Pali-Scholl, I., Kinaciyan, T., Untersmayr, E., and Jensen-Jarolim, E. 2010 *Clin.Exp.Allergy*
1099. Anti-acids lead to immunological and morphological changes in the intestine of BALB/c mice similar to human food allergy Pali-Scholl, I., Yildirim, A. O., Ackermann, U., Knauer, T., Becker, C., Garn, H., Renz, H., Jensen-Jarolim, E., and Fehrenbach, H. 2008 *Exp.Toxicol.Pathol.*
1100. If stomach acid helps digest food, how is food digested if you take an antacid after a meal? 2006 *Mayo Clin.Health Lett.*
1101. Vitamin C supplement use may protect against gallstones: an observational study on a randomly selected population Walcher, T., Haenle, M. M., Kron, M., Hay, B., Mason, R. A., Walcher, D., Steinbach, G., Kern, P., Piechotowski, I., Adler, G., Boehm, B. O., Koenig, W., and Kratzer, W. 2009 *BMC.Gastroenterol.*
1102. Nutritional approaches to prevention and treatment of gallstones Gaby, A. R. 2009 *Altern.Med.Rev.*
1103. Gallstone disease: Epidemiology of gallbladder stone disease Shaffer, E. A. 2006 *Best.Pract.Res.Clin.Gastroenterol.*
1104. The effect of vitamin C in high doses on plasma and biliary lipid composition in patients with cholesterol gallstones: prolongation of the nucleation time Gustafsson, U., Wang, F. H., Axelson, M., Kallner, A., Sahlin, S., and Einarsson, K. 1997 *Eur.J.Clin.Invest*
1105. [Vitamin C correction in patients with complicated cholecystitis] Fishchenko, A. I., Kolibaba, S. S., Oshovskii, I. N., and Zheliba, N. D. 1988 *Vrach.Delo*
1106. Chronic marginal vitamin C deficiency: biochemistry and pathophysiology Ginter, E. 1979 *World Rev.Nutr.Diet.*
1107. Vitamin C and gallstone formation: a preliminary report Jenkins, S. A. 12-15-1977 *Experientia*
1108. Motility abnormalities in irritable bowel syndrome Dupont, A. W., Jiang, Z. D., Harold, S. A., Snyder, N., Galler, G. W., Garcia-Torres, F., and DuPont, H. L. 2014 *Digestion*
1109. Methanobrevibacter smithii is the predominant methanogen in patients with constipation-predominant IBS and methane on breath Kim, G., Deepinder, F., Morales, W., Hwang, L., Weitsman, S., Chang, C., Gunsalus, R., and Pimentel, M. 2012 *Dig.Dis.Sci.*
1110. Small intestinal bacterial overgrowth (SIBO) in irritable bowel syndrome: frequency and predictors Sachdeva, S., Rawat, A. K., Reddy, R. S., and Puri, A. S. 2011 *J.Gastroenterol.Hepatol.*
1111. Methane on breath testing is associated with constipation: a systematic review and meta-analysis Kunkel, D., Basseri, R. J., Makhani, M. D., Chong, K., Chang, C., and Pimentel, M. 2011 *Dig.Dis.Sci.*
1112. Bacterial concepts in irritable bowel syndrome Lin, H. C. and Pimentel, M. 2005 *Rev.Gastroenterol.Disord.*
1113. Bacteria and irritable bowel syndrome: the evidence for small intestinal bacterial overgrowth Lee, H. R. and Pimentel, M. 2006 *Curr.Gastroenterol.Rep.*
1114. The influence of omega-3 polyunsaturated fatty acids (omega-3 pufa) on lactobacilli adhesion to the intestinal mucosa and on immunity in gnotobiotic piglets Bomba, A., Nemcova, R., Gancarcikova, S., Herich, R., Pistl, J., Revajova, V., Jonecova, Z., Bugarsky, A., Levkut, M., Kastel, R., Baran, M., Lazar, G., Hluchy, M., Marsalkova, S., and Posivak, J. 2003 *Berl Munch.Tierarztl.Wochenschr.*
1115. Diet and exercise orthogonally alter the gut microbiome and reveal independent associations with anxiety and cognition Kang, S. S., Jeraldo, P. R., Kurti, A., Miller, M. E., Cook, M. D., Whitlock, K., Goldenfeld, N., Woods, J. A., White, B. A., Chia, N., and Fryer, J. D. 2014 *Mol.Neurodegener.*

1116. Exercise and associated dietary extremes impact on gut microbial diversity Clarke, S. F., Murphy, E. F., O'Sullivan, O., Lucey, A. J., Humphreys, M., Hogan, A., Hayes, P., O'Reilly, M., Jeffery, I. B., Wood-Martin, R., Kerins, D. M., Quigley, E., Ross, R. P., O'Toole, P. W., Molloy, M. G., Falvey, E., Shanahan, F., and Cotter, P. D. 2014 Gut
1117. The gut microbiota, dietary extremes and exercise Hold, G. L. 2014 Gut
1118. Gut microbiota. Tackling the effects of diet and exercise on the gut microbiota Ray, K. 2014 Nat.Rev.Gastroenterol.Hepatol.
1119. Neural networks in intestinal immunoregulation Costes, L. M., Boeckxstaens, G. E., de Jonge, W. J., and Cailotto, C. 2013 Organogenesis.
1120. Absence of the gut microbiota enhances anxiety-like behavior and neuroendocrine response to acute stress in rats Crumeyrolle-Arias, M., Jaglin, M., Bruneau, A., Vancassel, S., Cardona, A., Dauge, V., Naudon, L., and Rabot, S. 2014 Psychoneuroendocrinology
1121. The gut microbiome and the brain Galland, L. 2014 J.Med.Food
1122. Neuropeptides and the microbiota-gut-brain axis Holzer, P. and Farzi, A. 2014 Adv.Exp.Med.Biol.
1123. Microbiota disbiosis is associated with colorectal cancer Gao, Z., Guo, B., Gao, R., Zhu, Q., and Qin, H. 2015 Front Microbiol.
1124. Exploring gut microbes in human health and disease: Pushing the envelope Sun, J. and Chang, E. B. 2014 Genes Dis.
1125. [Obesity and cancer] Ungefroren, H., Gieseler, F., and Lehnert, H. 2015 Internist (Berl)
1126. Cancer and the gut microbiota: An unexpected link Zitvogel, L., Galluzzi, L., Viaud, S., Vetzizou, M., Dailere, R., Merad, M., and Kroemer, G. 1-21-2015 Sci.Transl.Med.
1127. Uncovering Microbes' Role in Tumor Progression 1-21-2015 Cancer Discov.
1128. Gut microbial metabolism and colon cancer: Can manipulations of the microbiota be useful in the management of gastrointestinal health? Belcheva, A., Irrazabal, T., and Martin, A. 1-20-2015 Bioessays
1129. The microbiome of the urinary tract-a role beyond infection Whiteside, S. A., Razvi, H., Dave, S., Reid, G., and Burton, J. P. 2015 Nat.Rev.Urol.
1130. Galacto-oligosaccharides and Colorectal Cancer: Feeding our Intestinal Probiome Bruno-Barcena, J. M. and Azcarate-Peril, M. A. 2015 J.Funct.Foods
1131. Microbiota-Mediated Inflammation and Antimicrobial Defense in the Intestine Caballero, S. and Pamer, E. G. 1-2-2015 Annu.Rev.Immunol.
1132. Microbiome: the bacterial tightrope Bourzac, K. 12-4-2014 Nature
1133. Microbiome and cancer Ohtani, N. 2015 Semin.Immunopathol.
1134. Substantial decreases in the number and diversity of microbiota during chemotherapy-induced gastrointestinal mucositis in a rat model Fijlstra, M., Ferdous, M., Koning, A. M., Rings, E. H., Harmsen, H. J., and Tissing, W. J. 11-8-2014 Support.Care Cancer
1135. The immunity-diet-microbiota axis in the development of metabolic syndrome Brandsma, E., Houben, T., Fu, J., Shiri-Sverdlov, R., and Hofker, M. H. 2-16-2015 Curr.Opin.Lipidol.
1136. Does our gut microbiome predict cardiovascular risk? A review of the evidence from metabolomics Griffin, J. L., Wang, X., and Stanley, E. 2015 Circ.Cardiovasc.Genet.
1137. Dysbiosis of the gut microbiota in disease Carding, S., Verbeke, K., Vipond, D. T., Corfe, B. M., and Owen, L. J. 2015 Microb.Ecol.Health Dis.
1138. Gut microbiota composition correlates with changes in body fat content due to weight loss Remely, M., Tesar, I., Hippe, B., Gnauer, S., Rust, P., and Haslberger, A. G. 1-21-2015 Benef.Microbes.
1139. Intestinal Microbiota: a Regulator of Intestinal Inflammation and Cardiac Ischemia? Bashashati, M., Habibi, H. R., Keshavarzian, A., Schmulson, M., and Sharkey, K. A. 1-19-2015 Curr.Drug Targets.
1140. Fecal microbiota transplantation broadening its application beyond intestinal disorders Xu, M. Q., Cao, H. L., Wang, W. Q., Wang, S., Cao, X. C., Yan, F., and Wang, B. M. 1-7-2015 World J.Gastroenterol.
1141. The intestinal microbiota: its role in health and disease Biedermann, L. and Rogler, G. 2015 Eur.J.Pediatr.
1142. Insights into the role of the microbiome in obesity and type 2 diabetes Hartstra, A. V., Bouter, K. E., Backhed, F., and Nieuwdorp, M. 2015 Diabetes Care
1143. Gut microbiota and metabolic syndrome Festi, D., Schiumerini, R., Eusebi, L. H., Marasco, G., Taddia, M., and Colecchia, A. 11-21-2014 World J.Gastroenterol.
1144. Fecal microbiota transplantation: a new old kid on the block for the management of gut microbiota-related disease Cammarota, G., Ianiro, G., Bibbo, S., and Gasbarrini, A. 2014 J.Clin.Gastroenterol.
1145. Dynamic interplay between metabolic syndrome and immunity Paragh, G., Seres, I., Harangi, M., and Fulop, P. 2014 Adv.Exp.Med.Biol.
1146. Microbiota and diabetes: an evolving relationship Tilg, H. and Moschen, A. R. 2014 Gut
1147. The gut microbiota and its correlations with the central nervous system disorders Catanzaro, R., Anzalone, M. G., Calabrese, F., Milazzo, M., Capuana, M. L., Italia, A., Occhipinti, S., and Marotta, F. 11-12-2014 Panminerva Med.
1148. Dealing with ability of the microbiota to influence the brain, and ultimately cognition and behavioral Lyte, M. and Cryan, J. F. 2014 Adv.Exp.Med.Biol.
1149. The impact of microbiota on brain and behavior: mechanisms & therapeutic potential Borre, Y. E., Moloney, R. D., Clarke, G., Dinan, T. G., and Cryan, J. F. 2014 Adv.Exp.Med.Biol.
1150. Microbiota-gut-brain axis and cognitive function Gareau, M. G. 2014 Adv.Exp.Med.Biol.
1151. The effects of inflammation, infection and antibiotics on the microbiota-gut-brain axis Bercik, P. and Collins, S. M. 2014 Adv.Exp.Med.Biol.
1152. The effects of gut microbiota on CNS function in humans Tillisch, K. 2014 Gut Microbes.
1153. Cognitive decline, dietary factors and gut-brain interactions Caracciolo, B., Xu, W., Collins, S., and Fratiglioni, L. 2014 Mech.Ageing Dev.

1154. Microbial genes, brain & behaviour - epigenetic regulation of the gut-brain axis Stilling, R. M., Dinan, T. G., and Cryan, J. F. 2014 *Genes Brain Behav.*
1155. The human microbiome in autoimmune diseases Cojocaru, M. and Chicos, B. 2014 *Rom.J.Intern.Med.*
1156. Application of metagenomics in the human gut microbiome Wang, W. L., Xu, S. Y., Ren, Z. G., Tao, L., Jiang, J. W., and Zheng, S. S. 1-21-2015 *World J.Gastroenterol.*
1157. Autism, an extreme challenge to integrative medicine. Part 2: medical management Kidd, P. M. 2002 *Altern.Med.Rev.*
1158. Phospholipid association reduces the gastric mucosal toxicity of aspirin in human subjects Anand, B. S., Romero, J. J., Sanduja, S. K., and Lichtenberger, L. M. 1999 *Am.J.Gastroenterol.*
1159. Zwitterionic phospholipids enhance aspirin's therapeutic activity, as demonstrated in rodent model systems Lichtenberger, L. M., Ulloa, C., Vanous, A. L., Romero, J. J., Dial, E. J., Illich, P. A., and Walters, E. T. 1996 *J.Pharmacol.Exp.Ther.*
1160. NSAID enteropathy and bacteria: a complicated relationship Syer, S. D., Blackler, R. W., Martin, R., de, Palma G., Rossi, L., Verdu, E., Bercik, P., Surette, M. G., Aucouturier, A., Langella, P., and Wallace, J. L. 1-10-2015 *J.Gastroenterol.*
1161. Gut microbiota of healthy elderly NSAID users is selectively modified with the administration of *Lactobacillus acidophilus* NCFM and lactitol Bjorklund, M., Ouwehand, A. C., Forssten, S. D., Nikkila, J., Tiihonen, K., Rautonen, N., and Lahtinen, S. J. 2012 *Age (Dordr.)*
1162. The effect of age and non-steroidal anti-inflammatory drugs on human intestinal microbiota composition Makivuokko, H., Tiihonen, K., Tynkkynen, S., Paulin, L., and Rautonen, N. 2010 *Br.J.Nutr.*
1163. Effect of a zinc L-carnosine compound on acid-induced injury in canine gastric mucosa ex vivo Hill, T. L. and Blikslager, A. T. 2012 *Am.J.Vet.Res.*
1164. Effects of zinc-L-carnosine and vitamin E on aspirin-induced gastroduodenal injury in dogs Baan, M., Sherding, R. G., and Johnson, S. E. 2011 *J.Vet.Intern.Med.*
1165. Zinc L-carnosine protects against mucosal injury in portal hypertensive gastropathy through induction of heat shock protein 72 Mikami, K., Otaka, M., Watanabe, D., Goto, T., Endoh, A., Miura, K., Ohshima, S., Yoneyama, K., Sato, M., Shibuya, T., Segawa, D., Kataoka, E., Yoshino, R., Takeuchi, S., Sato, W., Odashima, M., and Watanabe, S. 2006 *J.Gastroenterol.Hepatol.*
1166. Zinc L-carnosine protects colonic mucosal injury through induction of heat shock protein 72 and suppression of NF-kappaB activation Odashima, M., Otaka, M., Jin, M., Wada, I., Horikawa, Y., Matsushashi, T., Ohba, R., Hatakeyama, N., Oyake, J., and Watanabe, S. 11-10-2006 *Life Sci.*
1167. The cytoprotective effect of zinc L-carnosine on ethanol-induced gastric gland damage in rabbits Cho, C. H., Hui, W. M., Chen, B. W., Luk, C. T., and Lam, S. K. 1992 *J.Pharm.Pharmacol.*
1168. Skin, muscle and joint disease from the 17th century: scurvy Lau, H., Massasso, D., and Joshua, F. 2009 *Int.J.Rheum.Dis.*
1169. Effects of vitamin C deficiency on the skin of the senescence marker protein-30 (SMP30) knockout mouse Arai, K. Y., Sato, Y., Kondo, Y., Kudo, C., Tsuchiya, H., Nomura, Y., Ishigami, A., and Nishiyama, T. 7-31-2009 *Biochem.Biophys.Res Commun.*
1170. Gene expression profiling reveals new protective roles for vitamin C in human skin cells Duarte, T. L., Cooke, M. S., and Jones, G. D. 1-1-2009 *Free Radic.Biol.Med.*
1171. Effect of vitamin C and its derivatives on collagen synthesis and cross-linking by normal human fibroblasts Boyera, N., Galey, I., and Bernard, B. A. 1998 *Int.J.Cosmet.Sci.*
1172. [Biological role and importance in the skin metabolism of vitamin C] Kleszczewska, E. 2007 *Pol.Merkur Lekarski.*
1173. Wrinkles Manriquez, J. J., Majerson, Gringberg D., and Nicklas, Diaz C. 2008 *Clin.Evid.(Online.)*
1174. Dietary nutrient intakes and skin-aging appearance among middle-aged American women Cosgrove, M. C., Franco, O. H., Granger, S. P., Murray, P. G., and Mayes, A. E. 2007 *Am.J.Clin.Nutr.*
1175. Relevance of vitamins C and E in cutaneous photoprotection Eberlein-Konig, B. and Ring, J. 2005 *J.Cosmet.Dermatol.*
1176. Improvement in the appearance of wrinkles with topical transforming growth factor beta(1) and l-ascorbic acid Ehrlich, M., Rao, J., Pabby, A., and Goldman, M. P. 2006 *Dermatol.Surg.*
1177. Topical vitamin C: a useful agent for treating photoaging and other dermatologic conditions Farris, P. K. 2005 *Dermatol.Surg.*
1178. Biological role of vitamin C in keratinocytes Catani, M. V., Savini, I., Rossi, A., Melino, G., and Avigliano, L. 2005 *Nutr.Rev.*
1179. Topically applied vitamin C increases the density of dermal papillae in aged human skin Sauermann, K., Jaspers, S., Koop, U., and Wenck, H. 9-29-2004 *BMC.Dermatol.*
1180. Vitamin C intake and the risk of gout in men: a prospective study Choi, H. K., Gao, X., and Curhan, G. 3-9-2009 *Arch.Intern.Med.*
1181. Vitamin C intake and serum uric acid concentration in men Gao, X., Curhan, G., Forman, J. P., Ascherio, A., and Choi, H. K. 2008 *J.Rheumatol.*
1182. Effect of antioxidants on knee cartilage and bone in healthy, middle-aged subjects: a cross-sectional study Wang, Y., Hodge, A. M., Wluka, A. E., English, D. R., Giles, G. G., O'Sullivan, R., Forbes, A., and Cicuttini, F. M. 2007 *Arthritis Res.Ther.*
1183. Effect of vitamin C administration in modulating some biochemical changes in arthritic rats Eldin, A. A., Hamdy, M. A., Shaheen, A. A., Motawi, T. K., and Abd el Gawad, H. M. 1992 *Pharmacol.Res.*
1184. Vitamin B12 in acute subdeltoid bursitis KLEMES, I. S. 1957 *Ind.Med.Surg.*
1185. Tendinitis and various joint involvements; observations on the therapeutic effect of a combination of muscle adenylic acid and vitamin B12 in their treatment DELUCIA, F. A. and STROSBURG, I. 1954 *Med.Times*
1186. Use of vitamin B12 in treatment of acute subdeltoid bursitis KLEMES, I. S. 1953 *Ind.Med.Surg.*
1187. Topical vitamins Burgess, C. 2008 *J.Drugs Dermatol.*

1188. Clinical, biometric and structural evaluation of the long-term effects of a topical treatment with ascorbic acid and madecassoside in photoaged human skin Haftek, M., Mac-Mary, S., Le Bitoux, M. A., Creidi, P., Seite, S., Rougier, A., and Humbert, P. 2008 *Exp.Dermatol.*
1189. Stability of vitamins C and E in topical microemulsions for combined antioxidant therapy Rozman, B. and Gasperlin, M. 2007 *Drug Deliv.*
1190. Topical activity of ascorbic acid: from in vitro optimization to in vivo efficacy Raschke, T., Koop, U., Dusing, H. J., Filbry, A., Sauermann, K., Jaspers, S., Wenck, H., and Wittern, K. P. 2004 *Skin Pharmacol.Physiol*
1191. Topically applied vitamin C and cysteine derivatives protect against UVA-induced photodegradation of suprofen in ex vivo pigskin Moison, R. M., Rijnkels, J. M., Podda, E., Riguele, F., Tomasello, F., Caffieri, S., and Beijersbergen van Henegouwen, G. M. 2003 *Photochem.Photobiol.*
1192. Cutaneous photodamage, oxidative stress, and topical antioxidant protection Pinnell, S. R. 2003 *J.Am.Acad.Dermatol.*
1193. Diagnosis and treatment of rosacea Cohen, A. F. and Tiemstra, J. D. 2002 *J.Am.Board Fam.Pract.*
1194. Topically applied vitamin C enhances the mRNA level of collagens I and III, their processing enzymes and tissue inhibitor of matrix metalloproteinase 1 in the human dermis Nusgens, B. V., Humbert, P., Rougier, A., Colige, A. C., Haftek, M., Lambert, C. A., Richard, A., Creidi, P., and Lapiere, C. M. 2001 *J Invest Dermatol.*
1195. Topical vitamin C in the treatment of photoaged skin Humbert, P. 2001 *Eur.J.Dermatol.*
1196. Effect of topical antioxidants on UV-induced erythema formation when administered after exposure Dreher, F., Denig, N., Gabard, B., Schwindt, D. A., and Maibach, H. I. 1999 *Dermatology*
1197. A double-blind, randomized, prospective trial to evaluate topical vitamin C solution for the prevention of radiation dermatitis. CNS Cancer Consortium Halperin, E. C., Gaspar, L., George, S., Darr, D., and Pinnell, S. 6-15-1993 *Int.J.Radiat.Oncol.Biol.Phys.*
1198. Topical vitamin C protects porcine skin from ultraviolet radiation-induced damage Darr, D., Combs, S., Dunston, S., Manning, T., and Pinnell, S. 1992 *Br.J.Dermatol.*
1199. Modification of membrane composition, eicosanoid metabolism, and immunoresponsiveness by dietary omega-3 and omega-6 fatty acid sources, modulators of ultraviolet-carcinogenesis Fischer, M. A. and Black, H. S. 1991 *Photochem.Photobiol.*
1200. Influence of omega-3 and omega-6 fatty acid sources on prostaglandin levels in mice Henderson, C. D., Black, H. S., and Wolf, J. E., Jr. 1989 *Lipids*
1201. Collagen-like peptide exhibits a remarkable antiwrinkle effect on the skin when topically applied: in vivo study Bauza, E., Oberto, G., Berghi, A., Dal, C. F., and Domloge, N. 2004 *Int.J.Tissue React.*
1202. Topical vitamin C: a useful agent for treating photoaging and other dermatologic conditions Farris, P. K. 2005 *Dermatol.Surg.*
1203. Topical application of 17beta-estradiol increases extracellular matrix protein synthesis by stimulating tgf-Beta signaling in aged human skin in vivo Son, E. D., Lee, J. Y., Lee, S., Kim, M. S., Lee, B. G., Chang, I. S., and Chung, J. H. 2005 *J.Invest Dermatol.*
1204. [Vitamin C] Valdes, F. 2006 *Actas Dermosifiliogr.*
1205. Photodamage of the skin: protection and reversal with topical antioxidants Burke, K. E. 2004 *J.Cosmet.Dermatol.*
1206. Changes in basal cell mitosis and transepidermal water loss in skin cultures treated with vitamins C and E Parish, W. E., Read, J., and Paterson, S. E. 2005 *Exp.Dermatol.*
1207. Histological evaluation of a topically applied retinol-vitamin C combination Seite, S., Bredoux, C., Compan, D., Zucchi, H., Lombard, D., Medaisko, C., and Fourtanier, A. 2005 *Skin Pharmacol.Physiol*
1208. Vitamin C derivative ascorbyl palmitate promotes ultraviolet-B-induced lipid peroxidation and cytotoxicity in keratinocytes Meves, A., Stock, S. N., Beyerle, A., Pittelkow, M. R., and Peus, D. 2002 *J.Invest Dermatol.*
1209. Ascorbic acid treatment, similarly to fluoxetine, reverses depressive-like behavior and brain oxidative damage induced by chronic unpredictable stress Moretti, M., Colla, A., de Oliveira, Balen G., Dos Santos, D. B., Budni, J., de Freitas, A. E., Farina, M., and Severo Rodrigues, A. L. 12-7-2011 *J.Psychiatr.Res.*
1210. Vitamin C transport and its role in the central nervous system May, J. M. 2012 *Subcell.Biochem.*
1211. Noninvasive quantification of ascorbate and glutathione concentration in the elderly human brain Emir, U. E., Raatz, S., McPherson, S., Hodges, J. S., Torkelson, C., Tawfik, P., White, T., and Terpstra, M. 2011 *NMR Biomed.*
1212. Neuroprotective effect of vitamin C against PTZ induced apoptotic neurodegeneration in adult rat brain Naseer, M. I., Ullah, I., Ullah, N., Lee, H. Y., Cheon, E. W., Chung, J., and Kim, M. O. 2011 *Pak.J.Pharm.Sci.*
1213. Vitamin C restores behavioral deficits and amyloid-beta oligomerization without affecting plaque formation in a mouse model of Alzheimer's disease Murakami, K., Murata, N., Ozawa, Y., Kinoshita, N., Irie, K., Shirasawa, T., and Shimizu, T. 2011 *J.Alzheimers.Dis.*
1214. Ascorbic acid-dependent GLUT3 inhibition is a critical step for switching neuronal metabolism Beltran, F. A., Acuna, A. I., Miro, M. P., Angulo, C., Concha, I. I., and Castro, M. A. 2011 *J.Cell Physiol*
1215. Ascorbate uptake is decreased in the hippocampus of ageing rats Siqueira, I. R., Elsner, V. R., Leite, M. C., Vanzella, C., Moyses, Fdos S., Spindler, C., Godinho, G., Battu, C., Wofchuk, S., Souza, D. O., Goncalves, C. A., and Netto, C. A. 2011 *Neurochem.Int.*
1216. Prolonged treatment with vitamins C and E separately and together decreases anxiety-related open-field behavior and acoustic startle in hooded rats Hughes, R. N., Lowther, C. L., and van, Nobelen M. 2011 *Pharmacol.Biochem.Behav.*
1217. High dietary fat and cholesterol exacerbates chronic vitamin C deficiency in guinea pigs Frikke-Schmidt, H., Tveden-Nyborg, P., Birck, M. M., and Lykkesfeldt, J. 2011 *Br.J.Nutr.*
1218. Neuronal damage and memory deficits after seizures are reversed by ascorbic acid? Tome, Ada R., Feitosa, C. M., and Freitas, R. M. 2010 *Arq Neuropsiquiatr.*
1219. The neurophysiology and pathology of brain zinc Sensi, S. L., Paoletti, P., Koh, J. Y., Aizenman, E., Bush, A. I., and Hershfinkel, M. 11-9-2011 *J.Neurosci.*

1220. New therapeutic targets in Alzheimer's disease: brain deregulation of calcium and zinc Corona, C., Pensalfini, A., Frazzini, V., and Sensi, S. L. 2011 Cell Death.Dis.
1221. Zinc, copper, and carnosine attenuate neurotoxicity of prion fragment PrP106-126 Kawahara, M., Koyama, H., Nagata, T., and Sadakane, Y. 2011 Metallomics.
1222. Effects of dietary supplementation of carnosine on mitochondrial dysfunction, amyloid pathology, and cognitive deficits in 3xTg-AD mice Corona, C., Frazzini, V., Silvestri, E., Lattanzio, R., La, Sorda R., Piantelli, M., Canzoniero, L. M., Ciavardelli, D., Rizzarelli, E., and Sensi, S. L. 2011 PLoS.One.
1223. New evidence on iron, copper accumulation and zinc depletion and its correlation with DNA integrity in aging human brain regions Vasudevaraju, P., Bharathi, T J, Shamasundar, N. M., Subba, Rao K., Balaraj, B. M., Ksj, R., and SR, T. S. 2010 Indian J.Psychiatry
1224. The essential toxin: impact of zinc on human health Plum, L. M., Rink, L., and Haase, H. 2010 Int.J.Envirn.Res.Public Health
1225. Brain trace element concentration of rats treated with the plant alkaloid, vincamine Fayed, A. H. 2010 Biol.Trace Elem.Res.
1226. [Zinc deficiency in the elderly] Miyata, S. 2007 Nihon Ronen Igakkai Zasshi
1227. Brain aging: The zinc connection Bertoni-Freddari, C., Fattoretti, P., Casoli, T., Di, Stefano G., Giorgetti, B., and Balietti, M. 2008 Exp.Gerontol.
1228. Defective DNA repair and neurodegenerative disease Rass, U., Ahel, I., and West, S. C. 9-21-2007 Cell
1229. Zinc dyshomeostasis, ageing and neurodegeneration: implications of A2M and inflammatory gene polymorphisms Mocchegiani, E. and Malavolta, M. 2007 J.Alzheimers.Dis.
1230. Effect of alpha-lipoic acid supplementation on trace element levels in serum and in postmitotic tissue in aged rats Kayali, R., Cakatay, U., Kiziler, A. R., and Aydemir, B. 2007 Med.Chem.
1231. Brain, aging and neurodegeneration: role of zinc ion availability Mocchegiani, E., Bertoni-Freddari, C., Marcellini, F., and Malavolta, M. 2005 Prog.Neurobiol.
1232. Selenoproteins and the aging brain Zhang, S., Rocourt, C., and Cheng, W. H. 2010 Mech.Ageing Dev.
1233. Seleno-L-methionine protects against beta-amyloid and iron/hydrogen peroxide-mediated neuron death Xiong, S., Markesbery, W. R., Shao, C., and Lovell, M. A. 2007 Antioxid.Redox.Signal.
1234. Plasma selenium over time and cognitive decline in the elderly Akbaraly, T. N., Hininger-Favier, I., Carriere, I., Arnaud, J., Gourlet, V., Roussel, A. M., and Berr, C. 2007 Epidemiology
1235. Selenium intake, mood and other aspects of psychological functioning Benton, D. 2002 Nutr.Neurosci.
1236. Oxidative stress and cognitive impairment in the elderly Berr, C. 2002 J.Nutr.Health Aging
1237. Effects of selenium deficiency on tissue selenium content, deiodinase activity, and thyroid hormone economy in the rat during development Bates, J. M., Spate, V. L., Morris, J. S., St Germain, D. L., and Galton, V. A. 2000 Endocrinology
1238. Effect of dietary vitamin E and selenium on susceptibility of brain regions to lipid peroxidation Meydani, M., Macauley, J. B., and Blumberg, J. B. 1988 Lipids
1239. Nutrient biomarker patterns, cognitive function, and MRI measures of brain aging Bowman, G. L., Silbert, L. C., Howieson, D., Dodge, H. H., Traber, M. G., Frei, B., Kaye, J. A., Shannon, J., and Quinn, J. F. 12-28-2011 Neurology
1240. Omega-3 polyunsaturated fatty acids and cognition throughout the lifespan: a review Karr, J. E., Alexander, J. E., and Winningham, R. G. 2011 Nutr.Neurosci.
1241. Omega-3 polyunsaturated fatty acids in the brain: metabolism and neuroprotection Zhang, W., Li, P., Hu, X., Zhang, F., Chen, J., and Gao, Y. 2012 Front Biosci.
1242. Dietary fatty acids and the aging brain Cole, G. M., Ma, Q. L., and Frautschy, S. A. 2010 Nutr.Rev.
1243. Omega-3 essential fatty acids modulate initiation and progression of neurodegenerative disease Palacios-Pelaez, R., Lukiw, W. J., and Bazan, N. G. 2010 Mol.Neurobiol.
1244. Omega-3 fatty acids: potential role in the management of early Alzheimer's disease Jicha, G. A. and Markesbery, W. R. 2010 Clin.Interv.Aging
1245. Food combination and Alzheimer disease risk: a protective diet Gu, Y., Nieves, J. W., Stern, Y., Luchsinger, J. A., and Scarmeas, N. 2010 Arch.Neurol.
1246. Omega-3 fatty acids reverse age-related decreases in nuclear receptors and increase neurogenesis in old rats Dyall, S. C., Michael, G. J., and Michael-Titus, A. T. 8-1-2010 J.Neurosci.Res.
1247. DHA may prevent age-related dementia Cole, G. M. and Frautschy, S. A. 2010 J.Nutr.
1248. Cognitive and cardiovascular benefits of docosahexaenoic acid in aging and cognitive decline Yurko-Mauro, K. 2010 Curr.Alzheimer Res.
1249. Fatty acid composition of frontal, temporal and parietal neocortex in the normal human brain and in Alzheimer's disease Fraser, T., Tayler, H., and Love, S. 2010 Neurochem.Res.
1250. Fish, docosahexaenoic acid and Alzheimer's disease Cunnane, S. C., Plourde, M., Pifferi, F., Begin, M., Feart, C., and Barberger-Gateau, P. 2009 Prog.Lipid Res.
1251. Exercise and the brain: something to chew on van, Praag H. 2009 Trends Neurosci.
1252. [Lifestyle-related diseases and anti-aging ophthalmology: suppression of retinal and choroidal pathologies by inhibiting renin-angiotensin system and inflammation] Ishida, S. 2009 Nihon Ganka Gakkai Zasshi
1253. Role of vinpocetine in cerebrovascular diseases Patyar, S., Prakash, A., Modi, M., and Medhi, B. 2011 Pharmacol.Rep.
1254. Reversing brain damage in former NFL players: implications for traumatic brain injury and substance abuse rehabilitation Amen, D. G., Wu, J. C., Taylor, D., and Willeumier, K. 2011 J.Psychoactive Drugs
1255. [Efficacy of cavinton in the treatment of patients with chronic blood flow insufficiency. Russian multicenter clinical-epidemiological program "CALIPSO"] Chukanova, E. I. 2010 Zh.Nevrol.Psikhiatr.Im S.S.Korsakova
1256. Decreased cGMP level contributes to increased contraction in arteries from hypertensive rats: role of phosphodiesterase 1 Giachini, F. R., Lima, V. V., Carneiro, F. S., Tostes, R. C., and Webb, R. C. 2011 Hypertension

1257. [Efficacy of vinpocetine in the therapy of initial signs of cerebrovascular pathology] Vorob'eva, O. V. and Tamarova, E. S. 2010 *Zh.Nevrol.Psikhiatr.Im S.S.Korsakova*
1258. [Chronic disorders of cerebral blood circulation: possibilities of the use of cavinton] Kamchatnov, P. R., Zaitsev, K. A., and Chugunov, A. V. 2010 *Zh.Nevrol.Psikhiatr.Im S.S.Korsakova*
1259. [Cavinton in the complex treatment of patients with chronic cerebrovascular insufficiency] Chukanova, E. I. 2009 *Zh.Nevrol.Psikhiatr.Im S.S.Korsakova*
1260. Neuroprotective effects of vinpocetine and its major metabolite cis-apovincaminic acid on NMDA-induced neurotoxicity in a rat entorhinal cortex lesion model Nyakas, C., Felszeghy, K., Szabo, R., Keijser, J. N., Luiten, P. G., Szombathelyi, Z., and Tihanyi, K. 2009 *CNS.Neurosci.Ther.*
1261. [The use of vinpocetine in chronic brain ischemia] Ivanova, N. E. and Panuntsev, V. S. 2008 *Zh.Nevrol.Psikhiatr.Im S.S.Korsakova*
1262. [Vinpocetine in the treatment of cerebral vascular diseases] Filimonov, V. A., Kliueva, V. N., and Kondrasheva, I. N. 2007 *Zh.Nevrol.Psikhiatr.Im S.S.Korsakova*
1263. Vinpocetine for acute ischaemic stroke Bereczki, D. and Fekete, I. 2008 *Cochrane.Database.Syst.Rev.*
1264. Adaptations of the aging animal to exercise: role of daily supplementation with melatonin Mendes, C., Lopes, A. M., do Amaral, F. G., Peliciari-Garcia, R. A., Turati, A. D., Hirabara, S. M., Scialfa Falcao, J. H., and Cipolla-Neto, J. 5-7-2013 *J.Pineal Res.*
1265. Melatonin-based therapeutics for neuroprotection in stroke Shinozuka, K., Staples, M., and Borlongan, C. V. 2013 *Int.J.Mol.Sci.*
1266. Melatonin and human skin aging Kleszczynski, K. and Fischer, T. W. 7-1-2012 *Dermatoendocrinol.*
1267. Effect of chronic melatonin administration on several physiological parameters from old Wistar rats and SAMP8 mice Tresguerres, J. A., Kireev, R., Forman, K., Cuesta, S., Tresguerres, A. F., and Vara, E. 2012 *Curr.Aging Sci.*
1268. Psychoneuroendocrine interventions aimed at attenuating immunosenescence: a review Bauer, M. E., Muller, G. C., Correa, B. L., Vianna, P., Turner, J. E., and Bosch, J. A. 2013 *Biogerontology.*
1269. Light-at-night-induced circadian disruption, cancer and aging Anisimov, V. N., Vinogradova, I. A., Panchenko, A. V., Popovich, I. G., and Zabezhinski, M. A. 2012 *Curr.Aging Sci.*
1270. Melatonin supplementation delays the decline of adult hippocampal neurogenesis during normal aging of mice Ramirez-Rodriguez, G., Vega-Rivera, N. M., Benitez-King, G., Castro-Garcia, M., and Ortiz-Lopez, L. 11-14-2012 *Neurosci.Lett.*
1271. Melatonin: an underappreciated player in retinal physiology and pathophysiology Tosini, G., Baba, K., Hwang, C. K., and Iuvone, P. M. 2012 *Exp.Eye Res.*
1272. Neurobiology, pathophysiology, and treatment of melatonin deficiency and dysfunction Hardeland, R. 2012 *ScientificWorldJournal.*
1273. Hormonal therapy of intrinsic aging Zouboulis, C. C. and Makrantonaki, E. 2012 *Rejuvenation.Res.*
1274. Pyrroloquinoline quinone modulates the kinetic parameters of the mammalian selenoprotein thioredoxin reductase 1 and is an inhibitor of glutathione reductase Xu, J. and Arner, E. S. 12-29-2011 *Biochem.Pharmacol.*
1275. The Neuroprotective Effect of Pyrroloquinoline Quinone on Traumatic Brain Injury Zhang, L., Liu, J., Cheng, C., Yuan, Y., Yu, B., Shen, A., and Yan, M. 12-20-2011 *J.Neurotrauma*
1276. Pyrroloquinoline quinone inhibits the fibrillation of amyloid proteins Kim, J., Kobayashi, M., Fukuda, M., Ogasawara, D., Kobayashi, N., Han, S., Nakamura, C., Inada, M., Miyaura, C., Ikebukuro, K., and Sode, K. 2010 *Prion.*
1277. Effect of vitamin E on learning and memory deficit in aged rats Takatsu, H., Owada, K., Abe, K., Nakano, M., and Urano, S. 2009 *J.Nutr.Sci.Vitaminol.(Tokyo)*
1278. Pyrroloquinoline quinone stimulates mitochondrial biogenesis through cAMP response element-binding protein phosphorylation and increased PGC-1alpha expression Chowanadisai, W., Bauerly, K. A., Tchapanian, E., Wong, A., Cortopassi, G. A., and Rucker, R. B. 1-1-2010 *J.Biol.Chem.*
1279. Aerobic exercise prevents age-dependent cognitive decline and reduces anxiety-related behaviors in middle-aged and old rats Pietrelli, A., Lopez-Costa, J., Goni, R., Brusco, A., and Basso, N. 12-8-2011 *Neuroscience*
1280. Exercise Increases Tryptophan Availability to the Brain in Older Men Aged 57-70 Years Melancon, M. O., Lorrain, D., and Dionne, I. J. 11-2-2011 *Med.Sci.Sports Exerc.*
1281. Reversal of glial and neurovascular markers of unhealthy brain aging by exercise in middle-aged female mice Latimer, C. S., Searcy, J. L., Bridges, M. T., Brewer, L. D., Popovic, J., Blalock, E. M., Landfield, P. W., Thibault, O., and Porter, N. M. 2011 *PLoS.One.*
1282. Metabolic Reserve as a Determinant of Cognitive Aging Stranahan, A. M. and Mattson, M. P. 11-1-2011 *J.Alzheimers.Dis.*
1283. Short bouts of mild-intensity physical exercise improve spatial learning and memory in aging rats: Involvement of hippocampal plasticity via AKT, CREB and BDNF signaling Aguiar, A. S., Jr., Castro, A. A., Moreira, E. L., Glaser, V., Santos, A. R., Tasca, C. I., Latini, A., and Prediger, R. D. 2011 *Mech.Ageing Dev.*
1284. Differential cognitive effects of cycling versus stretching/coordination training in middle-aged adults Hotting, K., Reich, B., Holzschneider, K., Kauschke, K., Schmidt, T., Reer, R., Braumann, K. M., and Roder, B. 9-5-2011 *Health Psychol.*
1285. Physical exercise as a preventive or disease-modifying treatment of dementia and brain aging Ahlskog, J. E., Geda, Y. E., Graff-Radford, N. R., and Petersen, R. C. 2011 *Mayo Clin.Proc.*
1286. Running is the neurogenic and neurotrophic stimulus in environmental enrichment Kobil, T., Liu, Q. R., Gandhi, K., Mughal, M., Shaham, Y., and van Praag, H. 2011 *Learn.Mem.*
1287. Voluntary wheel running reverses age-induced changes in hippocampal gene expression Kohman, R. A., Rodriguez-Zas, S. L., Southey, B. R., Kelley, K. W., Dantzer, R., and Rhodes, J. S. 2011 *PLoS.One.*
1288. Little exercise, big effects: reversing aging and infection-induced memory deficits, and underlying processes Barrientos, R. M., Frank, M. G., Crysdale, N. Y., Chapman, T. R., Ahrends, J. T., Day, H. E., Campeau, S., Watkins, L. R., Patterson, S. L., and Maier, S. F. 8-10-2011 *J.Neurosci.*
1289. The Impact of Physical and Mental Activity on Cognitive Aging Jak, A. J. 8-5-2011 *Curr.Top.Behav.Neurosci.*

1290. The influence of exercise on brain ageing and dementia Lautenschlager, N. T., Cox, K., and Cyarto, E. V. 7-24-2011 *Biochim.Biophys.Acta*
1291. Resistance training and functional plasticity of the aging brain: a 12-month randomized controlled trial Liu-Ambrose, T., Nagamatsu, L. S., Voss, M. W., Khan, K. M., and Handy, T. C. 7-6-2011 *Neurobiol.Aging*
1292. Improved cerebral vasomotor reactivity after exercise training in hemiparetic stroke survivors Ivey, F. M., Ryan, A. S., Hafer-Macko, C. E., and Macko, R. F. 2011 *Stroke*
1293. Neurophysiological and epigenetic effects of physical exercise on the aging process Kaliman, P., Parrizas, M., Lalanza, J. F., Camins, A., Escorihuela, R. M., and Pallas, M. 2011 *Ageing Res.Rev.*
1294. Exercise-induced cognitive plasticity, implications for mild cognitive impairment and Alzheimer's disease Foster, P. P., Rosenblatt, K. P., and Kuljis, R. O. 2011 *Front Neurol.*
1295. Revitalizing the aged brain Desai, A. K. 2011 *Med.Clin.North Am.*
1296. The Aging Hippocampus: Interactions between Exercise, Depression, and BDNF Erickson, K. I., Miller, D. L., and Roecklein, K. A. 4-29-2011 *Neuroscientist.*
1297. Physical activity and neural correlates of aging: a combined TMS/fMRI study McGregor, K. M., Zlatar, Z., Kleim, E., Sudhyadhom, A., Bauer, A., Phan, S., Seeds, L., Ford, A., Manini, T. M., White, K. D., Kleim, J., and Crosson, B. 9-12-2011 *Behav.Brain Res.*
1298. Resilience to chronic stress is mediated by hippocampal brain-derived neurotrophic factor Taliatz, D., Loya, A., Gersner, R., Haramati, S., Chen, A., and Zangen, A. 3-23-2011 *J.Neurosci.*
1299. Antibiotics as primary therapy for Crohn's disease Chamberlin, W., Hulten, K., and Graham, D. Y. 2000 *Drugs Today (Barc.)*
1300. Mycoplasma infection induces a scleroderma-like centrosome autoantibody response in mice Gavanescu, I., Pihan, G., Hallilovic, E., Szomolanyi-Tsuda, E., Welsh, R. M., and Doxsey, S. 2004 *Clin.Exp.Immunol.*
1301. Is Crohn's disease caused by a mycobacterium? Comparisons with leprosy, tuberculosis, and Johne's disease Greenstein, R. J. 2003 *Lancet Infect.Dis.*
1302. The pediatric autoimmune neuropsychiatric disorders associated with streptococcal infection (PANDAS) etiology for tics and obsessive-compulsive symptoms: hypothesis or entity? Practical considerations for the clinician Kurlan, R. and Kaplan, E. L. 2004 *Pediatrics*
1303. Sarcoidosis succumbs to antibiotics--implications for autoimmune disease Marshall, T. G. and Marshall, F. E. 2004 *Autoimmun.Rev.*
1304. Lyme borreliosis: from infection to autoimmunity Singh, S. K. and Girschick, H. J. 2004 *Clin.Microbiol.Infect.*
1305. Childhood-onset obsessive-compulsive disorder and tic disorders: case report and literature review Snider, L. A. and Swedo, S. E. 2003 *J.Child Adolesc.Psychopharmacol.*
1306. Eradication of *Helicobacter pylori* infection improves blood pressure values in patients affected by hypertension Migneco, A., Ojetti, V., Specchia, L., Franceschi, F., Candelli, M., Mettimano, M., Montebelli, R., Savi, L., and Gasbarrini, G. 2003 *Helicobacter.*
1307. Magnesium homeostasis and aging Barbagallo, M., Belvedere, M., and Dominguez, L. J. 2009 *Magnes.Res.*
1308. Chronic fatigue syndrome is associated with metabolic syndrome: results from a case-control study in Georgia Maloney, E. M., Boneva, R. S., Lin, J. M., and Reeves, W. C. 2010 *Metabolism*
1309. On commonness and rarity of thyroid hormone resistance: a discussion based on mechanisms of reduced sensitivity in peripheral tissues Tjorve, E., Tjorve, K. M., Olsen, J. O., Senum, R., and Oftebro, H. 2007 *Med.Hypotheses*
1310. Metabolic syndrome and mitochondrial function: molecular replacement and antioxidant supplements to prevent membrane peroxidation and restore mitochondrial function Nicolson, G. L. 4-15-2007 *J.Cell Biochem.*
1311. Evidence for prescribing exercise as therapy in chronic disease Pedersen, B. K. and Saltin, B. 2006 *Scand.J.Med.Sci.Sports*
1312. Associations between neuroendocrine responses to the Insulin Tolerance Test and patient characteristics in chronic fatigue syndrome Gaab, J., Engert, V., Heitz, V., Schad, T., Schurmeyer, T. H., and Ehler, U. 2004 *J.Psychosom.Res.*
1313. Strength training as a countermeasure to aging muscle and chronic disease Hurley, B. F., Hanson, E. D., and Sheaff, A. K. 4-1-2011 *Sports Med.*
1314. Hypothalamic-pituitary-adrenal axis, neuroendocrine factors and stress Tsigos, C. and Chrousos, G. P. 2002 *J.Psychosom.Res.*
1315. Soil-based organisms improve immune function: shift cytokine profile from TH2 to TH1 1998 *Posit.Health News*
1316. Nutrition and brain development in early life Prado, E. L. and Dewey, K. G. 2014 *Nutr.Rev.*
1317. Impact of mild thyroid hormone deficiency in pregnancy on cognitive function in children: Lessons from the Generation R Study Ghassabian, A., Henrichs, J., and Tiemeier, H. 2014 *Best.Pract.Res.Clin.Endocrinol.Metab*
1318. Health knowledge and iodine intake in pregnancy Martin, J. C., Savage, G. S., and Mitchell, E. K. 3-16-2014 *Aust.N.Z.J.Obstet.Gynaecol.*
1319. Oxidative stress increased in pregnant women with iodine deficiency Vidal, Z. E., Rufino, S. C., Tlaxcalteco, E. H., Trejo, C. H., Campos, R. M., Meza, M. N., Rodriguez, R. C., and Arroyo-Helguera, O. 2014 *Biol.Trace Elem.Res.*
1320. Children of mothers with iodine deficiency during pregnancy are more likely to have lower verbal IQ and reading scores at 8-9 years of age Leung, A. M. and Brent, G. A. 12-12-2013 *Evid.Based.Nurs.*
1321. Rickets: not a disease of the past Nield, L. S., Mahajan, P., Joshi, A., and Kamat, D. 8-15-2006 *Am.Fam.Physician*
1322. Vitamin D deficiency in the San Francisco Bay Area McAllister, J. C., Lane, A. T., and Buckingham, B. A. 2006 *J.Pediatr.Endocrinol.Metab*
1323. Vitamin D and the breastfed infant Henderson, A. 2005 *J.Obstet.Gynecol.Neonatal Nurs.*
1324. Reemerging nutritional rickets: a historical perspective Rajakumar, K. and Thomas, S. B. 2005 *Arch.Pediatr.Adolesc.Med.*
1325. Postnatal evaluation of vitamin D and bone health in women who were vitamin D-deficient in pregnancy, and in their infants Thomson, K., Morley, R., Grover, S. R., and Zacharin, M. R. 11-1-2004 *Med.J.Aust.*

1326. Probiotics and prevention of allergic disease Kopp, M. V. and Salfeld, P. 2009 *Curr.Opin.Clin.Nutr.Metab Care*
1327. Prenatal probiotic administration can influence Bifidobacterium microbiota development in infants at high risk of allergy Lahtinen, S. J., Boyle, R. J., Kivivuori, S., Oppedisano, F., Smith, K. R., Robins-Browne, R., Salminen, S. J., and Tang, M. L. 2009 *J.Allergy Clin.Immunol.*
1328. Gut microbiota and pregnancy, a matter of inner life Cani, P. D. 2009 *Br.J.Nutr.*
1329. Probiotics and dietary counselling contribute to glucose regulation during and after pregnancy: a randomised controlled trial Laitinen, K., Poussa, T., and Isolauri, E. 2009 *Br.J.Nutr.*
1330. Supplementation with Lactobacillus rhamnosus or Bifidobacterium lactis probiotics in pregnancy increases cord blood interferon-gamma and breast milk transforming growth factor-beta and immunoglobulin A detection Prescott, S. L., Wickens, K., Westcott, L., Jung, W., Currie, H., Black, P. N., Stanley, T. V., Mitchell, E. A., Fitzharris, P., Siebers, R., Wu, L., and Crane, J. 2008 *Clin.Exp.Allergy*
1331. Opportunities for improving the health and nutrition of the human infant by probiotics Salminen, S. and Isolauri, E. 2008 *Nestle.Nutr.Workshop Ser.Pediatr.Program.*
1332. Probiotics in infancy induce protective immune profiles that are characteristic for chronic low-grade inflammation Marschan, E., Kuitunen, M., Kukkonen, K., Poussa, T., Sarnesto, A., Haahtela, T., Korpela, R., Savilahti, E., and Vaarala, O. 2008 *Clin.Exp.Allergy*
1333. Neonatal microbial flora and disease outcome Vassallo, M. F. and Walker, W. A. 2008 *Nestle.Nutr.Workshop Ser.Pediatr.Program.*
1334. Dietary counseling and probiotic supplementation during pregnancy modify placental phospholipid fatty acids Kaplas, N., Isolauri, E., Lampi, A. M., Ojala, T., and Laitinen, K. 2007 *Lipids*
1335. Impact of diet on the immunological microenvironment of the pregnant uterus and its relationship to allergic disease in the offspring--a review of the recent literature Moore, D. C., Elsas, P. X., Maximiano, E. S., and Elsas, M. I. 9-7-2006 *Sao Paulo Med.J.*
1336. Probiotics affects vaginal flora in pregnant women, suggesting the possibility of preventing preterm labor Nishijima, K., Shukunami, K., and Kotsuji, F. 2005 *J.Clin.Gastroenterol.*
1337. Oral probiotics for maternal and newborn health Reid, G., Anukam, K., James, V. I., van der Mei, H. C., Heineman, C., Busscher, H. J., and Bruce, A. W. 2005 *J.Clin.Gastroenterol.*
1338. The potential for probiotics to prevent bacterial vaginosis and preterm labor Reid, G. and Bocking, A. 2003 *Am.J.Obstet.Gynecol.*
1339. Ingestion of probiotics: optional treatment of bacterial vaginosis in pregnancy Shalev, E. 2002 *Isr.Med.Assoc.J.*
1340. Establishment of the intestinal microbiota and its role for atopic dermatitis in early childhood Penders, J., Gerhold, K., Stobberingh, E. E., Thijs, C., Zimmermann, K., Lau, S., and Hamelmann, E. 7-27-2013 *J.Allergy Clin.Immunol.*
1341. Infant Feeding and Childhood Cognition at Ages 3 and 7 Years: Effects of Breastfeeding Duration and Exclusivity Belfort, M. B., Rifas-Shiman, S. L., Kleinman, K. P., Guthrie, L. B., Bellinger, D. C., Taveras, E. M., Gillman, M. W., and Oken, E. 7-29-2013 *JAMA Pediatr.*
1342. Breastfeeding and Cognition: Can IQ Tip the Scale? Christakis, D. A. 7-29-2013 *JAMA Pediatr.*
1343. Duration of breastfeeding and gender are associated with methylation of the LEPTIN gene in very young children Obermann-Borst, S. A., Eilers, P. H., Tobi, E. W., de Jong, F. H., Slagboom, P. E., Heijmans, B. T., and Steegers-Theunissen, R. P. 6-11-2013 *Pediatr.Res.*
1344. Does breastfeeding contribute to the racial gap in reading and math test scores? Peters, K. E., Huang, J., Vaughn, M. G., and Witko, C. 7-20-2013 *Ann.Epidemiol.*
1345. Breastfeeding and Adolescent Blood Pressure: Evidence From Hong Kong's "Children of 1997" Birth Cohort Kwok, M. K., Leung, G. M., and Schooling, C. M. 7-14-2013 *Am.J.Epidemiol.*
1346. Association between Child Cortisol Levels in Saliva and Neuropsychological Development during the Second Year of Life Forns, J., Vegas, O., Julvez, J., Garcia-Esteban, R., Rivera, M., Lertxundi, N., Guxens, M., Fano, E., Ferrer, M., Grelhier, J., Ibarluzea, J., and Sunyer, J. 7-1-2013 *Stress.Health*
1347. Breast feeding and intergenerational social mobility: what are the mechanisms? Sacker, A., Kelly, Y., Iacovou, M., Cable, N., and Bartley, M. 6-24-2013 *Arch.Dis.Child*
1348. Impact of breastfeeding on the intelligence quotient of eight-year-old children Fonseca, A. L., Albernaz, E. P., Kaufmann, C. C., Neves, I. H., and de Figueiredo, V. L. 2013 *J.Pediatr.(Rio J.)*
1349. Breastfeeding and early white matter development: A cross-sectional study Deoni, S. C., Dean, D. C., III, Piryatinsky, I., O'Muircheartaigh, J., Waskiewicz, N., Lehman, K., Han, M., and Dirks, H. 5-28-2013 *Neuroimage.*
1350. Protective effect of human lactoferrin in the gastrointestinal tract Queiroz, V. A., Assis, A. M., and Hda, R. Junior 2013 *Rev.Paul Pediatr.*
1351. Human milk glycoproteins protect infants against human pathogens Liu, B. and Newburg, D. S. 2013 *Breastfeed.Med.*
1352. Consumption of some polyphenols reduces fecal deoxycholic acid and lithocholic acid, the secondary bile acids of risk factors of colon cancer Han, Y., Haraguchi, T., Iwanaga, S., Tomotake, H., Okazaki, Y., Mineo, S., Moriyama, A., Inoue, J., and Kato, N. 9-23-2009 *J.Agric.Food Chem.*
1353. Rutin has therapeutic effect on septic arthritis caused by Candida albicans Han, Y. 2009 *Int.Immunopharmacol.*
1354. Phenolic compounds rutin and o-coumaric acid ameliorate obesity induced by high-fat diet in rats Hsu, C. L., Wu, C. H., Huang, S. L., and Yen, G. C. 1-28-2009 *J.Agric.Food Chem.*
1355. Bioactivation of flavonoid diglycosides by chicken cecal bacteria Iqbal, M. F. and Zhu, W. Y. 2009 *FEMS Microbiol.Lett.*
1356. In vitro catabolism of rutin by human fecal bacteria and the antioxidant capacity of its catabolites Jaganath, I. B., Mullen, W., Lean, M. E., Edwards, C. A., and Crozier, A. 10-15-2009 *Free Radic.Biol.Med.*
1357. Modulatory effects of rutin on biochemical and hematological parameters in hypercholesterolemic Golden Syrian hamsters Kanashiro, A., Andrade, D. C., Kabeya, L. M., Turato, W. M., Faccioli, L. H., Uyemura, S. A., and Lucisano-Valim, Y. M. 2009 *An.Acad.Bras.Cienc.*

1358. Protective mechanism of quercetin and rutin using glutathione metabolism on HO-induced oxidative stress in HepG2 cells Kim, G. N. and Jang, H. D. 2009 Ann.N.Y.Acad.Sci.
1359. Antibacterial, antifungal, and antiviral activities of some flavonoids Orhan, D. D., Ozcelik, B., Ozgen, S., and Ergun, F. 10-17-2009 Microbiol.Res.
1360. Effects of rutin on lipid profile in hypercholesterolaemic rats Ziaee, A., Zamansoltani, F., Nassiri-Asl, M., and Abbasi, E. 2009 Basic Clin.Pharmacol.Toxicol.

CHAPTER 16 OTHER PEOPLE'S IMPORTANT STUFF

Some of the information provided is absolutely true, some is speculation, but likely true, and some is simply opinion. Good information but read discriminately (recognize and weight the difference).

SUGAR'S GOOD SIDE

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"The Investigative works of Dr M. H. Beguin into dental decay and prevention by natural nutrition."

"Dental decay: A deficient disease caused by the refinement of food."

In civilised countries, where there is no shortage of food, few people get to adulthood without suffering dental decay. Its presence is accepted as normal. In spite of this we know that animals which live in the wild do not have bad teeth, one does not realize that mankind in Western Society had good teeth until the 18th Century. In reality, the number of bad teeth found in the skeletons of our forebears is very low - some 1 in every 100 - while today between 80% - 90 % of adults are affected.

Dental decay is an illness caused by civilization. In reality the supposedly called "primitives" in Asia, Africa, South Africa, and some of whose principal food consists of sugar cane have conserved good teeth. A study carried out in the remote valley of Valais has demonstrated that until 1900, while food came from their own soil, the mountaineers preserved good teeth. The railways and modern highways have brought the dental decay of civilization.

During rationing in 1939 - 1945 an enormous reduction in tooth decay was noticed in Swiss children of school age. In 1946 the school dentists registered that the enamel had become harder and more resistant and had two times less decay than before. Some forty years later, when there are no limits to sugar and you can eat and all the sweets produced, dental decay has returned to increase to their usual rate of ten teeth per child.

An attentive reader will understand on reflection why I, as a paediatrician, have carried out this investigation for the past 30 years. If the people who consume natural products on their own lands without refinement or alteration have been able to conserve their splendid teeth they must have a way that we can rediscover good dentistry for ourselves and our children. This is the reason that we need to replace refined products with natural unrefined products.

The equation will be: REFINED FOOD = TOOTH DECAY

The logical deduction of this: NON REFINED PRODUCTS = TOOTH DECAY DISAPPEARS

Of course the solution is more than the limits of simple mathematics. Those children who are now growing with the new form of nutrition will give the proof that the line taken is correct and viable. Today I can affirm by their good dentistry these children's food with healthy products is proof of my theory. This is the problem that I would like to view a little closer with the reader.

First Stage - Crude Sugar Cane

The previous assumptions seem to show that, white refined and granulated sugar stimulates tooth decay. It would be impossible to prohibit people from eating sugar. One gets accustomed to the taste of sweets in our youth, and it becomes very difficult to leave it. It is like preaching in the desert and the 49Kg of sugar, which according to the statistics is consumed by the average Swiss each year, is not reducing. This small consumption is approximately one kilo per week per person, which is more or less the same all over Europe.

What can replace refined sugar? In 1950, when I was working as a medical assistant in the prison, I asked my boss, Professor E. Freudenberg, if with his help (he was a paediatrician with chemistry), I could carry out some sugar analysis in my spare time. I wanted to compare the quantity of mineral salts in white sugar and granulated with brown sugar from crude honey.

First Result: If one fills two porcelain crucibles with 10g white sugar in one and 10g of crude sugar in the other and they are heated to combustion point you will find that the crucible with the white sugar is nearly empty after the experiment. With the crude sugar we are left with a small quantity of greyish seeds: the mineral salts. After weighing one discovers 30mg - 50 mg of mineral salts to 100g of white sugar and 300 mg - 500 mg to 100g of crude sugar, in other words ten times more. An analysis of these seeds shows phosphate, calcium, potassium, magnesium, iron and sulphur.

All these elements are vital for a healthy constitution but are lost during refining. One could hear my professor, who was very content and close to the results obtained say "The white sugar is the pride, but from a biological point of view it has no value."

After this analysis, Prof. Freudenberg decided to replace the white sugar that babies were taking with crude sugar. They enjoyed this and are growing more strongly and more healthily.

In 1953, when I was working as a paediatrician in the Chaux-de-Fonds, I convinced the mothers who were giving white sugar to their children to replace this with crude sugar. Ten years later the school dentist was astonished to see the children with such good teeth, just in the time of rationing. He interviewed the children and found that they received brown bread and brown sugar at home. This can be verified. In 1963, at our petition, the town authorities decided to undertake a survey with all 1420 children (between 6 - 10 years) and from first to third year. We asked the parents to complete questionnaires concerning the type of food that their children received: white sugar, brown sugar, white bread, brown bread, brown whole-wheat bread, fruit drinks, etc. The school dentist took note of the good teeth, lightly affected and heavily decayed for each child. The Federal Office of Statistics in Berne evaluated all of the documentation.

The results were unquestionably clear. Those children who had taken brown sugar had an average of 3.4 good teeth more than those who had taken white sugar. Those who had taken brown wholemeal could show an average of 1.9 good teeth more than those who had taken only white bread. Those children with a combination of the favourable factors had an average of 5.6 good teeth more than those with more traditional food. With refined food only 2% of the children had no bad

teeth, while 26%, that is to say $\frac{1}{4}$ of the children who had benefited from natural food had good teeth. It was particularly marked the difference in deep decay in teeth, that is to say: here 5.4 teeth were affected in the first group while only 0.7 in the second.

The first questionnaire was in 1963 with the student population (1420 children) showed that without doubt refined produce caused dental decay. Despite being so promising, these results were not satisfactory. In spite of selecting the best foods in the market, the children still had an average of 4.5 bad teeth. Before, the number was 10: this was certainly better, but was not the final victory.

Second Stage: Whole Sugar (Panela)

A study closer to the different types of bread: white, brown, wholemeal showed an obvious parallel between the quality of the bread and tooth decay.

Brown wholemeal bread conserves 95 - 100% of the elements of wheat, causing the smallest number of bad teeth. White bread, with a milling grade of 7.2% caused the greatest number of bad teeth. Brown bread with 84% is between the two in refinement and tooth decay. How much with sugar ? Crude sugar, which has been proved to be much better than white sugar and much more efficient than wholemeal, is not a type of whole sugar. Here it is how it is produced. The juice from sugar cane is evaporated in large bowls, and converted into molasses, which is concentrated. When that the physicists call the point of super saturation is reached, the crystals of the crude sugar separate from the molasses and drip through the valves. This substance is rich in mineral substances. Here the elements of sugar juice are separated in two parts: the crystals of crude sugar on one side and on the other the molasses which has been eliminated. It is used to make rum ! I had thought about these problems for such a long time that an idea started to form in my mind. Could there be a parallel between bread and sugar. The three grades in quality:

White bread - brown bread - wholemeal bread corresponding with an improvement in teeth. Here it is possible to make a similar parallel:

White sugar - brown sugar - whole sugar.

Crude sugar in the market corresponds with brown bread, in this way everything we have found is a type of whole sugar, which has all the elements of sugar cane juice and can equate with wholemeal bread.

This study was the principal of the decisive fight against dental decay.

The whole sugar, which I have in mind - sugar cane juice dried by evaporation - is unknown in Europe. Where could I ask or try to find information about this idea that everybody thought was mad. After three years arduous investigation into the material, an engineer from India, who was close to my investigation told me that this type of sugar was produced in his country. It is called GUR-JAGGARY. He knows that those people in India who consume this have good teeth.

A friend of mine returned from the Civil Service in India, where he had worked in a hospital for lepers, explained that he had seen country people producing this type of sugar. The sugar is crushed and pressed, the juice is collected in large basins of earth heated underneath by a bonfire, which is maintained for two or three days.

The juice is turned with enormous wooden spoons. Finally we are left with a dry material, dough in the shape of a brick. This is the sugar GUR - JAGGARY, the sugar of the poor people, which is sold in the market.

I carried out an analysis and the results exceeded my expectations, containing ten times the mineral salts of brown sugar and a hundred times more than white sugar. Here are the results obtained by analysis of the three types of sugar:

	100g of White and granulated sugar	100g of Brown Sugar	100g of Whole Sugar (panela)
Mineral salts	30 - 50 mg	330 - 740 mg	2850 mg
Phosphorus (P)	0.25 mg	3.0 - 3.9 mg	116 mg
Calcium (C)	14.0 mg	74 - 85 mg	118 mg
Magnesium (Mg)	0 mg	13 - 23 mg	136 mg
Potassium (K)	4.6 mg	40 - 100 mg	1056 mg
Iron (Fe)	0.1 mg	0.6 - 1.3 mg	3 mg

Purified and refined sugar consists of nearly 100% crystallised sucrose. The mineral salts, considered as impurities are removed and only leave a little behind, counted in milligrams. Whole sugar, without doubt is rich in the vitally important mineral salts: 2.8 grams per 100 grams, that is to say 28 grams per kilogram, while only 300 milligrams per kilogram is found in refined sugar.

Knowing that teeth are composed of calcium phosphate one understands, compared to the figures, that whole sugar, where there exists large quantities, is superior to white sugar, where there is only a little. The magnesium strengthens the nervous system. Potassium is vital to conserve the acid balance in the cells and combats acids and acetone. Iron, a composite of haemoglobin prevents anaemia.

Only the simple comparison of the mineral salts in the two types of sugar has to be an argument in favour of whole sugar.

Sucrose contains twelve atoms of carbon per molecule. Substituting by synthesis the fructose and the glucose - both sugars contain six atoms of carbon each. In the refined sugar these two types of sugars are eliminated, despite them having a high biological value, meanwhile 12% remained in the whole sugar. As well it contains around 1% of protein and an enormous variety of proteins especially the complete B: there is 1 mg of B6 or pyridoxine per 100 g. The analysis has revealed large quantities of vitamin B1, B2, folate, calcium pantothenate and inositol. Of course the oligo elements exist in all natural products. Small amounts of fluorine and selenium were also found.

RESULTS AFTER EIGHT YEARS: WHOLE SUGAR IS A PRODUCT OF HIGH QUALITY ALLOWING CHILDREN TO GROW HEALTHILY.

In 1967 the first sample of 300 Kg of Gur-Jaggary sugar arrived from India. First you have to examine and prove the tolerance. It is a granulated flour of a light orange to beige colour, which can

be easily dissolved in water or milk. It has an agreeable fruity smell, a little like honey or raisin juice. **Babies love it and soon they prefer it to white sugar.**

In its traditional form this sugar has some disadvantages. It contains grains of flour and fragments of cellulose, which can block the entry to a baby's drinking bottle. This has to be removed by the mothers. More, when it is dissolved and not sterilized it contains microbes. For this reason it needs to be treated in a laboratory.

Sugar comes from India by boat, it is redissolved, filtered, dried in a vacuum or low temperature and packed in tins. In this manner it does not lose any of its' characteristics, it is a product of irreproachable quality. There is one disadvantage which we have waited for since the beginning. This is due to the enormous quantity of mineral substances and ungranulated sugar, it is very hygroscopic, absorbs the humidity in the air and becomes hard and sticky. For this reason you have to keep it in a tin, which is air and water tight, and close it immediately after use.

1. Excellent tolerance. Babies and children love the flavour and take in doses normally of 5g per 100g. Constipation, which is very frequent with white sugar disappears. Babies are maintained healthily and their weight grows normally and regularly.
2. Prevention of nutritious anaemia. White sugar, refined flour and milk not poor in iron. Having to triplicate in one year the baby's weight from birth, they have to receive a sufficient quantity of iron. With the type of traditional food, a small number of paediatricians have found babies with pallid faces, transparent ears and colourless conjunctivitis. Suspecting anaemia, determine by analysis the haemoglobin and you will find it to be well below normal. For this we prescribe iron pills. For those babies who take whole sugar they do not have nutritional anaemia. All have rosy faces, ears and well coloured conjunctivitis.
3. Whole sugar prevents rickets. Growth of the skeleton is excellent. Historically paediatricians frequently found signs of rickets such as "cranial deprival" which is a softening of the cranial bones around the fontanel and the "rosary rickets". These cases are not registered yet.
4. Thrush or aphthae rarely returns. Thrush, white marks - fungus in the mucal membrane in the mouth - is frequent in young children and is a sign of low resistance. This effect practically disappears.
5. The children are more alive and full of vitality. The psychological factor most difficult to measure. But in place of these pallid faces, passive and quiet, the children now appear smiling, happy and lively.
6. Whole sugar prevents tooth decay.

You have to wait until the children grow in order to judge the influence that whole sugar has had on their teeth. Today, after eight years it is possible to measure the influence.

For two years, I was filling formulae's for each one with information from the mother, in respect of the type of sugar (white, brown or whole) that the child had taken each year.

I noted the number of good teeth, those lightly affected and those with severe decay. These results were passed to the University of Neuchatel, where they were evaluated by computer.

I have to state that I did not carry out these experiments, in the manner of a professor who is able to do these in small sections. I would recommend to all mothers to use the best products for their

children. The group examined who had been consuming white sugar came from other paediatricians or from families who had conserved the traditional form of nutrition. 1410 children of 2 - 16 years of age were examined in this way. The results were extraordinary and exceeded all expectations, while those with white sugar had regular tooth decay and approximately one quarter of their teeth affected, the majority of the children on whole sugar conserved good teeth. This tendency could be observed year on year.

The complete results fill a collection of documents. Here I would like to limit myself to two parts which summarize my study. The first graph shows the number of teeth affected by decay for 100 teeth - for each type of sugar measured and the consumption reduced progressively from 100% to 0%. With white sugar 25%, that is to say $\frac{1}{4}$ of the teeth are affected, with the whole sugar it is practically 20 times less: 1.4 teeth per 100. The brown sugar is between the two with 7 teeth affected per 100, which is much better than white sugar.

This graphic reveals something else interesting. If one takes a ruler to join the tops of the five columns which represent the whole sugar, we obtain a straight line from the points. There is no tooth decay when we consume only whole sugar! By this we can deduce that:

REFINED SUGAR IS THE MAJOR CAUSE OF TOOTH DECAY.

The second graphic, which was taken directly from the computer, shows the percentage of children with and without dental decay. With whole sugar 92% of the children have good teeth. With white sugar only 21%. Between raw whole sugar eliminated, that is to say between the highest grade of refining, the majority of teeth are affected by decay.

This study about whole sugar, which was a simple theoretical reflection at the beginning, has produced very interesting results. **This form of sugar has always existed, but it is unknown in Europe.** It is more, in all the countries and continents which produce sugar it is possible to find the old traditional methods where sugar juice is dried to form solids in the shape of bread. Today it is appreciated in the sugar producing countries for its flavour, nutritional value and curative character. The history and good reputation guarantee it is a healthy product and this cannot be confirmed for all the new products that appear in the market.

Dr. Max -Henri Beguin

translation into English by Nigel Rennie

ABOUT FATS, AGAIN

The OILING of AMERICA Part 1 of 2

Modern-day diets high in hydrogenated vegetable oils instead of traditional animal fats are implicated in causing a significant increase in heart disease and cancer.

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In 1954 a young researcher from Russia, named David Kritchevsky, published a paper describing the effects of feeding cholesterol to rabbits.¹ Cholesterol added to vegetarian rabbit chow caused the formation of atheromas - plaques that block arteries and contribute to heart disease. Cholesterol is a heavyweight molecule - an alcohol or a sterol - found only in animal foods such as meat, cheese, eggs and butter.

In the same year, according to the American Oil Chemists Society, Kritchevsky published a paper describing the beneficial effects of polyunsaturated fatty acids for lowering cholesterol levels.² (Polyunsaturated fatty acids are the kind of fats found in large amounts in highly liquid vegetable oils made from corn, soybeans, safflower seeds and sunflower seeds. Mono-unsaturated fatty acids are found in large amounts in olive oil, palm oil and lard; saturated fatty acids are found in large amounts in fats and oils that are solid at room temperature, e.g., butter, tallow and coconut oil.)

Scientists of the period were grappling with a new threat to public health: a steep rise in heart disease. While turn-of-the-century mortality statistics are unreliable, they consistently indicate that heart disease caused no more than 10 per cent of all deaths - considerably less than infectious diseases such as pneumonia and tuberculosis. By 1950, coronary heart disease (CHD) was the leading source of mortality in the United States, causing more than 30 per cent of all deaths. The greatest increase came under the rubric of myocardial infarction (MI) - a massive blood clot leading to obstruction of a coronary artery and consequent death to the heart muscle. MI was almost non-existent in 1910 and caused no more than 3,000 deaths per year in 1930. By 1960, there were at least 500,000 MI deaths per year in the US. What lifestyle changes had caused this increase?

One change was a decrease in infectious disease, following the decline of the horse as a means of transport, the installation of more sanitary water supplies and the advent of better housing, all of which allowed more people to reach adulthood and the heart attack age. The other was a dietary change.

Since the early part of the century when the US Department of Agriculture (USDA) had begun to keep track of food 'disappearance' data (the amount of various foods going into the food supply), a number of researchers had noticed a change in the kind of fats Americans were eating. Butter consumption was declining, while the use of vegetable oils, especially oils that had been hardened to resemble butter by a process called 'hydrogenation', was increasing dramatically. By 1950, butter consumption had dropped from 18 pounds per person per year to just over 10 pounds. Margarine filled in the gap, rising from about two pounds per person at the turn of the century to about eight. Consumption of vegetable shortening - used in crackers and baked goods - remained relatively steady at about 12 pounds per person per year, but vegetable oil consumption had more than tripled from just under three pounds per person per year to more than 10 pounds.³

The statistics pointed to one obvious conclusion: Americans should eat the traditional foods - including meat, eggs, butter and cheese - that nourished their ancestors, and avoid the newfangled, vegetable-oil-based foods that were flooding the grocers' shelves.

The Kritchevsky articles attracted immediate attention because they lent support to another theory - one that militated against the consumption of meat and dairy products. This was the lipid hypothesis: namely, that saturated fat and cholesterol from animal sources raise cholesterol levels in the blood, leading to deposition of cholesterol and fatty material as pathogenic plaques in the arteries.

Kritchevsky's rabbit trials were actually a repeat of studies carried out four decades earlier in St Petersburg, in which rabbits fed saturated fats and cholesterol developed fatty deposits in their skin and other tissues - and in their arteries. By showing that polyunsaturated oils from vegetable sources lowered serum cholesterol at least temporarily in humans, Kritchevsky appeared to show that the findings from the animal trials were relevant to the CHD problem, that the lipid hypothesis was a valid explanation for the new epidemic, and that, by reducing animal products in their diets, Americans could avoid heart disease.

In the years that followed, a number of population studies demonstrated that the animal model - especially one derived from vegetarian animals - was not a valid approach for the problem of heart disease in human omnivores.

A 1955 report on artery plaques in soldiers killed during the Korean War showed little difference in the number and severity of plaques between American soldiers and those of Japanese natives - 75 per cent versus 65 per cent - even though the Japanese diet at the time was lower in animal products and fat.⁴ A 1957 study of the largely vegetarian Bantu found that they had as much atheroma - occlusions or plaque build-up in the arteries - as other races from South Africa who ate more meat.⁵ A 1958 report noted that Jamaican Blacks showed a degree of atherosclerosis comparable to that found in the United States, although they suffered from lower rates of heart disease.⁶ A 1960 report noted that the severity of atherosclerotic lesions in Japan approached that of the United States.⁷

The 1968 International Atherosclerosis Project, in which over 22,000 corpses in 14 nations were cut open and examined for plaques in the arteries, showed the same degree of atheroma in all parts of the world - in populations that suffered from a great deal of heart disease, and in populations that had very little or none at all.⁸

All of these studies pointed to the fact that the thickening of the arterial walls is a natural, unavoidable process. The lipid hypothesis did not hold up to these population studies, nor did it explain the tendency toward fatal clots that caused myocardial infarction.

In 1956, an American Heart Association (AHA) fund-raiser was aired on all three major networks. The Master of Ceremonies interviewed, among others, Irving Page and Jeremiah Stamler of the AHA and researcher Ancel Keys. Panelists presented the lipid hypothesis as the cause of the heart disease epidemic and launched the Prudent Diet, one in which corn oil, margarine, chicken and cold cereal replaced butter, lard, beef and eggs.

The television campaign was not an unqualified success because one of the panelists, Dr Dudley White, disputed his colleagues at the AHA. Dr White noted that heart disease in the form of myocardial infarction was non-existent in 1900 when egg consumption was three times what it was in 1956 and when corn oil was unavailable. When pressed to support the Prudent Diet, Dr White replied: "See here, I began my practice as a cardiologist in 1921 and I never saw an MI patient until 1928. Back in the MI-free days before 1920 the fats were butter and lard, and I think that we would all benefit from the kind of diet that we had at a time when no one had ever heard the word 'corn' oil."

But the lipid hypothesis had already gained enough momentum to keep it rolling, in spite of Dr White's nationally televised plea for common sense in matters of diet and in spite of the contradictory studies that were showing up in the scientific literature.

In 1957, Dr Norman Jolliffe, Director of the Nutrition Bureau of the New York Health Department, initiated the Anti-Coronary Club in which selected businessmen, ranging in age from 40 to 59 years, were placed on the Prudent Diet. Club members used corn oil and margarine instead of butter, cold breakfast cereals instead of eggs and chicken, and fish instead of beef. Anti-Coronary Club members were to be compared with a 'matched' group of the same age who ate eggs for breakfast and had meat three times a day. Jolliffe, an overweight diabetic confined to a wheelchair, was confident that the Prudent Diet would save lives, including his own.

In the same year, the food industry initiated advertising campaigns that touted the health benefits of their products: low in fat or made with vegetable oils. A typical ad read "Wheaties may help you live longer". Wesson recommended its cooking oil "for your heart's sake". An ad in the Journal of the American Medical Association (JAMA) described Wesson oil as a "cholesterol depressant". Mazola advertisements assured the public that "science finds corn oil important to your health". Medical journal ads recommended Fleishmann's unsalted margarine for patients with high blood pressure.

In his syndicated column, Dr Frederick Stare, head of Harvard University's Nutrition Department, encouraged the consumption of corn oil - up to one cup a day. In a promotional piece specifically for Proctor and Gamble's Puritan oil, he cited two experiments and one clinical trial as showing that high blood cholesterol is associated with CHD. However, both experiments had nothing to do with CHD, and the clinical trial did not find that reducing blood cholesterol had any effect on CHD events. Later, Dr William Castelli, director of the Framingham Study, was one of several specialists to endorse Puritan. Dr Antonio Gotto, Jr, former AHA president, sent practising physicians a letter promoting Puritan oil - printed on Baylor College of Medicine, The De Bakey Heart Center letterhead.⁹

The irony of Gotto's letter is that De Bakey, the famous heart surgeon, co-authored a 1964 study involving 1,700 patients, which also showed no definite correlation between serum cholesterol levels and the nature and extent of coronary artery disease.¹⁰ In other words, those with low cholesterol levels were just as likely to have blocked arteries as those with high cholesterol levels.

But while studies like DeBakey's mouldered in the basements of university libraries, the vegetable oil campaign took on increased bravado and audacity.

The American Medical Association (AMA) at first opposed the commercialization of the lipid hypothesis and warned that "the anti-fat, anti-cholesterol fad is not just foolish and futile..it also carries some risk". The American Heart Association, however, was committed. In 1961, the AHA published its first dietary guidelines aimed at the public. The authors, Irving Page, Ancel Keys, Jeremiah Stamler and Frederick Stare, called for the substitution of polyunsaturates for saturated fat, even though Keys, Stare and Page had all previously noted in published papers that the increase in CHD was paralleled by increasing consumption of vegetable oils. In fact, in a 1956 paper, Keys had suggested that the increasing use of hydrogenated vegetable oils might be the underlying cause of the CHD epidemic.¹¹

Stamler showed up again in 1966 as an author of *Your Heart Has Nine Lives*, a little self-help book advocating the substitution of vegetable oils for butter and other so-called 'artery-clogging' saturated fats. The book was sponsored by makers of Mazola corn oil and Mazola margarine. Stamler did not believe that lack of evidence should deter Americans from changing their eating habits. The evidence, he stated, was "...compelling enough to call for altering some habits even before the final proof is nailed down.. the definitive proof that middle-aged men who reduce their blood cholesterol will actually have far fewer heart attacks waits upon diet studies now in progress." His version of the Prudent Diet called for substituting low-fat milk products such as skim milk and low-fat cheeses for cream, butter and whole cheeses, reducing egg consumption and cutting the fat off red meats. Heart disease, he lectured, was a disease of rich countries, striking rich people who ate rich food, including 'hard' fats like butter.

It was in the same year, 1966, that the results of Dr Jolliffe's Anti-Coronary Club experiment were published in JAMA.¹² Those on the Prudent Diet of corn oil, margarine, fish, chicken and cold cereal had an average serum cholesterol of 220, compared to 250 in the meat-and-potatoes control group. However, the study authors were obliged to note that there were eight deaths from heart disease among Dr Jolliffe's Prudent Diet group, and none among those who ate meat three times a day. Dr Jolliffe was dead by this time. He succumbed in 1961 from a vascular thrombosis, although the obituaries listed the cause of death as "complications from diabetes". The compelling "proof" that Stamler and others were sure would vindicate wholesale tampering with American eating habits had not yet been "nailed down".

The problem, said the insiders promoting the lipid hypothesis, was that the numbers involved in the Anti-Coronary Club experiment were too small. Dr Irving Page urged a National Diet-Heart Study involving one million men, in which the results of the Prudent Diet could be compared on a large scale with those on a diet high in meat and fat. With great media attention, the National Heart, Lung and Blood Institute organized the stocking of food warehouses in six major cities, where men on the Prudent Diet could get tasty polyunsaturated doughnuts and other fabricated food items free of charge. But a pilot study, involving 2,000 men, resulted in exactly the same number of deaths in both the Prudent Diet group and the control group. A brief report in *Circulation* (March 1968) stated that the study was a milestone "in mass environmental experimentation" that would have "an important effect on the food industry and the attitude of the public toward its eating habits". But the million-man Diet-Heart Study was abandoned in utter silence "for reasons of cost". Its chairman, Dr Irving Page, died of a heart attack.

Most animal fats - like butter, lard and tallow - have a large proportion of saturated fatty acids. Saturated fats are straight chains of carbon and hydrogen that pack together easily so that they are relatively solid at room temperature. Oils from seeds are composed mostly of polyunsaturated fatty acids. These molecules have kinks in them at the point of the unsaturated double bond. They do not pack together easily and therefore tend to be liquid at room temperature.

Judging from both food data and turn-of-the-century cookbooks, the American diet in 1900 was a rich one, with at least 35 to 40 per cent of calories coming from fats, mostly dairy fats in the form of butter, cream, whole milk, and also eggs. Salad dressing recipes usually called for egg yolks or cream; only occasionally for olive oil. Lard or tallow served for frying. Rich dishes like head cheese and scrapple contributed additional saturated fats

during an era when cancer and heart disease were rare. Butter substitutes made up only a small portion of the American diet, and these margarines were blended from coconut oil, animal tallow and lard - all rich in natural saturates.

The technology by which liquid vegetable oils could be hardened to make margarine was first discovered by a French chemist named Sabatier. He found that a nickel catalyst would cause the hydrogenation (the addition of hydrogen to unsaturated bonds to make them saturated) of ethylene gas to ethane. Subsequently, the British chemist Norman developed the first application of hydrogenation to food oils and took out a patent. In 1909, Procter & Gamble acquired the US rights to a British patent on making liquid vegetable oils solid at room temperature. The process was used on both cotton-seed oil and lard to give "better physical properties", to create shortenings that did not melt as easily on hot days.

The hydrogenation process transforms unsaturated oils into straight 'packable' molecules by rearranging the hydrogen atoms at the double bonds. In nature, most double bonds occur in the cis configuration - that is, with both hydrogen atoms on the same side of the carbon chain at the point of the double bond. It is the cis isomers of fatty acids that have a bend or kink at the double bond, preventing them from packing together easily. Hydrogenation creates trans double bonds by moving one hydrogen atom across to the other side of the carbon chain at the point of the double bond. In effect, the two hydrogen atoms then balance each other and the fatty acid straightens, creating a packable 'plastic' fat with a much higher melting temperature.

Although trans fatty acids are technically unsaturated, they are configured in such a way that the benefits of unsaturation are lost. The presence of several unpaired electrons presented by contiguous hydrogen atoms in their cis form allows many vital chemical reactions to occur at the site of the double bond. When one hydrogen atom is moved to the other side of the fatty acid molecule during hydrogenation, the ability of living cells to make reactions at the site is compromised or altogether lost. Trans fatty acids are sufficiently similar to natural fats that the body readily incorporates them into the cell membrane; once there, their altered chemical structure creates havoc with thousands of necessary chemical reactions - everything from energy provision to prostaglandin production.

After the Second World War, 'improvements' made it possible to plasticise highly unsaturated oils from corn and soybeans. New catalysts allowed processors to 'selectively hydrogenate' the kinds of fatty acids found in soy and canola oils - those with three double bonds. Called 'partial hydrogenation', this new method allowed processors to replace cotton-seed oil with more unsaturated corn and soybean oils in margarines and shortenings. This spurred a meteoric rise in soybean production from virtually nothing in 1900 to 70 million tons in 1970, surpassing corn production. Today, soy oil dominates the market and is used in almost 80 per cent of all hydrogenated oils.

The particular mix of fatty acids in soy oil results in shortenings containing about 40 per cent trans fats - an increase of about 5 per cent over cotton-seed oil and 15 per cent over corn oil. Canola oil, processed from a hybrid form of rape-seed, is particularly rich in fatty acids containing three double bonds and can contain as much as 50 per cent trans fats. Trans fats of a particularly problematic type are also formed during the process of deodorizing canola oil, although they are not indicated on labels for canola oil.

Certain forms of trans fatty acids occur naturally in dairy fats. Trans vaccenic acid makes up about four per cent of the fatty acids in butter. It is an interim product which the ruminant animal then converts to conjugated linoleic acid, a highly beneficial anti-carcinogenic component of animal fat. Humans seem to utilise the small amounts of trans vaccenic acid in butter fat without ill effects.

However, most of the trans isomers in modern hydrogenated fats are new to the human physiology. By the early 1970s, a number of researchers had expressed concern about their presence in the American diet, noting that the increasing use of hydrogenated fats had paralleled the increase in both heart disease and cancer. The unstated solution was one that could be easily presented to the public: eat natural, traditional fats; avoid newfangled foods made from vegetable oils; use butter, not margarine.

But medical research and public consciousness took a different tack - one that accelerated the decline of traditional foods like meat, eggs and butter, and fuelled continued dramatic increases in vegetable oil consumption.

Although the AHA had committed itself to the lipid hypothesis and the unproven theory that polyunsaturated oils afforded protection against heart disease, concerns about hydrogenated vegetable oils were sufficiently great to warrant the inclusion of the following statement in the organization's 1968 diet heart statement: "Partial hydrogenation of polyunsaturated fats results in the formation of trans forms which are less effective than cis, cis forms in lowering cholesterol concentrations. It should be noted that many currently available shortenings and margarines are partially hydrogenated and may contain little polyunsaturated fat of the natural cis, cis form."

While 150,000 copies of the statement were printed, they were never distributed. The shortening industry objected strongly, and a researcher named Fred Mattson of Procter & Gamble convinced Campbell Moses, medical director of the AHA, to remove it.¹³ The final recommendations for the public contained three major points: restrict calories; substitute polyunsaturates for saturates; reduce cholesterol in the diet.

Other organizations fell in behind the AHA in pushing vegetable oils instead of animal fats. By the early 1970s, the National Heart, Lung and Blood Institute, the AMA, the American Dietetic Association and the National Academy of Sciences had all endorsed the lipid hypothesis and the avoidance of animal fats for those Americans in the 'at risk' category.

Since Kritchevsky's early studies, many other trials had shown that serum cholesterol can be lowered by increasing ingestion of polyunsaturates. The physiological explanation for this is that when excess polyunsaturates are built into the cell membranes, resulting in reduced structural integrity or 'limpness', cholesterol is sequestered from the blood into the cell membranes to give them 'stiffness'. The problem was that there was no proof that lowering serum cholesterol levels could stave off CHD.

That did not prevent the American Heart Association calling for "modified and ordinary foods" useful for the purpose of facilitating dietary changes to newfangled oils away from traditional fats. These foods, said the AHA literature, should be made available to the consumer, "...reasonably priced and easily identified by appropriate labeling. Any existing legal and regulatory barriers to the marketing of such foods should be removed."

The man who made it possible to remove any "existing legal and regulatory barriers" was Peter Barton Hutt, a food lawyer for the prestigious Washington, DC, law firm of Covington and Burling. Hutt once stated: "Food law is the most wonderful field of law that you can possibly enter." After representing the edible oil industry, he temporarily left his law firm to become general counsel for the US Food and Drug Administration (FDA) in 1971.

The regulatory barrier to foods useful to the purpose of changing American consumption patterns was the Food, Drug and Cosmetic Act of 1938, which stated: "...there are certain traditional foods that everyone knows, such as bread, milk and cheese, and that when consumers buy these foods, they should get the foods that they are expecting.. [and] if a food resembles a standardized food but does not comply with the standard, that food must be labeled as an 'imitation'."

The 1938 Food, Drug and Cosmetic Act had been signed into law partly in response to consumer concerns about the adulteration of ordinary foodstuffs. Chief among the products with a tradition of suffering competition from imitation products were fats and oils.

In *Life on the Mississippi*, Mark Twain reports on a conversation overheard between a New Orleans cottonseed oil purveyor and a Cincinnati margarine drummer. New Orleans boasts of selling deodorized cottonseed oil as olive oil in bottles with European labels. "We turn out the whole thing - clean from the word go - in our factory in New Orleans.. We are doing a ripping trade, too." The man from Cincinnati reports that his factories are turning out oleomargarine by the thousands of tons, an imitation that "you can't tell from butter". He gloats at the thought of market domination. "You are going to see the day, pretty soon, when you won't find an ounce of butter to bless yourself with, in any hotel in the Mississippi and Ohio valleys, outside of the biggest cities.. and we can sell it so dirt cheap that the whole country has got to take it .. butter don't stand any show - there ain't any chance for competition. Butter's had its day - and from this out, butter goes to the wall. There's more money in oleomargarine than - why, you can't imagine the business we do."

In the tradition of Mark Twain's riverboat hucksters, Peter Barton Hutt guided the FDA through the legal and congressional hoops to the establishment in 1973 of the FDA "Imitation" policy which attempted to provide for "advances in food technology" and give "manufacturers relief from the dilemma of either complying with an

outdated standard or having to label their new products as 'imitation'.. [since] ...such products are not necessarily inferior to the traditional foods for which they may be substituted". Hutt considered the word 'imitation' to be oversimplified and inaccurate - "potentially misleading to consumers". The new regulations defined 'inferiority' as any reduction in content of an essential nutrient that is present at a level of two per cent or more of the US Recommended Daily Allowance (RDA). The new 'imitation' policy meant that imitation sour cream, made with vegetable oil and fillers like guar gum and carrageenan, need not be labeled 'imitation' as long as artificial vitamins were added to bring macronutrient levels up to the same amounts as those in real sour cream. Coffee creamers, imitation egg mixes, processed cheeses and imitation whipped cream no longer required the 'imitation' label, but could be sold as real and beneficial foods, low in cholesterol and rich in polyunsaturates.

These new regulations were adopted without the consent of Congress, continuing the trend instituted under Nixon in which the White House would use the FDA to promote certain social agendas through government food policies. They had the effect of increasing the lobbying clout of special-interest groups such as the edible oil industry, and short-circuiting public participation in the regulatory process. It allowed food processing innovations, regarded as 'technological improvements' by manufacturers, to enter the marketplace without the onus of economic fraud that might be engendered by greater consumer awareness and congressional supervision. They ushered in the era of ersatz foodstuffs, convenient counterfeit products - weary, stale, flat and immensely profitable.

Congress did not voice any objection to this usurpation of its powers, but entered the contest on the side of the lipid hypothesis. The Senate Select Committee on Nutrition and Human Needs, chaired by George McGovern during the years 1973 to 1977, actively promoted the use of vegetable oils.

"Dietary Goals for the United States", published by the committee, cited USDA data on fat consumption and stated categorically that "the overconsumption of fat, generally, and saturated fat in particular...have been related to six of the ten leading causes of death" in the United States. The report urged the American populace to reduce overall fat intake and to substitute polyunsaturates for saturated fat from animal sources - margarine and corn oil for butter, lard and tallow.

Opposing testimony included a moving letter (buried in the voluminous report) by Dr Fred Kummerow of the University of Illinois, urging a return to traditional whole foods and warning against the use of soft drinks. In the early 1970s, Kummerow had shown that trans fatty acids caused increased rates of heart disease in pigs. A private endowment allowed him to continue his research, but government-funded agencies such as the National Institutes of Health refused to give him further grants.

One study that was known to McGovern Committee members, but not mentioned in its final report, compared calves fed saturated fat from tallow and lard with calves fed unsaturated fat from soybean oil. The calves fed tallow and lard did indeed show higher plasma cholesterol levels than the soybean-oil-fed calves; fat-streaking was found in their aortas, and atherosclerosis was also enhanced. But the calves fed soybean oil showed a decline in calcium and magnesium levels in the blood, possibly due to inefficient absorption. They utilized vitamins and minerals inefficiently, showed poor growth and poor bone development, and had abnormal hearts. More cholesterol per unit of dry matter was found in the aorta, liver, muscle, fat and coronary arteries - a finding which led the investigators to the conclusion that the lower blood cholesterol levels in the soybean-oil-fed calves may be the result of cholesterol being transferred from the blood to other tissues. The calves in the soybean oil group collapsed when forced to move around and they were unaware of their surroundings for short periods. They also had rickets and diarrhea.

The McGovern Committee report continued dietary trends already in progress: the increased use of vegetables oils, especially in the form of partially hydrogenated margarines and shortenings. In 1976, the FDA established the GRAS (Generally Recognized As Safe) status for hydrogenated soybean oil. A report prepared by the Life Sciences Research Office of the Federation of American Scientists for Experimental Biology concluded: "There is no evidence in the available information on hydrogenated soybean oil that demonstrates or suggests reasonable ground to suspect a hazard to the public when it is used as a direct or indirect food ingredient at levels that are now current or that might reasonably be expected in the future."

When Mary Enig, a graduate student at the University of Maryland, read the McGovern Committee report, she was puzzled. Enig was familiar with Kummerow's research and she knew that the consumption of animal fats in

America was not on the increase. Quite the contrary: the use of animal fats had been declining steadily since the turn of the century.

A report in the Journal of American Oil Chemists - which the McGovern Committee did not use - showed that animal fat consumption had declined from 104 grams per person per day in 1909 to 97 grams per day in 1972, while vegetable fat intake had increased from a mere 21 grams to almost 60 grams.¹⁴ Total per-capita fat consumption had increased over the period, but this increase was mostly due to an increase in unsaturated fats from vegetable oils - with 50 per cent of the increase coming from liquid vegetable oils and about 41 per cent from margarines made from vegetable oils.

Enig noted a number of studies that directly contradicted the McGovern Committee's conclusions that "there is...a strong correlation between dietary fat intake and the incidence of breast cancer and colon cancer" - two of the most common cancers in America. Greece, for example, had less than one-fourth the rate of breast cancer compared to Israel, but the same dietary fat intake. Spain had only one-third the breast cancer mortality of France and Italy, but the total dietary fat intake was slightly greater. Puerto Rico, with a high animal fat intake, had a very low rate of breast and colon cancer. The Netherlands and Finland both used approximately 100 grams of animal fat per capita per day, but breast and colon cancer rates were almost twice in the Netherlands what they were in Finland. The Netherlands consumed 53 grams of vegetable fat per person compared to 13 grams in Finland. A study from Cali, Colombia, found a fourfold excess risk for colon cancer in the higher economic classes which used less animal fat than the lower economic classes. A study found that Seventh Day Adventist physicians, who avoid meat (especially red meat), had a significantly higher rate of colon cancer than Seventh Day Adventist physicians.

Enig analyzed the USDA data that the McGovern Committee had used and concluded that they showed a strong positive correlation with total fat and vegetable fat and an essentially strong negative correlation or no correlation with animal fat to total cancer deaths, breast and colon cancer mortality and breast and colon cancer incidence - in other words, use of vegetable oils seemed to predispose to cancer, and animal fats seemed to protect against cancer. She noted that the analysts for the committee had manipulated the data in inappropriate ways in order to obtain mendacious results.

Enig submitted her findings to the journal of the Federation of American Societies for Experimental Biology (FASEB), in May 1978, and her article was published in FASEB's Federation Proceedings¹⁵ in July of the same year - an unusually quick turnaround. The assistant editor, responsible for accepting the article, died of a heart attack shortly thereafter. Enig's paper noted that the correlations pointed a finger at trans fatty acids and called for further investigation. Only two years earlier, the Life Sciences Research Office, which is the arm of FASEB that does scientific investigations, had published the whitewash that ushered partially hydrogenated soybean oil onto the GRAS list and removed any lingering constraints against the number-one ingredient in factory-produced food.

Enig's paper sent alarm bells through the industry. In early 1979 she received a visit from S. F. Reipma of the National Association of Margarine Manufacturers. Short, bald and pompous, Reipma was visibly annoyed. He explained that both his association and the Institute for Shortening and Edible Oils (ISEO) kept careful watch to prevent articles like Enig's from appearing in the literature. Enig's paper should never have been published, he said. He thought that ISEO was "watching out". "We left the barn door open," he said, "and the horse got out."

Reipma also challenged Enig's use of the USDA data, claiming that it was in error. He knew it was in error, he said, "because we give it to them".

A few weeks later, Reipma paid a second visit, this time in the company of Tom Applewhite, an adviser to the ISEO and representative of Kraft Foods, Ronald Simpson with Central Soya, and a representative from Lever Brothers. They carried with them - in fact, waved in the air in indignation - a two-inch stack of newspaper articles, including one that appeared in the National Enquirer, reporting on Enig's Federation Proceedings article. Applewhite's face flushed red with anger when Enig repeated Reipma's statement that they had "left the barn door open and the horse got out" and his admission that Department of Agriculture food data had been sabotaged by the margarine lobby.

The other thing Reipma told Enig during his unguarded visit was that he had called in on the FASEB offices in an attempt to coerce them into publishing letters to refute her paper, without allowing Enig to submit any

counter-refutation as was normally customary in scientific journals. He told Enig that he was "thrown out of the office" - an admission later confirmed by one of the FASEB editors. Nevertheless, a series of letters did follow the July 1978 article.¹⁶ On behalf of the ISEO, Applewhite and Walter Meyer of Procter & Gamble criticized Enig's use of the data. Applewhite accused Enig of extrapolating from two data points, when in fact she had used seven. John Bailar, Editor-in-Chief of the Journal of the National Cancer Institute pointed out that the correlations between vegetable oil consumption and cancer were not the same as evidence of causation, and warned against changing current dietary components in the hope of preventing cancer in the future - which is, of course, exactly what the McGovern Committee did.

In reply, Enig and her colleagues noted that although the National Cancer Institute (NCI) had provided them with faulty cancer data, this had no bearing on the statistics relating to trans consumption and did not affect the gist of their argument - that the correlation between vegetable fat consumption, especially trans fat consumption, was sufficient to warrant a more thorough investigation. The problem was that very little investigation was being done.

University of Maryland researchers recognized the need for more research in two areas. One concerned the effects of trans fats on cellular processes once they are built into the cell membrane. Studies with rats, including one conducted by Fred Mattson in 1960, indicated that the trans fatty acids were built into the cell membrane in proportion to their presence in the diet, and that the turnover of trans in the cells was similar to that of other fatty acids. These studies, according to J. Edward Hunter of the ISEO, were proof that "trans fatty acids do not pose any hazard to man in a normal diet".

Enig and her associates were not so sure. Kummerow's research indicated that the trans fats contributed to heart disease; and Kritchevsky, whose early experiments with vegetarian rabbits were now seen to be totally irrelevant to the human model, had found that trans fatty acids raise cholesterol in humans.¹⁷ Enig's own research, published in her 1984 doctoral dissertation, indicated that trans fats interfered with enzyme systems that neutralized carcinogens and increased enzymes that potentiates carcinogens.¹⁸

Endnotes:

1. D Kritchevsky, et al, "Effect of Cholesterol Vehicle in Experimental Atherosclerosis", Am. J. Physiol. 178:30-32, July-September 1954
2. "Notice of Supelco-AOC Award to Kritchevsky", Inform 7:315, 1996
3. Enig, M., Trans Fatty Acids in the Food Supply: A Comprehensive Report Covering 60 Years of Research, Enig Associates, Inc., Silver Spring, MD, USA, 1995 (2ed), pp. 4-8
4. Groom, D., "Population Studies of Atherosclerosis", Annals of Int. Med. 55(1):51-62, July 1961; Enos, W. F. et al., "Pathogenesis of Coronary Disease in American Soldiers Killed in Korea", JAMA 158:912, 1955.
5. Laurie, W. et al, "Atherosclerosis and its Cerebral Complications in the South African Bantu", Lancet, February 1958, pp. 231-232
6. Robertson, W. B., "Atherosclerosis and Ischaemic Heart Disease," Lancet 1:444, 1959
7. Gordon, T., "Mortality Experience Among Japanese in the US, Hawaii and Japan", Pul. Health Rep. 51:270, 1957; Pollak, O. J., "Diet and Atherosclerosis," Lancet 1:444, 1959
8. McGill, H. C. et al., "General Findings of the International Atherosclerosis Project," Laboratory Investigations 18(5):498, 1968
9. Smith, R. L. and E. R. Pinckney, The Cholesterol Conspiracy, Warren H Green, Inc., St Louis, MO, USA, 1991, p. 125
10. De Bakey, M. et al., "Serum Cholesterol Values in Patients Treated Surgically for Atherosclerosis", JAMA 189(9):655-59, 1964
11. Keys, A., "Diet and Development of Coronary Heart Disease", J. Chron. Dis. 4(4):364-380, October 1956
12. Cristakis, G., "Effect of the Anti-Coronary Club Program on Coronary Heart Disease Risk-Factor Status", JAMA 198(6):129-35, November 7, 1996
13. "Dietary Goals for the United States - Supplemental Views", prepared by the Staff of the Select Committee on Nutrition and Human Needs, United States Senate, Government Printing Office, Washington, DC, November 1977, pp. 139-140
14. Rizek, R. L. et al., "Fat in Today's Food Supply - Level of Use and Sources", J. Am. Oil Chem. Soc. 51:244, 1974
15. Enig, M. G. et al., "Dietary Fat and Cance Trends - A Critique", Federation Proceedings 37(9):2215-2220, FASEB, July 1978
16. Applewhite, T. H., "Statistical 'Correlations' Relating Trans Fats to Cance: A Commentary", Federation Proceedings 38(11):2435-2439, FASEB, October 1979
17. Kummerow, F. A., "Effects of Isomeric Fats on Animal Tissue, Lipid Classes and Atherosclerosis", Geometrical and Positional Fatty Acid Isomers (E. A. Emken and H. J. Dutton, eds), American Oil Chemists Society, Champaign, IL, USA, 1979, pp. 151-180;
18. Kritchevsky, D., "Trans Fatty Acid Effects in Experimental Atherosclerosis", Federation Proceedings 41:2813, FASEB, 1982

18. Enig, M. G., "Modification of Membrane Lipid Composition and Mixed-Function Oxidases in Mouse Liver Microsomes by Dietary Trans Fatty Acids", Doctoral Dissertation for the University of Maryland, 1984

The OILING of AMERICA Part 2 of 2

Modern-day diets high in hydrogenated vegetable oils instead of traditional animal fats are implicated in causing a significant increase in heart disease and cancer.

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The other area needing further investigation concerned just how much trans fat there was in a 'normal diet' of the typical American. What had hampered any thorough research into the correlation of trans fatty acid consumption and disease was the fact that these altered fats were not considered as a separate category in any of the databases then available to researchers. A 1970 US Food and Drug Administration internal memo stated that a market-basket survey was needed to determine trans levels in commonly used foods. The memo remained buried in the FDA files.

The massive Health and Human Services National Health and Nutrition Examination Survey (NHANES II), conducted during the years 1976 to 1980, noted the increasing US consumption of margarine, French fried potatoes, cookies and snack chips - all made with vegetable shortenings - without listing the proportion of trans.

Mary Enig first looked at the NHANES II database in 1987 and, when she did, she had a sinking feeling. Not only were trans fats conspicuously absent from the fatty acid analyses, but data on other lipids made no sense at all. Even foods containing no trans fats were listed with faulty fatty-acid profiles. For example, safflower oil was listed as containing 14 per cent linoleic acid (a double-bond fatty acid of the omega-6 family) when in fact it contained 80 per cent; and a sample of butter crackers was listed as containing 34 per cent saturated fat when in fact it contained 78 per cent. In general, the NHANES II database tended to minimize the amount of saturated fats in common foods.

Over the years, Joseph Sampagna and Mark Keeney, both highly qualified lipid biochemists at the University of Maryland, applied to the National Science Foundation, the National Institutes of Health (NIH), the US Department of Agriculture (USDA), the National Dairy Council and the National Livestock and Meat Board for funds to look into the trans content of common American foods. Only the National Livestock and Meat Board came through with a small grant for equipment; the others turned them down. The pink slip from the NIH criticized items that weren't even relevant to the proposal. The turndown by the National Dairy Council was not a surprise. Enig had earlier learned that Phil Lofgren, then head of research at the Dairy Council, had philosophical ties to the lipid hypothesis. Enig tried to alert Senator Mettzanbaum from Ohio, who was involved in the dietary recommendations debate, but got nowhere.

A USDA official confided to the Maryland research group that they "would never get money as long as they pursued the trans work". Nevertheless, they did pursue it. Sampagna, Keeney and a few graduate students, funded jointly by the USDA and the university, spent thousands of hours in the laboratory analyzing the trans-fat content of hundreds of commercially available foods. Enig worked as a graduate student, at times with a small stipend, at times without pay, to help direct the process of tedious analysis. The long arm of the food industry did its best to put a stop to the group's work by pressuring the USDA to pull its financial support of the graduate students doing the lipid analyses - support which the University of Maryland received due to its status as a land-grant college.

In December of 1982, Food Processing carried a brief preview of the University of Maryland research¹⁹ and, five months later, printed a blistering letter from Edward Hunter on behalf of the Institute of Shortening and

Edible Oils (ISEO).²⁰ The University of Maryland studies on trans-fat content in common foods had obviously struck a nerve in the industry. Hunter stated that the Bailar, Applewhite and Meyer letters that had appeared in Federation Proceedings five years earlier, "severely criticized and discredited" the conclusions reached by Enig and her colleagues. Hunter was concerned that Enig's group would exaggerate the amount of trans found in common foods. He cited ISEO data indicating that most margarines and shortenings contain no more than 35 per cent and 25 per cent trans respectively, and that most contain considerably less.

What Enig and her colleagues actually found was that many margarines indeed contained about 31 per cent trans-fat, while later surveys by others revealed that Parkay margarine contained up to 45 per cent trans, and that many shortenings found ubiquitously in cookies, chips and baked goods contained more than 35 per cent trans-fat. Enig also discovered that many baked goods and processed foods contained considerably more fat from partially hydrogenated vegetable oils than was listed on the labels. The finding of higher levels of fat in products made with partially hydrogenated oils was reported by Canadian government researchers many years later, in 1993.²¹

The final results of Enig's ground-breaking compilation were published in the October 1983 edition of the Journal of the American Oil Chemists' Society.²² Her analyses of more than 220 food items, coupled with food disappearance data, allowed University of Maryland researchers to confirm earlier estimates that the average American consumed at least 12 grams of trans fat per day - directly contradicting ISEO assertions that most Americans consumed no more than 6 to 8 grams of trans fat per day. Those who consciously avoided animal fats typically consumed far more than 12 grams of trans fat per day.

The ensuing debate - between Enig and her colleagues at the University of Maryland, and Hunter and Applewhite of the ISEO - took the form of a cat-and-mouse game, running through several scientific journals. Food Processing declined to publish Enig's reply to Hunter's attack. Science published another critical letter by Hunter in 1984,²³ in which he misquoted Enig, but the journal refused to print her rebuttal. Hunter continued to object to assertions that average consumption of trans fat in partially hydrogenated margarines and shortenings could exceed six to eight grams per day - a concern that Enig found puzzling when coupled with the official ISEO position that trans fatty acids were innocuous and posed no threat to public health.

The ISEO did not want the American public to hear about the debate on hydrogenated vegetable oils. For Enig, this translated into the sound of doors closing. A poster presentation she organized for a campus health fair caught the eye of the dietetics department chairman who suggested she submit an abstract to the Society for Nutrition Education, many of whose members are registered dietitians. Her abstract concluded that "...meal plans and recipes developed for nutritionists and dietitians to use when designing diets to meet the Dietary Guidelines, the dietary recommendation of the American Heart Association or the Prudent Diet have been examined for trans fatty acid content. Some diet plans are found to contain approximately 7% or more of calories as trans fatty acids." The Abstract Review Committee rejected the submission, calling it of "limited interest".

Early in 1985, the Federation of American Societies for Experimental Biology (FASEB) heard more testimony on the trans-fat issue. Enig alone represented the alarmist point of view, while Hunter and Applewhite of the ISEO and Ronald Simpson, then with the National Association of Margarine Manufacturers, assured the panel that trans fats in the food supply posed no danger. Enig reported on University of Maryland research that delineated the differences in small amounts of naturally occurring trans fats in butter, which do not inhibit enzyme function at the cellular level, and man-made trans fats in margarines and vegetable shortenings, which do. She also noted a 1981 feeding trial in which swine fed trans fatty acids developed higher parameters for heart disease than those fed saturated fats, especially when trans fatty acids were combined with added polyunsaturates.²⁴ Her testimony was omitted from the final report, although her name in the bibliography created the impression that her research supported the FASEB whitewash.²⁵

In the following year, 1986, Hunter and Applewhite published an article, exonerating trans fats as a cause of atherosclerosis, in the prestigious American Journal of Clinical Nutrition²⁶ - which, by the way, is sponsored by companies including Procter & Gamble, General Foods, General Mills, Nabisco and Quaker Oats. The authors once again stressed that the average per-capita consumption of trans fatty acids did not exceed six to eight grams. Many subsequent government and quasi-government reports minimizing the dangers of trans fats used the 1986 Hunter and Applewhite article as a reference.

Enig testified again in 1988 before the Expert Panel on the National Nutrition Monitoring System (NNMS). In fact, she was the only witness before a panel which began its meeting by confirming that the cause of America's health problems was the overconsumption of "fat, saturated fatty acids, cholesterol and sodium". Her testimony pointed out that the 1985 FASEB report, exonerating trans fatty acids as safe, was based on flawed data.

Behind the scenes, in a private letter to Dr Kenneth Fischer, Director of the Life Sciences Research Office (LSRO), Hunter and Applewhite charged that "the University of Maryland group continues to raise unwarranted and unsubstantiated concerns about the intake of and imagined physiological effects of trans fatty acids and...they continue to overestimate greatly the intake of trans acids by typical Americans". They said, "No one other than Enig has raised questions about the validity of the food fatty-acid composition data used in NHANES II and...she has not presented sufficiently compelling arguments to justify a major re-evaluating."

The letter contained numerous other innuendos that Enig had mischaracterized the work of other researchers and had been less than scientific in her research. It was widely circulated among NNMS agencies. John Weihrauch - a USDA scientist, not an industry representative - surreptitiously slipped the letter to Dr Enig. She and her colleagues replied by asking: "If the trade association truly believes 'that trans fatty acids do not pose any harm to humans and animals'...why are they so concerned about any levels of consumption and why do they so vehemently and so frequently attack researchers whose findings suggest that the consumption of trans fatty acids is greater than the values the industry reports?"

The Maryland researchers argued that trans fats should be included in food nutrition labels; but the Hunter and Applewhite letter asserted that "there is no documented justification for including trans acids...as part of nutrition labeling".

During her testimony, Enig also brought up her concerns about other national food databases, citing their lack of information on trans. The Food Consumption Survey contained glaring errors - reporting, for example, consumption of butter in amounts nearly twice as great as what exists in the US food supply, and of margarine in quantities nearly half those known to exist in the food supply. "The fact that the database is in error should compel the Congress to require correction of the database and re-evaluation of policy flowing from erroneous data," Enig argued, "especially since the congressional charter for NHANES was to compare dietary intake and health status, and since this database is widely used to do just that." Rather than "correction of the database", NNMS officials responded to Enig's criticism by dropping the whole section pertaining to butter and margarine from the 1980 tables.

Enig's testimony was not totally left out of the National Nutritional Monitoring System final report, as it had been from the FASEB report three years earlier. A summary of the proceedings with the listing of panelists, released in July 1989 by Director Kenneth Fischer, announced that a transcript of Enig's testimony could be obtained from Ace Federal Reporter in Washington, DC.²⁷ Unfortunately his report wrongly listed the date of Enig's testimony as January 20, 1988, rather than January 21, thus making her comments more difficult to retrieve.

The Enig-ISEO debate was covered by the prestigious Food Chemical News and Nutrition Week²⁸ - both widely read by Congress and the food industry, but virtually unknown to the general public. National media coverage of dietary fat issues focused on the proceedings of the National Heart, Lung and Blood Institute (NHLBI), as this enormous bureaucracy ploughed relentlessly forward with the lipid hypothesis. In June of 1984, for example, the press diligently reported the proceedings of the NHLBI's Lipid Research Clinics (LRC) Conference which was organized to wrap up almost 40 years of research on lipids, cholesterol and heart disease. The problem with the 40 years of NHLBI-sponsored research on lipids, cholesterol and heart disease was that it had not produced many answers - at least not many answers that pleased the NHLBI.

The ongoing Framingham Study found that there was virtually no difference in coronary heart disease (CHD) "events" for individuals with cholesterol levels between 205 mg/dL and 294 mg/dL - the vast majority of the US population. Even for those with extremely high cholesterol levels - up to almost 1,200 mg/dL - the difference in CHD events compared to those in the normal range was trivial.²⁹ This did not prevent Dr William Kennel, then Framingham Study Director, from making claims about the Framingham results. "Total plasma cholesterol," he said, "is a powerful predictor of death related to CHD."

It was not until more than a decade later, in 1992, that the real findings at Framingham were published - without fanfare - in the Archives of Internal Medicine, an obscure journal. "In Framingham, Massachusetts," admitted Dr

William Castelli, Kannel's successor, "the more saturated fat one ate, the more cholesterol one ate, the more calories one ate, the lower people's serum cholesterol ... we found that the people who ate the most cholesterol, ate the most saturated fat, ate the most calories, weighed the least and were the most physically active."³⁰

The NHLBI's Multiple Risk Factor Intervention Trial (MRFIT) studied the relationship between heart disease and serum cholesterol levels in 362,000 men, and found that annual deaths from CHD varied from slightly less than one per thousand, for serum cholesterol levels below 140 mg/dL, to about two per thousand, for serum cholesterol levels above 300 mg/dL - once again, a trivial difference. Dr John LaRosa, of the American Heart Association (AHA), claimed that the curve for CHD deaths began to "inflect" after 200 mg/dL, when in fact the "curve" was a very gradually sloping straight line that could not be used to predict whether serum cholesterol above certain levels posed a significantly greater risk for heart disease. One unexpected MRFIT finding the media did not report was that deaths from all causes - cancer, heart disease, accidents, infectious disease, kidney failure, etc. - were substantially greater for those men with cholesterol levels below 160 mg/dL.³¹

What was needed to resolve the validity of the lipid hypothesis once and for all was a well-designed, long-term diet study that compared coronary heart disease events in those eating traditional foods with those whose diets contained high levels of vegetable oils - but the proposed Diet&Heart Study designed to test just that had been cancelled without fanfare years earlier.

In view of the fact that orthodox medical agencies were united in their promotion of margarine and vegetable oils over animal foods containing cholesterol and animal fats, it is surprising that the official literature can cite only a handful of experiments indicating that dietary cholesterol has "a major role in determining blood cholesterol levels".

One of these was a study, involving 70 male prisoners, directed by Fred Mattson³² - the same Fred Mattson who had pressured the AHA into removing any reference to hydrogenated fats from its diet/heart statement a decade earlier. Funded in part by Procter & Gamble, the research contained a number of serious flaws: selection of subjects for the four groups studied was not randomized; the experiment inexcusably eliminated "an equal number of subjects with the highest and lowest cholesterol values"; 12 additional subjects dropped out, leaving some of the groups too small to provide valid conclusions; and statistical manipulation of the results was shoddy. But the biggest flaw was that the subjects receiving cholesterol did so in the form of reconstituted powder - a totally artificial diet. Mattson's discussion did not even address the possibility that the liquid formula diet he used might affect blood cholesterol differently than would a whole-foods diet, when many other studies indicated that this is in fact the case.

The culprit in liquid protein diets actually seems to be oxidized cholesterol, formed during the high-temperature drying process, which seems to initiate the build-up of plaque in the arteries.³³ To give it 'body', powdered milk containing oxidized cholesterol is added to reduced fat milk - which the American public has accepted as a healthier choice than whole milk. It was purified, oxidized cholesterol that Kritchevsky and others used in their experiments on vegetarian rabbits.

The NHLBI argued that a diet study using whole foods and involving the whole population would be too difficult to design and too expensive to carry out. But the NHLBI did have funds available to sponsor the massive Lipid Research Clinics Coronary Primary Prevention Trial in which all subjects were placed on a diet low in cholesterol and saturated fat. Subjects were divided into two groups, one of which took a cholesterol-lowering drug and the other a placebo. Working behind the scenes, but playing a key role in both the design and implementation of the trials, was Dr Fred Mattson, formerly of Procter & Gamble.

An interesting feature of the study was the fact that a good part of the trial's US\$150 million budget was devoted to group sessions in which trained dietitians taught both groups of study participants how to choose "heart-friendly" foods: margarine, egg replacements, processed cheese, baked goods made with vegetable shortenings; in short, the vast array of manufactured foods awaiting consumer acceptance. As both groups received dietary indoctrination, study results could support no claims about the relation of diet to heart disease. Nevertheless, when the results were released, both the popular press and medical journals portrayed the Lipid Research Clinics trials as the long-sought proof that animal fats were the cause of heart disease. Rarely mentioned in the press was the ominous fact that the group taking the cholesterol-lowering drugs had an increase in deaths from cancer, stroke, violence and suicide.³⁴

LRC researchers claimed that the group taking the cholesterol-lowering drug had a 17 per cent reduction in the rate of CHD, with an average cholesterol reduction of 8.5 per cent. This allowed LRC trials Director Basil Rifkind to claim that "for each 1% reduction in cholesterol, we can expect a 2% reduction in CHD events". The statement was widely circulated, even though it represented a completely invalid representation of the data - especially in light of the fact that when the University of Maryland lipid group analyzed the LRC data, they found no difference in CHD events between the group taking the drug and those on the placebo.

A number of clinicians and statisticians, including Michael Oliver and Richard Krommel, who participated in a 1984 Lipid Research Clinics conference workshop, were highly critical of the manner in which the LRC results had been tabulated and manipulated. In fact, the conference went very badly for the NHLBI, with critics of the lipid hypothesis almost outnumbering supporters. One participant, Dr Beverly Teter of the University of Maryland's lipid group, was delighted with the state of affairs. "It's wonderful," she remarked to Basil Rifkind, "to finally hear both sides of the debate. We need more meetings like this." His reply was terse and sour: "No we don't."

Dissenters were again invited to speak briefly at the NHLBI-sponsored National Cholesterol Consensus Conference held later that year, but their views were not included in the panel's report for the simple reason that the report was generated by NHLBI staff before the conference convened. Dr Bev Teter discovered this when she picked up some papers by mistake just before the conference began, and found they contained the consensus report, already written, with just a few numbers left blank. Kritchevsky represented the lipid hypothesis camp with a humorous five-minute presentation full of ditties. Edward Ahrens, a respected researcher, raised strenuous objections about the "consensus", only to be told that he had misinterpreted his own data, and that if he wanted a conference to come up with different conclusions he should pay for it himself.

The 1984 Cholesterol Consensus Conference final report was a whitewash, containing no mention of the large body of evidence that conflicted with the lipid hypothesis. One of the blanks was filled in with the number '200'. The document defined all those with cholesterol levels above 200 mg/dL as "at risk" and called for mass cholesterol screening, even though the most ardent supporters of the lipid hypothesis had surmised in print that 240 should be the magic cut-off point. Such screening would in fact need to be carried out on a massive scale, as the federal medical bureaucracy, by picking the number 200, had defined the vast majority of the American adult population as "at risk". The report resurrected the ghost of Norman Jolliffe and his Prudent Diet by suggesting the avoidance of saturated fat and cholesterol for all Americans now defined as "at risk", and specifically advised the replacement of butter with margarine.

The Consensus Conference also provided a launching pad for the nationwide National Cholesterol Education Program (NCEP) which had the stated goal of "changing physicians' attitudes". NHLBI-funded studies had determined that while the general population had bought into the lipid hypothesis and was dutifully using margarine and buying low-cholesterol foods, the medical profession remained skeptical. A large "Physicians Kit" was sent to all doctors in America, compiled in part by the American Pharmaceutical Association whose representatives served on the NCEP coordinating committee. Doctors were taught the importance of cholesterol screening, the advantages of cholesterol-lowering drugs and the unique benefits of the Prudent Diet. NCEP materials told every doctor in America to recommend the use of margarine rather than butter.

In November of 1986, the Journal of the American Medical Association published a series on the Lipid Research Clinics trials, including "Cholesterol and Coronary Heart Disease: A New Era" by long-time American Heart Association member Scott Grundy, MD, PhD.³⁵ The article is a disturbing combination of euphoria and agony - euphoria at the forward movement of the lipid hypothesis juggernaut, and agony over the elusive nature of real proof. "The recent Consensus Conference on Cholesterol...implied that levels between 200 and 240...carry at least a mild increase in risk, which they obviously do...," said Grundy, directly contradicting an earlier statement: "Evidence relating plasma cholesterol levels to atherosclerosis and CHD has become so strong as to leave little doubt of the etiologic connection." Grundy called for "the simple step of measuring the plasma cholesterol level in all adults" and said, "...those found to have elevated cholesterol levels can be designated as at high risk and thereby can enter the medical care system ... an enormous number of patients will be included." Who benefits from "the simple step of measuring the plasma cholesterol level in all adults"? Why, hospitals, laboratories, pharmaceutical companies, the vegetable oil industry, margarine manufacturers, food processors and, of course, medical doctors.

"Many physicians will see the advantages of using drugs for cholesterol lowering...," said Grundy, even though "a positive benefit/risk ratio for cholesterol-lowering drugs will be difficult to prove". In the US alone, the cost of

cholesterol screening and cholesterol-lowering drugs now stands at \$60 billion per year, even though a positive risk/benefit ratio for such treatment has never been established.

Grundy was equally schizophrenic about the benefits of dietary modification. "Whether diet has a long-term effect on cholesterol remains to be proved," he stated, but "Public health advocates furthermore can play an important role by urging the food industry to provide palatable choices of foods that are low in cholesterol, saturated fatty acids and total calories." Such foods, almost by definition, contain partially hydrogenated vegetable oils that imitate the advantages of animal fats.

Grundy knew that the trans fats were a problem, that they raised serum cholesterol and contributed to the etiology of many diseases. He knew, because a year earlier, at his request, Mary Enig had sent him a package of data detailing numerous studies that gave reason for concern, which he acknowledged in a signed letter as an important contribution to the ongoing debate.

Other mouthpieces of the medical establishment fell in line after the Consensus Conference. In 1987, the National Academy of Sciences published an overview in the form of a handout booklet, containing a whitewash of the trans problem and a pejorative description of palm oil - a natural fat high in beneficial saturates and mono-unsaturates that, like butter, has nourished healthy population groups for thousands of years, and, also like butter, competes with hydrogenated fats because it can be used as a shortening.

he following year, the Surgeon General's Report on Nutrition and Health emphasized the importance of making low-fat foods more widely available. Project LEAN (Low-fat Eating for America Now) - sponsored by the J. Kaiser Family Foundation and a host of establishment groups such as the American Heart Association, the American Dietetic Association, the American Medical Association, the USDA, the National Cancer Institute, the Centers for Disease Control and the National Heart, Lung and Blood Institute - announced a publicity campaign to "aggressively promote foods low in saturated fat and cholesterol in order to reduce the risk of heart disease and cancer".

The next year, Enig joined Frank McLaughlin, Director of the Center for Business and Public Policy at the University of Maryland, in testimony before the National Food Processors Association (NFPA). It was a closed conference for NFPA members only. Enig and McLaughlin had been invited to give "a view from academia". Enig presented a number of slides and warned against singling out classes of fats and oils for special pejorative labeling. A representative from Frito-Lay took umbrage at Enig's slides which listed amounts of trans fats in Frito-Lay products. Enig offered to re-do the analyses if Frito-Lay were willing to fund the research. "If you'd talk different, you'd get money," he said.

Enig urged the association to endorse accurate labeling of trans fats in all food items, but conference participants - including representatives from most of the major food processing giants - preferred a policy of "voluntary labeling" that did not unnecessarily alert the public to the presence of trans fats in their foods. To date, they have prevailed in preventing the inclusion of trans fats on nutrition labels.

Enig's cat-and-mouse game with Hunter and Applewhite of the ISEO continued throughout the later years of the 1980s. Their modus operandi was to pepper the literature with articles that downplayed the dangers of trans fats, to use their influence to prevent opposing points of view from appearing in print, and to follow up the few alarmist articles that did squeak through with "definitive rebuttals".

In 1987 Enig submitted a paper on trans fatty acids in the US diet to the American Journal of Clinical Nutrition, as a reply to the erroneous 1985 FASEB report as well as to Hunter and Applewhite's influential 1986 article - which by even the most conservative analysis underestimated the average American consumption of partially hydrogenated fats. Editor-in-chief Albert Mendeloff, MD, rejected Enig's rebuttal as "inappropriate for the journal's readership". His rejection letter invited her to resubmit her paper if she could come up with "new evidence". In 1991, her article finally came out in a less prestigious publication, the Journal of the American College of Nutrition,³⁶ although Applewhite did his best to coerce editor Mildred Seelig into removing it at the last minute.

Hunter and Applewhite submitted letters and then an article of rebuttal to the American Journal of Clinical Nutrition,³⁷ which were published shortly thereafter. In their article, "Reassessment of Trans Fatty Acid Availability in the US Diet", Hunter and Applewhite argued that the amount of trans in the American diet had

actually declined since 1984 due to the introduction of soft margarines and tub spreads. The media fell in line with their pronouncements, with numerous articles by food writers recommending low-trans tub spreads, made from polyunsaturated vegetable oils, as the sensible alternative to saturated fat from animal sources. This was not surprising, as most newspapers rely on the International Food Information Council, an arm of the food processing industry, for their nutrition information.

Enig and the University of Maryland group were not alone in their efforts to bring their concerns about the effect of partially hydrogenated fats before the public.

Kummerow at the University of Illinois, blessed with independent funding and an abundance of patience, carried out a number of studies that indicated that trans fats increased the risk factors associated with heart disease and that vegetable-oil-based fabricated foods such as Egg Beaters cannot support life.³⁸

George Mann, formerly with the Framingham project, possessed neither funding nor patience and in fact was very angry with what he called the "Diet/Heart scam". His independent studies of the Masai in Africa,³⁹ whose diet is extremely rich in cholesterol and saturated fat and who are virtually free of heart disease, had convinced him that the lipid hypothesis was "the public health diversion of this century...the greatest scam in the history of medicine".⁴⁰

Mann resolved to bring the issue before the public by organizing a conference in Washington, DC, in November of 1991. "Hundreds of millions of tax dollars are wasted by the bureaucracy and the self-interested Heart Association," he wrote in his invitation to participants. "Segments of the food industry play the game for profits. Research on the true causes and prevention is stifled by denying funding to the 'unbelievers'. This meeting will review the data and expose the rascals."

The rascals did their best to prevent the meeting from taking place. Funding promised by the Greenwall Foundation of New York City was later withdrawn, so Mann paid most of the bills. A press release, sent as a dirty trick to speakers and participants, wrongly announced that the conference had been cancelled. Several speakers, including the prestigious Dr Roslyn Alfin-Slater and Dr Peter Nixon of London, did in fact renege at the last minute on their commitment to attend. Dr Eliot Corday of Los Angeles cancelled after being told that his attendance would jeopardize future funding.

The final pared-down roster included: Dr George Mann; Dr Mary Enig; Dr Victor Herbert; Dr Petr Skrabenek; Dr James McCormick, a physician from Dublin; Dr William Stehbens from New Zealand, who described the normal protective process of arterial thickening at points of greatest stress and pressure; and Dr Meyer Texon, an expert in the dynamics of blood flow.

Mann, in his presentation, blasted the system that had foisted the diet/heart-disease dogma on a gullible public. "You will see," he said, "that many of our contributors are senior scientists. They are so for a reason that has become painfully conspicuous as we organized this meeting. Scientists who must go before review panels for their research funding know well that to speak out, to disagree with this false dogma of Diet/Heart, is a fatal error. They must comply or go unfunded. I could show a list of scientists who said to me, in effect, when I invited them to participate, 'I believe you are right, that the Diet/Heart hypothesis is wrong, but I cannot join you because that would jeopardize my perks and funding.' For me, that kind of hypocritical response separates the scientists from the operators, the men from the boys."

By the 1990s the operators had succeeded, by slick manipulation of the press and of scientific research, in transforming America into a nation that was well and truly oiled. Consumption of butter had bottomed out at about 5 grams per person per day, down from almost 18 grams at the turn of the century. Use of lard and tallow had been reduced by two-thirds. Margarine consumption had jumped from less than 2 grams per person per day in 1909 to about 11 grams in 1960. Since then, consumption figures have changed little, remaining at about 11 grams per person per day - perhaps because knowledge of margarine's dangers has been slowly seeping out to the public.

However, most of the trans fats in the current American diet come not from margarine but from shortening used in fried and fabricated foods. American shortening consumption of 10 grams per person per day held steady until the 1960s, although the content of that shortening had changed from mostly lard, tallow and coconut oil - all natural fats - to partially hydrogenated soybean oil. Then shortening consumption shot up and by 1993 had

tripled to over 30 grams per person per day. But the most dramatic overall change in the American diet was the huge increase in the consumption of liquid vegetable oils, from slightly less than 2 grams per person per day in 1909 to over 30 grams in 1993 - a fifteen fold increase.

The irony is that these trends have persisted concurrently with revelations about the dangers of polyunsaturates. Because polyunsaturates are highly subject to rancidity, they increase the body's need for vitamin E and other antioxidants.

Excess consumption of vegetable oils is especially damaging to the reproductive organs and the lungs - both of which are sites for huge increases in cancer in Americans. In test animals, diets high in polyunsaturates from vegetable oils inhibit the ability to learn, especially under conditions of stress; they are toxic to the liver; they compromise the integrity of the immune system; they depress the mental and physical growth of infants; they increase levels of uric acid in the blood; they cause abnormal fatty acid profiles in the adipose tissues; they have been linked to mental decline and chromosomal damage; and they accelerate ageing.

Excess consumption of polyunsaturates is associated with increasing rates of cancer, heart disease and weight gain. The excessive use of commercial vegetable oils interferes with the production of prostaglandins, leading to an array of complaints ranging from autoimmune disease to premenstrual syndrome (PMS). Disruption of prostaglandin production leads to an increased tendency to form blood clots, and hence to myocardial infarction - which has reached epidemic levels in the US.⁴¹

Vegetable oils are more toxic when heated. One study reported that polyunsaturates turn to varnish in the intestines. A study by a plastic surgeon found that women who consumed mostly vegetable oils had far more wrinkles than those who used traditional animal fats. A 1994 study published in the Lancet showed that almost three-quarters of the fat in artery clogs is unsaturated. The 'artery-clogging' fats are not animal fats but vegetable oils.⁴²

Those who have most actively promoted the use of polyunsaturated vegetable oils as part of a Prudent Diet are well aware of their dangers. In 1971, William B. Kannel, former Director of the Framingham Study, warned against including too many polyunsaturates in the diet. A year earlier, Dr William Connor of the American Heart Association issued a similar warning, and Frederick Stare reviewed an article which reported that the use of polyunsaturated oils caused an increase in breast tumours. and Kritchevsky, way back in 1969, discovered that the use of corn oil caused an increase in atherosclerosis.⁴³

As for the trans fats produced in vegetable oils when they are partially hydrogenated, the results that are now in the literature more than justify the concerns of early investigators about the relation between trans fats and both heart disease and cancer.

The research group at the University of Maryland found that trans fatty acids not only alter enzymes that neutralize carcinogens and increase enzymes that potentiate carcinogens, but in nursing mothers they also depress milk-fat production and decrease insulin binding.⁴⁴ In other words, trans fatty acids in the diets of new mothers interfere with their ability to nurse successfully and increase their likelihood of developing diabetes.

Unpublished work indicates that trans fats contribute to osteoporosis. Hanis, a Czechoslovakian researcher, found that trans consumption decreased testosterone, caused the production of abnormal sperm and altered gestation.⁴⁵ Koletzko, a German paediatrics researcher, found that excess trans consumption in pregnant women predisposed them to having low-birth-weight babies.⁴⁶ Trans consumption interferes with the body's use of omega-3 fatty acids (found in fish oils, grains and green vegetables), leading to impaired prostaglandin production.⁴⁷ George Mann confirmed that trans consumption increases the incidence of heart disease.⁴⁸ In 1995, European researchers found a positive correlation between breast cancer rates and trans consumption.⁴⁹

Until the 1993 studies, only the disturbing revelations of Dutch researchers Mensink and Katan in 1990 received front-page coverage. Mensink and Katan found that margarine consumption increased coronary heart disease risk factors.⁵⁰ The industry - and the press - responded by promoting tub spreads which contain reduced amounts of trans compared to stick margarine.

For the general population, these trans reductions have been more than offset by changes in the types of fat used by the fast-food industry. In the early 1980s, the Center for Science in the Public Interest campaigned against the use of beef tallow for frying potatoes. Before that, it campaigned against the use of tallow for frying chicken and fish. Most fast-food concerns switched to partially hydrogenated soybean oil for all fried foods. Some deep-fried foods have been tested at almost 50 per cent trans.⁵¹

Epidemiologist Walter Willett at Harvard worked for many years with flawed databases which did not identify trans fats as a dietary component. He found a correlation with dietary fat consumption and both heart disease and cancer. After his researchers contacted Enig about the trans data, they developed a more valid database that was used in the analysis of the massive Nurses Study. When Willett's group separated out the trans component in their analyses, they were able to confirm greater rates of cancer in those consuming margarine and vegetable shortenings - not butter, eggs, cheese and meat.⁵² The correlation between trans-fat consumption and cancer was never published, but was reported at the Baltimore Data Bank Conference in 1992.

In 1993, Willett's research group at Harvard found that trans contributed to heart disease.⁵³ This study was not ignored but in fact received much fanfare in the press. Willett's first reference in his report was Enig's work on the trans content of common foods.

The industry continues to argue that American trans consumption is a low 6 to 8 grams per person per day - not enough to contribute to today's epidemic of chronic disease. Total per-capita consumption of margarine and shortening hovers around 40 grams per person per day. If these products contain 30 per cent trans (many shortenings contain more), then average consumption is about 12 grams per person per day.

In reality, consumption figures can be dramatically higher for some individuals. A 1989 Washington Post article documented the diet of a teenage girl who ate 12 doughnuts and 24 cookies over a three-day period; her total trans intake worked out to at least 30 grams per day, and possibly much more. The fat in the chips that teenagers consume in abundance may contain up to 48 per cent trans, which translates into 45.6 grams of trans fat in a small, 10-ounce (284-gram) bag of snack chips which a hungry teenager can gobble up in a few minutes. High school sex education classes do not teach American teenagers that the altered fats in their snack foods may severely compromise their ability to have normal sex, to conceive, to give birth to healthy babies and successfully nurse their infants.

Foods containing trans-fat sell because the American public is afraid of the alternative: saturated fats found in tallow, lard, butter, palm oil and coconut oil - fats traditionally used for frying and baking. Yet the scientific literature delineates a number of vital roles for dietary saturated fats: they enhance the immune system,⁵⁴ are necessary for healthy bones,⁵⁵ provide energy and structural integrity to the cells,⁵⁶ protect the liver,⁵⁷ and enhance the body's use of essential fatty acids.⁵⁸ Stearic acid, found in beef tallow and butter, has cholesterol-lowering properties and is a preferred food for the heart.⁵⁹ As saturated fats are stable, they do not become rancid easily, they do not call upon the body's reserves of antioxidants, they do not initiate cancer, and they do not irritate the artery walls.

Your body makes saturated fats, and your body makes cholesterol - about 2,000 mg per day. In general, cholesterol that the average American absorbs from food amounts to about 100 mg per day. So, in theory, even reducing animal foods to zero will result in only a five per cent decrease in the total amount of cholesterol available to the blood and tissues. In practice, such a diet is likely to deprive the body of the substrates it needs to manufacture enough of this vital substance.

Cholesterol, like saturated fats, stands unfairly accused. It acts as a precursor to vital corticosteroids (hormones that help us deal with stress and protect the body against heart disease and cancer) and to the sex hormones like androgen, testosterone, oestrogen and progesterone. It is a precursor to vitamin D, a very important fat-soluble vitamin needed for healthy bones and nervous system, proper growth, mineral metabolism, muscle tone, insulin production, reproduction and immune system function. and it is the precursor to bile salts which are vital for digestion and assimilation of fats in the diet.

Recent research shows that cholesterol acts as an antioxidant.⁶⁰ This is the likely explanation for the fact that cholesterol levels go up with age. As an antioxidant, cholesterol protects us against free-radical damage that leads to heart disease and cancer. Cholesterol is the body's repair substance, manufactured in large amounts

when the arteries are irritated or weak. Blaming heart disease on high serum cholesterol levels is like blaming firemen, who have come to put out a fire, for starting the blaze.

Cholesterol is needed for proper function of serotonin receptors in the brain.⁶¹ Serotonin is the body's natural 'feel-good' chemical. This explains why low cholesterol levels have been linked to aggressive and violent behaviour, depression and suicidal tendencies. Mother's milk is particularly rich in cholesterol and contains a special enzyme that helps the baby utilise this nutrient. Babies and children need cholesterol-rich foods throughout their growing years to ensure proper development of the brain and nervous system. Dietary cholesterol plays an important role in maintaining the health of the intestinal wall,⁶² which is why low-cholesterol vegetarian diets can lead to leaky gut syndrome and other intestinal disorders.

Animal foods containing saturated fat and cholesterol provide vital nutrients necessary for growth, energy and protection from degenerative disease. Like sex, animal fats are necessary for reproduction. Humans are drawn to both by powerful instincts. Suppression of natural appetites leads to weird nocturnal habits, fantasies, fetishes, bingeing and splurging. Animal fats are nutritious and satisfying and they taste good.

"Whatever is the cause of heart disease," said the eminent biochemist Michael Gurr in a recent article, "it is not primarily the consumption of saturated fats."⁶³ and yet the high priests of the lipid hypothesis continue to lay their curse on the fairest of culinary pleasures: butter and Béarnaise, whipped cream, soufflés and omelets, full-bodied cheeses, juicy steaks and pork sausages.

On April 30, 1996, senior researcher David Kritchevsky received the American Oil Chemists' Society's Research Award in recognition of his accomplishments as a "researcher on cancer and atherosclerosis as well as cholesterol metabolism". His accomplishments include co-authorship of more than 370 research papers, one of which appeared a month later in the American Journal of Clinical Nutrition.⁶⁴ "Position Paper on Trans Fatty Acids" continued the debate on trans fats that began in the same journal with Hunter and Applewhite's 1986 attack on Enig's research. "A controversy has arisen about the potential health hazards of trans unsaturated fatty acids in the American diet," wrote Kritchevsky and his co-authors.

Actually, the controversy dates back to 1954. In the rabbit studies that launched Kritchevsky on his career, the researcher actually found that cholesterol fed with Wesson oil "markedly accelerated" the development of cholesterol-containing low-density lipoproteins; and cholesterol fed with shortening gave cholesterol levels twice as high as cholesterol fed alone.⁶⁵ Enig's work - and that of Kummerow and Mann and several others - merely confirmed what Kritchevsky ascertained decades ago but declined to publicize: that vegetable oils, and particularly partially hydrogenated vegetable oils, are bad news.

However, "Position Paper on Trans Fatty Acids" took no position at all. Studies have given contradictory results, said the authors, and the amount of trans in the average American diet is very difficult to determine. As for labeling, the authors said: "There is no clear choice of how to include trans fatty acids on the nutrition label. The database is insufficient to establish a classification scheme for these fats." There may be problems with trans, says the senior researcher, but their use "...helps to reduce the intake of dietary fats higher in saturated fatty acids. Also, vegetable fats are not a source of dietary cholesterol, unlike saturated animal fats."

Kritchevsky and his co-authors concluded that physicians and nutritionists should "...focus on a further decrease in total fat intake and especially the intake of saturated fat... A reduction in total fat intake simplifies the problem, because all fats in the diet decrease and choices are unnecessary." However, even senior scientists find that fence-straddling is necessary. "We may conclude," wrote Kritchevsky and his colleagues, "that consumption of liquid vegetable oils is preferable to solid fats."

As a footnote, early in 1998 a symposium entitled "Evolution of Ideas about the Nutritional Value of Dietary Fat" reviewed the many flaws in the lipid hypothesis and highlighted a study in which mice fed on purified diets died within 20 days, but mice fed on whole milk stayed alive for several months.⁶⁶ One of the symposium participants was David Kritchevsky. He noted that the use of low-fat diets and drugs in intervention trials "did not affect overall CHD mortality". Ever with a finger in the wind, this influential founding father of the lipid hypothesis concluded thus: "Research continues apace and, as new findings appear, it may be necessary to re-evaluate our conclusions and preventive medicine policies."

Endnotes:

19. "New Focus on Trans Fatty Acids," *Food Processing*, December 1982, pp. 64-66
20. Hunter, E. J., "More on Those Trans Fatty Acids", *Food Processing*, May 1983, pp. 35-36
21. Ratnayake, W. M. N. et al., "Fatty Acids in Some Common Food Items in Canada", *J. Am. Coll. Nutr.* 12(6):651-660, 1993
22. Enig, M. G. et al., "Fatty Acid Composition of the Fat in Selected Food Items with Emphasis on Trans Components", *J. Am. Oil Chem. Soc.* 60(10):1788-1795, 1983
23. Hunter, J. E., Letter to the Editor, *Science* 224:659, 1984
24. Elson, C. E. et al., "The Influence of Dietary Unsaturated Cis and Trans and Saturated Fatty Acids on Tissue Lipids of Swine", *Atherosclerosis* 40:115-137, 1981
25. Senti, F. R. (ed.), *Health Aspects of Dietary Trans Fatty Acids*, Life Sciences Research Office (LSRO)/Fed. Am. Soc. Exp. Biol. (FASEB), Bethesda, MD, USA, 1985
26. Hunter, J. E. and T. Applewhite, "Isomeric Fatty Acids in the US Diet: Levels and Health Perspectives", *Am. J. Clin. Nutr.* 44:707-717, 1986
27. Ace Federal Reporter, Inc., *Stenotype Reporters*, 444 North Capitol Street, Suite 402, Washington, DC 20001, USA, tel (202) 347 3700
28. *Food Chemical News* 29(47):52, January 25, 1988;
Nutrition Week, Community Nutrition Institute (CNI), June 16, 1988, p. 6
29. Smith, R. and E. R. Pinckney, *Diet, Blood Cholesterol and Coronary Heart Disease: A Critical Review of the Literature*, Vector Enterprises, Sherman Oaks, CA, USA, 1991, vol. 2
30. Castelli, William, "Concerning the Possibility of a Nut...", *Archives of Internal Medicine* 152(7):1371-1372, July 1992
31. "Multiple Risk Factor Intervention Trial: Risk Factor Changes and Mortality Results", *JAMA* 248(12):1465, September 24, 1982
32. Mattson, F. H. et al., "Effect of Dietary Cholesterol on Serum Cholesterol in Men", *Am. J. Clin. Nutr.* 25:589, 1972
33. Addis, P., *Food and Nutrition News* 62(2):7-10, March/April 1990
34. "The Lipid Research Clinics Coronary Primary Prevention Trial Results: I. Reduction in Incidence of Coronary Heart Disease", *JAMA* 251:359, 1984
35. Grundy, S. M., "Cholesterol and Coronary Heart Disease: A New Era", *JAMA* 256(20):2849-2858, November 28, 1986
36. Letters to the Editor and Authors' Responses, *J. Am. Coll. Nutr.* 10(5):510-521, 1991
37. Hunter, E. J. and T. H. Applewhite, "Reassessment of Trans Fatty Acid Availability in the US Diet", *Am. J. Clin. Nutr.* 54:363-369, 1991
38. Kummerow, F. A., "Nutritional Effects of Isomeric Fats: Their Possible Influence on Cell Metabolism or Cell Structure", *Dietary Fats and Health* (E. G. Perkins and W. J. Visek, eds), The American Oil Chemists' Society, Champaign, IL, USA, 1983, pp. 391-402;
Kummerow, F. A., "Nutritional Aspects of Isomeric Fats", *Lipids in Modern Nutrition* (M. Horisberger and U. Bracco, eds), Nestlé Nutrition, Vevey/Raven Press, New York, 1987
39. Mann, G. V. et al., "Atherosclerosis in the Maasai", *Am. J. Epidemiol.* 95:6-37, 1972
40. Mann, George V. (ed.), *Coronary Heart Disease: The Dietary Sense and Nonsense*, Veritas Society, London, UK, 1993, p. 1
41. A general review of citations for problems with polyunsaturate consumption is found in E. R. Pinckney and C. Pinckney, *The Cholesterol Controversy*, Sherbourne Press, Los Angeles, CA, USA, 1973, pp. 127-131
42. Felton, C. V. et al., "Dietary Polyunsaturated Fatty Acids and Composition of Human Aortic Plaques", *Lancet* 344:1195, 1994
43. Kritchevsky, D., *Medical Counterpoint*, March 1969
44. Teter, B. B. et al., "Milk Fat Depression in C57B1/6J Mice Consuming Partially Hydrogenated Fat", *Journal of Nutrition* 120:818-824, 1990;
Barnard et al., "Dietary Trans Fatty Acids Modulate Erythrocyte Membrane Fatty Acid Composition and Insulin Binding in Monkeys", *J. of Nutritional Biochemistry* 1:190-195, 1990
45. Hanis, T. et al., "Effects of Dietary Trans Fatty Acids on Reproductive Performance of Wistar Rats", *British Journal of Nutrition* 61:519-529, 1989
46. Koletzko, B. and J. Muller, "Cis- and Trans- Isomeric Fatty Acids in Plasma Lipids of Newborn Infants and Their Mothers", *Biology of the Neonate* 57:172-178, 1990
47. Horrobin, D., "The Regulation of Prostaglandin Biosynthesis by Manipulation of Essential Fatty Acid Metabolism", *Reviews in Pure and Applied Pharmacological Sciences* 4:339-383, 1983
48. Mann, G. V., "Metabolic Consequences of Dietary Trans Fatty Acids", *Lancet* 343:1268-1271, 1994
49. Kohlmeier, L. et al., "Stores of Trans Fatty Acids and Breast Cancer Risk", *Am. J. Clin. Nutr.* 61:896, A25, 1995
50. Mensink, R. P. and M. Katan, "Effect of Dietary Trans Fatty Acids on High-Density and Low-Density Lipoprotein Cholesterol Levels in Healthy Subjects", *N. Eng. J. Med.* 323:439-445, 1990
51. Enig, M. G. et al., "Isomeric Trans Fatty Acids in the US Diet", *J. Am. Coll. Nutr.* 9:471-486, 1990
52. Willett, W. C. et al., "Consumption of Trans-Fatty Acids in Relation to Risk of Coronary Heart Disease Among Women", *Society for Epidemiology Research, Annual Meeting*, June 1992, Abstract 249
53. Willett, W. C. et al., "Intake of Trans Fatty Acids and Risk of Coronary Heart Disease Among Women", *Lancet* 341:581-585, 1993
54. Kabara, J. J., *The Pharmacological Effects of Lipids* (J. J. Kabara, ed.), The American Oil Chemists' Society (AOCS), Champaign, IL, USA, 1978, pp. 1-14;
Cohen, L. A. et al., *J. Natl Cancer Inst.* 77:43, 1986
55. Watkins, B. A. et al., "Importance of Vitamin E in Bone Formation and in Chondrocyte Function", *AOCS Proceedings*, Purdue University, Lafayette, IN, USA, 1996;

- Watkins, B. A. and M. F. Seifert, "Food Lipids and Bone Health", Food Lipids and Health (R. E. McDonald and D. B. Min, eds), Marcel Dekker, Inc., New York, NY, p. 101
56. Mead, J. F. et al., Lipids: Chemistry, Biochemistry and Nutrition, Plenum Press, New York, 1986
57. Nanji, A. A. et al., Gastroenterology 109(2):547-54, August 1995;
- Cha, Y. S. and D. S. Sachan, J. Am. Coll. Nutr. 13(4):338-43, August 1994
58. Garg, M. L. et al., The FASEB Journal 2(4), A852, 1988;
- Oliart Ros, R. M. et al., "Meeting Abstracts", AOCS Proceedings, Chicago, IL, USA, May 1998, p. 7
59. Lawson, L. D. and F. Kummerow, "B-Oxidation of the Coenzyme A Esters of Vaccenic, Elaidic and Petroselaiddic Acids by Rat Heart Mitochondria", Lipids 14:501-503, 1979
60. Cranton, E. M. and J. P. Frackelton, "Free Radical Pathology in Age-Associated Diseases: Treatment with EDTA Chelation, Nutrition and Antioxidants", Journal of Holistic Medicine, Spring/Summer 1984, pp. 6-37
61. Engelberg, H., "Low Serum Cholesterol and Suicide", Lancet 339:727-728, March 21, 1992
62. Alfin-Slater, R. B. and L. Aftergood, "Lipids", Modern Nutrition in Health and Disease (R. S. Goodhart and M. E. Shils, eds), Lea & Febiger, Philadelphia, USA, 1980, 6th ed., p. 134
63. Gurr, M., "A Fresh Look at Dietary Recommendations", Inform 7(4):432-435, April 1996
64. AIN/ASCN Task Force on Trans Fatty Acids, "Position Paper on Trans Fatty Acids", Am. J. Clin. Nutr. 63:663-670, 1996
65. Lemmon, R. M., D. Kritchevsky et al., "The Effect of Delta-7-Cholesterol Feeding on the Cholesterol and Lipoproteins of Rabbit Serum", Archives of Biochemistry & Biophysics (NY) 51(1):1161-9, July 1954;
- Kritchevsky, D. et al., "Effect of Cholesterol Vehicle in Experimental Atherosclerosis", Am. J. Physiol. 178:30-32, July-September 1954
66. Olson, R. E., "Evolution of Ideas about the Nutritional Value of Dietary Fat: Introduction", J. Nutr. 128:421S-425S, 1998

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SOY-SCIENTIFIC DEBATE

From Tofu and Tacos To Burgers and Baby Formula

By *Brian Ross* and Richard D. Allyn

Soy products have swept the nation as a healthy source of high protein, with a reputation for being all natural and all good. But a 20/20 investigation has found that amid all of this praise, some scientists are now challenging this popular wisdom, and suggesting there may be a downside to this "miracle food." "The safety issues are largely unanswered," says Daniel Doerge, a research scientist for the Food and Drug Administration and an expert on soy. New studies have raised questions over whether the natural ingredients in soy might increase the risk of breast cancer in some women, affect brain function in men and lead to hidden developmental abnormalities in infants.

This unresolved scientific debate continues to develop. Just last October, soy enjoyed a huge boost when the FDA issued a health claim, concluding that soy may lower both cholesterol levels and the risk of heart disease. But two of the FDA's experts on soy — Doerge and his colleague, Daniel Sheehan — have stepped forward to criticize their own agency's claim and even attempted in vain to stop the recommendation. Their main concern: that the claim could be misinterpreted as a much broader endorsement for soy protein, beyond benefits solely for the heart. Signing a highly unusual letter of protest to their employer, Doerge and Sheehan pointed to research that demonstrates a link between soy and fertility problems in certain animals. (You can find a copy of the letter in the related stories section on the right-hand column.)

"The animal data is a clear indication for adverse effects, the potential for adverse effects in humans," Doerge says to 20/20.

Debate Over Soy Infant Formula

The core of their concern rests with the chemical make-up of soy: in addition to all the nutrients and protein, exists a natural chemical that mimics estrogen, the female hormone. Some studies in animals show that this chemical can alter sexual development. and in fact, two glasses of soy milk a day, over the course of a month, contains enough of the chemical to change the timing of a woman's menstrual cycle.

"We are doing a large uncontrolled and unmonitored experiment on human infants," Sheehan says. "We're exposing infants to the chemicals in soy infant formula that are known to have adverse effects in experimental animals, and we have never looked in the human population to see if they have adverse effects." The infant formula industry, along with some scientists, have blasted this criticism of soy, calling it "scientifically unjustified claims that could unduly frighten thousands of parents."

Kenneth Setchell, a pediatrics professor at Children's Hospital in Cincinnati and a leading advocate of soy, contends that scientific studies on soy show promise in fighting a number of diseases and that adverse effects seen in animals do not apply to humans.

"There have been literally hundreds of thousands of infants that have been raised on those soy formulas," Setchell says to 20/20. "Some of those infants would be well into their late 30s, early 40s now. and you know, I don't see evidence of tremendous numbers of cases where there are abnormalities."

The debate over soy formula for infants poses a major issue throughout the country. Soy infant formula is an undeniable lifesaver for the 3 to 4 percent of babies who are allergic to or can not digest cow's milk. However, heavy marketing of soy infant formula has led to its much wider use, extending well beyond just those infants who are allergic to 25 percent of the entire formula market.

"My careful and considered professional opinion is that it makes more sense not to needlessly expose your baby to these compounds," says Dr. Claude Hughes, director of the Women's Health Center at Cedars-Sinai Medical Center in Los Angeles. He adds that while breast-feeding is preferred, mothers who don't breast-feed should use a milk-based formula and choose soy as a last resort.

Other Health Concerns

Aside from his concerns about soy's health effects on infants, Hughes has also raised potentially more serious questions about soy and breast cancer. In some cases, soy is thought to protect against breast cancer. But some studies now indicate, for other women, the chemicals found in soy may enhance a widely found kind of estrogen-feeding breast cancer.

"It can speed up divisions of those cells that are already cancer cells that depend on estrogen for their growth," Hughes tells 20/20.

The multibillion dollar soy industry has insisted that the health benefits of soy significantly outweigh any potential risk.

Soy — consumed in the form of tofu — may have a connection to accelerated aging in the brain, according to a three decade-long study begun by the National Institutes of Health. Dr. Lon White of NIH says that he found

greater brain aging and shrinkage among elderly men — all Japanese-American and living in Hawaii — who had eaten tofu at least twice a week during middle age.

“Their brains, looking at them in terms of how their brain functions, memory cognition, their brains seemed to be showing an exaggeration of the usual patterns we see in aging,” White says.

The soy industry countered that White’s study only shows an association between tofu consumption and brain aging, does not prove cause and effect and is in conflict with research on Asian populations and animals.

While the scientific research on soy is still emerging and is often contradictory, there are now some serious questions being raised about this miracle food, and some of its staunchest defenders acknowledge that these questions need to be answered.

Tragedy and Hype- The Third International Soy Symposium

Far from being the perfect food, modern soy products contain anti-nutrients and toxins and they interfere with the absorption of vitamins and minerals.

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Each year, research on the health effects of soy and soybean components seems to increase exponentially. Furthermore, research is not just expanding in the primary areas under investigation, such as cancer, heart disease and osteoporosis; new findings suggest that soy has potential benefits that may be more extensive than previously thought.

So writes Mark Messina, PhD, General Chairperson of the Third International Soy Symposium, held in Washington, DC, in November 1999.¹ For four days, well-funded scientists gathered in Washington made presentations to an admiring press and to their sponsors - United Soybean Board, American Soybean Association, Monsanto, Protein Technologies International, Central Soya, Cargill Foods, Personal Products Company, SoyLife, Whitehall-Robins Healthcare and the soybean councils of Illinois, Indiana, Kentucky, Michigan, Minnesota, Nebraska, Ohio and South Dakota.

The symposium marked the apogee of a decade-long marketing campaign to gain consumer acceptance of tofu, soy milk, soy ice cream, soy cheese, soy sausage and soy derivatives, particularly soy isoflavones like genistein and diadzen, the oestrogen-like compounds found in soybeans. It coincided with a US Food and Drug Administration (FDA) decision, announced on October 25, 1999, to allow a health claim for products "low in saturated fat and cholesterol" that contain 6.25 grams of soy protein per serving. Breakfast cereals, baked goods, convenience food, smoothie mixes and meat substitutes could now be sold with labels touting benefits to cardiovascular health, as long as these products contained one heaping teaspoon of soy protein per 100-gram serving.

MARKETING THE PERFECT FOOD

"Just imagine you could grow the perfect food. This food not only would provide affordable nutrition, but also would be delicious and easy to prepare in a variety of ways. It would be a healthful food, with no saturated fat.

In fact, you would be growing a virtual fountain of youth on your back forty." The author is Dean Houghton, writing for *The Furrow*,² a magazine published in 12 languages by John Deere. "This ideal food would help prevent, and perhaps reverse, some of the world's most dreaded diseases. You could grow this miracle crop in a variety of soils and climates. Its cultivation would build up, not deplete, the land...this miracle food already exists... It's called soy."

Just imagine. Farmers have been imagining - and planting more soy. What was once a minor crop, listed in the 1913 US Department of Agriculture (USDA) handbook not as a food but as an industrial product, now covers 72 million acres of American farmland. Much of this harvest will be used to feed chickens, turkeys, pigs, cows and salmon. Another large fraction will be squeezed to produce oil for margarine, shortenings and salad dressings.

Advances in technology make it possible to produce isolated soy protein from what was once considered a waste product - the defatted, high-protein soy chips - and then transform something that looks and smells terrible into products that can be consumed by human beings. Flavourings, preservatives, sweeteners, emulsifiers and synthetic nutrients have turned soy protein isolate, the food processors' ugly duckling, into a New Age Cinderella.

The new fairy-tale food has been marketed not so much for her beauty but for her virtues. Early on, products based on soy protein isolate were sold as extenders and meat substitutes - a strategy that failed to produce the requisite consumer demand. The industry changed its approach. "The quickest way to gain product acceptability in the less affluent society," said an industry spokesman, "is to have the product consumed on its own merit in a more affluent society."³ So soy is now sold to the upscale consumer, not as a cheap, poverty food but as a miracle substance that will prevent heart disease and cancer, whisk away hot flushes, build strong bones and keep us forever young. The competition - meat, milk, cheese, butter and eggs - has been duly demonised by the appropriate government bodies. Soy serves as meat and milk for a new generation of virtuous vegetarians.

Marketing costs money, especially when it needs to be bolstered with "research", but there's plenty of funds available. All soybean producers pay a mandatory assessment of one-half to one per cent of the net market price of soybeans. The total - something like US\$80 million annually⁴ - supports United Soybean's program to "strengthen the position of soybeans in the marketplace and maintain and expand domestic and foreign markets for uses for soybeans and soybean products". State soybean councils from Maryland, Nebraska, Delaware, Arkansas, Virginia, North Dakota and Michigan provide another \$2.5 million for "research".⁵ Private companies like Archer Daniels Midland also contribute their share. ADM spent \$4.7 million for advertising on *Meet the Press* and \$4.3 million on *Face the Nation* during the course of a year.⁶ Public relations firms help convert research projects into newspaper articles and advertising copy, and law firms lobby for favourable government regulations. IMF money funds soy processing plants in foreign countries, and free trade policies keep soybean abundance flowing to overseas destinations.

The push for more soy has been relentless and global in its reach. Soy protein is now found in most supermarket breads. It is being used to transform "the humble tortilla, Mexico's corn-based staple food, into a protein-fortified 'super-tortilla' that would give a nutritional boost to the nearly 20 million Mexicans who live in extreme poverty".⁷ Advertising for a new soy-enriched loaf from Allied Bakeries in Britain targets menopausal women seeking relief from hot flushes. Sales are running at a quarter of a million loaves per week.⁸

The soy industry hired Norman Robert Associates, a public relations firm, to "get more soy products onto school menus".⁹ The USDA responded with a proposal to scrap the 30 per cent limit for soy in school lunches. The NuMenu program would allow unlimited use of soy in student meals. With soy added to hamburgers, tacos and lasagna, dieticians can get the total fat content below 30 per cent of calories, thereby conforming to government dictates. "With the soy-enhanced food items, students are receiving better servings of nutrients and less cholesterol and fat."

Soy milk has posted the biggest gains, soaring from \$2 million in 1980 to \$300 million in the US last year.¹⁰ Recent advances in processing have transformed the grey, thin, bitter, beany-tasting Asian beverage into a product that Western consumers will accept - one that tastes like a milkshake, but without the guilt.

Processing miracles, good packaging, massive advertising and a marketing strategy that stresses the products' possible health benefits account for increasing sales to all age groups. For example, reports that soy helps

prevent prostate cancer have made soy milk acceptable to middle-aged men. "You don't have to twist the arm of a 55- to 60-year-old guy to get him to try soy milk," says Mark Messina. Michael Milken, former junk bond financier, has helped the industry shed its hippie image with well-publicized efforts to consume 40 grams of soy protein daily.

America today, tomorrow the world. Soy milk sales are rising in Canada, even though soy milk there costs twice as much as cow's milk. Soybean milk processing plants are sprouting up in places like Kenya.¹¹ Even China, where soy really is a poverty food and whose people want more meat, not tofu, has opted to build Western-style soy factories rather than develop western grasslands for grazing animals.¹²

CINDERELLA'S DARK SIDE

The propaganda that has created the soy sales miracle is all the more remarkable because, only a few decades ago, the soybean was considered unfit to eat - even in Asia. During the Chou Dynasty (1134&endash;246 BC) the soybean was designated one of the five sacred grains, along with barley, wheat, millet and rice. However, the pictograph for the soybean, which dates from earlier times, indicates that it was not first used as a food; for whereas the pictographs for the other four grains show the seed and stem structure of the plant, the pictograph for the soybean emphasizes the root structure. Agricultural literature of the period speaks frequently of the soybean and its use in crop rotation. Apparently the soy plant was initially used as a method of fixing nitrogen.¹³

The soybean did not serve as a food until the discovery of fermentation techniques, some time during the Chou Dynasty. The first soy foods were fermented products like tempeh, natto, miso and soy sauce. At a later date, possibly in the 2nd century BC, Chinese scientists discovered that a purée of cooked soybeans could be precipitated with calcium sulphate or magnesium sulphate (plaster of Paris or Epsom salts) to make a smooth, pale curd - tofu or bean curd. The use of fermented and precipitated soy products soon spread to other parts of the orient, notably Japan and Indonesia.

The Chinese did not eat unfermented soybeans as they did other legumes such as lentils because the soybean contains large quantities of natural toxins or "anti-nutrients". First among them are potent enzyme inhibitors that block the action of trypsin and other enzymes needed for protein digestion. These inhibitors are large, tightly folded proteins that are not completely deactivated during ordinary cooking. They can produce serious gastric distress, reduced protein digestion and chronic deficiencies in amino acid uptake. In test animals, diets high in trypsin inhibitors cause enlargement and pathological conditions of the pancreas, including cancer.¹⁴

Soybeans also contain haemagglutinin, a clot-promoting substance that causes red blood cells to clump together.

Trypsin inhibitors and haemagglutinin are growth inhibitors. Weanling rats fed soy containing these anti-nutrients fail to grow normally. Growth-depressant compounds are deactivated during the process of fermentation, so once the Chinese discovered how to ferment the soybean, they began to incorporate soy foods into their diets. In precipitated products, enzyme inhibitors concentrate in the soaking liquid rather than in the curd. Thus, in tofu and bean curd, growth depressants are reduced in quantity but not completely eliminated.

Soy also contains goitrogens - substances that depress thyroid function.

Soybeans are high in phytic acid, present in the bran or hulls of all seeds. It's a substance that can block the uptake of essential minerals - calcium, magnesium, copper, iron and especially zinc - in the intestinal tract. Although not a household word, phytic acid has been extensively studied; there are literally hundreds of articles on the effects of phytic acid in the current scientific literature. Scientists are in general agreement that grain- and legume-based diets high in phytates contribute to widespread mineral deficiencies in third world countries.¹⁵ Analysis shows that calcium, magnesium, iron and zinc are present in the plant foods eaten in these areas, but the high phytate content of soy- and grain-based diets prevents their absorption.

The soybean has one of the highest phytate levels of any grain or legume that has been studied,¹⁶ and the phytates in soy are highly resistant to normal phytate-reducing techniques such as long, slow cooking.¹⁷ Only a long period of fermentation will significantly reduce the phytate content of soybeans. When precipitated soy products like tofu are consumed with meat, the mineral-blocking effects of the phytates are reduced.¹⁸ The

Japanese traditionally eat a small amount of tofu or miso as part of a mineral-rich fish broth, followed by a serving of meat or fish.

Vegetarians who consume tofu and bean curd as a substitute for meat and dairy products risk severe mineral deficiencies. The results of calcium, magnesium and iron deficiency are well known; those of zinc are less so.

Zinc is called the intelligence mineral because it is needed for optimal development and functioning of the brain and nervous system. It plays a role in protein synthesis and collagen formation; it is involved in the blood-sugar control mechanism and thus protects against diabetes; it is needed for a healthy reproductive system. Zinc is a key component in numerous vital enzymes and plays a role in the immune system. Phytates found in soy products interfere with zinc absorption more completely than with other minerals.¹⁹ Zinc deficiency can cause a "spacey" feeling that some vegetarians may mistake for the "high" of spiritual enlightenment.

Milk drinking is given as the reason why second-generation Japanese in America grow taller than their native ancestors. Some investigators postulate that the reduced phytate content of the American diet - whatever may be its other deficiencies - is the true explanation, pointing out that both Asian and Western children who do not get enough meat and fish products to counteract the effects of a high phytate diet, frequently suffer rickets, stunting and other growth problems.²⁰

SOY PROTEIN ISOLATE: NOT SO FRIENDLY

Soy processors have worked hard to get these anti-nutrients out of the finished product, particularly soy protein isolate (SPI) which is the key ingredient in most soy foods that imitate meat and dairy products, including baby formulas and some brands of soy milk.

SPI is not something you can make in your own kitchen. Production takes place in industrial factories where a slurry of soy beans is first mixed with an alkaline solution to remove fibre, then precipitated and separated using an acid wash and, finally, neutralized in an alkaline solution. Acid washing in aluminum tanks leaches high levels of aluminum into the final product. The resultant curds are spray-dried at high temperatures to produce a high-protein powder. A final indignity to the original soybean is high-temperature, high-pressure extrusion processing of soy protein isolate to produce textured vegetable protein (TVP).

Much of the trypsin inhibitor content can be removed through high-temperature processing, but not all. Trypsin inhibitor content of soy protein isolate can vary as much as fivefold.²¹ (In rats, even low-level trypsin inhibitor SPI feeding results in reduced weight gain compared to controls.²²) But high-temperature processing has the unfortunate side-effect of so denaturing the other proteins in soy that they are rendered largely ineffective.²³ That's why animals on soy feed need lysine supplements for normal growth.

Nitrites, which are potent carcinogens, are formed during spray-drying, and a toxin called lysinoalanine is formed during alkaline processing.²⁴ Numerous artificial flavourings, particularly MSG, are added to soy protein isolate and textured vegetable protein products to mask their strong "beany" taste and to impart the flavour of meat.²⁵

In feeding experiments, the use of SPI increased requirements for vitamins E, K, D and B12 and created deficiency symptoms of calcium, magnesium, manganese, molybdenum, copper, iron and zinc.²⁶ Phytic acid remaining in these soy products greatly inhibits zinc and iron absorption; test animals fed SPI develop enlarged organs, particularly the pancreas and thyroid gland, and increased deposition of fatty acids in the liver.²⁷

Yet soy protein isolate and textured vegetable protein are used extensively in school lunch programs, commercial baked goods, diet beverages and fast food products. They are heavily promoted in third world countries and form the basis of many food giveaway programs.

In spite of poor results in animal feeding trials, the soy industry has sponsored a number of studies designed to show that soy protein products can be used in human diets as a replacement for traditional foods.

An example is "Nutritional Quality of Soy Bean Protein Isolates: Studies in Children of Preschool Age", sponsored by the Ralston Purina Company.²⁸ A group of Central American children suffering from malnutrition

was first stabilized and brought into better health by feeding them native foods, including meat and dairy products. Then, for a two-week period, these traditional foods were replaced by a drink made of soy protein isolate and sugar. All nitrogen taken in and all nitrogen excreted was measured in truly Orwellian fashion: the children were weighed naked every morning, and all excrement and vomit gathered up for analysis. The researchers found that the children retained nitrogen and that their growth was "adequate", so the experiment was declared a success.

Whether the children were actually healthy on such a diet, or could remain so over a long period, is another matter. The researchers noted that the children vomited "occasionally", usually after finishing a meal; that over half suffered from periods of moderate diarrhoea; that some had upper respiratory infections; and that others suffered from rash and fever.

It should be noted that the researchers did not dare to use soy products to help the children recover from malnutrition, and were obliged to supplement the soy-sugar mixture with nutrients largely absent in soy products - notably, vitamins A, D and B12, iron, iodine and zinc.

FDA HEALTH CLAIM CHALLENGED

The best marketing strategy for a product that is inherently unhealthy is, of course, a health claim.

"The road to FDA approval," writes a soy apologist, "was long and demanding, consisting of a detailed review of human clinical data collected from more than 40 scientific studies conducted over the last 20 years. Soy protein was found to be one of the rare foods that had sufficient scientific evidence not only to qualify for an FDA health claim proposal but to ultimately pass the rigorous approval process."²⁹

The "long and demanding" road to FDA approval actually took a few unexpected turns. The original petition, submitted by Protein Technology International, requested a health claim for isoflavones, the oestrogen-like compounds found plentifully in soybeans, based on assertions that "only soy protein that has been processed in a manner in which isoflavones are retained will result in cholesterol lowering". In 1998, the FDA made the unprecedented move of rewriting PTI's petition, removing any reference to the phyto-oestrogens and substituting a claim for soy protein - a move that was in direct contradiction to the agency's regulations. The FDA is authorized to make rulings only on substances presented by petition.

The abrupt change in direction was no doubt due to the fact that a number of researchers, including scientists employed by the US Government, submitted documents indicating that isoflavones are toxic.

The FDA had also received, early in 1998, the final British Government report on phytoestrogens, which failed to find much evidence of benefit and warned against potential adverse effects.³⁰

Even with the change to soy protein isolate, FDA bureaucrats engaged in the "rigorous approval process" were forced to deal nimbly with concerns about mineral blocking effects, enzyme inhibitors, goitrogenicity, endocrine disruption, reproductive problems and increased allergic reactions from consumption of soy products.³¹

One of the strongest letters of protest came from Dr Dan Sheehan and Dr Daniel Doerge, government researchers at the National Center for Toxicological Research.³² Their pleas for warning labels were dismissed as unwarranted.

"Sufficient scientific evidence" of soy's cholesterol-lowering properties is drawn largely from a 1995 meta-analysis by Dr James Anderson, sponsored by Protein Technologies International and published in the New England Journal of Medicine.³³

A meta-analysis is a review and summary of the results of many clinical studies on the same subject. Use of meta-analyses to draw general conclusions has come under sharp criticism by members of the scientific community. "Researchers substituting meta-analysis for more rigorous trials risk making faulty assumptions and indulging in creative accounting," says Sir John Scott, President of the Royal Society of New Zealand. "Like is not being lumped with like. Little lumps and big lumps of data are being gathered together by various groups."³⁴

There is the added temptation for researchers, particularly researchers funded by a company like Protein Technologies International, to leave out studies that would prevent the desired conclusions. Dr Anderson discarded eight studies for various reasons, leaving a remainder of twenty-nine. The published report suggested that individuals with cholesterol levels over 250 mg/dl would experience a "significant" reduction of 7 to 20 per cent in levels of serum cholesterol if they substituted soy protein for animal protein. Cholesterol reduction was insignificant for individuals whose cholesterol was lower than 250 mg/dl.

In other words, for most of us, giving up steak and eating veggieburgers instead will not bring down blood cholesterol levels. The health claim that the FDA approved "after detailed review of human clinical data" fails to inform the consumer about these important details.

Research that ties soy to positive effects on cholesterol levels is "incredibly immature", said Ronald M. Krauss, MD, head of the Molecular Medical Research Program and Lawrence Berkeley National Laboratory.³⁵ He might have added that studies in which cholesterol levels were lowered through either diet or drugs have consistently resulted in a greater number of deaths in the treatment groups than in controls - deaths from stroke, cancer, intestinal disorders, accident and suicide.³⁶ Cholesterol-lowering measures in the US have fuelled a \$60 billion per year cholesterol-lowering industry, but have not saved us from the ravages of heart disease.

SOY and CANCER

The new FDA ruling does not allow any claims about cancer prevention on food packages, but that has not restrained the industry and its marketeers from making them in their promotional literature.

"In addition to protecting the heart," says a vitamin company brochure, "soy has demonstrated powerful anticancer benefits...the Japanese, who eat 30 times as much soy as North Americans, have a lower incidence of cancers of the breast, uterus and prostate."³⁷

Indeed they do. But the Japanese, and Asians in general, have much higher rates of other types of cancer, particularly cancer of the oesophagus, stomach, pancreas and liver.³⁸ Asians throughout the world also have high rates of thyroid cancer.³⁹ The logic that links low rates of reproductive cancers to soy consumption requires attribution of high rates of thyroid and digestive cancers to the same foods, particularly as soy causes these types of cancers in laboratory rats.

Just how much soy do Asians eat? A 1998 survey found that the average daily amount of soy protein consumed in Japan was about eight grams for men and seven for women - less than two teaspoons.⁴⁰ The famous Cornell China Study, conducted by Colin T. Campbell, found that legume consumption in China varied from 0 to 58 grams per day, with a mean of about twelve.⁴¹ Assuming that two-thirds of legume consumption is soy, then the maximum consumption is about 40 grams, or less than three tablespoons per day, with an average consumption of about nine grams, or less than two teaspoons. A survey conducted in the 1930s found that soy foods accounted for only 1.5 per cent of calories in the Chinese diet, compared with 65 per cent of calories from pork.⁴² (Asians traditionally cooked with lard, not vegetable oil!)

Traditionally fermented soy products make a delicious, natural seasoning that may supply important nutritional factors in the Asian diet. But except in times of famine, Asians consume soy products only in small amounts, as condiments, and not as a replacement for animal foods - with one exception. Celibate monks living in monasteries and leading a vegetarian lifestyle find soy foods quite helpful because they dampen libido.

It was a 1994 meta-analysis by Mark Messina, published in *Nutrition and Cancer*, that fuelled speculation on soy's anticarcinogenic properties.⁴³ Messina noted that in 26 animal studies, 65 per cent reported protective effects from soy. He conveniently neglected to include at least one study in which soy feeding caused pancreatic cancer - the 1985 study by Rackis.⁴⁴ In the human studies he listed, the results were mixed. A few showed some protective effect, but most showed no correlation at all between soy consumption and cancer rates. He concluded that "the data in this review cannot be used as a basis for claiming that soy intake decreases cancer risk". Yet in his subsequent book, *The Simple Soybean and Your Health*, Messina makes just such a claim, recommending one cup or 230 grams of soy products per day in his "optimal" diet as a way to prevent cancer.

Thousands of women are now consuming soy in the belief that it protects them against breast cancer. Yet, in 1996, researchers found that women consuming soy protein isolate had an increased incidence of epithelial hyperplasia, a condition that presages malignancies.⁴⁵ A year later, dietary genistein was found to stimulate breast cells to enter the cell cycle - a discovery that led the study authors to conclude that women should not consume soy products to prevent breast cancer.⁴⁶

PHYTOESTROGENS: PANACEA or POISON?

The male species of tropical birds carries the drab plumage of the female at birth and 'colours up' at maturity, somewhere between nine and 24 months.

In 1991, Richard and Valerie James, bird breeders in Whangerai, New Zealand, purchased a new kind of feed for their birds - one based largely on soy protein.⁴⁷ When soy-based feed was used, their birds 'coloured up' after just a few months. In fact, one bird-food manufacturer claimed that this early development was an advantage imparted by the feed. A 1992 ad for Roudybush feed formula showed a picture of the male crimson rosella, an Australian parrot that acquires beautiful red plumage at 18 to 24 months, already brightly coloured at 11 weeks old.

Unfortunately, in the ensuing years, there was decreased fertility in the birds, with precocious maturation, deformed, stunted and stillborn babies, and premature deaths, especially among females, with the result that the total population in the aviaries went into steady decline. The birds suffered beak and bone deformities, goitre, immune system disorders and pathological, aggressive behaviour. Autopsy revealed digestive organs in a state of disintegration. The list of problems corresponded with many of the problems the Jameses had encountered in their two children, who had been fed soy-based infant formula.

Startled, aghast, angry, the Jameses hired toxicologist Mike Fitzpatrick, PhD, to investigate further. Dr Fitzpatrick's literature review uncovered evidence that soy consumption has been linked to numerous disorders, including infertility, increased cancer and infantile leukaemia; and, in studies dating back to the 1950s,⁴⁸ that genistein in soy causes endocrine disruption in animals. Dr Fitzpatrick also analyzed the bird feed and found that it contained high levels of phytoestrogens, especially genistein. When the Jameses discontinued using soy-based feed, the flock gradually returned to normal breeding habits and behaviour.

The Jameses embarked on a private crusade to warn the public and government officials about toxins in soy foods, particularly the endocrine-disrupting isoflavones, genistein and diadzen. Protein Technology International received their material in 1994.

In 1991, Japanese researchers reported that consumption of as little as 30 grams or two tablespoons of soybeans per day for only one month resulted in a significant increase in thyroid-stimulating hormone.⁴⁹ Diffuse goitre and hypothyroidism appeared in some of the subjects and many complained of constipation, fatigue and lethargy, even though their intake of iodine was adequate. In 1997, researchers from the FDA's National Center for Toxicological Research made the embarrassing discovery that the goitrogenic components of soy were the very same isoflavones.⁵⁰

Twenty-five grams of soy protein isolate, the minimum amount PTI claimed to have cholesterol-lowering effects, contains from 50 to 70 mg of isoflavones. It took only 45 mg of isoflavones in premenopausal women to exert significant biological effects, including a reduction in hormones needed for adequate thyroid function. These effects lingered for three months after soy consumption was discontinued.⁵¹

One hundred grams of soy protein - the maximum suggested cholesterol-lowering dose, and the amount recommended by Protein Technologies International - can contain almost 600 mg of isoflavones,⁵² an amount that is undeniably toxic. In 1992, the Swiss health service estimated that 100 grams of soy protein provided the oestrogenic equivalent of the Pill.⁵³

In vitro studies suggest that isoflavones inhibit synthesis of oestradiol and other steroid hormones.⁵⁴ Reproductive problems, infertility, thyroid disease and liver disease due to dietary intake of isoflavones have been observed for several species of animals including mice, cheetah, quail, pigs, rats, sturgeon and sheep.⁵⁵

It is the isoflavones in soy that are said to have a favourable effect on postmenopausal symptoms, including hot flushes, and protection from osteoporosis. Quantification of discomfort from hot flushes is extremely subjective, and most studies show that control subjects report reduction in discomfort in amounts equal to subjects given soy.⁵⁶ The claim that soy prevents osteoporosis is extraordinary, given that soy foods block calcium and cause vitamin D deficiencies. If Asians indeed have lower rates of osteoporosis than Westerners, it is because their diet provides plenty of vitamin D from shrimp, lard and seafood, and plenty of calcium from bone broths. The reason that Westerners have such high rates of osteoporosis is because they have substituted soy oil for butter, which is a traditional source of vitamin D and other fat-soluble activators needed for calcium absorption.

BIRTH CONTROL PILLS FOR BABIES

But it was the isoflavones in infant formula that gave the Jameses the most cause for concern. In 1998, investigators reported that the daily exposure of infants to isoflavones in soy infant formula is 6 to 11 times higher on a body-weight basis than the dose that has hormonal effects in adults consuming soy foods. Circulating concentrations of isoflavones in infants fed soy-based formula were 13,000 to 22,000 times higher than plasma oestradiol concentrations in infants on cow's milk formula.⁵⁷

Approximately 25 per cent of bottle-fed children in the US receive soy-based formula - a much higher percentage than in other parts of the Western world. Fitzpatrick estimated that an infant exclusively fed soy formula receives the oestrogenic equivalent (based on body weight) of at least five birth control pills per day.⁵⁸ By contrast, almost no phytoestrogens have been detected in dairy-based infant formula or in human milk, even when the mother consumes soy products.

Scientists have known for years that soy-based formula can cause thyroid problems in babies. But what are the effects of soy products on the hormonal development of the infant, both male and female?

Male infants undergo a "testosterone surge" during the first few months of life, when testosterone levels may be as high as those of an adult male. During this period, the infant is programmed to express male characteristics after puberty, not only in the development of his sexual organs and other masculine physical traits, but also in setting patterns in the brain characteristic of male behaviour. In monkeys, deficiency of male hormones impairs the development of spatial perception (which, in humans, is normally more acute in men than in women), of learning ability and of visual discrimination tasks (such as would be required for reading).⁵⁹ It goes without saying that future patterns of sexual orientation may also be influenced by the early hormonal environment. Male children exposed during gestation to diethylstilbestrol (DES), a synthetic oestrogen that has effects on animals similar to those of phytoestrogens from soy, had testes smaller than normal on maturation.⁶⁰

Learning disabilities, especially in male children, have reached epidemic proportions. Soy infant feeding - which began in earnest in the early 1970s - cannot be ignored as a probable cause for these tragic developments.

As for girls, an alarming number are entering puberty much earlier than normal, according to a recent study reported in the journal *Pediatrics*.⁶¹ Investigators found that one per cent of all girls now show signs of puberty, such as breast development or pubic hair, before the age of three; by age eight, 14.7 per cent of white girls and almost 50 per cent of African-American girls have one or both of these characteristics.

New data indicate that environmental oestrogens such as PCBs and DDE (a breakdown product of DDT) may cause early sexual development in girls.⁶² In the 1986 Puerto Rico Premature Thelarche study, the most significant dietary association with premature sexual development was not chicken - as reported in the press - but soy infant formula.⁶³

The consequences of this truncated childhood are tragic. Young girls with mature bodies must cope with feelings and urges that most children are not well-equipped to handle, and early maturation in girls is frequently a harbinger for problems with the reproductive system later in life, including failure to menstruate, infertility and breast cancer.

Parents who have contacted the Jameses recount other problems associated with children of both sexes who were fed soy-based formula, including extreme emotional behaviour, asthma, immune system problems, pituitary insufficiency, thyroid disorders and irritable bowel syndrome - the same endocrine and digestive havoc that afflicted the Jameses' parrots.

DISSENSION IN THE RANKS

Organizers of the Third International Soy Symposium would be hard-pressed to call the conference an unqualified success. On the second day of the symposium, the London-based Food Commission and the Weston A. Price Foundation of Washington, DC, held a joint press conference, in the same hotel as the symposium, to present concerns about soy infant formula. Industry representatives sat stony-faced through the recitation of potential dangers and a plea from concerned scientists and parents to pull soy-based infant formula from the market. Under pressure from the Jameses, the New Zealand Government had issued a health warning about soy infant formula in 1998; it was time for the American government to do the same.

On the last day of the symposium, presentations on new findings related to toxicity sent a well-oxygenated chill through the giddy helium hype. Dr Lon White reported on a study of Japanese Americans living in Hawaii, that showed a significant statistical relationship between two or more servings of tofu a week and "accelerated brain aging".⁶⁴ Those participants who consumed tofu in mid-life had lower cognitive function in late life and a greater incidence of Alzheimer's disease and dementia. "What's more," said Dr White, "those who ate a lot of tofu, by the time they were 75 or 80 looked five years older".⁶⁵ White and his colleagues blamed the negative effects on isoflavones - a finding that supports an earlier study in which postmenopausal women with higher levels of circulating oestrogen experienced greater cognitive decline.⁶⁶

Scientists Daniel Sheehan and Daniel Doerge, from the National Center for Toxicological Research, ruined PTI's day by presenting findings from rat feeding studies, indicating that genistein in soy foods causes irreversible damage to enzymes that synthesize thyroid hormones.⁶⁷ "The association between soybean consumption and goiter in animals and humans has a long history," wrote Dr Doerge. "Current evidence for the beneficial effects of soy requires a full understanding of potential adverse effects as well."

Dr Claude Hughes reported that rats born to mothers that were fed genistein had decreased birth weights compared to controls, and onset of puberty occurred earlier in male offspring.⁶⁸ His research suggested that the effects observed in rats "...will be at least somewhat predictive of what occurs in humans. There is no reason to assume that there will be gross malformations of fetuses but there may be subtle changes, such as neurobehavioral attributes, immune function and sex hormone levels." The results, he said, "could be nothing or could be something of great concern...if mom is eating something that can act like sex hormones, it is logical to wonder if that could change the baby's development".⁶⁹

A study of babies born to vegetarian mothers, published in January 2000, indicated just what those changes in baby's development might be. Mothers who ate a vegetarian diet during pregnancy had a fivefold greater risk of delivering a boy with hypospadias, a birth defect of the penis.⁷⁰ The authors of the study suggested that the cause was greater exposure to phytoestrogens in soy foods popular with vegetarians. Problems with female offspring of vegetarian mothers are more likely to show up later in life. While soy's oestrogenic effect is less than that of diethylstilbestrol (DES), the dose is likely to be higher because it's consumed as a food, not taken as a drug. Daughters of women who took DES during pregnancy suffered from infertility and cancer when they reached their twenties.

QUESTION MARKS OVER GRAS STATUS

Lurking in the background of industry hype for soy is the nagging question of whether it's even legal to add soy protein isolate to food. All food additives not in common use prior to 1958, including casein protein from milk, must have GRAS (Generally Recognized As Safe) status. In 1972, the Nixon administration directed a re-examination of substances believed to be GRAS, in the light of any scientific information then available. This re-examination included casein protein which became codified as GRAS in 1978. In 1974, the FDA obtained a literature review of soy protein because, as soy protein had not been used in food until 1959 and was not even in common use in the early 1970s, it was not eligible to have its GRAS status grandfathered under the provisions of the Food, Drug and Cosmetic Act.⁷¹

The scientific literature up to 1974 recognized many anti-nutrients in factory-made soy protein, including trypsin inhibitors, phytic acid and genistein. But the FDA literature review dismissed discussion of adverse impacts, with the statement that it was important for "adequate processing" to remove them. Genistein could be removed with an alcohol wash, but it was an expensive procedure that processors avoided. Later studies determined that

trypsin inhibitor content could be removed only with long periods of heat and pressure, but the FDA has imposed no requirements for manufacturers to do so.

The FDA was more concerned with toxins formed during processing, specifically nitrites and lysinoalanine.⁷² Even at low levels of consumption - averaging one-third of a gram per day at the time - the presence of these carcinogens was considered too great a threat to public health to allow GRAS status.

Soy protein did have approval for use as a binder in cardboard boxes, and this approval was allowed to continue, as researchers considered that migration of nitrites from the box into the food contents would be too small to constitute a cancer risk. FDA officials called for safety specifications and monitoring procedures before granting of GRAS status for food. These were never performed. To this day, use of soy protein is codified as GRAS only for this limited industrial use as a cardboard binder. This means that soy protein must be subject to premarket approval procedures each time manufacturers intend to use it as a food or add it to a food.

Soy protein was introduced into infant formula in the early 1960s. It was a new product with no history of any use at all. As soy protein did not have GRAS status, premarket approval was required. This was not and still has not been granted. The key ingredient of soy infant formula is not recognized as safe.

THE NEXT ASBESTOS?

"Against the backdrop of widespread praise...there is growing suspicion that soy - despite its undisputed benefits - may pose some health hazards," writes Marian Burros, a leading food writer for the New York Times. More than any other writer, Ms Burros's endorsement of a low-fat, largely vegetarian diet has herded Americans into supermarket aisles featuring soy foods. Yet her January 26, 2000 article, "Doubts Cloud Rosy News on Soy", contains the following alarming statement: "Not one of the 18 scientists interviewed for this column was willing to say that taking isoflavones was risk free." Ms Burros did not enumerate the risks, nor did she mention that the recommended 25 daily grams of soy protein contain enough isoflavones to cause problems in sensitive individuals, but it was evident that the industry had recognized the need to cover itself.

Because the industry is extremely exposed...contingency lawyers will soon discover that the number of potential plaintiffs can be counted in the millions and the pockets are very, very deep. Juries will hear something like the following: "The industry has known for years that soy contains many toxins. At first they told the public that the toxins were removed by processing. When it became apparent that processing could not get rid of them, they claimed that these substances were beneficial. Your government granted a health claim to a substance that is poisonous, and the industry lied to the public to sell more soy."

The "industry" includes merchants, manufacturers, scientists, publicists, bureaucrats, former bond financiers, food writers, vitamin companies and retail stores. Farmers will probably escape because they were duped like the rest of us. But they need to find something else to grow before the soy bubble bursts and the market collapses: grass-fed livestock, designer vegetables ...or hemp to make paper for thousands and thousands of legal briefs.

Endnotes:

1. Program for the Third International Symposium on the Role of Soy in Preventing and Treating Chronic Disease, Sunday, October 31, through Wednesday, November 3, 1999, Omni Shoreham Hotel, Washington, DC.
2. Houghton, Dean, "Healthful Harvest", *The Furrow*, January 2000, pp. 10-13.
3. Coleman, Richard J., "Vegetable Protein - A Delayed Birth?" *Journal of the American Oil Chemists' Society* 52:238A, April 1975.
4. See www.unitedsoybean.org.
5. These are listed in www.soyonlineservice.co.nz.
6. *Wall Street Journal*, October 27, 1995.
7. Smith, James F., "Healthier tortillas could lead to healthier Mexico", *Denver Post*, August 22, 1999, p. 26A.
8. "Bakery says new loaf can help reduce hot flushes", *Reuters*, September 15, 1997.
9. "Beefing Up Burgers with Soy Products at School", *Nutrition Week*, Community Nutrition Institute, Washington, DC, June 5, 1998, p. 2.
10. Urquhart, John, "A Health Food Hits Big Time", *Wall Street Journal*, August 3, 1999, p. B1
11. "Soyabean Milk Plant in Kenya", *Africa News Service*, September 1998.
12. Simoons, Frederick J., *Food in China: A Cultural and Historical Inquiry*, CRC Press, Boca Raton, 1991, p. 64.
13. Katz, Solomon H., "Food and Biocultural Evolution: A Model for the Investigation of Modern Nutritional Problems", *Nutritional Anthropology*, Alan R. Liss Inc., 1987, p. 50.

14. Rackis, Joseph J. et al., "The USDA trypsin inhibitor study. I. Background, objectives and procedural details", *Qualification of Plant Foods in Human Nutrition*, vol. 35, 1985.
15. Van Rensburg et al., "Nutritional status of African populations predisposed to esophageal cancer", *Nutrition and Cancer*, vol. 4, 1983, pp. 206-216; Moser, P.B. et al., "Copper, iron, zinc and selenium dietary intake and status of Nepalese lactating women and their breastfed infants", *American Journal of Clinical Nutrition* 47:729-734, April 1988; Harland, B.F. et al., "Nutritional status and phytate: zinc and phytate X calcium: zinc dietary molar ratios of lacto-ovo-vegetarian Trappist monks: 10 years later", *Journal of the American Dietetic Association* 88:1562-1566, December 1988.
16. El Tiney, A.H., "Proximate Composition and Mineral and Phytate Contents of Legumes Grown in Sudan", *Journal of Food Composition and Analysis* (1989) 2:6778.
17. Ologhobo, A.D. et al., "Distribution of phosphorus and phytate in some Nigerian varieties of legumes and some effects of processing", *Journal of Food Science* 49(1):199-201, January/February 1984.
18. Sandstrom, B. et al., "Effect of protein level and protein source on zinc absorption in humans", *Journal of Nutrition* 119(1):48-53, January 1989; Tait, Susan et al., "The availability of minerals in food, with particular reference to iron", *Journal of Research in Society and Health* 103(2):74-77, April 1983.
19. Phytate reduction of zinc absorption has been demonstrated in numerous studies. These results are summarised in Leviton, Richard, *Tofu, Tempeh, Miso and Other Soyfoods: The 'Food of the Future' - How to Enjoy Its Spectacular Health Benefits*, Keats Publishing, Inc., New Canaan, CT, USA, 1982, p. 1415.
20. Mellanby, Edward, "Experimental rickets: The effect of cereals and their interaction with other factors of diet and environment in producing rickets", *Journal of the Medical Research Council* 93:265, March 1925; Wills, M.R. et al., "Phytic Acid and Nutritional Rickets in Immigrants", *The Lancet*, April 8, 1972, pp. 771-773.
21. Rackis et al., *ibid.*
22. Rackis et al., *ibid.*, p. 232.
23. Wallace, G.M., "Studies on the Processing and Properties of Soymilk", *Journal of Science and Food Agriculture* 22:526-535, October 1971.
24. Rackis, et al., *ibid.*, p. 22; "Evaluation of the Health Aspects of Soy Protein Isolates as Food Ingredients", prepared for FDA by Life Sciences Research Office, Federation of American Societies for Experimental Biology (9650 Rockville Pike, Bethesda, MD 20014), USA, Contract No. FDA 223-75-2004, 1979.
25. See www.truthinlabeling.org.
26. Rackis, Joseph, J., "Biological and Physiological Factors in Soybeans", *Journal of the American Oil Chemists' Society* 51:161A-170A, January 1974.
27. Rackis, Joseph J. et al., "The USDA trypsin inhibitor study", *ibid.*
28. Torum, Benjamin, "Nutritional Quality of Soybean Protein Isolates: Studies in Children of Preschool Age", in *Soy Protein and Human Nutrition*, Harold L Wilcke et al. (eds), Academic Press, New York, 1979.
29. Zreik, Marwin, CCN, "The Great Soy Protein Awakening", *Total Health* 32(1), February 2000.
30. IEH Assessment on Phytoestrogens in the Human Diet, Final Report to the Ministry of Agriculture, Fisheries and Food, UK, November 1997, p. 11.
31. Food Labeling: Health Claims: Soy Protein and Coronary Heart Disease, Food and Drug Administration 21 CFR, Part 101 (Docket No. 98P-0683).
32. Sheegan, Daniel M. and Daniel R Doerge, Letter to Dockets Management Branch (HFA-305), February 18, 1999.
33. Anderson, James W. et al., "Meta-analysis of the Effects of Soy Protein Intake on Serum Lipids", *New England Journal of Medicine* (1995) 333(5):276-282.
34. Guy, Camille, "Doctors warned against magic, quackery", *New Zealand Herald*, September 9, 1995, section 8, p. 5.
35. Sander, Kate and Hilary Wilson, "FDA approves new health claim for soy, but little fallout expected for dairy", *Cheese Market News*, October 22, 1999, p. 24.
36. Enig, Mary G. and Sally Fallon, "The Oiling of America", *NEXUS Magazine*, December 1998-January 1999 and February-March 1999; also available at www.WestonAPrice.org.
37. *Natural Medicine News (L & H Vitamins*, 32-33 47th Avenue, Long Island City, NY 11101), USA, January/February 2000, p. 8.
38. Harras, Angela (ed.), *Cancer Rates and Risks*, National Institutes of Health, National Cancer Institute, 1996, 4th edition.
39. Searle, Charles E. (ed.), *Chemical Carcinogens*, ACS Monograph 173, American Chemical Society, Washington, DC, 1976.
40. Nagata, C. et al., *Journal of Nutrition* (1998) 128:209-213.
41. Campbell, Colin T. et al., *The Cornell Project in China*.
42. Chang, K.C. (ed.), *Food in Chinese Culture: Anthropological and Historical Perspectives*, New Haven, 1977.
43. Messina, Mark J. et al., "SoyIntake and Cancer Risk: A Review of the In Vitro and In Vivo Data", *Nutrition and Cancer* (1994) 21(2):113-131.
44. Rackis et al., "The USDA trypsin inhibitor study", *ibid.*
45. Petrakis, N.L. et al., "Stimulatory influence of soy protein isolate on breast secretion in pre- and post-menopausal women", *Cancer Epid. Bio. Prev.* (1996) 5:785-794.
46. Dees, C. et al., "Dietary estrogens stimulate human breast cells to enter the cell cycle", *Environmental Health Perspectives* (1997) 105(Suppl. 3):633-636.
47. Woodhams, D.J., "Phytoestrogens and parrots: The anatomy of an investigation", *Proceedings of the Nutrition Society of New Zealand* (1995) 20:22-30.
48. Matrone, G. et al., "Effect of Genistin on Growth and Development of the Male Mouse", *Journal of Nutrition* (1956) 235-240.
49. Ishizuki, Y. et al., "The effects on the thyroid gland of soybeans administered experimentally in healthy subjects", *Nippon Naibunpi Gakkai Zasshi* (1991) 767:622-629.

50. Divi, R.L. et al., "Anti-thyroid isoflavones from the soybean", *Biochemical Pharmacology* (1997) 54:1087-1096.
51. Cassidy, A. et al., "Biological Effects of a Diet of Soy Protein Rich in Isoflavones on the Menstrual Cycle of Premenopausal Women", *American Journal of Clinical Nutrition* (1994) 60:333-340.
52. Murphy, P.A., "Phytoestrogen Content of Processed Soybean Foods", *Food Technology*, January 1982, pp. 60-64.
53. Bulletin de L'Office Fédéral de la Santé Publique, no. 28, July 20, 1992.
54. Keung, W.M., "Dietary oestrogenic isoflavones are potent inhibitors of B-hydroxysteroid dehydrogenase of P. testosteroneii", *Biochemical and Biophysical Research Committee* (1995) 215:1137-1144; Makela, S.I. et al., "Estrogen-specific 12 B-hydroxysteroid oxidoreductase type 1 (E.C. 1.1.1.62) as a possible target for the action of phytoestrogens", *PSEBM* (1995) 208:51-59.
55. Setchell, K.D.R. et al., "Dietary oestrogens - a probable cause of infertility and liver disease in captive cheetahs", *Gastroenterology* (1987) 93:225-233; Leopald, A.S., "Phytoestrogens: Adverse effects on reproduction in California Quail," *Science* (1976) 191:98-100; Drane, H.M. et al., "Oestrogenic activity of soya-bean products", *Food, Cosmetics and Technology* (1980) 18:425-427; Kimura, S. et al., "Development of malignant goiter by defatted soybean with iodine-free diet in rats", *Gann.* (1976) 67:763-765; Pelissero, C. et al., "Oestrogenic effect of dietary soybean meal on vitellogenesis in cultured Siberian Sturgeon *Acipenser baeri*", *Gen. Comp. End.* (1991) 83:447-457; Braden et al., "The oestrogenic activity and metabolism of certain isoflavones in sheep", *Australian J. Agricultural Research* (1967) 18:335-348.
56. Ginsburg, Jean and Giordana M. Prelevic, "Is there a proven place for phytoestrogens in the menopause?", *Climacteric* (1999) 2:75-78.
57. Setchell, K.D. et al., "Isoflavone content of infant formulas and the metabolic fate of these early phytoestrogens in early life", *American Journal of Clinical Nutrition*, December 1998 Supplement, 1453S-1461S.
58. Irvine, C. et al., "The Potential Adverse Effects of Soybean Phytoestrogens in Infant Feeding", *New Zealand Medical Journal* May 24, 1995, p. 318.
59. Hagger, C. and J. Bachevalier, "Visual habit formation in 3-month-old monkeys (*Macaca mulatta*): reversal of sex difference following neonatal manipulations of androgen", *Behavior and Brain Research* (1991) 45:57-63.
60. Ross, R.K. et al., "Effect of in-utero exposure to diethylstilbestrol on age at onset of puberty and on post-pubertal hormone levels in boys", *Canadian Medical Association Journal* 128(10):1197-8, May 15, 1983.
61. Herman-Giddens, Marcia E. et al., "Secondary Sexual Characteristics and Menses in Young Girls Seen in Office Practice: A Study from the Pediatric Research in Office Settings Network", *Pediatrics* 99(4):505-512, April 1997.
62. Rachel's Environment & Health Weekly 263, "The Wingspread Statement", Part 1, December 11, 1991; Colborn, Theo, Dianne Dumanoski and John Peterson Myers, *Our Stolen Future*, Little, Brown & Company, London, 1996.
63. Freni-Titulaer, L.W., "Premature Thelarch in Puerto Rico: A search for environmental factors", *American Journal of Diseases of Children* 140(12):1263-1267, December 1986.
64. White, Lon, "Association of High Midlife Tofu Consumption with Accelerated Brain Aging", Plenary Session #8: Cognitive Function, The Third International Soy Symposium, November 1999, Program, p. 26.
65. Altonn, Helen, "Too much tofu induces 'brain aging', study shows", *Honolulu Star-Bulletin*, November 19, 1999.
66. *Journal of the American Geriatric Society* (1998) 46:816-21.
67. Doerge, Daniel R., "Inactivation of Thyroid Peroxidase by Genistein and Daidzein in Vitro and in Vivo; Mechanism for Anti-Thyroid Activity of Soy", presented at the November 1999 Soy Symposium in Washington, DC, National Center for Toxicological Research, Jefferson, AR 72029, USA.
68. Hughes, Claude, Center for Women's Health and Department of Obstetrics & Gynecology, Cedars-Sinai Medical Center, Los Angeles, CA.
69. Soy Intake May Affect Fetus", *Reuters News Service*, November 5, 1999.
70. "Vegetarian diet in pregnancy linked to birth defect", *BJU International* 85:107-113, January 2000.
71. FDA ref 72/104, Report FDABF GRAS - 258.
72. "Evaluation of the Health Aspects of Soy Protein Isolates as Food Ingredients", prepared for FDA by Life Sciences Research Office, Federation of American Societies for Experimental Biology (FASEB) (9650 Rockville Pike, Bethesda, MD 20014, USA), Contract No. FDA 223-75-2004, 1979.

SOY- REAL DANGERS

Brain Aging and Midlife Tofu Consumption

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Objective: To examine associations of midlife tofu consumption with brain function and structural changes in late life.

Methods: The design utilized surviving participants of a longitudinal study established in 1965 for research on heart disease, stroke, and cancer. Information on consumption of selected foods was available from standardized interviews conducted 1965-67 and 1971-74. A 4-level composite intake index defined "low-low" consumption as fewer than two servings of tofu per week in 1965 and no tofu in the prior week in 1971. Men who reported 2 or more servings per week at both interviews were defined as "high-high" consumers. Intermediate or less consistent "low" and "high" consumption levels were also defined. Cognitive functioning was tested at the 1991-1993 examination, when participants were aged 71 to 93 years (n=3734). Brain atrophy was assessed using neuroimage (n=574) and autopsy (n=290) information. Cognitive function data were also analyzed for wives of a sample of study participants (n=502) who had been living with the participants at the time of their dietary interviews.

Results: Poor cognitive test performance, enlargement of ventricles and low brain weight were each significantly and independently associated with higher midlife tofu consumption. A similar association of midlife tofu intake with poor late life cognitive test scores was also observed among wives of cohort members, using the husband's answers to food frequency questions as proxy for the wife's consumption. Statistically significant associations were consistently demonstrated in linear and logistic multivariate regression models. Odds ratios comparing endpoints among "high-high" with "low-low" consumers were mostly in the range of 1.6 to 2.0.

Conclusions: In this population, higher midlife tofu consumption was independently associated with indicators of cognitive impairment and brain atrophy in late life.

Soy Formulas and the Effects of Isoflavones on the Thyroid

In a paper published in the New Zealand Medical Journal (Volume 113, Feb 11, 2000), environmental scientist and long-time campaigner against soy-based infant formulas, Dr Mike Fitzpatrick, has warned about the risk of thyroid disease in infants fed soy formulas, high soy consumers and users of isoflavone supplements:

"There is potential for certain individuals to consume levels of isoflavones in the range that could have goitrogenic effects. Most at risk appear to be infants fed soy formulas, followed by high soy users and those using isoflavone supplements".

The report noted that infants fed soy formulas are exposed to high levels of isoflavones, which are potent anti-thyroid agents, and that the risks to normal growth and development were significant. Fitzpatrick stated that thyroid problems due to soy might not be recognized "due to difficulties in establishing a cause and effect relationship" and noted that even experienced soy researchers may be ignorant of the connection between isoflavones and goitre. Fitzpatrick also rejected claims that there was no evidence that isoflavones in soy formulas harmed infants citing the reported cases of goitre that have occurred in infants fed iodine sufficient soy formulas.

Fitzpatrick stated his support to the position of the New Zealand Ministry of Health:

"MOH has found that infants with a history of thyroid dysfunction should avoid soy formulas and soy milks. Additionally, there is potential for isoflavone exposure to cause chronic thyroid damage in all infants fed soy formulas"

Fitzpatrick stated that exposing infants to isoflavones was unnecessary and that the risk of harm could be avoided if manufacturers removed isoflavones from soy formulas. "In the interim" he stated "it is appropriate for medical practitioners to monitor the thyroid status of infants fed soy formulas"

Fitzpatrick also claimed that high soy consumers and users of isoflavone supplements were also at risk of thyroid disorders. He stated that the subtle effects of anti-thyroid agents on thyroid function would most likely be evidenced as subclinical, or even overt hypothyroidism.

Fitzpatrick also noted that a sporadic pattern of soy use may also not be without risk since the resulting thyroid stimulation parallels the classic method for inducing thyroid tumours in laboratory animals. He recommended "a more cautionary approach to the use of soy and isoflavone supplements".

Infantile Leukemia and Soybeans- a hypothesis

Abe T Leukemia 1999, 13:317-20

Abstract

Recent molecular-genetic studies have revealed that in the majority of patients with secondary leukemia induced by topoisomerase II (topo II) inhibitors and also with infantile acute leukemia (IAL), the breakpoints are clustered within scaffold attachment regions (SARs) of 3'-MLL-bcr near exon 9. Genistein, abundant in soybeans, is reported to be a potent nonintercalative topo II inhibitor. It interferes with the break-reseal reaction of topo II by stabilizing a cleavable complex, which in the presence of detergents, results in DNA strand breaks. The present study revealed that genistein induced chromatid-type aberrations, in which chromatid exchanges are often observed. Genistein seems to act in a manner very similar to that of VP-16, although the latter is reported to produce both chromatid- and chromosome-type aberrations. In view of this pharmacological similarity between genistein and VP-16, and also the similarity of breakpoint clustering regions within the MLL gene in reported cases with secondary leukemia and IAL, genistein may be largely responsible for the development of IAL.

Vegetarian Diet In Pregnancy Linked To Birth Defect

Mothers who ate a vegetarian diet during pregnancy had a five-time greater risk of delivering a boy with hypospadias, a birth defect of the penis. The research team suggests

that phytoestrogens, hormone-like compounds found in soy, may be responsible for the link. Interestingly, the researchers also found that mothers who took iron supplements and those who had influenza in the first 3 months of pregnancy also had a higher risk of having a baby boy with hypospadias. The authors suggest that more research is needed to see if any of the associations found in the study actually cause the birth defect.

There is biological evidence that vegetarians have a greater exposure to phytoestrogens and thus a causal link is biologically feasible. Hypospadias is a birth defect where the opening of the penis is found on the underside of the penis rather than at the tip. It is a common congenital defect, affecting about 1 in 300 newborn males. The condition requires surgery to correct it, where the foreskin is used to repair the problem. Untreated, it can interfere with urination and sexual function. The investigators asked mothers to fill out questionnaires during pregnancy regarding obstetric history, lifestyle, and dietary practices. Of 7,928 boys born to mothers participating in the study, 51 cases of hypospadias were identified. Mothers with a vegetarian diet in the first half of pregnancy had a 4.99 times greater risk of having a boy with hypospadias compared with mothers who included meat in their diets, the researchers report. In addition, mothers who took iron supplements had double the normal risk of having a boy with hypospadias, and influenza during the first 3 months of pregnancy increased the risk of by just over three times.

BJU International January 2000;85:107-113.

COMMENT: The evidence continues to mount. Just because you are a vegetarian does not mean you are healthy. One of the main reasons is due to the soy issue addressed here. It appears that the soy phytoestrogens increased the risk of the birth defect by 500%. Not only are the soy phytoestrogens an issue, but most vegetarians consume far too little protein and far too many grains. However, the vegetables, or course, are a huge benefit and to provide some partial compensation in some areas.

Soy Lowers Brain Calcium-binding Protein, A Brain Protector

Phytoestrogens decrease brain calcium-binding proteins but do not alter hypothalamic androgen metabolizing enzymes in adult male rats.

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Phytoestrogen [plant estrogenic-like molecule(s)] research has grown rapidly in recent years due to their potential health benefits. However, little is known about phytoestrogen's effects on the CNS. androgen metabolizing enzymes are known to regulate neuroendocrine functions and reproductive behaviors, while calcium-binding proteins are associated with protecting against neurodegenerative diseases. Therefore, we examined aromatase and 5alpha-reductase enzyme activities in the medial basal hypothalamic and preoptic area (mbh-poa) and characterized mbh-poa and amygdala (amy) calbindin and calretinin levels (via Western analysis) from animals fed a phytoestrogen-free (P-free) vs. a phytoestrogen-containing diet [(P-600); that had 600 microg/g of phytoestrogens]. After approximately 5 weeks on the diets, the male rats were killed at 105 days. P-600 plasma phytoestrogen

levels were 78-fold higher than the P-free values and the mbh-poa phytoestrogen content was 8-fold higher than the P-free group, demonstrating the passage of phytoestrogens into brain. In general, brain aromatase or 5alpha-reductase activity levels were not significantly altered by the experimental diets. However, independent of brain site (i.e., mbh-poa or amy) the abundance of calbindin from male P-600 rats was significantly lower than P-free animals. Conversely, for calretinin there were no significant alterations in the mbh-poa tissue site, while in the amy a similar pattern of expression was seen to that of the calbindin results. **These data suggest that consumption of phytoestrogens via a soy diet for a relatively short interval can significantly: (1) elevate plasma and brain phytoestrogens levels and (2) decrease brain calcium-binding proteins** without altering brain androgen metabolizing enzymes.

ADDENDUM

Suggested Reading List

There are many good books available to help you discover what you like and what works for you. A book may have just one small part of a much larger picture. You don't have to 'swallow' the whole concept. Pick out the books and ideas that work for you and remember that we are all different. There is no 'perfect', 'one-size-fits-all" in nutrition and health. All books will have some truth and some error. Discriminate and most important as you try new ideas and new foods listen to your body.

General Nutrition

Good Calories Bad Calories and Why We Get Fat Gary Taubes

Know Your Fats: The Complete Primer for Understanding Fats, Oils, and Cholesterol

Mary G. Enig, Ph.D.

Nourishing Traditions Fallon, Connelly, Enig A cookbook. Potassium, protein & good fats.

Nutrition and Physical Degeneration Weston Price A classic on the decline of health.

Nutritional Medicine Davies and Stewart MD General, current nutrition information; info on herbs.

Right Dose Hausman Safe use of supplements.

Traditional Foods are Your Best Medicine Schmidt History of foods and nutrition.

Cancer

Beating Cancer with Nutrition Patrick Quillin How to use supplements and diet in conjunction with standard, Western medicine, allopathic cancer treatments

Cancer and Natural Medicine Boik Very well-researched text. Covers all types of alternative therapies.

Children

Encyclopedia of Natural Health and Healing for Children Marcea Weber

How to Raise a Healthy Child In Spite of Your Doctor Mendelsohn, MD

Let's Have Healthy Children Adele Davis Out of print but worth searching for!

Parents Nutrition Bible Earl Mindell

The Family Bed Tine Thevenin Out of print but worth searching for!

The Crazy Makers : How the Food Industry Is Destroying Our Brains and Harming Our Children Carol Simontacchi, CN

Diet (all lower fasting insulin)

Charles Hunt's Diet Evolution Charles Hunt

It Starts with Food Hartwig and Hartwig

NeanderThin* Ray Audette

Paleo Diet Loren Cordain

Perfect Health Diet Jaminet

Protein Power Michael Eades

Rosedale Diet Rosedale

8 Hour Diet David Zinczenko Peter Moore Matt Goulding

Intermittent Fasting <http://leangains.com>

Doctors, Safe Use of

Matters of Life and Death Robin MD Stanford Alumni Press

Taking Charge of Your Medical Fate Horowitz

What Your Doctor Didn't Learn in Medical School Stuart Berger MD

Drugs, Safe Use of

Worst Pills Best Pills Public Citizen Health Research Group get the latest version

Fats

Fats and Oils Udo Erasmus

Fats that Heal Fats that Kill Udo Erasmus

The Cholesterol Myths Uffe Ravnskov, MD, PhD

Life Threatening or Chronic Diseases, Healing from

DMSO Nature's Healer Morton Walker Information on using DMSO in chronic disease.

Making Miracles Roud A must read!

Third Opinion 2nd Ed. John Fink

You Can't Afford the Luxury of a Negative Thought McWilliams and Roger

Magnesium

Magnesium and Man Warren Wacker

The Magnesium Factor Mildred S. Seelig, MD, MPH

Heart Healthy Magnesium Pierce

Nutrient Content Reference

Food Composition Ford Heritage Foundation (This book contains values for vegetables & fruits only)

Food Values of Portions Commonly Used Pennington (The Best)

Nutrition and the Mind

Mental and Elemental Nutrients Pfeiffer, MD amino acids

Change your Brain, Change your Life Daniel Amen, MD amino acids

Smart Fats Michael Schmidt Omega-3 in the developing and developed brain

Smart Nutrients Abram Hoffer, PhD

The Mood Cure Julia Ross depression, nutrition, and amino acids

Potassium

The High Blood Pressure Solution-Natural Prevention and Cure with the K Factor Richard Moore, MD

Thyroid Disease

Hypothyroidism Type 2: The Epidemic by Mark Starr, M.D.

Hypothyroidism, The Unsuspected Illness Broda Barnes, MD

Living Well with Hypothyroidism Mary Shomon best general info

Recovering with T3 Paul Robinson

Stop the Thyroid Madness Janie A Bowthorpe

The Great Thyroid Scandal and How To Survive It by Dr. Barry Durrant-Peatfield, MB, BS, LRCP, MRCS

The Thyroid Solution Ridha Arem, MD best clinical info

Why Do I Still Have Thyroid Symptoms When My Lab Tests Are Normal? A Revolutionary Your Thyroid and How to Keep it Healthy by Dr. Barry Durrant-Peatfield. MB BS LRCP MRCS

Vitamin C

How To Live Longer and Feel Better, by Linus Pauling, Ph.D., (Freeman, 1986)

The Healing Factor: Vitamin C Against Disease, by Irwin Stone (Putnam, 1972)

The Vitamin C Connection, by Emanuel Cheraskin, M.D. et al (Harper and Row, 1983)

Clinical Guide to the Use of Vitamin C, by Lendon H. Smith, M.D

Ascorbate: The Science of Vitamin C by Dr. Steve Hickey & Dr. Hilary Roberts

Vitamin C: The Real Story, the Remarkable and Controversial Healing Factor by Steve Hickey
Cancer and Vitamin C: A Discussion of the Nature, Causes, Prevention, and Treatment of Cancer With Special Reference to the Value of Vitamin C, Updated and Expanded by Ewan Cameron

Clinical Tests and Laboratories

I request very little testing in my practice. Testing is used only when it is critical to the success of your program. I believe these tests provide important information worth the cost.

BLOOD TESTS:

Blood is the last place you will find a deficiency. Long before serum levels drop body stores will be depleted. When an abnormal value appears on a blood test it is always serious.

Below available from <http://lef.org> or <http://www.healthcheckusa.com> or <http://www.privatemdlabs.com/>

- **25(OH)D** or 25-hydroxyvitamin D- The critical test for optimum levels of vitamin D necessary for all clients. If your physician will not order the test you may order for yourself. REQUIRED
- **Ferritin**- As a marker of iron sufficiency and make sure iron is not in excess REQUIRED
- **Fasting Insulin**- (NOT glucose) REQUIRED
- **Fasting Glucose**
- **Hemoglobin A1C**
- **Homocysteine**
- **Thyroid panel**- If you feel you have symptoms of thyroid disease or have a family member who has or had thyroid disease. Simple- just TSH, Problems/symptoms- TSH, free T4 and free T3 and reverse T3

Optional- Chemistry 25, CBC, Platelet Count and Differential- This is a standard blood panel similar to your yearly blood test and includes cholesterol. This test is important for clients with medical conditions requiring blood monitoring such as heart disease, diabetes, liver disease and the like. It is also a good 'yearly' test to see how you are responding to aging.

C-Reactive Protein- a marker of inflammation and aging

HAIR- Hair testing is appropriate if you are concerned with exposure to heavy metals including selenium, mercury, lead and cadmium. Hair is not a marker for nutritional sufficiency and cannot be used if you regularly use chemicals on your hair. If appropriate the cost is \$50 (approx.)

STOOL/Microbiome- Excellent way to see the members of your microbiome and retest after the Immune Restoration Protocol. The cost is under \$100 and with this link a 10% discount. <http://ubiome.refr.cc/XL3MGSK> Results take about 6 weeks. You may also order testing of skin, genitals, mouth and nose if you wish to know your surface biome.

23andme gene testing analysis is available. Cost to 23andme is about \$99. The analysis will cost another \$180 plus program prep. <http://refer.23andme.com/v2/share/6037539286874301729> Important if you have ongoing health issues.

Skin Type Sun Guidelines

Table 22 Skin Type Guidelines

SKIN TYPE # and DESCRIPTION	SKIN REACTION (UV overexposure)	COMMENTS ON SKIN TYPE
1 Typically: Red-blond hair. Blue eyes, very light skin.	Mostly burns, does not tan	Will often comment that they "Can never get a real tan." As teenagers, they sometimes resort to burning and waiting a day for the pigmentation to create the "illusion" of a tan, sometimes mixed with freckles.
2 Typically: Light to medium hair, light to medium eyes, light to medium skin.	Usually burns, seldom tans.	Most skin type 2 individuals will say that "I tan if I am careful the first few times out". The light burning or pinking of 1 erythemal dose will pigment to a "tan effect" by evening on a skin type 2, giving the impression of a tan. They often do not recognize the pinking as a burn, hence, the dermatological definition always burns, seldom tans.
3 Typically: Medium hair, medium to dark eyes, medium to olive skin.	Moderately burns usually tans.	Usually do not recognize that they burn moderately if exposure is moderate. A skin type 3 will comment that they "Can get a good tan with care."
4 Typically: Dark hair, dark eyes, dark olive to light brown skin.	Burns mildly, moderate brown.	Usually considers themselves to tan easily and with "moderate" exposure in orthern climates, will not experience a burn very often. Skin type 4 is usually surprised when they get a "little sunburn" while visiting higher intensity locations.
5 Typically: Dark hair, dark eyes, dark skin.	Seldom burns, dark brown.	Seldom experiences a burn. This experience usually will occur after having no previous exposure for many months, then being exposed to very high intensity levels (100+ on the SUNSOR Scale).
6 Typically: Dark hair, dark eyes, very dark skin.	Insensitive, does not burn.	Individuals have very good pigmentation that affords exceptional protection in ultraviolet light.

80% of body surface needs to be exposed for optimum D production.

These figures are for body surface exposure so this means 'per side'. Each 5% surface equals about 200 IU but only at mid-day. On August 15, 2000 at 12:30 PM 38° N near San Francisco UV-B was only 75% of Florida summer noon, a UVI of 6 requiring 30 minutes mid-day exposure per side, 60 minutes total, for lightest white skin.

The UV Index (UVI) is posted daily on any weather service and indicates the intensity of combined UV-B and low UV-A at noon on that day. The UVI does not apply to earlier or later in the day. If the posted value is 8 or greater most light skinned persons can get sufficient D in little time, near noon (between 11 AM and 2 PM).

At a UVI of 6 the lightest skins would need 30 minutes per side, a full hour mid-day. If the UVI is 5 or lower significant time would be needed to produce D, probably more time than available mid-day.

For each level of decrease in UVI add five minutes to type 1 exposure time for optimal production of D. San Francisco 11/15/00 UV 4 at noon would require 45 minutes exposure in white skin to attain an optimal level of D. This is impossible as 1.5 hours (remember- full time for each side) of UV 4 would not be available.

Sunning Chart

Table 23 Mid-day Minutes per Side to Maximize Vitamin D

UV Index	Skin Type 1	Skin Type 2	Skin Type 3	Skin Type 4	Skin Type 5	Skin Type 6
UVI 1-3	N/A	N/A	N/A	N/A	N/A	N/A
UVI 4-5	40 per side	50 per side	60 per side	N/A	N/A	N/A
UVI 6	20-30 per side	40 per side	50 per side	120 per side	N/A	N/A
UVI 7	20-25 per side	35 per side	45 per side	100 per side	150 per side	150+ per side
UVI 8	15-20 per side	30 per side	40 per side	80 per side	120 per side	120+ per side
UVI 9	10-15 per side	25 per side	30 per side	60 per side	90 per side	90+ per side
UVI 10	7-10 per side	20 per side	25 per side	50 per side	80 per side	80+ per side
10+ (Hawaii & altitude, tanning beds)	5-7 per side	10 per side	15 per side	30 per side	60 per side	60+ per side

Values are per side so must be doubled to calculate actual time needed. The sky must be clear. If there are clouds or haze UV-B is blocked and while you may burn you won't make optimal D. You also won't make D if you sun behind a glass barrier.

N/A means not enough time would be available mid-day to maximize D.

UV-B Meters

To calculate your own local UV-B get a meter. This is much more accurate than using the local estimate. The Sunsor is no longer available. I am looking for a replacement. Do not buy UVI meters sold for the sun as they calculate both A and B and won't work for our purposes. The following meters work with descending accuracy.

Solarmeter UV-B meter from SolarTech, Inc 1-800-798-3311

SafeSun personal sun meter, available from Optix Tech, Inc 1-888-327-6641 Tanita EC

Getting Started- How to Begin

Where do I start? Begin by collecting the supplements you will need for your program. Use the reference list of supplements and sources. Also check your local health food store for sources. At any time if you have problems CALL. Take notes; use sticky tabs, use highlighter, whatever helps get the information across. Write in the margins.

Start with the information on Protein and Potassium. Pick one and count your daily intake. Maximize your intake. Try the other (protein or potassium) and do the same.

Read the Basic Food Plan and Putting It All Together next. Visit your grocer and shop around the edges of the store (stay out of the middle). Everything fresh. Try to keep it simple. A slow cooker is great in winter months. Just pick your protein and vegetables and toss them in the pot with some seasonings you like and let it cook. A blender works for quick fruit smoothies in summer.

Remove all fats and foods from your home that are in the categories listed as Do Not Consume. If some of the fat information seems confusing it essentially boils down to

Do not use vegetable oils, canola, soy, safflower, sesame, cottonseed, corn, flax, etc. even if purchased at a health food store or foods containing them. Toss them all.

Do not use margarines or the new 'fake fats' even if purchased in a health food store. Toss.

Do not use foods, breads or other packaged products that contain vegetable oils, margarine, hydrogenated or partially hydrogenated fats and oils. Toss.

DO complete the Immune Restoration Protocol

Do use extra virgin olive oil (extra virgin only and check the label for harvest date)

Do use butter or ghee or clarified butter, cream and sour cream

Do use coconut oil (from your health food store, extra virgin only) or coconut milk available at your grocers. Do not use hydrogenated coconut oil.

Do use fresh sprouted or lightly dry-roasted nuts and seeds (you do the sprouting/roasting) in moderation. If you are deficient in omega-3 avoid nuts and seeds, except walnuts, when possible, for the first 2-4 months.

When you have gotten a start and are becoming comfortable with the protein and potassium guidelines read the information on vitamin D, calcium and magnesium.

The other sections of the book should be read as you develop interest in them. Special Formulas includes remedies for colds and flu, treatments for depression, insomnia, jetlag

and other useful and safe ways to deal with a number of conditions. The additional pages in the front and back of your workbook are for further education. Read as you have time and interest.

First Week and Second Week:

Look at protein and potassium goals. Pick the one you need to most work on. (Are you low on fruits and vegetables - both major sources of potassium, or low on proteins, the meat, fish, dairy, nuts and seeds stuff?) Just pick one. Don't try to change everything at once. The advantage of making only one major change at a time is that you learn in what way each contributes to the way you feel and function.

Third Week:

Concentrate on getting and taking the supplements and recording food and supplements; mood and symptoms. It's ok to take just 'some' of your supplements, adding one or more each day, or week. Go as rapidly or as slowly as you are willing.

Call if you have concerns or questions.

Forth Week:

Work on the other major component, either potassium or protein.

Fifth Week:

Continue recording and collecting concerns and questions. This is the week you will want to call in to report. Called sooner if there are problems.

NOTES & QUESTIONS FOR KRISPIN (or your healthcare practitioner):

Safe Supplement Information, check your multi-

More is not better. Vitamins and minerals have a reverse effect. Many of the symptoms of deficiency are the same as the symptoms of toxicity. Count daily totals carefully. Only take as much as you seem to need. Do not exceed upper amounts for any extended period of time.

Look for a good multiple that supplies most of the amounts below in 4-6 tablets or capsules daily. No supplement is perfect but these are the basics. Any reputable brand will do if you can swallow it (not too big) and it provides MOST of what is listed below. Supplement individually with items to reach your goals. You'll need extra iron and B-12 if you don't eat red meat and/or organ meats (liver, kidney) and folate if you don't eat 'greens'.

Supplement 'powders' like greens and reds or other powders are PROCESSED food. Don't be taken in by advertising. There are no supplements so special they cannot be duplicated by another brand, ever. Look for the basics and if you have special need for certain nutrients get them separately. No multiple can ever contain the perfect balance for you, not even those supposedly tailored to your 'genes'.

Table 24 Safe and Adequate Vitamins/Minerals

Vitamins	
A	Retinol 5,000-15,000 IU daily (extra only during infections) Not beta-carotene. Excess beta-carotene is implicated in chronic pain syndromes. Get beta-carotene and other carotinoids from vegetables.
B-complex	10-25 mg of most of the Bs NEVER containing synthetic folic acid
Folates	400 mcg of natural folates but if you have the MTHFR gene you'll need 5-MTHF Consume NOTHING (supplements or food) with added folic acid as it is synthetic
B-12	800-1,000 mcg of B-12 prefer methylcobalamin
C	2,000 mg twice daily, more if infection or injury is present and if under stress
Bioflavonoids	Rutin about 500 mg once or twice a day will provide both rutin and quercetin IF you have good gut flora and it will protect your brain, heart, liver and gut. <small>(1352, 1353, 1354, 1355, 1356, 1357, 1358, 1359, 1360)</small>
D3	800-4,000 IU from food, supplements and/or sun (must be determined by testing)
E	d'alpha tocopherol with mixed tocopherols 200-400 IU total, do not exceed 800 IU
K	Important for bone and every other tissue 1-3 mg (1,000-3,000 mcg) Life Extension Super K 2 mg, other brands are low.
Minerals	
Calcium	500-1,000 mg
Magnesium	400-800 mg
Zinc	15-50 mg more when infection is present, do not exceed 90 mg. daily for extended use. Use Zinc Status test to check levels.
Iron	10-25 mg if needed, ferrochel (Albion iron) is safe at any age; no iron if ferritin test exceeds 150 ng/ml Optimal ferritin test 70-90 ng/ml
Chromium	200 mcg more is not necessary
Selenium	200 mcg methylselenocysteine or selenomethionine is preferred, toxic when dose is too high (greater than 600 mcg extended use) or inorganic exposure..
Lithium	5-10 mg lithium orotate if mood disorder, diabetes or thyroid disease is present
Boron	3-6 mg if you have bone loss, arthritis, or elevated PSA
Molybdenum	100-150 mcg.

Copper	1-2 mg balanced with zinc
Vanadium	25-100 mcg. especially if diabetic
Iodine	225-1,000 mcg (1 mg.). unless you are allergic. Best source is dulse, not kelp.
Manganese	5-10 mg higher amount if you degenerative joint or disc disease
Other elements	Most supplements add 'window dressing', stuff you might need but in amounts that are NOT clinically relevant. Look for supplements with the least window dressing and if you need a special item, CoQ10, more D, extra iron, glutathione, probiotics, etc. get them separately in RELEVANT amounts.

Beta-carotene should be gotten from food not supplements as is true of potassium. Supplements of these items may be detrimental to your health. Most multiples now contain beta-carotene, which is unfortunate, and you won't be able to avoid it. Look for a supplement that has the lowest amount. Beta-carotene is NOT vitamin A.

Additional Options- lecithin granules, Carlson Labs cod liver oil (3 capsules or 1 teaspoon-9 caps or 1 tablespoon), brewer's yeast (Lewis Labs International Brewers Yeast has organic selenium and lots of potassium), bone meal, dolomite powder (Kal), liver powder, bioflavonoids, quercetin, fish oil

When counting your totals always include amounts from all supplements, including protein drinks and the like.

Supplements below are just giving safe/adequate ranges for use WHEN NEEDED. NONE of these are needed when you are eating right and healthy (not injured or ill)

Amino Acid Supplements

Table 25 Amino Acids-Applications

Name	Use: Amino acids are typically taken on an empty stomach (no food)
dl-phenylalanine	Used for pain management 2,000 mg 2-3 times a day
Arginine	Growth hormone releaser, NO (nitric oxide) production, heart 2,000-4,000 mg
Carnitine	Heart; fat burning 2,000-4,000 mg as needed
Cysteine	Heavy metal detoxification; hair loss; psoriasis 500-1,000 mg 2 times daily
Glycine	Used for wound healing; cholesterol; gout 3,000 mg 2-3 times a day
Glutamine	Gut repair, hypoglycemia, brain food, growth hormone 2,000-4,000 mg as needed
Histadine	Rheumatoid Arthritis 4,000 mg
Lysine	Herpes 2,000-4,000 mg 2 times a day
Ornithine	Growth hormone releaser 2,000-4,000 mg before bed
Taurine	Heart; gall bladder; mood disorder; obesity 1,000-2,000 mg 2-3 times daily
Tyrosine	Antidepressant, energy, anti-stress 1,000-2,000 mg as needed
Tryptophan	Sleep and mood 500-1,000 mg as needed before bed

For more information on therapeutic use of amino acids read [The Healing Nutrients Within](#) by Eric Braverman, M.D.

Additional Supplements

Supplement	Relevant Amounts (clinical studies support)
I-theanine	200 mg twice a day for stress, works in 30 minutes
Olive Leaf Extract	500-1,000 mg 1-3 times a day (Vitacost brand is best buy) infection/hypertension
CoQ10	100-400 mg less if using liposomal form for heart/brain
MSM	1,000-3,000 mg joint and skin health
Silymarin	300 mg twice a day, liver (chemical/toxin) detoxification

Probiotics	Minimum 100 BILLION active bacteria (one hundred, not 10)
Glucosamine-Chondroitin	Possible relevant amount 1500 mg of each.
Source Naturals Arthred	1-2 scoops daily for arthritis, best client response
Liposomal Glutathione	Only really absorbable form- 100-200 mg twice a day
Resveratrol	50-200 mg trans-resveratrol twice a day; less if liposomal
Rutin	500 mg excellent bioflavonoid and is reduced by gut bacteria to provide quercetin, enhances vitamin C bioavailability
EGCG (-)-epigallocatechin-3-gallate	200-400 mg for elevated lipids, heart disease, liver disease
Bromelain- a protease enzyme (digests proteins)	Variable dose pre and post surgery injury.500-1,000 mg up to 4 times a day. Must be taken on empty stomach. Use for any inflammation (empty stomach) or with food to aid simple protein indigestion.
Berberine a potent plant extract	For gut issues, elevated blood lipids or LDL. Lowers fasting insulin and glucose. Best brand is GlycoX 500 mg berberine HCl 2-3 times a day from http://amazon.com
PQQ pyrroloquinoline quinone	10-20 mg daily to restore mitochondrial function if there are issues with the heart or brain (stroke, fibrillation, heart failure, dementia)
Vinpocetin	20 mg once a day Plant extract useful for memory/brain issues including fatigue
Niacinamide	150-250 mg four to eight times a day for arthritis

The latest ‘special’ nutrient supplement, from noni juice to ‘greens’ to antioxidants to whatever the ‘latest’ is, should ONLY be used if you have consistently followed a good basic program and still have issues. There are NO magic elements.

Taking glucosamine for joint pain when you eat foods you do not tolerate, have insufficient vitamins D or A or K, lack of omega-3, low intake of potassium containing foods, low intake of vitamin C, insufficient zinc, low iron, or other lack of ESSENTIAL elements (glucosamine is NOT essential) will fix NOTHING.

Pregnancy Supplements

The amounts listed under Safe Supplements are all within range for pregnancy and nursing. During pregnancy what needs to increase is omega-3 and protein. Otherwise, a healthy diet as layed out in this workbook and a good multiple with some few additions, should make for beautiful babies and productive labor.

- Folicin or 5-MTHF (NEVER folic acid) 800 mcg in the multiple or an added supplement
- B-12 400-800 mcg (methylcobalamin if MTHFR)
- Albion Ferrochel Iron, 25 mg daily in the multiple or added (Solgar Gentle Iron)
- 1-2 mg (1,000-2,000 mcg) vitamin K must be added, not in any multiple

Nursing may require slightly more calcium and magnesium than you might usually consume in addition to continuing adequate omega-3 and protein (one extra serving of protein during both pregnancy and nursing).

Make sure to check your vitamin D, CBC, iron, homocysteine, ferritin, fasting insulin, fasting glucose and thyroid before and throughout your pregnancy and take the zinc test monthly. Keep your 25(OH)D between 40-60 ng/ml. and your ferritin 70-90 ng/ml. Take as much zinc as needed to pass the zinc test, always. Keep your fasting insulin low ≤ 5 .

Meet your daily potassium, protein, FIBER (for a healthy microbiota for your babe) and omega-3 goals. Get help if you carry the MTHFR gene.

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Program Worksheet

Protein Goal: _____ Actual: _____ Potassium Goal: _____ Actual: _____

Make copies of this sheet. Keep a food diary for the first week or so (as long as you need to get comfortable with your food/diet) Use this sheet to write down everything you eat and drink, including water, and when you get a chance in the evening add up your daily totals. Pick either your protein or potassium goal to work on first. Once you get familiar with amounts of one switch to the other.

List food and drink with amount and time eaten.

Be patient with yourself. It takes time to learn even simple basics. If you have a question or a concern, write it here and call in as needed. Call immediately if you are experiencing any problems or difficulties.

Program Worksheet

Protein Goal: _____ Actual: _____ Potassium Goal: _____ Actual: _____

Make copies of this sheet. Keep a food diary for the first week or so (as long as you need to get comfortable with your food/diet) Use this sheet to write down everything you eat and drink, including water, and when you get a chance in the evening add up your daily totals. Pick either your protein or potassium goal to work on first. Once you get familiar with amounts of one switch to the other.

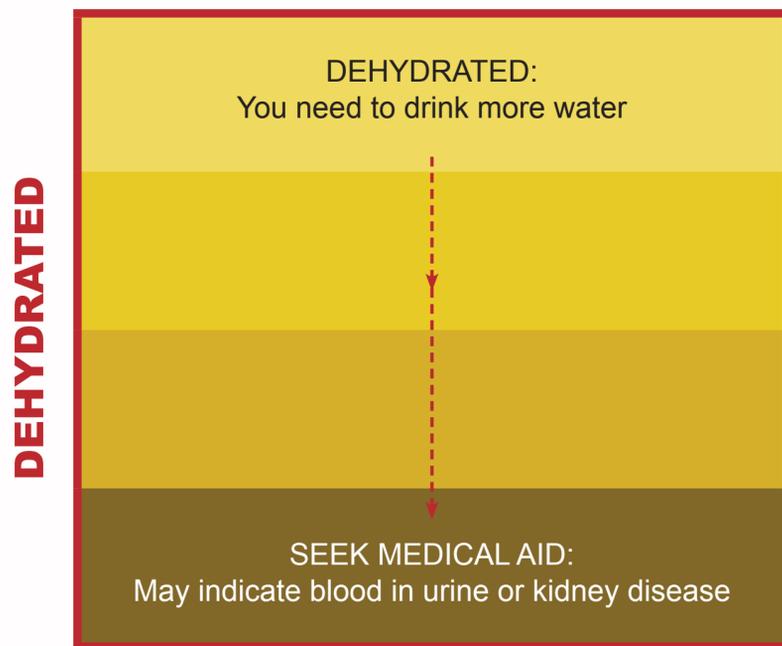
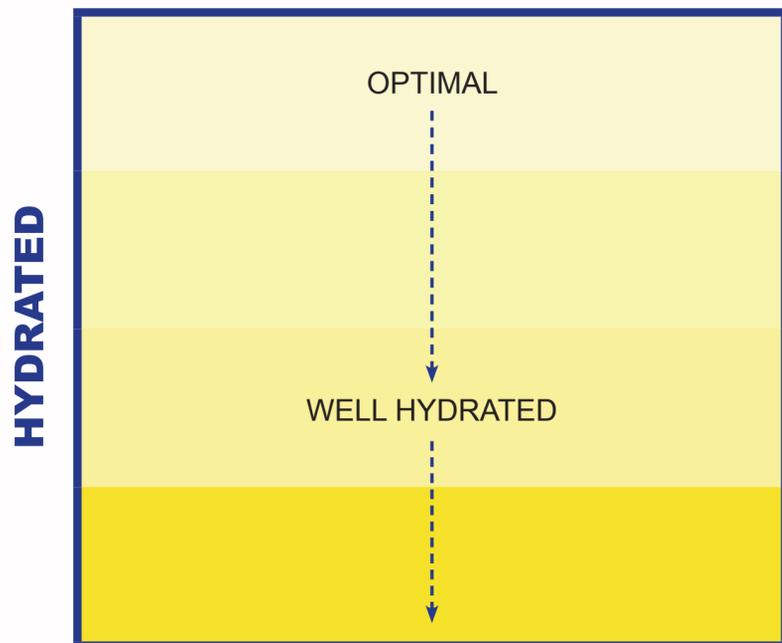
List food and drink with amount and time eaten.

Be patient with yourself. It takes time to learn even simple basics. If you have a question or a concern, write it here and call in as needed. Call immediately if you are experiencing any problems or difficulties.

Are You Hydrated?

Take the Urine Color Test

Urine Color Chart*



*This color chart is not for clinical use.

Water Consumption Table

Heat Category	WBGT Index, °F	Easy Work	Moderate Work	Hard Work
		Water Intake (Quart/Hour)	Water Intake (Quart/Hour)	Water Intake (Quart/Hour)
1	78° - 81.9°	½	¾	¾
2	82° - 84.9°	½	¾	1
3	85° - 87.9°	¾	¾	1
4	88° - 89.9°	¾	¾	1
5	> 90°	1	1	1
Body Armor = +5°		Easy Work – walking on a hard surface at less than 2 mph with less than a 30 pound load, weapon maintenance, marksmanship training; drill and ceremony	Moderate Work – patrolling, walking in the sand at 2.5 mph with no load, calisthenics; patrolling; individual movement techniques (i.e., high/low crawl)	Hard Work – walking in the sand at 2.5 MPH with a load, field assaults
MOPP 4 = +10°				
Rest - sitting or standing in the shade if possible				

The fluid replacement volumes will sustain performance and hydration for at least **4 HOURS** of work in the specified heat category. Fluid needs can vary based on individual differences and exposure to full sun or full shade.

CAUTION: Hourly fluid intake should not exceed 1.5 quarts. Daily fluid intake should not exceed 12 quarts.

Purpose

- With normal kidney function, your level of hydration is indicated by the color of your urine. Some vitamins and supplements may cause a darkening of the urine unrelated to dehydration.
- Since heat-related illness often follows dehydration, this simple test will help protect your health.
- Dehydration also increases your risk for kidney stones.

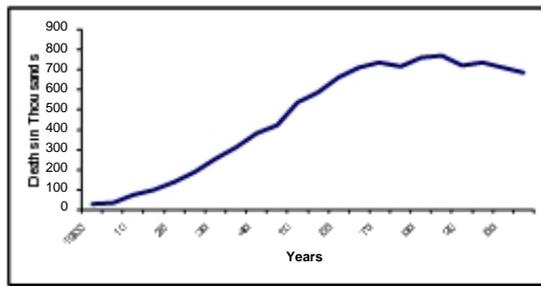
How does it work?

- Match your urine color to closest color in the chart and read the hydration level on the chart.
- Watch the urine stream not the toilet water, as the water in the toilet will dilute your urine color.
- In response to dehydration, the kidneys conserve water and excrete more concentrated urine; the more concentrated the urine the darker the color.

Prevent Dehydration

- No amount of training or acclimatization can reduce the body's requirement for water.
- Follow the water consumption guidelines in the water consumption table.

Death from Diseases of the Heart 1900-2003



CDC/NCHS

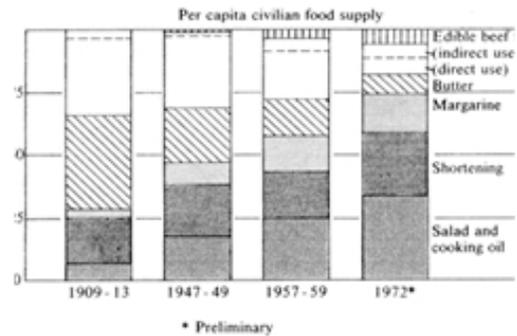


Figure 5-3: Sources of dietary fats and oils from 1909-1913 to 1972. From *Diet and Composition of Animal Products* (Washington, D.C.: National Academy of Sciences, 1972).

The dramatic increase in intakes of margarine, shortening (hydrogenated and partially hydrogenated oils) and salad and cooking oils (seed oils like sunflower, safflower, soy, cottonseed, not olive oil), from 1900-the current day, are the largest contributors to the increase in heart disease and cancer. Overall increases in these degenerative diseases closely match the per capita increased intake of these fats. All are processed (manmade) fats. There is no research supporting an increased intake of saturated, natural fats, lard (non-hydrogenated), palm (non-hydrogenated), coconut (non-hydrogenated), butter and heart disease or cancer though it is often repeated that these are the damaging fats. Our consumption of these fats has consistently declined as disease rates have increased. (Krispin's comment)

J Indian Med Assoc. 1998 Oct;96(10):304-7.

Choice of cooking oils--myths and realities.

Sircar S, Kansra U.

Department of Medicine, Safdarjang Hospital, New Delhi.

In contrast to earlier epidemiologic studies showing a low prevalence of atherosclerotic heart disease (AHD) and type-2 dependent diabetes mellitus (Type-2 DM) in the Indian subcontinent, over the recent years, there has been an alarming increase in the prevalence of these diseases in Indians--both abroad and at home, attributable to increased dietary fat intake. Replacing the traditional cooking fats condemned to be atherogenic, with refined vegetable oils promoted as "heart-friendly" because of their polyunsaturated fatty acid (PUFA) content, unfortunately, has not been able to curtail this trend. Current data on dietary fats indicate that it is not just the presence of PUFA but the type of PUFA that is important--a high PUFA n-6 content and high n-6/n-3 ratio in dietary fats being atherogenic and diabetogenic. The newer "heart-friendly" oils like sunflower or safflower oils possess this undesirable PUFA content and there are numerous research data now available to indicate that the sole use or excess intake of these newer vegetable oils are actually detrimental to health and switching to a combination of different types of fats including the traditional cooking fats like ghee, coconut oil and mustard oil would actually reduce the risk of dyslipidaemias, AHD and Type-2 DM.

Role of vitamin K and vitamin K-dependent proteins in vascular calcification.

Schurgers LJ, Dissel PE, Spronk HM, Soute BA, Dhore CR, Cleutjens JP, Vermeer C
Z Kardiol 2001 90 Suppl 3:57-63

Z Kardiol • Volume 90 Suppl 3

Abstract

OBJECTIVES: To provide a rational basis for recommended daily allowances (RDA) of dietary phylloquinone (vitamin K1) and menaquinone (vitamin K2) intake that adequately supply extrahepatic (notably vascular) tissue requirements. **BACKGROUND:** Vitamin K has a key function in the synthesis of at least two proteins involved in calcium and bone metabolism, namely osteocalcin and matrix Gla-protein (MGP). MGP was shown to be a strong inhibitor of vascular calcification. Present RDA values for vitamin K are based on the hepatic phylloquinone requirement for coagulation factor synthesis. Accumulating data suggest that extrahepatic tissues such as bone and vessel wall require higher dietary intakes and have a preference for menaquinone rather than for phylloquinone. **METHODS:** Tissue-specific vitamin K consumption under controlled intake was determined in warfarin-treated rats using the vitamin K-quinone/epoxide ratio as a measure for vitamin K consumption. Immunohistochemical analysis of human vascular material was performed using a monoclonal antibody against MGP. The same antibody was used for quantification of MGP levels in serum. **RESULTS:** At least some extrahepatic tissues including the arterial vessel wall have a high preference for accumulating and using menaquinone rather than phylloquinone. Both intima and media sclerosis are associated with high tissue concentrations of MGP, with the most prominent accumulation at the interface between vascular tissue and calcified material. This was consistent with increased concentrations of circulating MGP in subjects with atherosclerosis and diabetes mellitus. **CONCLUSIONS:** This is the first report demonstrating the association between MGP and vascular calcification. The hypothesis is put forward that undercarboxylation of MGP is a risk factor for vascular calcification and that **the present RDA values are too low to ensure full carboxylation of MGP.**



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A packet containing the Report on the Importance of Sunlight and Vitamin D with references, Patient Protocol and Physician Testing and Treatment Protocol and other important information for maintaining optimal D status is available for \$50. This packet explains how to test, treat and maintain optimal and safe levels of vitamin D. This packet allows my clients, their families, and their physician, to rapidly access important, up to date information on safe use of sunlight and vitamin D.

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The manuscript of Naked at Noon, Understanding the Importance of Sunlight and Vitamin D is available for \$50. Unedited, without an index. This is the 'story' of sunlight and vitamin D from early beginnings of understanding to the latest information on its importance for overall health and longevity. It does not explicitly explain how to maximize your vitamin D levels.

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Bristol Stool Chart

Type 1		Separate hard lumps, like nuts (hard to pass)
Type 2		Sausage-shaped but lumpy
Type 3		Like a sausage but with cracks on its surface
Type 4		Like a sausage or snake, smooth and soft
Type 5		Soft blobs with clear-cut edges (passed easily)
Type 6		Fluffy pieces with ragged edges, a mushy stool
Type 7		Watery, no solid pieces. Entirely Liquid

You just look at a simple chart, point to what approximates the content of your toilet bowl, and your doctor (or this book) tells you whether the form is right or wrong.

» Type 1: Separate hard lumps, like nuts

Typical for acute disbacteriosis. These stools lack a normal amorphous quality, because bacteria are missing and there is nothing to retain water. The lumps are hard and abrasive, the typical diameter ranges from 1 to 2 cm (0.4–0.8”), and they’re painful to pass, because the lumps are hard and scratchy. There is a high likelihood of anorectal bleeding from mechanical laceration of the anal canal. Typical for post-antibiotic treatments and for people attempting fiber-free (low-carb) diets. Flatulence isn’t likely, because fermentation of fiber isn’t taking place.

» Type 2: Sausage-like but lumpy

Represents a combination of Type 1 stools impacted into a single mass and lumped together by fiber components and some bacteria. Typical for organic constipation. The diameter is 3 to 4 cm (1.2–1.6”). This type is the most destructive by far because its size is near or exceeds the maximum opening of the anal canal’s aperture (3.5 cm). It’s bound to cause extreme straining during elimination, and most likely to cause anal canal laceration, hemorrhoidal prolapse, or diverticulosis. To attain this form, the stools must be in the colon for at least several weeks instead of the normal 72 hours. Anorectal pain, hemorrhoidal disease, anal fissures, withholding or delaying of defecation, and a history of chronic constipation are the most likely causes. Minor flatulence is probable. A person experiencing these stools is most likely to suffer from irritable bowel syndrome because of continuous pressure of large stools on the intestinal walls. The possibility of obstruction

of the small intestine is high, because the large intestine is filled to capacity with stools. Adding supplemental fiber to expel these stools is dangerous, because the expanded fiber has no place to go, and may cause hernia, obstruction, or perforation of the small and large intestine alike.

» **Type 3: Like a sausage but with cracks in the surface**

This form has all of the characteristics of Type 2 stools, but the transit time is faster, between one and two weeks. Typical for latent constipation. The diameter is 2 to 3.5 cm (0.8–1.4”). Irritable bowel syndrome is likely. Flatulence is minor, because of disbacteriosis. The fact that it hasn’t become as enlarged as Type 2 suggests that the defecations are regular. Straining is required. All of the adverse effects typical for Type 2 stools are likely for type 3, especially the rapid deterioration of hemorrhoidal disease.

» **Type 4: Like a sausage or snake, smooth and soft**

This form is normal for someone defecating once daily. The diameter is 1 to 2 cm (0.4–0.8”). The larger diameter suggests a longer transit time or a large amount of dietary fiber in the diet.

» **Type 5: Soft blobs with clear-cut edges**

I consider this form ideal. It is typical for a person who has stools twice or three times daily, after major meals. The diameter is 1 to 1.5 cm (0.4–0.6”).

» **Type 6: Fluffy pieces with ragged edges, a mushy stool**

This form is close to the margins of comfort in several respects. First, it may be difficult to control the urge, especially when you don’t have immediate access to a bathroom. Second, it is a rather messy affair to manage with toilet paper alone, unless you have access to a flexible shower or bidet. Otherwise, I consider it borderline normal. These kind of stools may suggest a slightly hyperactive colon (fast motility), excess dietary potassium, or sudden dehydration or spike in blood pressure related to stress (both cause the rapid release of water and potassium from blood plasma into the intestinal cavity). It can also indicate a hypersensitive personality prone to stress, too many spices, drinking water with a high mineral content, or the use of osmotic (mineral salts) laxatives.

» **Type 7: Watery, no solid pieces**

This, of course, is diarrhea, a subject outside the scope of this chapter with just one important and notable exception—so-called paradoxical diarrhea. It’s typical for people (especially young children and infirm or convalescing adults) affected by fecal impaction—a condition that follows or accompanies type 1 stools. During paradoxical diarrhea the liquid contents of the small intestine (up to 1.5–2 liters/quarts daily) have no place to go but down, because the large intestine is stuffed with impacted stools throughout its entire length. Some water gets absorbed, the rest accumulates in the rectum. The reason this type of diarrhea is called paradoxical is not because its nature isn’t known or understood, but because being severely constipated and experiencing diarrhea all at once, is, indeed, a paradoxical situation. Unfortunately, it’s all too common.

*Excerpted from *Fiber Menace*, page 117-120;
BSF Chart: wikipedia.org

To avoid referencing non-descriptive numbers, I use the following definitions: types 1, 2 and 3 = hard or impacted stools. Type 4 and 5 = normal or optimal. Type 6 = loose stool, subnormal, or suboptimal, and type 7 = diarrhea.

In such cases as acute hemorrhoidal disease, anal fissure, or the inability to attain unassisted

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For International orders-

The workbook is designed to be put in a 1" binder with any additions put in the front and back pockets. Format is as requested either A4 PDF or Letter PDF

Critical to Your Success- Start Here

Make sure to READ the protein, potassium, and omega-3 sections to set your minimum daily requirements. These three values cover much more than single nutrients and are critical to the success of any program.

Look through the workbook table of contents for chapters that seem important for you. Check the pockets front and back. This is second to the protein, potassium and omega-3 chapters which apply to everyone.

If your fasting insulin is $\Rightarrow 8$ focus on Time Restricted Feeding.

Read the information on Immune Restoration, digestion and immunity and if it applies to you begin in addition to your regular program.

Read the information on vitamin C in the vitamin section. Get no less than 1,000 mg LIPOSOMAL vitamin C or 4,000 mg regular ascorbic acid twice a day. You may need more.

Check the back of your workbook for a chart on dehydration. Make sure you drink enough water every day.

Make the vitamin C skin spray if you regularly sun or have current sun damage to your skin. It must be fresh so make just a small amount at a time. The skin spray protects from sun damage without blocking production of vitamin D. Sunscreens and sunblocks prevent D production.

Get the Sally Fallon cookbook, Nourishing Traditions. Available from Amazon or 877-707-1776

Make sure your serum 25(OH)D is between 40-60 ng/ml NOT higher or lower. Monitor your D YEARLY. Also test your zinc (info in workbook) every few months and ferritin and fasting insulin every year.

Take notes, mark up your workbook. USE it. Keep it handy for reference until you KNOW your numbers and your needs. Keep it handy for emergencies (section on Special Formulas).

There are solutions NOT included in this workbook. Some formulas and protocols are only prepared for my clients (phone, fax, mail, email) because they are non-traditional or specific to a certain disease or condition. Call in if you are not getting the results you need/expect. 775-831-0292

Keep working at your health until you achieve your goals and always LISTEN TO YOUR BODY.

Your job:

1. Take the time to count your average daily intake of protein in grams. Do not include incidental protein found in fruits and vegetables in your totals. More than the minimum is fine, but not less than the minimum.
2. Take the time to count your average daily intake of potassium. Count this from all sources but remember that when food is cooked by a method that uses water (boiling, like pasta or potato) or steam much of the potassium is in the 'drip' or the boiling water. You can't count the total unless you consume this also. If food is frozen and then thawed a significant portion of potassium is lost in the fluids you toss after thawing.
3. Listen to your body. Try things 'one at a time' and give time for response. New supplement? Give it 7-21 days to see results. New amino acid? Usually within 3 days you'll notice changes, or not. New mineral? Allow up to 12 weeks to see changes in bony tissues like nails, hair growth or tooth sensitivity, 6-12 months to see changes in bone mineral density.
4. If the food plan or supplements you are trying don't give results set by your goals, make sure to call in and have a list of all supplements tried and responses ready to report. It may take some experimentation to determine what works for you.
5. If you can't tolerate a food or supplement call for help to determine a substitute.
6. DON'T purchase the latest 'cure' for your symptom. There are no 'cures' just your body and what it needs to be whole. You need to determine that. Food is first choice. A poor diet of refined or processed foods (even if organic) won't build or maintain your health. Neither will a diet lacking potassium foods or a diet low in protein or essential fats.
7. Eat the whole food. If eating grains, eat all the parts. If eating fruits consume the skin or use in recipes (zest from citrus fruits, invest in a zester). A good blender, commercial quality or a Vita-Mix, can blend the entire fruit or vegetable, skin, seeds and all, into a drink or soup. Meat, fish and poultry were traditionally consumed in all parts. Organ meats are most nutritious and safest when gotten from 100% 'grass-fed' animals. Bones should always be made into stock and consumed by all family members as broth, or added to soup, sauces, or gravies.
8. Sun or supplement vitamin D and test once a year (or more)
9. When increasing your protein or potassium food intake use foods you like. Don't consume a food based on 'it's good for me' because if you don't like it, it probably isn't.
10. Take vitamin C every day twice a day, 2,000 mg ascorbic acid or 1,000 mg liposomal vitamin C. That is 4,000 mg ascorbic acid or 2,000 mg LC. It is difficult to get enough C from food.
11. Take omega-3 fish oil every day unless you eat fatty fish (with the fat) 4 or more times a week.
12. Food tables are inherently inaccurate. Think 'approximate'.

ON STARTING YOUR PROGRAM

A QUICK CHECK BEFORE BEGINNING-

You may have feelings of 'overwhelm' when beginning your new program. This is a common experience because so much information, often new or contradicting what you have been taught, is given.

If you have not yet tested your vitamin D get the vitamin D test as soon as possible.
http://www.bloodtestathome.com/vitamin_D_test.html.

Start by collecting the supplements you need from your source list in the front pocket of your booklet. Always call the store before hand to make sure they have the supplement(s) you need when you arrive. Buy small sizes at first to see if a particular supplement is tolerable or efficacious. If you buy locally first you can return supplements that do not agree with you. Later when you know what you will be using long term buy online or by mail to save money.

Make sure to look in the back pocket of your workbook for fatty acid information. Especially note the charts on US per capita changing use of fatty acids and disease states.

Read over the workbook at your leisure. Add protein, potassium and supplements as fast or as slow as you feel comfortable. Most clients can get a good start on the program within 2 weeks.

If you seem to be reacting to any part of your new program stop immediately until you reach me for a consult. If there are no adverse effects or unusual reactions continue to experiment with your program and record your results (and any questions) on your worksheets found in the front of your booklet. Call in after a week or so for a short check-in on your progress.

If you do not apply the information you have received from me you will not see the changes that we have set as your goals. I am truly serious about the protein and potassium goal numbers. These goals are the basis of your program. Supplements can help but without the basic food changes you will not attain long term health. These numbers come from predetermined values shown to promote the optimum level of health and longevity.

I want you to choose foods you like to meet your goals. Just because a food has potassium or protein does not mean that it is the best food for you. Begin to find foods that you like that are also truly good for you. REAL FOODS ONLY.

You may have been exposed to many different theories of health and nutrition before you began working with me, high carbohydrate, low fat, many or no supplements, food combining- the list may go on and on. You are the only person who can know what is right for you and you must determine your individual needs thru trial and error.

You will find that most of the information you need to begin and for support is covered in your workbook. You don't have to do it all at once. You don't have to change everything. You do need to work until you find your 'answers'.

If you have chronic, serious illness or have set long-term health goals you may need more time with me. Take the time. It is time and money invested for knowledge. There is no knowledge more priceless than how to maintain or regain your health.

Program Worksheet

Protein Goal:_____ **Actual:**_____ **Potassium Goal:**_____ **Actual:**_____

Make copies of this sheet. Keep a food diary for the first week or so (as long as you need to become comfortable with your food/diet) Use this sheet to write down everything you eat and drink, including water, and when you get a chance in the evening add up your daily totals. Pick either your protein or potassium goal to work on first. Once you get familiar with amounts of one switch to the other.

List food and drink with amount and time eaten.

Be patient with yourself. It takes time to learn even simple basics. If you have a question or a concern, write it here and call in as needed. Call immediately if you are experiencing any problems or difficulties.

Date:_____ Took supplements:_____ Mood:_____
Exercise type/amount:_____ How I slept:_____
Mental function:_____

Health, Immunity and Aging

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There is significant evidence a functioning immune system is key to health and longevity. Immune function is all about walls, walls that divide 'self' from 'not-self'. It is true good walls make good neighbors.

The human body is very much like the description of a cell (also repeated later in the Workbook)-

From chapter 9, The Plasma Membrane, Nutrition an Integrated Approach, Pike and Brown, 1986

All cells are units separated from their environment by a membrane. This is a barrier whose presence determine the shape and encloses the substance of the cell. Despite the variability and potential hostility of the outside environment, it is the membrane on which the constancy of the internal chemistry of the cell is dependent. The discharge of this responsibility is made possible by the ability of the membrane to discriminate among those organic and inorganic molecules in the surrounding medium, permitting the entrance to some and rebuffing others. This is a truly vital task since either mass invasion of potentially toxic material or rejection of essential nutrients can lead to cellular death by asphyxiation, hydration, desiccation, poisoning, starvation, or other equally effective means. The cell, thus dependent on the external environment for all the raw materials from which it is made and with which it operates, by means of the membrane barrier and it fastidious selectivity, can enjoy a distinct and separate existence.

A cell in equilibrium with its environment is a dead cell.

For survival, selectivity, that is discrimination, is the only choice. It is necessary that the cell allows those things that are needed and avoids those things that are unnecessary or toxic. This is equally true throughout your body as a whole. Your body must remain vigilant to accept that which is able to maintain life and become 'self' and to avoid or destroy that which is 'not self'. Tolerance of 'not self' brings dissolution of the cell and death.

Over a lifetime assaults include over-exposure to infectious pathogens including bacteria, virus, spirochetes, and mycoplasmas; damage to healthy gut microflora from pathogens or antibiotics resulting in immune failure of the gut wall; consumption of lectins, glycoproteins such as gluten or casein, that are not genetically appropriate resulting in immune dysfunction of the gut wall. These assaults can be intensified, meaning immune response does not result in full recovery, if sources of nutrients needed by the immune system, such as protein, zinc, selenium, iron, vitamin A, vitamin D, vitamin E, and others, are missing or insufficient.

The immune system exists to protect our bodies from invasion by toxins (chemicals, drugs, heavy metals, poisons), pathogens (infectious agents including virus, bacteria, parasites and fungi), allergens (injected, including vaccines, inhaled or ingested) and other environmental assaults.

Lack of exposure to 'other-not me' assaults (living in a bubble) prevents the development of critical parts of the immune system, hence the advice to allow children to have pets at an early age. BUT over stressing the immune system shortens life expectancy.

The immune system is keyed to all 'surfaces', the skin, the gut from mouth to anus, the cell walls and cell membranes. In infants the gut wall is semi-permeable at birth but rapidly develops closure in breast fed infants. Feeding of formula, even 'hypo-allergenic formula' seems to delay development of gut barrier function. (1)

Early introduction of inappropriate proteins can irreversibly alter immune function with dire results.(2-4) Evidence indicates breast feeding, even for a few months, feeding genetically appropriate foods, and early introduction of probiotics help to lower immune assaults early in life and reduce lifetime immune burden.(5) Vaccinations prevent a number of life-threatening diseases but over-vaccination, becoming more likely with the new policies of yearly flu vaccines and increasing insistence on vaccines for other viral diseases, are likely to lead to increases in autoimmune diseases. Some researchers suggest this may already be happening.

Evidence from veterinary medicine shows a steep increase in auto-antibodies in vaccinated versus unvaccinated dogs.(6-8) Our immune system has been most recently classified by stimulation of T cells, T helper cells, T Suppressor cells and T Killer cells. Assaults stimulate expression of T Helper cells 1 and/or T Helper cells 2 (TH1 and TH2).

Th1 function regulates the cellular or cell-mediated immune system designed to destroy, digest and expel foreign antigens out of the body via the lymph system. This is your body's 'acute inflammatory response' and is often accompanied by inflammation, fever, pain, malaise and discharge of mucus, pus, rash or diarrhea.

Th2 functions as your humoral immune system regulating the production of antibodies which recognize foreign antigens in blood.

The two types of T-helper cells are defined by the cytokines they produce. Th1 cells, involved in cellular immunity, produce IL-2, TNF-beta and IFN-gamma, while Th2 cells, with roles in humoral immunity, produce IL-4, IL-5 and IL-10. The cytokines produced by Th2 cells enhance Th2 development and inhibit Th1 development, while Th1 cytokines stimulate development of Th1 and inhibit development of Th2.

These two functions work together to protect us from 'not us'. Th2 functions act as a sense organ, 'tasting', identifying and remembering foreign invaders (not-self). Th1 functions digest and eliminate foreign invaders from the body. While cellular immunity (Th1) directs Natural Killer T-cells and macrophages to attack abnormal cells and microorganisms at sites of infection inside the cells, humoral immunity (Th2) results in the production of antibodies used to neutralize foreign invaders and substances outside of the cells.

We are daily assaulted by virus, bacteria, parasites, fungus and antigenic proteins.

In many cases, an infection is fought with both arms of the immune system. At other times predominantly one is needed to control an infection. A healthy immune system is balanced and dynamic, Th1 and Th2 activity switching back and forth as needed. This allows for a quick eradication of a threat and then a return to balance before responding to the next threat. The inability to respond adequately with a Th1 response can result in chronic infection and cancer; an overactive Th2 response can contribute to allergies, and play a role in the development of autoimmune diseases. In end stage illnesses, both arms of the immune system fail.

The food we eat, the drugs we use, the infectious agents we are intentionally or unintentionally exposed to and the health of our gut all potentially contribute to immune load. Enough but not too much is the rule. We need a certain amount of exposure to 'foreign invaders' to stimulate immune function but chronic over stimulation results in acute or chronic illness and aging of the immune system.

An example of 'stress but not too much' would be using 'exfoliation' to stimulate regeneration of sun-damaged skin. Infrequent use in some persons will produce the desired results but chronic use or even light use in susceptible persons will damage underlying structures in the skin and increase the risk of skin cancer. In all cases exfoliation renders the skin more vulnerable to chemical and sun damage for 7-10 days following treatment.

As we age there is a shift from Th1 to Th2 dominance resulting in less ability to resist and recover from infectious disease, a generalized increase in inflammation and an increased likelihood of autoimmune disease.(9-11) This change increases the risk of altered cell-cell communication resulting in higher rates of cell hyperplasia (over production of cells as found in benign prostatic hyperplasia). Chronic inflammation is recognized as a promoter in heart disease, hypertension, diabetes, osteoporosis and cancer.

*Inflamm Res. 2000 Nov;49(11):561-70. **Unregulated inflammation shortens human functional longevity.** Brod SA. University of Texas Health Science Center at Houston, Department of Neurology, 77225, USA. Staley.a.brod@uth.tmc.edu*

Systemic inflammation, represented in large part by the production of pro-inflammatory cytokines, is the response of humans to the assault of the non-self on the organism. Three distinct types of human ailments -namely autoimmunity, presenile dementia (Alzheimer's disease), or atherosclerosis - are initiated or worsened by systemic inflammation. Autoimmunity is unregulated hyperimmunity to organ-specific proteins, inducing rapid turnover of antigen-specific T cells of the acquired immune system with ultimate exhaustion and loss of acquired immunity IL-2 and IFN-gamma production and proliferative decline, conforming to the limited capacity of clonal division (Hayflick phenomenon). In Alzheimer's disease (AD), the primary degenerative process of amyloid-beta (A β) protein precedes a cascade of events that ultimately leads to a local "brain inflammatory response". Unregulated systemic immune processes are secondary but important as a driving-force role in AD pathogenesis. Atherosclerosis, an underlying cause of myocardial infarction, stroke, and other cardiovascular diseases, consists of focal plaques characterized by cholesterol deposition, fibrosis, and inflammation. The presence of activated T lymphocytes and macrophages indicate a local immunologic activation in the atherosclerotic plaque that

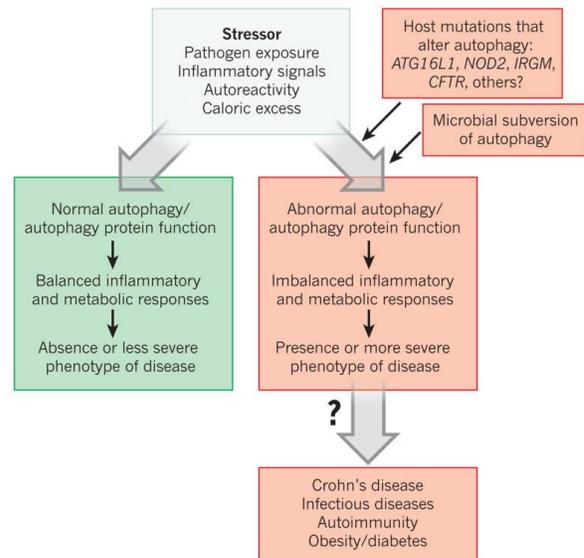
may be secondary to unregulated pro-inflammatory cytokines too. The premature hyperimmunity of autoimmunity, the local "brain inflammatory response" to A β protein in AD, and the immune response to fatty changes in vessels in atherosclerosis all signal the critical importance of unregulated systemic inflammation to common neurological and cardiovascular disease that shortens the nominal longevity of humans.

Elevated fasting insulin precedes chronic inflammation and suppresses autophagy.

A primary, yet to be fully understood, component of healthy aging and immunity is autophagy.

Autophagy (self-eating) is a process whereby the body removes (digests) dead and dying cells, bacteria, virus, and other damaged and/or potentially harmful proteins. Autophagy is a primary component of both innate and adaptive immunity. When autophagy is able to function normally our bodies are able to remove damaged DNA and useless cell components and better fight bacterial and viral loads.

Nature. 2011 January 20; 469(7330): 323–335.doi: 10.1038/nature09782 **Autophagy in immunity and inflammation** Beth Levine,1,2,3 Noboru Mizushima,4 and Herbert W. Virgin55



...Perturbations in autophagy-protein-dependent functions in immunity may contribute not only to increased susceptibility to infection, but also to chronic inflammatory diseases and autoimmune diseases.

For autophagy to function optimally the body requires:

- adequate vitamin D (40-60 ng/ml)
- normal thyroid function (TSH less than 2)
- rest (with adequate melatonin production)
- fasting insulin <6 uU/ml (elevated insulin suppresses autophagy)
- time restricted feeding or intermittent fasting

Clearly much of this aging of the immune system is modifiable, including improving/normalizing autophagy. An adequate diet, rest, normal thyroid function and adequate vitamins C and D support immune health even in centenarians.(12-15)

Consumption of whole, fresh foods, genetically appropriate, (Did your ancestors eat it?) including fish, shell fish, poultry, meat and organ meats supports immune health at any age. Organ meats, especially livers, provide the important fat soluble vitamins and key minerals required for immune function.(16-18) Fresh foods provide abundant anti-oxidants, protein, minerals and vitamins.

Regular exercise stimulates (think 'exercises') immune functions, both Th1 and Th2 in a positive way.(19-23) Regular moderate sun exposure also enhances immunity at any age. Lack of sunlight or overexposure to sunlight suppresses immune response.(24)

Vaccination may be important in areas where exposure to the disease is likely but vaccination when exposure is unlikely may increase immune load without long-term benefit. Yearly flu vaccine will more rapidly push the immune system into Th2 response found in aged individuals. Why? Here is the hypothesis from Gary Null.

http://www.garynull.com/Documents/niin/how_vaccinations_work.htm

...A vaccination consists of introducing a disease agent or disease antigen into an individual's body without causing the disease. If the disease agent provoked the whole immune system into action it would cause all the symptoms of the disease! The symptoms of a disease are primarily the symptoms (fever, pain, malaise, loss of function) of the acute inflammatory response to the disease.

So the trick of a vaccination is to stimulate the immune system just enough so that it makes antibodies and "remembers" the disease antigen but not so much that it provokes an acute inflammatory response by the cellular immune system and makes us sick with the disease we're trying to prevent! Thus a vaccination works by stimulating very much the antibody production (Th2) and by stimulating very little or not at all the digesting and discharging function of the cellular immune system (Th1).

Vaccine antigens are designed to be "unprovocative" or "indigestible" for the cellular immune system (Th1) and highly stimulating for the antibody-mediated humoral immune system (Th2).

Perhaps it is not difficult to see then why the repeated use of vaccinations would tend to shift the functional balance of the immune system toward the antibody-producing side (Th2) and away from the acute inflammatory discharging side (the cell-mediated side or Th1). This has been confirmed by observation especially in the case of Gulf War Illness: most vaccinations cause a shift in immune function from the Th1 side (acute inflammatory discharging response) to the Th2 side (chronic auto-immune or allergic response).

... There is no system of the human being, from mind to muscles to immune system, which gets stronger through avoiding challenges, but only through overcoming challenges. The wise use of vaccinations would be to use them selectively, and not on a mass scale. In order for vaccinations to be helpful and not harmful, we must know beforehand in each individual to be vaccinated whether the Th1 function or the Th2 function of the immune system predominates.

In individuals in whom the Th1 function predominates, causing many acute inflammations because the cellular immune system is over reactive, a vaccination could have a balancing effect on the immune system and be helpful for that individual.

In individuals in whom the Th2 function predominates, causing few acute inflammations but rather the tendency to chronic allergic or autoimmune inflammations, a vaccination would cause the Th2 function

to predominate even more, aggravating the imbalance of the immune system and harming the health of that individual.

Sleep also plays an important role in immune health.(25-31) Studies show sleep deprivation decreases production of NK and NKT cells and as mentioned before impaired sleep with low melatonin production reduces autophagy.

Natural Killer cells destroy cells that have become infected with a virus or cells that are replicating abnormally such as pre-cancerous cells. Natural Killer T cells secrete cytokines of both the Th1 and Th2 family and destroy infectious agents as well as protecting against autoimmune disease. Both of these sleep modifiable cell types (as well as autophagy) are critical players in immune maintenance.

Our environment, those around us, family, friends and co-workers, and even the thoughts we think alter immune function. Positive thinking, a positive human support system, and faith in God improve immune health.(32-37)

To remain healthy into advanced age we need a lifetime of good friends, genetically appropriate fresh, real, whole food, faith, exposure to and full recovery from common pathogens and infectious agents, quality and quantity of good sleep, time-restricted feeding or intermittent fasting to enhance autophagy, intermittent doses of probiotics or naturally fermented foods, and regular exercise.

Things to avoid for long-term health: Excessive exercise, avoidance of exercise, excessive food, dead fake food, processed food, genetically inappropriate food, refined sugar, excessive alcohol, chronically depressed or angry friends or family, chronically angry or paranoid politics, a bad attitude, and sleep deprivation.

Reference List

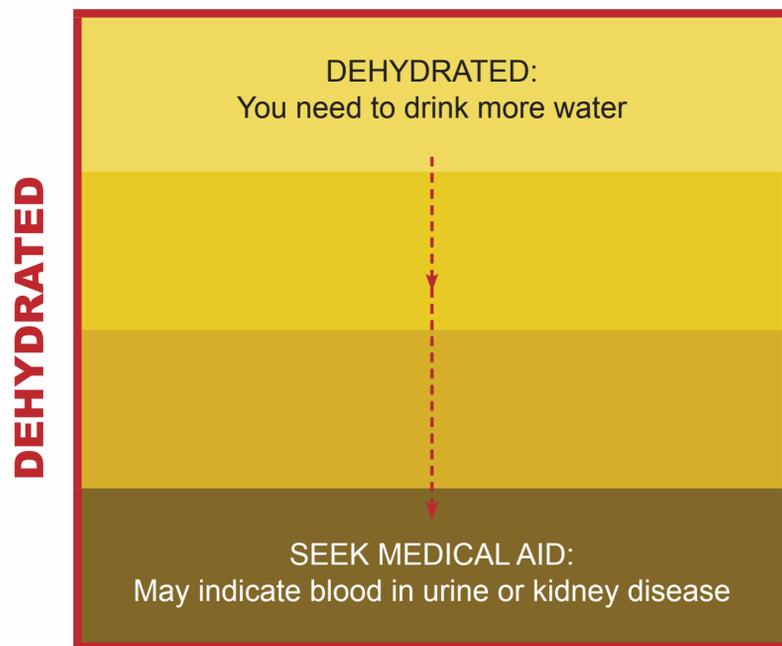
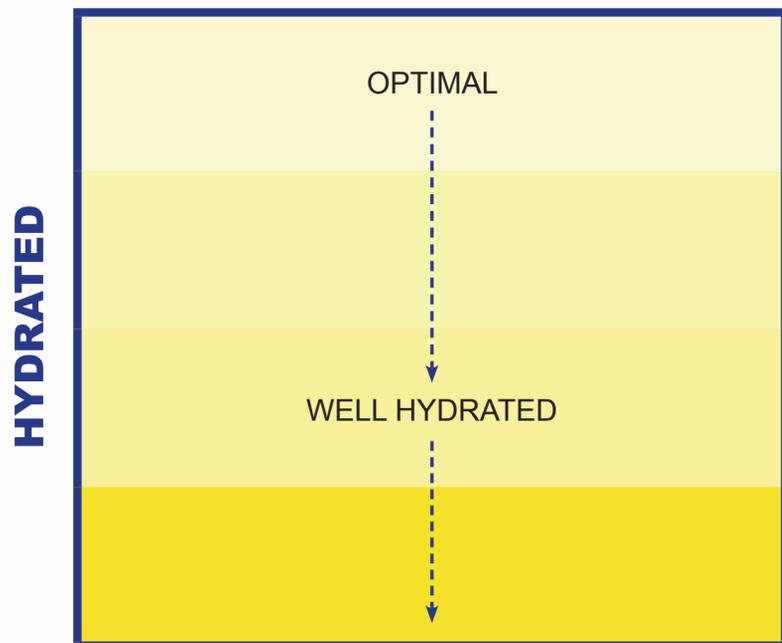
- (1) Catassi C, Bonucci A, Coppa GV, Carlucci A, Giorgi PL. Intestinal permeability changes during the first month: effect of natural versus artificial feeding. *J Pediatr Gastroenterol Nutr* 1995 November;21(4):383-6.
- (2) Coombs RR, McLaughlan P. Allergenicity of food proteins and its possible modification. *Ann Allergy* 1984 December;53(6 Pt 2):592-6.
- (3) Dupont C, Heyman M. Food protein-induced enterocolitis syndrome: laboratory perspectives. *J Pediatr Gastroenterol Nutr* 2000;30 Suppl:S50-S57.
- (4) Husby S. Dietary antigens: uptake and humoral immunity in man. *APMIS Suppl* 1988;1:1-40.
- (5) Majamaa H, Isolauri E. Probiotics: a novel approach in the management of food allergy. *J Allergy Clin Immunol* 1997 February;99(2):179-85.
- (6) Shoenfeld Y, Ron-Maor A. Vaccination and autoimmunity-'vaccinosis': a dangerous liaison? *J Autoimmun* 2000 February;14(1):1-10.
- (7) HogenEsch H, Zcona-Olivera J, Scott-Moncrieff C, Snyder PW, Glickman LT. Vaccine-induced autoimmunity in the dog. *Adv Vet Med* 1999;41:733-47.
- (8) Garlepp MJ, Kay PH, Farrow BR, Dawkins RL. Autoimmunity in spontaneous myasthenia gravis in dogs. *Clin Immunol Immunopathol* 1984 May;31(2):301-6.
- (9) Gardner EM, Murasko DM. Age-related changes in Type 1 and Type 2 cytokine production in humans. *Biogerontology* 2002;3(5):271-90.
- (10) Hsu HC, Scott DK, Mountz JD. Impaired apoptosis and immune senescence - cause or effect? *Immunol Rev* 2005 June;205:130-46.
- (11) Ibs KH, Rink L. [The immune system in aging]. *Z Gerontol Geriatr* 2001 December;34(6):480-5.
- (12) Kmiec Z, Mysliwska J, Rachon D, Kotlarz G, Sworczak K, Mysliwski A. Natural killer activity and thyroid hormone levels in young and elderly persons. *Gerontology* 2001 September;47(5):282-8.
- (13) Mariani E, Ravaglia G, Forti P et al. Vitamin D, thyroid hormones and muscle mass influence natural killer (NK) innate immunity in healthy nonagenarians and centenarians. *Clin Exp Immunol* 1999 April;116(1):19-27.

- (14) Provinciali M, Pieri C, Fabris N. Reversibility of age associated NK defect by endocrinological and/or nutritional intervention. *Ann Ist Super Sanita* 1991;27(1):61-6.
- (15) Thomasset M. [Vitamin D and the immune system]. *Pathol Biol (Paris)* 1994 February;42(2):163-72.
- (16) Chandra RK. Nutrition and the immune system from birth to old age. *Eur J Clin Nutr* 2002 August;56 Suppl 3:S73-6.:S73-S76.
- (17) Chew BP, Park JS. Carotenoid action on the immune response. *J Nutr* 2004 January;134(1):257S-61S.
- (18) Field CJ, Van AA, Drager KL, Goruk S, Basu T. Dietary folate improves age-related decreases in lymphocyte function. *J Nutr Biochem* 2005 August 9;.
- (19) Bengmark S. Acute and "chronic" phase reaction-a mother of disease. *Clin Nutr* 2004 December;23(6):1256-66.
- (20) d'Alessio P. Aging and the endothelium. *Exp Gerontol* 2004 February;39(2):165-71.
- (21) De la FM, Hernanz A, Vallejo MC. The immune system in the oxidative stress conditions of aging and hypertension: favorable effects of antioxidants and physical exercise. *Antioxid Redox Signal* 2005 September;7(9-10):1356-66.
- (22) Kohut ML, Arntson BA, Lee W et al. Moderate exercise improves antibody response to influenza immunization in older adults. *Vaccine* 2004 June 2;22(17-18):2298-306.
- (23) Kohut ML, Senchina DS. Reversing age-associated immunosenescence via exercise. *Exerc Immunol Rev* 2004;10:6-41.:6-41.
- (24) Heck DE, Gerecke DR, Vetrano AM, Laskin JD. Solar ultraviolet radiation as a trigger of cell signal transduction. *Toxicol Appl Pharmacol* 2004 March 15;195(3):288-97.
- (25) Anisman H, Merali Z. Cytokines, stress, and depressive illness. *Brain Behav Immun* 2002 October;16(5):513-24.
- (26) Dickstein JB, Moldofsky H. Sleep, cytokines and immune function. *Sleep Med Rev* 1999 September;3(3):219-28.
- (27) Gabor JY, Cooper AB, Hanly PJ. Sleep disruption in the intensive care unit. *Curr Opin Crit Care* 2001 February;7(1):21-7.
- (28) Horohov DW, Pourciau SS, Mistic L, Chapman A, Ryan DH. Increased dietary fat prevents sleep deprivation-induced immune suppression in rats. *Comp Med* 2001 June;51(3):230-3.
- (29) Irwin M. Effects of sleep and sleep loss on immunity and cytokines. *Brain Behav Immun* 2002 October;16(5):503-12.
- (30) Malik SW, Kaplan J. Sleep deprivation. *Prim Care* 2005 June;32(2):475-90.
- (31) Ozturk L, Pelin Z, Karadeniz D, Kaynak H, Cakar L, Gozukirmizi E. Effects of 48 hours sleep deprivation on human immune profile. *Sleep Res Online* 1999;2(4):107-11.
- (32) DeKeyser F. Psychoneuroimmunology in critically ill patients. *AACN Clin Issues* 2003 February;14(1):25-32.
- (33) Glaser R, Kiecolt-Glaser JK. Stress-induced immune dysfunction: implications for health. *Nat Rev Immunol* 2005 March;5(3):243-51.
- (34) Khansari DN, Murgu AJ, Faith RE. Effects of stress on the immune system. *Immunol Today* 1990 May;11(5):170-5.
- (35) Kiecolt-Glaser JK, McGuire L, Robles TF, Glaser R. Psychoneuroimmunology: psychological influences on immune function and health. *J Consult Clin Psychol* 2002 June;70(3):537-47.
- (36) Koenig HG. Psychoneuroimmunology and the faith factor. *J Gend Specif Med* 2000 July;3(5):37-44.
- (37) Prolo P, Chiappelli F, Fiorucci A, Dovic A, Sartori ML, Angeli A. Psychoneuroimmunology: new avenues of research for the twenty-first century. *Ann N Y Acad Sci* 2002 June;966:400-8.:400-8.

Are You Hydrated?

Take the Urine Color Test

Urine Color Chart*



*This color chart is not for clinical use.

Water Consumption Table

Heat Category	WBGT Index, °F	Easy Work	Moderate Work	Hard Work
		Water Intake (Quart/Hour)	Water Intake (Quart/Hour)	Water Intake (Quart/Hour)
1	78° - 81.9°	½	¾	¾
2	82° - 84.9°	½	¾	1
3	85° - 87.9°	¾	¾	1
4	88° - 89.9°	¾	¾	1
5	> 90°	1	1	1
Body Armor = +5°		Easy Work – walking on a hard surface at less than 2 mph with less than a 30 pound load, weapon maintenance, marksmanship training; drill and ceremony	Moderate Work – patrolling, walking in the sand at 2.5 mph with no load, calisthenics; patrolling; individual movement techniques (i.e., high/low crawl)	Hard Work – walking in the sand at 2.5 MPH with a load, field assaults
MOPP 4 = +10°				
Rest - sitting or standing in the shade if possible				

The fluid replacement volumes will sustain performance and hydration for at least **4 HOURS** of work in the specified heat category. Fluid needs can vary based on individual differences and exposure to full sun or full shade.

CAUTION: Hourly fluid intake should not exceed 1.5 quarts. Daily fluid intake should not exceed 12 quarts.

Purpose

- With normal kidney function, your level of hydration is indicated by the color of your urine. Some vitamins and supplements may cause a darkening of the urine unrelated to dehydration.
- Since heat-related illness often follows dehydration, this simple test will help protect your health.
- Dehydration also increases your risk for kidney stones.

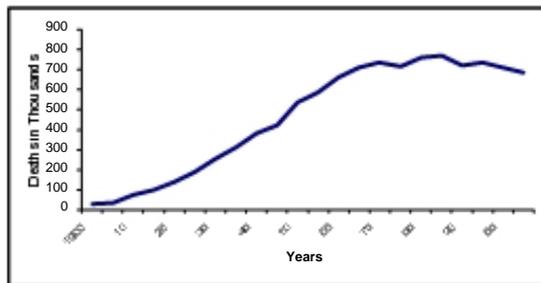
How does it work?

- Match your urine color to closest color in the chart and read the hydration level on the chart.
- Watch the urine stream not the toilet water, as the water in the toilet will dilute your urine color.
- In response to dehydration, the kidneys conserve water and excrete more concentrated urine; the more concentrated the urine the darker the color.

Prevent Dehydration

- No amount of training or acclimatization can reduce the body's requirement for water.
- Follow the water consumption guidelines in the water consumption table.

Death from Diseases of the Heart 1900-2003



CDC/NCHS

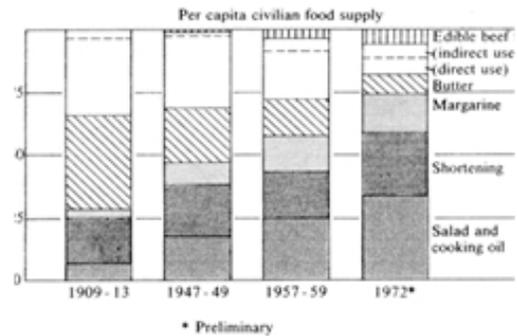


Figure 5-3: Sources of dietary fats and oils from 1909-1913 to 1972. From *Diet and Composition of Animal Products* (Washington, D.C.: National Academy of Sciences, 1972).

The dramatic increase in intakes of margarine, shortening (hydrogenated and partially hydrogenated oils) and salad and cooking oils (seed oils like sunflower, safflower, soy, cottonseed, not olive oil), from 1900-the current day, are the largest contributors to the increase in heart disease and cancer. Overall increases in these degenerative diseases closely match the per capita increased intake of these fats. All are processed (manmade) fats. There is no research supporting an increased intake of saturated, natural fats, lard (non-hydrogenated), palm (non-hydrogenated), coconut (non-hydrogenated), butter and heart disease or cancer though it is often repeated that these are the damaging fats. Our consumption of these fats has consistently declined as disease rates have increased. (Krispin's comment)

J Indian Med Assoc. 1998 Oct;96(10):304-7.

Choice of cooking oils--myths and realities.

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In contrast to earlier epidemiologic studies showing a low prevalence of atherosclerotic heart disease (AHD) and type-2 dependent diabetes mellitus (Type-2 DM) in the Indian subcontinent, over the recent years, there has been an alarming increase in the prevalence of these diseases in Indians--both abroad and at home, attributable to increased dietary fat intake. Replacing the traditional cooking fats condemned to be atherogenic, with refined vegetable oils promoted as "heart-friendly" because of their polyunsaturated fatty acid (PUFA) content, unfortunately, has not been able to curtail this trend. Current data on dietary fats indicate that it is not just the presence of PUFA but the type of PUFA that is important--a high PUFA n-6 content and high n-6/n-3 ratio in dietary fats being atherogenic and diabetogenic. The newer "heart-friendly" oils like sunflower or safflower oils possess this undesirable PUFA content and there are numerous research data now available to indicate that the sole use or excess intake of these newer vegetable oils are actually detrimental to health and switching to a combination of different types of fats including the traditional cooking fats like ghee, coconut oil and mustard oil would actually reduce the risk of dyslipidaemias, AHD and Type-2 DM.

Role of vitamin K and vitamin K-dependent proteins in vascular calcification.

Schurgers LJ, Dissel PE, Spronk HM, Soute BA, Dhore CR, Cleutjens JP, Vermeer C
Z Kardiol 2001 90 Suppl 3:57-63

Z Kardiol • Volume 90 Suppl 3

Abstract

OBJECTIVES: To provide a rational basis for recommended daily allowances (RDA) of dietary phylloquinone (vitamin K1) and menaquinone (vitamin K2) intake that adequately supply extrahepatic (notably vascular) tissue requirements. **BACKGROUND:** Vitamin K has a key function in the synthesis of at least two proteins involved in calcium and bone metabolism, namely osteocalcin and matrix Gla-protein (MGP). MGP was shown to be a strong inhibitor of vascular calcification. Present RDA values for vitamin K are based on the hepatic phylloquinone requirement for coagulation factor synthesis. Accumulating data suggest that extrahepatic tissues such as bone and vessel wall require higher dietary intakes and have a preference for menaquinone rather than for phylloquinone. **METHODS:** Tissue-specific vitamin K consumption under controlled intake was determined in warfarin-treated rats using the vitamin K-quinone/epoxide ratio as a measure for vitamin K consumption. Immunohistochemical analysis of human vascular material was performed using a monoclonal antibody against MGP. The same antibody was used for quantification of MGP levels in serum. **RESULTS:** At least some extrahepatic tissues including the arterial vessel wall have a high preference for accumulating and using menaquinone rather than phylloquinone. Both intima and media sclerosis are associated with high tissue concentrations of MGP, with the most prominent accumulation at the interface between vascular tissue and calcified material. This was consistent with increased concentrations of circulating MGP in subjects with atherosclerosis and diabetes mellitus. **CONCLUSIONS:** This is the first report demonstrating the association between MGP and vascular calcification. The hypothesis is put forward that undercarboxylation of MGP is a risk factor for vascular calcification and that **the present RDA values are too low to ensure full carboxylation of MGP.**



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Bristol Stool Chart

Type 1		Separate hard lumps, like nuts (hard to pass)
Type 2		Sausage-shaped but lumpy
Type 3		Like a sausage but with cracks on its surface
Type 4		Like a sausage or snake, smooth and soft
Type 5		Soft blobs with clear-cut edges (passed easily)
Type 6		Fluffy pieces with ragged edges, a mushy stool
Type 7		Watery, no solid pieces. Entirely Liquid

You just look at a simple chart, point to what approximates the content of your toilet bowl, and your doctor (or this book) tells you whether the form is right or wrong.

» Type 1: Separate hard lumps, like nuts

Typical for acute disbacteriosis. These stools lack a normal amorphous quality, because bacteria are missing and there is nothing to retain water. The lumps are hard and abrasive, the typical diameter ranges from 1 to 2 cm (0.4–0.8”), and they’re painful to pass, because the lumps are hard and scratchy. There is a high likelihood of anorectal bleeding from mechanical laceration of the anal canal. Typical for post-antibiotic treatments and for people attempting fiber-free (low-carb) diets. Flatulence isn’t likely, because fermentation of fiber isn’t taking place.

» Type 2: Sausage-like but lumpy

Represents a combination of Type 1 stools impacted into a single mass and lumped together by fiber components and some bacteria. Typical for organic constipation. The diameter is 3 to 4 cm (1.2–1.6”). This type is the most destructive by far because its size is near or exceeds the maximum opening of the anal canal’s aperture (3.5 cm). It’s bound to cause extreme straining during elimination, and most likely to cause anal canal laceration, hemorrhoidal prolapse, or diverticulosis. To attain this form, the stools must be in the colon for at least several weeks instead of the normal 72 hours. Anorectal pain, hemorrhoidal disease, anal fissures, withholding or delaying of defecation, and a history of chronic constipation are the most likely causes. Minor flatulence is probable. A person experiencing these stools is most likely to suffer from irritable bowel syndrome because of continuous pressure of large stools on the intestinal walls. The possibility of obstruction

of the small intestine is high, because the large intestine is filled to capacity with stools. Adding supplemental fiber to expel these stools is dangerous, because the expanded fiber has no place to go, and may cause hernia, obstruction, or perforation of the small and large intestine alike.

» **Type 3: Like a sausage but with cracks in the surface**

This form has all of the characteristics of Type 2 stools, but the transit time is faster, between one and two weeks. Typical for latent constipation. The diameter is 2 to 3.5 cm (0.8–1.4”). Irritable bowel syndrome is likely. Flatulence is minor, because of disbacteriosis. The fact that it hasn’t become as enlarged as Type 2 suggests that the defecations are regular. Straining is required. All of the adverse effects typical for Type 2 stools are likely for type 3, especially the rapid deterioration of hemorrhoidal disease.

» **Type 4: Like a sausage or snake, smooth and soft**

This form is normal for someone defecating once daily. The diameter is 1 to 2 cm (0.4–0.8”). The larger diameter suggests a longer transit time or a large amount of dietary fiber in the diet.

» **Type 5: Soft blobs with clear-cut edges**

I consider this form ideal. It is typical for a person who has stools twice or three times daily, after major meals. The diameter is 1 to 1.5 cm (0.4–0.6”).

» **Type 6: Fluffy pieces with ragged edges, a mushy stool**

This form is close to the margins of comfort in several respects. First, it may be difficult to control the urge, especially when you don’t have immediate access to a bathroom. Second, it is a rather messy affair to manage with toilet paper alone, unless you have access to a flexible shower or bidet. Otherwise, I consider it borderline normal. These kind of stools may suggest a slightly hyperactive colon (fast motility), excess dietary potassium, or sudden dehydration or spike in blood pressure related to stress (both cause the rapid release of water and potassium from blood plasma into the intestinal cavity). It can also indicate a hypersensitive personality prone to stress, too many spices, drinking water with a high mineral content, or the use of osmotic (mineral salts) laxatives.

» **Type 7: Watery, no solid pieces**

This, of course, is diarrhea, a subject outside the scope of this chapter with just one important and notable exception—so-called paradoxical diarrhea. It’s typical for people (especially young children and infirm or convalescing adults) affected by fecal impaction—a condition that follows or accompanies type 1 stools. During paradoxical diarrhea the liquid contents of the small intestine (up to 1.5–2 liters/quarts daily) have no place to go but down, because the large intestine is stuffed with impacted stools throughout its entire length. Some water gets absorbed, the rest accumulates in the rectum. The reason this type of diarrhea is called paradoxical is not because its nature isn’t known or understood, but because being severely constipated and experiencing diarrhea all at once, is, indeed, a paradoxical situation. Unfortunately, it’s all too common.

*Excerpted from Fiber Menace, page 117-120;
BSF Chart: wikipedia.org

To avoid referencing non-descriptive numbers, I use the following definitions: types 1, 2 and 3 = hard or impacted stools. Type 4 and 5 = normal or optimal. Type 6 = loose stool, subnormal, or suboptimal, and type 7 = diarrhea.

In such cases as acute hemorrhoidal disease, anal fissure, or the inability to attain unassisted

For non-clients who have ordered this workbook.

In the front pocket you will find two new additions, one on complex systems and a second on health, the immune system and aging.

This workbook is designed for my clients, those who actively work with me in a process of discovery to find their individual nutrient needs. The ideas in this workbook are overviews, generalizations and guidelines which require you to experiment, record and reflect on the success or failure of your varying choices.

Any article or book on nutrition suggesting there is a 'healthy diet' speaks to few. There are many healthy diets, but likely only one version that will be healthy for you. Keep on in your process of discovery until you find 'your food'.

When you are successful in your journey do not make the mistake of thinking 'your food' is also your neighbors' food, it may or may not be.

If you would like to become a client email or phone your Name, Address and Zip and request the information packet. 775-831-0292 or krispin@krispin.com

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The workbook is designed to be put in a 1" binder with any additions put in the front and back pockets. Format is as requested either A4 PDF or Letter PDF

Critical to Your Success- Start Here

Make sure to READ the protein, potassium, and omega-3 sections to set your minimum daily requirements. These three values cover much more than single nutrients and are critical to the success of any program.

Look through the workbook table of contents for chapters that seem important for you. Check the pockets front and back. This is second to the protein, potassium and omega-3 chapters which apply to everyone.

If your fasting insulin is $\Rightarrow 8$ focus on Time Restricted Feeding.

Read the information on Immune Restoration, digestion and immunity and if it applies to you begin in addition to your regular program.

Read the information on vitamin C in the vitamin section. Get no less than 1,000 mg LIPOSOMAL vitamin C or 4,000 mg regular ascorbic acid twice a day. You may need more.

Check the back of your workbook for a chart on dehydration. Make sure you drink enough water every day.

Make the vitamin C skin spray if you regularly sun or have current sun damage to your skin. It must be fresh so make just a small amount at a time. The skin spray protects from sun damage without blocking production of vitamin D. Sunscreens and sunblocks prevent D production.

Get the Sally Fallon cookbook, Nourishing Traditions. Available from Amazon or 877-707-1776

Make sure your serum 25(OH)D is between 40-60 ng/ml NOT higher or lower. Monitor your D YEARLY. Also test your zinc (info in workbook) every few months and ferritin and fasting insulin every year.

Take notes, mark up your workbook. USE it. Keep it handy for reference until you KNOW your numbers and your needs. Keep it handy for emergencies (section on Special Formulas).

There are solutions NOT included in this workbook. Some formulas and protocols are only prepared for my clients (phone, fax, mail, email) because they are non-traditional or specific to a certain disease or condition. Call in if you are not getting the results you need/expect. 775-831-0292

Keep working at your health until you achieve your goals and always LISTEN TO YOUR BODY.

Your job:

1. Take the time to count your average daily intake of protein in grams. Do not include incidental protein found in fruits and vegetables in your totals. More than the minimum is fine, but not less than the minimum.
2. Take the time to count your average daily intake of potassium. Count this from all sources but remember that when food is cooked by a method that uses water (boiling, like pasta or potato) or steam much of the potassium is in the 'drip' or the boiling water. You can't count the total unless you consume this also. If food is frozen and then thawed a significant portion of potassium is lost in the fluids you toss after thawing.
3. Listen to your body. Try things 'one at a time' and give time for response. New supplement? Give it 7-21 days to see results. New amino acid? Usually within 3 days you'll notice changes, or not. New mineral? Allow up to 12 weeks to see changes in bony tissues like nails, hair growth or tooth sensitivity, 6-12 months to see changes in bone mineral density.
4. If the food plan or supplements you are trying don't give results set by your goals, make sure to call in and have a list of all supplements tried and responses ready to report. It may take some experimentation to determine what works for you.
5. If you can't tolerate a food or supplement call for help to determine a substitute.
6. DON'T purchase the latest 'cure' for your symptom. There are no 'cures' just your body and what it needs to be whole. You need to determine that. Food is first choice. A poor diet of refined or processed foods (even if organic) won't build or maintain your health. Neither will a diet lacking potassium foods or a diet low in protein or essential fats.
7. Eat the whole food. If eating grains, eat all the parts. If eating fruits consume the skin or use in recipes (zest from citrus fruits, invest in a zester). A good blender, commercial quality or a Vita-Mix, can blend the entire fruit or vegetable, skin, seeds and all, into a drink or soup. Meat, fish and poultry were traditionally consumed in all parts. Organ meats are most nutritious and safest when gotten from 100% 'grass-fed' animals. Bones should always be made into stock and consumed by all family members as broth, or added to soup, sauces, or gravies.
8. Sun or supplement vitamin D and test once a year (or more)
9. When increasing your protein or potassium food intake use foods you like. Don't consume a food based on 'it's good for me' because if you don't like it, it probably isn't.
10. Take vitamin C every day twice a day, 2,000 mg ascorbic acid or 1,000 mg liposomal vitamin C. That is 4,000 mg ascorbic acid or 2,000 mg LC. It is difficult to get enough C from food.
11. Take omega-3 fish oil every day unless you eat fatty fish (with the fat) 4 or more times a week.
12. Food tables are inherently inaccurate. Think 'approximate'.

ON STARTING YOUR PROGRAM

A QUICK CHECK BEFORE BEGINNING-

You may have feelings of 'overwhelm' when beginning your new program. This is a common experience because so much information, often new or contradicting what you have been taught, is given.

If you have not yet tested your vitamin D get the vitamin D test as soon as possible.
http://www.bloodtestathome.com/vitamin_D_test.html.

Start by collecting the supplements you need from your source list in the front pocket of your booklet. Always call the store before hand to make sure they have the supplement(s) you need when you arrive. Buy small sizes at first to see if a particular supplement is tolerable or efficacious. If you buy locally first you can return supplements that do not agree with you. Later when you know what you will be using long term buy online or by mail to save money.

Make sure to look in the back pocket of your workbook for fatty acid information. Especially note the charts on US per capita changing use of fatty acids and disease states.

Read over the workbook at your leisure. Add protein, potassium and supplements as fast or as slow as you feel comfortable. Most clients can get a good start on the program within 2 weeks.

If you seem to be reacting to any part of your new program stop immediately until you reach me for a consult. If there are no adverse effects or unusual reactions continue to experiment with your program and record your results (and any questions) on your worksheets found in the front of your booklet. Call in after a week or so for a short check-in on your progress.

If you do not apply the information you have received from me you will not see the changes that we have set as your goals. I am truly serious about the protein and potassium goal numbers. These goals are the basis of your program. Supplements can help but without the basic food changes you will not attain long term health. These numbers come from predetermined values shown to promote the optimum level of health and longevity.

I want you to choose foods you like to meet your goals. Just because a food has potassium or protein does not mean that it is the best food for you. Begin to find foods that you like that are also truly good for you. REAL FOODS ONLY.

You may have been exposed to many different theories of health and nutrition before you began working with me, high carbohydrate, low fat, many or no supplements, food combining- the list may go on and on. You are the only person who can know what is right for you and you must determine your individual needs thru trial and error.

You will find that most of the information you need to begin and for support is covered in your workbook. You don't have to do it all at once. You don't have to change everything. You do need to work until you find your 'answers'.

If you have chronic, serious illness or have set long-term health goals you may need more time with me. Take the time. It is time and money invested for knowledge. There is no knowledge more priceless than how to maintain or regain your health.

Program Worksheet

Protein Goal:_____ **Actual:**_____ **Potassium Goal:**_____ **Actual:**_____

Make copies of this sheet. Keep a food diary for the first week or so (as long as you need to become comfortable with your food/diet) Use this sheet to write down everything you eat and drink, including water, and when you get a chance in the evening add up your daily totals. Pick either your protein or potassium goal to work on first. Once you get familiar with amounts of one switch to the other.

List food and drink with amount and time eaten.

Be patient with yourself. It takes time to learn even simple basics. If you have a question or a concern, write it here and call in as needed. Call immediately if you are experiencing any problems or difficulties.

Date:_____ Took supplements:_____ Mood:_____
Exercise type/amount:_____ How I slept:_____
Mental function:_____

Health, Immunity and Aging

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There is significant evidence a functioning immune system is key to health and longevity. Immune function is all about walls, walls that divide 'self' from 'not-self'. It is true good walls make good neighbors.

The human body is very much like the description of a cell (also repeated later in the Workbook)-

From chapter 9, The Plasma Membrane, Nutrition an Integrated Approach, Pike and Brown, 1986

All cells are units separated from their environment by a membrane. This is a barrier whose presence determine the shape and encloses the substance of the cell. Despite the variability and potential hostility of the outside environment, it is the membrane on which the constancy of the internal chemistry of the cell is dependent. The discharge of this responsibility is made possible by the ability of the membrane to discriminate among those organic and inorganic molecules in the surrounding medium, permitting the entrance to some and rebuffing others. This is a truly vital task since either mass invasion of potentially toxic material or rejection of essential nutrients can lead to cellular death by asphyxiation, hydration, desiccation, poisoning, starvation, or other equally effective means. The cell, thus dependent on the external environment for all the raw materials from which it is made and with which it operates, by means of the membrane barrier and it fastidious selectivity, can enjoy a distinct and separate existence.

A cell in equilibrium with its environment is a dead cell.

For survival, selectivity, that is discrimination, is the only choice. It is necessary that the cell allows those things that are needed and avoids those things that are unnecessary or toxic. This is equally true throughout your body as a whole. Your body must remain vigilant to accept that which is able to maintain life and become 'self' and to avoid or destroy that which is 'not self'. Tolerance of 'not self' brings dissolution of the cell and death.

Over a lifetime assaults include over-exposure to infectious pathogens including bacteria, virus, spirochetes, and mycoplasmas; damage to healthy gut microflora from pathogens or antibiotics resulting in immune failure of the gut wall; consumption of lectins, glycoproteins such as gluten or casein, that are not genetically appropriate resulting in immune dysfunction of the gut wall. These assaults can be intensified, meaning immune response does not result in full recovery, if sources of nutrients needed by the immune system, such as protein, zinc, selenium, iron, vitamin A, vitamin D, vitamin E, and others, are missing or insufficient.

The immune system exists to protect our bodies from invasion by toxins (chemicals, drugs, heavy metals, poisons), pathogens (infectious agents including virus, bacteria, parasites and fungi), allergens (injected, including vaccines, inhaled or ingested) and other environmental assaults.

Lack of exposure to 'other-not me' assaults (living in a bubble) prevents the development of critical parts of the immune system, hence the advice to allow children to have pets at an early age. BUT over stressing the immune system shortens life expectancy.

The immune system is keyed to all 'surfaces', the skin, the gut from mouth to anus, the cell walls and cell membranes. In infants the gut wall is semi-permeable at birth but rapidly develops closure in breast fed infants. Feeding of formula, even 'hypo-allergenic formula' seems to delay development of gut barrier function. (1)

Early introduction of inappropriate proteins can irreversibly alter immune function with dire results.(2-4) Evidence indicates breast feeding, even for a few months, feeding genetically appropriate foods, and early introduction of probiotics help to lower immune assaults early in life and reduce lifetime immune burden.(5) Vaccinations prevent a number of life-threatening diseases but over-vaccination, becoming more likely with the new policies of yearly flu vaccines and increasing insistence on vaccines for other viral diseases, are likely to lead to increases in autoimmune diseases. Some researchers suggest this may already be happening.

Evidence from veterinary medicine shows a steep increase in auto-antibodies in vaccinated versus unvaccinated dogs.(6-8) Our immune system has been most recently classified by stimulation of T cells, T helper cells, T Suppressor cells and T Killer cells. Assaults stimulate expression of T Helper cells 1 and/or T Helper cells 2 (TH1 and TH2).

Th1 function regulates the cellular or cell-mediated immune system designed to destroy, digest and expel foreign antigens out of the body via the lymph system. This is your body's 'acute inflammatory response' and is often accompanied by inflammation, fever, pain, malaise and discharge of mucus, pus, rash or diarrhea.

Th2 functions as your humoral immune system regulating the production of antibodies which recognize foreign antigens in blood.

The two types of T-helper cells are defined by the cytokines they produce. Th1 cells, involved in cellular immunity, produce IL-2, TNF-beta and IFN-gamma, while Th2 cells, with roles in humoral immunity, produce IL-4, IL-5 and IL-10. The cytokines produced by Th2 cells enhance Th2 development and inhibit Th1 development, while Th1 cytokines stimulate development of Th1 and inhibit development of Th2.

These two functions work together to protect us from 'not us'. Th2 functions act as a sense organ, 'tasting', identifying and remembering foreign invaders (not-self). Th1 functions digest and eliminate foreign invaders from the body. While cellular immunity (Th1) directs Natural Killer T-cells and macrophages to attack abnormal cells and microorganisms at sites of infection inside the cells, humoral immunity (Th2) results in the production of antibodies used to neutralize foreign invaders and substances outside of the cells.

We are daily assaulted by virus, bacteria, parasites, fungus and antigenic proteins.

In many cases, an infection is fought with both arms of the immune system. At other times predominantly one is needed to control an infection. A healthy immune system is balanced and dynamic, Th1 and Th2 activity switching back and forth as needed. This allows for a quick eradication of a threat and then a return to balance before responding to the next threat. The inability to respond adequately with a Th1 response can result in chronic infection and cancer; an overactive Th2 response can contribute to allergies, and play a role in the development of autoimmune diseases. In end stage illnesses, both arms of the immune system fail.

The food we eat, the drugs we use, the infectious agents we are intentionally or unintentionally exposed to and the health of our gut all potentially contribute to immune load. Enough but not too much is the rule. We need a certain amount of exposure to 'foreign invaders' to stimulate immune function but chronic over stimulation results in acute or chronic illness and aging of the immune system.

An example of 'stress but not too much' would be using 'exfoliation' to stimulate regeneration of sun-damaged skin. Infrequent use in some persons will produce the desired results but chronic use or even light use in susceptible persons will damage underlying structures in the skin and increase the risk of skin cancer. In all cases exfoliation renders the skin more vulnerable to chemical and sun damage for 7-10 days following treatment.

As we age there is a shift from Th1 to Th2 dominance resulting in less ability to resist and recover from infectious disease, a generalized increase in inflammation and an increased likelihood of autoimmune disease.(9-11) This change increases the risk of altered cell-cell communication resulting in higher rates of cell hyperplasia (over production of cells as found in benign prostatic hyperplasia). Chronic inflammation is recognized as a promoter in heart disease, hypertension, diabetes, osteoporosis and cancer.

*Inflamm Res. 2000 Nov;49(11):561-70. **Unregulated inflammation shortens human functional longevity.** Brod SA. University of Texas Health Science Center at Houston, Department of Neurology, 77225, USA. Staley.a.brod@uth.tmc.edu*

Systemic inflammation, represented in large part by the production of pro-inflammatory cytokines, is the response of humans to the assault of the non-self on the organism. Three distinct types of human ailments -namely autoimmunity, presenile dementia (Alzheimer's disease), or atherosclerosis - are initiated or worsened by systemic inflammation. Autoimmunity is unregulated hyperimmunity to organ-specific proteins, inducing rapid turnover of antigen-specific T cells of the acquired immune system with ultimate exhaustion and loss of acquired immunity IL-2 and IFN-gamma production and proliferative decline, conforming to the limited capacity of clonal division (Hayflick phenomenon). In Alzheimer's disease (AD), the primary degenerative process of amyloid-beta (A β) protein precedes a cascade of events that ultimately leads to a local "brain inflammatory response". Unregulated systemic immune processes are secondary but important as a driving-force role in AD pathogenesis. Atherosclerosis, an underlying cause of myocardial infarction, stroke, and other cardiovascular diseases, consists of focal plaques characterized by cholesterol deposition, fibrosis, and inflammation. The presence of activated T lymphocytes and macrophages indicate a local immunologic activation in the atherosclerotic plaque that

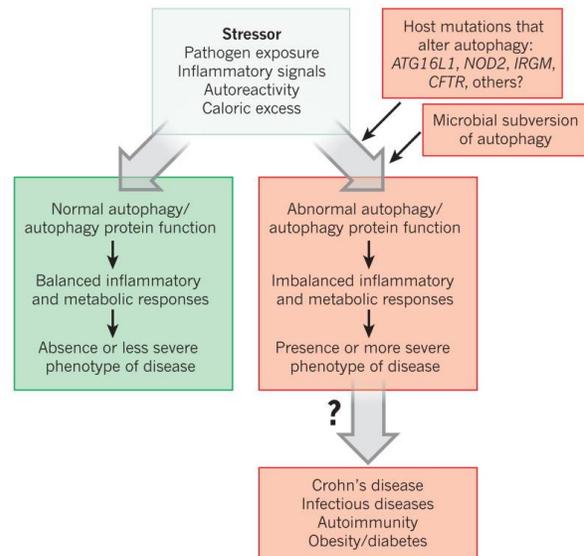
may be secondary to unregulated pro-inflammatory cytokines too. The premature hyperimmunity of autoimmunity, the local "brain inflammatory response" to A β protein in AD, and the immune response to fatty changes in vessels in atherosclerosis all signal the critical importance of unregulated systemic inflammation to common neurological and cardiovascular disease that shortens the nominal longevity of humans.

Elevated fasting insulin precedes chronic inflammation and suppresses autophagy.

A primary, yet to be fully understood, component of healthy aging and immunity is autophagy.

Autophagy (self-eating) is a process whereby the body removes (digests) dead and dying cells, bacteria, virus, and other damaged and/or potentially harmful proteins. Autophagy is a primary component of both innate and adaptive immunity. When autophagy is able to function normally our bodies are able to remove damaged DNA and useless cell components and better fight bacterial and viral loads.

Nature. 2011 January 20; 469(7330): 323–335.doi: 10.1038/nature09782 **Autophagy in immunity and inflammation** Beth Levine,1,2,3 Noboru Mizushima,4 and Herbert W. Virgin55



...Perturbations in autophagy-protein-dependent functions in immunity may contribute not only to increased susceptibility to infection, but also to chronic inflammatory diseases and autoimmune diseases.

For autophagy to function optimally the body requires:

- adequate vitamin D (40-60 ng/ml)
- normal thyroid function (TSH less than 2)
- rest (with adequate melatonin production)
- fasting insulin <6 uU/ml (elevated insulin suppresses autophagy)
- time restricted feeding or intermittent fasting

Clearly much of this aging of the immune system is modifiable, including improving/normalizing autophagy. An adequate diet, rest, normal thyroid function and adequate vitamins C and D support immune health even in centenarians.(12-15)

Consumption of whole, fresh foods, genetically appropriate, (Did your ancestors eat it?) including fish, shell fish, poultry, meat and organ meats supports immune health at any age. Organ meats, especially livers, provide the important fat soluble vitamins and key minerals required for immune function.(16-18) Fresh foods provide abundant anti-oxidants, protein, minerals and vitamins.

Regular exercise stimulates (think 'exercises') immune functions, both Th1 and Th2 in a positive way.(19-23) Regular moderate sun exposure also enhances immunity at any age. Lack of sunlight or overexposure to sunlight suppresses immune response.(24)

Vaccination may be important in areas where exposure to the disease is likely but vaccination when exposure is unlikely may increase immune load without long-term benefit. Yearly flu vaccine will more rapidly push the immune system into Th2 response found in aged individuals. Why? Here is the hypothesis from Gary Null.

http://www.garynull.com/Documents/niin/how_vaccinations_work.htm

...A vaccination consists of introducing a disease agent or disease antigen into an individual's body without causing the disease. If the disease agent provoked the whole immune system into action it would cause all the symptoms of the disease! The symptoms of a disease are primarily the symptoms (fever, pain, malaise, loss of function) of the acute inflammatory response to the disease.

So the trick of a vaccination is to stimulate the immune system just enough so that it makes antibodies and "remembers" the disease antigen but not so much that it provokes an acute inflammatory response by the cellular immune system and makes us sick with the disease we're trying to prevent! Thus a vaccination works by stimulating very much the antibody production (Th2) and by stimulating very little or not at all the digesting and discharging function of the cellular immune system (Th1).

Vaccine antigens are designed to be "unprovocative" or "indigestible" for the cellular immune system (Th1) and highly stimulating for the antibody-mediated humoral immune system (Th2).

Perhaps it is not difficult to see then why the repeated use of vaccinations would tend to shift the functional balance of the immune system toward the antibody-producing side (Th2) and away from the acute inflammatory discharging side (the cell-mediated side or Th1). This has been confirmed by observation especially in the case of Gulf War Illness: most vaccinations cause a shift in immune function from the Th1 side (acute inflammatory discharging response) to the Th2 side (chronic auto-immune or allergic response).

... There is no system of the human being, from mind to muscles to immune system, which gets stronger through avoiding challenges, but only through overcoming challenges. The wise use of vaccinations would be to use them selectively, and not on a mass scale. In order for vaccinations to be helpful and not harmful, we must know beforehand in each individual to be vaccinated whether the Th1 function or the Th2 function of the immune system predominates.

In individuals in whom the Th1 function predominates, causing many acute inflammations because the cellular immune system is over reactive, a vaccination could have a balancing effect on the immune system and be helpful for that individual.

In individuals in whom the Th2 function predominates, causing few acute inflammations but rather the tendency to chronic allergic or autoimmune inflammations, a vaccination would cause the Th2 function

to predominate even more, aggravating the imbalance of the immune system and harming the health of that individual.

Sleep also plays an important role in immune health.(25-31) Studies show sleep deprivation decreases production of NK and NKT cells and as mentioned before impaired sleep with low melatonin production reduces autophagy.

Natural Killer cells destroy cells that have become infected with a virus or cells that are replicating abnormally such as pre-cancerous cells. Natural Killer T cells secrete cytokines of both the Th1 and Th2 family and destroy infectious agents as well as protecting against autoimmune disease. Both of these sleep modifiable cell types (as well as autophagy) are critical players in immune maintenance.

Our environment, those around us, family, friends and co-workers, and even the thoughts we think alter immune function. Positive thinking, a positive human support system, and faith in God improve immune health.(32-37)

To remain healthy into advanced age we need a lifetime of good friends, genetically appropriate fresh, real, whole food, faith, exposure to and full recovery from common pathogens and infectious agents, quality and quantity of good sleep, time-restricted feeding or intermittent fasting to enhance autophagy, intermittent doses of probiotics or naturally fermented foods, and regular exercise.

Things to avoid for long-term health: Excessive exercise, avoidance of exercise, excessive food, dead fake food, processed food, genetically inappropriate food, refined sugar, excessive alcohol, chronically depressed or angry friends or family, chronically angry or paranoid politics, a bad attitude, and sleep deprivation.

Reference List

- (1) Catassi C, Bonucci A, Coppa GV, Carlucci A, Giorgi PL. Intestinal permeability changes during the first month: effect of natural versus artificial feeding. *J Pediatr Gastroenterol Nutr* 1995 November;21(4):383-6.
- (2) Coombs RR, McLaughlan P. Allergenicity of food proteins and its possible modification. *Ann Allergy* 1984 December;53(6 Pt 2):592-6.
- (3) Dupont C, Heyman M. Food protein-induced enterocolitis syndrome: laboratory perspectives. *J Pediatr Gastroenterol Nutr* 2000;30 Suppl:S50-S57.
- (4) Husby S. Dietary antigens: uptake and humoral immunity in man. *APMIS Suppl* 1988;1:1-40.
- (5) Majamaa H, Isolauri E. Probiotics: a novel approach in the management of food allergy. *J Allergy Clin Immunol* 1997 February;99(2):179-85.
- (6) Shoenfeld Y, Ron-Maor A. Vaccination and autoimmunity-'vaccinosis': a dangerous liaison? *J Autoimmun* 2000 February;14(1):1-10.
- (7) HogenEsch H, Zcona-Olivera J, Scott-Moncrieff C, Snyder PW, Glickman LT. Vaccine-induced autoimmunity in the dog. *Adv Vet Med* 1999;41:733-47.
- (8) Garlepp MJ, Kay PH, Farrow BR, Dawkins RL. Autoimmunity in spontaneous myasthenia gravis in dogs. *Clin Immunol Immunopathol* 1984 May;31(2):301-6.
- (9) Gardner EM, Murasko DM. Age-related changes in Type 1 and Type 2 cytokine production in humans. *Biogerontology* 2002;3(5):271-90.
- (10) Hsu HC, Scott DK, Mountz JD. Impaired apoptosis and immune senescence - cause or effect? *Immunol Rev* 2005 June;205:130-46.
- (11) Ibs KH, Rink L. [The immune system in aging]. *Z Gerontol Geriatr* 2001 December;34(6):480-5.
- (12) Kmiec Z, Mysliwska J, Rachon D, Kotlarz G, Sworczak K, Mysliwski A. Natural killer activity and thyroid hormone levels in young and elderly persons. *Gerontology* 2001 September;47(5):282-8.
- (13) Mariani E, Ravaglia G, Forti P et al. Vitamin D, thyroid hormones and muscle mass influence natural killer (NK) innate immunity in healthy nonagenarians and centenarians. *Clin Exp Immunol* 1999 April;116(1):19-27.

- (14) Provinciali M, Pieri C, Fabris N. Reversibility of age associated NK defect by endocrinological and/or nutritional intervention. *Ann Ist Super Sanita* 1991;27(1):61-6.
- (15) Thomasset M. [Vitamin D and the immune system]. *Pathol Biol (Paris)* 1994 February;42(2):163-72.
- (16) Chandra RK. Nutrition and the immune system from birth to old age. *Eur J Clin Nutr* 2002 August;56 Suppl 3:S73-6.:S73-S76.
- (17) Chew BP, Park JS. Carotenoid action on the immune response. *J Nutr* 2004 January;134(1):257S-61S.
- (18) Field CJ, Van AA, Drager KL, Goruk S, Basu T. Dietary folate improves age-related decreases in lymphocyte function. *J Nutr Biochem* 2005 August 9;.
- (19) Bengmark S. Acute and "chronic" phase reaction-a mother of disease. *Clin Nutr* 2004 December;23(6):1256-66.
- (20) d'Alessio P. Aging and the endothelium. *Exp Gerontol* 2004 February;39(2):165-71.
- (21) De la FM, Hernanz A, Vallejo MC. The immune system in the oxidative stress conditions of aging and hypertension: favorable effects of antioxidants and physical exercise. *Antioxid Redox Signal* 2005 September;7(9-10):1356-66.
- (22) Kohut ML, Arntson BA, Lee W et al. Moderate exercise improves antibody response to influenza immunization in older adults. *Vaccine* 2004 June 2;22(17-18):2298-306.
- (23) Kohut ML, Senchina DS. Reversing age-associated immunosenescence via exercise. *Exerc Immunol Rev* 2004;10:6-41.:6-41.
- (24) Heck DE, Gerecke DR, Vetrano AM, Laskin JD. Solar ultraviolet radiation as a trigger of cell signal transduction. *Toxicol Appl Pharmacol* 2004 March 15;195(3):288-97.
- (25) Anisman H, Merali Z. Cytokines, stress, and depressive illness. *Brain Behav Immun* 2002 October;16(5):513-24.
- (26) Dickstein JB, Moldofsky H. Sleep, cytokines and immune function. *Sleep Med Rev* 1999 September;3(3):219-28.
- (27) Gabor JY, Cooper AB, Hanly PJ. Sleep disruption in the intensive care unit. *Curr Opin Crit Care* 2001 February;7(1):21-7.
- (28) Horohov DW, Pourciau SS, Mistic L, Chapman A, Ryan DH. Increased dietary fat prevents sleep deprivation-induced immune suppression in rats. *Comp Med* 2001 June;51(3):230-3.
- (29) Irwin M. Effects of sleep and sleep loss on immunity and cytokines. *Brain Behav Immun* 2002 October;16(5):503-12.
- (30) Malik SW, Kaplan J. Sleep deprivation. *Prim Care* 2005 June;32(2):475-90.
- (31) Ozturk L, Pelin Z, Karadeniz D, Kaynak H, Cakar L, Gozukirmizi E. Effects of 48 hours sleep deprivation on human immune profile. *Sleep Res Online* 1999;2(4):107-11.
- (32) DeKeyser F. Psychoneuroimmunology in critically ill patients. *AACN Clin Issues* 2003 February;14(1):25-32.
- (33) Glaser R, Kiecolt-Glaser JK. Stress-induced immune dysfunction: implications for health. *Nat Rev Immunol* 2005 March;5(3):243-51.
- (34) Khansari DN, Murgu AJ, Faith RE. Effects of stress on the immune system. *Immunol Today* 1990 May;11(5):170-5.
- (35) Kiecolt-Glaser JK, McGuire L, Robles TF, Glaser R. Psychoneuroimmunology: psychological influences on immune function and health. *J Consult Clin Psychol* 2002 June;70(3):537-47.
- (36) Koenig HG. Psychoneuroimmunology and the faith factor. *J Gend Specif Med* 2000 July;3(5):37-44.
- (37) Prolo P, Chiappelli F, Fiorucci A, Dovic A, Sartori ML, Angeli A. Psychoneuroimmunology: new avenues of research for the twenty-first century. *Ann N Y Acad Sci* 2002 June;966:400-8.:400-8.