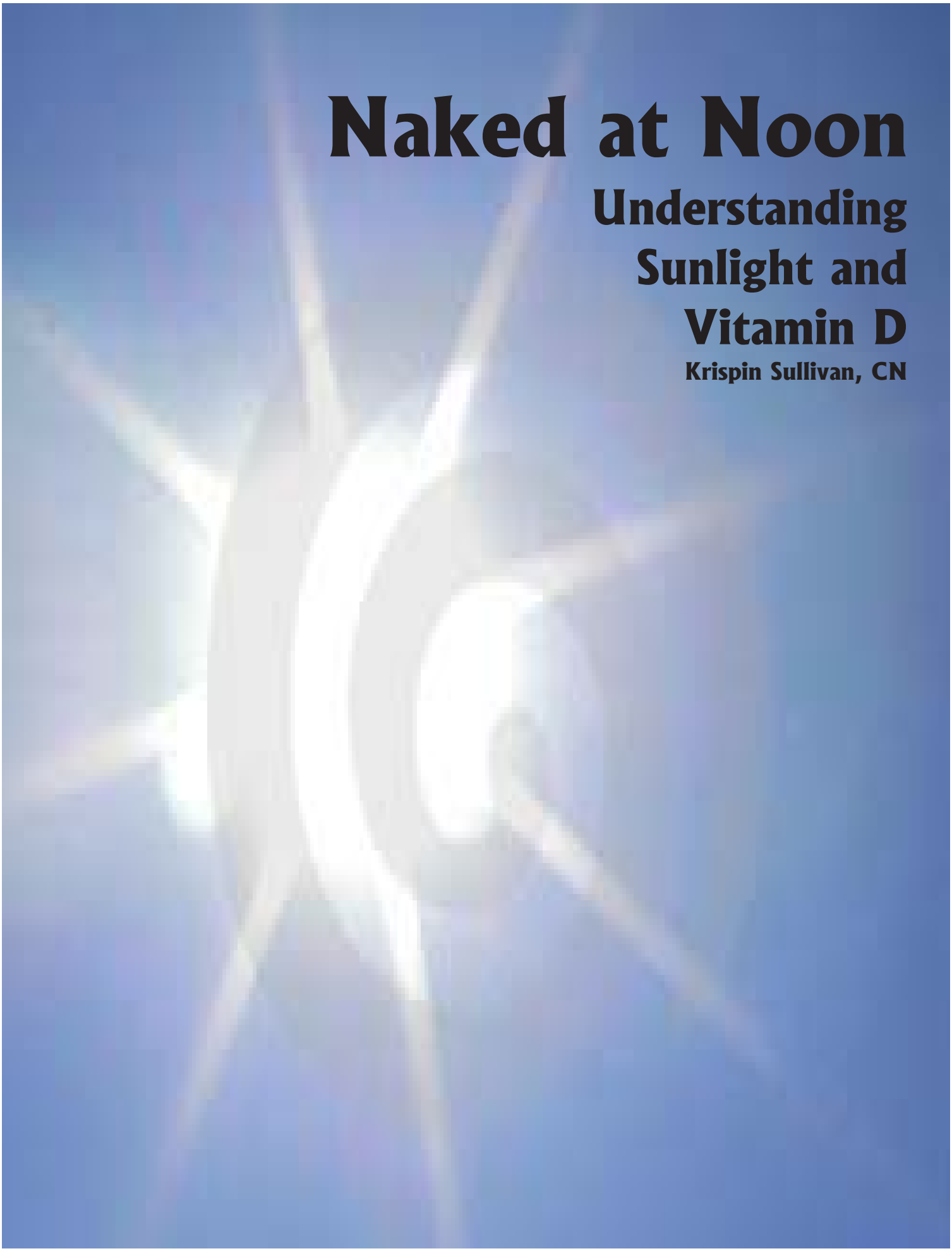


Naked at Noon

Understanding Sunlight and Vitamin D

Krispin Sullivan, CN

Naked at Noon

Understanding the Importance of Sunlight and Vitamin D

Updated 2013

This book is dedicated to my mother who introduced me to the wonder of God‘s love; my father who taught me ‗solutioning‘ and the marvels of life on earth; my grown children who continue to fill my world with wonder and delight and most of all James Leland, Riley Justus and Bishop Clayton, my three grandsons, perfect examples of life emerging. It is my hope this book will help make their world brighter.

Forward

There is a band of light, a very narrow band, upon which all life depends. Too much and cells are rapidly destroyed, too little and life becomes dark, corrupted, filled with depression, deformity, degeneration and disease.

This narrow band of light is known as ultraviolet-B (UV-B) and it is this band of light that induces the production of an amazing life critical hormone we call vitamin D.

This book is about this band of light, its capture and storage in our bodies as vitamin D, and the research of some of the most brilliant and dedicated scientists of our age, the men and women investigating the wonders of vitamin D.

This book could not have been written without the ever-increasing volume of research, beginning in the late 1890's and growing exponentially to this day. I am deeply grateful to the researchers, past and present, whose work has made this book possible. I mention the names of some few of these important persons but others remain unnamed.

If I have improperly credited or left out credit well-deserved, I am truly sorry. The communities of scientists who study light and those who study the various forms of vitamin D are relatively small. I do not mean to intentionally deny recognition to those who well deserve it. Sometimes I mention a name and 'others' or 'colleagues' or 'associates'. It would be appropriate to include all the names as they all deserve the credit, but it would make the book much longer and it would not help readers get the important bits of information needed to make informed decisions.

I hereby offer a blank check of deepest gratitude to all of these men and women, both living and those still present through their work, which remains, who have brought us to our present understanding of sunlight and vitamin D.

The most difficult part in preparing this book has been trying to reduce so much history and science to material that could be found useful in everyday life. Studies build on studies. Early explorers in sunlight and vitamin D forged the way for later adventurers who continue to broaden our understanding. While researching and writing this book the volume of data was at times overwhelming and choices had to be made as to what I would include. For each references cited in this book there are others, equally on topic and important, not referenced. I have tried, to the best of my ability, to ferret out those bits of knowledge that will help readers understand and safely use sunlight and vitamin D

Just as it must be our personal responsibility to feed ourselves nutritious foods to keep our bodies well it is equally our responsibility to ensure we have sufficient

sunlight and vitamin D. The intent of this work is to provide you, the reader, with knowledge and tools that will allow you to determine how much D you have, how much D you need, and how to get and maintain your optimum level of vitamin D.

GP: This book has been written expressly for the General Public, henceforth fondly referred to as the GP. GP this book is for you, the real people in the real world. This term, whether we acknowledge it or not, includes us all.

We need sunlight, we need vitamin D. Belief systems, attitudes and policies that prevent us from getting what we need are bad beliefs, attitudes and policies adding to national healthcare costs in a dollar value incalculable. Making sunlight a villain and vitamin D a prescription drug leads us into darkness, of body, spirit and intellect. There is no sound reason for anyone, whether the General Public, a journalist, an academician, or a healthcare professional, to fear sunlight or vitamin D.

Knowledge about safe use of sunlight and vitamin D should be an intrinsic part of our basic health education. For this to happen there will have to be significant changes in popular, medical, and governmental, understanding, attitudes, and policies. This need for transformation of understanding exists within all developed and developing countries as changing diets and lifestyles continue to increase the numbers of world citizens suffering from a lack of sunlight and vitamin D.

Heartfelt personal thanks to Dr. Fred Kummerow; Bill Grant, PhD; Dr. Bruce Hollis; Dr. Michael Holick; CC Kartha, PhD; Steve Mackin of Solartech, Reinhold Vieth, PhD; John Adams, MD; Dr. Robert P. Heaney; Dr. Walter Stohl, Yaneer Bar-Yam; Dr. Barbara Boucher; Dr. Hector DeLuca; the organizers and participants of the Vitamin D Workshops; the organizers and participants in the Biologic Effects of Light Symposiums. A special note of gratitude to Dr. Elias Ilyia from Diagnos-Techs. Without his kindness and support this book could not have been written. Robert Sayre, PhD., deserves special mention as his work provided the inspiration for the naming of this book.

CHAPTER 1 WHAT'S SO IMPORTANT ABOUT SUNLIGHT AND VITAMIN D?

VITAMIN D MAKES THE NEWS

Sunlight is man's primary source of vitamin D.[1] Vitamin D was first recognized for its role in the prevention of rickets, a disease of the bones in infants and children. From this humble beginning, making our bones straight and strong, vitamin D is now surfacing as an important prehormone once activated perhaps protecting us from cancers, autoimmune diseases and much more. Vitamin D influences the growth and regulation of all body cells and systems in amphibians, reptiles, birds, mammals and humans. [2,3]

To maintain optimum levels of vitamin D sunlight UV-B exposure or oral intake of vitamin D is essential. Reports of D insufficiency continue to increase which suggests current recommendations for sunlight exposure, fortification of milk, or use of supplements containing vitamin D are either inadequate or misunderstood and misapplied.

In April of 2000, Dr. Anu Prabhala and colleagues reported on five patients with severe muscle weakness and fatigue.[4] So great were their patients' disabilities, they had been confined to wheelchairs for mobility. Initially causes were thought to vary from simple consequences of aging to diabetic neuropathy or unexplained general debility but after further testing these wheelchair-bound patients were found to be suffering from severe vitamin D deficiency. All five patients became wheelchair free after 6 weeks of treatment with 50,000 IU of vitamin D given once a week. This is a dose equivalent to 7,000 IU of vitamin D a day, well beyond the 200-400 IU Recommended Dietary Allowance.

People in wheelchairs got up and walked when supplied with vitamin D, even those of advanced age! What had I missed in understanding this amazing vitamin? Prabhala's paper inspired me to search for more information on vitamin D; its actions in

the human body, how much D we really need, and how we get D (or not). Sunlight and vitamin D researchers have been busy these past 30+ years and what they have learned and continue to learn demands our attention.

EVIDENCE OF WORLDWIDE VITAMIN D DEFICIENCY

International research presents a picture of hidden vitamin D insufficiency and deficiency including moderate winter declines in vitamin D, general deficiencies across entire population groups and severe vitamin D deficiency evidenced by the return of rickets in industrialized nations.[5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21] Studies like these and the unusual expression of vitamin D deficiency seen in the wheelchair bound patients from upper New York State, suggest a need for a significant change in monitoring and maintaining optimal levels of this important nutrient. The research includes reports of osteomalacia (adult rickets), muscle disorders (myopathies), immune disorders, osteoporosis, hip fractures, and more. Deficiencies of vitamin D are being reported in Saudia Arabia, Asia, Turkey, Australia, Pakistan, South Africa, the U.K., France, Canada, and Norway as well as other locations.[4,6,7,8,13,16,22,23,24,25,26,27,28,29,30,31,32,33,34,35,36,37,38,39,40,41,42,43,44,45])

Studies repeatedly reject the idea vitamin D from food sources will be sufficient to maintain D when sunlight is avoided or unavailable. [22,46,47] It is difficult to know exactly why vitamin D insufficiency is increasing. As you will discover there are many possible reasons. It may be clinicians are diagnosing D deficiency and insufficiency more accurately or it may be we live in a location that cannot provide us with the sun we need. Our problem becomes more interesting as many reports of vitamin D deficiency are from countries in lower latitudes with abundant sunlight such as Saudi Arabia, Kuwait and Nigeria. [48,49,50,51]

Insufficiency or deficiency may be a result of modern lifestyles which reduce access to the vitamin from sunlight or D containing foods, or increase the need for D. Whatever the cause, vitamin D insufficiency appears to be increasing as are incidences of diseases associated with low levels of vitamin D. Making sure we all have enough and not too much D will contribute to improved health and decreased healthcare costs.

THE WORK OF REINHOLD VIETH

The idea that vitamin D deficiency could mask itself in symptoms not normally associated with vitamin D and that these symptoms could be severely debilitating, the wheelchair-bound New Yorkers, brought me to the work of Dr. Reinhold Vieth.

In the paper *Efficacy and safety of vitamin D(3) intake exceeding the lowest observed adverse effect level Vieth, R., et al*. [52] Vieth argues convincingly that the current vitamin D recommendations are woefully inadequate. The recommended dose of 200-400 IU will prevent rickets in most children but Vieth suggests it does not come close to the dose needed to maintain vitamin D sufficiency. According to Dr. Vieth, the minimal daily requirement for vitamin D is more likely to be in the range of 2,000-

4,000 IU from all sources, food, supplement and sunlight equivalents, rather than the 200-400 IU currently recommended.

In several studies, subjects were given 1000 IU or 4000 IU of vitamin D daily for 3-5 months. Vitamin D, that is serum 25(OH)D, rose to normal or high normal levels without any signs of excess.[53] These doses are ten times the Recommended Daily Allowance (RDA) and 4000 IU is double the current vitamin D UL of 2,000 IU. The UL, Tolerable Upper Intake Level, is a value determined by a panel of experts to be the highest safe dose of a studied nutrient. This upper limit is calculated by review of scientific data which includes reported adverse events.

There are significant benefits to having adequate vitamin D in our bodies. Vieth's work at the University of Toronto, published, not yet published, and currently ongoing, strongly suggests that higher doses of vitamin D, in his research from supplements, not sunlight, can achieve and maintain levels of serum vitamin D in ranges that promote a maximally functioning vitamin D endocrine system (vitamin D as hormone).

Vieth has a habit of asking interesting questions and trying to determine the answers. His basis for believing we need more D makes sense. In his article *Vitamin D Nutrition and Its Potential Health Benefits for Bone, Cancer, and Other Conditions* [54] he asks "If evolution effectively designed our genome for higher levels of vitamin D nutrition than are prevalent today, might this not suggest health benefits of higher intakes?"

To Vieth's question I would add:

'What range of 25(OH)D might provide optimal health to a majority of humans?" and "What amount of sunlight or vitamin D might maintain that level in any given individual?'.

As you already know and will read repeatedly, we are not the same. We have different diets, different ethnicities, different skin colors, and different habits of dress. We live at different latitudes (distance from the equator). We all need vitamin D. We are not 'normal', we are individual. Determining the 'mean' (average) of all of us combined and making this our "normal" would be meaningless.

Vieth is a man with a mission and he deserves our attention. In the chapter, *How Much D Do We Need*? Vieth's work and others will be discussed. What these researchers have shown, convincingly to my mind, is that many people do not get sufficient vitamin D and may benefit from increased D or sunlight resulting in higher levels of 25(OH)D. Serum 25(OH)D is determined by a blood test and used to determine and monitor vitamin D sufficiency.

Vieth's specialty is studying supplementation of vitamin D which makes sense because he is located at the University of Toronto, Toronto, Canada. His latitude is about 43° north, not a great location to source adequate vitamin D from sunlight. This location problem (how much actual UV-B containing sun is available where you live) is reflected in studies done in Toronto and western Canada which show a high prevalence of vitamin D insufficiency.[6,55]

Other researchers have concluded too much D from supplements or sunlight may contribute to disease. For these clinicians and researchers the high levels of supplementation suggested by Vieth are considered potentially dangerous to long-term

health.[56,57,58,59,60,61] Further, concerns expressed by Muskiet [62] over the shortness of studies using higher doses of vitamin D, 4,000 IU or greater should be a caution to us all.

There are studies showing lower doses of vitamin D may equally increase 25(OH)D levels and as the possibility of higher doses of vitamin D causing vitamin D excess increases over a longer term, more moderate dosing or other ways to get D deserve our serious consideration.

What becomes apparent, after reading Vieth's work and the research of others, is that we, the researchers, physicians, you, and I, really don't have any consensus about how much sunlight and vitamin D humans need or don't need. We do not fully understand the complexities of determining the individual need for vitamin D, nor do we yet understand how we might get the right amount of D safely.

Hopefully this book will provide you with facts, about what has been learned in the past and may have been forgotten, what currently is accepted but may not be true, and enough of what is known to make the job of getting and keeping enough D not too difficult and very safe.

It is my intention to present information that will allow you to make knowledgeable choices. To completely embrace, good under all conditions, or to demonize and fear, bad under all conditions, sunlight, or vitamin D, are equally unsupportable positions.

Please join me on a fascinating journey of en'light'enment. (Sorry, I just couldn't resist.) This book is for those who have learned that leaving ones' well-being to others often results in losing one‘s' well-being.

CHAPTER 2 SHEDDING LIGHT ON THE COMPLEXITIES OF SUNLIGHT AND D

HERE COMES THE SUN

We live in fast times. In 21st century America when individuals believe they understand a particular topic the sum total of our latest discovery becomes a seven-second news flash or a shortened phrase on a news ticker. These bits are sometimes called factoids.

> *factoid, def. Encarta® World English Dictionary [North American Edition]*
> *unreliable information: something that may not be true but is widely accepted as true because it is repeatedly quoted, especially in the media (emphasis mine)*
> *single fact: a small and often unimportant bit of information*

On our topic of vitamin D often repeated factoids include:

- Vitamin D is important for bones.
- Vitamin D is made in our skins from UV-B found in sunlight or gotten from food or supplements.
- We can get all the D we need from sunlight, 20 minutes, arms and legs, three times a week
- Vitamin D from summer sun stores in our bodies for winter
- If we must avoid the sun a multivitamin with 400 IU of D supplies our daily need.
- Vitamin D from fortified milk provides adequate D for infants and children.
- Rickets has been eliminated in developed countries by supplements and fortification of foods.

(GP: Only the first two factoids in our list are true; the last five are NOT true.)

On sunlight:

(GP: before you read these be aware all of these factoids are either NOT true or at best partially true.)

- There is a fixed, average, amount of sunlight and vitamin D needed by all of us (Sunning arms and legs 3 times a week .)
- The ozone layer destruction is causing higher levels of toxic UV-B to reach the ground and this is the cause of increased skin cancers and the need to avoid the sun. This so called fact is repeated many places including in the June 1999 issue of Nursing.
- Sunlight must be avoided by all, especially between 10 AM and 2 PM.
- Sunscreen is necessary at all times for all children and adults to prevent skin cancer and skin aging.

To make this subject even more confusing, consider these news bites:

7/2002 Letter to the Editor, *Cardiovascular Research,* for Fremantle, Western Australia- Dr. Paul Norman, et al, Department of Surgery, Fremantle Hospital, The University of Western Australia, studying the role of vitamin D in heart disease found excessive vitamin D given to rats during pregnancy and while nursing caused changes in cells of the aortas of offspring. These changes could possibly lead to the development of atherosclerosis and hypertension in adulthood.(63)

GP: What is not immediately obvious is the vitamin D the rats were given the active hormone D, calcitriol, (more on this later) and not what a pregnant woman would ever be exposed to. The study has little application to human health. While too much D is not a good thing lack of vitamin D also presents significant problems. Pregnant women with low levels of vitamin D pass this deficiency on to the fetus, which has profound implications for later health. *(26,31,64,65,66,67,68,69,70,71,72,73,74,75,76)*

8/2002 *The Lancet,* Dr. Caryl A Nowson, Deacon University, Victoria , Australia, reports in the August issue of the Medical Journal of Australia that 23% of Australian women and 76% of nursing home residents tested had a marginal vitamin D deficiency. 80% of veiled dark-skinned pregnant women had a serious vitamin D deficiency. (22) Australia has a strong policy of sun avoidance as they have the highest rates of skin cancer in the world. (77)

GP: Trying to balance the need for sunlight to produce vitamin D and sun avoidance for skin protection is obviously not working out for us, the GP.

11/2001 *BBC News,* London A Finnish study published in the Lancet found infants given 2000 IU of vitamin D had an 80% reduced risk of developing Type 1, insulin dependent, diabetes. Infants given any dose of vitamin D had a somewhat lower risk than unsupplemented infants. [78]

GP: Finland has one of the highest rates of type 1 diabetes in the world. Finland is located in the far north, latitudes between 60-68°. At these latitudes little UV-B light is available at any time of year. In July, one of the few months when UV-B is present at the intensity needed to make D, at noon on a clear day sunbathers would require 24 minutes exposure to equal 5 minutes of tropical UV-B, nearly a 500% difference.

2000 IU D is a significant dose, which may be safe in Finland where vitamin D levels and UV-B are very low but this same dose may be unsafe for children of other ancestries or children in other locations with more available UV-B containing sunlight.

In the June 2003 issue of Parents magazine, page 146, Sally Kuzemchak warns parents,

> "Infants under 6 months shouldn't be in direct sunlight at all…"

Earlier in the April 2003 Pediatrics article Prevention of Rickets and vitamin D deficiency; new guidelines for vitamin D intake, [79] Gartner wrote,

> "Rickets in infants attributable to inadequate vitamin D intake and decreased exposure to sunlight (emphasis mine) continues to be reported in the United States. It is recommended that all infants, including those who are exclusively breast fed, have a minimum intake of 200 IU of vitamin D per day beginning during the second month of life."

What you need to know:

Like the Australians in the Lancet study a large percent of Americans are deficient in vitamin D but before you run out and buy a vitamin D supplement or head for the beach read on. It is possible to get excess levels of vitamin D from sunlight (though not easily); supplements; or a combination of both.

- In the U.S. and other countries, even those with enough UV-B sunlight, sun avoidance contributes to vitamin D deficiency. [16,40,80,81,82,83]
- Overuse of supplements with or without sunlight may result in vitamin D excess. [56,84,85,86]
- Vitamin D receptors, sites inside our cells on our DNA where vitamin D actively regulates many processes, are located in most of our tissues and organs which indicates vitamin D is important for the health of skin, muscle, glands, brain and blood and other body parts, as well as bone, some yet to be determined. [87,88,89,90,91]
- Rickets has reappeared, especially among people of color. Older successful preventative treatments like cod liver oil and sunbathing have been abandoned. [6,44,79,92,93,94,95,96]

- UV-B sunlight, the wavelength that produces vitamin D, varies by time of day, season, latitude and altitude. [97,98]

- Part of our current problem of widespread vitamin D deficiency relates to migration, immigration, ethnicity, and skin color.[6,81,99,100,101]

- Whole foods are not generally tested for D content. While there are some natural food sources of vitamin D, they are in short supply in most modern diets. Fish, especially cold water fish, historically the best food source of D, store D in fat. To get maximum D from eating fish requires consumption of the whole fish, especially the fat, organs, and skin, not a common habit in the U.S.

- Vegetarians and vegans are at greater risk of vitamin D deficiency, as the vegetarian diet provides no natural source of vitamin D. [41,102,103,104]

- Breast milk is a poor source of vitamin D in mothers with insufficient D which includes much of the population of the U.S. [71,105,106,107,108,109,110] Even when cod liver oil is used vitamin D content of breast milk may be low.[111]

The only way to know how much vitamin D you have is by testing. Vitamin D deficiency or excess will impair health and increase our chance of suffering from degenerative conditions that reduce both length and quality of life.

WHY NAKED AT NOON?

Is This About Sex?

Just in case you thought this was a book about sex, it is, but only briefly. It is likely vitamin D alters fertility in humans but to date there is little published research that makes a direct connection. [87,112,113]

It is known that vitamin D is necessary for reproduction in cows, chickens, quail, and rats. [114,115,116,117,118,119,120,121,122,123] In rats vitamin D deficiency caused uterine abnormalities and elevated luteinizing hormone (LH) and follicle-stimulating hormone (FSH), hormones controlling the fertility cycle. Male mice had fewer and less active sperm.[124] It seems possible humans might need vitamin D too. Perhaps researchers should consider testing the vitamin D levels of infertile couples.

Polycystic Ovarian Syndrome (PCOS), which results in infertility, has been treated successfully by Dr. Susan Thys-Jacobs.[125] Supplementing vitamin D and calcium restored normal menstrual cycles to most participants and two women became pregnant. The study was very small and treatment just two months long but it is an indication of a link between D and fertility and of more work needing to be done.[126,127]

There is one tantalizing bit of research on sex and sunlight. In his book Sunlight, World Health Publications, 1980, author Zane Kime, M.D. referenced a 1939 study published in the journal Endocrinology suggesting enhanced testosterone levels with sunlight exposure. Kime's review of the research fascinated me. I contacted the

staff at Endocrinology and they were kind enough to send me a copy. Just the title grabs your attention., I*nfluence of Ultraviolet Radiation upon Excretion of Sex Hormones in the Male*. [128].

Researchers Myerson and Neustadt used a quartz mercury lamp containing 52% infrared, 20% visible light, and 28% ultraviolet, a mix of UV-B and UV-A. The intent of the researchers was to determine if ultraviolet light would exert an influence on formation and excretion of sex hormones. They also wondered if skin was the most important factor or was it the photo-pituitary reaction (general exposure to bright light). Earlier studies with birds found ultraviolet (UV-B) irradiation was more effective than luminous (visible light) irradiation resulting in a sustained elevation of sex hormones.[129] Apparently many tropical birds with high UV-B exposure have two breeding cycles instead of one.

As the experiment progressed, different areas of the body were isolated for UV exposure; full front including genitalia; chest and head alone; genital region alone; full back; and a small portion of the back equal in size to the irradiated genital area. At no time did the intensity of exposure cause an adverse reaction of the skin such as sunburn.

In 1938 methods for determining hormone levels were limited. Researchers analyzed the excretion of androsterone in urine as a marker of sex hormone production. Androsterone is a breakdown product of testosterone and they assumed greater testosterone production to be the cause of any increase in androsterone excretion.

After receiving five irradiations of the full front of the body average excretion of androsterone increased by 120%. This level returned to normal 8 days following the last exposure. Researchers noted it took five exposures for maximum effect and continuing exposure did not further increase androsterone excretion.

What gets even more interesting is repeated irradiation of just the genitals, other skin covered, increased androsterone in urine from 110 to 320 IU per liter while whole body irradiation (with genitals covered) resulted in androsterone excretion of just 240 IU per liter.

Study limitations are important when interpreting the results. The patients in this study were hospitalized, not free-living, and the research was conducted between November and February when little UV-B is present in sunlight. Myerson and Neustadt stressed that men living under normal conditions and values taken during months when significant UV-B is present might show completely different responses.

On page 217 in Sunlight, Kime surmises this hormonal response to light might be why Greek soldiers practiced arenation- ~~–e~~xercising nude on the beach" to capture sunrays downwards and upwards reflected from the sand. He explains the Greeks thought this practice built muscles and suggests the mechanism might be muscle increase stimulated by increase in testosterone.

Kime believed this increase in testosterone was a direct effect of sunlight and had nothing to do with vitamin D.

Current knowledge suggests participants in his study would have had increased levels of vitamin D but, as you will see in a later chapter, full body exposure would have increased vitamin D more than limited genital irradiation. This analysis suggests

Kime's assumption is correct. Sunlight, even simulated sunlight as provided in those early sunlamps, may provide us with more than just vitamin D.

GP: This is just one of the many reasons I believe getting D from sunlight rather than supplements is the preferred method unless contraindicated or impossible.

In April 2003 researchers at the University of California, San Diego, reported one hour exposure to bright light, 1000 lux from a light box, increased luteinizing hormone (LH) by 69%. [130] LH controls secretion of sex hormones in men and women. The placebo was a regular light emitting less than 10 lux, which had no effect.

Lux is the light bulb equivalent of brightness or intensity of visible light. It makes one wonder what would happen if they had tried sunlight or simulated sunlight instead.

Research shows there is a link between testosterone and vitamin D [131,132,133] though exactly how they are linked is still unknown. In some studies testosterone raised levels of 25(OH)D, the form of circulating vitamin D used by our bodies to make the active hormone D. This connection combined with Myerson and Neustadt's work may mean sunlight exposure is a better way to get vitamin D than supplements. Sunlight would increase D and testosterone, a synergistic plus.

The testosterone connection may also help explain less osteoporosis in men and why men tend to have higher 25(OH)D levels. Another explanation for increased 25(OH)D in men may just be that men use less sunscreen, spend more time out-of-doors, and can remove their shirts without breaking the law. This would mean greater skin exposure to UV-B sunlight and thereby greater D production.

Vitamin D, whether from sun or supplements, does have an effect on muscle function and extreme muscle weakness can be a symptom of vitamin D deficiency.[4,30,134,135,136] Muscles do have something to do with sex.

The Naked Part

The 'naked' part of the title comes from understanding how vitamin D is produced in our skins. Your skin is composed of a thin surface layer of protective dead cells, the stratum corneum, covering the epidermis and dermis. Skin cells contain 7-dehydrocholesterol, 7-DHC for short, a cholesterol metabolite. (see Terms section) When 7-DHC is exposed to UV-B, it is converted to precholecalciferol and body heat then converts precholecalciferol to vitamin D_3.

The amount of available 7-DHC in a given area of skin is limited and the amount converted to precholecalciferol is also limited, an estimated 10-15% of initial concentrations.[137] Aging further reduces our supply of 7-DHC because we actually do become, relatively, thin-skinned.[138]

After 7-DHC completes its two step conversion to vitamin D_3 (cholecalciferol), it is carried by vitamin D-binding proteins from the skin to the liver for conversion to 25(OH)D. This cycle of D production, UV-B conversion, 7-DHC, precholecalciferol,

vitamin D_3, from skin to the liver, and replacement of 7-DHC in skin takes time. Conversion of precholecalciferol to D_3 takes about 8 hours. [137]

For any given area of skin only so much D will be produced within a given period of sun exposure. Some estimates used to determine our need for sunlight have been made calculating something like:

Surface area of skin X light intensity (of UV-B) adjusted for skin color = vitamin D

There are any number of problems with the calculation (in real world conditions), which include difficulties in knowing how intense the light actually is; calculating the actual effect of skin color; various parts of the body having more or less 7-DHC and alterations in liver function resulting in lower production of 25(OH)D. Under real world conditions time in the sun will produce a wide variation of 25(OH)D in the blood of persons seemingly similar.

The current recommendations, which suggest exposing the tops of your arms and legs for 20 minutes three times a week, under many real world settings will not produce much D at all.

When skin is exposed to a 295-300 nm narrowband UV-B light about 60% of 7-DHC is converted to D_3, cholecalciferol. When skin is exposed to full sunlight, a maximum of 20% conversion of 7-DHC to cholecalciferol occurs.

Other UV wavelengths found in sunlight photolyze (breakdown caused by light) the intermediate precholecalciferol to inactive substances other than vitamin D_3. Both precholecalciferol and vitamin D_3 are photolyzed to inactive metabolites if sunlight exposure continues. Obviously there is a time factor to consider in sunlight vitamin D production as well as skin surface volume.

GP: This means spending excess time (any time greater than you personally need to make D) in sunlight won't increase your D and may even deplete some of the D you've already made, and it will damage your skin.

While overexposure just doesn't make any sense, underexposure won't promote health either.

What has been determined is when UV-B is abundant in sunlight (more tropical locations or high altitudes, summer time, midday) the more skin exposed the more D produced AND in less time. In higher latitudes (more distant from the equator) with less available UV-B light, exposing 80% of your skin, mostly naked, to the highest available UV-B can produce maximum levels of vitamin D in the shortest period of time.[139,140,141,142] This is very good news. It means we can minimize our total sun exposure and still reap maximum benefits.

And The Noon

BUT this maximum production-minimum exposure concept won't work before 10 AM or after 2 PM in latitudes above 30° north or south. Uh-oh!

This is actually a book about the complex system, which encompasses man's (the universal male and female sense) relationship with the sun.

In most of the United States and countries with latitudes greater than 30°, north or south, the band of light necessary to produce vitamin D within our skin SAFELY is only present in sufficient quantities midday, the noon part, and then only certain months of the year. (143)

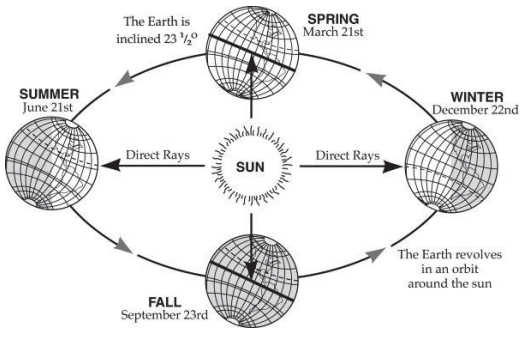
I capitalized 'safely' to get your attention. Throughout this book you will read 'too much, too little and just right' repeated many times. I think of it as the Goldilocks' Principle. Goldilocks was only interested in what fit her. Too little, too much or the wrong kind of sunlight exposure, for you, will not support your health and longevity. We need vitamin D and as of today, many of us, of all ages and races, don't have enough. What has yet to be determined is how much you need and that is a determination that, at present, can only be made by you.

Our primary source of D, actually our only source of D, is sunlight. Even if we get D from fish or cod liver oil or eggs or any other natural source that source made it from sunlight or got it from eating plants containing vitamin D produced from sunlight.(144) The most 'artificial' vitamin D supplement is still made by sunlight, sort of, and isn't really artificial at all.

Any vitamin D supplement not derived from fish liver oil is made by irradiating either 7-DHC or ergosterol. The term irradiation when used in conjunction with vitamin D means exposure to that narrow band of UV-B light.

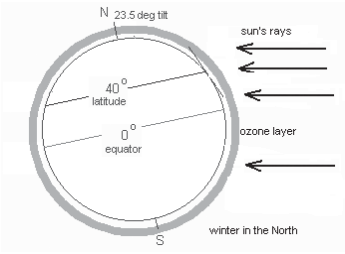
Exposing your full body, front and back, to sunlight when UV-B is at its greatest intensity, produces your maximum quantity of vitamin D very rapidly. Robert Sayre and colleagues studied the effect of solar angle on production of vitamin D.(143).

Movement, the earth's rotation on its axis and its path around the sun, alter the angle of light reaching the earth. This causes the dramatic changes in UV-B availability throughout the day and in more northern and southern latitudes, throughout the year.



The angles, north and south, east and west, of sunlight reaching earth's surface are called the solar angles. In latitudes between 23.5° and –23.5° the seasonal shift of earth's position causes the north-south solar angle to reach 0° twice a year.

In latitudes above 23.5° and below –23.5°, including all locations in the U.S., sunlight is never actually 'overhead' (0°) at any season. The daily east-west solar angle changes from 90° at 6 AM to 0° at noon and -90° at 6 PM.



Solar angle determines the path sunlight travels through the ozone layer surrounding the earth. UV-B, the band of light that produces vitamin D, is absorbed by ozone. The greater the angle the more ozone there is to be penetrated which absorbs UV-B. This solar angle is greatest in early morning, evening, and winter, allowing little UV-B to reach earth's surface in latitudes more distant from the equator. The angle is least, the sun closest to overhead, at noon in summer.

Sunlight contains UV-B and UV-A. Both bands of light cause skin damage when there is excessive exposure. UV-B will damage skin more quickly than UV-A. Its intensity is much greater. UV-A penetrates ozone so the amount of UV-A remains relatively stable throughout the day and year. Approximately 99% of the UV light reaching the earth‘s surface is UV-A.

When the sun takes a more direct route through the ozone, as in summer and/or midday, allowing the greatest percent of UV-B, Sayre found maximum amounts of vitamin D were produced before MED. You'll read more about MED later. The short explanation is a MED is the Minimal Erythemal Dose, the minimum amount of ultraviolet light needed to produce *erythema*.

Erythema means redness produced by congested capillaries. A number of things can cause erythema. One of them is ultraviolet light. Erythema doesn't mean sunburn though erythema is present when you get a sunburn.

In the world of UV light researchers and dermatologists erythema is:

Any, however slight, redness or tenderness occurring within 24 hours after exposure to ultraviolet light.

Erythema is NOT sunburn. Erythema occurs some significant period of time before sunburn, depending on skin type.

Very light skins can _pinken‘ rapidly when exposed to UV light. (Yes, I did make up the word but it looks like pinkness to me.) While UV-B is primarily responsible, wavelengths at the lower end of the UV-A band also contribute to erythema; it just takes longer as UV-A energy is not as intense (scientists say 'biologically active').

If sunning takes place when UV-B is present but low in intensity, because of greater solar angle, such as occurs early or late in the day or in winter, erythema, produced by shorter wave UV-A with a bit of UV-B, will occur before appreciable amounts of vitamin D are produced.

What Sayre's research means in simple terms:

If we try to get vitamin D when little UV-B is present, by hour of the day or season of the year, we are likely to suffer skin damage before we make much D.

If we sun when UV-B is most intensely present many of us can get all of the D we need before sun damage occurs. (As long as we stop sunning before we 'pinken'.)

Example: In the Bay area, just north of San Francisco, sufficient sunlight for optimal D production is available on clear days from May through August, midday, between 10 AM and 2 PM.[145] Sunning near noon on a clear day, mostly naked, persons with very light skin could make all the D they need from 10 minutes exposure of front and back, 20 minutes total, and without 'pinkening'.

So now you know why I am promoting 'naked at noon', well nearly naked, unless you spend your lunch hour in a very private setting. I am also promoting long lunch hours, outdoor sidewalk and rooftop cafés, and romantic, loose, drapey, clothing, and hats, easily arranged to allow skin exposure to sun when desired and otherwise act as an exceptionally efficient sunscreen.

COMPLEX SYSTEMS AND BIOCHEMICAL INDIVIDUALITY

How do we sometimes go wrong (so very wrong) in developing health information and policies? Much of physiologic and biologic science to date has been developed and defined with linear methodology.

linear def. of or in or along or relating to a line; involving a single dimension.

We look for the one thing, one answer, one key that fits.

Man's manipulations, of life, of living systems, are always a trade off. If we truly wish to understand a living system, which includes our own body, it becomes necessary to develop information within a complex systems model.

Complex systems are dynamic, in constant motion, composed of many moving parts that act, interact, and adapt. Complex systems require us to see the parts and the whole, and the movement, the relationship between the parts and the whole.

Example: To understand a tree we need to see the variety of trees and other life in the forest and the location of the forest; the differences of environment surrounding a forest's location, including latitude, altitude, water, sunlight and soil. As we study a tree‘s 'system‘ we begin to recognize there various kinds of forests and trees and each need different elements to survive. Not all trees grow in all locations and as soils change, over time, the trees and other life within the ecosystem‘ also change.

A further complication arises as we are hoping to understand humans, not trees, and humans have the unnerving habit of getting up and moving about whenever they like causing them to show up in 'forests' not designed for them.

Traditional medicine describes a symptom and gives a treatment BUT, how interesting, the treatment almost always has a side effect, something unwanted and often not positive. It is impossible to shift one single thing without many other things moving, sometimes in ways that are positive but sometimes in ways we cannot foresee and may not want.

Where did the unwanted result come from? How do we then treat the side effect and what new conditions, positive or negative, will then appear?

reductionism def
simplification: the analysis of something into simpler elements or organized systems, especially with a view to explaining or understanding it
oversimplification: the oversimplifying of something complex, or the misguided belief that everything can be explained in simple terms

We are born reductionists, quantifiers and qualifiers. Adam was given the job of naming and we are still at it. We dissect and isolate; put name and number to all manner of things. In our quest for knowledge we stop time and space to define the thing we are analyzing.

We try endlessly to capture the essence, in whatever field we explore, by removing the subject of our study from its system. Think about that for a moment. Just how smart are we?

What happens between a drug and a cancer cell in a test tube or in the skin of a specially bred naked rat exposed to simulated sunlight often won't happen in a living human in the real world.

Today science looks for answers to our ills in such elevated disciplines as the Genome Project, stem cell research, and genetic engineering. Forty years ago it was antibiotics that were to save the world from infectious disease and to an amazing degree they did. All of these disciplines continue to contribute to new knowledge and benefit our general health and longevity but none of them is 'the answer'. We will still continue to suffer from diseases and conditions inherited, contagious, or degenerative.

In alternative medicine the quest for ultimate truth is routinely reported as FOUND in the latest vitamin, mineral, homeopathic medicine, herb, amino acids or derivatives thereof, or of late, 'natural' hormones applied topically, injected, swallowed or sucked.

This book isn't about the fountain of youth, the genetic key, or the ultimate answer to all mankind‘s ills. It is about one very specific and very complex problem. I hope to change the way you look at things; the earth, the sun, your body.

Here we are, you and I, on a planet traveling through time, spinning in space, around an immense, fiery, globe we have named the Sun, center of our solar system, which is just a small part of something so vast it is unimaginable.

Note to the GP: The 'spinning in space' part is responsible for the way we get vitamin D. It is the rotations of the earth, on its axis and around the sun, that create solar angle and the cycles of space and time. This interrelationship of earth and sun determines the availability of D producing light.

Why Understanding Complex Systems Modeling Is Important

The birth of complex systems theory began in the 1700s among mathematicians trying to solve the Three Body Problem. The problem involved predicting the orbits of

three bodies, the sun, moon, and earth, using certain known quantities, things like position, mass, and velocity. In the mid-1890s Henri Poincaré showed the problem could not be solved with an absolute, precise answer.

The initial problem involved a desire to know 'what will happen if'. One should be able to figure out the answer 'if they had sufficient facts', like an algebra problem. What seemed simple turned out to be impossible. The future was not precisely predictable. This discovery marks the beginnings of chaos theory and complex systems.

Like the Three Body Problem or the problem of predicting weather (including global warming or cooling or any other form of ‗scientific' divination) understanding the complexities of an individual's health and disease are not exactly predictable. Whatever you do or don't do there are no guarantees.

A quote from An Introduction to Complexity in Social Science by Bernard Pavard & Julie Dugdale GRIC-IRIT, Toulouse, France:

> "It is often very difficult to determine the boundaries of a complex system. The boundary is based on the observer's needs, the actors and the context, rather than on any intrinsic property of the system itself.
>
> …The reduction of complexity is an essential stage in the traditional scientific and experimental methodology (also known as analytic). After reducing the number of variables (deemed most relevant), this approach allows systems to be studied in a controlled way, i.e. with the necessary replication of results. This approach in itself need not be questioned. . However, when considering complex socio-technical systems it is appropriate to analyze precisely the limits of the approach."

Note to the GP- Within the complexities of life, sunlight, and vitamin D, the individual is key to the boundary. While it is true we need to continue clinical research in nutrition and health, researchers must be willing to admit study limitations. The current approach in medical and nutritional research often reduces 'variables' (the complexities) to such an extent that the outcomes and applicable conclusions must be questioned.

'Variables' are the essence life. When researchers reduce variables in a study for control, extrapolate the results and then use this data to determine harm or benefit or to market a drug or nutrient, it is from a place of ignorance, not intelligence. Ignorance ignores the variables; which in understanding our topic, sunlight and D, include race, sex, location, diet, lifestyle, gastrointestinal health, nutrient interactions, and genetic anomalies as well as other known and as yet unknown variables.

> *extrapolate def. to use known facts as the starting point from which to draw inferences or draw conclusions about something unknown*

Yaneer Bar-Yam's definition of complex systems may be found on the New England Complex Systems Institute website, a great place to learn more about this expanding discipline. His work is offered here with permission from the New England Complex Systems Institute and Yaneer. Yaneer is responsible for my tree and forest images earlier. The comments in parenthesis are mine.

Author: Yaneer Bar-Yam Website: http://www.necsi.org

" Keys to the complex system, complexity and emergence:

Emergence is…

1) ...What parts of a system do together that they would not do by themselves: collective behavior.

(KS- the human body is an example of a collective society, the cells communicating among themselves, old cells dying and new cells being born, cells in a body do not act like cells isolated in a Petri dish)

2) ...What a system does by virtue of its relationship to its environment that it would not do by itself: e.g. its function.

(KS- cells communicate with one another and bodies as a whole, influence and are influenced by the temperature of the air, the sun, food, water and much more These interactions occur in just seconds or over much longer periods of time to sustain life in whatever its form. Recent research is discovering that it is not just DNA that influences how cells replicate, mRNA once thought to just carry instructions is now considered to dynamically interact between the cell and its environment with the ability to change the message in response to current conditions.)

3) ...The act or process of becoming an emergent system.

(KS- the act of becoming includes birth, growth, organization, and maintenance of a living body, a family, a community, a state)

According to number 1 emergence refers to understanding how collective properties arise from the properties of parts. More generally, it refers to how behavior at a larger scale of the system arises from the detailed structure, behavior, and relationships on a finer scale. In the extreme, it is about how macroscopic behavior arises from microscopic behavior.

According to this view, when we think about emergence we are, in our mind's eye, moving between different vantage points. We see the trees and the forest at the same time. We see the way the trees and the forest are related to each other. To see in both these views we have to be able to see details, but also ignore details. The trick is to know which of the many details we see in the trees are important to know when we see the forest.

In conventional views the observer considers either the trees or the forest. Those who consider the trees consider the details to be essential and do not see the patterns that arise when considering trees in the context of the forest. Those who consider the forest do not see the details. When one can shift back and forth between seeing the trees and the forest one also sees which aspects of the trees are relevant to the description of the forest. Understanding this relationship in general is the study of emergence.

… emergence refers to all the properties that we assign to a system that are really properties of the relationship between a system and its environment."

GP- Understanding the properties of the sunlight and vitamin D 'system' include answering the questions where did my ancestors live, where do I live, how much UV-B sunlight is available, do I go in the sun, if I do go out how much skin do I expose to the sun, do I use sunscreen, what nutrients do I need, get?

—One of the problems in thinking about the concepts of complex systems is that *we often assign properties to a system that are actually properties of a relationship between the system and its environment*. Why do we do this? Because it makes thinking about what is going on simpler. Why can we do this? Because when the environment does not change, then we only need to describe the system and not the environment in order to give the relationship. Thus, the relationship is often implicit in what we think and what we say."

(GP- Our problem, regarding sunlight and vitamin D, is the relationship between our individual genes and our immediate environment. Location, lifestyle, and diet, are essential factors in vitamin D sufficiency or insufficiency and to further complicate our situation, the environment itself changes on a daily, even hourly, basis. These inter-relationships are often ignored in research and in diagnosis and treatment of vitamin D deficiency. They are regularly ignored when formulating public health policy regarding sunlight and vitamin D.)

—The role of relationship:
… when a system is related to parts of a larger system we talk about its ecosystem.

The role of pattern:
When there are relationships that exist between parts of a system we talk about the existence of patterns of behavior.

The idea of emergence is often contrasted with a reductionist perspective. The reductionist perspective thinks about parts in isolation. It is the often-vilified "anti-complex systems" view of the world. However, even the idea of a system is based upon a partial reductionism. To understand this, one should carefully understand the notion of approximation or "partial-truth" which is essential for the study of complex systems."

Thank-you Yaneer.

Why put you through a mini explanation of complex systems? Because unless you get even the slightest 'feel' for this you will not understand sunlight, vitamin D, nutrition, or 'health', what it is, and how to reach for it.

In the last paragraph Yaneer explains "notion of approximation" or 'partial-truth'. Science and medicine can give us generalities, approximations that can point us in the right direction, for some of us, some of the time. Science and medicine cannot 'fix everything' or determine the absolute correct path for us on an individual basis, not now, not ever. Over and over in this book you will see the words –may, perhaps, is associated with, seems to, is likely, suggests", and other very fuzzy terms.

Complex systems are inherently fuzzy. Life is very fuzzy. What research can do is give us a sense of general outcomes and directions. The value and application of information must be self-tested and self-determined.

The failings of the linear, reductionist, approach in the field of health may be demonstrated with any number of examples. The promotion of the low fat diet which has contributed to dramatic increase in carbohydrate intake and associated obesity, insulin resistance and increased incidence of adult onset diabetes.(146) Adult onset diabetes is currently considered an epidemic with a current incidence of 18.2 million (6.3 % of US population; CDC Diabetes Fact Sheet 2003) and a projection 48.3 million cases in the US by 2050.(147,148) Type II diabetes, once called _adult onset' diabetes is now appearing at younger and younger ages. (149,150,151).

Weinberg, S. L. 3-3-2004 J.Am.Coll.Cardiol. 43 731-733
The diet-heart hypothesis: a critique

The low-fat "diet-heart hypothesis" has been controversial for nearly 100 years. The low-fat-high-carbohydrate diet, promulgated vigorously by the National Cholesterol Education Program, National Institutes of Health, and American Heart Association since the Lipid Research Clinics-Primary Prevention Program in 1984, and earlier by the U.S. Department of Agriculture food pyramid, may well have played an unintended role in the current epidemics of obesity, lipid abnormalities, type II diabetes, and metabolic syndromes. This diet can no longer be defended by appeal to the authority of prestigious medical organizations or by rejecting clinical experience and a growing medical literature suggesting that the much-maligned low-carbohydrate-high-protein diet may have a salutary effect on the epidemics in question.

The determination of elevated cholesterol levels as the primary cause of heart disease is also questionable since between 30-50% of persons with heart disease have normal cholesterol levels. (152) Factors including deficiencies of B-12, B-6 and folate with associated hyperhomocysteinemia may be another equally important cause of heart disease in some persons.(153,154,155,156,157,158) Low levels of vitamin D, magnesium, calcium, potassium or other essential nutrients or high intake of omega-6 fats and low intake of omega-3 fats also play a role in heart disease. (159,160,161,162,163,164)

In African Americans and in Arab women low levels of vitamin D are strongly associated with hypertension and congestive heart failure and correction of vitamin D insufficiency may improve their condition.(165,166)

The simplistic idea that the use of sunscreens will protect us from skin cancer has been an abysmal failure when you look at the statistics. Sales of sunscreens have grown from tens of millions to more than half a billion dollars yearly. At least locally I can confirm it is being used according to instructions as I have watched moms at local parks faithfully and frequently applying sun blocks to all exposed body parts. Yet the rate of melanoma has more than doubled during the same time period. [167,168]

Basal and squamous skin cancers also show an increase in white populations. The idea that this occurs because we get too much sun and do not use enough sunscreen is disingenuous and perhaps even intentionally deceptive.

Recently members of the health community blamed the sunscreen manufacturers for overstating the protective effects of sunscreen. Noting that UVA protection may be as important as UVB there are no standards and as yet no full protection UVA sunscreen has been concocted.[169,170,171]

GP: Clothing protects from both UVA and UVB and has been used successfully throughout history by persons in high sunlight locations AND it doesn't have to be UV rated clothing either.

Our individual, personal, response to the sun is directly related to our genes born out of the habitat, both latitude and altitude, of our ancestors (at least 6 generations prior). Ancestry, our ancestral history, must then be combined with our current location, the idea of a rootless moving tree now outside its ancestral forest.

Location for our purposes is determined by latitude and altitude because we are discussing vitamin D produced by UV-B sunlight, only available in significant amounts year round in the tropics and subtropics. In all other locations more distant from the equator many parts of the day or year lack significant amounts of UV-B, and no, the suspected depletion of ozone has not changed this.

Beginning with the industrial revolution and continuing to the present day massive increase in urban living, this ‗location factor' of available access to UV-B must be corrected for countryside and city. The correction is necessary because while some suggest the ozone is failing, pollution in cities worldwide blocks UV-B light by producing pockets of ozone in the troposphere. (See *How Do We Get D?*) UV-B is critical for production of vitamin D and these urban ozone covers are contributing to vitamin D deficiencies in even our most sunny cities like Los Angeles as well as other cities worldwide. [10,92,172,173]

Location plays an important role in timing, daily and seasonally. As mentioned previously, the title of this book, Naked at Noon, in part reflects the importance and variability of the hourly, daily and yearly positioning of the sun and consequently UV-B light..

An individual's location on planet earth is a rarely considered element in understanding health. If your skin is dark and designed for intense exposure to ultraviolet B and you have migrated or immigrated to an area with less UV-B; or your skin is light and you now live where UV-B levels are high; taking a supplement or medication or using a protective lotion may not alter the reality that your circumstances, lifestyle, location, latitude and/or altitude, no longer support optimal health and well being for your ancestral type.

You may well be a tree in a hostile forest.

As children one of our earliest lessons in understanding complex systems was recognizing appropriate portion size and 'fitting' in. This principal is demonstrated in the story of Goldilocks. Too hot, too cold, too much, too little, too big, too small and just right begin the understanding that even the term moderation has different meanings in different situations with different subjects at different stages of growth.

Life individually, and collectively all life on earth, requires just enough and not too much, sun, air, water and food. All living organisms have specific requirements for optimal health. These requirements fit within a narrow range and even this narrow range varies at different life stages and when life is challenged by injury or illness.

Your essential requirements are not necessarily the requirements of your neighbor or nowadays even a family member. Until the 1800s most humans grew up within 100 miles of where they were born eating foods grown locally in season, drinking local water, and getting UV light exposure specific to their ancestral type. They married locally, someone with similar needs, and had children predisposed to the environment.

Migration, immigration, and intermarriage have altered us in ways yet unknown and usually not even considered. Food and water nutrient content are specific to various soils and climates and UV light exposure. We may be able to move about but we may not be able to find the elements we need in our new environment.

Just how do you best supply the food, water, and light requirements of a Hawaiian-Inuit or an African-Anglo, or a light skinned person in the tropics or dark skinned person in the higher latitudes?

GP: Quick geography refresher: Lower latitudes are near the equator, at 0°-30° which include the tropics and sub-tropics. Higher latitudes are those more distant, both north and south.)

As amounts of essential elements change, the nature of life changes. We change and are changed by the food, water, sunlight, and air we consume. Our biochemical individuality and complexity, as it relates to ancestral location and lifestyle and current location and lifestyle, become our most personal experience of a complex system.

The Arrow of Time- There Are No "Do-Overs"

The idea of complex systems and cycles is further developed with 'the arrow of time' as described in Prigogine's The End of Certainty, Free Press, 1997. This arrow of time is important to our topic. If we try to reduce the understanding of sunlight and vitamin D to our few opening statements we are powerless to change our current situation, which includes dramatic increases in diseases associated with too much or too little sunlight, vitamin D, or substances depending on vitamin D.

If you ignore the 'arrow of time', that there is an irreversibility of processes, we end up with missed opportunity.

It is clear that early bone development strongly influences lifetime bone mass and the structure and function of the jaw and teeth.[174,175,176]

Adequate or deficient D during pregnancy and infancy influences the development of the entire vitamin D endocrine system.[177,178,179,180,181,182,183,184,185,186,187] While we need to understand the complexities of vitamin D and sunlight, our sources, individual responses, environmental factors and dangers, we also need to grasp that the longer we wait and the slower we respond the more irreversible the outcomes, societal and personal, and costs, of misunderstanding sunlight and vitamin D.

We so love to believe in a static linear system that allows us to push just one button and have just one result, the one we want. We love the idea of reversibility, being able to 'take it back', of getting a 'do over'. We love the people who sell us the products or politics that promise the 'answer', to fix it all, but we are growing up to find there is no one button nor one pill nor one answer and some decisions made earlier in our lives, by ourselves or others, have consequences later we cannot change at all..

Adequate nutrition which includes optimal vitamin D and minerals for pregnant moms may help prevent low bone mass, malformed teeth, myopia, childhood diabetes, and much, much, more. In dealing with human health, when we wait too long to apply what we know, there are often no 'go backs'.

When Complexity Allows Experts to Perpetrate Poor Science

In A God Within, Charles Scribner Sons, New York, 1972 author Rene Dubos wrote:

"A new form of panic is being generated among the general public by the thought that the human mind cannot possibly apprehend the complexity of the interrelationships between the social structure and scientific technology.'

Further he continues,

'The alarm over the possibility of a technological takeover of our own lives was made more vivid, plausible, and fashionable by the French philosopher, Jacques Ellul in La Technique ou L'Enjeu du Siecle, first published in 1954… From the point of view of technique, efficiency is the ultimate criterion of success. For the sake of efficiency social institutions and customs must be continuously changed, and traditions must be rejected even though they are the expression of ancestral wisdom. Technique demands that life be regimented, mechanized, and automated to fit the efficiency of machines…

'John Kenneth Galbraith concludes … the modern technological society is an almost self-contained system. The system still depends on the public, but it secures acceptance of its products through an artificial demand created by advertising and government policies. In practice, it is accountable only to an essentially autonomous 'techno-structure'…

In Galbraith's techno-structure as in Ellul's technique,

_the efficiency of the social system is more important than the individual life of the human person.'

When customs and traditions, ancestral wisdom, and individual life become variables to be ignored, our experts become highly educated ignoramuses who control public knowledge and worse, public policy.

ignoramus def. late 16th century.
Via modern Latin, we ignore, from Latin, a form of ignorare

When persons, because of medical promotion or governmental policy, buy and use sunscreens, which they may or may not need, and which may or may not work, to prevent skin cancers; or habitually avoid sunlight though they may be persons who need more light; they become victims of public health policies, supported by limited, though often peer supported and promoted, scientific evidence.

Science and government have repeatedly and shortsightedly contributed to more disease throughout our history.

In the same light, governments also have, in the case of sunscreens, 'secured acceptance' of products 'through artificial demand created by advertising and government policies', exactly as stated by Galbraith.

THE ELEMENTS OF LIFE

"The sum total of human knowledge consists of an endless series of doubtful bulletins."
Thomas L. Masson, The City of Perfection, The Century Co.1927

Since sunlight is our major source of vitamin D and sunlight is variable, by latitude, altitude, season and time of day and response to light is inherited, involving both skin color and genetic propensities for production and storage, the whole idea of source and production shows itself to be one very complex and dynamic system.

When I began this book, I wanted a word to describe this amazing complexity that comprises our existence in relationship to everything, food, water, air, light, the whole thing. I realized, on a late summer, foggy, morning walk in the hills near my home in northern California, that there already was a word that encompassed it all.

LIFE is the whole fuzzy, messy, spectrum of things including the parts and the movement itself. We, in relationship to each other, in relationship to the earth, in relationship to the sun, in relationship to space, in relationship to time. As we move through space and time it changes and we change and it all changes again… LIFE.

Policies to promote health as recommended by experts have limitations. Experts are limited by current knowledge, which at the present time, in matters of health, is continually changing; that endless series of doubtful bulletins.

Often past knowledge, and the policies put in place derived from that knowledge, are found to be 'not such a good idea' when we discover new relationships and interrelationships. It is my hope this book helps its readers understand that when

we 'discover' and 'fix' this thing that is bothering us, whatever it may be, something else may bother us even more.

We can keep people alive with antibiotics but then we have to feed, house, and clothe them. We can use fertilizers and pesticides to grow more crops but we then pollute our air, food, water, the life in the water, and eventually ourselves. We can use DDT, pollute the soils and water and save lives or stop using DDT and contribute to 500 million new cases of malaria since the demise of DDT and 1-3 million new deaths each year.[188]

We make pesticides and the bugs become tolerant to them. We make and use antibiotics, including anti-bacterial hand soaps and room sprays, to kill invisible 'bugs', and the bacteria become tolerant to them and evolve into new, ever-changing super bugs. We can treat conditions and diseases with drugs and then watch those 'saved' die from the side effects of the drugs that ‗saved' them.

We can genetically engineer a new trait into an existing species of plant but have little understanding and no control over its mutations or its spread, or new problems that may emerge over time.

This is not about stopping progress. We are far beyond any such choice and given real human health history we wouldn't like the living conditions or lifespan of our ancestors much anyway. You would be amazed at the amount of air pollution caused by open-hearth fires.

What we need is the will to admit the potential and actual problems we create from our solutions and we need to be prepared to deal with them in a more honest and realistic way.

There is a point to this, stay with me. I am not suggesting we stop trying to combat degeneration, disease, and pestilence. I just want to get across the idea of unintended consequence as inevitable and a consideration when undertaking any change.

As this applies to our current topic there is increasing evidence that sun avoidance and use of sunscreens has led us, in the United States and abroad, to large populations suffering from chronic low-level or even serious, acute, vitamin D deficiency. Thus, unintentionally, we may be contributing to any number of life-threatening or chronic degenerative diseases.

We need better understanding and thereby better solutions.

LIFE'S REQUIREMENTS

In general, the requirements of life are clean fresh food, clean air, and water, respite from the more adverse elements, and LIGHT. With rare exceptions, none of them applying to humans, all life requires light. When I think about it, it is likely there are no exceptions, as even those things that don't need light depend on things that do.

For humans, birds, mammals and reptiles UV-B is of primary importance as life‘s only source of vitamin D. For all mammals, birds, and reptiles life is not possible without sunlight vitamin D. In reality there is no life without the sun.

solar def. adjective
1. from the Sun: relating to or originating from the Sun
2. operating using energy from the Sun: using the Sun's radiation as a source of energy
3. measured by the Sun's position: measured with reference to the Earth's movement in relation to the Sun

Our sun has "burned" for more than 4.5 billion years and will continue to shine for several billion more. Our world revolves around our sun. Historically humans have feared, loved or worshiped the sun, and in our time, now with 'scientific evidence', we once again fear, love, or worship the source of life in our solar system.

A day in the sun, an outdoor picnic, a ballgame at the park, a day at the beach with friends, may lead to profit for the sunscreen manufacturer, a healthy glow, or a miserable night of sunburned skin against the sheets.

The current round of experts has determined that the sun is bad for us. It will, at its worst, kill us fairly quickly by causing the dreaded cancer, melanoma, or produce cancers not as deadly, but serious none the less, squamous or basal cell carcinoma, or if we escape cancer at least prematurely age our skins.

We have been told to keep our children and ourselves out of the sun and if that is impossible to compulsively use on every surface of our bodies a waterproof, sweat proof, SPF 45 sunscreen applied frequently. I am only slightly exaggerating.

Other experts have determined the ozone is being destroyed, exposing us to ever more hazardous levels of UV-B and this excessive sunlight is responsible for the current epidemic levels of skin cancer with more devastating damage predicted for our future. The problem with this expert opinion is that it is just that, opinion. The truth is much less clear.

Our ancestors lived in the light. Surviving childbirth, infectious disease, war or famine (big killers all) many of our ancestors died with teeth intact, a fact noted and photographed by Weston Price, DDS, researching the dental health of indigenous peoples throughout the world. Price published his findings and photographs in 1939 in his book Nutrition and Physical Degeneration. [189]

Prior to improvements in sanitation and food supply, the numbers of these early survivors were relatively few but they were hardy stock providing excellent survival genes for their offspring. Each of these survivors would have expressed genes that complimented their access to and storage of locally available nutrients necessary for life including variations of sunlight and vitamin D.

Whether located in tropical or temperate climates our ancestors were, by necessity, physically active and most waking hours were spent out of doors, a lifestyle in direct contrast to that of children and adults today. Prior to the industrial revolution, agricultural societies and hunter-gatherers lived outside, shelters providing protection for sleep or during extreme weather.

Our ancestors (and many today in lower latitudes) were aware of the need for sunscreen and used clothing and shade to block too intense rays of light. In tropical and subtropical locations midday activities were avoided, replaced with the siesta or its regional equivalent.

Prior to the 1700s rural life provided an outdoor lifestyle with regular sun exposure, and for many, access to wild game, fish, meat, poultry, eggs, and dairy, all natural sources of vitamin D.

The industrial revolution beginning in England and Wales in 1740 with factories for textile production, started the human exodus out of the countryside and into the cities. America's industrial revolution was not far behind. By 1813 British workers in industry outnumbered agricultural workers for the first time in human history.

Factory production kept workers inside during most daylight hours and provided abundant air pollution to block the sun from city streets during the day. This profound change in developed countries marks the beginning of a cultural decline in access to sunlight vitamin D. Such a dramatic change in lifestyle, food, physical labor and sunlight exposure, had never occurred in man's history.

It is during this time of movement, from rural to city living, rickets, the most severe expression of vitamin D deficiency, began to be recognized and described by physicians.

Today the move to an indoor lifestyle and sun avoidance continues to grow worldwide, expanding in both developed and developing countries.

White-collar workers became a force in the marketplace in the late 1800s. Today white-collar workers compose almost 50% of the work force in America outnumbering manual workers by 11 million persons. The white-collar revolution keeps more of us inside even longer than our factory employed brethren of the past and present. We spend most of our day behind a desk and behind the wheel.

Both changes, from agricultural to industrial and industrial to white-collar and service work, have contributed to a new level of prosperity for many Americans and at the same time to possible serious complications of a city lifestyle. Our children start school at a younger age, indoors, and continue education, indoors, for more years than any prior generation.

Recess (outside play) and physical education as a daily activity has been in decline for more than 10 years. In high school approximately 38% of females and 46% of males were active in PE for 20 minutes or longer which means greater than 50% of those who managed to get to PE daily managed to remain inactive during class. (Participation in High School Physical Education --- United States, 1991—2003) As of 2005 high schoolers watching more than 3 hours of TV a day is estimated to be about 38%. (National Youth Risk Behavior Survey 1991-2005) If you add in time spent on cell phones, computers, and video games the amount of outdoor and physical activity is further reduced.

More of us will live longer. That is called life expectancy. It doesn't mean that we live to be 120 but that more of us reach 70, 80, or even 90. In the United States and other developed countries we have access to more and better food than at any time in history, though some would disagree given our equal access to junk food. We have cleaner water and better sanitation, all important components of health and longevity.

Many of the changes that contribute to our longevity are quite recent. Our food supply is more abundant and safer than ever before providing essential protein, fresh fruits, and vegetables year round. Antibiotics keep alive many who in earlier times

would have died from infection in infancy or childhood, from injuries suffered fighting wars, or during childbirth.

Great stuff this 'progress of civilization'. To understand our present (and future) it is important to understand our past.

For more information on our health history, how health happens, and why we are doing better, not worse as some suggest, take time to read some health history. Informative choices include
Mainsprings of Civilization, Ellsworth Huntington, Mentor, 1945;
Health and the Rise of Civilization, Mark Nathan Cohen, Yale University Press, 1989;
Mirage of Health, Rene Dubos, Rutgers University Press, 1987: and a personal favorite
Plagues and Peoples, William H McNeill, Anchor Books, 1976.
Each of these books offers a slightly different view of the role of health and disease in the progress of man. All offer deep insights into what health means and how it affects our history and our present, collectively and individually.

The Complex Health Issues We Face Today

Between 1900-2000 the western world and the United States in particular has seen a dramatic increase in depression, obesity, degenerative diseases including hypertension, adult onset diabetes, heart disease, and osteoporosis. An equally steep increase in cancer incidence, especially breast, prostate, skin and colon cancers, has brought grief to every family touched personally by loss, or near loss, of a family member or friend. We have also seen a rise in autoimmune disorders including Multiple Sclerosis, Rheumatoid Arthritis, Lupus, Graves Disease, Hashimoto's Thyroiditis, Addison's disease and others. There has been a frightening increase in disorders of the brain, from simple dementia to Alzheimer's, schizophrenia, and autism.

Some experts remind us that we should expect these things because more of us live longer. This may be true for reasons explained by our geneticists but all of these diseases have also been associated with various nutritional deficiencies, insufficiencies, or excesses. Many of these conditions have been associated with insufficient sunlight or vitamin D. So here is just some of the problem:

- We may or may not have enough UV-B sun exposure or supplemental D.
- As a policy we don't test vitamin D, in our bodies or in our foods though this policy is changing.
- If serum testing does occur, current normal values may not reflect optimal levels of vitamin D. Until 2007 lab values reflected suboptimal 25(OH)D values but as of 2008 labs may now reflect values that may be too high.

As symptoms of less than optimal vitamin D are broad and may include fatigue, cavities, gum disease, PMS, bone loss, obesity, hypertension, degenerative joint diseases, depression, or muscle weakness, all of which can be attributed to other conditions, vitamin D insufficiency is rarely considered.

Until 2007 members of both the research and the medical community generally found the idea of regular monitoring of vitamin D too expensive, too complicated, or not yet supported by _science'. This community includes HMO's, physicians, healthcare policy makers in business and government, vitamin D researchers, and pretty much everyone who might make a difference in our understanding of vitamin D. Fortunately this has begun to change..

The price of our ignorance, ignoring the problem or the solution, can be calculated in billions of dollars in healthcare related costs as well as incalculable costs in human suffering. The estimated direct and indirect 2002 costs for adult onset diabetes alone is $132 billion. (Lewin Group, Inc. for the American Diabetes Association, 2002) The chapters that follow take up the individual issues that make this problem of sunlight and vitamin D so complex and offer an immediate safe solution for most persons while we wait for research to bring us more answers.

CHAPTER 3 A QUICK REVIEW- TERMINOLOGY AND RESEARCH PROTOCOLS

THE TERMINOLOGY

When the term vitamin D is used in research papers, conference proceedings, textbooks, and medical news reports it may mean any one of many different molecules, metabolites of vitamin D. Actually, the IUPAC-IUB Joint Commission on Biochemical Nomenclature prepared the Nomenclature of Vitamin D in 1981.[190]

Their definition of the term Vitamin D?

"The term vitamin D should be used as a general term to describe all steroids that exhibit qualitatively the biological activity of calciol."

Note to the GP: Any molecule that is like vitamin D is vitamin D. Calciol is the 'base' name for the kind of D produced in our skins from sunlight. or found in cod liver oil.

There are many vitamin D metabolites. For our purposes we only need to know about three of the Ds. Unfortunately each of these very different molecules are often referred to by the exact same name, vitamin D. As each of these forms of D has a different structure, potency, and action it is necessary to define them.

When reading an abstract or news report it may not tell you which D was tested or used for treatment. You may need to do more in-depth research to determine what is actually being reported. The 3 Ds are not equivalent.

Vitamin D, The Many and Varied

When reviewing the studies or listening to one of those news flashes if you are interested in understanding the conclusions it is important to pay attention to which D is being investigated. In the sample news flash at the beginning of this book, the study showing damage from D in baby rats, the vitamin D used was not the D from sunlight or supplements that you or I have access to, but the active hormone D, available only as a prescription drug and an unlikely source of D for any pregnant human. This form of D does not rise or drop significantly in our bodies even in moderate D deficiency or toxicity.

Active, hormone D, calcitriol, rises to toxic levels only in some rare genetic or immune disorders, such as sarcoidosis.[191] This means that the study with the rats does not and cannot apply to humans unless perhaps they suffered from one of the rare disorders.

Not only are there individual effects of the different Ds, relative amounts of one may alter amounts and perhaps functions of the others. One example:

A deficiency of 25(OH)D, calcidiol, the precursor to the active hormone and the D metabolite most often tested for D sufficiency, may initially result in a rise in serum levels of the active hormone, $1,25(OH)_2D$, calcitriol, but as 25(OH)D drops to very low levels, $1,25(OH)_2D$ also declines.

(GP: Watch where the numbers go, this is $1,25(OH)_2D$ not D_2, where the numbers go gives different meanings.)

All of the vitamin Ds will have a subscript $_{(2)}$ or $_{(3)}$ behind them, often not shown but recognized. Tests typically look for _total' D, both D_2 and D_3 and unless it is a research study _which' may not be defined. All sunlight D, be it calciferol, calcidiol or calcitriol is D_3. Any animal derived D is also D_3. Only a few plants or man-made supplements have and provide D_2.

There are other metabolites of vitamin D, not listed here, just beginning to be explored. They may prove to be important as research continues. For now, we'll stick with the short list, hopefully making this topic somewhat manageable.

Substances Typically Called Vitamin D:

Calciferol or calciol is the basic name for vitamin D produced by sunlight in our skin, or gotten from food or supplements. It may be vitamin D_2, ergocalciferol or vitamin D_3, cholecalciferol.

Chole-calciferol is the stuff produced in our skins from UV-B light and the D found in cod liver oil, eggs, dairy (fortified and unfortified) and the flesh and fat of

fish, birds, reptiles and mammals. It is a precursor to other D metabolites essential for mammals, reptiles, and birds.

> *precursor def. a chemical compound that leads to another product in a series of connected reactions*

Cholecalciferol is produced when a cholesterol-based molecule, 7-dehydrocholesterol, 7-DHC, found in human and reptilian skin and in the skin, feathers and fur of birds and animals, is exposed to UV-B light.

Ergo-calciferol, vitamin D_2, is produced when ergosterol, found in a number of plants, yeasts, and fungi is exposed to UV-B light from the sun or a UV-B lamp. It is also a precursor to other D metabolites (the things it gets turned into)

Ergocalciferol, labeled as Calciferol, is available by prescription in the United States. Prescription Calciferol contains 50,000 IU of vitamin D_2. This is an extremely high dose, 125 times the RDA of 400 IU.

Ergocalciferol and cholecalciferol have different molecular structures. Both can be used to treat vitamin D deficiency but cholecalciferol is more biologically active in humans than ergocalciferol.[192]

Humans, reptiles, birds, and egg-producing mammals (think Australia and platypus) preferentially bind cholecalciferol (D_3). Other mammals bind the two D metabolites equally. [193]

Studies done with fish and chickens found lower doses of cholecalciferol (rather than ergocalciferol) were able to resolve conditions of D insufficiency suggesting higher biological activity in these species as well as humans.[194,195,196]

Pre or prohormone D, also called vitamin D by researchers and clinicians:

25(OH)D is a short term for 25-hydroxyvitamin D, or 25-hydroxycholecalciferol ($25(OH)D_3$) or 25-hydroxyergocalciferol ($25(OH)D_2$) depending on the precursor D_2 or D_3. It is also called calcidiol.

Calcidiol is the intermediate storage metabolite of vitamin D formed in the liver from either cholecalciferol or ergocalciferol. This metabolite of D is used in the body for transport and storage and may have other as yet unknown activities important to our health. Found primarily in the blood and muscles, but also in other tissues and fluids including saliva, it assures a constant supply of calcidiol for the production of the active hormone, calcitriol.

Calcidiol is the D metabolite considered to be the most accurate determinant of vitamin D status. Blood tests can be for total 25(OH)D, the most common, or for values of each of the forms, $25(OH)D_2$ or $25(OH)D_3$.

In humans, other mammals, reptiles, or birds there is very little ergocalciferol, D_2, found naturally. Most circulating 25(OH)D is in the form of $25(OH)D_3$. High levels of $25(OH)D_2$ are only found when the person (or animal) has taken a supplement of vitamin D_2, ergocalciferol. Labs often give independent values for each plus combined.

25-hydroxyvitamin D, that is 25(OH)D, calcidiol, is available as a prescription medication, and has been recently receiving more attention in the research community for various treatments of D insufficiency. It is especially useful for patients with liver

disease who are unable to efficiently convert oral or sunlight D, cholecalciferol, to calcidiol, 25(OH)D.

Calcitriol, The active hormone D, also called vitamin D by researchers and clinicians:

Calcitriol is the name given to the active hormone vitamin D. It is the term I will use most of the time in this book. It is written as $1,25(OH)_2D$, or 1,25-dihydroxycholecalciferol or 1,25-dihydroxyergocalciferol. There are several other ways to write the chemical name but these are the most common.

Calcitriol is primarily produced in the kidney from 25(OH)D though other tissues and organs also contain the enzyme necessary to make this D metabolite. In more recent research finding indicate many tissues may have the ability to convert calcidiol to calcitriol and this ability may protect us from any number of cancers including skin cancers.[197]

This is the metabolite considered to be essential for bone development and maintenance. $1,25(OH)_2D$ also controls production of various enzymes and other proteins throughout the body by its binding with vitamin D receptors within the nucleus of cells. It is currently considered the most active metabolite of the many forms of D in living systems.

Calcitriol is available by prescription only under the name Rocalcitrol®. This, or analogs created to be very like it, is the version of vitamin D used in research to treat cancer and some bone disorders. It is sometimes required for persons on dialysis because their kidneys can no longer make sufficient quantities of this important hormone.

Other Important Terms

- 7-dehydrocholesterol (7-DHC)-a zoosterol (see last item in terms) in skin and other animal, reptile and avian tissues that upon activation by ultraviolet light becomes antirachitic (prevents or cures rickets) and is then referred to as cholecalciferol (vitamin D_3). It is made from cholesterol metabolite.

- calbindin- vitamin D induced (levels of D regulate its production) calcium-binding protein found in neuronal tissues. A vitamin D-dependent variant that is a protein playing a fundamental role in the vitamin D mediated transport of calcium in reptiles, amphibians, birds and mammals. It is found in the intestine, kidneys, eggshell, gland, brain, and possibly other organs.

- calcitonin- calcium-controlling hormone produced by the thyroid and parathyroid glands that increases the deposition of calcium in bones. Also called thyrocalcitonin

- calcium-binding protein- There are two main groups of calcium binding proteins. Many other proteins will bind calcium. They can act as transport proteins, regulator proteins, or activator proteins.

- cholesterol- a pearly, fatlike steroid alcohol, found in animal fats and oils, in bile, blood, brain tissue, milk, yolk of egg, myelin sheaths of nerve fibers, the liver, kidneys and adrenal glands. Cholesterol is a sterol. Because of its hydrophilic (attracts water) property at the -OH

end and hydrophobicity (repels water) at the hydrocarbon side chain, it can be incorporated into the lipid bilayers of the membrane. Most of the body's cholesterol is synthesized in the liver, but some is absorbed from the diet. It is a precursor of bile acids and is important in the synthesis of steroid hormones (including vitamin D).

- epithelium- the covering or lining of internal and external surfaces of the body, including the lining of vessels and other small cavities. It consists of cells joined by small amounts of cementing substances. Epithelium is classified into types on the basis of the number of layers deep and the shape of the superficial cells.

- ions- atoms or radicals having a charge of positive (cation) or negative (anion) electricity owing to the loss (positive) or gain (negative) of one or more electrons.

- melanin- pigments largely of animal origin. Colors include black/brown, yellow, red and violet. Found in feathers, cuttle ink, human skin, hair, and eyes and in cellular immune responses and wound healing in arthropods.

- metabolite- byproduct of metabolism: a substance that is involved in or is a byproduct of metabolism. Basically it means any products that something turns into as it is processed. Cholecalciferol becomes 25(OH)D which becomes $1,25(OH)_2D$ which becomes yet another metabolite

- mucous membrane- The lubricated inner lining of the mouth, nasal passages, vagina, intestinal tract and urethra, any membrane or lining which contains mucous secreting glands.

- myelin- the fatty substance that covers myelinated nerves. Myelin is a layered tissue surrounding the axons or nerve fibers. This sheath acts as a conduit in an electrical system, allowing rapid and efficient transmission of nerve impulses. Myelination refers to the process in which nerves acquire a myelin sheath.

- myopathy- any disease of muscle

- photolyze- photolysis any process of disassociation driven by the sun's rays

- physiologic dose- the normal dose or intake level of a nutrient associated with the prevention of deficiency or the maintenance of health. A physiologic dose is no greater than that which could be achieved through a conscientious diet, as opposed to the use of supplements.

- placebo- a sugar pill or false treatment that is given to a control group while the experimental group is given the experimental treatment. Placebo-controlled studies are conducted to make sure that significant outcomes of a trial are due to the experimental treatment rather than another factor associated with participating in the study.

- -plasia -the suffix means formation (especially of cells). Example: hypoplasia (insufficient formation), hyperplasia (overabundant formation) and dysplasia (abnormal formation).

- plasma- the liquid part of blood (as opposed to blood cells) that makes up about half its volume.

- precursor -chemical compound preceding another: a chemical compound that leads to another, usually more stable, product in a series of connected reactions [Early 16th century. From Latin praecursor , from praecurs- , the stem of praecurrere , literally to run before, from currere to run.]

- precholecalciferol -pre-vitamin D_3 an intermediate metabolite of 7-DHC in our skins. UV-B exposed 7-DHC is photolyzed to precholecalciferol. Precholecalciferol is further metabolized, by heat, to become cholecalciferol, or by other bands of UV light to inactive metabolites.

- retinol-binding protein -a protein that binds retinol (a form of vitamin A). Retinol-binding protein is found in plasma. The protein has one binding site for retinol and is responsible for the transport of vitamin A from the liver to all other tissues and organs of the body. It is a zinc dependent protein so low levels of dietary zinc can cause an insufficiency of retinol binding protein and mimic vitamin A deficiency.

- steroid -any of numerous naturally occurring or synthetic fat-soluble organic compounds having as a basis 17 carbon atoms arranged in four rings and including the sterols and bile acids, adrenal and sex hormones, certain natural drugs such as digitalis compounds, and the precursors of certain vitamins.

- sterol -any steroid-based alcohol. Any substance with -sterol at the end starts with this molecule. Sterols can be animal or plant based.

- vitamin D-binding protein -an alpha-globulin found in the plasma of man and other vertebrates. It is synthesized in the liver and carries vitamin D and its metabolites (our D family) through the circulation. It is also known as group-specific component (gc). Gc subtypes are used to determine specific phenotypes (phenotype indicates interactions between a particular set of genes and the environment) and gene frequencies. This data is employed in the classification of population groups, paternity investigations, and in forensic medicine.

- hypervitaminosis D -excess vitamin D from supplements

- zoosterol -an animal sterol. I like this word. Vitamin D in its active form is a zoosterol.

HOW RESEARCH STUDIES ARE CONDUCTED

Nutritional research studies generally fall into one of two categories, observational studies, and randomized controlled trials.

One type of observational study is prospective cohort. Researchers watch a large group of people over a set period of time. Some of the participants will have certain characteristics, behaviors, dietary habits, or lifestyle variables, and others won't. Subjects do whatever it is they normally do with variables determined by what the researchers hope to learn.

Variables may include such things as diet, exercise, alcohol intake, smoking, or supplement or medication intake. Researchers then compare outcomes within the group.

As an example: Some may drink alcohol, in small or large quantities, others may not drink at all. Do these differences in behavior influence the particular outcome the researchers are interested in, such as incidence of cancer or depression or diabetes?

The second type of observational study is case-controlled. Case-controlled studies take a very different approach. Researchers look very carefully at any number of past variables common to people who currently have the condition being studied and

compare these variables, sex, age, habits, intake of fruits and vegetables, whatever has been set by the study guidelines, in matched persons who do not have the condition.

The researchers then try to determine which, if any, of these variables might contribute to or help prevent the condition of interest. What is it? That is, what variable is different between those who become ill and those who remain well? Possible variables might be a particular diet or dietary element, exercise, sunlight, vitamins, medications, or some other factor such as where they live (possible toxics in the environment).

Unlike observational studies, randomized controlled trials involve intervention. The researchers change something in some of the participants and not in others to see how or if it alters their health status. The change could be a change in diet, low fat, low carbohydrate, low calorie; adding a diet supplement or medication; or altering lifestyle by behavior modification, exercise, or some other intentional intervention. Participants are chosen randomly to receive or not receive the particular intervention.

If the trial is 'blinded or double-blinded' participants and/or researchers do not know who got what. This type of trial is commonly used to test medications to avoid the 'placebo' effect. The placebo effect is best described as no longer having a headache because you thought you took aspirin, but you really took some other pill which has no known affect on headaches. Blinded trials try to avoid the problem of 'it works because I believe it will work (or not)'.

Both observational and randomized controlled trials are necessary because researchers can't ethically ask people to do things that clearly are harmful like drink too much or get sunburns intentionally or take up or increase smoking or participate in random unprotected sex.

All three types of studies have strengths and weaknesses. Case controlled studies are the least expensive but are prone to inaccuracy because they use information from the past. Not only do most of us have difficulty remembering accurately what we used to do, especially things like what and how much we ate or drank or smoked, but in case-controlled studies participants with the condition being studied may see the past with a bias caused by their feelings and judgments about their current disease or condition.

Prospective cohort studies get around the 'clouded memory' problem of case control studies by gathering information moving forward in time, no memory problem, and before the disease or condition appears, no disease induced bias. These types of studies are less used as they take a considerable amount of record gathering and recording and require willing participants who must record and report regularly and aren't getting paid. Without a captive group a high percent of participants can and often do disappear over time. For these and other reasons prospective cohort studies tend to be very expensive with a high dropout rate.

Randomized controlled trials are considered by many researchers to be the 'gold standard' for determining if a particular variable produces a particular outcome. An example would be "Does radiation therapy prolong cancer survival time?" or "Does taking a (specific) vitamin supplement protect from heart disease?" Because these trials follow participants over time, like prospective cohort studies, they are very expensive

to run. Because of the expense, trials may be too short to see positive or negative effects.

The value of any of the studies depends on how well the study was put together in all of its parts, from beginning to end.

Did they ask the right question? Does the answer have any application to anything in real life? Was the study long enough to know what might happen to real people in the real world over time?

Example-
Studies too short to give long term answers occur frequently, possibly because of the costs involved in longer studies. Studies considering the safety of supplementation with high doses of vitamin D, 2,000-4,000 IU, lasted 6 months or less, far too short a period of time to tell what might occur if supplementation continued over two, three or more years.

Vitamin D is a fat-soluble vitamin, which stores in our bodies and builds up, slowly or rapidly depending on dose, over time.

Did the researchers look at all important variables? There may be less incidence of a particular disease in latitudes with more UV-B but there may also be more access to fresh fruits and vegetables (year round growing season). Other variables could be dietary intake of fatty fish containing D, lifestyle sunlight exposure, skin color, etc.

Are the study conclusions actually supported by the data? Sometimes the studies I read drew conclusions that were very poorly supported by the data presented. In other studies the data presented was so limited, because of number of participants or 'variables' or a misunderstanding of what vitamin D values are important, it held little value for increasing our understanding and safe use of sunlight or vitamin D.

The Susan B. Koman Breast Cancer Foundation has a website with a very helpful guide to understanding epidemiological studies. You can visit their website for more information about understanding research studies or information about breast cancer. http://www.komen.org/abc/dc/dc_studies.asp

For more information about types of research studies and their positive and negative aspects read Epidemiology in Medicine by C.H. Hennekens and J.E. Buring (Lippincott Williams & Williams 1987)

HOW RESEARCH CAN MAKE US DUMBER

Research isn't real, particularly the double blind placebo controlled studies and the studies involving simulated sunlight. This is important. You cannot determine what will happen in real life with real people and real sun from these studies. You can get an approximation, sometimes.

Few of us fall into the mean.

The mean is the number used in research to set 'normals' and to determine how well a treatment works. The mean is defined as the average value determined by taking the sum of all values and dividing by the total number of values.

The general idea as far as I can gather is that if the _mean‘ suggests a thing is good or bad (works or fails to work), it is then to be avoided or undertaken by the GP, *en masse*.

An example:
Sunlight has an association with skin cancer in naked mice and in persons with light skin and light eyes. Sunscreens are thought to protect or slow development of cancerous (non-melanoma and melanoma) skin changes.

Humans are told to use sunscreen, all humans.

Blacks, Hispanics, and others with darker skins, rarely get skin cancer and if they do it is NOT associated with UV exposure. [198,199]
Though darker skins are at high risk for vitamin D insufficiency and are at low risk for skin cancers they are included in warnings to avoid sun and use sunscreen.

Most studies contain an underlying premise as a basis of the question asked and the conclusion. In a number of studies you will read about in this book the premise, while widely accepted as true, turned out to be untrue. This occurred because either past research was not verified or the 'fact' had been repeated so often no one even bothered to check and see if it was true.

> *premise*
> *1. evidence for conclusion: a statement given as the evidence for a conclusion*
> *2. basis of argument: a proposition that forms the basis of an argument or from which a conclusion is drawn. 'I question the premise on which your whole theory is based.'*

Several unfortunate assumptions regarding sunlight and vitamin D have led to some scientific conclusions being quite wrong and these conclusions, more unfortunately, are difficult to challenge or change.

One _premise‘ clouding our topic of discovery seems to be a misunderstanding of how and why vitamin D stores in the human body, which will be discussed in its own section.

Another accepted premise, that excess levels of vitamin D cannot occur from exposure to UV-B light, has never been _proven‘. Later you will see that this, also, appears to be incorrect, potentially leading to a series of other problems.

And then there is research bias

Expectations

We have expectations. Depending on past experiences they may be positive or negative but we have them. Even when we try not to have them, they are there, somewhere, expectations of others, of the situation, of ourselves.

Expectations have this almost mystical ability to cloud what we see, like the memories of participants in case-control studies or the placebo effect.

Expectations cloud researcher brains just like the rest of us. In the world of scientific inquiry expectations may have monetary considerations. This can cloud a brain more than usual.

Politics

Political correctness can infect research influencing what questions researchers decide to ask, answer, and publish. Currently it is NOT politically correct to find anything good about sunlight. The possible benefits of UV-B exposure in the prevention of cancers and autoimmune diseases is currently politically incorrect and funding difficult to find as no marketable product can result from any outcome.

Peers

Research is an interesting life path. Once you gain status within your field of expertise and your work is published in the correct journals, you become an authority. Authorities are persons who author an idea or theory. Authors of ideas and theories get very attached to their ideas and theories and more so if these ideas become the generally accepted 'truth'. As new information becomes available shifting an authority's opinion may be a very difficult undertaking.

Often when a shift in view brings new light and a new understanding of what is true the new information is ignored, or attacked by authorities of the old school. It is human nature. We just really get attached to our ideas, especially if we are an authority.

Anecdotal Evidence

It is unfortunate that some very well educated people believe in the outcomes of clinical double blind studies and out of hand reject personal evidence. Personal evidence is what I/you report as our experience of a medication, food, supplement, condition, and the like.

My personal experience or your personal experience as reported to an authority, such as a physician, healthcare professional or researcher may be discounted as 'anecdotal' and not therefore not relevant.

anecdotal- based on anecdotes or hearsay: consisting of or based on secondhand accounts rather than firsthand knowledge or experience or scientific investigation

(GP- it says firsthand experience OR scientific investigation!) GP listen up: My experiences and your experiences are not anecdotal when we experience them and report them. This whole journey is about you, finding out who you are in relation to the sun and discovering what your personal need for sunlight and vitamin D is. You are the person to determine how much sunlight, or what foods or supplements might supply your need. You will be given tools to help you do this safely but the actual 'knowing and doing' is up to you.

What Is A Study Worth?

The bottom line, a study regarding nutrition and health is only worth its time and expense if the end value brings benefit to the individual, the GP. Whatever the conclusion of the latest research paper, its value rests in the potential positive application of the results in our daily lives. Can the knowledge be put to practical use in your daily life or in mine? What you and I need are not always the same. A study may offer us an approximate direction but even if using the information made "all the difference in the world" to me it may have no application whatsoever to you.

Well-done studies at best can only offer us an approximation, a direction in which we may begin to look for a solution to a problem. Research may shed light on a missing element or clues about lifestyle changes that can shorten or lengthen our lives. Yet every study is only an approximation. There will always be that 100 year old who smokes and drinks and that guy down the street that exercises every day and 'eats right' and dies of cancer at an early age. Whatever the latest conclusions of the experts only you can determine what is right for you.

One last important comment about studies, the types I have described in this section usually involve people. Many of the studies mentioned in this book about vitamin D and sunlight use specially bred animals, vitamin D in a form not usually found in humans, artificial light instead of direct actual sunlight, artificial skin, or cells no longer attached to a living being. These are pretty big variables to use when trying to draw conclusions that apply to real people in the real world but sometimes they are very helpful is suggesting a direction.

Let me repeat for emphasis, the difficulty in using studies to support any theory is that the value of the study is not the study outcome but how its conclusions play out in the life of an individual.

A study may show soy consumption lowers the incidence of breast cancer. Does it really? Who were the people being studied? Was their use of soy a part of a traditional diet meaning generations of acclimation to the diet? How was the study done? Were people or animals used? Was the soy an extract put in a Petri dish with a cell, outside a living system? How long was the study? How much and what kind of

soy was used? Could a real person actually consume that amount and kind? Even if all of the above could be answered sensibly does the study outcome apply to you?

FACT: Soy eaters get breast cancer and all of the other diseases suffered by non-soy eaters. The lower incidence may not be associated with soy at all and even if it is (extremely hard to prove) would it make a difference to you? Would you be one of the participants who lucked out, or not?

Common Sense

Almost every night on the news I hear "the latest research shows _____" (fill in the blank with whatever disease or cause of disease or treatment or cure) or 'the answer to _____is_____'(name of disease and treatment or cure).

So if the research shows almost everything studied, drugs, vitamins, alcohol, caffeine, diet, exercise, sun, sleep, is good/ is bad, will kill you, will cure you, what is a mere human to do? Hopefully you have learned that a study may or may not have value to you or anyone else and that you probably shouldn't believe everything you hear, no matter how many authorities are cited. Look for approximation and use common sense.

> *common sense*
> *good judgment: sound practical judgment derived from experience rather than study Encarta® World English Dictionary [North American Edition]*

Asking the right questions is important in every sphere of learning but especially health research, for you as well as the researchers. Healthcare is costly. Enjoying health requires knowing what you need to be healthy. There is more information available about health than at any other time in history. Wading through the information would take several lifetimes or more. Learning to ask the right questions saves time and helps sort out the information, the wheat from the chaff so to speak.

Schools often teach students what to think but rarely teach students how to think. If you are interested in learning how to get better answers by asking better questions my favorite book on the topic is a college textbook, currently in its sixth edition.

Asking the Right Questions, M. Neil Browne and Stuart M. Keeley, Prentiss Hall. is a gem of great price. Browne and Keeley offer information, exercises and self-exams to rapidly increase your ability to ask the right questions and get answers that can make the information you process every day work for you.

This book is a boot camp for your brain to develop and exercise your critical thinking skills. Put to use the information will truly 'change your mind'.

CHAPTER 4 SUNLIGHT, D, AND DISEASE

Most of the conditions that respond to vitamin D sufficiency (getting enough) are related to whether cells communicate with each other and grow normally, or not. We again come back to our Goldilocks' Principle, not too much, not too little; just right. Historically we got minimally sufficient D or we did not live long enough to reproduce.

For most of our ancestors sunlight provided the primary source of vitamin D. For a few of our most northern and southern ancestors in latitudes lacking significant UV-B, D was provided by diet, almost exclusively from a diet of fish including the skin, fat and organs.

Our history tells us that D and sunlight are natural components of our external environment. As amounts of available light and vitamin D are dependent on location, diet, and lifestyle, changes over the last two centuries have greatly increased the complexities of ensuring vitamin D adequacy.

This book is not about treating disease. WE ALL NEED D. Needing D is not a disease. There is a television ad to encourage viewers to visit the Caribbean. It says-

'Life needs direct sun".

Life does.

The linear model of medicine diagnoses a disease and prescribes a treatment, a drug, surgery, or therapy. Nutrition has evolved from a healthy whole food diet to supplements available as pills, potions, powders, and bars. Popular nutrition books have lists of nutrients or other supplements, or more recently herbs, suitable for addressing any number of diseases or conditions.

I promise you a headache is not an aspirin deficiency nor is it a deficiency of feverfew. There are nutrient insufficiencies and deficiencies. They can be recognized

and treated. Lack of essential nutrients contributes to disease states because when our bodies don't get what is needed they cannot function optimally. When an insufficiency of one or more nutrients continues over time our bodies develop conditions, which we define as disease or degenerative.

Nutrient sufficiency is preventative medicine. If your body gets what it needs to function optimally you are much less likely to need medicine or herbs. Food can provide more than adequate amounts of essential nutrients if the diet is composed of ancestrally appropriate real (not processed), whole, fresh, foods consisting of meat, fish, and poultry including the organs; eggs, dairy, and fermented foods; fresh fruits and vegetables. Amounts and types will vary by taste and need. The wiser your choice of foods the less you will pay for supplements or later medical care.

What may not be provided (or available) to fit your genetic need is vitamin D. A significant number of studies show the RDA of 400 IU is not sufficient to maintain optimal levels of vitamin D year round in a large portion of the American public.[46,200]

Health is about a person, an individual, you. In two different people the reason for the exact same symptom/s may be completely different and completely unrelated.

Taking a medication or supplement may give a completely different response in different people, even persons sharing DNA. Many conditions are associated with lower levels of vitamin D. Instead of focusing on a condition the sunlight and vitamin D issue should be addressed by finding out how much D you have, how much D you need and how you can safely get what you need. It is this individual determination of need and how to supply it that is the important thing, not a 'condition'. .

SUNLIGHT AND D, DEFICIENCY OR DISEASE?

Within the medical and research communities when treating disorders with vitamin D, clinicians use extremely high doses of the vitamin chole- or ergo- calciferol, or prescription calcidiol, or prescription calcitriol, or more recently, specially designed vitamin D analogs. Some of the conditions being treated, tumors, cancers, genetic anomalies, or conditions caused by loss or impaired function of an organ or gland need the diagnosis and treatment provided by skilled medical personnel.

Yet in other situations, like many of the conditions associated with marginal deficiencies of D, the greatest concern for the GP, it may be difficult for doctors and researchers to step out of the 'diagnose disease' and 'prescribe treatment' model.

Deficiencies occur because the living organism, human, animal, or plant, lacks something it needs. The disease-treatment model typically defines the 'enemy' and sets out to determine the best weapon to destroy it. The weapon is a drug, which is defined as any compound used to treat disease, injury, or pain. This model works fairly well with infectious disease, unless the organism develops drug resistance, but not so very well with degenerative diseases particularly when the underlying cause relates to a nutritional imbalance, excess, or deficiency.

When the anti-rachitic (to prevent or cure rickets) factor was first discovered, isolated, and named, it was considered to be a vitamin.

vitamin def. organic substances essential in small quantities to normal metabolism

This factor was found in cod liver oil, which is sort of a food. The discovery caused rickets and vitamin D deficiency to fall into the domain of the nutritionist or dietician, which is a problem since the largest part of our supply of vitamin D comes from sunlight.

Sunlight really isn't in anyone's domain except perhaps for the atmospheric specialists who aren't very well informed on human biochemistry and physiology.

Later when the active end product of vitamin D, calcitriol, became fully recognized as a hormone the field of D sufficiency seemed as if it should belong to the domain of the endocrinologist but most endocrinologists don't know much about light or vitamin D.

Which in part brings us to our current crisis…

Quality research is a tool that helps us understand the way our world is put together. Because elements are often isolated from other elements and studied in artificial environments research outcomes and conclusions may often not have value or application to the GP (General Public, you and me)

Nutrition research typically studies individual nutrients to consider their role in a particular condition or disease or to determine drug-like actions, to prevent or cure disease.

Early researchers isolated cholecalciferol in cod liver oil but soon after determined antirachitic factor could be produced in vegetable sterols by irradiation (UV-B our sunlight friend). This discovery led to the rapid development of irradiated ergosterol, vitamin D_2, followed by its promotion and sale for treatment of rickets.

Prior to the production and marketing of irradiated ergosterol the primary form of vitamin D found in humans was cholecalciferol from sunlight, animal, fish and poultry sources. Ergocalciferol, isolated, concentrated and manufactured, transformed a natural nutrient into a drug, one that is still used today.

physiological-of organism's function: relating to the way that living things function, rather than to their shape or structure
pharmacological- drug's effects: the effects that a drug has when taken by somebody, especially as a medical treatment
drug- medicine used in the treatment of disease, injury, or pain

Physiological dose, as applies to nutritional elements, means a form and amount of the substance that could be found in a natural diet or life style.

‗Pharmacological dose' is used as a way of saying a natural substance, like vitamin C or vitamin D, is being used to treat a disease, like a drug, a medical treatment. When herbs or vitamins are used in 'pharmacological doses' it indicates an amount far beyond any amount typically consumed in a natural diet. In a natural state, meaning derived from food intake, the nutrient would not be able to be consumed in such large amounts.

Currently the issue of vitamin D sufficiency is addressed by a number of different authorities and protocols.

- Public health authorities tell us sunning arms and legs three times a week for 15 minutes provides all the D we need. In June 2005 Dr. Cheryl Rosen, national director of the Canadian Dermatology Association's National Sun Awareness Program was quoted as saying "… Only brief sun exposure to either the back of the hands, arms, or face, two to three times a week from May to September, is required to maintain sufficient vitamin D levels through production of vitamin D in the skin."

- Public health also tells us if we don't sun, adequate D is found in infant formula or in 1 quart of fortified milk.

- Alternative medicine proponents are somewhat split suggesting relatively high dose, 1,000-4,000 IU, vitamin D supplements, or cod liver oil.

- Pediatricians have been advised, April 2003, by the American Academy of Pediatrics, to recommend 200 IU of supplemental vitamin D to all breast-fed infants and other infants who consume less than 17 ounces of fortified milk or formula daily.

- Osteoporosis specialists and clinics commonly use doses ranging from 400-1,000 IU of D daily combined with calcium. Earlier researchers used much higher doses. Some use the active hormone calcitriol.

- Endocrinologists treating vitamin D related disorders might suggest use of one of the more potent prescriptions, ergocalciferol, calcidiol, or calcitriol. The typical dose of ergocalciferol is 50,000 IU given at various intervals.

In action and response vitamin D is a hormone, with all of the implications of that term. Supplementing hormones without sufficient cause and without testing may create new health problems. An example of the dangers of hormone tapering has been seen in women exposed to estrogen from the 'pill' and hormone replacement therapy (HRT), demonstrating increases in breast cancer and dementia. [201,202]

Vieth has suggested labeling cholecalciferol a hormone is a misnomer leading to a failure to adequately address the issues of D insufficiency.

Vieth, R. 2004 J.Steroid Biochem.Mol.Biol. 89-90 571-573
Why "Vitamin D" is not a hormone, and not a synonym for 1,25-dihydroxy-vitamin D, its analogs or deltanoids

Official nutrition committee reports in both North America and Europe now state that Vitamin D is more of a hormone than a nutrient. These statements are wrong, and do not reflect the definitions of either vitamin or hormone. Researchers often compound the problem by referring to calcitriol or other deltanoids as "Vitamin D". These things have serious consequences: (1) The literature is burdened by an ongoing confusion that presumes that the reader will somehow "know" what the writer refers to by "Vitamin D". (2) Medical practitioners not familiar with the ambiguities administer Vitamin D inappropriately when calcitriol or a deltanoid analog would be correct, or vice versa. (3) Attempts to promote Vitamin D nutrition are hindered by alarmist responses justifiably associated with the widespread administration of any hormone. Vitamin D is a vitamin in the truest sense of the word, because "insufficient amounts in the diet may cause deficiency diseases". The term, prohormone, is not relevant to the Vitamin D system, but 25-hydroxy-Vitamin D (calcidiol) is appropriately described as a

prehormone, i.e. a glandular secretory product, having little or no inherent biologic potency, that is converted peripherally to an active hormone

The unfortunate reality is actions of excess cholecalciferol are as yet not well studied. It is true that excess cholecalciferol does not elevate serum (blood) calcium but there appear to be other potential side-effects unrecognized by Vieth and other researchers.

Sekkarie, M.
2006 Clin.Nephrol. 65 91-96

The impact of over-the-counter vitamin D supplements on vitamin D and parathyroid hormone levels in chronic kidney disease

BACKGROUND: In addition to the known disturbances in mineral metabolism and vitamin D activation, the majority of patients with chronic kidney disease (CKD) do not have sufficient vitamin D stores. The impact of supplementation with low-dose, non-active forms of vitamin D (calciferol) on parathyroid hormone (PTH) levels in this population is unknown, however. METHODS: A cross-sectional evaluation of vitamin D levels, intact parathyroid hormone (iPTH) and other laboratory results in 108 stage 3 and stage 4 CKD patients according to their intake of over-the-counter vitamin D. RESULTS: 37 patients took 400 IU of vitamin D daily with supplemental calcium and 71 did not. Compared to subjects who did not take it, patients who were on the supplement had higher 25(OH)D (31 +/- 15 vs. 17 +/- 9) ng/ml, higher 1,25(OH)D (21 +/- 12 vs. 16 +/- 9) pg/ml, lower iPTH (75 +/- 48 vs. 144 +/- 100) pg/ml and were more likely to meet K-DOQI PTH guidelines. However, these subjects were more likely to have over-suppressed iPTH values. The groups did not differ with regard to demographics, glomerular filtration rate and calcium and phosphorus levels. CONCLUSIONS: Vitamin D supplements may be a valuable tool in the prevention and treatment of hyperparathyroidism in patients with stages 3 and 4 CKD. CKD patients who have over-suppressed PTH need to be asked about their vitamin supplement intake.

This study shows that even when kidneys are failing dietary D elevates the active hormone, and this at a very low dose of only 400 IU.

Hormone, pre-hormone or pro-hormone, we have much to learn about vitamin D in all of its forms.

Hormones and You

Medicine recognizes thyroid hormone, pituitary hormone, parathyroid hormone, and similar substances should never be supplemented without testing and monitoring but the medical community regularly prescribes estrogen and progesterone for birth control or menopausal symptoms.

The alternative healthcare community frequently promotes human growth hormone, progesterone, testosterone, melatonin and DHEA as 'natural' substances that may be utilized simply because we think perhaps they will benefit us, extend life, improve our mood, improve our sex life or otherwise make us feel better.

Hormones are funny things, they communicate with each other and balance each other, and taking them, just because, without testing and monitoring, is a huge

mistake. Even if you test and determine you really need a specific hormone it won‘t mimic life. The daily interplay of our hormones is like an immense choir, all of the members adjusting tone and pitch to food, energy, rest, light, darkness, exercise, stress, relaxation and more.

There is a huge difference between a nutrient deficiency and a hormone deficiency. Nutrients are by definition supplied from outside our bodies. A nutrient deficiency occurs because we aren't getting enough of the essential element from our food. The solution is to increase consumption of foods containing the element.

Hormones are produced inside of our bodies. Deficiencies occur because elements necessary for their production are lacking or an organ or gland is aged, diseased or damaged. Damaged glands or organs rarely repair themselves. The only solution is to acquire the hormone from a compatible species, like Armour thyroid from pigs, or create it in a lab, like Humulin (for diabetes), and follow up with careful replacement to hopefully mimic the body's production.

If it is determined, by extensive testing, that an insufficiency exists, prescriptive treatment and regular monitoring may help restore health. Yet after many years of talking with persons needing to take thyroid, insulin, cortisol, or other hormone to survive, none have recovered the level of health they had prior to onset of their need for treatment. This lack of well-being occurs because in a healthy functioning body individual hormones perform like members of a choir.

The music of life varies in pitch, tone, and song day-by-day and even minute-by-minute. Our natural hormones faithfully listen to one another and follow after the grand conductor while the pitch and rhythm of a supplemented hormone remains constant or nearly constant all the time. Supplemental hormones should become adjuncts to long-term health only when deficiencies are determined to be significant enough to need medical treatment.

When one hormone, the one you or others decide is 'right for you', unable to _listen‘, without understanding the song, begins to shout, all the time, every day, the same pitch (dose), unable to respond to the conductor or the tune, the harmony of your internal choir is disrupted, the song damaged or even destroyed. It is wiser to let the body be in harmony with itself unless there is a serious medical need for hormone supplementation.

Nutritional Insufficiency is Not a Disease

Having presented my thoughts about hormone supplementation and since calcitriol is a hormone does this mean vitamin D should only be used as a prescription treatment? Well, I also consider vitamin D to be a nutrient and yet more strange a nutrient we can produce from sunlight in our skins.[203] There is the rub. Clinical books about vitamin D see it as a treatment for disease. Nutrition books see it as a vitamin.

I am attempting to address the issues involved in ensuring sufficiency of a sunlight dependent hormone. Our topic is real sun, real food, and real people in the real world. How much do we need? How much do we get? How can we get what we need?

A nutritional insufficiency is not a disease. Lack of sunlight is not a disease either. A nutritional deficit does not require huge doses of a substance to correct it. A deficiency requires that the nutrient or sunlight be supplied in the most natural form in amounts that are appropriate to the nutritionally deficient or sunlight deprived organism, be it man or beast (or plant for that matter).

We would never consider giving massive doses of other nutrients to treat deficiency. If I need more protein I don't need hundreds of grams of protein. If I need iron just a bit will do.

Living things with nutritional deficiencies should be appropriately treated, by replenishing their supply of the needed nutrient to levels that are optimal for the organism, in this case human. Because we have traveled far from out ancestral habitats and food supplies and have altered our access and exposure to sunlight it is quite likely our supply of sunlight or vitamin D is inappropriate.

> Giving an excessive, pharmacological dose of any nutrient, no matter how natural the substance, to a plant or animal can result in illness, damage, or even death. Excessive doses of boron, copper, zinc, vitamin A, vitamin D, vitamin B-1, vitamin B-6 or synthetic folic acid have each been demonstrated to cause damage in animals or humans, sometimes permanent.
> (204,205,206,207,208,209,210,211,212,213,214,215,216,217,218,219,220,221,222,223,224,225)

Within the medical community the typical dose of vitamin D prescribed for deficiency is 50,000 IU of D_2 given daily or weekly. In the mood study you'll read shortly participants were given a single dose of 100,000 IU. For comparison the current DRI (Dietary Reference Intake) Estimated Adequate Requirement (EAR) is 5-15 mcg. which is 200-600 IU (International Units). A microgram (mcg) is 1/1000 of a gram, not much at all.

While the use of high dose prescription vitamin D has shown positive results in research the potential for harm is also present. The most frequent reason for single or intermittent high doses is ease of compliance. This is an unsatisfactory and unnecessary solution. There is no reason to use high dose vitamin D in normal humans wishing to maintain optimal levels of D. There is a better and safer way to get your D, without a prescription.

WHY WE NEED TO KNOW MORE ABOUT SUNLIGHT AND D

Some of the items listed here will not be covered in later topics. The prevailing premise of this book is that MANY conditions and diseases will disappear or be greatly reduced if all of us (or as many as possible) have optimal levels of sunlight, vitamin D, and accessory nutrients (things that go with sunlight and vitamin D such as calcium). While D is associated with various conditions it is a nutrient, not a drug and we all need D.

- Vitamin D is a more effective anti-oxidant than vitamin E in reducing lipid peroxidation and increasing superoxide dismutase and glutathione in hepatocytes (liver cells).[226]
- Vitamin D is a cell membrane anti-oxidant inhibiting liposomal peroxidation. [227]
- Research suggests low levels of D, altering calcium metabolism, may contribute to or be a cause of Syndrome X with associated hypertension, obesity, diabetes, and heart disease. [228]
- Clinical vitamin D deficiency decreases biosynthesis and release of insulin. [229,230,231]
- Glucose intolerance has been inversely associated with the concentration of 25(OH)D. That is low D may predispose to glucose intolerance. [228,232]
- Risk of senile cataract is reduced in persons with optimal levels of vitamin D and carotenoids. [233]
- Estimations of clinically evident serum D deficiency in the U.S. range from 41%-57% of the general population. [234] Clinical deficiency does not define optimal amounts of D.[235,236,237,238]
- Northern countries have higher levels of cardiovascular disease and more heart attacks occur in winter months. [239,240]
- 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.[163,164]
- Sunlight, containing UV-B, and vitamin D contribute to normal appetite and blood sugar thereby helping to prevent obesity. Normal weight is associated with higher levels of D and adequate calcium.[241,241,242,243]
- Obesity is associated with vitamin D deficiency or insufficiency. [244,245]
- Obese persons have impaired UV-B stimulated production of vitamin D and impaired absorption of food source and supplemental D. [246]
- PCOS (Polycystic Ovarian Syndrome) has been corrected by supplementation of vitamin D and calcium.[125] Much of Thys-Jacobs work reports on the benefits of calcium for this condition but in her studies all participants also receive significant amounts of vitamin D.
- Vitamin D plays a role in regulation of both the 'infectious' immune system and the 'inflammatory' immune system. [247]
- Low vitamin D is associated with an increasing number of autoimmune diseases including Multiple Sclerosis, Sjogren's Syndrome, rheumatoid arthritis, and Crohn's disease. [248] [249,250]
- D deficiency has been mistaken for fibromyalgia, chronic fatigue, or peripheral neuropathy. [4,251]
- Infertility is associated with low vitamin D.[252]
- Menstrual migraine is associated with low levels of vitamin D and calcium.[253]
- Breast, prostate, skin and colon cancer have a strong association with low levels of D and lack of sunlight. [254,255,256,257]

- Michael Holick and others suggest that an optimal level of 25-hydroxyvitamin D may contribute to lower levels of all epithelial cell cancers including, breast, prostate, colon and skin.[258,259,260]

- Activated vitamin D, calcitriol, regulates tyrosine hydroxylase in the adrenal gland, the rate-limiting enzyme necessary for the production of dopamine, epinephrine, and norepinephrine. Low D may contribute to chronic fatigue and depression. [261] [262]

- Seasonal Affective Disorder has been treated successfully with vitamin D.[263]

- High stress may increase the need for D or sunlight (UV-B) and calcium.[264,265,266]

- People with Parkinson's and Alzheimer's have been found to have lower levels of D.[267,268]

- Hospitalized or immobilized patients may need more D. Immobilization may require active $1,25(OH)_2D$ as conversion of D_3 seems to fail. [269,270]

- Low levels of D, and perhaps calcium, in a pregnant mother and/or later in the child are a contributing cause of cavities, 'crooked teeth' and myopia.[271]

- Behavior and learning disorders may respond well to D and/or calcium combined with an adequate, well-balanced diet and trace elements.[272]

- Single, infrequent, intense, skin exposure to UV-B light suppresses the immune system but chronic, low level exposure (as per the Safe Sun guidelines later in this book) normalizes immune function, enhancing NK (Natural Killer) cell and T cell production, reducing abnormal inflammatory responses such as found in autoimmune disorders, and reducing occurrences of infectious disease. [248] [273,274] [275,276]

In presenting this information I am not attempting to suggest that taking vitamin D in any form, sunbathing, or visiting a tanning salon can cure or prevent any of these diseases. I am trying to demonstrate there is significant evidence vitamin D status needs to be considered when evaluating our health status. This review covers a small part of what we seem to know.

Lack of light containing sufficient UV-B needed to make vitamin D or lack of vitamin D directly, as a supplement or in food, has been associated with numerous diseases.

In the studies that follow often there are assumptions about vitamin D status, that the subject has enough or too little, WITHOUT testing actual levels of vitamin D. This is unfortunate, as conclusions from these studies must fall into the category of _facts not in evidence'. What we can do by considering the studies is get some pretty good hunches. Think once again of the idea of 'approximation' in complex systems as covered in the beginning of this book. Let's take a look at some of the research.

LACK OF SUNLIGHT AND DISEASE

Some studies seem to show that sunlight improves health. If it is sunlight that makes the difference is it light, any or all, or a particular band of light, visible light, UV-A, UV-C or UV-B? If it is UV-B, since that is the band that produces D, the next

step needed to solve the puzzle is to determine what levels of D persons with and without these diseases actually have. Unfortunately this has rarely been done.

This is a short section with research specifically about sunlight and disease. It is short because the variables are tough to work with. Sunlight where? When? How? How much? It isn't a researchers dream. Even if you found sunlight worked how would you 'prescribe' the treatment?

There are problems relating the results of research connecting vitamin D from sunlight or just sunlight to health and disease.

1. Often the studies do not determine how much D the participants actually have.

2. Many studies are retrospective and assume that living in an area that has more UV-B, the ultraviolet range that produces vitamin D, increases general population vitamin D. It is very likely this is true but no one actually knows.

3. Studies using light are done in a clinical setting with controlled light. They may use UV-A or UV-B or a combination of various bands of light, something called simulated sunlight. If this light causes or prevents something from happening, good, or bad, it remains difficult to suggest this has direct application to you or me within the context of our current location and lifestyle.

The light outside your door does not and cannot mimic these completely artificial sources and when and how you would expose yourself to this light also modifies outcome.

The idea of simulated sunlight is a bit bizarre. Sunlight by its very nature is constantly changing by the minute as the earth moves around the sun spinning on its axis and the sun‘s rays travel around the earth and back and forth across the equator.

Natural sunlight varies depending on time of day, season, location, and presence or absence of clouds, haze, fog or smog. Studies using simulated sunlight or individual or mixed bands of light are limited in value because the conclusions are applicable to simulated sunlight

Data derived from these studies may or may not have any correlation with the lives of the General Public, you know, us, the real people in the real world living under the real sun. This limitation has shown itself in studies with sunscreen where results in the lab determining SPF (sun protection factor) under simulated sunlight don't necessarily apply in the outside world.[277]

Cancer and Sunlight

The Garland brothers, Cedric and Frank, both MDs and professors, work in San Diego, California. They have been studying the relationships between sunlight, vitamin D, calcium and cancer incidence over many years. In 1980 they first proposed an association between colon cancer and sunlight exposure. [278] Their research found

higher rates of colon cancer in higher latitudes, temperate zones north and south, which have less UV-B, the band of light that produces vitamin D in our skins. They also found higher rates of cancer in cities where UV-B light is blocked by pollution.[137]

In 1988 the brothers published The Calcium Connection, G.P. Putnam's Sons, New York, which offers an overview of supporting research and further describes disease relationships and sunlight. The book also offers high calcium recipes to help prevent disease. Calcium is vitamin D sparing. If supplies of vitamin D are low extra calcium can help keep bones, and perhaps other cells as well, protected.[191,279,280]

In their book the Garlands propose a novel calcium and cancer connection.

"Decoupling

Decoupling is the process of cells splitting apart from one another. It happens when the amount of calcium in the extracellular fluid is low. It is due to loss of tight junctions that bind cells of the intestine, breast, and some other tissues together. … .cells in many tissues will divide unless they receive a signal from neighboring cells. If the signal is blocked, as with a piece of plastic film between the cells, than cells on both sides of the film begin to divide.

…If for any reason the close contact between cells were interrupted, it would be as if you had cut an important wire in an electrical circuit. The signal cannot be transmitted and the cells that make new epithelium will begin to proliferate."

Thus the Garlands propose a possible explanation for our hyperplasic cells.

The GP version- Cells like having neighbors and depend on constant communication with them. When they can't communicate the cells seem to think they are alone and start producing neighbors. This is a premise. It may be true.

Very recent research supports the idea of damaged cell communications causing abnormal cell growth. Researchers altered skin cells in a way that damaged communication with neighboring cells and they began behaving badly, hyperproliferating (hyperplasia).[281]

The brothers suggest calcium as the primary modifier of communication with vitamin D as a helper.

Another view of this communication problem is offered by the work of Stahl's group in Germany. They found vitamin D, just the plain old vitamin D, cholecalciferol like we make in our skins or take in cod liver oil, induced cell communication in gap junctions.

Both high and low levels of cholecalciferol vitamin D reduced communication.[282]

Stahl determined the membrane modifier was cholecalciferol not calcitriol (considered the active hormone D) which suggests multiple roles for D metabolites

(more on this later). These findings support the Goldilocks‘ Principle, there is a 'right' amount of vitamin D, all of its metabolites, not too much and not too little.

Stahl's study also found that vitamin A and carotenoids influence cell communication. It appears that vitamin D, vitamin A, and calcium are several of the important communicators responsible for cells being good neighbors and not contributing to overpopulation, in a cellular sort of way.

What a cell does before it becomes cancerous is 'proliferate' as the Garlands describe. The first stage of proliferation is hyperplasia, the second dysplasia, and finally malignancy. Not all cells that are hyperplasic or dysplasic become cancerous but when you read the word, hyperplasic, on a lab report it should get your attention that something not so good is beginning to happen and 'dysplasic' means cells have altered even further from the healthy, normally proliferating cell.

Cancers of our Age; Prostate, Breast, and Colon

WB Grant and others have found a strong association between latitudinal UV-B and disease with increased cancers of the prostate, breast, and colon in latitudes more distant from the equator. [172,173,254,278,283,284,285,286,287,288,289,290]

Researchers argue, a lot, about the association, with more experts on the 'sunlight is dangerous' side than on the 'sunlight might help' side at the present time. Much of this prejudice is based on fears stemming from the rapidly increasing rates of skin cancer; especially the most deadly, melanoma, which has been attributed to excess sunlight exposure.

Clinicians seem to feel if anyone says anything nice about sunlight the entire population of the planet will immediately jump naked into endless summer and die. (I did say 'feel' not think.)

My own opinion is that you are smart enough to understand how sunlight works, once someone explains it, and will use moderation and common sense in applying the information. If you choose to ignore the information you may find yourself over or under-done in a sunlight way and less healthy than you might have been.

Melanoma

In several studies men with more moderate chronic exposure to sunlight had less melanoma than those with very little sunlight exposure.[284] These studies reaffirm the need to understand that value or danger, when it comes to sunlight, is relative. There is too much, too little, and just right. Intense intermittent exposure seems to up the risk for melanoma, especially in sunny climates and in those persons with lighter skins.

This makes sense as historically persons with lighter skins lived in places with relatively little UV-B. In other locations (the 'place' thing again) workers with regular

sun exposure had less melanoma and to further confuse the issue most melanomas appear on our bodies in areas that are typically not exposed to sunlight. [291,292,293,294]

Now we're all really confused. We have so much to learn and may not even be asking the right questions.

What may be suggested by these observations is that moderate chronic exposure to sunlight may increase vitamin D levels, which could be important in protecting against melanoma.

Our skins can directly convert sunlight from pre-D to cholecalciferol to calcidiol to the active vitamin D, calcitriol, which does play a role in melanoma, inhibiting growth in some studies. [295] In addition low levels of vitamin D have been reported in persons with melanoma.[296] and persons living in South East Queensland, Australia, an area having the highest rates of skin cancer in the world, were found to have vitamin D deficiency and insufficiency of 8% and 23% respectively.[297]

Calcitriol or similar analogs are being researched as a possible treatment for melanoma and have shown some positive results.[298,299,300]

Non-melanoma Skin Cancers

Too much sun contributes to skin cancer, no argument about it.[301,302,303,304,305,306,307,308,309,310,311,312]. But if you look at the references it isn't just UV-B that causes a problem, UV-A contributes too. Sunscreens were not originally developed to block UV-A and even the newer formulations are rarely effective in blocking UV-A for an extended period of time.

The best sunscreen is clothing or sun avoidance. Any good thing I say about sunlight means just enough and not too much, truly.

Susceptibility to these less aggressive forms of skin cancer can be reduced by good nutrition, getting enough vitamin A and vitamin D, using curcumin or topical nutrient preparations such as virgin olive oil, curcumin, green tea, vitamin E, aloe and vitamin C.[313,314,315,316,317,318,319,320,321,322,323,324]

Immune Function

UV light is often associated with immune suppression. In animal studies excess UV exposure, both UV-A and UV-B, changes certain blood values that indicate impairment in immune function.[325,326,327,328,329,330,331,332,333] The generally accepted idea is too much sun equals a suppressed immune system and this impairment leads to a number of problems including greater incidence in skin cancers, increased virulence of infectious diseases and possible reduced effectiveness of vaccinations.[334,335]

This immune suppression has been associated with the intensity of the UV light, skin sensitivity, and skin color. In the chapter on light you will find information on intensity.

As an example of what the study demonstrated light skinned persons who burn in 10-30 minutes, types 1-3, with sensitive skin, had a 50% suppression in immune response with UV exposure equivalent to 60 minutes, twice the highest safe level of exposure for these skin types.

In persons with less sensitive skin, skin types 4-6, the dose of UV needed to alter immune response by 50% could not be determined.[336]

> Clearly excess sunlight does us no good. Some of us need less sunlight than others. This does not mean avoiding sunlight improves immune function.

Researchers from Humbolt University in Germany and Boston University in the U.S. reported on the treatment of 21 children suffering from chronic colds with UV light containing both UV-A, 96.5% and UV-B 3.5% over 6-8 weeks. Vitamin D, 25(OH)D, values at the end of treatment increased reaching a range of 38.2-71 ng/ml. (Optimal is probably between 35-65 ng/ml) A number of immune markers altered to indicate improved immune function. The study doesn't say if participants then got fewer than expected colds but the indicators seemed positive.[337]

Once again we have an example of complex systems and our Goldilocks' Principle at work. Enough sunlight but not too much for your genetic type may very well help strengthen the immune system, as shown in studies with centenarians, while sun avoidance or sun enthusiasm may contribute to any number of diseases to shorten your life span or reduce the quality of your life.

Vitamin D, Immunity and Aging

In seniors 90-100 years of age vitamin D levels were a marker of longevity and immune health.[338] All the seniors in the study got their D from sunlight. We know this for two reasons. Researchers questioned participants and none reported supplement use and because the vitamin D they tested, D_3, is a marker of sunlight D.

The researchers sought to determine what might be contributing to the longevity of 37 women and 25 men between 90-106 years of age. They looked at thyroid hormones, TSH, growth hormone, estrogen, testosterone, DHEA, IGF-1, parathyroid hormone, and $1,25(OH)_2D_3$.

Only vitamin D values correlated with natural killer cell (NK) number and activity, a strong predictor of immune health. NK cells attack and destroy foreign, infectious, or cancerous cells. The authors suggest this elevation of NK cells compensates for decreased number and function of T cells (from your thymus, they help regulate your immune system and you have less as you age) protecting the seniors from infectious disease and cancer.

These same seniors, with adequate D and abundant, perky NK cells, also had normal thyroid function and preserved muscle mass and function.

While on the topic of aging gracefully, one other study of 55 centenarians is worth noting. Cell membranes are important to the health of your cells acting as a gateway to allow entrance to nutrients and release of spent molecules and protecting the cell nucleus from destruction.

Centenarians were found to have higher levels of the omega-3 fats, EPA and DHA in erthrocyte membranes than any other age group tested. These membranes contained less arachidonic acid and linoleic acid and less saturated fat and expressed higher membrane fluidity. This unusual balance caused a dramatic decrease in peroxidation; the omega-3 fats or some other component protecting the cells from oxidative damage.[339].

It is likely this group got these higher levels of omega-3 by eating fish., not by taking supplements. Unfortunately this group was not tested for vitamin D. Fatty fish contain vitamin D as well as omega-3 fats so enjoying fatty fish frequently may be a boon to longevity for more than one reason.

At the very beginning I discussed a study linking low vitamin D and muscle weakness. In seniors muscle and D are very related, lower levels of D repeatedly showing reduced muscle strength.[4,134,135,340,341,342,343,344,345,346] A decline in muscle function increases falls. Just the simple act of getting around is made much more difficult.

Vitamin D is important for muscle health and do remember, the heart is a muscle. Fish, like us, suffer from muscle problems if they don't get enough D. They develop a condition known as 'droopy tail'[347] Sounds familiar to me. Interesting isn't it, how all our parts and life's other parts are connected?

Hypertension

Epidemiological studies find greater incidence of hypertension at locations more distant from the equator. Hypertension incidence goes up in winter too. It is very likely optimal levels of vitamin D from UV-B sunlight modify blood pressure.[348] Krause and colleagues reported a significant drop in blood pressure in untreated mild essential hypertension. Treatment consisted of three weekly suberythemal UV-B exposures over a one-month period.[349] Suberythemal means exposure to UV-B light ending just before any, however slight, skin pinkening. Depending on the strength of the UV-B source this may be as little as just a few minutes. This treatment increased vitamin D levels from an average of 23 ng/ml to 60 ng/ml.

Studies showing an association between sunlight, D, and hypertension show sunlight to be a better reducer of blood pressure than supplementing with vitamin D.[350,351] Could it be that sunlight has the advantage of providing both vitamin D and relaxation? Other studies relate lower incidence in blood pressure with an active lifestyle, which is most likely out of doors providing more UV-B. As early as the 1960s high altitude UV-B exposure (there's more UV-B the higher your go) was shown to influence blood pressure.[352]

Multiple Sclerosis

One of the first diseases to be studied in relation to latitude, (our location problem), multiple sclerosis, still remains a mystery. Many studies have shown a correlation between latitude, climate, ultraviolet light and MS.[353,354,355,356,357,358,359,360,361,362,363]

Because of the proliferation of this research some MS sufferers have sought out sunlight, which has in a few cases been unfortunate, as heat tolerance is impaired with this disease and actual fatalities have occurred. [364,365] This is one more example of complex systems and should be a reminder to look at the whole picture before deciding how to approach understanding diseases and treating them.

The references listed here are just regarding sunlight and multiple sclerosis. Later in Vitamin D and Disease the relationship between vitamin D and MS is further reviewed.

Sunlight and Depression

Some absolutely anecdotal evidence, definitely second-hand, at its most unscientific best: In every class I have ever taught a nonscientific 99% majority of students raise their hands when asked if they 'feel better after a day in the sun'. I am well aware of the dangers of using the words all, ever and never but I still maintain the truth of my observation. The students raise their hand quite high.

Many light studies seem to show benefits for seasonal depression known as seasonal affective disorder- SAD. I am not referencing them here because this book is about sunlight and vitamin D and SAD studies have used artificial light. To my knowledge none have used actual sunlight. This is probably because it would require transporting persons with winter SAD, all located in the higher latitudes, to locations in the tropics, which would tend to make anyone feel better.

VITAMIN D AND DISEASE

The last time I searched there were more than 39,500 (increasing daily) citations on PubMed that reference vitamin D. These include studies on how vitamin D functions and research using vitamin D analogs (man-made substances like vitamin D but not found in real life and mimicking only some of the functions of D) to treat disease. of the studies relating vitamin D to disease states some are about not enough D and some about too much D. A relative few, about 1000, reference sunlight or UV-B

light. The following sections discuss conditions that are associated with having too little D and studies that have shown improvement in the conditions by improving D nutriture.

> *nutriture def. The state of the body in regard to nourishment, especially in regard to a specific nutrient, such as protein.*

Building and Maintaining Bones

Osteopenia and Osteoporosis

"There are 10 million Americans who have osteoporosis, 8 million of whom are women. According to the National Osteoporosis Foundation, another 34 million women have low bone density, which is a precursor to osteoporosis." Colette Bouchez, HealthScout News Reporter, June 23, 2002

Adding up the numbers it seems 44 million Americans have some level of degenerative bone disease. The population as of 2003 is estimated to be about 290,000,000. If these figures are even near correct it shows approximately 15% of the population suffering from poor bone maintenance. If dental health is related to bone health, which as you will see later it is, this percent reaches much higher. In 1985 the CDC (Centers for Disease Control) reported that 87% of 17 year olds had had cavities.

What is osteopenia and osteoporosis?

In 1994 the World Health Organization formed a committee to define osteoporosis.

Table 1 Osteoporosis Source: WHO

WHO definitions of osteoporosis and osteopenia	
Bone density value in relation to young adult mean	Classification
Within 1 SD	Normal
Between 1-2.5 SD	Osteopenia
> 2.5 SD	Osteoporosis
> 2.5 SD plus fragility fracture	Established osteoporosis

You are diagnosed as having osteopenia if your bone density is found to be 1-2.5 standard deviations below average bone mass for young adults. Bone density naturally declines with age. Some 16% of American white women in their 20s have osteopenia; less than 1% have osteoporosis. By age 65 about 38% of U.S. women have osteopenia and 20% have osteoporosis. Only 15% of women 80 years old have normal bone density.

In the research persons with higher levels of sunshine or vitamin D seem to suffer less from bone loss and low levels of vitamin D are associated with decreased bone density. (30,33,36,366,367,368,369,370,371,372,373) Other studies suggest that levels of vitamin D, serum 25(OH)D, the precursor to the active D, that are too high or too low contribute to or actually cause bone loss. (368,374,375,376,377,378,379,380,381)

Aging and bone loss combine to greatly increase fracture risk, which doubles every decade past 50. This fracture risk increase occurs even if bone density remains constant. Though studies using vitamin D to increase bone density in osteoporosis have shown mixed results vitamin D has shown significant benefit in reducing and

preventing fractures.[382,383,384,385,386] This is important because fractures limit mobility and cause pain.

Vitamin D has been used in varying amounts to treat osteopenia and osteoporosis with some successes and some failures. There are studies where vitamin D is not seemingly related to bone loss [387].

As suggested in the complex systems model, vitamin D is not the only factor in osteoporosis. Vitamin D-binding proteins and vitamin D receptors, both important to the way vitamin D works in our bodies, are inherited. These factors and others alter the way we absorb, store, and utilize vitamin D.

In some osteoporosis studies when supplements are used for treatment either the way in which they are administered or the amounts used may be a large part of the reason for poor response. Studies in Asia associate osteoporosis with lack of vitamin D, lack of calcium or lack of both[388].

A three-year study, published in 2002 from the University of California, Berkeley, Department of Epidemiology, looked at three different osteoporosis intervention protocols, a controlled diet, supplementing calcium and vitamin D, or supplementing with a multi-nutrient containing calcium, vitamin D, and other accessory nutrients. Ninety-nine late-postmenopausal women began the study. Eighty-three subjects completed the full three years of evaluation. Researchers found no bone sparing nor bone building benefit.[389] This study is a good example of the current problems understanding bone loss, calcium and vitamin D status.

Robert Heaney, M.D., Professor of Medicine at Creighton University, is a long time researcher studying bones, vitamin D, and calcium. Dr. Heaney suggests that the current acceptable serum values of vitamin D used to define deficiency or sufficiency for bone health are incorrect. His work has explored the lowest level of serum 25(OH)D needed to maintain bone health. His findings, supported by other researchers, suggest 32 ng/ml as a minimum value for bone health.[390]

In the Berkeley study researchers monitored 25(OH)D levels,. All three groups started with serum 25(OH)D averaging between 15-17 ng/ml, well below Heaney's minimum value for bone health.

At the beginning of the study only 7 women had D levels greater than 30 ng/ml. Over the three years of the study 25(OH)D did increase in all three groups but only the multi-nutrient supplemented women reached a group average level of D equal to or greater than the 32 ng/ml minimum and they did not reach this level until the third year when the study ended.

39 of 83 women ended with levels of 25(OH)D greater than 30 ng/ml. As this may be the beginning (lowest) value for bone building and bone keeping there might have been a different outcome had the study continued or had the researchers sought to optimize serum vitamin D.

If Heaney and other researchers are correct the lack of improvement in bone retention found in this intervention trial may have been because vitamin D either never reached levels necessary for bone building and bone retention or, in the 32 who did increase their D into Heaney's suggested range, the important value was not achieved until the last year of the study, too late to show an effect on bone.

Studies showing problems with too much D are extremely important and may be overlooked or ignored. This topic is covered in the chapter *How Much D Do We Need?* Regarding osteoporosis giving vitamin D when levels are already adequate can contribute to vitamin D excess, which may cause bone loss.[56] Once again, not too much, not too little; whether D or sunlight. There is an amount that is just right, for you.

There is strong evidence vitamin D testing should be a part of yearly health exams but at present it seems most clinicians are not yet willing to recognize and support the need for testing though some may be coming around.[391]

Better understanding of our individual needs for vitamin D, calcium, magnesium, and other bone elements is important for both prevention and treatment of osteoporosis.

Several of the current medical treatments for low bone mineral density are not without dangers, the familiar side-effects problem. Estrogen has been considered the best hope to rebuild bone but with the increasing incidence of breast cancer, and a definitive connection, however small, between estrogen intake and increased risk for cancer of the breast it becomes a much less agreeable choice.[392]

In the 1960's hip fracture incidence varied depending on race and location. [388] Caucasians in Northern Europe and North American had a higher prevalence of hip fracture than Asian and Black populations. African-Americans have very low levels of vitamin D and yet retain bone. This is attributed to yet unknown factors and an alteration in the vitamin D endocrine system in which calcium is reabsorbed in the kidney rather than being lost in the urine.[244]

Hip fracture is associated with osteoporosis however there can be low bone mineral density defined as osteoporosis without fracture and fracture can occur, particularly in older women, even when osteoporosis is not present.

Japan and other Asian countries have found success in treating osteoporosis with vitamin D and calcium. [366] Their treatment success rate has been greater than that in the U.S. There are a number of possible reasons for this. Fujita suggests that D receptor gene variations play a role. It is also likely that components of our Western diet, low in calcium and vitamin D with high levels of grains, sugar, and fats may interfere with positive treatment outcomes in the U.S. [393]

The common treatment for osteoporosis with fracture in Japan is the active hormone, calcitriol, a prescription drug. Asians have less side effects and better response to this treatment than Caucasians.[388] This reminds us once more of the problems underlying individuality and complexity.

In the U.S. treatments for vitamin D deficiency related osteoporosis use an injection or oral dose of pharmacological levels of ergocalciferol or cholecalciferol, or use the active hormone, calcitriol, as in Japan. None of these methods have been as successful as researchers and physicians would like. [394,395,396]

Bones undergo a constant 'remodeling'; they are torn down and rebuilt 24 hours a day. One of the diagnostic tests for osteoporosis involves a 24-hour urine sample. By

determining calcium intake from food and supplements and the amount of calcium spilled into the urine over a 24-hour period clinicians can make a rough estimate of daily bone loss.

Excess vitamin A, excess or low vitamin D, and low vitamin K have all been shown to increase urinary calcium loss reflecting bone loss.[397,398,399,400,401,402]

There are many studies suggesting that calcium and vitamin D have positive actions on bones, participating in building, keeping and remodeling them.[376,380,380,382,394,403,404,405,406,407,408]

Some of the most critical variables researchers consider when trying to understand the incidence of osteoporosis include genetics relating to variations in vitamin D receptors (VDR) and D-binding proteins (DBP), skin color (melanin content), and sun exposure at different locations, both latitude and altitude.

In Hong Kong, a sub-tropical location, one study found seniors, who spend much of every day out of doors due to crowded living conditions, had 25(OH)D levels of 57.7 ng/ml -+ 2.5, a value quite high compared to most Americans but within normal range. Osteoporosis in this group responded to calcium supplementation.

Seniors in institutions who did not have free access to sunlight had much lower levels of 25(OH)D showing better response with addition of both D supplements and calcium. [409]

Osteoporosis occurs worldwide, more frequently and with more serious side effects in women than men, greatly increases with aging, menopause, surgical menopause (removal of the ovaries) or andropause.

Treatment of osteoporosis in the U.S. currently consists of HRT (hormone replacement therapy, using estrogen alone or estrogen with progestin, synthetic or progesterone, natural) to encourage new bone production and/or bisphosphonates such as Fosamax, which slow bone loss by reducing the natural process of bone breakdown. These prescriptions may be combined with calcium supplements providing from 1,000 mg-2,000 mg of calcium a day with or without magnesium. Protocols may also use vitamin D supplements with doses ranging from 400 IU-1,000 IU a day.

For those with more serious bone loss or those with poor response to standard treatments calcium supplementation may be combined with the active hormone vitamin D, prescription calcitriol. More recently researchers and physicians have begun to use a genetically engineered parathyroid hormone that builds bone even after dramatic losses have occurred. [410] Other treatments under investigation include DHEA and recombinant human growth hormone.[411,412,413,414]

Preventing low bone density begins at an early age by first building dense bones. (Remember our _arrow of time‘?) Bone is built during pregnancy, infancy, childhood and adolescence and inadequate nutrition during any of these stages of growth will create less dense bone.

Trying to rebuild what was poorly built or lost through inadequate nutritional practices, lack of sunlight, or vitamin D is difficult and may require serious medical intervention. As yet no drug or hormone treatment rebuilds bone density to optimal young adult levels. Prevention is always better than treatment. Building and keeping dense bone improves health and quality of life and saves many healthcare dollars.

Often overlooked is the need for vitamin K [415,416,417,418,419,420] and other elements such as potassium, manganese, copper, zinc, and boron.[404,421,422,423,424,425,426,427]

GP The important lesson to learn from research is that developing nutritional habits, in our children and in ourselves, that build bone from pregnancy to old age, is the best bone defense.[110,428,429] AND you'll need more than calcium and vitamin D to guarantee healthy bones.

To build great bones and teeth our (parents and children alike) daily protocol needs to include weight-bearing exercise; adequate vitamin D from sunlight or supplements; and a diet that contains sufficient minerals and vitamins.

While bones have a high calcium and phosphorus content, bones contain other trace minerals and need yet other minerals to produce the elements that are responsible for bone health. These accessory minerals include zinc, copper, iron, manganese, magnesium, and boron.[426,430,431] Potassium, abundant in fruits and vegetables, reduces loss of calcium in the urine.[432] Vitamins associated with bone production (building new bone) include vitamin A, C, B_{12}, B_6, folate and vitamin K.[404,423]

Your best source of nutrients will always be whole, fresh food. Fresh fruits and vegetables, dairy if tolerated, and high quality proteins supply the major nutrients necessary to build and keep bone. Supplements may help but supplements cannot take the place of a good diet nor can they make up for a bad diet.

If you have been diagnosed with low bone density you have a good reason to regularly test your vitamin D level. When bone loss is evident the process of bone breakdown is occurring at a more rapid rate than new bone production. Make sure you have enough but not too much vitamin D and a diet that promotes bone growth.

To deal with the increasing costs and suffering related to osteoporosis in the United States we need to recognize the importance of vitamin D and the value of regular determination of serum levels of 25(OH)D to verify D sufficiency.

Education, from the government, schools, media, and mom, should emphasize nutrition FROM FOOD. We need to put in the time and effort necessary to understand how to get sufficient calcium and other minerals from our diets, the best way, and from supplements when necessary. A good beginning is consumption of whole foods and if tolerated dairy including milk, yogurt, kefir and cheese.

GP CAVEAT: Early research seemed to show vitamin D did little to prevent or reverse bone loss. Many of these studies used supplements too low to show change or too high, which may contribute to bone loss. Testing counts. It isn't the amount of D you take but what you actually get that counts. Vitamin D works along with ather essential elements so a study that doesn't monitor diet to make sure all the elements are present has little value. D tells cells what to do but they won't be able to do it without the essential

elements; the needed fruits, vegetables, protein, vitamin K, calcium, magnesium and other vitamins and minerals, necessary to build strong bones.

Hyperparathyroidism

Parathyroid hormone in our blood increases as we age. Parathyroid hormone goes up when vitamin D levels are low. As we currently rarely test D it makes me wonder if our ‗grown-up' lifestyles promote D insufficiency. We may spend more time indoors and use sunscreen when out of doors and most adults drink less or no vitamin D fortified milk.

Primary hyperparathyroidism (elevated above normal parathyroid hormone in our blood) may be caused by benign tumor, gland hypertrophy (overgrowth), or rarely, malignancy. Long-term deficiency of vitamin D and/or calcium may also contribute to primary hypothyroidism.[433,434,435,436,437] This makes sense when you understand the relationship of adequate vitamin D and calcium to normalizing cell growth.

Incidence of hyperparathyroidism is associated with reduced VDR (vitamin D receptors). [124,438,439,440,441,442] Parathyroid hormone down regulates VDR and vitamin D stimulates production of VDR. VDRs (vitamin D receptors) are the places where vitamin D acts to regulate your cells.

Primary hyperparathyroidism is diagnosed by elevated parathyroid hormone and usually, but not always, elevated serum calcium. Secondary hyperparathyroidism may be caused by a number of conditions, one, very common, being vitamin D deficiency.[443,444,445]

Unfortunately many physicians treating hyperparathyroidism, primary or secondary, do not regularly test for levels of vitamin D. Some who do test accept older, lower values of D as being sufficient, yet adequate vitamin D, reflected in optimal serum calcidiol levels, repeatedly lowers PTH. Internationally researchers have found men, women and children maintaining a 25(OH)D between 35-60 ng/ml build and maintain bone and do not test with elevated PTH.
[8,28,46,236,367,433,446,447,448,449,450,451,452,453,454,455,456,457,458,459,460,461,462,463,464,465,466,467,468,469,470,471,472]

Vitamin D deficiency and insufficiency both may result in elevated parathyroid hormone and hyperplasia (excess growth of cells) of the parathyroid gland. First line defense is to check vitamin D and optimize 25(OH)D levels. If low D is the issue vitamin D combined with calcium supplementation can lower parathyroid hormone in a matter of weeks. [65,386,463,473,474,475]

Diagnosis of insufficiency, of calcium or vitamin D, followed by nutritional intervention should be the first consideration in treating elevated PTH. Waiting until a need for surgery develops is sometimes the only option given to patients when only slight enlargement of the parathyroid gland is present. Some physicians do not routinely test 25(OH)D when PTH is elevated. This needs to change.

Teeth are bones too

Or at least they are 'boney'. Understanding the associations between teeth health (sounds weird, maybe I mean tooth health) bone status and vitamin D, opens a new

world of possibilities; living without braces, dental fillings, or brutal gum surgery for periodontal disease. Vitamin D plays a critical preventive role in all of these conditions (along with vitamin A, calcium and magnesium and trace minerals).
(174,476,477,478,479,480,481,482,483)

First to study and record the association between vitamin D and mouth health were Dr. and Mrs. Mellanby, a husband and wife team from England, early researchers in the use of cod liver oil to treat rickets. The Mellanbys were not only interested in rickets, the first recorded disease associated with lack of vitamin D, but everything about vitamin D and the boney structures of the human body.

Preventing and Healing Cavities

May Mellanby, working with dogs and later with children, found adequate vitamin D during pregnancy and infancy produced the best tooth enamel, the hard outer covering of your teeth. Mrs. Mellanby's work also showed that even if moms and babes didn't get enough D during pregnancy, causing impaired enamel formation (called enamel hypoplasia), children's teeth could be strengthened by adequate vitamin D and calcium creating a strong 'secondary dentin'. This process of improving secondary dentin was also shown to heal small erosions (beginning cavities) and protect from new cavities. (484,484,485,486,487,488,489)

In Ultraviolet Light and Vitamin D in Nutrition, Chapter 5, Teeth and the Antirachitic Vitamin, authors Blunt and Cowan consider the 'fermentation theory' of tooth decay first mentioned by Aristotle-

He asked

"Why do figs, when they are soft and sweet, produce damage to the teeth?" and answered "Perhaps because the viscous softness of the fig causes small particles to adhere to the gums and insinuate themselves into dental interstices, where they very easily become the cause of putrefaction processes."

In 1885 Miller proved Aristotle‘s premise on a more scientific basis which lead to the idea that cleaning the sticky particles from the mouth would retard the process of decay. Cleaning the teeth did indeed retard decay but did not eliminate it. Cowan and Blunt continue on page 45

"In fact, the 'fermentation' theory as the sole explanation for the prevalence of tooth decay fails to cover many situations. For example, adjacent teeth in the same mouth are by no means always acted on in the same way by the same organisms

… Why also, we might ask, do the teeth of primitive peoples the world over- Eskimos, New Zealander, Africans, and North American Indians- deteriorate so rapidly when they are brought under the influence of civilization? Certainly their primitive ideas of mouth hygiene have not been superior to ours

….why has there been no decline, but rather an increase in the occurrence of dental decay in spite of the fact that methods for the daily care of the teeth similar to those in use today have been known and advocated by doctors and dentists for the last five hundred years?"

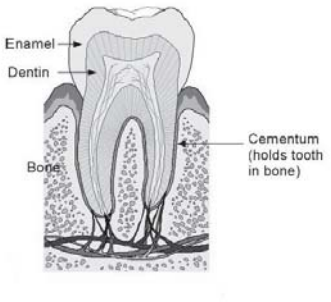
(and we still haven't quite learned that Crest is not enough!)

Great questions. Weston Price asked the same questions in Nutrition and Physical Degeneration published some 9 years after Blunt and Cowan's textbook.(271,490)

In 1925 researchers first demonstrated the existence of a circulatory mechanism inside the tooth, which allows for its continuous nutrition both during growth and after full growth has been attained. It was also demonstrated that calcium and phosphorus could be withdrawn from teeth when these minerals are needed during times of stress. Teeth are made up of three main parts, enamel (the outer covering), dentin (also called ivory) and pulp.

dentin def.
bone (calcified tissue) surrounding the pulp cavity of a tooth
a calcareous material harder and denser than bone that comprises the bulk of a tooth

Healthy enamel should be hard, brittle, and (Blunt and Cowan Chapter 5 page 46) "semitransparent…which to the naked eye has a smooth, lustrous, and whitish appearance. It is non-cellular and is built up of prisms…The pulp is soft… composed largely of cells, blood vessels, and nerves…The dentine, which makes up the largest portion of the tooth and is the most like bone in its composition, is a yellowish white, translucent substance consisting of a non-cellular, homogenous material … "



Dr. and Mrs. Mellanby published numerous studies between 1922 and 1928 reviewed by May Mellanby in "The Influence of Diet on the Structure of Teeth" Physiological Reviews October, 1928.

May's husband, Dr. E. Mellanby, used dogs as the primary subjects in his many studies concerning the cause, cure, and prevention of rickets. Mrs. Mellanby believed teeth, being part of the bony structure of the body, might also be affected by the same factors controlling the calcification of bones and that abnormalities of bones and teeth might be expected to run parallel. Mrs. Mellanby was given free access to her husband's canine research subjects to prove her hypothesis.

When teeth first develop there can be defects in the enamel. These defects may include slight roughness, discoloration, pits, grooves, or even entire absence of enamel over certain areas. Mrs. Mellanby found she could control development of defective enamel and dentin by feeding diets lacking vitamin D.

Normal, strong, healthy teeth were produced and protected by adding cod liver oil; egg yolks which contain vitamin D (the amount depending on the laying hens exposure to UV-B sunlight); irradiated food; irradiated olive oil; or irradiated plant sterols (such as found in yeast). In this case irradiation means exposure to UV-B light.

GP: A short sun bath of UV-B light converts pre-D in food fats to vitamin D, which gives a whole new meaning to outdoor lunchtime (high UV-B) cooking and eating.

Recent research continues to confirm May Mellanby‘s findings showing ultrastructural changes in the tooth root and demineralization of cementum and dentin with low dietary levels of calcium and vitamin D.[83,369,491,492,493,494,495,496,497,498,499]

While exposing dogs to sunlight or sunlamps improved teeth, Mrs. Mellanby found the results were not equivalent to giving cod liver oil. What was not known at that time is that dogs and cats do not make significant vitamin D in their skins.[500,501,502] Carnivorous animals primarily get vitamin D from their prey. A minor source may be from the natural oils on their coats exposed to sunlight and orally absorbed during grooming of their own or others' coats or fur.

Tooth development occurs very early in mammals and defects are difficult or impossible to change at a later stage of growth. Dentin responds to the current diet. An adequate diet for several days, followed by poor diet, and then improvement to adequate once again, can create a tooth with successive layers of poorly constructed and well-constructed substance. This, once again, brings in our ‗arrow of time‘, the importance of timely action.

What pregnant moms, infants, and young children are fed will influence dental and orthodontic visits (and costs) for the rest of the child's life. In the 1920's most infants had normal first teeth. Problems began after weaning. Some teeth were protected, having a more normal dentine, such as the incisors, because they formed first and were more fully calcified before weaning occurred.

Mrs. Mellanby's original research involved dogs, rabbits, and rats. During the late 1920's she began working with children‘s extracted teeth. Over the course of her research she examined more than one thousand temporary (deciduous) and 266 permanent teeth. Temporary teeth were largely used because they fall out naturally. Permanent teeth are only available from cases where they had fallen out due to gum disorders or had been intentionally extracted due to crowding of teeth, conditions that attest to prior poor conditions of the mouth.

Teeth were categorized as normal- enamel smooth, little pigmentation, and the dentin free from 'interglobular spaces', slightly underdeveloped, moderately underdeveloped and severely underdeveloped, showing defects in enamel, dentin or both. What she found disturbed her greatly. Out of 1,036 teeth only 149 were soundly constructed. About one quarter were slightly underdeveloped, but nearly two-thirds showed moderate or severe 'hypoplasia'. (underdevelopment because of a decrease in the number of cells)

As with the animals, the incisors (front teeth), early formers, were relatively well constructed.

Mrs. Mellanby observed,

"The first and second molars, or 'grinders,' were very poorly constructed, three-quarters of the first and nine-tenths of the second molars being classed as moderately or grossly underdeveloped."

The diets of these children were not available to analyze. All the participating children were located in England, 52° north, where the Mellanbys lived and worked, so little UV-B sun exposure was possible. Mrs. Mellanby did note that teeth from private sources were in better condition than teeth from dental clinics. Page 54

"Even among the more well-to-do children, however, only a little over one-fourth of the total teeth were really well formed, and about one-third showed 'hypoplasia or severe hypoplasia.' Poor temporary teeth presaged permanent teeth, which were equally poor in quality and in some cases worse."

So we have a tooth; enamel, dentin and pulp (there is cementum too, but not a factor in our story). It appears that if diet and timing are right you get 'good' teeth, or not. Well, maybe.

Generally, poor tooth structure promotes tooth decay. It is those later-forming back teeth that are most often found to suffer from decay. In examples of teeth with normal or nearly normal teeth Mrs. Mellanby found less decay, about one quarter having cavities as compared to 85% decay in the poorly formed teeth. Incisors (front teeth) were much less carious while molars (back teeth) suffered 100%. Size and extensiveness of decay also bore a direct relation to tooth structure in 90% of cases. What about the other 10%?

Mrs. Mellanby made an interesting discovery. Completely calcified and full-grown teeth can, under certain circumstances, produce something called 'secondary' dentine.

In dogs this process can be stimulated by rubbing of the teeth, perhaps one of the reasons chewing bones protects your dog's mouth. In humans this secondary dentin occurs naturally, if it appears at all, under decayed spots or portions of the tooth that have been worn away by use. It is evidence of effort by the tooth to repair the damage and protect vital tissues of the pulp.

Like the original tooth, secondary dentin may be well or poorly made. In dogs the quality of the diet determined quality of secondary dentine. Vitamin D deficiency may result in secondary dentin of poor quality or even complete absence of secondary dentine.

In Mellanby's study the children's teeth having normal calcification and decay, that unexplained 10%, were found to have abnormal secondary dentine. In these cases secondary dentin was found to be absent or defective in structure.

So, whether your childhood diet was abundant or deprived, the long-term health of your teeth depends on what you do every day, right now. You do have a second chance, for good or ill. Even as a senior you can make a difference in long-term retention of your own teeth by dietary modifications.[369]

Mrs. Mellanby joined forces with Dr. C.L. Pattison, medical superintendent of the King Edward VII Hospital, of Sheffield, England and J. W. Proud, an English dentist to provide groups of children with varying amounts of 'antirachitic' factor, vitamin D. The variables used in the studies were interesting and I refer you to the text if you want or need more details.

The short version of the studies‘ settings and participants; children were under 12 years of age and in a hospital setting being treated for bone tuberculosis. They were bed ridden but daily exposed to significant light through a window. Unfortunately the text doesn't tell us if the window was ever opened. You will see later that this is important because the particular band of sunlight that provides vitamin D does not penetrate glass. Three separate studies were completed with different variables and controls used.

Many of these children had very poor teeth. To truly test the influence of 'antirachitic factor' on tooth decay the children with the worst teeth, defined as having the most cavities, were given the best diets. The basic diet consisted of milk and meat daily with moderate amounts of fruit and vegetables. (I am not sure what 'moderate amount' might mean in the 1920's in England)

Children received more or less vitamin D from various combinations of light, food, and cod liver oil or irradiated ergosterol, depending on the study. At the time, as I am sure would happen now, investigators argued about the meanings, doses, and conclusions. BUT in all three of these studies higher amounts of vitamin D, whatever the source, produced fewer new cavities and the arrest of some cavities already present.

To quote the authors "…the indications are very clear that vitamin D is an important factor in building up the resistance of the teeth and preventing the spread of caries."

Exactly why enriching the diet with vitamin D promoted healthy teeth had yet to be determined.

Our conclusion is that adequate D, currently an unknown amount but more than what the participants began with, promotes development, growth, and maintenance of healthy teeth.

The researchers never knew how much D their subjects had at the beginning, or end, of the study as they had no way to determine the serum level of vitamin D. The ability to test serum vitamin D did not become available until many years later. They also did not know how much D they were actually giving. An accurate test for vitamin D, in food, cod liver oil, or supplements, was yet some years away.

In the 1930's the mechanisms by means of which the secondary dentin is formed remained controversial. Some believed the calcium being laid down in dentin was derived from the saliva, being deposited externally rather than internally from the blood. Turns out they were right.

Modern thoughts on healing cavities can be found in an excellent text, Applied Oral Physiology, R.J.C.Wilding. BDS, Dip Pros. M.Dent. Ph.D. Dr. Wilding's website offers an online look at how cavities form and how they can be treated and arrested in the early stages.[503]

Wilding agrees that replacement of calcium occurs in secondary dentin but adds the process is also active in the enamel. While Wilding's current treatment focuses on increasing saliva flow to bathe the teeth in salivary calcium, and fluoride applied topically (something I don't agree with), the role of vitamin D is not diminished.

Working with Mrs. Mellanby, Dr. Pattison found the calcium content of children's saliva doubled or trebled when changing from a diet low in vitamin D to one that was adequate in this nutrient. More recent studies with rats (and levels of vitamin D in persons with diseased salivary glands) suggest that vitamin D is essential to healthy saliva, both quality and quantity.

Increasing vitamin D to optimal levels increases salivary ionized calcium and increases salivary flow. [504,505,506,507,508]

When we eat carbohydrates bacteria naturally found in our mouths begin a process of carbohydrate fermentation, in agreement with Aristotle's premise. This fermentation dramatically lowers the pH of the mouth.

From 'Evidence based management of dental caries; a review of the repair potential of the pulp-dentine', Dr. Wilding:

"Provided the pH does not drop below 5.3 the enamel remains intact, but below this critical level, crystals of apatite dissolve. Fortunately both plaque and saliva are saturated with calcium and phosphate ions, so that if the pH returns fairly rapidly above the 5.3 level, ions will go back into the enamel and recrystalize."

The work of earlier researchers showed that the level of calcium in the saliva is altered by vitamin D status. Accordingly, increasing calcium alters pH in a way favorable to tooth health. Later research confirms this and adds that that there are other important components controlled by vitamin D, which contribute to healthy saliva and thereby tooth health. Research old and new confirms the need for calcium and vitamin D to avoid 'the drill'.

We have somehow, in spite of all evidence, managed to miss (or ignore) this connection between bone health and teeth. Citizens of developed countries not only have degenerative disease at alarming rates we have really bad teeth. Cavities and braces are accepted as normal. They are actually expected. There is a connection between our nutrition, our bones, and our teeth. Vitamin D levels, for good or for ill, alter the health of our bodies. All our body parts are connected.

It isn‘t just bones and teeth that are connected. Heart disease has been associated with osteoporosis and with loss of teeth. [509,510,511,512] Multiple sclerosis has been associated with low levels of sunlight or vitamin D but also with more cavities.[513]

Tooth health reflects bone health as both require the same elements for normal structure and function.[482,514,515,516] Elisabeth Krall and colleagues found supplementing extra calcium and vitamin D reduced tooth loss in seniors.[369] Tooth and bone complications of aging may be prevented or treated with a good diet, vitamin D, and adequate minerals works.

In Vitamin D, Feldman, Academic Press, 1997, Chapter 27, *Vitamin D Action on Tooth Development and Biomineralization* Adrian Berdal gives an update and confirmation to the vitamin D and tooth health story. Dr. Berdal tells us that enamel is the only mineralized tissue of 'epithelial' origin.

Vitamin D's relationship to development of normal epithelial cells is discussed in the section on vitamin D and cancer. Low levels of vitamin D, or high levels, result in impaired formation of tooth enamel.[69,499,517,518,519,520]

Periodontal Disease, an indicator of bone health

Periodontal disease comes in two different forms, disease of the gingiva (gums to you and me) and disease of the bone (but which also involves the gums). In The Nutrition Crisis, a reader , 1975, West Publishing Co., Theodore P. Labuza, Editor, Chapter 21, *Dietary Calcium and the Reversal of Bone Demineralization*, last page of the chapter, page 204, Leo Lutwak, M.D., Ph.D. says (emphasis mine)

"Based on our research findings there is a hierarchy of change when bones start to demineralize under osteoporotic conditions. First, decreases in bone density are detected in the jawbone, then in the vertebrae and other bones in the body. If

periodontal disease is correctly diagnosed (my comment- meaning the disease in this case is related to bone) and correctly treated by increasing the dietary calcium at the time it's first found, then the vertebral disease (osteoporosis) doesn't progress to the point where fracture can occur.

People visit dentists on a regular basis but only go to physicians after trouble is well established. An excellent example of preventive medicine in action can be illustrated by the dentist who detects early jawbone demineralization. If his diagnosis is substantiated, he can initiate proper therapeutic regimens to improve calcium intake before the disease has progressed to osteoporosis of the vertebrae."

In 1974 Dr. Lutwak was a Professor of Medicine at UC Los Angeles. Lutwak's work concentrated on calcium, phosphorus, and magnesium metabolism. While he did not consider our topic, vitamin D, these elements, the macro-minerals and vitamin D, are intimately related in the human body, including our teeth. His recognition that the mouth, that is the condition of the jaw bones, gums and teeth, reflects bone health combined with our early researchers' findings regarding vitamin D and mouth health suggest there is a great deal of common sense in dentists screening for bone problems and vitamin D sufficiency. More recent research confirms the vitamin D connection in young and old.[521,522,523,524,525]

Some dentists in America do inform patients of bone loss and its possible implications and even offer referral or treatment, but many don't. In questioning persons across the U.S. diagnosed with gum disease and bone loss few had been told their condition might be reversible. At the present time even if patients are alerted to the degenerative processes occurring in their mouths treatment typically focuses on replacing calcium, which used alone, rarely succeeds in reversing the degenerative condition.

Recent research concerning periodontal disease and vitamin D continues to show the benefits of D.[369,526,527,528,529,530,531]

The work of early researchers, Mrs. Mellanby, Pattison, and Proud, and confirmation by later researchers, demonstrates that vitamin D plays an important role in the health of bone, gums, and teeth. [174,476,479,481,482,532,533] The large body of work in this area demonstrates the wisdom of consuming a balanced diet with plenty of calcium, other accessory nutrients, and vitamin D at any age.

Testing and monitoring serum 25(OH)D to make sure vitamin D is sufficient is an important part of any bone-building (and tooth building/saving) treatment protocol. Supplying adequate vitamin D along with minerals and trace minerals provides the elements needed to reverse bone loss, tooth destruction, and gum disease.

Making sure mothers have sufficient minerals and vitamin D throughout their pregnancies and during lactation, guarantees stronger, healthier teeth and bones for their newborns. Assuring a continuing sufficient supply of these same nutrients to infants, children, and adolescents supports life-long health of teeth and bones. For those who have not been fortunate to have a wise mother, providing the elements necessary for good bones and teeth, two very simple, cost effective, steps, early detection of tooth and bone disorders, by examination and x-ray, and follow-up treatment with minerals and vitamin D, can restore and maintain the health of the mouth at any age.

Saliva and the health of your teeth

Vitamin D plays a critical role in the amount and composition of your saliva. You may not be aware that your saliva is a dynamic substance that contains an amazing number of substances including hormones, enzymes, minerals and electrolytes.[534] In fact, serum (blood) electrolytes including ionized calcium, and other serum elements such as estrogen, testosterone, DHEA, and cortisol are reflected in saliva values.

The two vitamins and one mineral that have been documented to have direct impact on saliva production are vitamin A, vitamin D, and zinc.[476,504,508,535,536,537,538,539,540] Zinc is most strongly associated with the immune capabilities of the mouth while vitamin D and vitamin A promote normal cell replication. As you may have noticed the inside of your mouth is always sloughing off. Old cells die and new cells are produced daily. Low levels of key nutrients may cause alterations in the structure and function of new cells, especially cells that replace at a rapid rate like those composing the lining of the mouth and digestive tract.

Saliva contains vitamin D[541] and other markers of bone health. Ionized calcium, also known as free calcium, is the active calcium in our bodies, immediately available for cellular functions. Low levels of ionized calcium are found in states of vitamin D deficiency.[542] Most calcium in our bodies is bound in bony tissues including hair and nails, bones and teeth, or in the blood to a protein- CBP Calcium-Binding Protein (there are many of these). What is important about free calcium is its ability to move about in our bodies and be readily accessed as needed for any number of functions.

Note to the GP:
My comments on ionized calcium do not mean that buying supplements advertised as being ionized calcium will bring about specific or favorable results. The way the body works is much more complex. Serum ionized calcium is regulated by vitamin D and parathyroid hormone and has nothing to do with the type of calcium you consume. Calcium in food is the best calcium for all of us. If supplementation is necessary, calcium, whatever the source, is best utilized by your body if taken in small doses, not greater than 200-300 mg at a time, throughout the day, with meals.

Osteoarthritis

While watching cable news one of those CNN tickers that go across the bottom of the screen read, "One third of all Americans suffer from arthritis or joint problems." Turns out it was an AP press release from a report issued by the Centers for Disease Control and Prevention. The numbers were shocking. 69.9 million of us suffer joint pain and swelling every day.

Cartilage is destroyed and remade. As aging and injury slow this regenerative process abnormal conditions of the joints occur causing pain and disability. Injury contributes to a more rapid degeneration of cartilage. Vitamin D plays a role here too. Osteoarthritis is a disease of degeneration defined as 'inflammation of the joint causing loss of cartilage'. It is also called 'degenerative joint disease'. Most persons I meet accept this condition as normal to aging.

Treatments are always some form of anti-inflammatory medication or nutritional supplements with anti-inflammatory action or joint support formulas containing some form of glucosamine and chondroitin.

In several studies low levels of vitamin D intake and low serum levels of vitamin D were related to progression of osteoarthritis. In one of the studies *moderate and low levels of serum 25(OH)D were associated with destruction of joint cartilage*. No current studies have yet connected low levels of vitamin D with 'cause' of osteoarthritis but two of three did associate low vitamin D with more rapid degeneration and loss of joint space. (543,544,545)

Consider the CDC report. In 2001 degenerative joint disease cost Americans $80 billion dollars in medical care and lost wages. What made this report more interesting is:

"The arthritis level ranged from 17.8 percent of adults in Hawaii to 42.6 percent of adults in West Virginia. States in the central and northwestern parts of the country had the highest rates."

Makes you wonder if that Hawaiian sunshine doesn't have some very beneficial effect.

Back Pain

In January of 2003 researchers in Saudi Arabia reported on the ability of vitamin D to correct back pain.(49) 360 patients, 90% women, attending spinal and internal medicine clinics experienced lower back pain continuing for 6 months or more with no obvious cause. 83% were found to have very low levels of 25(OH)D. After one month of treatment with very high doses of vitamin D all of the patients with low levels of D experienced improvement. A total of 95% of those treated, including those beginning with normal levels of vitamin D, experienced a resolution of back pain.

Saudi Arabia has very high levels of UV-B making it easy to produce vitamin D IF skin is exposed. Local religious and cultural traditions support customs requiring women to be covered when out of doors. Women are also unlikely to participate in outdoor activities such as sports. Our lesson is that sun can't help us, no matter where we live, if we don't go out in it and expose our skin. The results also show that _normal' levels of vitamin D may not be enough. Optimal levels bring optimal health, which in this case meant relief from back pain.

Note to the GP: This study also shows clearly how effective clothing is in preventing exposure to UV light.

Cancer

In pre-cancerous states (cells aren't cancerous but things don't look and behave quite right) there is always a condition of abnormal 'plasia' (function), whether hyperplasia or dysplasia. Cancer cells are classified as 'malignant'. "Malignant" has four meanings, one is 'harmful', that works. Another meaning is defined as 'evil', which I also like. Cancer certainly seems evil to me. The medical definitions are 'likely to grow or spread' and 'likely to cause death'. Obviously malignant cells should be avoided whenever possible.

The suffix of each word is 'plasia' which means 'formation'.
hypoplasia, def below, under, deficient, formation (you read this before about tooth enamel and vitamin D)
hyperplasia, def. above, beyond, excessive formation
dysplasia, def. faulty, bad, improper, formation

First, before cells become malignant, they start reproducing in abnormal ways. You have heard the word pre-cancerous, used perhaps when your dermatologist looked at the funny skin on your nose or the top of your ears, or after a biopsy of any number of body tissues or following a colonoscopy. You don't have cancer BUT you have these funny cells.

Because we make new cells all the time growth of these new cells must be carefully regulated. We want normal 'plasia', I know it isn't a word but you get the idea- normal new cells. The other -plasias, what causes them? A number of studies with animals, especially rats, have determined the Western diet, low in vitamin D and high in fat and refined carbohydrates, causes hyperplasia in various organs and tissues.[546,547,548,549,550] What is interesting is that when these animals are given extra vitamin D and calcium, while still eating the animal version of the high fat Western diet, the hyperplasia reverses.

I just have to say that again. Not so great a diet, similar to the human high fat, high sugar diet, plus extra vitamin D and calcium reversed hyperplasia. So far only rats have been studied but it certainly is very interesting.

Other studied causes of hyperplasia include several vitamin deficiencies including low levels of vitamin E, vitamin A and folate.[155,546,550,551,552,553] Drugs, chemicals, hormones, and medications can also initiate or contribute to hyperplasia and abnormal cell growth. [201] Excess exposure to UV-A or UV-B in sunlight induces hyperplasia of skin cells.[302]

So, is it possible that the diet we consume in developed countries, all that added fat and refined carbohydrates, is a primary contributor to the dramatic increased incidence of cancers, especially cancers of the prostate, breast, colon and skin? It is very likely. What these most common cancers, prostate, breast, colon and skin, have in common is that the first abnormal cells are found in the epithelium.

New word-
epithelium, def: The nonvascular cellular layer that covers the internal and external surfaces of the body.

These epithelial cells compose our inside and outside walls. Walls are important to keep things out and let things in. These cells are nonvascular. That means they don't have a direct blood supply, no vessels or capillaries. Epithelial cells are found in your skin, all of the mucous membranes in your body including the surface of the digestive tract from mouth to anus, your respiratory tract including lungs and sinuses, and the lining of the vagina. They line the ducts found in the breast and prostate. Tooth enamel, the outside of your teeth, is formed from mineralized epithelial cells.

What is it about these cells that make them more vulnerable to environmental influences like diet and damage from chemicals and sunlight? One reason is simply exposure. They get the brunt of chemical exposure, physical damage from injury, or any other kind of abuse that comes from the outside environment. There is another reason.

Many epithelial cells have very short lives, with good cause. Epithelial cells are constantly being replaced from underneath. That means that the top cells slough off. You notice it when you realize it is time to soak your feet because there is a lot of dead skin to remove. The fancy word, used by cosmetologists, estheticians, and make-up sales persons is exfoliate. You may have been told you need to do this.

This loss of surface cells is important for the health of your whole body. When old cells slough off, dead skin cells or the cells lining your mouth, throat, stomach, and intestinal tract, they take any bacteria, toxins, or other pathogenic organisms that have hopped on, with them. Think of the lizard who when attacked gives up his tail and grows a new one. He does this because by giving up his tail he retains his life. It increases his chances of survival. Like the lizard's tail, surface cell sloughing takes potentially invasive organisms away so that these substances can't harm you. Our outer and inner walls are our first line of defense. Pathogens or toxins (bad things, living or otherwise) can't get us if they can't get inside us. Sloughing and renewal is an important part of our immune defense.

Over time, because these epithelial cells are replaced so frequently and because the underlying cells are exposed to outside elements that may cause damage, there is a greater chance for chromosome errors. Fast replicating cells are also more likely to suffer from nutritional deficiencies. Rapid growth, as we see in children, during pregnancy, and here with rapid growing epithelial cells, requires excellent nutrition or the cells cannot form naturally.

Cells composing the lining of the colon have one of the shortest life spans of any cells in the body renewing every few days. Colon epithelial cells consequently have high nutritional needs. Daily nutritional intake becomes critical whenever rapid growth occurs so that gene expression is accurate and the elements of each newly formed cell are chemically complete.

The Western Diet

You read the association of the Western diet and cell hyperplasia. Mice and rats are often fed a 'Western Diet' in research. There are a number of versions of the Western diet. One is high in cholesterol. The Western diet used for the hyperplasia studies was formulated to be high in fat and refined carbohydrates and low in calcium and vitamin D. Unfortunately I was unable to gain access to the exact formulations, often different studies use very different formulations with the same name, and this raises some problems. There is no indication of the fats used and different fats make huge differences in outcomes. A second consideration is that rats may not respond exactly to diet and supplements as humans do. Even with this being true the addition of calcium and vitamin D did alter outcome.

When the American or Western diet is compared to traditional diets composed of whole foods the potassium content is very low. Traditional diets contain about 2 mg of potassium for each calorie consumed which means about 4,000 mg of potassium in 2,000 calories. The typical U.S. diet contains less than 0.5 mg of potassium for each calorie consumed.

Potassium is the body's choice to neutralize acid in the kidney. When foods are refined the potassium content drops precipitously, whole sugar cane containing 2 mg potassium for each calorie, white sugar containing none. Whole peas lose ¾ of their potassium when canned, cooked and drained.

The modern dietary shift to refined, processed, foods which are thereby low in potassium alters pH from alkaline to acidic which is why the U.S. diet is considered acidogenic.[554,555]The Western diet is not only acidogenic it increases cortisol production, a symptom of bodily stress.[556,557]

The Western diet is typically very low in potassium as the highest potassium containing foods are fresh fruits, vegetables, whole grains (the potassium is in the bran), and unrefined sugars. This lowering of dietary potassium is responsible for an increase is calcium in the urine in some persons. When potassium is sufficient (from whole foods or supplements) calcium is retained in bone.[483,558,559,560] The kidney is preferentially designed to use excess potassium as the buffer. As shown in research, when the diet is low in potassium your body will actually rob calcium from your bones to neutralize acids in the kidney.[561].

Humans eating higher amounts of whole fruits and vegetables have significantly higher bone mineral density.[562] They also have less cancer and heart disease. Cats given a chance to choose between acid, neutral, or base diets will always pick the neutral or basic formulas over the acidic trying to preserve pH balance.[563] Smart cats.

When dietary potassium is low and calcium, either from bone or from supplemental excess, is excreted in the urine there is a greater chance of kidney stones developing. Adequate potassium helps prevent stone formation by neutralizing pH reducing the need for dumping of calcium.[558,564,565,566]

The ability of the kidney to utilize calcium does not mean extra calcium is a good solution. Calcium as a pH neutralizer is second best, a necessity when potassium intake is low. When whole foods are consumed sufficient potassium is available to act as a buffer and calcium, and thereby bone, is spared. When dietary potassium is high much less calcium is necessary to keep cells and bones functioning normally.

The promotion of whole foods and the recognition that processed foods, even when fortified, provide little nutritional value should constitute the core of national health policy but this is unlikely to occur. The acid load of the Western diet which currently contains high intakes of sodas, including diet sodas, refined sugars, refined grains, proteins, and fats, all acid producing, would require excessive amounts of calcium to act as a primary buffer in the kidney.

It isn‘t just your kidneys that need potassium. The lowest level of potassium associated with protection from stroke and heart disease is 4,000 mg a day. The RDA is 2,000 mg a day and the typical intake in the U.S. is 1,500 mg a day.

My point? The complex systems thing again; it isn't just a lack of calcium and vitamin D causing us problems. We consume diets high in fat and refined carbohydrates and low in fresh vegetables and fruits. These are diets typically found in hospital cafeterias, school breakfast and lunch programs, school and hospital snack machines, and the homes of many (most?) Americans. Quick serve processed foods contribute empty calories and are primary causes of the current health crisis encompassing increasing rates of degenerative diseases including cancer, osteoporosis, caries, diabetes, and obesity.

Not even rats should have to eat a Western diet.

Colon Cancer

Colon cancer is one of the most deadly cancers and one of the most common causes of cancer mortality in developed countries. Calcium and vitamin D have shown specific benefit in the prevention of this cancer.[285,286,547,567,568,569,570,571,572,573,574,575] While diet may be the inducer, low fiber in the processed foods we eat, all that fat and refined carbohydrate, there is mounting evidence that correcting vitamin D and calcium balance may make a big difference in colon cancer incidence and outcome.

In the Faroe Islands, a group of small islands in the north Atlantic, 62° north, the incidence of colon cancer is the lowest in all of Europe and North America.[576] The Faroese diet is high in fish, calcium, and vitamin D. Favorite foods include whale and blubber, a full 25% of total meat intake and 9.5% of dinner meals; fresh fish, 44% of dinner meals; seabirds and seabird eggs all exceptionally high sources of vitamin D. Dairy cows, which graze on local forage, provide fresh milk, butter and cream. Local sheep provide both wool and mutton. The diet is low in processed foods, grains, and sugar. The major vegetable is potato (high in potassium when you eat the skin) grown locally.

Breast Cancer

A number of studies show a relationship between sunlight and breast cancer, consistently suggesting more sunlight, less breast cancer. [259,288,290,577,578,578] This puts women in a difficult predicament as they are repeatedly instructed to use sunscreen and practice sun avoidance by their physicians and dermatologists. Often they comply

hoping to prevent skin aging and skin cancer and their cosmeticians and dermatologists applaud their vigilance. At this moment you may wonder, at what cost?

Could our national obsession with sun avoidance have anything to do with the large increases in breast cancer in the U.S.? Ainsleigh suggests the 17% increase in breast cancer between 1990-1992 may be the result of 10 years of sun avoidance. He estimates 30,000 cancer deaths, from various cancer types, could be avoided by regular sun exposure.[284] Estrogen-containing hormones have also made a contribution to the breast cancer increase.[392,579]

Unfortunately it is very likely women using sunscreens and avoiding the sun are the same women using the Pill or hormone replacement therapy. Vitamin D is an antioxidant protecting cell membranes and this includes those of the breast tissues. It has been favorably compared to vitamin E and tamoxifen in antioxidant activity. [226,227] As sunlight is our major source of vitamin D, women (and their physicians and estheticians) need a new attitude.

In experimental high fat, high sugar (Western) diets abnormal changes occurred in breast tissue. These changes were reversed by additional vitamin D and calcium.[577] These changes in breast tissue weren't cancerous but abnormal hyperplasia. Hyperplasia does occur before cells become malignant. Since high intake of fat is associated with hyperplasia wouldn't a low fat diet be advisable?

Besides the unpalatably of such diets they lack critical essential fatty acids. Moderate intake of fats as they *naturally occur in foods* as has been the custom of our ancestors seems more appropriate. Our only sources of dietary A and D are found in natural fats like butter, cream, egg yolk and fatty fish. Fish, the highest natural source of D, store most of their D in the fatty organs and fat under the skin, not parts eaten by most American women (or men for that matter).

So we have two sets of hints from breast cancer studies, research that found higher breast cancer in women getting less UV-B sunlight; and research that fed animals high fat and carbohydrate diets and saw abnormal changes in the breast that reversed when the animals were given more vitamin D and calcium.

So let's take a look at the studies testing vitamin D levels in women with and without breast cancer.

Here is where I have to rant just a little. D is important for normal cell growth and more sun seems to correlate with less breast cancer. I live in Marin County, California with one of the highest rates of breast cancer in America. [580] Someone must have tested women for vitamin D. Imagine that you find out there are few studies. Researchers have looked at 25(OH)D in a few studies but most focus on 1,25(OH)D. There are reasons.

At some point in time the research with D and breast cancer turns to the active metabolite calcitriol; partly because it does participate in cell expression and because breast cancer cells do respond to 1,25(OH)D. Researchers are certain vitamin D has anti-cancer potential but instead of determining how much D we have and perhaps how much D we might need many researchers shift to studies using $1,25(OH)_2D$, the hormone form of D. in pharmacological doses; or creating and experimenting with vitamin D analogs.

Analogs are not bad things. They are vitamin D like substances that researchers hope to use to treat people who already have cancer. This is good, sort of. A growing number of studies are using vitamin D in its hormone form or created analogs to treat active cancer and some are showing positive results but so far only in cancer cell lines or animal studies, not in humans.[581,582,583,584,585]

BUT wait a minute. What about not getting cancer in the first place? I am a strong proponent of disease preventative and pro-active health habits. What about finding out how much D or sunlight we really need (and what goes with it) so that we have a better chance of avoiding cancer? How about finding out what levels of 25(OH)D were in those women who lived where there was more sunlight and less cancer?

In 1999 Janowsky looked at 25(OH)D and 1,25(OH)D in women with and without breast cancer.[586] It was a controlled study matched by age, race, clinic and time of year. (the season and D factor) The conclusion of this study was higher levels of 1,25(OH)D, calcitriol, are protective against breast cancer.

The difficulties:

Black women with breast cancer had a higher mean level of calcitriol than white women with cancer, and black and white controls.

All subjects and controls had 25(OH)D levels below the 32 ng/ml which may be closer to an optimal value for normal cell function and most had levels below Holick's suggested minimum 20 ng/ml.

In the section *People with Color* you'll read about alterations in the vitamin D endocrine system of blacks. The response to a vitamin D deficiency causes elevation of calcitriol and parathyroid hormone and retention of calcium. It is likely the changes in the black women are significant as the mean 25(OH)D was below 10 ng/ml the typical cutoff value for clinical vitamin D deficiency.

Vitamin D does have something to do with cancer, including cancer of the breast. When 25(OH)D is within a healthy range, still being determined, it is likely all our cells express in a healthier way. But it isn't calcitriol deficiency that is causing the rise in cancers of all types. It has to be a more widespread alteration in our diet or lifestyle.

The Marin County breast cancer rate, one of the highest in the world, has most recently been associated with higher alcohol intake.[587] One study in Finland found slightly higher mean levels of D in those who used alcohol. [588] But other studies have found an alteration of vitamin D metabolites in persons using alcohol, including lower 25(OH)D.[589,590] Combining hormones, alcohol, sunscreens, and sun avoidance can't bode well.

Which leads me to my rant point.

The current focus on individual diseases and treatments needs to be broadened to include funding for research determining causes and possible paths of prevention. We need to really look at how much D we need (not what we now have) and support optimum D nutriture. The research must take into account the incredible variances in

sunlight, dietary D, skin colors, and racial differences in the vitamin D endocrine system, all found within the borders of our country. America ranges from the Arctic to Hawaii with skin colors from the very lightest albino to the darkest, most melanized, black.

Also included in these studies must be a consideration of the interaction between nutrients such as vitamin A (more later) and other essential elements. We must start recognizing and acknowledging the importance of the variables. (End of rant.)

A simplistic change in the Recommended Daily Requirement will never, not ever, deal with the complexities of sunlight and vitamin D. Fortification of food will not solve vitamin D deficiency, insufficiency or potential problems of excess.
This is one very unusual situation where never really does mean never.

GP it is time to get your D tested. Insist that this is a part of your annual physical. Pay for it yourself if need be. If the researchers and physicians have not yet begun to understand our biochemically VERY individual need for sunlight and vitamin D, and the financial (and spiritual) benefits of disease preventive grab them and lead them. Please be aware I am promoting finding out your individual nutritional and sunning need. I am NOT promoting any herb, supplement, or other non-food (or uni-food) item.

Leukemia

Leukemia has an association with vitamin D. Both vitamin D and sunlight seem to work against this disease. Vitamin D stores in bone marrow. Whether adequate vitamin D will prevent this disease is unknown but vitamin D has been shown to 'differentiate' leukemic cells. [137,284,300,591,592] Differentiate means that abnormal cells begin to look and behave like normal cells.

BPH (not cancer) and Prostate Cancer

BPH is the short term for benign prostatic hypertrophy. It is not cancer and does not cause cancer. It is a condition of benign hyperplasia (overgrowth of cells causing enlargement), which has been associated with a diet high in refined carbohydrates and fat in animal studies.[393,593] Between ages 50 and 80 30% of men have symptoms and 10% seek medical treatment. Medical epidemiologists suggest most men, 95%, will have some slight enlargement of the prostate by the time they are 80 years old. The condition can make urination difficult and the need to urinate more frequently can disrupt sleep. There is a higher incidence of heart disease in men diagnosed with BPH.[594]

No determination of vitamin D levels has been done in men with BPH but the reversal of prostatic hyperplasia has occurred in animals given adequate vitamin D and calcium. BPH is short for benign prostatic hyperplasia, it's the last ‗h' that gives us a clue. Checking vitamin D status and making sure to get enough vitamin D and calcium might help and won't hurt.

Prostate cancer is a malignant overgrowth of cells. In the U.S. it is the second leading cancer cause of death in men following lung cancer. It is strongly associated with latitude and sun exposure.[595,596,597] Men in higher latitudes with African heritage have the highest incidence of prostate cancer and Asians the lowest.[598,599,600] Prostate cancer incidence is 1.6 times higher in African-Americans. The disease is also more aggressive in blacks and more likely to return after treatment.

Vitamin D may be associated with prostate cancer. 25(OH)D has been found to be low, normal or elevated in studies causing researchers to dismiss its importance yet the indications are vitamin D is important in expression and progression of the disease.[257,601,602,603,604,605] A 2008 study showed little association of 25(OH)D and prostate cancer when values fall with normal limits, meaning it did not protect, but higher values were found in men having aggressive forms of prostate cancer.[606] As vitamin A also protects against hyperplasia and prostate cancer the balance between these two nutrients is likely also important.[607,608,609,610,611] You will read more about this balance between vitamins A and D and cell health later.

What may turn out to be very important in preventing this disease is a healthy diet and adequate sunlight for reasons you'll read next.

Depression

A number of studies have associated lack of light with depression. In 1999 Gloth, Alam and Hollis [263] at Union Memorial Hospital in Baltimore Maryland completed a small study of 15 subjects with SAD, seasonal affective disorder. Subject's serum 25(OH)D was measured before and after the study. As mentioned before serum 25(OH)D is considered by many researchers to be the best marker of overall vitamin D status. Eight received a single dose of 100,000 IU of vitamin D at the beginning of the study and seven received two hours of phototherapy with full spectrum lights, daily, for one month. Subjects took three tests, the Hamilton Depression scale, the SIGH-SAD and the SAD-8 depression scale.

The phototherapy group showed no significant changes in any of the test measures. Their serum levels of 25(OH)D were increased by 38 % using the light box demonstrating that the light contained some small amount of UV-B but the change was not enough to improve mood. In the vitamin D group all subjects improved in all measures tested. The single dose of D significantly increased serum 25(OH)D by.78%. The higher levels of serum vitamin D achieved by supplementation were significantly associated with improvement in depression scale scores.

It appears that vitamin D and not light may be the critical substance able to profoundly alter the chemicals in our brains that control our moods or at least those dark moods of dark seasons with inadequate UV-B. As with a number of vitamin D studies the dose of vitamin D used is pharmacologic and probably unnecessary. It is likely a more 'physiologic' dose would work as well and with greater safety. It is also

likely that regular supplementation of vitamin D would maintain their good mood. You have heard of a sunny disposition, right?

Consider the choice of treatments, spending two hours every day sitting in front of a light box or taking a safe amount of daily vitamin D, which would you choose?

Or another choice- what about lunch on the rooftop terrace above your city office or at the sidewalk café or outdoor seating at your favorite mall restaurant or picnic tables at your local park filled with children and smart moms during summer exposing your meal and some skin to the sun?

I have this vision of dashing men and womanly women wearing hats, wonderful sun shading big brimmed hats. The men wear loose gauzy shirts with a tank T underneath so they can shed their shirt for sun. The women wear long or not so long skirts or baggy early Hollywood pants easily drawn up to expose bare legs and tops that let light in, when you want it.

Clothing is the greatest sunscreen ever because it does block the rays, both UV-A and UV-B, and you can remove it when and for however long you need to get your daily dose of sunlight vitamin D.

In Australia skin cancer incidence began to drop after the health department switched from suggesting sunscreen to promoting the use of clothing as a sun barrier. (612)

In Medical Hypothesis 1998 Partonen (613) suggests that vitamin D control of an adrenal enzyme, tyrosine hydroxylase, affects both serotonin and melatonin production. There is a relationship between vitamin D status and neurotransmitters including serotonin, dopamine, and epinephrine and vitamin D has been shown to alter expression of tyrosine hydroxylase, necessary for production of dopamine, in adrenal chromaffin cells.(261,262,614,615,616,616) Vitamin D also protects dopamine-producing cells in the brain. (617,618,619)

Lansdowne and Provost(614) at the University of Newcastle, Callaghan NSW, Australia found that in 44 subjects given 400 IU or 800 IU of vitamin D or placebo, for just 5 days, the higher level of vitamin D supplementation was associated with improvements in sleep, carbohydrate cravings, lethargy and depression. Unfortunately they did not test serum vitamin D. What is exciting is how quickly the improvement occurred and that a physiologic dose, as little as 800 IU daily, was effective.

Syndrome X

Syndrome X was originally a name given to a specific type of angina (heart pain) but between 1989 and 1992 the name was expanded, by Dr. Gerald Reaven, to

include a complex of conditions including hypertension, central obesity (wide around the middle), reduced insulin sensitivity, hyperinsulinemia (over production of insulin in response to glucose), low high-density lipoprotein (HDL, the good cholesterol) and increased likelihood of heart attack.

In the U.K. Barbara Boucher, M.D. has studied the relationship between vitamin D status and insulin resistance. [228,620,621] Her findings suggest that better vitamin D status may result in less incidence of Syndrome X. Dr. Boucher faces the problem of living and working in a country with national healthcare. Testing is not currently considered an option outside of research or clinical conditions of severe vitamin deficiency because of cost. Later I will offer arguments in favor of overcoming this resistance and changing national and international policies.

Zemel has done significant work showing the relationship of calcium intake and diabetes, hypertension, and insulin resistance. [622,623,624,625,626] Other researchers note that the vitamin D endocrine system is related, as yet not fully understood, to blood sugar and insulin production and response. *[627,628]*

The increase in incidence of Syndrome X may share common cause with the studies on cell hyperplasia; the Western diet altering the need for or access to vitamin D and calcium. Vitamin D and calcium regulate movement of calcium in and out of cells. This movement alters the cells response to any number of substances including neurotransmitters and hormones like insulin. Since vitamin D plays an important role in calcium movement and calcium ionization[629] this all begins to fit together. Calcium in the wrong place, inside the cell, can increase insulin resistance and contribute to hypertension and obesity.

Obesity

There is increasing evidence that obesity is a factor in the development of Syndrome X. Obesity is now widespread and continuing to grow at a rapid rate in the U.S. Recent data suggests that a full 1/3 of our population is now obese.

Overweight is any weight greater than that defined as normal within the standard body mass, weight and height charts..

Obesity is defined as being overweight by more than 1/3 of your ideal body weight. This would be >200 pounds for a person whose normal weight should be about 150 pounds. The Centers for Disease Control and Prevention have found 13% of children between 6 and 19 years of age are overweight (not all of them meeting the definition of obese). This percent has doubled since the 1970s.

Obese persons tested for 25(OH)D exhibit a high incidence of vitamin D deficiency or insufficiency. [244,630,631,632] Obese persons also respond poorly to vitamin D supplementation or sun exposure.[246] They apparently just don't utilize vitamin D as efficiently as the non-obese. In Wortsman's study when obese and normal weight subjects were exposed to sunlight obese persons produced serum 25(OH)D levels 57% lower than normal weight participants.

There are a number of suggested reasons for these differences. One theory is that the D is being stored in the excess fat tissue. My questions: Does this D

insufficiency and altered response precede or follow obesity? Would maximizing vitamin D and calcium produce weight loss? At present no one knows. BUT Zemel has found increasing intake of calcium is associated with weight loss.

In 2000 Zemel studied the possible role of calcium in causing and preventing obesity.[241] In an unrelated previous clinical trial investigating the effects of calcium on hypertension in African-Americans Zemel had noted that hypertensive obese persons given calcium supplements for one year lost an average of 10-11 pounds without a change in diet or physical activity. The weight loss was unexpected and Zemel and his colleagues wanted to know why it occurred.

In the current study the subjects were rats that maintain normal weight on regular rat chow (a research formula balanced chow designed for rat health) but become fat when fed a diet high in refined carbohydrates and fat, similar to our Western diet. Zemel divided them into four groups. Group one was given the basal diet, a specially modified rat diet designed to provide high levels of sugar and fat. Group two ate the basal diet supplemented with calcium carbonate. Groups three and four ate the basal diet but with part of the protein replace with two different levels of non-fat dry milk. The substitution of non-fat dry milk provided two different levels of calcium both significantly greater than that provided in the basal diet. All variations of the diet contained the same amount of calories.

The calcium-supplemented diet prevented, to some degree, the weight gain that occurred in the group on the high fat and sugar basal diet alone. One of the changes recorded in response to the basal diet was a drop in core body temperature. In some way the excess sugar and fat decreased the rats normal metabolic rate as determined by body temperature.

Energy produces heat. In our bodies this is called thermogenesis. This process of thermogenesis was suppressed by the basal diet. All three diets supplemented with calcium increased core body temperature, which is an indication of a return to a more normal metabolism and thermogenesis. The two diets supplemented with the non-fat dry milk powder were more effective in normalizing core body temperature than the basal diet plus calcium carbonate.

Genesis means the beginning of a process. Thermogenesis is production of heat, thermo-, lipogenesis the production of fat, lipo-. Lysis means destruction of a cell. When used as a suffix the prefix indicates the type of cell.

Lipogenesis is the process that turns calories (proteins, sugars and fats work equally well) into stored body fat. Zemel calculated the amount of adipocyte fatty acid synthase, one of the rate-controlling enzymes involved in lipogenesis. The high fat, high sugar, low calcium basal diet greatly increased the activity of this enzyme, 2.6-fold over the amount found in rats fed regular rat chow. The addition of calcium carbonate decreased this effect by 27% and moderate and high calcium diet using non-fat milk powder decreased enzyme activity by 51%. The extra calcium blunted the fat storing response to the basal diet. Once calories are stored as fat a process called lipolysis must occur releasing the stored energy. In our fat rats adding calcium to the high fat, high sugar diet decreased the production of new fat cells and it also increased lipolysis by 3.4-5.2-fold.

Since the high fat, high sugar diet has also been known to alter glucose and insulin response Zemel tested fasting glucose and insulin. Rats on the basal diet had higher levels of glucose and insulin, a condition in humans called hyperinsulinemia. This is one of the markers for Syndrome X. Added calcium in the form of calcium gluconate at high levels or dairy calcium at moderate levels reduced this response.

The diet with the highest level of dairy based calcium prevented the glucose insulin response completely.

The idea Zemel was testing suggested that levels of a vitamin D and calcium regulated hormone, $1,25(OH)_2D$, calcitriol, might increase calcium inside the fat cell and this state of elevated internal (intracellular) calcium might be responsible for the abnormally increased production of fat cells and decreased fat burning. Indeed, giving calcium while on the high fat and sugar diet lowered the active hormone D.

Zemel believes this is the cause for decreased production and activity of fatty acid synthase, increased lipolysis (fat burning), lower glucose and lower insulin production. Suppressing $1,25(OH)_2D$ and intracellular calcium by supplying extra calcium seems to mean that calories may be more readily burned as energy not stored as fat. Zemel's hypothesis worked.

Since we are learning about vitamin D, and elevated $1,25(OH)_2D$ facilitated weight gain, it might seem that less vitamin D would help with weight loss but remember our complex systems model? Active calcitriol, the value Zemel studied, tends to stay within normal ranges unless there is a disease state or 25(OH)D is very low OR calcium is needed. Zemel's mice had moderately elevated levels of calcitriol. This increased conversion of 25(OH)D into active $1,25(OH)_2D$ (calcitriol) occurs when the body requires more calcium. Calcitriol participates in regulating absorption of calcium.

The study does not explain why sugar and fat increase the need for calcium only what happens when this occurs. The treatment is to supply more calcium to restore normal metabolism. As this process relates to vitamin D, the kind we get from sun and the kind we take in supplements, low levels of vitamin D and 25(OH)D also contribute to elevated $1,25(OH)_2D$ as the body tries to maintain the vitamin D endocrine system.

What if in summer vitamin D from sunlight and calcium from an adequate food supply, are in abundance? The body burns calories readily, producing energy important during this time for mating, reproduction, and growth, and few calories are stored as fat. As the rays of summer decline vitamin D, 25(OH)D, levels in the blood drop. Later as food supplies disappear calcium in the diet also drops.

As available vitamin D and dietary calcium decline there is a parallel decline in serum ionized (free) calcium. In response parathyroid hormone and calcitriol ($1,25(OH)_2D$) increase..

In Zemel's study ionized calcium is one of the regulators of the fat storing and burning enzymes. This actually makes sense. The body prepares for the winter, less sunlight, less D, less food, less calcium, by storing fat. During the dark months reduced supplies of food allow the fat stored to be burned for energy to keep the body alive and warm, though at a reduced rate. In spring the cycle begins again. What a great system.

BUT what if we have winter's light with summer's food year round or worse, instead of the nutrient dense, whole foods diet of our ancestors, we eat a diet loaded

with added fat, refined carbohydrates and much less calcium and to make matters even worse we are intentionally advised by experts avoid summer's sun?

Fat is stored energy. Obese persons often describe being hungry, tired and cold. In this cycle energy is consumed but instead of being burned for heat or physical movement it is stored. As mentioned researchers have found obese persons have a great difficulty in getting and maintaining normal vitamin D and surgical obesity treatments make this bad situation worse.[633]

How do we get our calories, those eaten today, and those previously stored, to burn instead of being endlessly stored for a calorie-deprived winter that never comes? (There is no lack of calories in the developed countries.)

Exercise burns fat. Lack of exercise contributes to obesity but given our busy schedules and the amount of exercise needed to burn a pound of fat exercise is not going to be the total answer to our current obesity crisis..

Zemel also cites a trial where dieters using dairy were compared to dieters consuming equal calories without dairy. The dairy consumers lost more weight. He suggests that the higher calcium in the dairy based diet made the difference by suppressing active $1,25(OH)_2D$ and the enzymes under its influence, like fatty acid synthase, and thereby decreasing fat cell production and increasing fat burning.

There is another reason why study participants may have noted greater success with dairy calcium than other forms. Dairy calcium contains calcium lactate and calcium lactate is better absorbed and utilized than some other forms of calcium.[634]. This could make a significant difference in calcium absorption and response.

There is another point to be taken from Zemel‘s study, one that would confuse his outcome but have meaning for us. Dairy contains more than calcium.[635] It is a significant source of potassium which plays a role in altering calcium balance and cellular calcium levels,[636,637] and zinc which facilitates insulin‘s entry into the cell and is important for other vital functions as well.[425,638,639,640,641]

Note to the GP and others more sinister: Before anyone decides to use this book to promote or sell a particular kind of calcium, let it be noted here that these are suppositions and NOT to be used as 'research findings' to promote the sale of products of any kind. We need vitamin D and we need calcium and when rats were fed non-fat dried milk they were somewhat protected from the obesity and altered glucose-insulin response associated with high fat and high sugar diets. If there is anything to sell here it might be dried milk powdered for fat rats. This study also might, if you are not dairy intolerant, cause you to think about dairy in a more favorable way.

If vitamin D and calcium together play an important role in regulating whether we store or burn calories and if our national health policies and modern lifestyles prevent us from getting enough vitamin D and further if the diet we consume is high in fat and sugar we are in trouble. Sunscreens do prevent D production[642,643] as does staying inside, out of noon day sun. This means our current national health policies may very well be helping to make us fat and keep us fat.

The child (or adult for that matter) kept out of the sun, restricted in physical activities and fed a diet high in calories containing excess fats and refined carbohydrates and insufficient calcium doesn't have a chance. Obesity is inevitable.

Avoiding sunlight and using sunscreen has been policy in the U.S. for some time. Often latchkey children in urban areas stay inside for reasons of safety. School policies encourage sun avoidance. We have also seen moms off to work and kids left to feed themselves with microwave food and juice snacks or junk food and sodas. Foods offered in schools are rarely designed for optimal nutrition. These practices alter vitamin D and calcium levels and the need for sunlight or supplementation.

Some people may just have a harder time getting and/or storing D, or their diet and/or lifestyle may create a relative deficiency. A relative deficiency can occur when something we are doing causes us to need more of a substance. Dieting, especially low calorie, low fat dieting as is currently promoted, may further decrease levels of vitamin D and thereby calcium absorption, raising calcitriol and altering fat metabolism. When this occurs and the diet is abandoned as calories are increased weight gain (fat storage) may occur with a vengeance. Sound familiar?

There are other indications that vitamin D and obesity are linked though just how will require more research. In a 'Petri dish' study both vitamin A and vitamin D seem to regulate leptin, now strongly associated with obesity. [644] Low levels of vitamin A and D stimulate the development of adipose (fat) tissue.[645] and giving cod liver oil which contains both A and D decreased weight gain in genetically obese mice.[646]

Diabetes

Diabetes is categorized as Type I, insulin dependent, considered to be an autoimmune condition and Type II, non-insulin dependent developing over time perhaps from dietary changes including excess intake of fats and carbohydrates. When serum levels of 25(OH)D have been tested in diabetics results are mixed.

Low levels of vitamin D have been associated with Type I insulin dependent diabetes.[647] In Europe a large epidemiological study found populations giving supplements of vitamin D to infants had a significantly reduced incidence of Type I diabetes.[648]. Once the disease is diagnosed and insulin treatment is initiated vitamin D is one of the factors important for building and protecting bone.[649,650]

Baynes and Boucher found an inverse association between glucose tolerance and 25(OH)D in Dutchmen.[232] Scragg studied serum 25(OH)D in 5,677 New Zealand Polynesians and Caucasians. Low levels of D were found in those diagnosed with Type II diabetes and glucose intolerance. Scragg's study suggests the higher incidence of diabetes among Polynesians is caused by lower levels of vitamin D.[651] The Europeans had significantly higher 25(OH)D than the Polynesians, comprised of Maori and Pacific Islanders, and lower incidence rates of Type II diabetes.

Latitudes in New Zealand range from 35-45° south, similar to latitudes between Virginia and upstate New York. Pacific Islanders originate from latitudes 10-25° south providing significant amounts of UV-B. The Maori traveled from these islands to New

Zealand around 1200 AD. Traditional diets were fish based which would have provided additional dietary source of vitamin D at their new location more distant from the equator. Early Maori inhabitants hunted marine mammals, whales, and seals.

Europeans, with lighter skins are able to get sufficient sunlight in less exposure time with less intense UV-B. In the study sample the Europeans and Polynesians were members of the workforce, which means well-clothed and indoors during daylight hours. The darker skins and D endocrine systems of the Polynesians would be unable to get sufficient UV-B sun to manufacture and maintain adequate vitamin D. Mean 25(OH)D in the Polynesians, Maori 26 ng/ml; Pacific Islanders 23 ng/ml and Europeans 32 ng/ml, the new minimum value for D sufficiency.

Many of the people most devastated by diabetes are native peoples, including African Americans, Native Americans, Native Alaskans, Pacific Islanders and Native Hawaiians. In each situation changes in vitamin D sourcing because of changes in location or lifestyle, or dietary changes restricting access to traditional foods, coincide with increases in Syndrome X, obesity, hypertension, heart disease and diabetes.

The role vitamin D may play in development of two very different types of diabetes is not well understood. Not all persons with either of these conditions will have lower serum vitamin D and not all people with low serum D develop diabetes. Once again, sufficient sunlight and vitamin D seem to contribute to generally better health. Low levels of 25(OH)D express in different conditions in different races and locations. Researchers continue exploring the relationships and genetic variables. While waiting for their conclusions we need to get sunlight and vitamin D.

Hypertension

Recently the ‗healthy' values for blood pressure were altered so that what was formerly considered normal is now pre-hypertensive. Approximately 1 billion persons worldwide suffer from hypertension of which 30 million are Americans. Hypertension is an independent predictor of heart attack, heart failure, stroke, and kidney disease.

The Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure in the May 21, 2003 issue of JAMA determined a reading of 120/80 should alert the physician to potential danger and a responsibility to inform the patient of lifestyle changes. In the report lifestyle changes included weight loss, high intake of fruits and vegetables, reduction of salt intake, physical exercise and moderate alcohol intake. These are without question important for health overall not just to avoid hypertension.

Calcium has shown positive results in the prevention and treatment of hypertension. [641,652,653,654,655] When vitamin D and/or calcium are low parathyroid hormone (PTH) is elevated. Changes in ionized calcium and elevations of PTH are found in hypertension and heart disease contributing to calcium deposits in the arteries.[656,657,658,659,660,661,662] [663,664,665,666]

When levels of 25(OH)D were checked in 186 patients newly diagnosed with hypertension Scragg found levels to be 'normal'. Normal meant an average 25(OH)D of

25.6 ng/ml.[667] This is above Holick's suggested 20 ng/ml but lower than the 32-40 ng/ml considered by a number of researchers to normalize PTH. What if extra calcium and vitamin D were given to these patients?.

When our levels of vitamin D are marginal wintertime brings a steady decline often leading to an increase in parathyroid hormone. Vitamin D lowers winter increases in parathyroid hormone.[668] Blood pressure is higher in winter which strongly suggests an association with calcium and vitamin D.[669] It is likely we all have individual responses to vitamin D and calcium. Some of us will genetically need more of one or both to optimize health.

Heart Disease

Along with the studies suggesting a relationship between vitamin D and Syndrome X, which includes precursors to heart disease there are many direct studies showing a relationship between vitamin D and heart disease. The heart disease story is very complex. Further on you will read about the reverse effect. Often in the human body too much or too little of a substance has a similar symptom. A deficiency or excess of vitamin A has many similar symptoms, one example being dry skin. This is also true of several of the B vitamins. Some symptoms of deficient or excessive nutritional elements can be severe and even life threatening.

Too much or too little vitamin D has been shown in research to be related to changes in the arteries which contribute to heart failure, been a factor in hypertension which damages the heart, or altered heart function in other ways, sometimes beneficial and sometimes not.[61,162,163,509,670,671,672,673,674,675,676,677,678,679,680,681,682,683,684,685,686,687] Low levels of vitamin D may contribute to congestive heart failure[688,689] Interestingly other researchers found congestive heart failure and bone loss to be related.[690]

Scragg and colleagues have been accessing 25(OH)D levels in relationship to heart disease and found lower levels in myocardial infarction. They also noted men with higher levels of outdoor activity and lower risk for heart disease had higher levels of 25(OH)D.[680,691] Sunlight just can‘t be all bad.

Animals used in research don't easily develop heart disease. To study heart disease experimental animals, rats, rabbits, or pigs, are given toxic amounts of vitamin D and fed high cholesterol diets, the perfect combination to develop atherosclerotic plaque (the stuff that clogs up your arteries).[685,692,693,694]

Dr. Fred Kummerow, a professor and researcher at the University of Illinois specializing in heart disease, found even moderately high doses of vitamin D caused damage to arteries and has long considered vitamin D atherogenic (bad for your heart). His research found elevated levels of 25(OH)D, independent of serum calcium values, contributed to bone resorption (loss of calcium from bones) and changes in the structure of soft tissues including arteries and kidneys.[60] The comment _independent of serum calcium‘ is important as some current researchers suggest that excess vitamin D is only harmful if serum calcium is elevated. Kummerow found serum calcium could be quite normal and damage still occur.

One of the most complete reviews of the complexities of vitamin D nutriture was published in the Journal of the American College of Nutrition Feb. 1983.[58] Authors Holmes and Kummerow offer an excellent overview of what was known at that time and present lots of questions. They really asked great questions. Unfortunately, 20 years later, most of the questions they proposed are still unanswered. Kummerow is the oldest practicing professor in the US and the man who first isolated and warned of the dangers of trans fats.

One of their concerns was the potential for damage by excess vitamin D to soft tissue of the body. In particular they considered research that showed damage to soft tissues, like arteries, with relatively low doses of vitamin D whether from supplements or sunlight. Recognizing the association between elevated 25(OH)D and heart disease researchers in Southern India wondered about possible connections between excess exposure to sunlight in the tropical environment, serum D levels and the incidence of heart disease.

Rajasree and colleagues did indeed find a link between sunlight, elevated $25(OH)D_3$ and heart disease incidence and published the results in the European Journal of Epidemiology June, 2001. They found 59.4% of those with diagnosed heart disease had levels of $25(OH)D_3$ greater than 89 ng/ml. In the control group having no evidence of heart disease 22.1% tested in excess of 89 ng/ml. In researcher lingo this reaches 'statistical significance'.

Note to the GP: There is approximation at work here. Elevated levels of 25(OH)D from supplements or sunlight seem to contribute to changes that relate to calcium entering soft tissues where it does not belong instead of entering or staying in bone, hair, and nails. One of the primary locations of soft tissue accumulation of calcium is the arteries. This process has been documented in animals, in tissue samples (Petri dish), and humans. No one has yet determined how much D is too much, that is, what the highest safe level of 25(OH)D might be. Make sure to read the chapter How Much D Do We Need?

Because feeding excess vitamin D and cholesterol rapidly induces heart disease in animals it has been difficult for some researchers and clinicians to consider that too little D might also contribute to heart disease. There are significant changes in heart function in those with rickets, the most severe D deficiency state, and similar changes in heart function may also be present in persons with osteoporosis. [679,695,696] Low levels of D like elevated levels of D have been associated with calcification of arteries and heart attack. In 2002 Varosy reviewed data from 9704 women enrolled in the Study of Osteoporotic Fractures and calculated a 43% lower risk of death from heart disease in women currently using a vitamin D supplement.[697]

Scottish Beards

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. Researchers tested beard calcium because beard hair grows faster thereby showing changes more rapidly, and men are more willing to give it up.

Vitamin D raised beard calcium and this rise continued as long as the vitamin D supplement was consumed. Almost immediately after stopping the D, beard calcium fell to pre-supplement levels. [674]

Scotland is quite north, with latitudes 55-56°. Southern India covers latitudes between 10-18°. The variation of UV-B light between these two locations is extreme. In southern India any season and any time of day would provide significant amounts of UV-B while in Scotland much of the year lacks any significant vitamin D producing sunlight. The UV-B percent of ultraviolet reaching Scotland is less at any time of day or year.

Considering the body of research suggesting both too much and too little D may play a significant role in heart health it would seem very important that regular vitamin D testing become a part of heart disease prevention and treatment programs and protocols.

Autoimmune Diseases

Autoimmune diseases have seemed to respond to supplementation with calcium and vitamin D. [248,698,698,699,700,701,702,703,704,705] A review of the subject, by Cantorna in 2000, considers vitamin D status to be an important environmental factor to be considered in prevalence of autoimmune disorders. [248]

Because autoimmune disorders are frequently linked to vitamin D or sunlight the question that bothered me and did not seem to be answered was whether some autoimmune diseases are moderate or extreme expressions of deficiencies or imbalances of vitamin D. The only way to test this idea is to test for deficiency or over abundance of vitamin D.

This has been done in some few studies. These studies often suggest that vitamin D has a very beneficial outcome on autoimmune disease states. Considering that vitamin D in appropriate amounts (to be determined) is very safe, checking levels of vitamin D and supplementing with sun or vitamin D if needed could be of great value.

Other studies relating vitamin D and/or calcium to autoimmune conditions use the supplements in forms, those analogs mentioned earlier, or in amounts that are clearly not 'physiologic', meaning the amounts used are such that one could never get that amount in the real world under any conditions. At very high doses supplements become pharmacological and must be considered drugs with a great likelihood of side effects.

These studies do not contribute to answering the question of D sufficiency still waiting to be answered.

—Will getting just the right amount of vitamin D from sunlight or supplements benefit in prevention or remission of disease?"

Crohn's Disease

In this autoimmune disorder there is chronic inflammation and consequent destruction of the intestine wall. The role of vitamin D deficiency as an underlying cause is questionable. In a state of active disease all of the fat-soluble vitamins, A, D, E, K and beta-carotene are poorly absorbed and an insufficiency or deficiency is likely and common.

Problems associated with this disease, which includes bone loss, may be related to low levels of vitamin D because of malabsorption (I took it but it didn't get in.) of nutrients by the damaged gut wall Yet newer research studying gene markers has found an association between a vitamin D receptor (VDR) and the disease. [706] Gene studies may or may not turn out to be useful for diagnosis and treatment. Most certainly persons with Crohn's Disease need to make sure they get and utilize all of the fat-soluble vitamins and that they get sufficient minerals. Appropriate supplementation is likely critical to long-term health. [707,708,709,710]

A single study of a single participant with Crohn's Disease determined the outcome of using a suntan bed for 10 minutes three times a week to increase vitamin D levels. The choice, of using UV-B light on the skin as the source of vitamin D, was made because the woman had lost most of her upper intestinal tract as a result of her disease. Without most of the ileum and jejunum (small intestine beginning just below the stomach, it is the area where most nutrients, including the fat soluble vitamins, are absorbed) her ability to absorb vitamin D from a supplement was severely compromised. This treatment protocol raised levels of D from 7 to 32 ng/ml in four weeks without erythema (she didn't pinken or burn).

erythema, def.
redness of skin: redness of the skin as a result of a widening of the small blood vessels near its surface. It has various causes, including fever and inflammation. (not sunburn)

This term, erythema, is used in all research involving sunlight and skin, (from animals or man) to designate the dose of light that causes skin damage. If any, even very slight, redness occurs it is considered to signify damage, altering underlying cells, and potentially setting the stage for later cancers of the skin.

Erythema is to be avoided and as you will see in the chapter on light we can get enough UV-B from sunlight to produce vitamin D without erythema just as this woman did. We can do this only if we understand and apply the variables of light intensity and exposure time to our individual skin type. Using sunlight or tanning beds to increase levels of vitamin D may be an important choice for those who have lost the ability to absorb nutrients, whatever the cause.

Multiple Sclerosis and D

As noted in the section on sunlight and disease Multiple Sclerosis is one of the first diseases to be strongly associated with latitude.[361,711] This has caused some

researchers to suggest this connection relates to UV-B sunlight and therefore vitamin D. [712,713,714]

In 1978 Craeluis looked at a possible association between Multiple Sclerosis and the prevalence of decayed, missing and filled teeth. Reviewing epidemiological data from studies in Australia and the United States he found a strong correlation between Multiple Sclerosis incidence and the number of bad teeth.

The author suggests common causes may be at work such as lack of vitamin D or inappropriate dietary fats.[513] He isn't suggesting you get MS if you have bad teeth but that as numbers of decayed teeth increase in a population there is a parallel increase in the number of persons diagnosed with MS. In 1994 Nieves found low levels of 25(OH)D and low bone mineral density in 80 female MS patients.[715] The lowest bone mineral density was found in the women with more severe MS.

A small study, 22 placebo and 17 supplemented, gave 1,000 IU of vitamin D and 800 mg of calcium for six months. The beginning levels of 25(OH)D were 11-23 ng/ml and in the supplemented group this rose to 20-36 ng/ml. One peptide suspected to be a marker of MS activity TGF-β1 (a protein that controls how certain cells grow) significantly increased but three other markers tested showed no significant change.[716]

The premise concerning MS and sunlight or D is often associated with the suggestion that sunlight and/or D suppress the immune system. This may be a poor understanding of the research. High, intense exposure to UV-B light does suppress the immune system.[335] But moderate exposure enhances immune system function. Immune suppression is a completely different state, typically induced by drug treatment and not the same as a normal, functioning immune system.

The normal immune system maintains a balance and is neither over nor under active. In a mouse model of MS, autoimmune encephalomyelitis, calcitriol normalized a number of immune markers.[713] Unfortunately this doesn't tell us much about any benefits of taking supplemental vitamin D.

Calcitriol production is tightly regulated by calcium, parathyroid hormone, and other factors. Taking or not taking vitamin D will make very little change in calcitriol unless the dose or deficiency is extreme. It may be that calcitriol or one of its analogs may be developed as a drug treatment for the condition at some time in the future.[688]

One uncontrolled study suggested a decrease in relapsing-remitting incidence in MS patients given vitamin D, calcium, and magnesium for one to two years.[712] The participants were young persons with histories of frequent relapse. After supplementation, relapses were half that expected, which also doesn't give us solid data as MS can sometimes seem to come and go for no apparent reason.

These participants were not tested for levels of vitamin D. I found this inadequacy in studies with good, mixed or no results. If you don't know how much vitamin D a study participant had to begin with and how much they have after treatment you cannot know if vitamin D is a critical factor in success or failure. Perhaps some did not respond because the dose was not large enough to raise D into optimal values or perhaps the dose caused an abnormally high level of vitamin D.

Some support groups for MS have suggested that high doses of vitamin D should be taken. There are a number of problems with this approach; the most serious being that the doses suggested are sometimes more than double the levels considered

the upper limit of safety and there is the possibility vitamin D excess might make MS worse.

The metabolite of vitamin D that has worked to successfully treat the MS model in rats is calcitriol. Excess 25(OH)D, calcitriol _s precursor, which is elevated when vitamin D is supplemented, may displace calcitriol in cell membranes and processes.[58]

Continuing research hopes to define the action of vitamin D in multiple sclerosis. [717]

Other Autoimmune Diseases

The diseases in this section may have an association, yet not understood, with low levels of vitamin D BUT rarely is vitamin D tested. A further complication of understanding any relationship is that many of these diseases are treated with corticosteroids. Corticosteroids can be a direct cause of bone loss.[718] Vitamin D status and calcium supplementation may be critical for all of these conditions either because low vitamin D or calcium may play a part in initiation of the condition or because the medication used to treat the condition increases the need for calcium or vitamin D.

Researcher note that alterations of vitamin D (in the genomic function of messenger) have a profound effect on both innate immunity and development of autoimmune disorders.[448,719,720]

Lupus Erythematosus

Lupus is a chronic autoimmune disease occurring in about 1 in 1000 white persons and 1 in 250 blacks. The ratio of female to male victims is 9:1. About 1/3 of those with systemic lupus are photosensitive and must avoid sunlight. Vitamin D supplementation is a consideration during treatment of this disease due to a large number of victims suffering from osteoporosis.[721,722,723].

Some of the association between Lupus, vitamin D, and osteoporosis may be related to sun avoidance. Another may be use of corticosteroids, one of the types of medications used to treat the disease. Many Lupus victims have very low levels of 25(OH)D before treatment with any medication.[722,723,724,725] Studies support supplementation of vitamin D and calcium to improve and maintain bone in this disease.[726,727]

Myasthenia Gravis

No studies have noted vitamin D status in Myasthenia Gravis. The condition is commonly treated with corticosteroids making it one of the conditions where, during treatment, maximizing calcium and vitamin D is important. [728,729]

Rheumatoid Arthritis

Few studies have been done to determine the effects of vitamin D in the treatment of this autoimmune form of arthritis. This was surprising to me because there are studies showing a positive response to cod liver oil [730,731] and books have been

written about using cod liver oil to reverse arthritis. There are a number of studies that have found low levels of vitamin D in this condition as well as disordered calcium metabolism which is associated with vitamin D.[732,733,734,735,735,736,737,738] The Iowa Women's Study found higher intakes of vitamin D associated with lower incidence of rheumatoid arthritis.[739]

Sjogren's Syndrome

Sjogren's is an interesting condition because it relates to 'secretions' (secreting saliva). Adequate saliva production and secretion requires adequate vitamin D.[504,505,506,507,508]

Sjogren's is a disease caused by an autoimmune attack against moisture secreting cells including tear and salivary glands. Antibodies cause destruction of these glands resulting in dry eyes and dry mouth. This is not only uncomfortable it is devastating to the health of the mouth and teeth. Saliva has many elements including ionized minerals that contribute to remineralization of enamel and dentine.[740] and protect the mouth and teeth from harmful bacteria.[536]

Two studies testing the levels of 25(OH)D in Sjogren's patients found decreased levels compared to controls.[249,741] In both studies those with the highest disease activity had the lowest levels of 25(OH) D. Testing and supplementing vitamin D when indicated may someday be found to help normalize immune function and help reverse or prevent Sjogren's.

PEOPLE WITH COLOR, SUNLIGHT, VITAMIN D, AND DISEASE

This is about people whose skins are very dark, often called black and somewhat about others with lighter darkness. (Smile)

Skin (and people) may be described using such terms as black, brown, white (really it's pinkish or yellowish or reddish) or dark and light. The terms used are meant to represent the amount and coloration of the person's melanin, the pigmented cells that give color to our skins.

The difficulty using African-American or Mexican-American or Asian-American (or African, Mexican, etc.) or similar terms denoting origin is that none of these terms actually describe the color of the skin which is a primary factor altering our relationship with the sun.

The intensity and tone of melanin in an individual's skin make a great difference in the person's need for sunlight. Skin color is a determinant of how efficiently our skin is able to make vitamin D from UV-B sunlight.

To produce adequate vitamin D very dark skins need lots of UV-B, even hours a day if they are located far distant from the equator, while very light skinned persons, depending on location, may need just minutes a day.[742]

Albinos, having no melanin, and persons with a disease called Xeroderma Pigmentosum or XP, a rare genetic disorder, must avoid all UV light and need to supplement D to achieve values within an optimal range.

Dark Skins and Disease

Diseases with higher incidence in persons having very dark skins living in more northern or southern latitudes include:

Pretty much everything!

Blacks in American have a 70% higher rate of adult onset diabetes. Diabetes incidence, both types I and II, is associated with vitamin D and calcium.[228,232,648,659,743,744]

Hypertension disables more blacks in American than any other race or ethnic group.[745] The outcomes of this disease include stroke, kidney failure, and death. Hypertension in blacks is associated with salt sensitivity and alterations in calcium metabolism.[746]

African-Americans have more arthritis, asthma, diabetes, and heart disease. They also have the highest rates of cancer incidence and cancer deaths of any race or ethnic group. Blacks have the highest rate of prostate cancer, much higher than any other group. As of 2000 prostate cancer incidence in white males was 164 per 100,000 people per year. In blacks the number was 272 per 100,000 per year.

Breast cancer incidence in white women was higher than in black women but deaths from breast cancer were higher in blacks which suggests delayed diagnosis and treatment.

Obesity hits hard in the African American community. 50% of black women are considered overweight, the highest percentage of any group in the U.S.[747]

Much of the research trying to determine why blacks suffer from a greater incidence of so many conditions focuses on altered genetics. Researchers have found variations in testosterone and specific genes that might contribute to the higher incidence of prostate cancer and other diseases seeming to favor blacks.[600,748] African-Americans in the U.S. have lower levels of 25(OH)D and higher levels of testosterone.[749] If it is genes then blacks in Africa should also suffer from similar diseases at similar rates, but they don't.

White and black women in South Africa have similar bone mass.[750,751] In the U.S. black women have greater bone density, less osteoporosis and fewer fractures when compared to whites at all age levels.[752,753]

Colon cancer is rare in South African blacks even after they move to urban areas and change their diets.[754] Colon cancer rates among blacks in the U.S. are very high, equal to the rates of this disease found in whites.[755]

Hypertension and heart disease have begun to increase in African populations moving from a rural to urban lifestyle [158,756,757] While a change from traditional to modern (processed, refined) diets may contribute to cancer incidence, lifestyle changes also deserve review. Spending greater amounts of time indoors, or wearing non-traditional clothing that blocks skin exposure to sunlight, makes for poor D production, compromised vitamin D status, and perhaps an increase in cancer risk at any latitude.

The incidence of prostate cancer is high in some parts of Africa.[758,759] But incidence in blacks in American is still higher.[760]

In Nigeria men eating a diet higher in fish and lower in animal fat had a reduced incidence of prostate cancer.[761] In traditional diets the whole fish is typically consumed, skin, organs, fat and bone, thus providing essential omega-3 fatty acids known to be good for the prostate, as well as zinc, vitamin D and vitamin A and significant amounts of calcium, all shown to reduce the incidence of many types of cancer.

Several studies have confirmed intake of fish (containing omega-3 fats and vitamin D) and liver (which contains vitamin A) decreases risk of prostate cancer.[762,763,764,765,766]

Genetic predisposition has to be a factor but what exactly does that mean? We have become fascinated with 'genetic markers'. Even if there are genetic variants, recent work on vitamin D receptor gene variants (you'll see this again) found these variants ‗express' just fine if vitamin D is adequate.[767] Problems occur when vitamin D is low.

GP: What genes may really indicate is that some of us need more of or less of certain nutrients. If we get enough but not too much of what we need our cells will develop normally.

The Purpose of Melanin

Many experts have argued and continue to argue about the purpose of skin color. Some of the reasoning is just plain dumb. One researcher suggested skin color had nothing to do with UV-B sunlight because some indigenous people near the equator had lighter skin. The amount of UV-B actually reaching the earth's surface is extremely varied. If your ancestors lived in a rain forest they didn't get as much UV-B as people living in sunnier places with fewer trees, clouds, and rain, whatever the latitude.

Locations at the equator, 0°-15°, don't get as much UV-B sunlight as locations between 15°and 30°. Much of the equatorial belt has high atmospheric humidity and cloud cover which allows less UV light to reach the ground. The number of sunny hours per year averages 2,500 near the equator and increases to 3,000 hours per year in latitudes between 15° and 30°. At any given location this may vary greatly. Some areas on the planet at any latitude are just sunnier (Think Las Cruces, NM, 350 days of sun a year) and others consistently more cloudy and damp. (Think Portland, OR, with less than 140 clear or partly cloudy days a year.) UV-B doesn't penetrate clouds or fog. Interestingly, UV-A does penetrate and it is UV-A that causes sunburn on a cloudy day.

Skin color most likely evolved, at least in part, to modify vitamin D production.[768] In tropic and sub tropic climates the high melanin content of darker skins protects the skin from excess UV rays, greatly reducing the risk of skin cancer and over-production of vitamin D. Melanoma incidence is very low in blacks in the U.S. and lower in Africa even though UV-B is more intense.[769] Basal and squamous cell skin cancers are also rare.[770,771,772]

As humans moved to less UV-B abundant locations it is likely melanin production decreased to allow continued production of adequate vitamin D. You will find the explanation of this process in the chapter *How Do We Get D?*

Skin color is just one of the ways our bodies may have adjusted over time to ensure adequate vitamin D.

Some natives of northern Asian countries and the far north have darker skins with less UV-B. These groups have a history of high fish consumption, one of the few dietary sources of vitamin D. As the sea grows colder and darker the amount of D in sea life increases. Seals and whales have exceptionally large stores of vitamin D which provided adequate vitamin D in the traditional Eskimo or Inuit diet.[773,774]

It is possible fish and seafood as a significant source of vitamin D in some way alters patterns of melanization. The Japanese have higher mean levels of 25(OH)D than white Americans even though Japan is far enough north to be a relatively poor source of UV-B in winter months (like much of the U.S).[373] This increased D level is attributed to higher fish intake.

Both high levels of vitamin D and high levels of fish intake are associated with less cancer of the breast, colon and prostate.[283] It has been demonstrated in one study cholecalciferol in skin stimulates melanocytes, cells producing melanin.[775] When levels of dietary or supplemental D, are very high the skin is one of the storage sites of excess cholecalciferol.[776] This suggests the possibility that persons who had very moderate exposure to UV-B and were consuming traditional diets high in vitamin D may have, over many generations developed more melanin producing cells and relatively darker skins. Both dietary and sunlight D influence melanin and melanocytes.

Our bodies have other ways to maintain just enough and not too much D including alteration of enzymes so that high exposure to sunlight or dietary D results in rapid breakdown of 25(OH)D to inactive metabolites as occurs in the skin of Asian Indians.[43] It is possible this occurs in other races as well which would mean they must have a constant source of sunlight to maintain adequate D.

Seals consume levels of D that would be toxic in other species but remain healthy by rapid conversion of 25(OH)D to inactive metabolites and by storing excess in blubber.[777]

What this means:

As long as each of us eats what our ancestors ate and do not intermarry and get the same amount of sun at the same location as our ancestors we should be able to maintain adequate D.

Uh, oh! There are so many impossibilities in that sentence it boggles the mind. You and sunlight and D are a very complex system.

The Need for Vitamin D

All of the conditions I listed as frequently occurring in blacks in the U.S. are associated with vitamin D and calcium. Adequate D and calcium have improved hypertension, diabetes, insulin resistance, obesity, and heart disease. Blacks have low to very low levels of vitamin D in all northern latitudes.[18,93,108,391,778,779,780,781]

The latest National Health and Nutrition Examination Survey, NHANES, found 42% of African American women suffering from hypovitaminosis D as compared to 4% of whites.

It gets worse. The standard they used to determine vitamin D adequacy was 15 ng/ml. Holick determined a minimum of 20 ng/ml to prevent disorders related to bone and higher levels, above 32 ng/ml, to provide adequate D for cellular functions, perhaps preventing cancer, reducing hypertension, diabetes and obesity. Other researchers suggest values equal to or greater than 40 ng/ml.[782]

The lowest levels of D found in black women were less than 10 ng/ml and the highest 25 ng/ml.

In whites low D usually means a reduction in bone mass. Blacks with low levels of vitamin D retain bone. The retention of bone occurs because the vitamin D endocrine system in blacks is altered.[244] There seems to be a compensatory shift in hormones and minerals, which causes a recycling of calcium in the kidney, thereby sparing bone. Even though levels of D are low or very low due to lack of UV-B, bone mass in blacks is greater at puberty and remains higher throughout the lifespan in the U.S.[783,784]

Black men and women may also have higher levels of estrogen and testosterone and perhaps growth hormone, which contribute to the building of greater bone density during adolescence. The calcium sparing action of the kidney slows bone loss when levels of sex hormones begin to decline with age.[785,786]

Most researchers and clinicians just don't think about D unless there is bone loss or a serious abnormality in one or more bone markers like serum calcium or PTH (parathyroid hormone).

In addition, my not so good friend 'norm' plays a part in the omission of recognizing the true significance of vitamin D deficiency in blacks. Normals in blood samples are defined as what a majority of 'normal' persons have. Women typically have less serum iron than men so 'normal' on lab iron and hemoglobin values are lower for women than men. Having values equal to men might alter, in a good way, energy and immune function in women, we haven‘t checked.

Blacks consistently have higher PTH (parathyroid hormone), higher calcitriol (the active hormone D) and lower 25(OH)D than whites. As most blacks have these values this has been considered 'normal', for blacks. Yet when blacks are given vitamin

D or prescription 25(OH)D the altered values become similar to whites. PTH lowers, calcitriol lowers and 25(OH)D increases, all to _white' normal values.[407,787]

In a study on vitamin D supplementation of postmenopausal black women, which showed supplements did improve bone health markers, the authors wrote, "These findings strongly support the hypothesis that the reduced levels of serum 25(OH)D in black women is physiologically significant. If this were not the case, dietary supplementation with vitamin D would not have reduced PTH levels and decreased serum 1,25-$(OH)_2$D levels" [407]

As true of most hormones parathyroid hormone levels vary throughout the day but remains within a normal range. PTH exhibits both stimulating and inhibiting effects on the formation of bone. When PTH is chronically elevated, as occurs in hyperparathyroidism, calcium is released from the bone contributing to net bone loss. Lowering PTH with vitamin D supplementation, only possible if vitamin D insufficiency is present, would reduce bone calcium losses and help keep bones mineralized.

GP Interpretation: Blacks in America have low 25(OH)D, elevated calcitriol and elevated PTH but as this is true for most darker skinned persons it is considered 'normal' for them. The researchers noted, when black, postmenopausal women were given vitamin D serum 25(OH)D increased, calcitriol decreased and PTH fell. "This probably means their low levels of vitamin D are physiologically significant." It seems to me …probably physiologically significant… is a gross understatement.

The seeming lack of connection in blacks between bone loss and low vitamin D levels and the concept of 'normal' as _the serum value which others like you also have', have blinded clinicians to considering other effects of D deficiency.

Vitamin D plays multiple roles in maintaining our health. It's not just about bone. Clinicians also seem to have completely disconnected from the reality that darker skins need more UV-B, both intensity and exposure time to make equivalent amounts of D.[97,768,788] This becomes particularly bizarre when you realize blacks are encouraged to use sunscreen though they have the lowest rates of all skin cancers.[789]

Rickets occurs in some areas of Nigeria. While rickets in Africa is most commonly associated with lack of calcium the mean 25(OH)D in Nigerian children with rickets has tested to be 12-15 ng/ml. well below Holick's 20 ng/ml. Mean levels of 25(OH)D in healthy Nigerian children, children without rickets, tested between 20-28 ng/ml. [790,791]

Rickets in Caucasian infants and osteomalacia in Caucasian adults is associated with levels of 25(OH)D less than 10 ng/ml.[792]

Some interesting points:

- Blacks in Africa suffer from rickets with levels of D considered adequate in the U.S. This suggests that persons with African heritage may need higher levels of vitamin D than whites to maintain equal cell health.

- Alternatively it may mean African children with rickets have insufficient calcium.
- Research suggests both intense UV-B sunlight and exposure of a large percent of the body's surface is needed to make sufficient vitamin D.
- In traditional African cultures (or any other tropic or subtropic cultures) life evolved out of doors and significant amounts of skin were exposed to sunlight.
- Dark skins may need as much as six times longer exposure, at any level of UV-B intensity, to make the same amount of vitamin D as light skinned persons because melanin quenches UV-B before it reaches 7-DHC in the skin to produce D.[203,793]
- The sun in the U.S. is a much poorer source of UV-B than sunlight in tropical or subtropical locations.[97,98]
- In the U.S. blacks have greater bone mass even with low levels of vitamin D. This is thought to be because they have a genetic alteration that causes the kidney to hold on to calcium, recycling it rather than excreting it as is common in most Europeans.[244,794]
- Calcium is hard to find in African diets so lack of calcium is a greater problem for infants and children than lack of sunlight vitamin D.[795,796] America has, relatively, more calcium available.
- In Africa, where available calcium is very low, children black and white have similar bone density. [751,797,798]
- Black women in Africa with low calcium intake do not retain bone mass.[752]
- Blacks in the U.S. have higher bone mass at all ages and black women are able to retain bone after menopause.[753,783,799,800]

In Africa vitamin D producing sunlight is plentiful but calcium is very hard to find. In the U.S. calcium is relatively easier to access contributing to denser bone in blacks due to calcium retention. But blacks in the U.S. have much higher incidence of all other diseases related to low vitamin D.

Vitamin D is not just about calcium and bones. As you will read vitamin D regulates our cells, the way they grow. If we lack D, or any of the other regulators, our cells grow 'funny'(instead of sunny).

Young Ethiopians in Ethiopia, 10° latitude, were found to have lower levels of 25(OH)D than Norwegians in Norway at 60° latitude.[801] The Ethiopians 25(OH)D averaged 9.4 ng/ml; the Norwegians 32.4 ng/ml.

This doesn't mean people with darker skin need or make less D. What it shows us is that to make vitamin D you not only must live where there is sun with UV-B, you must actually go out in it, exposing some skin. The amount of D we make is based on intensity of UV-B in the sunlight, skin color, time in the sun, and the amount of skin exposed.

When persons with darker skins, at any latitude, spend many daylight hours inside it is likely they have difficulty producing adequate vitamin D. There just isn't enough time. As the amount of skin exposed also is a factor in D production excess clothing as well as reduced exposure time would contribute to diminished D.

As D deficiency is being reported in blacks worldwide it appears indoor lifestyles and excess clothing may be a stumbling block to D production in darker skins at any latitude.

The conditions plaguing blacks in the U.S. relate to alterations in cell replication (how our bodies make new cells) or calcium distribution within or outside of the cell. These roles for D have to do with regulation of cell membranes, allowing entrance or exit of calcium and other electrolytes, and actions of vitamin D within the nucleus of various cells. If vitamin D, from sunlight or food or supplement, is low fewer nuclear receptors are expressed.[802] This could lead to an imbalance between the other cell regulators, testosterone, estrogen, retinoids (vitamin A) and thyroid.

Bodies compensate. They learn how to survive with less of something they need, to a point. There are strong indications persons with darker skins would do well with more D, whether from sunlight or supplements. There are few studies.

Zemel experimented with the usefulness of extra calcium for diabetic hypertension in blacks and found more calcium helped.[803,803] Not only did blood pressure improve, participants lost weight without any change in diet or exercise.

Calcium supplementation, if calcium is low, can alter vitamin D levels, improving them. In Nigerian children with rickets 1,000 mg of calcium daily, just calcium, no supplemental vitamin D, increased 25(OH)D from a mean of 16 ng/ml to 21 ng/ml in six months and resolved symptoms.[804] Adding vitamin D to the calcium produced even better responses. Using vitamin D alone, without calcium, gave a higher value of 25(OH)D but serum and bone markers of rickets remained.

Earlier studies in the U.S. have also demonstrated the sparing effect of calcium on 25(OH)D. A 2,000 mg calcium supplement given to men with no obvious disease demonstrated an increase in 25(OH)D from a mean of 29.2 ng/ml to 37.6 ng/ml in just 6-7 weeks.[279]

As Nigerian study participants had little calcium in the diet, about 200 mg. a day, and UV-B sunlight is abundant it is yet to be determined if calcium alone would work equally well in higher latitudes having less UV-B sunlight. The study does suggest that when we are trying to understand sunlight and D, daily intake of calcium is an equally important part of understanding what tested levels of serum 25(OH)D might really mean.

The Real Meaning of Roots

Our roots are found in the land (latitude, longitude and altitude) of our far distant ancestors. A given amount of sun exposure, time plus intensity plus skin surface, produces D in all skin types but amounts vary. When exposed to UV-B at equal intensity and time vitamin D increases most in whites and least in blacks with East Asians (Chinese, Japanese and Korean) and South Asians (Indian) in-between.[805] This suggests very different needs for sunlight.

Any ethnic group with ancestors from the lower latitudes must consider vitamin D when moving north or south to higher latitudes more distant from the equator. UV-B just won't offer itself easily in these locations.

Hispanics have the lowest cancer incidence and death rates in the U.S. Hispanics, like blacks, seem to retain bone but have very low levels of serum 25(OH)D.[806] Members of this group suffer from a number of the conditions discussed in this book and these conditions are increasing within the population over time.[807,808] Obesity and heart disease are the fastest growing health problems in Mexican Americans.[809,810]

Native Americans, Alaskan natives and Asians also have lower overall rates of cancer than blacks or whites but high rates of certain types of cancer.

Inuit in Greenland eating traditional diets have low levels of calcium but very high levels of D.[811] Traditional Inuit diets provide very little calcium. Normal growth in children occurs on as little as 20 mg of elemental calcium a day. When Inuit children were given extra calcium serum calcium remained normal but urinary calcium increased in half of the test subjects. [812]

Like blacks the Inuit seem to have developed mechanisms well suited to an environment low in calcium and high in vitamin D.

In the far north fatty fish and seal oil provide large amounts of D. Eskimos, Inuit's and Canadian Indians are experiencing the effects of leaving behind traditional sources of vitamin D. Prevalence of rickets and cavities in 70% of teeth demonstrate just some of the damage caused by modern diets and too little D.[813]

Rates of diabetes, arthritis, osteoporosis, tuberculosis, hypertension and obesity are increasing rapidly.[814,815,816,817,818,819,820,821,822,823,824,825,826,827,828] All of these conditions are strongly associated with vitamin D and calcium.

In this far north location dietary D is the primary source. Intake of fatty fish, seal oil, and other traditional foods are critical for adequate D nutriture. Supplements won't replace all of the nutrients lost in such a huge dietary change and even if supplements could be used are unlikely to be available or affordable.

Without question vitamin D isn't the only problem created by changing from traditional diets to modern processed food. The Western diet that makes rats sick makes people sick too. Traditional foods contain important nutrients necessary to survival of the peoples consuming them. Modern processed foods don't do any of us much good and clearly contribute to ever increasing obesity..

Asian Indians are less well studied in U.S. epidemiology. They do need plenty of sunlight to make D as you'll see in the Delhi study. In the U.S. the greatest risks for this ethnic group are diabetes and heart disease.[153,829,830,831,832,833] What has been noted is that like Hispanics, Inuits, Eskimos, and blacks they have 'an alteration of the vitamin D endocrine system' which causes them to need more sunlight.[43]

I have to say I have come to think of that term as pretty stupid.

Alteration from what? Whites? When our ancestors lived at different latitudes with different diets our incredible bodies evolved in our ancestral _forest' with the adjustments necessary, to soil, sun, temperature, food and water, to survive.

We are all different and we can all be Americans but we, all of us, have to make allowances for these differences. Whites aren't doing all that well so comparing to them

or seeing them as 'normal' is not such a good idea. If normal is what most people in a group demonstrate then perhaps obesity is normal, right?

Quick PROBLEM CHECK for people of any color:

- Moving from ancestral locations causing increased or decreased exposure to UV-B (example-whites in northern Australia, blacks in America or Europe)
- Changing traditional skin exposure to UV-B by putting on or taking off clothing
- Changing exposure patterns to sunlight; spending daylight hours inside/outside
- Changing ancestral diets; in Africa and the tropics fresh palm oil, native vegetables, and tropical fruits provide vitamin A to balance sunlight D, important to prevent vitamin A deficiency; in the far north seal oil, whale, and fish contain high levels of vitamin D and A, when the skin, organs and fat are consumed.

Blacks, Inuits, Eskimos, and Mexican Americans need to be concerned about getting enough but not too much calcium and adequate vitamin D. We all do. If your genetics suggest high levels of D, from sunlight or food, and low levels of calcium, life in the U.S. may be very complicated. America has easy access, relatively speaking, to calcium but sources of D from food or sunlight are limited.

Sunlight above 30° is just not adequate to provide D for persons with darker skins. Vitamin D deficiencies have been reported in every race and ethnic group.[76,100,108,520,813,834,835,836]

There are solutions. Read on.

SOME THOUGHTS ON SUNLIGHT, D AND DISEASE RESEARCH

While pursuing the causal agent of a disease or condition researchers may test vitamin D and find it to be within 'normal' range. This may cause them to discount the role vitamin D might play in the disease or condition. In some of the studies values of D were low normal, which, as you will see later, may be 'normal' but not adequate to prevent or modify the condition or disease being studied.

In other studies, the studies on bone health and the backache study, people with 'normal' levels of D were given more D and got better, meaning D very likely did have something to do with it, and challenging the usefulness of normal values. Accepted normal values for 25(OH)D in the year 2003 are most probably not healthy or optimal. In the section on testing you'll read more about 'normal'.

A single study done in Finland comparing hormone replacement therapy and vitamin D supplementation in postmenopausal women found vitamin D increased LDL and decreased HDL levels. Vitamin D levels were not tested before the study began so there was no demonstrated need for D. The amount of vitamin D given was just 300 IU, less than the 400 IU used frequently in the U.S. The conclusion, that hormone replacement therapy decreases and vitamin D may increase the risk of heart disease

suggests the promotion of hormones for postmenopausal women more than it presents any real evidence of danger from vitamin D.[837]

Well after this study other studies determined HRT does not protect from heart disease and has other problems such as an increase in breast cancer. These later studies actually show an increase in heart disease among HRT users.[838,839,840,841]

I mention this because if you really want to know what a study says you may need to read the full text and find out what it doesn't say. In the moderate doses from supplements or sunlight as suggested in this book the likelihood of problems from sunlight or vitamin D are minimal. My 7+ years of study and actual experience with persons trying sunlight, supplementation, or a combination, have caused me to consider sunlight the safest source of vitamin D. If you decide to proceed with maximizing D using supplements, remember:

Supplementation beyond the DRI Tolerable Upper Intake Level should be undertaken with the support of an experienced healthcare provider and with repeated testing, before and while using supplemental D.

Anyone can react to anything at any time. If what you're doing doesn't seem right, stop. Find a knowledgeable, experienced healthcare provider to help you.

The studies I reference ni this book do not prove lack of sunlight or vitamin D caused or corrected the diseases and conditions being associated with sunlight or D. Rickets, osteomalacia, and some cases of hyperparathyroidism are the only conditions proven to be caused by D deficiency.

The studies do suggest very many miserable moments may be related to lack of sunlight or vitamin D.

You get to prove or disprove the importance of D, for you. If you have a backache or arthritis or a family history of prostate cancer or any of the other conditions I‘ve discussed and you test your D and make sure you get the right amount of sun or supplements and you get better or stay well (don't develop the disease) D works, for you.

Your future is in your hands.

CHAPTER 5 WHAT IS VITAMIN D?

A SHORT HISTORY OF VITAMIN D AND HUMAN HEALTH

Holick, DeLuca and others [377,793,842,843,844,845,846] have written extensively on the history of vitamin D within the academic and research community. An excellent short text for an overview of vitamin D including historical data is Vitamin D: Metabolism and Function written by Dr. Hector F. DeLuca, [847] Dr. DeLuca has been working with vitamin D since the early 60s and is currently the Steenbock Research Professor and Chairman of the Department of Biochemistry at the University of Wisconsin-Madison.

DeLuca tells us diseases of the bone from lack of sunlight have been described in writings throughout recorded history. Reporting from a work by Hess in 1929 [848] DeLuca writes:

"The apparently softer skulls of Persians compared to those of Egyptians were discerned in the field of battle. It is possible that the Egyptians, who shave their hair and wore scanty clothing, permitted ultraviolet light to be incident on their skins, whereas the Persians, who wore turbans and covered much of their bodies, prevented ultraviolet light from reaching their skin. … resulting in thinner bones. Whether this actually occurred is a matter of speculation."

Early work leading up to the discovery of vitamins involved methods of determining essential elements for life. F. Magendie in France in 1816, Justus von Liebig in 1841 in Germany and F. G.Hopkins in 1906, reasoned that if they knew the chemical composition of foodstuffs they could support life with the purified elements. Liebig worked primarily with soils and plants. Initially the isolated elements he used failed to support life. Each of the other early investigators worked with animals and also found it impossible to support life with purified mixtures of carbohydrates, proteins, and fats.

C. Funk introduced the idea of 'vital amines' in 1911. This was his term for the substances yet to be discovered that would provide the essential elements, beyond carbohydrates, proteins and fats, which sustain life. Later as various essential elements necessary to life were discovered and isolated they were given names. The term vital amine was shortened to vitamin and the essential elements labeled according to discovery, vitamin A, vitamin B, vitamin C, vitamin D and so on. .

The history of vitamin D is forever entwined with the awful disease rickets. Most of us have not seen the crippling effects of this disease as even when it appears today, as it still does in some communities, it is quickly identified, treated, and reversed. [520,813,849,850,851,852,853,854,855,856,857,858,859] The disease is disturbing to view. It is painful to imagine the sufferings of so many children before the discovery and use of cod liver oil and vitamin D.

Rickets, the most severe expression of vitamin D deficiency, is a terrible, painful, and permanently deforming condition when not treated in early stages. Understanding the cause and finding a cure in the early 1900s was a great discovery for all mankind.

rickets, def. a disease, especially of children, caused by a deficiency in vitamin D that makes the bones become soft and prone to bending and structural change.

Glisson in 1650 or perhaps Whistler in 1645 recorded the first description of a bony disease thought to be rickets. Definitive research into the cause and cure of rickets does not appear until 1919 with the work of Dr. E. Mellanby, which shortly follows. The name rickets may have come from the term rucket, meaning to breathe with difficulty, a problem in rickets because of malformed ribs [848,860]. Or it may be from the Welch term "wrygates", which meant crooked goings or twisted legs.[860]

DeLuca and others cover the research history of vitamin D, carefully, and with the respect due these brilliant early explorers and discoverers, listing researcher names, discoveries, and dates.

What is more useful to our current understanding of D was a history of vitamin D research in the early years, which I found in a 1930 textbook Ultraviolet Light and Vitamin D in Nutrition, Blunt and Cowan, University of Chicago Press, Chicago, IL. In the forward the then editor of the Journal of the American medical Association, Morris Fishbein, tells readers

'of all of the vitamins most seems to be known concerning vitamin D, which forms the subject of this book.'

Fishbein then relates the ways in which one can get vitamin D including the new Viosterol, a standardized irradiated ergosterol, just then developed. It was the first standardized D supplement listed in New and Nonofficial Remedies, a publication of the Council on Pharmacy and Chemistry of the American Medical Association. This was important because it was the first 'medicinal, man-made, vitamin D supplement' and its selling point, according to Fishbein, was that

"the infant who needs vitamin D for the prevention of rickets or for the cure of that disorder, the persons with disease of the bone or teeth who should have vitamin D, may obtain all that he needs in a preparation that can be taken in drop-doses, and without the smell, the taste or the other disagreeable qualities of cod liver oil."

GP: Cod liver oil has a long history of distaste. Researchers and subjects were obviously delighted by this discovery.

Fishbein continues

"Only seven years have passed since the identification of vitamin D as distinct from vitamin A. Yet… such progress has been made as no one would have dreamed possible seven years ago. … In this book Dr. Blunt and Miss Cowan have assayed the literature, have collected it under significant headings, skimmed the truth from the fantastic notions and exaggerations of those commercially minded and yielded what seems to me to be a fundamental work for all interested in this field. It will not be necessary for writers in the future again to review all that has been done in arriving at the point where the authors have paused to take inventory."

The book contains a wealth of information to help us today, much of it forgotten or unused.

The Mellanbys and Cod Liver Oil

The early understanding, of the relationship between sunlight and bones and the relationship between vitamin D and bones, started in separate places.

The industrial revolution ushered in a high incidence of rickets in Europe and North American. City dwellers spent days inside and should they venture out the air over their cities was filled with smoke and pollution blocking the needed ultraviolet rays.

The Englishman, Mellanby, first published the effects of diet on bone growth in several studies in 1918 and 1919 in the Lancet. He had succeeded in producing a condition in puppies resembling rickets, the condition then becoming so prevalent in children. He first designed and fed the animals diets deficient in 'antirachitic factor', which caused the symptoms of rickets to appear. He then proceeded to cure the disease

"by giving cod liver oil, or, less effectively, butter fat or suet and in others he failed entirely to cure it by lard, by cottonseed, olive or linseed oil."

His research was the first to clearly define rickets as a disease of dietary insufficiency, a lack of what was called "antirachitic factor".

At the time Mellanby carried out his studies cod liver oil had already been determined to contain 'fat soluble vitamin A', so named by McCollum in 1913. Professor McCollum executed classical experiments demonstrating the presence of a factor in butterfat and cod liver oil essential to the growth and health of animals. It was this 'fat soluble vitamin A' that was considered to be the active component of cod liver oil so Mellanby initially misconstrued vitamin A to be the antirachitic (anti-rickets) vitamin.

Researchers in the U.S. were "loath to accept" this role for vitamin A. AF Hess found that some infants consuming a diet rich in milk and cream (both are naturally high in vitamin A) developed rickets more readily than other babies having a diet with

skimmed milk, low in vitamin A. (Vitamin A works with vitamin D and is important for other reasons yet to come.) The research confirming vitamin A and vitamin D were two different vitamins came from the work of A McCollum and colleagues at Johns Hopkins University in 1922.

At almost the same time McCollum isolated and named fat soluble vitamin A, in 1916, he discovered a new water soluble factor he named vitamin B. Antirachitic factor, being separated out and determined to be different than vitamin A in 1922, got the next available letter in the alphabet, fat soluble vitamin D. The method McCollum used to isolate the difference in function between the vitamin A and antirachitic factor provides insight into important characteristics of vitamin D.

The researchers were aware vitamin A could be destroyed by oxidation. They passed a stream of oxygen through heated cod liver oil. This treated oil was then fed to two sets of rats. Vitamin A prevents the development of xerophthalmia, an eye disease causing blindness, and cod liver oil prevents it.

The rats on a diet devoid of vitamin A developed xerophthalmia when fed the oxidized cod liver oil but rats on a rickets producing diet (no D but some A) receiving the oxidized oil did not develop rickets. This proved that cod liver oil had two active components, one critical to the health of the eyes and skin, and the other critical for the formation of bone.

xerophthalmia, def.: an eye disease caused by vitamin A deficiency, marked by dryness and ulceration of the conjunctiva and cornea.

If untreated, xerophthalmia may cause blindness. It is still a common cause of blindness in third world countries today.(861)

It should get your attention that treatment of the cod liver oil with a combination of heat and oxygen destroyed the vitamin A BUT left the vitamin D. This is an amazing example of the anti-oxidant and membrane stabilizing potential of vitamin D.

Vitamins, including vitamin A, beta-carotene, vitamin E, the B vitamins, and vitamin C are destroyed, some more quickly than others, by light, heat and oxygen. Compare them to vitamin D, which is MADE by light and remains stable even when exposed to direct heat and oxygen as was the cod liver oil in the experiment.

D can be destroyed but it is very stable. The more we learn, the more amazing this substance becomes.

Lack of Sunlight; Bones Gone Awry

The second track of discovery, regarding sunlight and rickets, begins with Huldschinsky working in Berlin, Germany just after the war, between 1919 and 1920. Cities at this time were dark, smelly, foul places. Pollution from burning coal used for heat filled the air covering every surface with soot and blocking what little UV-B light was available at higher latitudes Without this critical band of light necessary for production of vitamin D, severe deficiencies abounded.

Huldschinsky found an appalling amount of rickets in infants and children. He began his research with children from the Oscar-Helene Home for Crippled Children. His patients were between 3 and 5 years old with deformed limbs or spinal curvature, severely impaired growth, and active rickets.

Huldschinsky exposed these children to sunlight and to a quartz mercury lamp like the light in the testosterone study, a lamp containing high levels of UV-B light. He was encouraged in his work because the treatment strengthened the softened bones BUT it did not correct the deformities.

Remember my earlier comments on the arrow of time? Nutrition is important at all points of development, but especially during pregnancy and infancy. Once abnormal growth occurs often it cannot later be corrected. The children's bones hardened in the abnormal shapes formed by the stress of growth and activity when the bones were soft. Severely bowed legs, abnormally curved spines, poorly developed pelvises and other severe abnormalities remained. Frustrated, Huldschinsky turned his efforts, with much success, to the prevention of rickets in younger children using his ultraviolet light treatment.

Researchers before him, like others before Mellanby, had noted the connection between rickets and children kept in "the crowded dark rooms of city tenements" but the condition was ascribed to bad air or noxious gases. A few physicians had tried sunlight but none with the definitive results and proofs of Huldschinsky.

Later, other researchers confirmed the favorable effect of the artificial ultraviolet light. In 1921 Hess and Unger in New York showed that sunlight alone could quickly and effectively cure infantile rickets. Steenbock and Hart and in another location McCollum continued to explore the connection between sunlight and calcium using rats, cows and goats. Steenbock and Hart found that lactating goats kept indoors lost bone mass but if kept outdoors in sunlight on the same diet retained bone.[862] NO sunscreen for goats!

Vitamin D and Sunlight; Connecting The Discoveries

Initially the co-ordination of these two sets of discoveries, cod liver oil and sunlight or ultraviolet light, baffled researchers. They had no idea of the relation between these two treatment protocols. What did sunlight or ultraviolet light have in common with cod liver oil?

In 1924 two groups of investigators, Steenbock and Black, and Hess and Weinstocks, almost simultaneously made the connection.

"Foods which were themselves without antirachitic power were discovered to develop it on irradiation with ultraviolet!"

Hess in New York irradiated (meaning that he exposed to UV-B light from the quartz mercury lamp, not x-rays) cottonseed and linseed oils and found them as potent to cure rickets as cod liver oil. Steenbock and co-workers at the University of Wisconsin irradiated the whole mixed diet of the rat with equal success. Apparently ultraviolet light (UV-B) made vitamin D where none had been before. These

investigations led to the irradiation of many foods and successful feeding of these foods to rachitic animals and children.

GP: Just imagine, a sunbath for you and your dinner! Makes you wonder if this may be part of the reason why food is more satisfying when cooked and eaten outdoors.

Initially it was believed that the raw material for D production was ergosterol, a natural plant sterol. The first standardized vitamin D supplement, Viosterol, was made by irradiating ergosterol. In 1930 researchers considered ergosterol to be the precursor molecule to vitamin D in man, animals and plants. Later ergosterol would be determined to be the precursor in plant foods leading to production of vitamin D_2 when exposed to UV-B light. It would be some time before researchers could identify the structural differences between vitamin D from plants and animals and use D_2 and D_3 to differentiate them.

Cod liver oil contains vitamin D_3, which is based on the cholesterol molecule. When the cholesterol metabolite, 7-dehydrocholesterol, 7-DHC, present in the skin, of mammals, birds, and reptiles is exposed to sunlight containing UV-B, the molecule is rapidly converted into vitamin D_3. Ergocalciferol is made by exposing ergosterol, found in plants and abundant in fungus and yeasts, to narrowband UV-B light.

FYI: The dry, often labeled vegetarian, cholecalciferol (D_3) sold in health food stores is made by chemical and UV-B light conversion of extracted sheep's wool grease. It is from an animal, well from its wool, but no animal is killed in the making. There is no non-animal source of cholecalciferol.

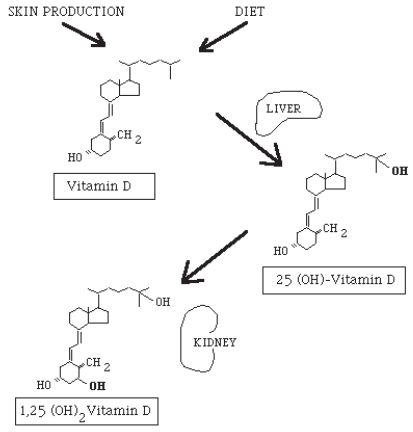
Most of the studies in the early research reviewed in Ultraviolet Light and Vitamin D in Nutrition used cod liver oil. Because cod liver oil contains both A and D, and because people didn't like the taste, nor could it be masked for 'double blind' research, later researchers used the new Viosterol, vitamin D_2. It cured rickets and worked well for the researchers studies because it only contained vitamin D.

Science first isolates the element they wish to study and these early researchers were still trying to isolate essential nutrients and determine individual actions in the animal and human body. The benefits to bones and teeth found by the Mellanbys are attributed to vitamin D and that is confirmed by results with isolated D. But the early researchers saw other health benefits with the application of cod liver oil that are lost to us when vitamin D becomes an isolated nutrient or a pharmaceutical.

Cod liver oil, used as the primary source of D in early studies, contains vitamin A, vitamin D_3 the form naturally found in humans, and relatively large amounts of omega-3 fatty acids. It may be considered the first recognized and researched 'health food supplement'.

CHAPTER 6 THE VITAMIN D ENDOCRINE SYSTEM

Vitamin D biochemistry fills a number of really big books with many, many pages and the research in the field is still growing and will continue to grow for some time. What follows is just a small portion of what has been written to give you some idea of the complexities involved in understanding vitamin D's multiple roles in building and maintaining healthy bodies. It includes explanations of vitamin D related elements that help or that may impede vitamin D functioning. These explanations are skeletal. They are missing lots of parts and steps. The idea is to give an overview of how things work.



VITAMIN D, THE MOLECULES

After Mellanby and others determined the need for antirachitic factor and McCollum named it, scientists still didn't know the structure. Initially the product was labeled D_1, structure unknown. As mentioned before, the first "man-made" vitamin D was extracted from plant sterols irradiated by UV-B light. Askew and others in Britain, isolated and determined and Windaus confirmed this molecule to be ergocalciferol, which became vitamin D_2.

Windaus and Bock later isolated the precursor from skin, 7-dehydrocholesterol, which sunlight UV-B converts to vitamin D_3, cholecalciferol. Hope you remembered to mark the Terms section. For more complex details and references look to Vitamin D, Feldman, Academic Press, 1997, one of those really big books.

The term vitamin D means any of the metabolites of cholecalciferol or ergocalciferol made in our skins or gotten from food. We are looking at the three most well studied, chole- or ergo- calciferol, calcidiol, and calcitriol, but there are others.

Egan Kodicek conducted experiments over a period of 10 years at Dunn Nutritional Laboratory to determine the active D molecule, active meaning the vitamin D metabolite that had significant biological activity. These experiments seemed to prove that vitamin D, cholecalciferol, the kind in food or made by sunlight in our skins, was the 'active' vitamin D.

The D metabolites, 25(OH)D and $1,25(OH)_2D$ (and others we won't even mention here) don't enter the picture as important players until the late 1960's. Groups headed by Kodicek, DeLuca and Norman in the years between the late 1960s and early1970s, completed research determining the presence and structure of $1,25(OH)_2D$, calcitriol, then considered to be the active metabolite. Understanding the structure of the vitamin D endocrine system led to the recognition that calcitriol‘s actions made it a hormone, not a vitamin.

$1,25(OH)_2D$ or calcitriol, is a hormone. The distinction is important because as long as we continue to see vitamin D as a vitamin, and its name doesn't help us much, we misconstrue the importance of its role in our long-term health. Seeing D as a hormone helps bring into focus the difficulties determining and supplying safe and adequate amounts

> *vitamin, def. An essential low molecular weight organic compound required in trace amounts for normal growth and metabolic processes. They usually serve as components of coenzyme systems. (My note- Vitamins must be gotten from outside the body, from food. We don't make them.)*

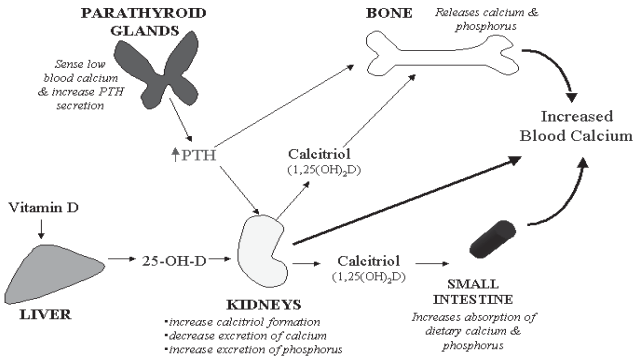
For humans vitamins A, the B series that includes folic acid as methylfolate, C, D, E and K are required. Deficiencies of one or more vitamins in the diet result in deficiency diseases such as rickets, scurvy, pellagra, and beriberi.

> *hormone def. A naturally occurring substance secreted by specialized cells that affects the metabolism or behavior of other cells possessing functional receptors for the hormone. Hormones may be hydrophilic (affinity for water), like insulin, in which case the receptors are on the cell surface or lipophilic (affinity for fat), like the steroids, where the receptor can be intracellular (inside the cell).*

Note to the GP: Hormones are made inside our bodies. They have receptors, places on cells designed to receive instructions from the hormone. These receptors transmit the hormone's instructions to our genes. Hormones are sometimes called signaling molecules which I think describes them well. They signal our cells with instructions including messages to grow, stop growing, produce a specific enzyme or die.

THE VITAMIN D ENDOCRINE SYSTEM

This is a brief (skeletal) description of the vitamin D endocrine system. It is not this simple. There are many more components and some parts of the system are still being discovered. The description is intended to give you a very general map of the major stops vitamin D takes on its journey throughout bodies.



-

- Vitamin D, either chole-or ergo- calciferol, is made from the interaction of UV-B light with 7-dehydrocholesterol in our skins or taken in from food or supplements. From skin or gut it then makes its way through the bloodstream or lymphatic system to the liver.

- Reaching the liver some of the vitamin D (calciferol) is converted to 25(OH)D, calcidiol, and other less well-studied metabolites.

- Leaving the liver unconverted calciferol and 25(OH)D are transported through the bloodstream by vitamin D-binding proteins. Bound and unbound excess calciferol and 25(OH)D are carried to fat cells, muscle cells, and other tissues for participation in cell structure or storage.

- The remaining calciferol and 25(OH)D circulate in the blood, calciferol available for later conversion in the liver

- Some 25(OH)D is converted to calcitriol as it travels through the kidney

- Calcitriol, $1,25(OH)_2D$, again carried by D-binding protein travels throughout the body to cell membranes where it is released from its protein to pass into the cell and deeper into the nucleus combining with a waiting receptors to activate gene expression and perform other critical cellular duties.

-

The kidney is the primary site of 25(OH)D conversion to calcitriol, the active hormone $1,25(OH)_2D$. The rate at which D becomes activated, that is 25(OH)D becomes $1,25(OH)_2D$, is controlled by parathyroid hormone, which in turn is regulated by calcium levels in the blood.

This basic understanding of the system occurred between 1970 and 1974. Researchers are still exploring the roles the various metabolites of D may play, and just how much of each form of D is necessary or optimal. Some are beginning to consider that each of the three different forms of vitamin D we have been discussing may be important to the balance of the vitamin D endocrine system.

A short review of our three Ds:

-calciferol

cholecalciferol, vitamin D_3, made in our skins or gotten from food or supplements, converted to $25(OH)D_3$

ergocalciferol , vitamin D_2, made by man by irradiation of ergosterol derived from plants, converted to $25(OH)D_2$

calcidiol 25(OH)D, the D in the middle, the intermediate, or precursor to calcitriol. The _storage' form of vitamin D used in testing as a marker for D sufficiency.

calcitriol $1,25(OH)_2D$, the hormonal D that binds to vitamin D receptors on the plasma membrane and DNA. Calcitriol activates processes regulating cell birth, growth, and death.

In 1988 Berlin and Bjorkhem tested 25(OH)D, and $1,25(OH)_2D$, in rats and found that amounts varied with calcium intake. When calcium intake was high, levels of $1,25(OH)_2D$ were lower and 25(OH)D higher. [279] This is the same system interaction explored by Zemel and the fat rats. Sufficient calcium is important when interpreting levels of vitamin D.

The interplay seems to work like this:

- We have enough calcium; calcium in the diet and in our bloodstream is sufficient or even abundant.
- The parathyroid finds everything to be just right. No need for extra calcium absorption
- No signal is sent to the kidney. $1,25(OH)_2D$, calcitriol, is low (normal) and 25(OH)D is high (normal).

or

- Dietary and serum calcium is low; we need calcium.
- This signals the parathyroid to produce more PTH
- which tells the kidney to increase the enzyme that converts 25(OH)D to $1,25(OH)_2D$, calcitriol
- $1,25(OH)_2D$ production from 25(OH)D increases
- 25(OH)D is depleted by conversion to calcitriol lowering serum 25(OH)D
- More calcium is absorbed from available calcium in the diet or if not available taken from bone to restore serum calcium balance.

While the metabolite, calcitriol, is the most biologically active, especially in raising serum (blood) calcium, and is critical for gene expression, the other forms of D may also being doing things, important things, not yet understood.

Barger-Lux and other researchers found absorption of calcium depended more or 25(OH)D which had been and is still by some considered an intermediate, not the

active player.[863] Heaney also suggests 25(OH)D to be a more potent regulator of intestinal calcium absorption than calcitriol.[864]

Earlier I wrote about cholecalciferol playing a part in membrane communication.[282,865] Not all of the cholecalciferol from sun or supplements is converted into 25(OH)D. Like 25(OH)D, cholecalciferol stores in tissue, particularly fat, and travels in the blood bound by D-binding protein.

There are other D metabolites that may or may not serve a function in our bodies. We have a long way to go to fully understand how very important sunlight and D are for our well-being. This brings us to new questions.

The Problem of Which D 'Rules'

In searching for the 'essence' (most basic element or feature) we may miss the complex interplay of substances. From the early beginnings of nutritional research scientists have been looking for 'the most biologically active element'. Complex systems are composed of many parts.

Justus von Leibig, a chemist of great renown in the first half of the 1800s, wished to understand the organic (living) substances in soils and plants.

Liebig claimed that because "perfect agriculture is the true foundation of all trade and industry," a "rational system of agriculture cannot be formed without the application of scientific principles." Only the chemist, he argued dogmatically, could tell the farmer the best means of feeding plants, the nature of the different soils, and the action of particular manures upon them.

"Liebig, Justus, Freiherr von" Encyclopædia Britannica

Liebig sought to find the pure elements and make 'super food'. Leibig began the work that later led to the first artificial fertilizers containing the well-known NPK, nitrogen, phosphorus and potassium formula, the essentials, but devoid of trace elements and other necessary elements to sustain the long term life and health of the soils. If only these inorganic elements are used initially plants thrive, because some organic elements still remain in the treated soils, but later these treated soils become less able to support life and plants that survive become more susceptible to insects and diseases.

In the early 1900s other scientists, studying nutrition in animals, were able to reduce the elements in foods to proteins, fats and carbohydrates, but when these purified substances were fed to the animals they died, just as earlier purified fertilizers were unable to support plant life. Single, or even a few, isolated elements cannot support life. Looking for these missing elements in food helped early nutrition researchers to discover vitamins (elements necessary for life). It was a small beginning towards understanding life and health as a complex system.

In the late 1930s Weston Price in Nutrition and Physical Degeneration page 256 tells us:

"of the 18 elements of which the human body is composed, all of which are presumably essential, several are needed in very small quantities. A few are required in liberal quantities."

At the time, the 1930's, he was trying to support and promote the notion of consuming whole foods, as nature supplied them, instead of the fast growing production and consumption of refined flours and refined sugar. Yet even his more holistic view left out a lot of 'stuff'.

We are composed of much more than 18 elements. Our bodies are known to contain some 59 elements, Emsley, John, The Elements, 3rd ed., Clarendon Press, Oxford, 1998. These elements are not elemental, that is, they are not in an isolated 'pure' form. The elements are parts of other substances made from the elements, vitamins, minerals, enzymes, thousands of different proteins, many different fats and fat based substances, carbohydrates, lipoproteins, glycoproteins and all of the many thousands of distinctly different cells composing a human body.

Nutrition texts prior to the 1960s still saw human nutrition in terms of protein, fat, carbohydrate and calories and some texts continue to do so even today. Very little is said about the differences in fats, including chain length, and saturation, or the nutritional effects of processing and hydrogenation, though this is now beginning to change.

There is no mention of the differences in proteins, both quality and that they are the most frequent food allergen. Nor are differences between complex, simple, or refined carbohydrates considered. Every few years another trace element or vitamin-like substance or conditionally essential amino acid comes up for consideration as being important to life and health. Many are marketed at great cost in pills and powders.

Proteins, fats, and carbohydrates are not created equal; have different roles in our bodies; and cannot be interchanged for each other, with few exceptions, in chemical processes. Our individual need, to get or avoid, a specific type of protein, fat or carbohydrate has a genetic link.

Some of us need more of a particular type of fat than others. Some of us must avoid certain proteins due to genetic intolerance, like gluten intolerance or peanut allergy. Some must avoid certain carbohydrates such as persons with lactose (milk sugar) intolerance.

Carbohydrates are simple, complex or refined, each reacting differently in nutrient availability, digestion time and insulin response. Carbohydrate sensitive individuals may develop adult onset diabetes when over consuming certain types of carbohydrates over many years. Lack of essential elements such as vitamin D, vitamin K, biotin, or chromium can make this carbohydrate intolerance even worse.[230,866,867,868,869]

Our needs for things and the way things go together make a difference in outcomes of health and longevity. Individual need, biochemical individuality, for various vitamins and minerals has been demonstrated in many research studies. An example particular to our topic, some persons need a significantly greater supply of

calcium than others to maintain bone mass. Others need large amounts of sunlight or vitamin D.

Science has been hell-bent on reducing foods to elements 'research has found' essential, ignoring the elements found in natural whole foods determined by the 'experts' to be non-essential or inconsequential. This betrayal (of the wisdom of wholes) has profited the researchers, the drug companies, and the nutritional supplement industry. It has not profited the consumer.

Every few months researchers 'discover' a new element (not so new as these elements are found in whole foods) to protect us from cancer or lower our cholesterol or otherwise improve our health. Rather than suggesting consumption of the whole food from which the element was isolated a new nutrient is manufactured and marketed, often within months. Does anyone truly believe you can get 5 fruits and vegetables in a pill?

The whole, to be whole, requires all of its parts. Sunlight and vitamin D are like this. Food sources of vitamin D contain more than just vitamin D and sunlight has many rays not just UV-B. It is likely these things 'go together' and since we have lots of vitamin D metabolites in our bodies it is quite likely they are there in some order, also a part of the whole.

The question was 'Which D rules?' In our bodies we have places for them all. The biochemical miracle of life constantly renewing within us very likely needs and uses all of its elements.

No D rules. Each of the metabolites is there in our bodies for a reason. We may not understand the reason right now. We may never understand the reason.

Man did not make the human body and cannot create life where none existed before. Our parts are all important. We need to see the forest and the trees and the leaves, soil, water, and sun, together.

New Roles For 25(OH)D and Calcitriol

While vitamin D is associated primarily with calcium regulation the research is exploding with new roles for D. In 1995 Stumpf reported

:" the vast majority of the target tissues appear not to be primarily related to calcium metabolism, but rather to the activation and regulation of exo- and endocrine secretory and somatotrophic processes such as cell differentiation and proliferation." (870)

Our Vitamin D Endocrine System explanation demonstrated vitamin D quite simply; a path from oral or skin produced D to the liver, converted and then on to the kidney for conversion to the hormone calcitriol.

While the kidney is the primary location for production of calcitriol, some of our cells have the ability to manufacture this hormone locally. In the 70s researchers isolated the responsible enzyme, 25-hydroxyvitamin D-1 alpha-hydroxylase (1α-OHase is the short version), in locations other than the kidney.(871) This means many cells in

your body, not just your kidney, contain the enzyme necessary to convert 25(OH)D into the cell active hormone calcitriol. [872,873,874] [875].

What researchers have yet to determine is why local production of calcitriol is possible, when it actually occurs, and whether it plays a significant or insignificant role in cell health. Studies continue to show this ability to produce active D plays a role in health and disease.[876,877,878,879,880]

Schwartz and colleagues cultured three types of prostate cancer cells, normal prostate cells, benign prostatic hyperplasic cells (enlarged prostate), and keratinocytes (skin cells) with 25(OH)D. With the exception of one cancer cell line, the remaining cultures produced calcitriol.[873] For the researchers working on cancer treatments these and similar findings suggest the potential for powerful new weapons in the war on cancer.

The active hormone, calcitriol, has demonstrated anti-proliferation activity (to stop or slow formation of fast growing cells).[295,585,881] While calcitriol, available as a prescription drug for oral or injectable use, does inhibit cell growth, at the doses needed to treat cancer it also does a number of nasty things such as raising blood calcium to dangerous levels and depositing calcium in soft tissues like arteries and the kidney.

The search for a 'low-calcemic' vitamin D analog, one that will stop cancer growth without dangerously elevating calcium, is ongoing. Numerous vitamin D analogs are being created to mimic the anti-proliferative action of calcitriol but avoid the problem of too much calcium in blood and tissues.

Chen's group[882] looked at the ability of two substances, 25(OH)D and a calcitriol analog, to inhibit prostate cell growth, in normal and cancerous cells. In a lab, not in a human body, both inhibited growth of prostate cells, but 25(OH)D inhibited growth only if the particular cells being cultured contained 1α-OHase. Some cancer cells do not produce this enzyme or produce it in much lower amounts than normal cells.

In cancer cells not producing 1α-OHase there may be the possibility of restoring the cells ability to do so, or in some other way provide the enzyme. New analogs, which bypass the need for 1α-hydroxylase, are also in the pipeline toward human testing, very hopeful research with some distance to human testing or solid conclusions.

Since calcitriol has been shown to inhibit cancers of the breast, prostate, colon, and skin, this ability of the healthy cell to produce calcitriol in the presence of 25(OH)D is likely to be important. It just might be a possibility that having 25(OH)D in our blood and tissues in optimal amounts, just in case it might be needed locally to repair some funny cells, could be a very good thing.

So just what are optimal amounts? Michael Holick, PhD, MD from Boston University School of Medicine has been studying vitamin D for many years. You'll find his name as editor of three of the academic texts used to prepare this book. Dr. Holick believes that the level of 25(OH)D currently accepted to be within normal (remember 'norm') range is too low to support normal calcium function. Further he suggests the level of 25(OH)D needed to sufficiently supply cells, for local conversion to active D, may be even higher.[258].

How much 25(OH)D you have is dependent on your exposure to sunlight or vitamin D supplements or consuming seal oil and fatty northern fish. That's it. There is

no other way. You get it or you don't. Without sunlight exposure, food is not an adequate source for most people, young or old, not even including fortified dairy products.[22,883,884]

D-BINDING PROTEINS (DBP)

Vitamin D had to get from our skins to the liver and from the liver through the bloodstream to the rest of the cells in our bodies. Carrier proteins have the job of carrying things around in our body fluids including blood. They carry hormones, vitamins, minerals, and other vital substances acting as both a transporter and a site of short-term storage. Vitamin D-binding proteins, hereafter shortened to DBP, were identified in 1959.

D-binding protein belongs to a family of binding proteins, which includes thyroid, cortisol, retinol, and sex hormone binding protein. Thyroid, cortisol, estrogen, testosterone, retinoic acid, and vitamin D are hydrophobic, relatively insoluble in water. To allow these messengers to travel through the watery bloodstream and body fluids that surround our cells they attach to water-soluble binding proteins.

DBP is made in the liver and circulates throughout the body. It is DBP in fluids between cells in or near the skin that carry D created by sunlight to the liver for conversion to 25(OH)D.[885] D-binding proteins have developed within gene families (similar to blood types), with a number of different groups currently identified. These variations of D-binding proteins are sometimes used as genetic markers. Another name for DPB is Gc-globulin.

Once made, DPB lasts just about one week. Vitamin D-binding proteins bind and transport all of the metabolites of D, calciferol, 25(OH)D, and $1,25(OH)_2D$ as well as other substances. Bound metabolites of D are carried throughout our bodies to sites where they may be acted upon by enzymes and converted to another metabolite, be released to enter a cell, or enter into tissues for storage. D-binding protein protects us from both deficiency[886] and overload of vitamin D and ensures delivery of 25(OH)D to the kidneys[887] for activation to calcitriol.

Binding proteins have affinities. They may bind many different substances but they prefer and bind some substances more readily than others. DBP has a stronger affinity for 25(OH)D than it does for calciferol or $1,25(OH)_2D$. This is a shared pathway, which leaves open the possibility of imbalances. Elevated or deficient levels of any of our three vitamin Ds have proved to be detrimental to health.[888,889,890,891,892] In the storage study you'll read shortly and a few other studies that checked, when D was given in high doses the primary metabolite found in blood bound to D-binding protein was unconverted D, cholecalciferol.

D-binding proteins also bind substances other than vitamin D. This should grab your attention when you consider the next bit of research. As early as 1989 researchers recognized an interaction between fats, DBP and 25(OH)D.[893] In 1992 Bouillon and colleagues discovered that monounsaturated oleic acid (found in olive oil), and polyunsaturated omega-6 linoleic acid (found in flax, sunflower, safflower, canola and corn oils) can displace vitamin D in binding proteins. [894] The studies are the 'Petri

dish' variety so may not apply to the GP, we real people in the real world, but consider this, in the study polyunsaturated fatty acids significantly decreased vitamin D binding. Saturated fats and cholesterol had no effect.

In the United States the per capita intake of fats containing linoleic acid, an omega-6 fatty acid, increased from 9 pounds per person per year in 1909 to nearly 56 pounds per person per year in 1998. Source: USDA Added Fats and Oils U.S. Pounds Per Capita Intake 1909-1998

This increase specifically reflects intake of margarines, shortenings, hydrogenated and partially hydrogenated vegetable oils, and salad oils all containing omega-6 fatty acids, those same polyunsaturated fats that blocked (actually, filled up) D-binding proteins.

Back to our study: The amount of polyunsaturated fat needed to displace 25(OH)D was very high, but at these elevated levels binding decreased by 20%.

"Much smaller ratio's of FFA:DBP (25 for arachidonic and 45 for oleic acid) however, decreased the binding of $1,25(OH)_2D_3$ to DBP."

The interpretation? Arachidonic acid is found in meat and dairy and is the fatty acid your body produces from omega-6 linoleic acid, the primary fatty acid in vegetable oils.[895] When the ratio of arachidonic acid reached 25:1 arachidonic acid displaced the active hormone calcitriol. This ratio may be physiologically possible. That is, it may be possible to consume enough of these fats to compete with and displace calcitriol on D-binding proteins.

Maybe. We have lots of D-binding protein, lots.

Given the dramatic change in fat intake in the United States some consideration may need to be given to the interactions between dietary fats and vitamin D metabolism. There is a possibility that dramatically increased consumption of omega-6 polyunsaturated fatty acids since the end of World War II, alters the availability of vitamin D contributing to some of our current vitamin D difficulties.

As mentioned in the section on cancer, rats on a Western high fat diet experienced abnormal cell growth that was corrected when they received higher levels of vitamin D and calcium.[393,549,896] Perhaps the alteration in D status or increased need for D had something to do with dietary fat and D-binding proteins. Perhaps some researchers will ask this question and find an answer.

There are other connections between D and fats. Fatty acids are needed as structural components of cell membranes. A vitamin D deficiency increases the amount of arachidonic acid in some cell membranes and membranes lipids are restored to normal when D sufficiency is restored.[897] Arachidonic acid is a precursor to the inflammatory prostaglandins. Increased amounts within a cell membrane increase cellular damage when exposed to UV-A the ultraviolet band of light equally present from morning until eve.[898] One of the jobs of vitamin D is to regulate cell communication, sometimes by alteration of cellular fatty acids.[899]

GP: When vitamin D is low cell membranes contain excess proinflammatory fat, arachidonic acid (AA), which is readily damaged by UV-A light. Getting enough D causes cell membrane lipids to normalize, lowering levels of AA..

D RECEPTORS (VDR) AND THE LIFE OF OUR CELLS

The next discovery of importance to our understanding of sunlight and D comes from Brumbagh and Haussler publishing in 1973. Looking into the cell they found calcitriol, $1,25(OH)_2D$, interacts within the nucleus of cells by binding to a vitamin D receptor. This is a genomic action.

genomic, def relating to genes

Very short explanation: Cells with a nucleus have a cell membrane and deeper inside a second nuclear membrane or envelope containing our chromosomes. Chromosomes package our DNA and genes. A gene is one unit of hereditary information. Genes are formed from DNA carried on chromosomes. We each have about 100,000 genes inherited from our parents.

Gene expression, the information in the gene converted into an actual physical structure, like a new cell or molecule, is regulated by signaling molecules, such as hormones, telling the cell what to do or not do. The messages are transmitted through receptors designed specifically for the particular signaling molecule. One of the messengers telling our cells what to do is vitamin D, calcitriol. This particular role of vitamin D is genomic, meaning it controls the behavior of our genes.

Vitamin D receptors (VDR) within the nuclear membrane vary between different types of cells. Our VDRs alter the way we respond to vitamin D and perhaps may alter how much vitamin D we need or can get along without.

Recently research has demonstrated VDRs on other cell membranes, not just within the nuclear membrane.[(900)] A big piece of the health and vitamin D puzzle has to do with vitamin D and VDR interactions which, along with other messengers, regulate the birth, growth, and death of cells.

In the early 1990's Samuel Edelstein and Miriam Lev-Ran, Dept. of Biochemistry, Wiezmann Institute of Science, Rehovot, Israel wrote:

"Despite the intensive research in the past twenty years in the field of vitamin D, very little is understood about the mode of action of vitamin D and about the reason for the curious metabolic pathway of the vitamin."

Cells have to communicate with each other, signaling and responding to changes in internal and external environments, in an organized way, to survive. Elements of communication are sometimes called signaling molecules.

We have both water soluble and fat-soluble signaling molecules in our bodies. Water-soluble signaling molecules, such as neurotransmitters, are short lived, and are removed or broken down within minutes or seconds. These molecules mediate responses of short duration. Fat-soluble signaling molecules, which include vitamin D, vitamin A retinoids, thyroid and steroid hormones persist in the blood for hours or days and regulate longer-lasting responses.

Vitamin D as $1,25(OH)_2D$, retinoids (think vitamin A), thyroid, and steroid hormones cross cell membranes and bind with intracellular receptor proteins which are

bound to specific gene sequences. The presence or sometimes the absence of a signaling molecule activates the receptor which delivers messages that direct (sometimes saying go, sometimes saying stop) gene expression, cell replication, growth and death.[901]

Dying is important. Cells die naturally because they have reached the maximum number of cell divisions or because they're supposed to. In the life of a cell dying according to plan is called apoptosis meaning programmed cell death. The natural process of apoptosis provides for old or abnormal or damaged cells to die making room for new, healthy cells.

At any age, 24 hours a day, 7 days a week, old cells are dying and new cells are born. We are constantly changing yet remain the same, sort of. As we grow older this process of cell replacement begins to slow down. At times the new cells replacing the old cells have coding errors and are functionally impaired, improperly producing hyperplasia or dysplasia or even cancer. In very old age these regenerative processes become extremely impaired and eventually no longer function leading to failure of some critical organ or system and death of the organism.

The only immortal cells are cancer cells, which do not experience apoptosis. Many cancer therapies are focused on restoring this cellular process, apoptosis-death. One of the reasons vitamin A and vitamin D have been associated with and used for treatment of cancer is because they both play an important role in regulation of apoptosis.[90,299,902,903,904,905,906,907,908,909] The location of their anti-oncogenic (anti-abnormal growth inducing) actions is within the cell, binding with their respective receptors.

In 1998 Zineb, [442] explored the relationship of nutritional factors on the cellular production of vitamin D receptors, VDRs. In the study control animals were given standard rat chow with rat equivalent recommended amounts of calcium and vitamin D. Vitamin D deficient rats received the same diet containing adequate calcium but minus vitamin D and were kept in the dark to prevent any synthesis of vitamin D.

During the last week of the eight-week study some of the vitamin D deficient rats were given supplements of vitamin D at the rat recommended dose. Others in the D deficient group were switched to a diet still deficient in vitamin D but with extra calcium and lactose to enhance its absorption.

In testing cells from the skin, duodenum (part of the upper intestine where nutrients are absorbed) and kidney, vitamin D deficient rats had decreased vitamin D receptors in all tested tissues. Adding vitamin D at recommended rat levels or extra calcium restored VDRs in the skin cells, extra calcium restored VDRs in tissue from the duodenum, and vitamin D restored VDRs in the kidney cells. <u>When vitamin D is deficient cells express fewer vitamin D receptors.</u>

More recently Vieth confirmed Zineb's finding.[802] This is important because, to quote Zineb:

"The biological activity of $1,25(OH)_2D_3$ in cells is directly proportional to the tissue VDR concentration"

This means for optimal cellular functioning of $1,25(OH)_2D_3$ we need cholecalciferol or ergocalciferol, from food, supplements or sunlight, and adequate calcium to insure optimal expression of vitamin D receptors.

Dietary D and calcium aren't the only elements that regulate VDR expression. The number of vitamin D receptors in a cell is regulated by many factors including the levels of $1,25(OH)_2D$, retinoic acid (vitamin A), glucocorticoids (adrenal hormones), protein sufficiency, and estrogen.

Estrogen loss at menopause contributes to more rapid bone loss. One reason for this may be that estrogen stimulates the expression of vitamin D receptors, giving hormonally active growth promoting D more sites upon which to act. Loss of estrogen by natural or surgical menopause reduces the number of vitamin D receptors in cells.[910,911,912]

Receptors for each of the other signaling molecules also exist within the cell, which should remind us of the amazing complexity of each and every single living cell. All of these components and others not mentioned here and yet others still unknown are constantly moving and changing minute by minute within and outside of our cells working harmoniously with each other to allow the cell to live a normal life span, replicate, and die, making room for new cells.

Vitamin D receptor and Vitamin D-binding protein research continues to expand. These carriers and receptors are the focus of a growing number of research groups trying to understand the vitamin D endocrine system and its confounding vitamin D variables. Genetically determined variations in carriers and receptors may help to explain the sometimes-dramatic differences in our individual requirements for and response to sunlight and vitamin D.

VITAMIN D AND THE CELL MEMBRANE

One of the targets of vitamin D activity is the cell membrane. The actions of D within the membrane are not yet understood but D may help to control what enters and exits the cell; act as a cell membrane anti-oxidant (protection against free radicals that damage the cell); and influence the way cells communicate with each other. A number of research groups are exploring non-genomic actions of vitamin D, the actions of vitamin D outside the nucleus, searching for vitamin D receptors within the membrane and studying the rapid biological events that can occur in cells exposed to calcitriol.[913,914,915]

Why should you care? The research supports vitamin D's role as essential to every part of you, not just your bones. Vitamin D is an essential regulator of the creation of life; the birth and death of cells. As D research continues the emerging non-genomic rapid actions of vitamin D in cell membranes, taking just seconds to occur, provide further evidence of the importance of supporting the vitamin D endocrine system.

There follows a definition of the role cell membranes play taken from the third edition of Nutrition, An Integrated Approach, Chapter 9, Pike and Brown, Macmillan, 1984. I find these few paragraphs describe much more than membranes. After your first reading, try reading it again replacing the word cell with people, or trees and membrane with skin, or bark.

"All cells are units separated from their environment by a membrane. This is a barrier whose presence determines 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 materials 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."

Not enough oxygen, too much water, too little water, toxins, or starvation (for nutrients great or small) may end the life of a cell or group of cells. That is what we are, a very large group of cells. Various experts estimate the number of cells in any given human to range from 10 trillion to 100 trillion. The large number of cells and range difference in estimates, by experts, should suggest to you that experts (and you and I) have a very long way to go to fully understand the human body.

Every day new cells are born and others die. For survival we do not search for equilibrium but how to abide within a constantly changing kaleidoscope of LIFE. Not only do we need certain elements only available in our external environment, we must take in enough of each of these elements but not too much.

The paragraph on cell membranes is to help you get the sense of our situation. Some things need 'in' and others must be kept 'out'. and some things need to be able to go in and out. I call it discriminatory flux. I made that up but it does describe what happens.

flux, def. constant change and instability

The environment of our cells (and our world) is really weird, stable instability.

We have within each of us a sort of living gyroscope (self-stabilizing device). We may not spin but we are most certainly in constant movement, experiencing constant change and yet remaining somewhat the same.

The list of roles for vitamin D in cellular processes, such as regulating cell membrane composition and function, continues to expand as D research continues.[227,897,916,917,918,919]

Vitamin D As Antioxidant

Cholecalciferol, ergocalciferol, 7-hydrocholesterol and calcitriol inhibit lipid peroxidation (free radical damage) in cell membranes. [90,227] Earlier when discussing how D was first isolated I pointed out the importance of the vitamin D in the cod liver oil surviving both heat and oxygen. Vitamin D joins two other fat-soluble vitamins, A and E, offering protection from free radical damage within cell membranes.

Studies of damage to brain cells, currently of deep concern due to the increase in Alzheimer's and Parkinson's disease, show the active hormone D, calcitriol, to protect brain cells under chemical attack. [619] So far these studies are of the 'Petri dish' variety. What makes this study more interesting is that other studies have shown people with Alzheimer's and Parkinson's have low levels of D and suffer from diseases associated with low D and calcium, like osteoporosis. [267,268,920,921]

One study by Sardar comparing oral vitamin D_3 to vitamin E demonstrated cholecalciferol to be a more potent antioxidant resulting in less lipid peroxidation and a greater increase of superoxide dismutase, an enzyme that reduces free radicals, in the liver than vitamin E.[226] This was one study, with rats, but it gives us another hint at the many possible, yet to be clarified, roles of vitamin D.

It is very likely having adequate levels of vitamin D, all of the D metabolites, in all the right places, will have a positive effect on our longevity and vitality.

How Humans Store D and Why This Is Really Important

The fat-soluble vitamins A and D store in the human body.

The upside of storage? Mechanisms and capacity for storage imply we have the ability to hold onto a reserve available for use when environmental or dietary sources are low.

The downside? This capacity for storage can be dangerous. Hypervitaminosis is the term used to indicate the presence of excess A or D and the metabolic consequences, which in the case of too much D can be very serious indeed.

In 1972 a team from the University Department of Medicine, The Royal Infirmary, Manchester, England set out to determine if and where vitamin D is stored in the human body. Vitamin D metabolites, including the three we are focusing on, are very very small. Vitamin D in blood and tissue is measured in nanogram or nanomole amounts. To give you an idea of just how small, a nanogram is one billionth of a gram and if you haven't got around to metrics yet it takes 28,349,520,000,000 nanograms to make one ounce. As our bodies contain 'nano' amounts of any of the D metabolites, tissue storage studies need comparatively large amounts of tissue to analyze.

The Royal Infirmary study design used radioactively labeled vitamin D_3. As the study explains 'Because of the small dose of radioactivity used in these studies, large samples were required…adequate material could be obtained only at autopsy or from an amputated limb.' The authors explain further that this is an 'opportunistic study' which I will define as meaning, 'under these conditions, dying or having a limb amputated to be able to complete the study, you take whatever you can get'. 60 patients volunteered and received the radioactively labeled vitamin D injection. of these 60 an

unfortunate 6 supplied the samples for the study. Two other patients, who did not receive the D_3 injection, but had been treated with oral ergocalciferol (D_2) up until time of their deaths, also provided tissue samples.

With one exception all tissue donors were patients suffering from illness or injury serious enough to cause death or amputation. Four died from chronic renal (kidney) failure, one from cancer, one from post-operative complications, and one from biliary disease. In addition to the problem of serious illness possibly clouding the outcome, one of the subjects had been treated with large amounts of ergocalciferol (D_2) before receiving the injection of radioactive vitamin D_3. The remaining volunteers receiving the injection were low or deficient in vitamin D. A few of the limitations of the storage study include small sample size, time elapsed between the injection and analysis of samples, possible complications due to kidney failure as the kidney plays a major role in D metabolism and prior treatment with vitamin D. Even considering the limitations the study does offer us an approximation of D storage.

The researchers analyzed tissue samples of liver, spleen, kidney, heart, lung, thyroid, pancreas, adrenal, intestine, skin, bone, marrow; muscle, tendon, and fat to see where the radioactive vitamin D ended up and how much ended up in each part. They looked for just two of our Ds, cholecalciferol, and 25(OH)D.

and the results: Every tissue studied demonstrated vitamin D activity. This is interesting because at the time very little was known about the actions of D in tissues other than bone. Later researchers would locate receptors for vitamin D in all parts of our bodies as you have learned.[3] Walter Stumpf working at the University of North Carolina, Chapel Hill has found more than 50 distinct cell binding sites so far.

After the injection the cholecalciferol cleared rapidly from the blood.

Quick review: Whether from skin production, oral intake or an injection vitamin D travels first to the liver where the cholecalciferol begins its metabolic journey by conversion to metabolite 25(OH)D and other less well known metabolites. In this study some of the injected cholecalciferol was excreted in bile, either unchanged or as one of several metabolites of D, some was converted to 25(OH)D circulating in the bloodstream, and some, both cholecalciferol and 25(OH)D, was removed from circulation by being partitioned off into fat cells or bound to tissue proteins. Our livers play an important role in handling all of the fats and fat-soluble substances we ingest or produce in our bodies.

Your body has metabolic pathways designed to break down and get rid of excesses thereby maintaining the normal balance, homeostasis, necessary for functioning. The liver breaks down fat-soluble toxins and other fat-soluble elements such as estrogen and excretes them in bile. Fat-soluble toxins, drug residues from antibiotics or chemicals such as DDT or PCBs that overload the system are unable to be metabolized and excreted in bile. Excesses can be kept out of the bloodstream by being stored in fat tissues as a protection from toxicity.

In this study the path of vitamin D excess appears to be similar. When serum levels were elevated by the injection the body responded by storing excess in fat cells.

Perhaps this occurred because the dose given was much greater than a physiological dose, like a toxin needing to be trapped outside of circulation to prevent damage. Circulating in the bloodstream high levels of vitamin D can be dangerous causing damage to arteries and promoting calcification of soft tissues.[58,922] At a minimum, excessively elevated serum D may disrupt normal feedback mechanisms necessary to regulate the D endocrine system. Perhaps this occurred as a natural process to keep blood levels of vitamin D within normal ranges and store any extra for later use.

.Back to the study-The tissues containing the highest amounts of vitamin D, totals that include both cholecalciferol and 25(OH)D, were fat and bone marrow (high in fat content). Total D activity recovered from voluntary muscle nearly equaled that found in fatty tissue because while concentrations of D were lower, total body mass was greater; the body contains more muscle than fat. As discussed before, vitamin D goes through many changes over time becoming any one of a number of metabolites.

The time between the initial injection and the analysis of tissue ranged from 4 days to 90 days. At any time point the blood and skin samples contained primarily 25(OH)D with one exception. In the samples from patients on prior vitamin D therapy the blood and skin contained higher levels of unmetabolized D, cholecalciferol. The liver, kidney and lung tissues had a significantly higher percentage of 25(OH)D than cholecalciferol. As the interval of time increased, D in muscle shifted from cholecalciferol to the metabolite 25(OH)D. In bone marrow and fat there was a mix of cholecalciferol and 25(OH)D with the unmetabolized cholecalciferol predominating in most samples.

GP overview: An injection of D moderately raises levels of serum 25(OH)D over a number of days. Excess (my word, not the study's) is stored in tissues, in fatty tissues as the unmetabolized pre-hormone D, cholecalciferol (D3), and in muscle initially as unmetabolized D but shifting to 25(OH)D over time. The skin contains vitamin D primarily as the metabolite 25(OH)D.

Vitamin D's fate is to be finally broken down and excreted in bile, as is the fate of all fat-soluble substances in our bodies. D is also removed as our bodies shed the cells of our mucous linings and skin, both of which contain all 3 metabolites of vitamin D. Traveling from initial intake, by mouth or skin, to active metabolites to degradation and elimination takes a significant period of time.

When vitamin D supplies are diminished or absent vitamin D stored in tissues and organs is rapidly released while fat stores of D release very slowly.[58] In patients who had previously been on extended D therapy large amounts of vitamin D activity were detectible in tissues even after 15-20 months.

What this study doesn't tell us: It does not offer any insight into optimal levels of vitamin D, in blood or in tissues. It doesn't tell us if storage in fat offers a useful reserve of vitamin D when serum levels decline. Holmes and Kummerow found

vitamin D in fat (also from excess doses of D) loath to leave, dispersing extremely slowly.[923]

This storage study doesn't tell us what normal humans, getting their D from sunlight and diet, actually do with vitamin D. Do they have D stored in their fat? If so in what form and how much is where?

Storage studies, all using excessive D, have firmly entrenched the idea we store D in fat, as a reserve. From this premise experts suggest getting D from sunlight in summer produces excess vitamin D, which is stored and may be accessed by the body in winter to maintain vitamin D. This assumption is either not true or we are gravely 'under-sunned'.

Studies in the United States and other countries, many of them in tropical or sub-tropical countries, show winter time levels of D to be deficient or insufficient and frequently associated with bone loss.[27,390,924,925,926] [8,36,98,367,927,928,929,930,931].

These studies all confirm that while D might be sufficient in summer women, men, children, seniors, healthy, or infirm, all have lower values of D during winter months, frequently dropping to seriously deficient values. So much for storage.

The data suggests that, in the real world with real people, storage is not a large factor in year round vitamin D sufficiency, especially if summer D is insufficient. In persons living at latitudes greater than 35° only those who spent significant time (months) in the tropics during the winter maintained optimal D. All others using sunlight their major source of D saw a significant drop in serum 25(OH)D by the end of October with a slow but continuous further decline until spring.

In a study published in 2002 Barger-Lux and Heaney checked the 25(OH)D levels of men spending the summer out of doors participating in activities including landscaping, construction, farming and recreation. The average value of D reached at summer's end was 48.8 ng/ml. Approximately 5 ½ months later the average of the 26 participants dropped to 29.6 ng/ml. Three of the men had values less than 20 ng/ml and 15 had less than 30 ng/ml.[932]

GP, the reality of storage looks quite different from the premise doesn't it?

Studies evaluating the system overload of an injection, with or without prior D therapy, or single or chronic high dose D as used in animal storage studies, may offer clues to D metabolism. The doses of D used in these studies may also completely imbalance the system so that the primary question answered is 'What happens to vitamin D in the human or animal body when an overload is given?' [923]

At no time, ever, from any source, could the human or animal body have gotten the massive doses of vitamin D being used today in research, in medicine, as additives in feed in animal husbandry and most recently as so called dietary supplements..

This storage study helps to show some of the difficulties encountered in understanding the relationship between our bodies and vitamin D. As there is general acceptance within and outside of the medical community that vitamin D stores in the body as a natural process clinicians have developed the protocol of giving high dose vitamin D. The idea is very user friendly. An injection once every three months or a pill

once a week or other prescription allows the physician to treat the condition and not have to be concerned about compliance.

More recently some clinicians have found giving oral drops of prescription calcidiol, that is 25(OH)D, once a week a better solution to D insufficiency because patient compliance was poor when asked to take a supplement of calcium and vitamin D.[933] Like the use of 50,000 IU D_2, this turns a lack of sunlight into a medical condition requiring office visits for diagnosis and follow-up and prescription medication.

Many of the studies using D for osteoporosis or other D related disorders used tens of thousands and even hundreds of thousands of International Units of vitamin D. The current prescription vitamin D supplement Calciferol, contains 50,000 IU of vitamin D_2. Protocols for various conditions continue to suggest 50,000 IU to as much as 700,000 IU daily or intermittently (weekly, monthly or once every 3 or 6 months) to treat hyperparathyroidism, vitamin D resistant rickets, osteoporosis, osteomalacia, vitamin D myopathies or just to build or maintain levels of 25(OH)D.[429,934,935,936]

As of August 2008 in personal communications and on sites found on the internet physicians and other healthcare providers are suggesting 4,000 IU daily to as much as 50,000 IU twice a week, and this larger amount to treat a man whose D was not even deficient but simply ‗low normal'.

When high doses were given in the past they had to be prescribed and monitored by the physician. At the doses used there is always a possibility of toxicity[937] and if the patient inadvertently combines the treatment with sun exposure[885] or with supplements that contain vitamin D, the possibility for toxicity increases exponentially. What is unclear to me is why these doses are/were ever used and even more frightening why these high doses are now available without a prescription and are commonly advised by so called experts.

Physiological doses of D and sunlight are effective.

VITAMINS A AND D, PARTNERS IN OUR CELLULAR DESTINIES

Vitamin A is a fat-soluble vitamin like vitamin D. It is an essential dietary element stored in our livers. In our bodies vitamin A undergoes a number of conversions to a number of metabolites similar to the journey of vitamin D.

At least three of the metabolites play a functional role in human health. Retinal influences vision, retinol, is critical for reproduction and retinoic acid and other retinoids (vitamin A metabolites) are active within the nucleus of the cell regulating cell differentiation and gene expression (genomic actions like D). Vitamin A has a retinol binding-protein and two nuclear receptors, labeled RAR, retinoic acid receptor, and RXR, retinoid X receptor.

Vitamin A influences the production and balance of sex hormones and adrenal hormones. Low levels of vitamin A result in an impaired immune system, increased rates of infections, and increased inflammation in epithelial cells including skin and mucous membranes. The skin contains all of the vitamin A metabolites, retinol-binding protein, and RAR and RXR receptors.

Humans get vitamin A as retinol from egg yolk, cod liver oil, fish, animal and poultry livers, and full fat milk and cream, some of the same sources of vitamin D.

The carotenoids with pre-vitamin A activity, alpha-carotene, beta-carotene, and beta-cryptoxanthin are present in certain orange, red, green, and dark-yellow fruits and vegetables. Beta-carotene is often called vitamin A but it is actually a precursor.

The three carotenoids with pre-vitamin A activity must be split by enzymes in our intestines or liver to yield two molecules of retinol, but only of the molecules is biologically active in humans. Further, carotenoids are poorly absorbed and utilized making it difficult to get sufficient vitamin A from plant sources.

The retinol-carotene equivalent set in the 80s suggested 1 mcg of retinol was equivalent to 6 mcg of beta-carotene but this has been reevaluated. Generally accepted at the present time- The vitamin A activity of 21 mcg of carotenoids with pre-vitamin A activity equals 1 mcg of retinol.[938] The reasoning behind the reevaluation of equivalency are an excellent example of nutritional complexities.

Factors determining the availability of vitamin A from carotenoids include "Species of carotenoid, molecular linkage, amount in the meal, matrix properties, effectors, nutrient status, genetics, host specificity, and interactions between factors"[939]

I can add to this list because pre-vitamin A activity is also dependent on the freshness of the fruits and vegetables eaten. It readily oxidizes. In addition, like vitamin A, carotenoids are fat-soluble requiring them to be consumed with fat for digestion and absorption. So unless your fruits and veggies are served with fat, be it salad dressing, butter or cream, it is likely much of the nutrient will fail to make it to your liver, blood and cells.

Vitamin A activity is determined by Retinol Equivalents (RE) but sold in International Units. 1 mcg of retinol is 1 RE is 3.33 International Units. I did apologize. The current DRI Estimated Average Requirement, EAR, to avoid deficiency is 900 mcg RE for men and 700 mcg RE for women, which work out to be 3,000 IU and 2,330 IU respectively. The EAR for pregnancy increases to 2,500 IU and for nursing 4,000 IU. The UL, tolerable upper intake levels, for vitamin A has been set at 3,000 RE or 10,000 IU of vitamin A.

Vitamin A deficiency is still a major problem in underdeveloped countries with inadequate access to animal foods or other sources containing the nutrient. Lack of vitamin A is a cause of blindness and increased susceptibility to serious infections in infants and children in these countries.[861,940,941,942]

Large doses of vitamin A, 50,000 IU-400,000 IU have been used by the World Health Organization to prevent blindness and to treat measles. [940,943,944] Deficiency may also occur in persons consuming diets restricted in fat or persons having a condition that alters their ability to absorb fat from the diet such as bile insufficiency or removal of their gallbladder.[945,946,947,948]

No study has yet shown whether vitamin A from plants is sufficient or if preformed A, retinol, is required. Persons with ancestors from Northern Europe, which includes the Scandinavian countries, and the British Isles, often exhibit improved vitamin A status, higher resistance to infection, better condition of the skin, improved

night vision, and normal fertility cycles, when eating beef liver once or twice a week or consuming moderate amounts of cod liver oil.

Records show the use of liver to cure eye diseases among ancient Egyptians and Greeks. The element was first isolated in 1913 by McCollum and Davis from butter and cream and by Osborn and Mendel from cod liver oil and butter. It was the first element determined to be essential for survival (remember those purified diets that could not sustain life) and hence named vitamin A.

In the history of vitamin D you learned the antirachitic properties of vitamin D were initially credited to vitamin A by Dr. Mellanby. It was not a difficult conclusion for him to make as five years earlier cod liver oil and butter were found to be the richest sources of 'fat soluble growth promoting vitamine' These are the same fats Mellanby found most potent in curing rickets.

As mentioned earlier Alfred Hess found that some babies consuming a diet rich in full fat milk and cream, rich sources of vitamin A, developed rickets more easily than babies having a diet containing skimmed milk, very low in vitamin A.

This tells us two very important things.

- It shows us not all dairy fat contains vitamin D naturally. It depends on the cows‘ UV-B sunlight exposure.
- It is the first recognition that vitamin A might cause or worsen a vitamin D deficiency.

Why is this important? In recent years numerous studies have sought to understand the benefits of vitamin A, particularly in treatment of cancers. The possible role of vitamin A and pre-vitamin A carotenoids in cancer prevention has been published in over 1000 studies, some suggesting it is of primary importance and others finding no correlation or benefit. The studies suggesting benefit were most often observational studies relating a higher intake of vitamin A or pre-vitamin A containing foods to less cancer incidence.

The CARET study, using a high-dose beta-carotene supplement, actually found an increase of cancer incidence in smokers who were taking the supplement.[949] For some reason vitamin A just doesn't seem to work as expected in cancer prevention.

Hypervitaminosis A causes bone demineralization. In searching for clues to the causes of osteoporosis various studies have found a link between excess vitamin A and increased bone loss.[950,951,952,953,954] One study sought to determine the relationship of vitamin A from food and supplements to bone mineral density and bone retention. 958 men and women between 55-92 years of age participated. When vitamin A intake was very low or when total vitamin A intake exceeded the RDA bone loss increased. While vitamin A is essential for growth, including bone growth, the study points out the narrow range between enough and too much vitamin A.[955]

Now you know way more than you ever wanted about vitamin A. Why is knowing about vitamin A important? Because fat-soluble vitamins A and D both have genomic actions, including actions between the two nutrients. They have nuclear

receptors and when binding to their respective receptors they also interact with each other.[901,956,957]

The amounts of active A and active D alter the way the cell functions. The location of this interaction is within the nucleus of the cell.[958]

Goldilocks' Principle: We need enough of what we need but not too much. When vitamins A and D are both deficient growth is impaired. When either of the nutrients is given in excess and the other is present in low or normal amounts growth is also impaired. Symptoms of genomic (cellular) vitamin A or vitamin D deficiency express in different ways.

The response to excess vitamin A and low or normal D mimics vitamin D deficiency. The growth response to excess D with low or normal A is similar to vitamin A deficiency. In the studies blood levels of the lesser nutrient typically remained within normal range.

A relative excess of vitamin A or D seems to result in a relative or functional deficiency of the other vitamin. When both nutrients are supplied in excess fewer abnormalities occur and growth is almost normal.[959,960,961,962,963] Vitamin A toxicity causes bone loss and fragility in animals. Vitamin A deficiency may cause kidney calcification.

In toxicity studies giving vitamin A in the presence of vitamin D excess prevents some of the worst symptoms of D toxicity including bone demineralization and calcium deposits in soft tissues.[962,964,965,966]

- Excess vitamin A may cause a functional vitamin D deficiency
- Excess D may cause a functional vitamin A deficiency

This explains Hess's observation that some of the babies getting higher levels of vitamin A from milk and cream were more susceptible to rickets, the classic expression of vitamin D deficiency. The small amount of vitamin A in the milk was enough to significantly worsen the effects of vitamin D deficiency.

It also may explain the association of even moderately excess vitamin A to bone demineralization, a functional deficiency of vitamin D.[951,967] Recognition of the interactions between A and D fit nicely into the complex systems model and help explain why supplementing the isolated nutrient, vitamin A or vitamin D, may produce unexpected results in disease prevention and treatment protocols.

When considering genomic actions regulated by A and D balance is everything.
Well, maybe not everything, but a very big thing.

Vitamin A deficiency is severe and common in tropical locations including many parts of Africa, Philippines, Vietnam, Thailand, India and Brazil.[941,942,968,969,970,971,972,973,974,975,976,977,978] While much of this deficiency can be blamed on diets lacking vitamin A the relationship between A and D and sunlight needs to be explored.

Vitamin A is a component in skin and eyes. The melanin in the color of our eyes contains high levels of vitamin A. When exposed to UV light vitamin A is depleted which may cause a functional vitamin A deficiency.[324,979,980]

The combination of abundant UV light in tropical countries and low dietary vitamin A creates the worst possible situation. Traditional diets often supplied local vegetables, or other foods, high in vitamin A or carotenoids. In many cultures modern introduction of grains has supplanted fruits and vegetables as a dietary mainstay. Grains provide no vitamin A.

Red palm oil and tropical fruits are a source of pro-vitamin A carotenoids but pre-formed A may be necessary for health.[981,982,983] If this is true the new genetically engineered rice high in carotenoids may not help much to prevent vitamin A deficiencies. Beta-carotene is not equivalent to vitamin A and requires a much larger amount to satisfy the need for vitamin A. World Health Organization field studies suggest 21 mcg. of pro-vitamin A carotenoids from fruit and vegetable sources are needed to equal 1 mcg of vitamin A found in liver and cod liver oil.[938]

UV-A and UV-B both deplete vitamin A.[324,980,984,985] Increased exposure to UV light apparently increases the need for vitamin A. Vitamin A and carotenoids are not equal in protective effects.[986]

Just enough and not too much should be the primary consideration when supplementing vitamins A and D. Both are essential. It is important to get a sufficient supply, but enthusiastic over-supplementation for prevention or treatment of a condition or disease with either of these fat-soluble signaling molecules could produce an unexpected and undesired outcome. As to how much of each we need? We'll tackle that next.

CHAPTER 7 HOW MUCH D DO WE NEED?

VITAMIN D DEFICIENCY OR SUFFICIENCY. HOW MUCH IS ENOUGH?

When you have enough of something it is sufficient, not enough, deficient, and then there are the gray areas. Within the area of 'I don't have obvious disease' and 'I am on top of the world' there is this area of 'I just don't feel quite right'. In 1941 the U.S. Food and Nutrition Board first proposed the RDA, Recommended. Dietary Allowance. These guidelines were developed as an assessment tool and a standard for determining dietary adequacy. The intent was to incorporate current nutrition knowledge to avoid nutrient deficiencies and improve the nutrition of all Americans. The last volume of the RDAs was published in 1989.

Beginning in 1997 the National Academy of Sciences Institute of Medicine began compiling the DRIs, Dietary Reference Intakes. The goal of the Academy is to determine optimal amounts of individual nutrients and also to set safety limits, determining doses that should be avoided to prevent toxicity. Many of the volumes are completed; others are yet to be compiled. Each step of the exhaustive review of the research literature and derived recommendations shows a growing awareness of the need for more broad based consideration of individual dietary needs.

The DRI is composed of three values; the Estimated Average Requirement (EAR); the Adequate Intake (AI); and the Tolerable Upper Intake Level (UL). The EAR is the amount of a nutrient that will meet the needs of at least 50% of healthy people based on significant research. Currently there is no EAR for vitamin D because the available scientific research data is not conclusive. When this is true for any nutrient the DRI uses Adequate Intake, the AI, instead.

The AI for vitamin D is 200 IU if you are between 0 and 50 years old; 400 IU if you are 51-70 years old and 600 IU if you are over 70. The Tolerable Upper Intake Level (UL) is 2,000 IU.

Our need for vitamin D requires new guidelines but Dietary Reference Intakes won't ever be the place to determine correct values. This vitamin AKA hormone just doesn't fit the typical definition of a nutrient and the standards and recommendations currently used just don't and won't work.

There really is no way to know how much D you currently have or how much you need without testing. Making a suggestion for supplementation may cause harm or lead to better health. The outcome depends on the person, skin color, season, lifestyle, diet; calcium intake, too many variables to consider in a one-size-fits-all (or most) prescription.

To determine if the GP, you and I, have too much, too little or just enough some standard must be used. In addition an accepted test must be agreed upon.

When $1,25(OH)_2D$ was determined to be the active 'hormone' D, it became the D most frequently tested to determine a deficiency state. This hormone, calcitriol, remains within a narrow normal range unless the body is suffering from either a severe deficiency of vitamin D or calcium, [987] or there is an underlying disease present, such as sarcoidosis where various cells produce $1,25(OH)_2D$ in large quantities leading to calcification of soft tissue.[191]

Testing calcitriol has turned out not to be a marker for vitamin D status. It is still tested in severe deficiency states and should always be tested in persons with unexplained elevations of calcium in the blood or sarcoidosis as vitamin D may be normal but calcitriol elevated with dire consequences.

25(OH)D, calcidiol, is the storage D carried on D-binding proteins in your blood and stored in your blood and muscle. Serum 25(OH)D is considered by experts to be the best test for determining vitamin D status. The test tells us how much storage and transport D we have but what do the numbers mean?

Various researchers over many years have tried to determine what 'adequate vitamin D' might mean. For many years D sufficiency was determined by a combination of the RDA, the Recommended Dietary Allowance, and research relating rickets and osteomalacia (adult rickets) and other bone abnormalities with levels of 25(OH)D below 9 ng/ml. 400 IU of vitamin D daily and some sun provided enough vitamin D to prevent or correct rickets or osteomalacia. These two values, less than 10 ng/ml 25(OH)D, to detect deficiency and 200-400 IU vitamin D to prevent deficiency became the standards.

One argument against testing is that the values may be different when tested by different laboratories or by different methods. 25(OH)D testing in the U.S. initially used HPLC, high performance liquid chromatography, an expensive and labor-intensive test still available and used in some studies. Since the early 1990s RIA testing, much less work and therefore less expensive to the consumer, has been in use in the U.S. as the preferred test for 25(OH)D. Some researchers argue that it is not as accurate as HPLC. Hollis suggests that RIA is more accurate.[988]

At present there are significant difficulties in standardization of 25(OH)D testing. It may take some time for labs to work out the problems with the available methods and problems with repeatable accuracy. [989]

Whatever the current arguments among researchers, testing is available and accurate enough to tell us if we have too little or too much D. Using the same lab for testing and retesting will show improvement or lack thereof over time.

What is 'normal'?

Initially researchers determined normal values through testing levels found locally in persons without obvious disease, in this case rickets or osteomalacia (adult rickets). Depending on the lab, values listed as normal are usually quite close to 10-55 ng/ml (nanograms per milliliter) or more recently, a huge shift, 32-100 ng/ml or using the scale common to Europe, Canada, and the U.K. 25-137.5 nmol/l. or 80-250 nmol/l. Some labs in the U.S. show normal values as low as 9 ng/ml and as high as 100 ng/ml. In Mexico normal values are 17 ng/ml to 74 ng/ml. If you decide to look at the research studies have a calculator on hand (or maybe you can do the math in your head).

The conversion for amounts of 25(OH)D:1 ng/ml = 2.5 nmol/l.

Today most researchers agree that less than 10 ng/ml (25 nmol/l) is a clinical deficiency. This was the low number in the normal column typically seen on older lab values for 25(OH)D. In 1999 Michael Holick edited Vitamin D Physiology, Molecular Biology and Clinical Applications, Humana Press. Holick also authored the first chapter. On page 12, section 3.11. *Redefining Vitamin D Deficiency* he suggests a new standard. Rather than using frank bone disease, rickets, he determined the minimum amount of 25(OH)D needed to keep PTH, parathyroid hormone, in normal range. Just a little review of D biochemistry here-

When vitamin D, in this case 25(OH)D, is low parathyroid hormone, PTH, rises to increase calcitriol (active D) and thereby calcium absorption, repeating what you already learned.

In Holick's research some people having levels of vitamin D considered 'normal' between 10-20 ng/ml also had elevated PTH. When given vitamin D their 25(OH)D went up and PTH came down. This is a good thing. Elevated PTH is associated with a number of not so good outcomes including cancer.[990] So, Holick suggests, the new value for deficiency should probably be <20 ng/ml and more recently some labs reflect this in their testing norms. Researchers in France found a minimum of 31 ng/ml was necessary to normalize PTH.[8] This seems to have influenced several labs in the US who now use 32 ng/ml as minimum value for ‗normal'.

The Third National Health and Nutrition Examination Survey (NHANES III) conducted by the National Center for Health Statistics, Centers for Disease Control and Prevention, determined 25(OH)D in 9,393 females and 8,590 males 12 years of age or older. The average 25(OH)D in females was 28.1 ng/ml and for males 31.1 ng/ml. This was the overall average. Many were below these levels, like those discussed in the chapter *People of Color, Sunlight, D, and Disease*, and many above. Older men and women had lower levels, which is a common finding in most studies of seniors. If 20 ng/ml is sufficient D it seems Americans, with the exception of African Americans, are doing all right.

The Eleventh Workshop on Vitamin D met in Nashville, TN in 2000. On page 904 of the workshop proceedings, Vitamin D Endocrine System, John Pettifor of Johannesburg, South Africa discusses

WHAT IS THE OPTIMAL LEVEL FOR BONE IN CHILDREN?

His answer should give us pause.

First he explains that a minimum of >12 ng/ml (>30 nmol/l) is necessary in children to prevent the development of bone disease. That is higher than the currently accepted deficiency value of <10 ng/ml. He then explores the idea presented by Docio [(991)] that higher levels of 25(OH)D appear to promote better bone growth and help lay down bone for later life, especially in adolescent girls.

What Docio did was give children with 25(OH)D values between 10-20 ng/ml a vitamin D supplement and active D, calcitriol, increased. This would improve bone (and, my comment, tooth) health. In his study and Pettifor's patient group most children fell below the desired levels at least during winter months.

Here are Pettifor's comments:

"Acting on such a recommendation would result in many children requiring vitamin D supplements as over 80% of children in the above study (Spain) had 25(OH)D values less than 20 ng/ml during winter. Similar high proportions of children would be found in many countries in Europe and other parts of the world. The public health and economic costs of such a recommendation need to be considered, before being implemented nationally."

Ok. Let's see if I understand-

Children need D. It's important to have sufficient D to prevent rickets BUT figuring out how much kids really need, which we already know is higher than the dose needed to avoid rickets, may not be such a good idea.

Why? Because making sure children have enough D to avoid osteoporosis (remember, the bones must be built early) will be difficult and cost us (public health, insurance companies, HMOs and the GP) a lot of money and since we aren't sure what D might do (unless perhaps we finally admit poor tooth development and decay, childhood diabetes, and reduced lifetime bone density is related to vitamin D deficiency) we need do more studies and evaluate the cost:benefit ratio.

I do understand the hesitancy about D. It is complex, but if <u>we</u> understand, even somewhat, how it works we can take care of ourselves. This is especially true if we quit thinking what we're told to think and use some common sense.

I consider vitamin D researchers to be incredibly valuable persons. You might even say I am a D researcher 'groupy'. I am most grateful for their painstaking and meticulous work. Some of them also make me crazy.

I have a question. How much does it cost, per person, in a lifetime, to have marginal status of teeth and bones, cavities and hip fractures, increased rates of cancer and heart disease, obesity and diabetes?

GP: Moms and dads unite. Your children need calcium and vitamin D. You do too. We all need the right amount. Not too much. Not too little.

Before we leave Pettifor's paper he mentions an important issue when trying to understand vitamin D. Calcium intake alters 25(OH)D.

Earlier I wrote about the Nigerian children with rickets treated with calcium alone, that 25(OH)D rose from an average of 16 ng/ml to 18 ng/ml at 3 months and 21 ng/ml at six months. In addition to the children's diets providing about 200 mg of calcium, they were given a supplement of 200 mg chewable calcium carbonate and instructed to chew two in the morning and three in the evening. The supplements provided 1,000 mg of calcium carbonate daily for each child. (804)

Other researchers have also found maximizing calcium intake raises 25(OH)D.(992) This is very important because if we use 25(OH)D as a marker of D status and dietary calcium is low, giving more vitamin D won't solve the problem.

The Thacher study had a control group given a placebo, a group receiving vitamin D 600,000 IU (injection) at the beginning and again at 12 weeks; a group getting the D injections plus 1,000 mg of calcium (split dose AM and PM); or a group just taking the calcium supplements. The calcium alone or the calcium plus D healed rickets. Both raised serum calcium levels and normalized calcitriol, the active hormone D.

In the Nigerian children given calcium alone, no supplementation of vitamin D, levels of 25(OH)D improved over 6 months reaching an average level just above Holick's 20 ng/ml. Supplementation of calcium may be all that some ‗apparently D deficient' persons need.

Calcium is a primary need of humans. If dietary calcium is low and vitamin D is given calcium may be withdrawn from bone. In the study 25(OH)D reached 35 ng/ml in the group given vitamin D alone and yet serum calcium remained low, calcitriol remained elevated and the radiographic score showed the least improvement of the three treatment protocols.

Making sure every one of us maintains calcium sufficiency should be the first step in optimizing the vitamin D endocrine system.

Kids (and parents) seem to need a minimum value of 25(OH)D of 20 ng/ml with adequate calcium but even at that level improvement in markers of bone health have been reported as supplementation further increased values of D.

Also submitting to the workshop, Pierre Meunier from France took on the question *What Is The Optimal Serum 25(Oh)D Level Appropriate For Bone?* Reviewing studies he determined the answer to be not less than 30 ng/ml, a full 10 ng/ml higher than Holick's suggested level of D for bone health(258).

That the higher value determined by Meunier is closer to 'optimal' is demonstrated by the study above showing adolescents with a serum 25(OH)D of 20 ng/ml, a level considered sufficient for bone production and maintenance, when given a vitamin D supplement, experienced further improvement in markers of bone health.

Meunier's 30 ng/ml is closely matched with the value that normalized PTH in Chapuy's study of French citizens in an urban environment, 31 ng/ml.(8) Chapuy

concluded it was impossible to get sufficient vitamin D from the diet when exposure to sunlight is limited. His study looked at 1569 subjects in 20 French cities.

Meunier began his paper with the divisions of D status: Vitamin D deficiency, vitamin D insufficiency, and vitamin D sufficiency. I would add another category, the elusive 'optimal' vitamin D. With normal sun exposure, in areas where UV-B is available, typical values of 25(OH)D appear to range from 40-65 ng/ml. perhaps dropping to the low 30s during winter months.

While researchers haven't yet tested indigenous natives in equatorial settings consuming traditional diets, very hard to find these days, they have tested the vitamin D level of black rhinoceros living free near the equator. The average value of free-ranging black rhinoceroses is 55.7 ng/ml.[993]

Two women participating in 25(OH)D screenings over the past six years maintained levels between 55-60 ng/ml year round. Both live just north of San Francisco, latitude 38°. One is a regular user of sunscreen during prolonged exposure to sunlight, the other uses sunscreen rarely. Both actively seek sun for brief periods, 15-30 minutes most summer days, without sunscreen. Neither intentionally tans. They both have Type II skin, relatively light, with ancestors from varying parts of northwestern Europe.

Both women are fortunate to be able to spend 3-4 months each winter in Hawaii or the Virgin Islands. They do not supplement vitamin D, however, both regularly eat eggs and fish, moderate sources of vitamin D. Both have very optimal calcium intake, 1,200-1,600 mg daily. Given most humans in moderate climates historically depended upon sunlight for adequate D and both of these women sun but do not tan or 'pinken', it is my sense (not a proven fact and not in any way scientific) these values reflect the upper range of healthy levels.

While lower values may protect bone, they may not be adequate for our other cells. Holick suggests that levels above 20 ng/ml may be necessary for normal function of prostate, colon and skin cells.[258] A recent evaluation of 25(OH)D makes this a bit more interesting.

Earlier you learned PTH (parathyroid hormone) may be elevated when calcium is low or when 25(OH)D is low. Researchers in Europe took blood samples from 356 subjects chosen randomly from participants in the European Vertebral Osteoporosis Study. Subjects ranged in age from 54 to 89. Only those men and women who had never received treatment of any kind for osteoporosis were included in the analysis. Subjects were considered to have secondary hyperparathyroidism if their PTH was >65 ng/ml.

Elevated PTH and low serum 25(OH)D has been found to be a useful indicator of hip fracture risk.[994]

Secondary hyperparathyroidism was determined to be present in 33% of those having 25(OH)D <10 ng/ml; 16% in those with 10-18 ng/ml and 12 % in participants having values 19-40 ng/ml. None of the participants with 25(OH)D above 40 ng/ml had elevated PTH.[995]

Asking the experts: When trying to determine a range of safe and optimal D I asked five experts, researchers studying D for 10 or more years, two questions.
What is the optimal level of vitamin D? None were able to give a better answer than Holick, 'more than 20 ng/ml'.
My second question was 'Are values between 40-60 ng/ml likely to do harm?' The experts' answers? 'No". The researchers queried felt comfortable with the safety of this range. So do I and it is the range I suggest as optimal (enough AND safe).

In some countries nearer the equator higher levels of D are common. Laboratories in Mexico typically list the 25(OH)D normal range as 16-74 ng/ml. Vieth reports studies showing values of D from sunlight as high as 90 ng/ml but the averages, from farmers in Puerto Rica to lifeguards in St. Louis, MO, summer, lots of sun, were between 54 ng/ml and 65 ng/ml.[53]

These numbers can be considered in another way. We evolved within our ancestral ecosystems, which included food, sunlight, cloud cover, and tree cover (the rain forests), the complex systems trees and forest analogy. It is clear from what research is available depending on our heritage we respond differently to sunlight and to vitamin D. Some of us need more vitamin D or sunlight and tolerate higher levels without harm. Others don't.

In a study we'll review shortly Dr. Adams reported D excess with excess calcium in the urine and bone loss, 25(OH)D at just above 50 ng/ml. This is unusual but it does happen. Perhaps there was another reason besides vitamin D, but when levels of 25(OH)D dropped, bone density increased.

When values of 25(OH)D are used in studies often the number given is the mean. Mean is the middle between the highs and lows. Life is fuzzy. This is important because there isn't a number, there is a range. If you decide to be a sun or D enthusiast and get your D right up to the top of normal, somebody's normal, and summer comes, you may over shoot your goal. It's normal to have higher levels of D in the summer and lower in the winter and spring. As long as winter values don't drop significantly below your 'just right' minimum you're bones will be just fine.

Common sense tells me that levels that can commonly be gotten from sunlight, without skin damage, and that are not associated with toxicity or deficiency, are most likely 'optimal'. These levels seem to fall between 35 and 60 ng/ml.

Remember the black rhino? Free-living rhinoceroses under tropical sun eating from the land have average 25(OH)D levels between 55-60 ng/ml. Three white women living in northern California, sunning midday, but never pinkening, produced levels of D between 52-60 ng/ml. The farmers in Puerto Rica averaged 54 ng/ml. Seems like a trend to me.

Table 2 How Much 25(OH)D?

25(OH)D values (but only if you know your calcium intake is sufficient):
Too little-

Severe Clinical Deficiency <10 ng/ml or 25 nmol/l Indicator for rickets and osteomalacia Clinical Deficiency: <20 ng/ml or 50 nmol/l Sub-clinical Deficiency <30 ng/ml or 75 nmol/l
Just right-
Sufficiency: >30 ng/ml or 75 nmol/l Optimal: 35-56 ng/ml or 100-140 nmol/l (think winter/summer) (Maybe 40-60 ng/ml)
Too much
Possible marginal low-level toxicity: >70 ng/ml or >175 nmol/l In this range serum calcium and PTH values may be normal but bone loss may occur in some people and will be indicated by declining bone mass and elevated urinary calcium. Possible soft tissue calcifications. Possible low-level chronic toxicity: >80 ng/ml or 200 nmol/l Serum calcium and PTH values may be normal but bone loss may occur in some people and will be indicated by declining bone mass and elevated urinary calcium. Calcium deposits in soft tissues may also accompany elevation in D.
Way too much- Hypervitaminosis D
>125 ng/ml or 312 nmol/l Any level of D accompanied by excess calcium in the urine and elevated calcium in the blood.
Clinical Intoxication or Poisoning: Unlike marginal deficiency or elevation this level of excess vitamin D has obvious serum markers (blood abnormalities) and/or obvious symptoms. This condition can only occur by direct exposure to high levels of ergocalciferol or cholecalciferol, usually by oral intake. The most common clinical signs associated with cholecalciferol or ergocalciferol hypervitaminosis depend on the body system that is affected.

.

Chronic Toxicity:

Elevated serum calcium levels of 12 to 16 mg/dL (3 to 4 mmol/L)
Excess calcium in the urine
Any of the symptoms listed below under acute poisoning but occurring over time

Acute poisoning:

Clinical signs appear 12- 36 hours after ingestion and may include:

Table 3 Acute D Poisoning Symptoms

abdominal pain
anorexia (loss of appetite)
arrhythmias (irregular heart beat)
constipation.
dehydration
depression
elevated serum calcium
elevated urinary calcium
severe itching
joint pain
muscle weakness
vomiting

As excessive vitamin D intake progresses additional clinical signs include hypertension, polyuria (excessive urination), and polydipsia (excessive thirst). There is rapid calcification of the soft tissues including the arteries and the kidney, which may lead to heart and/or kidney failure. The condition may present with extremely elevated levels of vitamin D_2 or D_3 (the vitamin you take or make on your skin), or 25(OH)D, or calcitriol, the active hormone. Rarely D toxicity symptoms may be caused by a genetic or immune disorder like sarcoidosis in which

vitamin D intake and serum 25(OH)D are normal but active hormone D, calcitriol, is overproduced in the affected tissues.

Vitamin D poisoning may be caused by over consumption of a supplement, knowingly or unknowingly, causing elevated levels of either vitamin D or 25(OH)D or both.[996,997]

Poisoning may be caused by consumption of a food contaminated with vitamin D, a 'spill' in fortified milk or other food[998] or consuming food contaminated with some other source of cholecalciferol such as some types of rat poison, listed below, or an animal feed additive. Yes, some rat poison is pure vitamin D.

Non-food, potentially toxic sources of vitamin D: Quintox, True Grit Rampage, Ortho Rat-B-Gone, and concentrated cholecalciferol as a livestock feed additive.

WHY TESTING IS CRITICAL AND PROBLEMATIC

There is no policy, in the U.S. or in other developed countries, supporting regular testing of 25(OH)D levels. While gathering information for this book I have spoken with many researchers. My persistent question was 'Why not just test vitamin D?" In screening 25(OH)D multiple times more than 300 people over a 3 year period it became clear their values of D could not have been estimated, by me or anyone else. Testing is the only way we can know if we need or do not need vitamin D (or sunlight).

There is every indication from existing research that testing 25(OH)D gives an accurate evaluation of vitamin D status, intoxication, hypervitaminosis, sufficient, insufficient, or deficient, with the exception of persons with unusual conditions. As discussed, researchers have even come to some agreement on what the numbers might be. Yet in every case in personal conversation I was told that 'broad individual testing of vitamin D is not possible'. Researchers in Canada, the U.S. and the U.K. all agreed that including this test in a yearly physical would not be cost effective and, even more astounding to me, 'it wasn't needed' Comments in studies and reviews echo this position.

The researcher and physician responses to widespread D deficiency include 'Let's wait' 'More testing" or 'Give everyone a supplement' with suggested doses ranging from 400 IU to 4,000 IU or more a day. Only one researcher supported more sun or possibly using a tanning bed.

In the early 1990's Adams and Lee found bone loss in patients with elevated levels of 25(OH)D.[56] Just for the record they also found bone loss in those who lacked vitamin D.[473] In response to their recommendation for routine testing, in an Editorial, Vitamin D Supplementation: A Word of Caution, Annals of Internal Medicine 1 August 1997. 127:231-233. Bernadette M. Marriott, PhD National Institutes of Health Bethesda, MD tells us:

"In their discussion, Adams and Lee express concern about the potential for more widespread occult hypercalciuria and vitamin D toxicity given the high level of dietary supplement use in the United States today. They recommend that physicians test economically advantaged osteopenic patients for hypercalciuria and high 25-hydroxyvitamin D levels.

Although such testing is unlikely to be cost-effective the simple addition of routine screening for dietary supplement use to practice routines may reduce the risk for toxicity and adverse drug and nutrient interactions."

Continuing later in the same editorial:

"Fall-related injuries, such as hip fracture, increase with age because of numerous factors, including osteoporosis. In one study, fall-related traumas accounted for 5.3% of all hospitalizations for older adults in Washington State. Yet hospitalization for falls accounted for only a small portion of the total cost of such trauma to the person and society. Heaney commented that a 20% reduction in hip fractures alone in the United States would lead to an estimated annual savings of $1.5 billion to $2.0 billion."

(GP: The underlining is all mine and I omitted some references for the Washington State study and Heaney's comments.)

A test for 25(OH)D is available for $50-$100+, a cost that is likely to drop should testing become a standard practice. To determine how much D one has and monitor sun or supplement results might take as many as 6 tests over a 3 year period for a total yearly cost of $300-600 per person. After the three year monitoring you have a pretty good idea of individual need and response to sunlight and/or vitamin D. Cost savings in reduction of adult onset diabetes, heart disease, obesity, degenerative joint disease, tooth loss, gum disease, back pain, and other D related conditions would result in cost reductions that I am unable to imagine. Just exactly what does cost effective mean?

Why not just give everyone in the U.S. extra vitamin D? Even at 800 IU daily the yearly cost per person would be about $36, much cheaper than testing.

At 800 IU of D a day, if everyone took their D, a certain percent of us would experience little change because of malabsorption or because of a need for higher amounts of D. Asian Indians have an excess of a particular enzyme that degrades vitamin D, a genetic modification most likely evolved to prevent D toxicity from chronic exposure to tropical sun.[43] Others may also have this enzyme and require higher amounts of D. A certain percent would sooner or later have excess vitamin D with some or all of the possible complications.

While it is very likely many people in the U.S. would benefit from 800-1,000 IU of D daily the only way to make sure, enough and not too much, is by testing.

An additional argument against broad recommendations for supplementing D is that vitamin D works to maintain blood levels of calcium, not bone, and D will remove calcium from bone if dietary calcium is low contributing to increased bone loss.[999,1000]

My last argument against broad recommendations for vitamin D is that in much of the U.S. sun is available at least part of the year. Combining supplements and sun can be a problem particularly in lighter skinned persons. In much of the rest of the world supplements aren't available.

We need to get over our fear of sunlight and learn how to use it safely and teach others how to do the same, throughout the world. Supplements as a solution to

worldwide or even national vitamin D insufficiency is not a realistic or viable option. Supplements of vitamin D replete D if used carefully but it is light that gives us life.

If we really want optimal health we need to know what it takes and do it. Making sure you and your family gets safe and adequate D can't be the responsibility of your physician.

TOO MUCH VITAMIN D?

A review from the section on testing: Normal values of 25(OH)D range from 20 ng/ml – 57 ng/ml (changed in 2007-08 to 32 ng/ml -100 ng/ml which worries me) Optimal levels are probably 40-60 ng/ml or the range may turn out to be as broad as 31-70 ng/ml. In Vieth's review of vitamin D he was unable to find studies showing toxicity at levels of 25(OH)D below 56 ng/ml.[53] As mentioned earlier chronically sun-exposed individuals in the tropics or subtropics reach higher values. Some researchers have made comments that these naturally derived elevations of D, such as found in one farmer in Puerto Rico, 90 ng/ml, are from sun and therefore normal and without danger. Past and recent research suggests the absolute safety of elevated levels of D from sun is less clear.

When I first began exploring vitamin D in 2000 I spoke with Barbara Boucher, M.D. from the Department of Diabetes and Metabolic Medicine, Medical and Dental School, Queen Mary, University of London, Royal London Hospital, Whitechapel, London, U.K. Dr. Boucher is one of the world's top researchers regarding vitamin D and Syndrome X, that is the complex comprised of insulin resistance, obesity, hypertension and adult onset non-insulin dependent diabetes. At the time of our conversation I had mentioned Reinhold Vieth's idea of higher doses of D being safe and perhaps even necessary. Dr. Boucher was unaware of Vieth's work but strongly disagreed with any suggestion that D in high doses for extended periods of time would be safe and suggested that I review this problem carefully. Her tone was so intense and serious the caution stuck with me over the 7+ years of book preparation.

Studies, however scientific, don't prove as much as the researchers, health promotion agencies, media and advertising would like us to think. Journals are filled with researchers comments arguing amongst themselves on why results often differ. Methods, testing procedures, number of participants, kind of participants and contrary results ruffle feathers frequently. Studies don't give us truth they give us approximations.

While there may not be sufficient evidence to say levels of 25(OH)D above 70 ng/ml are absolutely harmful there is equally no sufficient evidence to support values above 70 ng/ml as natural, necessary, optimal, or safe.

Hypervitaminosis D indicates excess intake of vitamin D leading to elevated levels of 25(OH)D. Vitamins D_2 or D_3, ergo or chole- calciferol, the vitamin you take or make, may also be elevated in hypervitaminosis. Vitamin D toxicity, intoxication, or poisoning, are terms reserved for very high levels of D accompanied by elevated serum calcium and potential or actual calcification of soft tissues. The research community

continues to discuss these terms among themselves and define what they might 'really mean'.

hy·per·vi·ta·min·osis
Function: noun
: an abnormal state resulting from excessive intake of one or more vitamins

The term hypervitaminosis D is used here to expressly mean chronically elevated, >70 ng/ml, levels of 25(OH)D, caused by supplementation and/or UV-B light exposure whether from sunlight or UV-B lamps.

In August 1997 a letter was published in the Annals of Internal Medicine. The title,- *Gains in Bone Mineral Density with Resolution of Vitamin D Intoxication*, should give us pause. The authors, Dr. John S. Adams and Gene Lee found 4 patients they determined to have hypervitaminosis D. These patients were discovered during a 1992-93 admittance screening at the Cedar-Sinai Bone Center in Los Angeles, CA. The purpose of the screening was to determine if a policy of giving a standard testing profile including fasting blood levels of parathyroid hormone, TSH (thyroid stimulating hormone), calcium and 25(OH)D and fasting urine levels of calcium and creatinine would help evaluate patients for osteoporosis or low bone mineral density. (56)

The four women had high levels of calcium in fasting urine, three times greater than normal values, demonstrated bone loss, and a 25(OH)D >50 ng/ml. There were no other abnormalities in the blood with the exception of a lower level of parathyroid hormone. TSH, $1,25(OH)_2D$ and serum calcium were all within normal ranges. All four patients had experienced demonstrable bone loss.

Two of the four women had unknowingly been taking supplements containing high levels of vitamin D. All of the women had been taking a minimum of 1,000 mg of calcium prior to and at the time of their diagnosis. This is important to note because the extra calcium did not protect them from the loss of bone attributed to excess 25(OH)D. In a manner as yet undetermined the elevated level of 25-hydroxyvitamin D caused or contributed to loss of calcium in the urine and increased bone loss.

While there are some arguments among experts about whether these women actually had hypervitaminosis D and whether it was the cause of their bone loss all four patients regained bone mass when elevated 25(OH)D and urinary calcium decreased to more normal values. The drop in D and decrease in urinary calcium took several months. Bone mass increased by an average of 2% a year following the resolution of hypervitaminosis D, very good news.

In the two women with the highest levels of 25(OH)D, 89 ng/ml and 80 ng/ml, the vitamin D causing the elevation was being taken without their knowledge. The high amounts of vitamin D were found to be an unlisted ingredient in preparations purchased from health food stores. None of the patients KNOWINGLY took more than 1,200 IU of vitamin D daily. One of the supplements tested contained 3,600 IU of D, not listed on the label.

According to the vitamin D endocrine system model $1,25(OH)_2D$ (calcitriol) is the active D, the hormone. All of the women with elevated 25(OH)D had normal levels of $1,25(OH)_2D$. Adams doesn't know why bone loss occurred but he suggests that the

high levels of 25(OH)D may have displaced $1,25(OH)_2D$ in cell function, potentially stopping or slowing the formation of new bone or otherwise altering production of elements necessary for bone maintenance.

Adams, Holmes, Kummerow, and the next study from India have documented damage to bones or arteries when 25(OH)D is elevated. In some of the studies done by them or reviewed by them damage occurred when the only abnormalities were elevated 25(OH)D and excess calcium in the urine.[56,59,60,922,923] Some very experienced vitamin D researchers believe there isn't a known upper limit on 25(OH)D if serum calcium remains normal. They accept hypercalcemia (too much calcium in the blood) as the indicator of excess D. This may be a mistake.

Researchers from the Department of Cardiology and Achutha Menon Centre for Health Science Studies, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum, India considered that high levels of D are used to cause heart disease in experimental animals.[61,1001] They wondered if high levels of 25(OH)D generated from exposure to tropical sun would also contribute to heart disease. In comparing $25(OH)D_3$ levels between a control group of 70 men without heart disease and 143 men with known heart disease, either recent heart attack or coronary artery blockage, levels equal to or greater than 89 ng/ml were present in 22.1% of the controls and 59.4% of the heart disease patients. The numbers indicate a strong association yet to be understood.[57] As low and high levels of D may contribute to heart disease I asked one of the study's authors the percentage of those with heart disease in the range I believe is optimal, 40-60 ng/ml. Fifteen percent had 25(OH)D within this range, 85% had levels higher or lower.

The researchers in India knew these elevated levels were from sunlight, not supplements, because the test was specifically for $25(OH)D_3$. D_3 is only produced on the skin or taken in vitamin D_3 supplements such as cod liver oil. Vitamin D_3 supplements are not generally available in many parts of the world including India. The test used commonly in the U.S. tests total 25(OH)D, which includes $25(OH)D_2$ and $25(OH)D_3$. Both D_2 and D_3 supplements are available here and both will raise 'total' 25(OH)D. This is important because the Indian research suggests the possibility of too much D from sun, generally thought not to be possible. (That old assumption trap.)

In December of 2001 a patient being medically treated for psoriasis with a special narrowband UV-B light prescribed by his dermatologist tested 25(OH)D at 97 ng/ml. The light treatment was immediately stopped by the choice of the patient, not the dermatologist. The patient then left for his yearly trip to Hawaii staying three months from Jan-March of 2002. He did not intentionally avoid the sun, believing, as I did at the time, hypervitaminosis D from natural sunlight was impossible. He ate local Hawaiian foods, including eggs and fish. On his return to northern California his 25(OH)D had risen to 127 ng/ml.

This man used no supplements containing D. His calcium supplementation was between 1,000-1,200 mg daily in addition to food sources. His D dropped slowly, just 6 ng/ml each month with complete avoidance of sunlight and any foods that might

contain a significant amount of D. After 8 months of sun avoidance and avoidance of fish and eggs his D dropped to 78 ng/ml.

His dermatologist refused to request the initial test for vitamin D. After being presented with the results the dermatologist stated he had no information on elevations of vitamin D from UV-B light treatment nor did he know if this was good, bad, or insignificant. After several attempts to get medical advice the patient was referred to an endocrinologist who also didn't know anything about elevated D and UV-B light treatment. He was willing to order testing, one time. The patient‘s last test reported a 25(OH)D of 57 ng/ml. after 12 months of complete sun avoidance and no fish, eggs, or supplements containing vitamin D.

His elevated 25(OH)D was caused by prescription psoriasis treatment with narrowband UV-B light made worse by exposure to tropical sun. This is iatrogenic (induced by a physician's treatment) hypervitaminosis D. When he first reported the elevation of vitamin D to his dermatologist a partner in the practice admitted they had seen excessively elevated levels of 25(OH)D before in persons treated with narrowband UV-B before. They did not know what it meant, or whether or not it might be a problem, nor was it their policy to monitor D. They demonstrated no interest in testing serum calcium, PTH, or fasting urinary calcium and refused a request to do so. Narrowband UV-B light can raise 25(OH)D to hypervitaminosis D levels.

A woman with severe osteoporosis, demonstrating a lumbar SD –4.6 and low 25(OH)D began taking D_3, cholecalciferol, 3,000 IU a day. Her serum 25(OH)D rose from below 20 ng/ml to 42 ng/ml within 4 months and a follow up bone scan after 8 months of D supplementation showed some not significant (very slight) bone gain had occurred. The patient did not want the expense of testing, it was not supported by her physician or HMO, so did not test D again. She continued to take the original 3,000 IU of D about five days a week. This dose is slightly lower than the dose of 4,000 IU sometimes suggested or used by some D researchers and clinicians. She also took between 1,000-1,500 mg calcium in addition to food sources and did not avoid foods containing D. The next bone scan, about 1 year after the scan showing a slight gain and 2 years after starting vitamin D, showed normal PTH (43 ng/ml); 25(OH)D 95 ng/ml; and lumbar SD –4.8 in addition to more loss in the femur for SD –2.2 to –2.5. Overall she experienced a 6% loss of bone density.

Her blood and urine tests confirmed her bone loss to be a case of excess D. She had the requisite elevated calcium in the urine with all other tests normal, serum calcitriol, PTH and serum calcium, just as Dr. Adams had found in his screenings.

When the patient‘s second scan showed bone loss her doctor, an osteoporosis specialist, did not want to test her D. Her physician believed the problem was hormonal and insisted on tests for TSH and PTH, both normal, and other similar studies. The only reason the patient got her D tested is because she stood her ground and demanded it, forcing her doctor to order the test.

Had the vitamin D test not been done her physician would have determined 'bone loss with unknown cause'. The physician had immediately prescribed Fosamax and estrogen for treatment. These treatments would have been ineffective in treating

the problem, excess supplementation of vitamin D, though Fosamax does help correct bone loss from hypervitaminosis D. What she needed to do was to stop taking the D

The test showing 95 ng/ml was done in July. All supplements were stopped and foods with vitamin D, fish, eggs and fortified dairy were avoided. Summer sunlight was neither avoided nor sought out. In November 25(OH)D reached 110 ng/ml. Vitamin D levels dropped slowly over the next six months, about 8 ng/ml per month. At last testing her D was 61 ng/ml.

For about six months prior to the July test showing 95 ng/ml she had been experiencing 'bone ache', fatigue and depression. Within several weeks of stopping vitamin D the pain resolved and energy and mood returned to normal, interesting because her 25(OH)D continued to climb during this time. Her serum calcium remained normal at all times.

Message: Don't take vitamin D in amounts beyond the 800 IU range without testing and when you begin to take D test every three or four months the first year and every six months the second and third year to make sure you have the right dose.

Retest if you move to a different latitude or increase or decrease your exposure to UV-B (summer or tropical sun). Find a healthcare provider that will support you in this process. In many cases elevated D doesn't appear until the second or third year of supplementation.

Lessons To Be Relearned

There are several important points to consider in these real stories.

First and foremost test, test, and retest D. There is no way to know your levels without testing and there are no obvious symptoms of too much or too little D. While some persons with elevated levels did complain of a general feeling a weakness and fatigue this is hardly a specific symptom and most persons with elevated D had no symptoms. While initial supplementation with vitamin D may normalize values, <u>continued supplementation over time at the same dose may cause hypervitaminosis D.</u> Doses above 800-1,000 IU a day may contribute to problems in persons particularly sensitive to vitamin D. The risk increases further at doses greater than the UL of 2,000 IU.

Second, it is possible to produce hypervitaminosis D from UV-B containing light, either that in UV-B rich environments as in the case of the heart disease patients in southern India or through treatments with narrowband UV-B light for medical conditions such as psoriasis. I am unable to say at the current time if suntan beds could also contribute to excess. It's a question for researchers. When UV-B makes up 5% or less of total UV (UV-B and UV-A combined) as in most tanning bed lights in the U.S. and natural sunlight at latitudes higher than 35° north or south, the UV-A present in the light will break down precholecalciferol in the skin before conversion to vitamin D or 25(OH)D.

Sunning midday in summer in latitudes between 35-40° has rarely produced levels of calcidiol beyond the mid 50-60 ng/ml in light skinned persons. This does not prove more intense exposure levels of UV-B rays from sunlight in the tropics won't raise D to excessive levels, especially in persons with little melanin. Narrowband UV-B and tropical sun clearly can, and in certain situations do, raise 25(OH)D beyond known safe values. While we wait for further research to clarify this issue response is ALWAYS individual, whether to supplements or light. Test, test, and retest.

Third, combining vitamin D supplementation, at a dose that maintains optimal values of D in winter, 40-55 ng/ml, with summer sun may rapidly elevate 25(OH)D in some persons in some locations. Having plenty of vitamin D doesn't stop your skin from producing more.[885,1002] In the summer of 2002 several persons reported going from 50 ng/ml or thereabouts to levels greater than 75 ng/ml within weeks of summer sun exposure. They had continued to take an appropriate 'winter' dose of D into the sunlight of summer.

You need to make a choice. Because you have enough D, from supplements or food, you do not stop producing D in your skin. Vitamin D levels continue to increase as you increase either D or sun or both. You may take D and avoid the sun or figure out your winter D dose and stop in the summer or combine some D and some sun. To do any of these safely you must test, test, and retest. You need to get to know your personal response to sunlight and to supplemental D.

Am I sounding paranoid? I worry. I remember the tone of concern in Dr. Barbara Boucher's voice speaking from the U.K. She had seen the problems with too much D given in infant formulas and fortified foods. There the problem stemmed from well-intentioned but unwise supplementation. The U.K. 51-52° north, with often overcast skies has little UV-B any time of year. Getting excess D from sunlight at any season would be extremely difficult. Here in the U.S. the situation is much more complex. We have a higher UV-B range at any season and in some areas subtropical sun.

I firmly believe that we all need vitamin D and having too little contributes to both chronic and acute conditions that could be corrected if we got enough.

I also firmly believe getting too much vitamin D from supplements or light or a combination can create a serious and potentially dangerous situation.

There are rarely obvious symptoms of D marginal deficiency or overabundance. Conditions associated with too much or too little vitamin D involve inappropriate mineralization or demineralization of bone, or joints or calcification of tissues and organs that include arteries, bone, kidneys, brain, or muscles.

I have seen an advertisement on TV for a calcium supplement that seems to suggest very high levels of vitamin D and calcium are safe and will cure any number of things. I have also visited websites produced by well-meaning persons suggesting massive doses of D, cod liver oil or a 'natural' source of D, is safe in any amount and they provide 'references' to prove this. The references are without merit and the statements are dangerously false.

You can take too much of anything but the consequences of too much D are extreme and many of these consequences may not be reversible. In seeking light (or using supplemental vitamin D) we must use moderation. We need a little sunlight and D, more perhaps than we get right now but there is no reason to believe we need levels higher than reasonably available from food or natural sunlight.

The moral of all of these stories is simple. America is a BIG melting pot with latitudes tropical, subtropical, temperate, and arctic and skins from very light to very dark. We are all different. We get different light. We respond to light and supplements differently. We live in different places. We have different skin colors and varied ability to produce and store D. We can all avoid damage by testing and responding sensibly to the results.

Below I quote Dr. Adams in his reply to criticism regarding his observations as published in the Annals of Internal Medicine Letter, March 1998:

"The most crucial point raised is the importance of detecting the opposite condition, vitamin D deficiency. We agree with the recommendation to increase the current recommended daily allowance for oral vitamin D consumption by 50% to 100% (from 400 to 600 or 800 IU daily), particularly in elderly persons who have limited sunlight exposure and cutaneous vitamin D synthetic capacity. This intake level is safe and will not cause hypercalciuria. What is not always safe and reliable is the label of a food supplement not regulated by the U.S. Food and Drug Administration. In our patients, the vitamin D content of the supplement was at least one order of magnitude greater than that advertised on the label. It is fortunate that the serum 25(OH)D level is the best screen for both hypervitaminosis D and hypovitaminosis D. Physicians should take better advantage of this versatile screening tool."

(GP: emphasis is mine)

A complicating addition to Dr. Adams' comments: Remember the two women with optimal D, the lucky ones who got to spend winters in the tropics? Both women were postmenopausal and candidates for a blanket prescription. of calcium and D. ANY supplementation would have elevated D to unnecessary levels. Even Dr. Adams' moderate dose of 800 IU is inappropriate if 25(OH) D is adequate. Testing really is critical.

The Causes- A Review

In our examples the elevated vitamin D came from supplements or sunlight or a combination of both. Remember the complex systems model and my warning about the devil being in skipping the details? Not getting enough vitamin D is clearly an issue in many parts of the world and so is getting too much. With all the voices, research, opinion, sales, media, the only safe path is working out your own need and your response and knowing that it works, safely, because you have tested.

The following list concerns low level excess D as that seen with Adam's cases of bone loss or the calcification of arteries in the southern Indians NOT clinical intoxication with elevated serum calcium.

- Vitamin D excess may be caused by too much sunlight.[57]
- Vitamin D excess may be caused by supplementation of D from unlabeled vitamin products. [473]
- Vitamin D excess may be caused by knowingly taking high doses of vitamin D over a short or long period of time.[936,1003,1004]
- Vitamin D excess may occur when supplements and sunlight are mixed. The body does not have an effective feedback mechanism to stop production or absorption of vitamin D either in the skin or from oral intake. A level of supplementation that might work well in winter may become too much when combined with summer sun.[885]

The Complications of Too Much D

Our few examples showed bone loss and calcification of soft tissue, in this case the arteries. In research extremely high levels of vitamin D are given to lab animals, rats in most cases, to cause a condition similar to heart disease with calcifications in arteries. While the doses of vitamin D used to cause artery damage in rats are extreme after considering the Indian study, with a strong association between heart disease and elevated 25(OH)D, there should be a concerned response and more research in this area. It certainly appears that both low and elevated levels of vitamin D may contribute to heart disease.

Holmes and Kummerow found elevations of 25(OH)D, independent of elevated serum calcium, caused damage to tissues. Excess 25(OH)D was found primarily in the kidney, liver, lung, aorta, and heart. places known to develop calcifications with D intoxication. As in our cadaver storage study Holmes found unconverted D, cholecalciferol, primarily in fat and 25(OH)D in blood. Remember DBP (D-binding protein) prefers 25(OH)D. Research suggests DBP entry into cells may be a normal process. Usually only 1% of DBP contains vitamin D, any of its metabolites. Holmes suggests elevations of vitamin D may increase DBP binding of D to as much as 40%.

The question of what constitutes hypervitaminosis D revolves around whether deposits of calcium in soft tissues are a result of excess calcium in the blood or excess 25(OH)D. Holmes and others have found calcium deposits related most to elevations of 25(OH)D. The pathologic changes he found in tissues, calcium infiltration of cells, occurred at levels lower than those causing elevated serum calcium. His theory as to why this happens suggests D-binding protein excess 25(OH)D may alter cell membrane permeability allowing entry of calcium.[923,1005] Increased calcium influx in a cell leads to calcium deposits, cell damage or death.[1006,1007]

Most researchers have noticed excess calcium in the urine as 25(OH)D levels increase and this has been attributed to improved absorption of calcium. Dr. Adams did not find that to be true and even if you aren't concerned about arteries or bone loss

consider this- Excess calcium in the urine combined with elevated 25(OH)D has been associated with kidney stones.[279]

Vitamin D moves calcium around our bodies; into and out of bone, muscle, hair, arteries, and cells. Both low and high levels of vitamin D appear to contribute to misbehaving calcium. Goldilocks' Principle: Not too much, not too little, just right.

In vitamin D poisoning calcification of the kidney and kidney failure are listed as cause of death. These unfortunate conditions have occurred in rare instances when children or adults have unknowingly been exposed to hundreds of thousands of units in a very short period of time or a somewhat lower dose of vitamin D over weeks or months. It is unlikely that any of you will find yourself suffering from poisoning in any of these ways. My concern is that in trying to be as healthy as you can be you may, in your enthusiasm, raise levels of 25(OH)D above the upper limit of safety, which to my mind is lower than some experts seem to believe.

CHAPTER 8 HOW DO WE GET D?

SUNLIGHT

Sunlight is our primary source of vitamin D, historically and currently. A continuing supply of sunlight or vitamin D is necessary for our survival. Trying to understand sunlight as a source of vitamin D in the 21st century turns into a quagmire of science, myth, fear, and questionable public health policy. Life as we know it would not be possible without the sun. It is the globe around which we spin and it is light from that fiery globe that allows us to be; to see, to eat, to grow, to multiply.

It seems very strange to me that there are massive campaigns worldwide to create fear of sunlight. Life has enough problems and complications without making the sun our enemy. Daily in news reports in every media market, supported by sunscreen manufacturers, well-meaning foundations, physicians, especially dermatologists, and researchers, we are bombarded with the message, avoid the sun, use sunscreen, cover up your children, hide quickly, the ozone is failing, the sun is burning, we are doomed.

What Does Light Have To Do With D?

Light is electromagnetic energy categorized as non-ionizing radiation. Non-ionizing radiation includes:

Table 4 Ionizing Radiation

UV-C	100-290 nm	In space, little reaches the earth, it‘s a killer.
UV-B	290-315 nm	This is the band of light that produces D
UV-A	315-400 nm	Invisible but very much present.
Visible	400-800 nm	The light we see, all the colors.
Infrared	800-1700 nm	Heat, including the heat from a fire.
Radio waves	3 Hz-300 GHz	This you know.

Electromagnetic energy produces waves. If you think of ocean waves the wavelength is the distance between the two peaks. The wavelength gives certain qualities to the energy; the effects it produces in different environments. A quick example, the wavelength of UV-A can pass through glass and nearly 80% of it will. UV-B wavelengths are unable to penetrate glass, allowing only a small percent to enter your home or car or office.

Ultraviolet (UV) light is invisible. You can't see it. It is divided into 3 bands or wavelength ranges, UV-C, UV-B and UV-A. [(1008)]

UV-C has very short wavelengths and is deadly to life should it reach earth's surface. It is completely absorbed by the ozone layer. UV-C in small amounts may be present in some fluorescent and halogen lights and other specialty lights.

UV-A wavelengths are the longest of the ultraviolet spectrum. When you step outside your home in the morning the primary band of ultraviolet light waiting to greet you is UV-A. It isn't the light you see. It's invisible but it‘s there. UV-A is present in all sunlight and makes up >95% of the total ultraviolet present, about 1.7% of total sunlight. UV-A does increase and decrease in intensity as our orbit around the sun moves us through the seasons. Some of the qualities of UV-A are in the table following.

UV- B is in sunlight too but at U.S. latitudes its presence is constantly and dramatically increasing or decreasing throughout the day and throughout the year. Early and late in the day during any season and most of the day during winter months very little UV-B makes it through the ozone to reach earth's surface. The greatest amount of UV-B at any location north of the equator will be present on June 21 at noon. South of the equator maximum UV-B reaches the ground on December 21 at noon.

Only UV-B produces vitamin D.

When you read the news, watch TV, or visit your dermatologist or esthetician it may seem UV-B is present everywhere just waiting to get you. The truth? With the exception of some of our most southern states UV-B is present in negligible amounts when you leave your house in the morning and when you go for a run after work. In much of America so little UV-B is available in winter you would need to spend most of

the day outside, mostly naked, to provide even a tiny amount of D, and you would likely freeze long before making any D. Indoor sunning won't do because UV-B doesn't penetrate glass.

As you learned in the section on sunning naked at noon, the angle of sunlight determines how much ozone must be penetrated for sunlight to reach the earth's surface. Ozone absorbs UV-B. Most of the ultraviolet reaching your skin is UV-A. This is the band responsible for aging of the skin. Sunscreens didn't block this band until very recently and many sunscreens still don't.[1009] UV-A is not much absorbed by the ozone layer and penetrates window glass so you get it inside your office, car, and home.

Bob Sayre presented a study at the 1998 symposium of the Biologic Effects of Light.[143] It is an amazing insight into maximizing vitamin D. UV-B ranges from 290-315. The particular wavelengths of UV-B light that generate D in our skins range between 295-300 nm. It is a very narrow band. While some UV-B may be present early and late in the day and during winter the amount of this narrow band is insufficient to generate significant D production.

Dr. Eddy at Columbia University performed experiments with sunlight in New York city during the winter of 1927.[1010] He demonstrated that 4 hours of direct sunlight midday was necessary to prevent rickets in rats. Rats don't need clothes and can just hang out for four hours in special cages that protect from the cold but let in UV-B light. The demonstration that four hours of full midday winter sun prevented rickets does not equal the amount of UV-B needed to produce optimal D. For us it clearly shows the impossibility of getting D year round. I have to mention that this four-hour exposure would have to be without sunscreen, not much clothing, and skin would get a good dose of UV-A at the same time.

Hess tried to prevent rickets in babies using sunlight in Boston and New York during the same period and failed. Dr. Wyman, also in Boston in 1927, succeeded by placing rachitic babies in front of windows made of quartz or Corning glass (these allow UV-B light to pass, regular glass doesn't) naked for the full day. He again found four hours in the middle of the day sufficient for most of the infants. of the nine babies with rickets seven recovered. The two babies of African heritage did not.

In 1927 the medical professions and researchers were really excited about the invention of a new type of glass, produced by Corning, that would allow UV-B to pass through. Now we are hiding from the sun blocking in every way possible, the same rays these early researchers so desperately sought for prevention of disease. It's kind of funny is a sad sort of way.

A quote from the book, pg. 89

'Finding enough antirachitic value for animals does not prove that human beings, with all their clothing and their short exposures to light can get much help.'

Sayre found the necessary intensity of the narrowband UV-B for D production was available during the middle of the day during summer months. Even though some of this band may be available at other times of the day or year it just isn't of great

enough intensity to make much D without staying in it for many minutes or hours. This is not a good idea because other rays do damage skin. Just for the record light bulbs can put out some not so healthy UV too.

It isn't that sun is bad, it's about enough and not too much. Research showing UV damage in persons with xeroderma pigmentosa or naked rats (commonly used for ultraviolet experiments) does not translate into data to insist on sun avoidance in healthy humans. We have melanin, we have repair mechanisms that exist for a reason. Surely we are not designed to spend our lives indoors or in darkness.

Our relationship with the sun is a dynamic complex system. This much-ignored fact has led to any number of false conclusions, inaccurate press releases, and poor public health policies.

Only light in the UV-B spectrum produces vitamin D. I keep repeating this because it's important.

GP: Your local weather channel broadcasts the UV Index daily. As I write this the weather channel UV Index listed, for my location at 10 AM, is UVI 3. I used an inexpensive UV Index meter to check this outside and my meter read 3. Sometimes that won't happen because local clouds or fog will block the rays. UV Index information is somewhat unhelpful regarding presence of UV-B because the UV Index uses a calculation that doesn't really tell how much UV-B is present.

I also own a UV-B meter. My UV-B meter indicates I would need 45 minutes to produce maximum D, if I stopped writing to sunbathe. If I want a full dose of sun, front and back, it would mean an hour and a half. Not only is the time unavailable I would also be exposed to lots of UV-A. I'll just keep writing.

UV-B and UV-A

When you spend time in the sun you are exposed to UV-A and UV-B. The intensity variables in the UV table are for higher latitudes, those above 30° north and south. As you learned in the section on sunning naked at noon, the angle of sunlight determines how much ozone must be penetrated for sunlight to reach the earth's surface.

UV-B	UV-A
UV-B is the only range of ultraviolet to activate D on human skin and in plants, animals, birds, and reptiles	UV-A may be implicated in melanoma (1011,1012,1013,1014)
UV-B is intensity varies greatly from dawn to dusk and is strongest near noon	UV-A is present from sunrise to sunset and only slightly greater in intensity near noon.
UV-B intensity varies throughout the year being strongest in summer	UV-A is present throughout the year with much less variance
UV-B is strongest at the equator.	UV-A is near full strength at any latitude
UV-B is stronger at high altitudes.	UV-A is near full strength at any altitude

UV-B composes from 0-0.5% of the sun's energy reaching the earth's surface at any given time, 0-1% of the UVR	UV-A composes 5.5% of the solar energy reaching earth's surface, 98-99% of the UVR
UV-B is 1000 times more biologically active than UV-A but intermittently present.	UV-A 1000 times more constantly present than UV-B.
UV-B, often called the "burning ray", is the primary cause of sunburn (erythema)	UV-A turns melanin dark (moles, sun or "age" spots). Some call it the "tanning ray"
UV-B does not penetrate deeply into the skin, only a small portion reaching the dermis	UV-A penetrates deeply into the skin reaching through all layers into the subcutaneous tissues
UV-B does not penetrate glass (about 5% only)	UV-A penetrates glass (78%, including car windows)
UV-B is blocked by ozone, smog, fog, and clouds. It is reflected by snow and sand. It penetrates water.	UV-A penetrates ozone, smog, clouds, and fog. It is reflected by snow and sand.
UV-B enhances the skin barrier [1015]	UV-A exposure causes significant damage to deep cellular processes in the skin [311,1016,1017]
UV-B is blocked by sunscreens and clothing, plastic, glass	UV-A is blocked by some sunscreens (not all) and clothing,
UV-B is linked to incidence of melanoma, basal and squamous cell carcinoma [292]	UV-A contributes to skin aging with cross-linking of skin fibers and loss of elasticity[1018]

Table 5 UV-B and UV-A

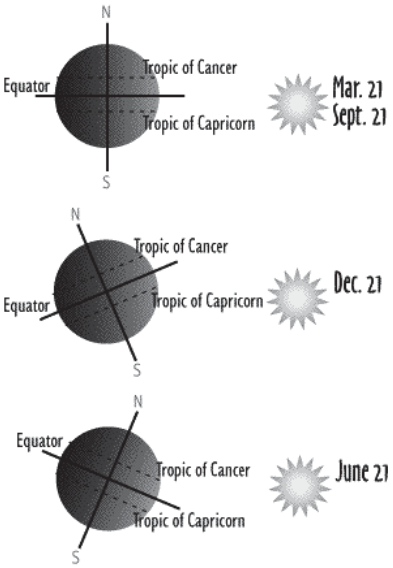
Since we are interested in UV-B why am I telling you about UV-A? Because it causes skin damage like UV-B, it just takes longer.[1019,1020,1021] But since UV-A is always present (all sunlight) and everywhere present (all latitudes) you will have a greater exposure to UV-A throughout your life than you will UV-B no matter where you live. When you use a sunscreen it blocks erythema, you won't burn as rapidly and can stay in the sun longer and most do.[1022] Many sunscreens don't block UV-A so that when you use a sunscreen and stay in the sun longer you greatly enhance your UV-A exposure, which some researchers believe is a very bad thing.[306,311] I happen to agree with them.

Remember, clothing is the perfect sunscreen, removable, replaceable and it blocks UV-A and UV-B.

The amount of vitamin D produced depends on exposure time, UV-B intensity, latitude, and altitude of location, amount of skin surface exposed, skin pigmentation and season.

The reason to sun is to get UV-B to make D. For persons with light skin in summer months it doesn't take long. Otherwise use shade, clothing, hats, or stay out of the sun.

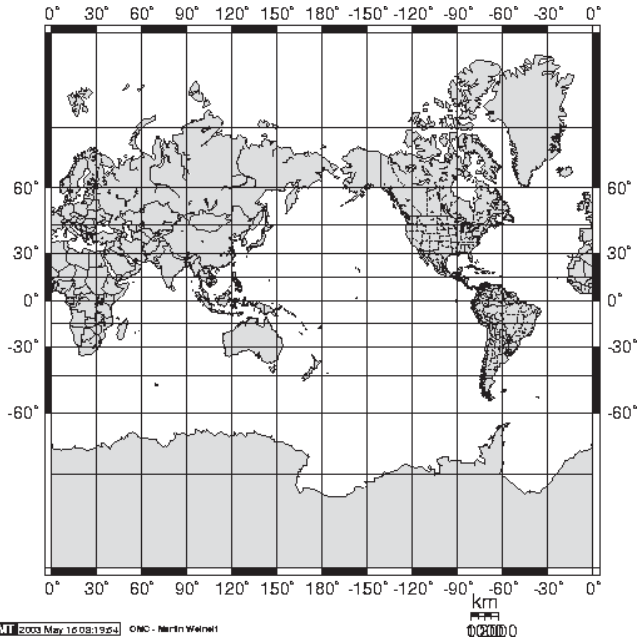
Location and Light



The first step in getting D from sunlight is to know where UV-B is found. We have two primary coordinates. Where are we on earth and where is the sun?

As the earth travels around the sun tilted on its axis the location of the sun directly overhead shifts from the tropic of Capricorn, 23.5° south, in winter, over the equator in March, directly above the tropic of cancer 23.5° north, in summer and back across the equator in September. Without making a model of the sun and earth it is hard to imagine because it most certainly seems it is the sun that moves.

We aren't just rotating around the sun we are spinning on our axis too. This rotation on our tilted axis gives us night and day. (I am definitely feeling dizzy.)



The light reaching the surface of the planet is altered in angle, east and west and north and south. These shifting angles cause a constant change the intensity of the sun's energy reaching the earth's surface and is responsible for day and night and our seasons.

Where is the sun? It depends, on time of day or day of year and where you live.

Where are you?

Most of the United States is located above 30° latitude. The problem of vitamin D and light becomes more difficult as distance from the equator increases because UV-B is *less available* (shorter mid-day span and shorter summer) and when UV-B is present it has *less intensity*. In the U.S. the UV Index (international rating of mid-day UV intensity) rarely exceeds 10 and then only in the most southern locations or high altitudes and only during summer midday.

Quick note- the UV Index is valid only for the middle of the day. They don't exactly tell you that but it is. It identifies the highest UV of the day, which is always near noon.

If you want to know how much UV-B is available to you the best way is to use a UV-B meter. (See resources) Without using a meter there are general guidelines to help you find the UV-B in light.

- Above 30° latitude UV-B and therefore vitamin D production will be greatest and skin damage the least (if you don‘t stay out long) between 11 AM and 2 PM
- Above 40° midday UV-B is present from May through August
- Latitudes 35° -40° significant UV-B is present midday from mid-April to mid-September.
- Arizona UV-B months begin in April and last through September; higher elevations (think mountains) have more UV-B and a longer UV-B season.
- Florida and Texas have optimal UV-B from mid-February through mid-October.

In the tropics and subtropics, located between latitudes 30° north and south, the intensity of UV-B is generally present most of the day with little change summer or winter. In these latitudes vitamin D producing light is available most any time unless clouds or rain block the light. The UV Index of these areas typically ranges from 10-16. A few locations near the equator and at high altitudes can reach a UVI as high as 21+, though rarely.

The Minimal Erythemal Dose, MED, is a measurement of the ultraviolet energy necessary to cause erythema. Remember, erythema is NOT sunburn. It means any redness caused by expansion and congestion of the tiny capillaries just under our skins. It is the very slight pinkening that may occur anytime within 24 hours of exposure to too much (for you) UV light. Erythema occurs in dark skins too, we just can't see it.

The MED is based on Skin Type II defined as light skin, light eyes and light hair, easy burning and little capacity to tan.

1 MED equals the UV energy required to produce erythema, to 'pinken' the skin of a person with Type II skin.

The UV Index is based on the MED, minimal erythemal dose. The calculation is 1 MED/hr equals 2.3 on the UV Index. What it means is if the UV is 2.3 at your location, you are very white, and you expose your skin to the sun for 1 hour you might turn pinkish sometime within the following 24 hours. It would be great if the UV Index could be used to determine UV-B but it can't. The UV Index (UVI) contains a mix of UV-B and some shorter waves of UV-A.

Just before erythema is the cut off point for midday summer sunning indicating you've got your D. Erythema occurring at other times of the day and year has little to do with adequate D. One hour of naked skin at UVI 2.3 might produce erythema in type 1I skin but would produce little or no D. The time of day and time of year (because these indicate the angle of the UV rays) determine the intensity of UV-B reaching the earth.

In latitudes above 30° north or south sun exposure before 10AM or after 2PM, will cause erythema (from UV-A plus UV-B) before it will supply adequate D (295-300 nm UV-B).

It means safe sunning for vitamin D must occur during the hours we have been told to avoid. Sunning near noon in summer months (or winter months in lower latitudes) for 5-90 minutes, depending on skin type (melanin, color and type), will form maximum vitamin D before erythema (skin damage) occurs in all but the darkest skins.[143]

Midday, summer months, is the only time providing adequate intensity of UV-B in locations more distant from the equator.

In 179 Korean women ages 20-75 the mean 25(OH)D tested at 25.8 ng/ml. 16% had values <10 ng/ml. *The Korean women with the largest seasonal variations of D spent the most time out of doors between 12 PM and 2 PM.* Older women in the study group had less D but it was explained by less dietary D and less time outside midday.[1023] South Korean latitudes range from 34°-39°, similar to many locations in the U.S.

GP the perspective: If you have light skin you don't need much sun, ever. If you have dark skin you may need significant amounts of UV-B containing sun frequently. Whatever the color of your skin or the length of exposure the sun you need, containing UV-B, is primarily found only midday in summer months, unless you live near the equator.

Sunning briefly midday during summer months can provide maximum amounts of vitamin D without skin damage in skin types I-III if you follow the guidelines and never stay long enough to 'pinken'. For full sun/vitamin D benefit this is 'per side' meaning front and back. Lying out in the sun briefly, mostly naked, front and back generates an abundance of vitamin D in most ‗light-colored' skins. ‗Briefly' is determined your location and skin type and may range from as little as 5-7 minutes (total front and back 10-14 minutes), skin type I in Florida, to as much as 30 minutes (60 total), skin type III in more northern states.

Whatever your skin type even slight redness or tenderness (the darkest skins do burn with excess exposure, you just can't see it, but skin will feel tender) within 24 hours of UV exposure IS sun damage. Reduce your exposure.

Skin types IV-VI need more exposure time to produce vitamin D. If melanin is abundant and you live in northern states really adequate light may not be available at any time of the year. (Portland, OR comes to mind.) UV-B doesn't penetrate clouds. (It can penetrate some haze, which is why a meter is helpful.)

Skin Damage at Any Exposure Level?

Dermatologists insist any UV light on normal skins will cause damage. We live in light. We need light. Erythema is a sign of damage. We can avoid it with a little knowledge and a great sunrise wardrobe.

How Much D Does The Sun Make? It doesn't. We do.

It has been determined by some studies that lifeguards and farmers in latitudes below 30° make the amount of D equivalent to an oral dose of 10,000 IU vitamin D a day providing a serum level of 25(OH)D equal to or greater than 100 nmol/l or 40 ng/ml.[53] I strongly disagree with this finding. Detailed information and supporting research about why I disagree can be found in the section on vitamin D supplementation.

Taking vitamin D and making D from sunlight are two very different things. Over a three year period persons of similar age, with similar skin types, similar locations and similar midday exposure of 70-80% of body surface, using sunlight only as a source of D produced very different levels of 25(OH)D.

Exposing skin to UV-B makes D, but other factors and processes determine how much you make and how much of it stays around. If you decide to use sunlight to produce D test before you start, and every few months thereafter, to see how well sunning works in summer and to make sure your D is still adequate in winter.

There have been a number of estimates relating body surface to sun exposure and amount of D produced. The commonly accepted calculation, as mentioned, is that a day in the sun produces 8,000-10,000 IU vitamin D.[1024] In body weights from 100-300 lbs, body surface area ranges from 1.5-2.66 square meters. This suggests an equivalent of 225 IU per 5% skin exposure.

In persons exposed to real sun, not simulated sunlight, a more accurate estimate may be 100-150 IU of D for 5% of surface skin exposure per day. This estimate is similar to the sun exposure:skin surface 25(OH)D figures found in a Delhi, India study. Indians with light skins.

At 20% summer sun skin exposure the physicians and nurses in this study had 25(OH)D levels similar to many in the U.S. taking a supplement of 400 IU.

Unfortunately even in Delhi this amount of sun was not enough to raise D to bone supporting levels.[1025]

Sunlight can provide all the D you need if you live in the right place, are not heavily melanized (dark skin) and know how to use the light available.

> It is possible, if you know how and when to sun, even persons with darker skins can get sufficient D. You'll need to experiment with your location and seasons to determine your sunlight and D equation. Don't forget, even members of the same family may have different responses and there is NEVER a reason to pinken, or burn.

Light skinned persons sunning midday five days a week, NEVER getting pink or tan, may produce enough D to maintain 25(OH)D between 40-60 ng/ml. (There are exceptions.) What I have just said is true for latitudes around 35°-40°, if and when they are sunny with UV-B containing rays. By mid-September there isn't much UV-B in many (not all) states and productive sun won't appear again until mid-April.

GP: Note I said 'with light skins'. If you tan or have darker skin you'll need more sun to produce the D you need.

Ozone and Light

The world seems to have gone completely nuts about ozone. Whether the ozone is disappearing depends on whom you talk to or what you read. There is an ozone hole in the Antarctic. At its worst the UV light reaching land under the ozone hole is equivalent to the UV found in summer in San Diego, CA., not even as intense as tropical sun. The repeated conclusion is that ozone thinning will seriously damage all life and increase rates of skin cancer. The last sentence is speculation.

> *speculation, def:*
> *a conclusion, theory, or opinion based on incomplete information or evidence*
> *reasoning based on incomplete information or evidence*

Whether speculations about ozone have any effect on U.S. citizens getting more UV-B, and therefore more skin cancer, is known. Speculations have had no effect on UV-B and skin cancer rates in the United States of America. The ozone hole is not over the U.S. It's over Antarctica, which is quite some ways away. UV-B reaching the ground in the United States has not changed for some time.[1026]

In the U.S. there is absolutely no way to relate increases in melanoma or other skin cancers to increases in UV-B *caused by a decrease in ozone*. It just isn't a factor. It isn't a factor because the ozone over the U.S. is just fine. That does not mean these cancers are unrelated to ultra-violet or visible light. They are. In the US and most other countries *it isn't the ozone causing the problem, it's human behavior.*[1027]

UV-B has not significantly increased and ozone has not significantly decreased but, for arguments sake, what if they had? I'll quote Dr. Fred Singer, an atmospheric physicist and president of The Science & Environmental Policy Project

"In spite of the fact that a downward ozone trend should result in an upward trend of UV, no such trend has ever been reported. In November 1993 two Canadian researchers, J.B. Kerr and C.T. McElroy, published a paper in Science claiming to have measured large upward trends of UV, as much as 35 percent per year for certain wavelengths. Their results were deemed suspicious since they showed no error bars or other measures of uncertainty. Indeed, a re-analysis of their data, also published in Science, showed that the "trend" was consistent with zero percent.

The Kerr/McElroy paper created great excitement. Even though they no longer claim the existence of a trend, researchers in other fields continue to blame a UV trend for such things as the disappearance of frogs and the rise in melanoma skin cancers. *Ignored is the undisputed fact that UV increases strongly as one approaches the equator; the feared 10% increase due to ozone thinning—if it were to exist—would correspond to a 60 mile move towards the equator.*"

GP: The emphasis is mine. Relax. The ozone is still with us and we are going to be just fine. The very worst case scenario is that your home would be 60 miles more tropical.

What is happening in the U.S., especially over urban areas, is *too much ozone*. The ozone up high, in the stratosphere, is currently staying where it belongs with the exception being near the poles. Lower down in the troposphere, where we live and breathe, we have managed to create our own ozone umbrellas.

Ozone is the principle component of summer smog.[1028] These ozone umbrellas are particularly strong during summer at midday. Unfortunately summer midday is exactly the time of maximum UV-B, which is blocked by ozone.[137]

Several researchers have made a connection between lower UV-B exposure, because of latitude or smog/ozone cover, and cancer incidence.[173,575,575,1029] Children in Delhi, India were determined to have 25(OH)D levels half that of children in rural areas. The study authors found one of the causes to be less UV-B reaching the ground due to ozone pollution.[92] Ozone air pollution is listed as a contributing factor to rickets incidence in Philadelphia, PA in a susceptible population. [95] The susceptible population had darker skins needing higher, not lower, UV-B.

Ozone is with us, especially too much ozone, from air pollution. We should not pollute. We should give up chemicals that mess up the atmosphere. However, experts should stop scaring people when the science available does not back up their projected ozone doomsday scenario. As of 2006 the ozone hole continues to recover, though perhaps more slowly than projected.

THE SKIN WE'RE IN

Skin, Light and Vitamin D

Skin is our outside wall. It is very important to our survival.[1030] A lifetime puts hard use to skin. It's important we take care of our skins and it helps to understand some things about skin and sunlight.

Skin color is caused by blood under the skin, pinkness or redness, and melanin.

> *melanin, def. a protein produced by a melanocyte containing pigment that may be black, brown, yellow, red, and violet. It is found in feathers, human skin, hair, and eyes.*

Actually melanin is the coloring pigment in all hair, fur, and skin of mammals, birds, amphibians, fish, and reptiles. Melanocytes are cells that make melanin in mammals and birds. Humans are born with about 5 million melanocytes no matter what our race or skin color. Our heredity dictates how much and what kind of melanin our melanocytes produce.

The primary pigments in human melanin are eumelanin, with brown-black pigments and pheomelanin, producing yellow-red pigments. Dark skin produces a

greater quantity of melanin primarily containing eumelanin. Light skin produces less total melanin and varying ratios of eumelanin and pheomelanin. Disorders of hypo- and hyperpigmentation, like vitiligo or darkening of skin with pregnancy, can result from a change in the number of melanocytes or a decrease or increase in the activity of the melanocytes.

People with dark hair and skin make relatively more eumelanin and their skins contain a greater total amount of melanin. Natural redheads produce proportionately more, pheomelanin and overall less total melanin. An example in hair composition- very black hair contains 99% eumelanin and 1% pheomelanin. Red hair, having the highest percent of pheomelanin, contains 67% eumelanin and 33% pheomelanin. Brown and blonde hair contain various mixtures. This same genetically variable combination of melanin pigments is responsible for determining whether a bear is brown or black.

Eumelanin interacts with UV light to protect skin by absorbing the rays.[1031,1032] Pheomelanin doesn't do a very good job protecting from UV damage and may itself be damaged by UV light creating free radicals.[1033,1034]

Genes associated with pheomelanin are also associated with melanoma.[1035,1036] High content of pheomelanin, more red or golden tones, in any skin type, suggests a more serious problem may occur with excess UV exposure. [1032,1037] Please don't skip over the word 'excess'.

In our skin's basal layer we have approximately 1 melanocyte for each 10 keratinocytes. Keratinocytes are cells that make the protein composing our skin, hair, and nails. Each melanocyte provides melanin for 30 nearby keratinocytes. Melanin's chemical structure and biological role is still being studied and debated. What is known- to make melanin a melanocyte needs the amino acid tyrosine and an enzyme, tyrosinase, to convert the tyrosine to melanin.

Tyrosinase activity is increased when vitamin D is adequate and decreased when vitamin D is insufficient.[1038]. Some scientists suggest this is one way of regulating vitamin D production.[1039] Less D, less tyrosinase activity, less conversion of tyrosine to melanin allowing more UV-B to penetrate our skins. Vitamin D plays an important role in normal melanocyte function.[1040] Melanocytes can be damaged by UV-A.[1041]

The darker the natural pigmentation or more tanned the skin, the less UV-B is available to cells for D conversion.[97,1042,1043] Eumelanin 'quenches' UV-B, like an anti-oxidant quenches free radicals.[1044] This is a good thing if you live where there‘s lots of sun. This is not such a good thing if sunlight with UV-B is not readily available. It is important to remember in much of the U.S. and latitudes greater than 30° north and south UV-B is absent from sunlight significant portions of each day and throughout much of the year.

Sunlight activates production of vitamin D by UV-B photolysis of 7-dehydrocholesterol in the skins basal layer. The intensity of natural sunlight UV-B is critical for conversion of 7-DHC to vitamin D.

Light intensity is called irradiance by light scientists. Intensity or irradiance follows the curve of the solar angle, the greatest irradiance being June 21 at noon in northern latitudes and December 21 at noon in the southern latitudes. Irradiance alters

throughout the day too so that noon is always the time of greatest irradiance (though daylight savings alters this a bit).

To make vitamin D your skin needs lots of irradiance and even at noon in winter in most of the U.S. there just isn't enough.[1045]

Your skin isn't very deep and only so much 7-DHC is present in a given area. A brief exposure to sufficiently intense UV-B efficiently converts 7-DHC to precholecalciferol. Once made, precholecalciferol follows one of two paths becoming either vitamin D_3,, transformed by heat, or it is photolyzed by other wavelengths of sunlight to inactive metabolites. This breakdown of precholecalciferol by sunlight to inactive metabolites prevents further production of vitamin D_3.[97]

Holick estimates only 10-20% of 7-DHC actually completes the metabolic pathway to D_3. [97] In persons with light skins sunning for a short period when UV-B is present makes full use of your 7-DHC. With short midday exposure you won't _over do' and damage your skin and you can sun again another day.

GP: A little sun over lots of your body, just enough and not too much, depending on your skin color, has the capacity to make all the D you need. Staying out longer won't make more D. Tanning actually makes getting D more difficult.[1046]

Skin thickness alters amount of 7-DHC. As we age our skins get thinner and our ability to make vitamin D declines.[138,1047,1048] The skins ability to repair also diminishes, which includes the ability to repair UV damage. Using the 'naked at noon' guidelines for sun allows maximum D and minimum skin damage at any age.

A fact to consider- there is only so much 7-DHC in a given area of skin, which means the amount of skin exposed limits production of vitamin D. You will make more D if you expose more skin, not by staying out longer. The function of time in production of D is skin type limited; light skins need very little time, dark skins need a longer time, determined by UV-B irradiance. Exposure to UV-B stops, or should stop, just before the amount of UV-B penetrating the skin might begin to cause erythema, that redness or pinkness, or in darker skins, tenderness. At that point, just prior to erythema, the amount of D produced is proportional to the area of skin exposed.

Note to the GP: Getting 10 minutes of summer sun on arms and legs, you might increase your serum D by an amount not measurable on any current test. Exposing my entire body (the naked thing) will produce much greater amounts of D because much more 7-DHC will be exposed to UV-B for conversion.

In a Delhi, India study, you'll read more details later, the physicians, nurses and pregnant women exposing face, arms and legs for 25 minutes a day managed to maintain 25(OH)D levels between 4-10 ng/ml for the physicians and nurses, and 4.8-12.8 ng/ml for the pregnant women. Not one person in either group managed to reach Holick's minimum 25(OH)D of 20 ng/ml.

Delhi, India is at about 28°, equivalent latitude to about 120 miles south of San Diego, CA. Values were taken in summer when the sun delivers 4 MED, lots of irradiance. Delhi soldiers exposing just face and hands for 360 minutes a day in winter, irradiance 1 MED, fared better. Their 25(OH)D was 14-23 ng/ml with daily exposure of 370 minutes. More than 6 hours of sun a day and yet only a few soldiers made it into

the 20 ng/ml minimum range. Unnoted in the study is that this amount of total exposure includes lots of UV-A which contributes to loss os skin elasticity and skin aging.

This study provides us with an excellent example of the necessity of showing lots of skin if you want to make D. Whoever began the myth Americans (Which Americans, black, white, or in-between? Do they live in Hawaii? Alaska?) could get all the D they needed exposing arms and legs for 20 minutes three times a week before 11AM or after 2PM needs to recant. For many of us it just isn't true.

National and International Sunlight Advisories

GP: The advice to limit midday sun exposure isn't appropriate for any number of dark skinned individuals. To minimize or limit exposure doesn't mean complete avoidance. WHEN YOU'VE HAD ENOUGH SUN the suggestions about wearing hats, sunglasses and clothing work, as does shade.

On the subject of sunlight the current, April 26, 2002, CDC guidelines for school programs to prevent skin cancer are:

- Minimize exposure between 10AM and 4PM
- Seek shade from the midday sun (10AM-4PM)
- Wear clothing, hats, and sunglasses that protect the skin
- Use a broad-spectrum sunscreen, UV-A and UV-B, with a sun protection factor of >=15
- Avoid sunlamps and tanning beds.

The Canadian news media CBC quoting the Canadian Dermatology Association warns:

- Limit your outdoor activities between 11:00AM and 4:00PM
- Wear sunscreen with a minimum rating of SPF 15 or higher
- Wear a wide-brimmed hat and wrap-around sunglasses with UVA and UVB protection

To stay safe, Cancer Research U.K. recommends people should:

- Avoid the sun at its height (usually 11am-3pm)
- Use shade wherever possible
- Take extra care of babies skin
- Never put babies under six months in the sun
- Wear a wide brimmed hat and sunglasses with UV protection

- Use clothes to cover-up
- Use a sunscreen of at least SPF 15 with UVA protection, even if you have a tan
- Avoid sun beds and tanning lamps
- Check skin and report unusual changes immediately.

And from the SunWise program, U.S. Environmental Protection Agency, to be promoted in the public schools:

- Limit Time in the Midday Sun- The sun's rays are strongest between 10 a.m. and 4 p.m. Whenever possible, limit exposure to the sun during these hours.
- Seek Shade- Staying under cover is one of the best ways to protect yourself from the sun. Remember the shadow rule: "Watch Your Shadow-No Shadow, Seek Shade!"
- Always Use Sunscreen- Apply a broad spectrum sunscreen of an Sun Protection Factor (SPF) of at least 15 or higher liberally on exposed skin and reapply every 2 hours when working, playing, swimming, or exercising outdoors. Consult your doctor about sunscreen use for children under six months of age.
- Wear a Hat- A hat with a wide brim offers good sun protection to your eyes, ears, face, and the back of your neck - areas particularly prone to overexposure to the sun.
- Cover Up- Wearing tightly woven, loose-fitting, and full-length clothing is a good way to protect your skin from the sun's UV rays.
- Wear Sunglasses that Block 99-100% of UV Radiation[Sunglasses that provide 99-100% UVA and UVB protection will greatly reduce sun exposure that can lead to cataracts and other eye damage. Check the label when buying sunglasses.
- Avoid Sunlamps and Tanning Parlors- The light source from sun beds and sunlamps can damage the skin and unprotected eyes.
- Watch for the UV Index- The UV Index provides important information to help you plan your outdoor activities in ways that prevent overexposure to the sun. Developed by the National Weather Service (NWS) and EPA, the UV Index is issued daily in selected cities across the United States. Please take special care to adopt sun safety practices when the UV Index is moderate or higher.

We have general agreement between health officials in the U.S., U.K. and Canada that we should avoid the sun. We also have strong governmental support for topical sunscreens. Hmmm…

The Problem of Total Sun Avoidance

Sunlight is the best source of vitamin D. Vitamin D produced in our skin and transported by our vitamin D-binding protein, that is sunshine-made 25(OH)D, rises more slowly and is sustained longer than when vitamin D supplements are given.[1049] While sunlight may excessively elevate 25(OH)D in light skinned persons in the tropics there is little danger of overdose in the U.S. The potential for problems with vitamin D fortification of foods or excess supplementation are much greater.

Brief or moderate exposure to midday sun increases D and once you understand how much you need you won't damage your skin. Placing a naked baby in midday summer sun for a few minutes, depending on sun, season and skin, will provide perfect baby sized amounts of vitamin D and babies love it. The rule remains the same for baby, a quick sunbath, never pinken, or tan, no erythema. Before and after a sunbath, use clothing or shade. The chemicals in sunscreens aren't needed by anyone. Allergic reactions are more common that reported.[1050,1051,1052,1053]

The Problems:

- UV-B is the only band of light that makes vitamin D. We need this ray.
- Sunscreens of SPF 8 used according to instructions block 97% of vitamin D production. Higher levels completely block production.[137,1054]
- Sunscreens block UV-B. Few protect from UV-A, none protect fully, and some loose effectiveness after just 20 minutes.[1009]
- Skins that have graded (regular but minimal) exposure to UV-B develop a skin change that protects the skin from UV-A. If no UV-B reaches the skin, because of avoidance or sunscreen, this protection is never developed and the skin is more susceptible to damage from UV-A, which, I repeat, is not blocked very effectively by most sunscreens[1015,1055,1056]
- Before we began broad use of sunscreens we had a problem with vitamin D deficiency. Now skin cancer rates are not dropping AND broad vitamin D deficiency is occurring.

Southern Asia has abundant UV-B and a very high levels of rickets and osteomalacia (adult rickets) which indicates the most severe deficiency of vitamin D. Researchers trying to understand this paradox analyzed the 25(OH)D levels in various groups of healthy Indians

The South Asian city of Delhi India is 28° N, offering UV-B sunlight year round. 123 subjects from Delhi participated and were divided into groups according to lifestyle and season. Groups were soldiers in winter; physicians and nurses in summer; physicians and nurses in winter; depigmented persons in winter; pregnant women in summer; and infants in summer.[1025]

GP read this carefully: According to the authors only those with "maximum direct sunlight exposure" had sufficient D. The soldiers, spending a great deal of time in the sun, had an

average 25(OH)D of 19 ng/ml, the highest in any of the groups. Wait a minute, that doesn't even reach Holick's minimum suggested value of 20 ng/ml. The others in the study faired much worse.

Table 6 Indian Study

Group and Season	Soldiers Winter	Physicians and nurses Winter	Physicians and Nurses Summer	Depigmented Persons Winter	Pregnant Summer	Newborn Summer
Daily minutes of sunlight	370 +- 30	25 +- 5	25 +- 5	5 +- 5	25 +- 5	None
25(OH)D	18.8 ng/ml +- 4.4	3.2 ng/ml +-1.4	7.2 ng/ml +-3.2	7.3 ng/ml +- 4.5	8.8 ng/ml +- 4.3	6.7 ng/ml +- 2

This gives us lots to think about. Remember, optimal 40-60 ng/ml?

- Delhi is more southern than any location in the United States. At 28° UV-B is significantly present summer and winter most of the day. (Washington, DC and San Francisco, CA are 38° Austin, TX 30°).
- In winter the ground received 1 MED and in summer 4 MED (This was checked, important because Delhi sufferers from ozone umbrella-see ozone section)
- Skin colors were categorized as dark, wheatish, fair. >60% were wheatish in all pigmented groups
- The depigmented persons (no color melanin, like albino or vitiligo) had higher levels of D even though they spent less time in the sun. (But not anywhere near enough.)
- The physicians and nurses in summer exposed 20% of body surface to the sun; face, neck, arms, and legs.
- The others exposed 10%; hands, neck, and face.

Even with 370 minutes of sun a day soldiers couldn't produce adequate D with 10% exposure of body surface.

The UV Index in Delhi during the time of exposure, winter, averages 7-8. Los Angeles has a winter UV Index maximum between 2 and 4; Florida between 4 and 6. Moreover 20% exposure in summer for 15 minutes daily wasn't sufficient for the physicians and nurses. The UV Index in summer in Delhi ranges from 12 to 15.

Given the facts, the location and the date, can anyone imagine we can get enough vitamin D year round from 20 minutes three times a week, arms, and legs, before 10 AM and after 2 PM?

The authors Discussion begins with

"The reported paradox of the prevalence of rickets and osteomalacia in the sun-drenched South Asian countries remains unexplained."

I think I can explain this. By now I'll bet you can too. You actually have to get in the sun to make D. You have to brave your fears and the wrath of experts and put out some flesh.

If we need D and the sun is our best source, and free if we live in the right places, just what are we doing?

UV Light and Cataracts

There are two reasons physicians go a bit batty about sunlight exposure. Skin cancer is discussed in the next section. Here I want to address the issue of cataracts. It is true in the tropics pterygia, pinquecula and cortical cataracts, all associated with excess UV exposure, are major health problems.[1057,1058,1059]

A pterygium is a fleshy growth that usually starts in one corner of the eye and grows inward toward the cornea. Eventually, the pterygium will grow onto the cornea.
A pinguecula is one or more soft yellowish patches of tissue growing on the white (sclera) of the eye just beyond the colored part of the eye. Typically, pinguecula are located toward the corners of the eye at the 3 or 9 o'clock position. They are usually harmless, but can be precursors of ptergia.

cortical cataract, def. The most common form of senile cataract.

But cataract incidence is also related to diabetes, increasing cataract risk fourfold, being female, not having finished high school and corticosteroid use which includes prednisone and equivalent drugs.[1060]

Our eyes contain melanin just like our skins and dark eyes are protected from UV if vitamins A, E and C, riboflavin; the carotenoids, and the minerals calcium, selenium, copper, and zinc are sufficient. It is important to maintain levels of these nutrients over time.[323,1061,1062,1063,1064,1065,1066,1067] Our bodies, in the active processes of living, _use up‘ nutrients. If these nutrients aren‘t replaced regularly the body (or eye) is unable to repair damage. Both vitamin A and vitamin C levels in our skins AND eyes are reduced by sun exposure and we need to make sure to replace, in sufficient amounts, these important dietary nutrients.[1068,1069] The human lens has one of the highest concentrations of vitamin C. Abundant vitamin C, throughout our lives, helps keep lens ascorbate sufficient and reduces risk of cataract.[1061,1070,1071,1072,1073,1074,1075]

Blue eyes, or very light eyes, contain less melanin and need all of the vitamins and minerals plus UV filtered contact lenses or sunglasses.

Hats serve a purpose. They protect your eyes from general UV exposure. If you are on the lake or at the beach in summer or spending time out of doors in winter or high altitude snow, add wrap-around UV-B and UV-A blocking sunglasses or goggles.[1076] Protect your eyes.

The amount of time you need to spend in the sun to get D will not increase cataract risk over a lifetime

The Sun, Skin Cancer and Sunscreen

Medical professionals everywhere on earth promote sunscreen. They have a reason.

From the CDC: .The Burden of Skin Cancer

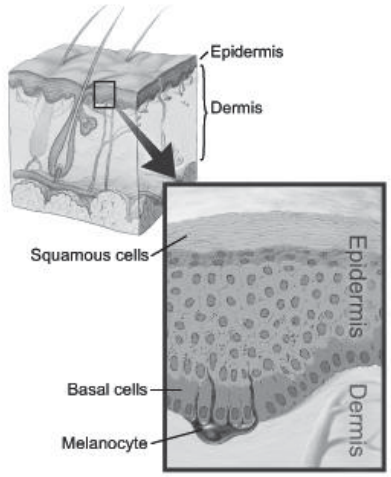
Skin cancer is the most common form of cancer in the United States. More than 1 million new cases of skin cancer will be diagnosed in 2002. The three major types of skin cancer are basal cell carcinoma, squamous cell carcinoma, and melanoma. Although basal cell and squamous cell carcinomas can be cured if detected and treated early, these cancers can cause considerable damage and disfigurement. Melanoma is the deadliest form of skin cancer, causing more than 75% of all skin cancer deaths. About 53,600 people in the United States will be diagnosed with a melanoma skin cancer in 2002, and approximately 7,400 will die.

Skin cancer facts from the American Cancer Society

Half of all new cancers are skin cancers.

About 1.2 million new cases of skin cancer will be diagnosed in the United States each year.

About 80% of skin cancers are basal cell carcinoma, 16% squamous cell carcinoma, and 4% melanoma.



Health officials estimated about 2,000 deaths as a result of basal cell or squamous cell carcinoma for the year 1998.

75% of skin cancer deaths are due to malignant melanoma.

Melanoma represents 2% of all cancers and 1% of all cancer deaths in the United States.

The absolute dictate to avoid sun is based on these statistics.

Abnormal growth of skin cells resulting in malignancy (cancer) can occur in the basal cell, the squamous cell or the melanocyte.

Cancer located in basal or squamous layers of the skin are classed at non-melanoma skin cancers. About 40-50% of all Americans who live ot age 65 will have skin cancer at least once. Anyone can get skin cancer but persons with light skin that freckles, light hair and blue or light-colored eyes, are the most susceptible. Black skins are very resistant to all forms of skin cancer.

All types of skin cancers can be cured, 100%, if detected and treated early so any usual skin changes or new growths should be checked by a physician as soon as they are noted.

75% of all skin cancers are basal cell carcinomas. Basal cell skin cancers do have a relationship to sunlight exposure but sun exposure alone won't produce these malignant growths. They typically appear on sun exposed areas especially the head and neck. They rarely spread to other organs if treated when they are discovered. About 35-50% of persons diagnosed with basal cell skin cancer will have a reoccurrence within 5 years. This form of skin cancer was typically found in middle aged or elderly people but is beginning to appear more frequently in younger persons. It is rarely fatal.

Squamous cell carcinomas make up about 20% of non-melanoma skin cancers. They are more aggressive than basal cell skin cancers. Like basal cell carcinomas they usually, but not always, appear on sun-exposed areas of the body such as the face, ears, neck, lips, or the back of the hands. This type of skin cancer can also develop in scar tissue or skin ulcers.

Non-melanoma skin cancers are poorly recorded in the U.S. It is estimated the yearly occurrence is 1,000,000 incidence. There cancers are highly curable and less than 2,200 persons die from non-melanoma skin cancers yearly, always because they did not seek treatment early. Men are twice as likely to develop these cancers as women.

Malignant growth in the melanocyte is melanoma, highly invasive and deadly. It is the skin cancer most likely to spread to other organs and tissues and the most likely to be fatal.

From the 2003 SEER's data on melanoma: [1077]

White males in 1975 had an incidence rate of 9.3 per 100,000; white females, 8.2 per 100,000. The incidence for blacks is not available or is non-existent. In 2000 the incidence for white males rose to 26.2 per 100,000 and in white women 17.4 per 100,000. In 1999 the total recorded diagnosis of melanoma in blacks, women and men combined was 1.2 per 100,000. Most melanoma, 60%, is diagnosed after age 65.

Deaths from melanoma in 1975 per 100,000- White men, 2.9; white women, 1.7; black men 0.6; black women, 0.4. Deaths, per 100,000 in 2000 were white men, 4.3; white women, 2.0; black men, 0.6; black women, 0.5.

As of 2004, the National Cancer Institute determined an estimated melanoma prevalence of 29,900 men and 25,200 women in the United States. Blacks, Asians and Hispanics combined accounted for about 5% of the total number of diagnosed cases.

Table 7 Melanoma in the US 2002 Estimates

New Cases	53,600
Deaths Per Year	7,400
5-Year Overall Survival Rate*	89%

Source: American Cancer Society

The states with the highest incidence are Oklahoma, Vermont, Delaware, Massachusetts, and Wyoming. The states with the lowest incidence are New York, Louisiana, North Dakota, Hawaii, and District of Columbia. Another hmmm…

With the exception of Oklahoma, all of the states with the highest incidence are in latitudes above 35° which get insignificant UV-B for 4 or more months each year. Even Oklahoma is partly above 35°. The states with low incidence also get fairly low UV-B exposure except for Hawaii which gets the most intense UV-B of all U.S. locations. One consideration is skin color because heavily melanized people, that eumelanin genetic trait, is protective when it comes to all forms of skin cancer including melanoma. Areas with greater populations of darker skinned persons will have a lower overall incidence.

The idea behind sunscreen, the reason it is produced and sold, is prevention of skin cancer. There are, however, a number of problems.

The suggested preventative measures for all forms of skin cancer are sun avoidance and/or use of sunscreens.

From Sunscam authored by Michael Castleman in the 1998 May/June issue of Mother Jones magazine:

> "Melanoma was rare until 1950 when it began to slowly increase until the mid-1960s when it accelerated into the current epidemic."

Castleman goes on to explain that while sunbathing is blamed for the increase in melanoma beaches were crowded in the 1930s and skin cancer did not increase until much later. He suggests the introduction of tanning lotions and sunscreens may play an important role in the development of this disease epidemic. According to Castleman sales of sunscreens have grown from $18 million in 1972 to $500 million in 1998. Between 1980 and 1998 melanoma incidence in whites increased from 1 in 250 to 1 in 84.

Castleman's ideas are supported by at least one epidemiologist. In 1998 at an American Association for the Advancement of Science meeting in New York Dr. Marianne Berwick, an epidemiologist from Sloan-Kettering, reviewed the efficacy of sunscreens in preventing skin cancer. Papers around the world reported it and dermatologists worldwide and the Skin Cancer Foundation united to refute her data. Dr. Berwick said,

> "After examining the available epidemiological data and conducting our own large case-control papulation-based study, we have found no relationship between sunscreen use at any age and the development of melanoma skin cancer."

More of Dr. Berwick's findings-Sunburns at an early age don't cause or predict later melanoma but people who sunburn easily are in the higher risk group and more likely to eventually have melanoma. No studies proved sunscreen prevented squamous cell carcinoma. Two found sunscreen prevented a skin condition thought to lead to

squamous cell carcinoma. The two studies she reviewed for basal cell carcinoma showed sunscreen use actually increased risk. The studies suggesting sunscreen protects against melanoma were as conflicting. In five studies sunscreen users were more likely to get melanoma, in three studies there was no association and in two sunscreen seemed to protect.

The concern is not just that sunscreens may not work but that they may actually increase risk. UV-B damages skin. Sunscreens, all of those used until perhaps the end of 2000, block UV-B. Until recently no sunscreen consistently blocked UV-A and even as of 2006 none block UV-A completely or for extended periods of time (and that's important because UV-A is always present, no matter what the time of day).

Assuming your sunscreen blocks UV-B allowing you hang out in the sun longer without getting burned you will get lots of UV-A. The potential for damage may be worse because UV-A penetrates skin deep into subcutaneous tissue. UV-A is present in light from morning to night and it penetrates glass and clouds. Excess UV-A exposure may alter our immune system.[1078,1079] UV-A damages skin and is the primary ray for skin aging.[306,311,1009,1080] Not only does UV-A damage skin is may be the primary band responsible for melanoma.[1011,1012,1014,1016,1081,1082,1083,1084]

GP: If you use sunscreen you can stay out in the sun longer without burning but it means you will be getting a very large dose of UV-A. The research suggests you may be in trouble, lots of trouble.

Dr. Berwick also found rather than the generally accepted idea we are spending more time in the sun, we are spending less time. What we are doing is getting 'intense intermittent sun'; the weekend warrior kind of sun. This is the exact type of sun exposure associated with melanoma.[1085]

The idea we suffer more melanoma because we spend more time in UV-B sunlight didn't make sense to me. I thought about this as I was writing this book, before I read Dr. Berwick's review. UV-B is present during the day and most people work or are in school. Now days most of us work inside, go to school inside, and because of national campaigns pretty much avoid sun midday. Schools nationwide are being warned to keep children inside midday to avoid sun. Besides, if we were getting so much UV-B we couldn't and wouldn't be deficient in vitamin D, and we most certainly are deficient. When you expose your skin to sunlight midday, when UV-B is present, without sunscreen, you make D, absolutely.

Melanoma is more about genes and pheomelanin. If you have the yellow-red pigment, pheomelanin, you are more likely to develop the disease whether you sun or not. Less total melanin plus less eumelanin and more pheomelanin are the worst combination. This is the combination found in light-skinned natural redheads with light eyes and freckles, the most at risk.

BUT Dr. Berwick also noted as have other researchers, people who have moderate regular exposure to sunlight have less incidence of melanoma. [284,294]

GP: Lots to think about here- moderate frequent exposure to sunlight is likely to increase levels of D in the blood and in the skin. Vitamin D abundance is associated with less cancers of all types.

Our skins naturally contain vitamin D, 25(OH)D, and calcitriol. New research, lots of it recently, is finding skin cells can all by themselves transform 7-DHC to precholecalciferol to vitamin D_3 to 25(OH)D_3 to calcitriol.[295,1086,1087]

We have a complete endocrine system right in our skins.[1086,1087,1088,1089] This fits with Holick's discovery that cells can convert 25(OH)D if there's enough of it around and this ability of the cell may function to keep cells from behaving badly.

The suggestion is our skin cells need D just like the rest of our cells. Vitamin D helps skin cells grow normally and may protect from melanoma. [284,296,871,1090,1091]

Just for the record skins need vitamin A too, so diet does count.[1092]

Sunscreens block UV-B and prevent the production of vitamin D. [97,137,642,1054,1093] There are three studies showing sunscreens don't block production of vitamin D.[1094,1095,1096] But in all three studies none of the users or controls produced optimal D, a level shown to protect cells and prevent bone loss, Holick's higher suggested range of >32 ng/ml.

In one study vitamin D actually was lower with sunscreen use but researchers said it was fine because it did not reach standards of ‗D deficiency', the old value of <10 ng/ml.

In another of the three studies users of sunscreen and non-users (placebo) had a similar rise in serum vitamin D. BIG problem. If their D did go up it means the *sunscreen was not blocking UV-B*. Only UV-B makes D. In the study the author comments on the possibility the sunscreen may not have been used properly.

Participants in the third study used rigorous sunscreen protection as they had a hereditary condition, xeroderma pigmentosum, which requires strict avoidance of ultraviolet light. Evaluations of 25(OH) showed levels that were low or very low, but not considered clinically deficient, therefore just fine by the researchers' standards.

As these low values don't take into account the possible benefits of optimal levels of D it really doesn't show the subjects were fine at all. It does show sunscreens work to prevent skin exposure to UV-B light. It also may show persons with xeroderma pigmentosum might benefit from some vitamin D.

GP-Xeroderma pigmentosum is a rare hereditary condition in which the skin cannot repair ultraviolet light damage, especially sunlight. Victims develop malignant skin cancers at an early age. All ultraviolet light, whatever the source, must be avoided.

What about non-melanoma skin cancers, at least the ones in sun exposed areas? If sunscreen won't help what can be done to reduce skin cancer incidence?

This next bit is from emedicine.com. Author: Stanley B Levy, MD, Clinical Professor, Department of Dermatology, University of North Carolina at Chapel Hill. The quote is from the web article Sunscreens and Photoprotection, which also provides information on how to evaluate a sunscreen for UV-A protection.

"The US Food and Drug Administration (FDA) regulates sunscreen products as over-the-counter drugs. The Final "Over-the-Counter Drug Products Monograph on Sunscreens (Federal Register 1999: 64: 27666-27963) established the conditions for safety, efficacy, and

labeling of these products. The sun protection factor (SPF) is defined as the dose of UVR required to produce 1 minimal erythema dose (MED) on protected skin after the application of 2 mg/cm^2 of product divided by the UVR required to produce 1 MED on unprotected skin. A water-resistant product maintains the SPF level after 40 minutes of water immersion, whereas a very water-resistant (formerly waterproof) product maintains the SPF level after 80 minutes of water immersion. A broad-spectrum or full-spectrum sunscreen provides both UV-B and UV-A protection, ideally through the entire UV-A I and UV-A II range."

For sunscreen to work an adult needs a minimum of 1 full ounce of product to cover the body per application. An ounce is about two tablespoonfuls (a shot glass). SPF has nothing to do with UV-A, no matter how high the number. Even if you use a 45 you'll still be getting UV-A, unless the product specifically indicates UV-A protection. Even then the UV-A protection may last only for a very brief period of time.

For sunscreen to work you have to use it properly and if you do you will not make any vitamin D.

The best protection from the sun is clothing.[1097,1098,1099,1100,1101,1102,1103] Clothing may be put on or removed any time you like. Evidence from early drawings suggest people used clothing to filter damaging sunlight, veils, and large brim hats, in ancient Greece, umbrellas in ancient Egypt, Mesopotamia, China, and India. In 1887 Veiel used a tightly woven red veil.[1104]

T-shirts work.[1105]

My favorite T-shirt experimenters are Gelsor, Sigernes, Gjessing and Kocbach. You'll find their work at http://fred.unis.no/Tibet/Tshirt.

These four men traveled to Lhasa, the capital of Tibet located 3,650 meters (2.26 miles) above sea level. They performed their experiment on June 9, 2000, a clear day. Given the season and altitude UV had to be very intense. Typical UV Index for the area is greater than 10 and can reach 20+ in summer. They tested T-shirts. 1. white, thin; 2. light gray with dark pattern, thin; 3. black, thick, closely woven; 4. light gray, normal thickness; 5. brown, tightly woven, thin; 6. dark blue, closely woven. All except number 4, the light gray, normal thickness, were 100% cotton. The light gray was 94% cotton and 6% polyester.

Results: Dark, thick, tightly woven T-shirts can protect human skin from solar UV even under the most extreme conditions. A UVI of 20 is as extreme as it gets.

The light colored and thin cotton shirts protect too but not as well under extreme conditions. The polyester cotton T-shirt was extremely poor at providing protection allowing more than twice the ultraviolet radiation to pass through compared to the thin white cotton, and sixteen times as much UV as the black, thick, tightly woven T-shirt. I never have liked polyester.

A large percentage of non-melanoma skin cancers, basal cell and squamous cell carcinomas, are located on the head and neck. This is why people used to wear hats. Hats have been around for a very long time and in every culture. Hats are the best

summer defense. Broad-brimmed hats are just the thing. Men and women look quite dashing and sexy in hats.

The other frequent site for non-melanoma cancers is our arms. Shirts and T-shirts work. We are not on a mountain in Tibet nor are we in the Arabian Desert. Even when UV-B is most intense it rarely exceeds UV Index 9 in the U.S. and then only for short portions in the middle of the day.

From some of the comments from public health officials and sunscreen companies you get the sense the light is so bright leaving your home will rapidly produce death.
We truly need some reality here and common sense.

Clothing can be removed to get a little D. You can't take sunscreen off; though it may wear off or wash off when you really want or need it. Clothing protects from UV-A and UV-B and it is reusable. Think about it. I really did mean what I said about outdoor cafes, long lunch hours, and loose clothing and think of all the money you'd save not buying sunscreen.

Sunscreens can serve a purpose when traveling to areas of intense UV or to protect after you've gotten your UV-B vitamin D at the pool or beach. I don't hate sunscreens I just prefer cotton and big hats. Lotions make my skin itch. When used in the amounts necessary for protection allergic reactions are more common that reported and some experts believe sunscreen to be the most common cause of contact dermatitis.[1051,1053,1106,1107] Allergic reactions are frequent. Other researchers worry about a number of chemicals in sunscreens which may be estrogenic, a whole other topic.[1108]

All in all sunscreens are not all they are cracked up to be.

Tsukahara, K., Moriwaki, S., Hotta, M., Fujimura, T., Sugiyama-Nakagiri, Y., Sugawara, S., Kitahara, T., and Takema, Y. 2005 Biol.Pharm.Bull. 28 2302-2307

The effect of sunscreen on skin elastase activity induced by ultraviolet-A irradiation

It has been reported that application of sunscreens prevents the photoaging of skin in animal models and in humans. We irradiated the dorsal skin of hairless mice with ultraviolet-A (UVA), and investigated the effects of sunscreens on skin elastase activity and on *skin* properties. Six-week-old female HR/ICR hairless mice were used in these experiments. After being treated with either a *UV*A sunscreen (also containing ultraviolet-B (*UV*B) sunscreen to eliminate any slight *UV*B in the *UV*A lamps; Protection Factor of *UV*A (PFA)=6, Sun Protection Factor (SPF)=20) or a vehicle, the dorsal *skin*s of mice were irradiated with the *UV*A lamps at 22.3 J/cm(2)/d, 5 times a week. At the end of 15 weeks *skin* properties were evaluated and elastase activities were measured. In the vehicle control group, *UV*A irradiation increased the brightness and yellowing of the *skin*, decreased the water content of the stratum corneum, increased *skin* thickness, decreased *skin* elasticity, increased *skin* elastase activity, and decreased the ability of the *skin* to recover in a pinch test, as compared to an un-irradiated group. All these differences were statistically significant. In the *UV*A sunscreen group, both the *UV*A induced *skin* damage and the increase in *skin* elastase activity were significantly inhibited, as compared to the vehicle group. However, as compared to the un-irradiated group, *skin* elastase activity was significantly increased and immediate extensibility of *skin* (Ue) was significantly decreased, thereby indicating that the *UV*A sunscreen did not prevent photoaging to the same level as the un-irradiated group. These results suggest the partial efficacy of the topical photoprotection from *UV*A by the sunscreen in inhibiting elastase activation, and also suggest the possibility of reducing photoaging.

If you must use a sunscreen just make sure you know what your sunscreen contains, really know, and that it blocks all of the bands, UV-A and UV-B. Don't forget, if you use a sunscreen, for it to work you have to really slop it on. You'll need a full ounce, 1/8 of a typical bottle, per application for an adult. You'll also need to reapply every two hours, and after swimming, and after sweating.
(Clothes, I am telling you, clothes!)

Defend Your Stratum Corneum (and Avoid Sun Damage)

In 2004 I received an email-

"… I am Australian (living in California) of English descent and have fair skin, so just the right amount of sun exposure is of importance to me, for I too believe in the merits of controlled amounts of vitamin D.

Each year, for 10 years, I would have about 50 pre cancerous sun spots burned off my skin. I still go to the same skin specialist but now the difference is, I am skin cancer free. But instead of being praised for my condition, I am reprimanded for having a slight tan and lectured about the need to stay completely out of the sun and always slather block out onto my skin.

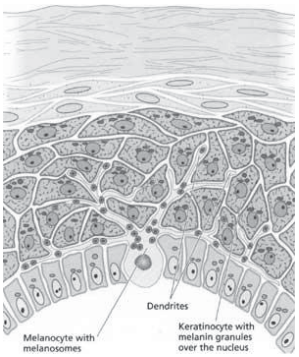
However, since I have completely avoided using skin care products containing propylene glycol or sodium laurel sulfate (among many other ingredients)

I have been skin cancer free for 5 years. My turn around came when I heard a skin scientist, Linda Chae, say in a lecture, „The sun is not your enemy," and follow that statement with well researched and correct information that I followed to the letter."

This email immediately sent me hunting for reasons one might experience such a dramatic change. Following up on the Linda Chae connection I read about the damage being done to our skins by chemicals in our soaps, detergents, shampoos, bubble baths, and other cleansers and cosmetics.

Even substances once thought to be safe now have been found to increase damage to the skin, such as methylparaben, a common preservative in cosmetics.[1109] This chemical increases skin damage when exposed to UV light. As chemicals are not tested together one wonders about cosmetics formulated with sunscreen and methylparaben or other photoenhancers.

More interesting is the increase in melanoma and an association with chemicals in water. An early study (seemingly never followed up) showed swimmers in polluted or chemically treated waters at a significantly higher risk for melanoma.[1110] Chemicals in water damage more than just skin. Swimmers seem to have a higher incidence of asthma and allergy. There is an association of adverse risk in particular with chlorine derivatives. Chlorine by-products are found in the human body after swimming, bathing or showering in chlorinated water.[1111,1112,1113,1114,1115,1116,1117,1118]



The part of our skin most altered by topical chemicals, which include the list mentioned by the author of the intriguing email, is the stratum corneum, the outer most layer of your epidermis (outside skin).

epidermis, def The outer layer of your skin. The epidermis is the thinnest layer of your skin, but it's responsible for protecting you from the harsh environment. The epidermis has five layers of its own: stratum germinativum, stratum spinosum, stratum granulosum, stratum lucidum, and stratum corneum. The epidermis also hosts different types of cells: keratinocytes, melanocytes and Langerhans cells. Keratinocytes produce the protein known as keratin, the main component of the epidermis. Melanocytes produce your skin pigment, known as melanin. Langerhans cells prevent foreign substances from getting into your skin.

You were created with the perfect skin, a living, breathing, covering to protect your inner parts from the elements and hold in all your fluids.

Originally this thin outer layer, about as thick as a piece of paper, was thought to be unimportant, just old, dead skin cells. This view is rapidly changing as new discoveries show the importance of skin design.

In The Essential Stratum Corneum, Marks, Leveque, and Voegeli, Dunitz Press 2002 the introduction begins with

"The stratum corneum appears thin and wispy and completely insignificant in routine formalin fixed and paraffin embedded histological sections. It was only when new techniques arrived on the scene allowing *a glimpse into structure as it exists in life* that some appreciation of its importance developed."

Emphasis is mine. Hmmm… Things look different viewed inside a living system as compared to viewing cells removed from that system.

Continuing in chapter 3, *One more look into the stratum corneum*, R Marks, pg. 25,

"Even amongst both physicians and biologists, the stratum corneum (SC) has been a much undervalued structure and dermatologists have not until quite recently, thought of this membrane as being of major importance. The reasons for this misperception are, first, that routine histological preparations deform and distort the stratum corneum so that is appears wispy and insignificant. Secondly, there has been paucity of techniques that can afford an accurate view of this horny structure."

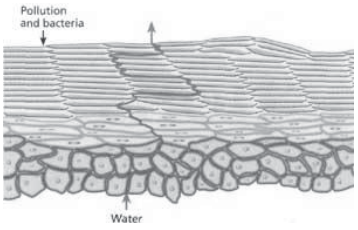
The primary function of the stratum corneum is its 'barrier function'. Seems this layer has value. It is important to understand this value. In the diagram the stratum corneum is responsible for keeping the 'outside', pollution, chemicals, and other damaging elements, out and the 'inside' including water, in.

The stratum corneum is made up of degraded keratinocytes. $1,25(OH)_2D$, the active form of vitamin D along with vitamin A gene regulators and vitamin C[1119,1120], control production of keratinocytes in the skin.

Keratinocyte, def. skin cell located in the basal layer of the skin separating the dermis and epidermis.

The number of layers of cells in your stratum corneum varies. The average number of cell layers ranges from about 10-28. As mentioned one job of the stratum corneum is to keep bad things out. This includes UV radiation. Your stratum corneum reflects some of the UV rays, making your skin safer when sunning.

Another important function of your stratum corneum is to keep water in. Water is a critical element inside and outside of your cells. Scientists call the natural process of water evaporation from within our skins TEWL (trans-epidermal water loss).Damage to the stratum corneum alters its barrier function and allows underlying cells to lose more than the normal amount of water.



When chemicals alter out TEWL we end up with aging, drying, barrier impaired skin more susceptible to infection, scarring, and other environmental assaults which includes UV damage.

Skin is an entire endocrine system and UV light alters its function. _Just enough and not to much', may be the most important health tip of the year.

Slominski, A. and Wortsman, J. 2000 Endocr.Rev. 21 457-487

Neuroendocrinology of the skin

The classical observations of the *skin* as a target for melanotropins have been complemented by the discovery of their actual production at the local level. In fact, all of the elements controlling the activity of the hypothalamus-pituitary-adrenal axis are expressed in the *skin* including CRH, urocortin, and POMC, with its products ACTH, alpha-MSH, and beta-endorphin. Demonstration of the corresponding receptors in the same cells suggests para- or autocrine mechanisms of action. These findings, together with the demonstration of cutaneous production of numerous other hormones including vitamin D_3, PTH-related protein (PTHrP), catecholamines, and acetylcholine that share regulation by environmental stressors such as *UV* light, underlie a role for these agents in the *skin* response to stress. The endocrine mediators with their receptors are organized into dermal and epidermal units that allow precise control of their activity in a field-restricted manner. The *skin* neuroendocrine system communicates with itself and with the systemic level through humoral and neural pathways to induce vascular, immune, or pigmentary changes, to directly buffer noxious agents or neutralize the elicited local reactions. Therefore, we suggest that the *skin* neuroendocrine system acts by preserving and maintaining the *skin* structural and functional integrity and, by inference, systemic homeostasis.

In a review of the literature Krause found the benefits of sun exposure to outweigh the dangers. Fewer people regularly getting sun died from cancer as compared with those avoiding sunlight..

"…The literature was analyzed in terms of reviews, controlled and epidemiological studies for the relationships between sunshine exposure and overall cancer mortality, as well as mortality from cancer of the prostate, colon and breast. The residential and/or occupational sun exposure rate seemed to be positively correlated with a lower risk of overall morality due to organ cancer. A normal vitamin D status appeared to be an important precondition,…"[1121]

The best way to care for your skin (and the rest of you) is to avoid chemicals in your food, water, and cosmetics and get some sun. Less is more and while cosmetics are relatively expensive, sunlight is free.

Major Toxic Ingredients to Avoid (Save Your Skin)

Consider a real milk bath or making your own natural cleansers. Look for products without the _Dirty Dozen'. I didn't make up this list. The first time I saw it was on Linda Chae's site. I don't know the author but do believe avoiding these chemicals will enhance our cell/skin health. If you know or are the source let me know and I will credit you in the next edition.

Table 8 The Dirty Dozen

1. Propylene, Ethlylene and Butylene Glycol: Found in Anti-freeze. Acts as a .surfactant. (wetting agent and solvent). Penetrates the skin and weakens protein and cellular structure. Strong enough to remove barnacles from boats, factory workers are required by the FDA to wear protective clothing when producing products containing these chemicals and are required to dispose of PG as toxic waste. Baby wipes, diaper creams, baby lotion, facial cleansing cloths, facial cleansers, body washes, shampoos, toothpastes, etc.
2. Sodium Lauryl Sulfate (SLS) and Sodium Laureth Sulfate (SLES): Detergents pose serious health threats. Used in garage floor cleaners and engine degreasers and in 90% of all personal-care products that foam. Young eyes may not develop properly if exposed to SLS. SLS may damage the skin's immune system. Baby body washes, baby shampoos, anti-bacterial hand washes, shaving cream, body lotions, shampoos, etc.
3. DEA (diethanolamine), MEA (monoethanolamine) & TEA (triethanolamine): Hormone-disrupting chemicals that can form cancer-causing nitrates. Dr. Samuel Epstein (Professor of Environmental Health at the University of Illinois) says that repeated applications of DEA-based detergents result in major increase in liver and kidney cancer. The FDA.s John Bailey says .the risk is significantly increased for children.. Body lotions, body washes, cleansers, shampoos, etc.
4. Polyethylene Glycol (PEG): Carcinogenic petroleum ingredient that reduces the skin's natural moisture. Increases the appearance of aging and leaves you vulnerable to bacteria. Baby wipes, diaper creams, baby lotions, cleansers, body washes, deodorants, etc.
5. Sodium Hydroxide: This is a poison (caustic lye) found in drain cleaners. The warning label on sodium hydroxide products reads .POISON, May be fatal or cause permanent damage if swallowed. May cause blindness. Avoid contact with skin, eyes, mouth and clothing.. Toothpastes, baby lotions, hand and body lotion, etc.
6. Triclosan: Synthetic .antibacterial. with a chemical structure similar to Agent Orange! The EPA registers Triclosan as a pesticide, giving it high scores as a risk to human health and the environment. It is in a class of chemicals suspected of causing cancer in humans. Tufts University, School of Medicine says Triclosan can force the emergence of .super bugs that it cannot kill. Anti-bacterial hand wash, antibacterial toys, etc.
7. DMDM and Urea (Imidazolidnyl): Two of many preservatives that often release formaldehyde which cause joint pain, skin reactions, allergies, depression, headaches, chest pains, ear infections, chronic fatigue, dizziness, and loss of sleep. Body lotions, body washes, anti-bacterial hand washes, cleansers, shampoos, etc.
8. Parabens: Studies show that parabens . alkyl hydroxy parabens . alpha hydroxy benzoate (methyl-, ethyl-, propyl- and butyl-parabens) are weakly estrogenic. Baby Wipes, baby body washes, anti-bacterial hand washes, facial wipes,

body lotions, shampoos, etc. In addition these chemicals may make skin more sensitive to UV-B.
9. Alcohol, Isoproplyl (SD-40): Drying, irritating solvent that strips skin‘s moisture and immune barrier, making you vulnerable to bacteria and viruses. Made from the same petroleum derivative used in shellac and antifreeze as well as personal care products. Promotes brown spots and premature aging. Lotions, creams, deodorants, etc.
10. Mineral Oil: Petroleum by-product that coats the skin similar to plastic wrap, clogging the pores. Interferes with skin‘s ability to eliminate toxins, promoting acne and other disorders. Slows down skin function and cell development, resulting in premature aging. Lotions, Creams, etc.
11. FD&C Color Pigments: Synthetic colors from coal tar that deposit toxins onto the skin, causing skin irritation. Absorption of certain colors can cause depletion of oxygen in the body and death. Shampoos, toothpastes, body washes, cleansers, baby products, wipes, hand washes, deodorants, lotions, creams, etc.
12. Fragrances: Can contain up to four thousand ingredients (including animal urine), many toxic or carcinogenic. Causes headaches, dizziness, allergic reactions, skin discoloration, violent coughing, vomiting, and skin irritation. Fragrances affect the nervous system, causing depression, hyperactivity, irritability, inability to cope and other behavioral changes. Shampoos, toothpastes, body washes, cleansers, baby products, wipes, hand washes, deodorants, lotions , creams, etc

Skin, Light and Regeneration

Skin loves to repair itself after sun. UV exposure uses up vitamin E, C and vitamin A in skin. [320,321,322,324,985,986,1122,1123] These vitamins absorb UV radiation protecting skin cells. [985]Wang found UV exposure if skin in real people (not in a petri dish) not only depleted vitamin A it reduced the mRNA and protein of the vitamin A receptors, RAR and RXR. You remember that these are two of the important nuclear receptors for regulation of cell growth. Wang suggests that sunlight causes a functional vitamin A deficiency that may have deleterious effect on skin function contributing to skin cancer and skin aging.[1124]

Adequate levels of vitamin A are important in cancer prevention, including skin cancers.[1125,1126] When the skin is exposed to UV-B or UV-A levels of vitamin A drop rapidly.[324,980,986] If the diet is low in vitamin A the inability of the body to replenish the skin's need may cause the skin to be more susceptible to UV damage and skin aging. Vitamin A is found in fatty foods including egg yolk (not the white), butter, cream, and animal or poultry livers.[1127]

All of these foods are dramatically reduced or avoided on the advice of nutritional experts in the current 'healthy' diet pyramid.

Let's assume nature intended us to get some sunlight. Before 1955 butter, cream, and whole milk, daily, and liver once a week were commonly served in many American homes. In 1909 the per capita intake of butter was 17 pounds per person per year. By 1945 this had dropped to 11 pounds per person per year and by 1970 a further drop to 5 pounds per person per year. Egg consumption has dropped from 309 eggs per person per year in 1970 to under 200 in 2000.

The current dietary recommendations are confusing as they seem to suggest vitamin A can be gotten from fruits and vegetables. Fruits and vegetables do not necessarily provide adequate vitamin A.

Nutritional guidelines suggesting carotenoids are equivalent to vitamin A are misleading.[938] Conversion of carotenoids to retinoic acid is not well understood and very little conversion takes place if the foods consumed are low in fat. Beta-carotene is fat soluble and requires fat to absorb whether from food or a supplement.[1128,1129,1130] While carotenoids play a role as anti-oxidant which may protect skin cells from lipid peroxidation[1131,1132], retinoic acid is essential to gene expression.

Omega-3 fatty acids are found in fish and protect the skin from UV damage, reducing the risk of non-melanoma skin cancers. Adding fish or fish oil to the diet improves skin health and reduces erythema when skin is exposed to sunlight.[1133] Omega-6 fatty acids as found in vegetable oils and margarine may increase the inflammatory response of human skin to sunlight and development of skin cancers.[898,1134]

Vitamins A, E and C can be used topically and are easily incorporated into home recipes. Home recipes are best because the key to all antioxidants is *freshness* which means they must be mixed and used up within a few days, few means less than 3. Once exposed to air oxidation is rapid. Don't keep mixtures longer than 7 days, ever. You may refrigerate them to protect the vitamins' potency but even with refrigeration don't make more than you will use in a few days.

If you decide to use vitamin A on your skin make sure it‘s retinol, as found in fish oil or sold dry as retinol palmitate. Beta-carotene may play a role in skin protection but studies indicate oral intake may be preferable to topical application and large doses don't work at all.[1135] You might mix a little vitamin A in extra virgin olive oil. (see below) Excess topical vitamin A may have internal complications. Don‘t overdo.

All suggestions here are for AFTER sun, never just before. Any antioxidant sitting on your skin will be rapidly oxidized by sunlight before being absorbed. Antioxidants work 'in' your skin, not on it.

Pigs and Light

In 1992 I read a study about pigs and UV light. My cousins are farmers and I grew up in the Midwest when farms still had animals not just corn and soybeans. I know something about pigs. Pink pigs get sunburned. Pink pigs in the tropics can get sunstroke and die. They used pink pigs in this study. The researchers put a dilute solution of l-ascorbic acid on a pig's skin and exposed the skin to different doses of UV-A and UV-B. From the abstract-

"Topical application of vitamin C has been shown to elevate significantly cutaneous levels of this vitamin in pigs, and this correlates with protection of the skin from *UV*B damage as measured by erythema and sunburn cell formation… Further, we provide evidence that the vitamin C levels of the skin can be severely depleted after *UV* irradiation, which would lower this organ's innate protective mechanism as well as leaving it at risk of impaired healing after photo induced damage. In addition, vitamin C protects porcine skin from *UV*A-mediated phototoxic reactions (P*UV*A) and therefore shows promise as a broad-spectrum photoprotectant"[1136]

The recipe is simple. Water, with a drop of pure rose oil or lavender oil if you like, and ascorbic acid powder available from a number of vitamin companies. The fine powder mixes more easily than the crystals. The ratio is 4 ounces of water to 2.5 level-measuring teaspoons of ascorbic acid (or a little less if your skin is sensitive). Spray all over once or twice a day and always spray again after sunning. The after is important. Don't spray before or during sunning, you'll turn orange from the unabsorbed vitamin C oxidizing on your skin.

How does it work? Your skin is oxygen intensive and vitamin C is critical to skin. UV (both UV-A and UV-B) exposure of your skin reduces cellular vitamin C, which is there to protect your DNA among other reasons. When you spray the solution on your face and body the ascorbic acid is absorbed into your skin and into the cells. Like melanin it quenches UV light. Numerous studies confirm the benefit of topical vitamin C.[1137,1138,1139,1140,1141,1142,1143,1144]

The ascorbic acid solution works because once absorbed it doesn't wash off like sunscreen. The vitamin C is incorporated into your skin cells. Other great news is that it doesn't block production of vitamin D either.

Taking extra vitamin C (orally) during summer months when you are sun exposed may also enhance skin/sun protection, but so far only mice have benefited. The likely protective dose is 2,000 mg. [1145,1146]

You need to spray twice a day for a minimum of 3 days before your first UV exposure. From that point on continue to spray just once a day and after sunning to keep your skin fully supplied.

Keep a spray bottle next to the shower. Towel dry and apply a light mist everywhere. Let it dry on your skin, don't wipe it off. Don't make it stronger and don't mix it with 'stuff'. It works just the way it is. People have tried to improve it by using other types of vitamin C or adding more ingredients. These very creative combinations never worked as well as the very simple original recipe and often caused irritation or in one case, using an ascorbate, reportedly even burned the skin.

Some vitamin C products used in skin care actually intensify UV damage. Ascorbyl palmitate is one of these.[1147] Don‘t use skin products that contain this form of vitamin C. Ascorbyl palmitate may actually increase UV-B damage to the skin.

Your skin likes to be ever so slightly acid so very dilute ascorbic acid works well. Don't vary the recipe, don't use another kind of vitamin C no matter what the experts tell you and don't keep it, the mixture, longer than 5 days. Vitamin C is very unstable in water. It begins to oxidize. Make new as you need it. Fresh, think fresh.

Ascorbic acid won‘t prevent sun damage when you expose yourself to more light than is genetically appropriate. It can help keep your skin younger as you grow older when combined with a diet appropriate for you and _wise sunning‘. Research shows it will also reverse sun damage.

If you aren't up for the spray there are other choices.

Extra virgin olive oil after sunning prevents cell damage. The three key words in the sentence are 'extra virgin' and 'after'. It must be extra virgin and applied after sun not before. [316,317] The researchers know this because they applied extra virgin olive oil to the skin of nude mice after exposing them to intense UV light and the mice were somewhat protected from developing skin cancers. Regular olive oil or any type of olive oil applied before UV exposure did not protect them. Mediterraneans have known this secret for a very long time.

Green tea or silymarin are protective too.[314,1148,1149,1150] The part of green tea being experimented with is (-)-epigallocatechin-3-gallate (EGCG). One study actually showed EGCG mixed in a culture with skin cells restored energy and renewed DNA.[1151] Expect to see it in skin care products in the future. This gives a whole new meaning to the trick of applying used tea bags to your closed eyes to get rid of dark circles and bagginess. We need super giant tea body bags for overall skin renewal (just kidding).

Silymarin, an extract from milk thistle is also showing promise as an anti-inflammatory and anti-oxidant when applied to the skin. Silymarin tested on mouse skin or in a culture with human skin cells helped cells repair damage from UV light. It has also shown some ability to prevent tumor growth, again in mice or culture.[1150,1152,1153,1154,1155]

We make new skin all the time, new cells rising from the epidermis to the surface and dropping off about every 30-40 days.[1156] Our skins need nutrients, whether exposed to UV or not, to be able to make new healthy skin. Vitamin A and zinc in the diet are important for healthy skin as are the B-complex vitamins.[1157,1158,1159] Of most importance is vitamin C. Skin is collagen. The key to healthy collage production and renewal is vitamin C.[1160,1161,1162,1163]

If you have very sensitive skin adding fatty fish or fish oil will improve your skin and protect from sun damage.[1133,1164] Extra fatty fish or fish oil is important for black skins that form keloids too.[1165] One study found omega-3 fatty acids (fish oil) may prevent the immunosuppression typical of excess UV-B exposure.[1166]

While sunlight is associated with skin cancers, clearly, so is nutritional insufficiency. An appropriate amount of sunlight with a diet of whole foods including, organ meats, fruits, vegetables and omega-3 fats makes good sense. A balanced diet includes quality protein; fish, meat, poultry; organ meats; eggs and dairy if you tolerate them; and lots of in season fruits and vegetables.

If you don't eat fresh venison, beef, or pork liver (liverwurst doesn‘t count) once a week, a multivitamin containing not more than 5,000 IU of retinol vitamin A and 15-30 mg of zinc (plus other essential nutrients) may help make your new skin healthy and happy. Venison, beef and pork livers contain significant amounts of vitamin A, zinc, copper, B vitamins, and even some D, all good for skin.

VITAMIN D IN OUR FOOD

Testing D in The Food Supply

There just isn't much D in food. If you look at the foods in the USDA National Nutrient Database vitamin D isn't listed. To test for vitamin D in a single food costs about $250. To test for vitamin C in a food costs about $60. Vitamin D is very potent in very small amounts. Testing is complex compared to many other nutrients. The government just doesn't do it. Even if testing were done the amount of D in food varies by location and season and/or supplementation, sound familiar? If animals are kept inside vitamin D supplements must be used. There is no regulation and amounts used, and the type of vitamin D supplemented, some supplement with 25(OH)D, is up to the individual producers.

Early experiments by Hess in 1923 found egg yolk cured rickets in rats. He and other researchers then proceeded to cure children of rickets by feeding one or two eggs a day. Hess had a source of outdoor chickens. I know this because they contained antirachitic factor. In the Journal of Biological Chemistry LXVI 1925 Hughes offered a paper on chickens and UV-B light. Kansas chickens, living about 39° N, were divided into four pens receiving sunlight in the yard plus 30 minutes treatment with a quartz mercury vapor lamp; sunlight through glass plus the lamp; outdoor sunlight and sunlight through glass alone. The eggs produced behind glass had no D (judged by the ability to cure rickets). The eggs behind glass plus the lamp and the outdoor eggs had some D; but the highest antirachitic power was in the eggs from outside chickens with an additional 30-minute UV-B light bath.

The amount of vitamin D in food is proportional to UV-B sunlight exposure or supplementation.

The poultry, dairy, pork and beef industry use vitamin D supplements. As excess D stores in fat and the industry uses varying types and amounts of vitamin D, we currently have no idea how much D is in our food. So until the powers that be think about this and do some testing foods that have some D might include the following.

Fatty fish contain D. Cold water fatty fish in locations without much UV-B contain high amounts. So do whales and seals but the D is in their fat. Eating the fat and skin of salmon gives more D than the flesh. Animal liver has some, but not much, as vitamin D is not stored in the liver as vitamin A is. Eggs of sunny southern chickens have D. Cow's milk has tiny amounts of D unless it is fortified, then it has about 100 IU/cup. In the chart below 100 grams is equal to about 3 ½ ounces.

Table 9 Vitamin D in Food

Cod Liver Oil, 1 teas.	450-500 IU
Swordfish, 100 grams	1,800 IU
Sardines 100 grams (can)	1,160-1,560 IU
Mackerel 100 grams	1,120 IU
Salmon 100 grams (can)	240-480 IU
Salmon 100 grams raw	160-560 IU
Herring 100 grams raw or canned	320 IU
Tuna raw Processing of tuna in the US removes all D in canned tuna.	288 IU
Eel, cooked, 100 grams	200 IU
Halibut 100 grams	40 IU
Shrimp 100 grams	160 IU
Oysters 3-4 medium	4 IU
Evaporated milk 2 T.	24 IU
Coffee cream 1 oz	16 IU
Milk, nonfat, reduced fat, and whole, vitamin D fortified, 1 c	98 IU
Margarine, fortified, 1 Tbs.	60 IU
Liver Beef, cooked, 3 1/2 oz Calf, 3 ½ oz. Chicken, 3 ½ oz	 8 IU 0-12 IU 46-68 IU
Egg, 1 whole (vitamin D is present in the yolk)	25 IU

Source: Fuller [1167]

What vitamin D there is in foods is found primarily in the fat portion.. Canned tuna doesn't have D because it has very little fat. To absorb vitamin D you need fat, even if you take supplements. Avoiding organ meats, animal and fish fat or the yolk of the egg reduces what little D we get from foods.

Supplementing D in the Food Supply

Supplementing the food supply began in England to prevent rickets. The fortification of milk and cereal was a disaster. Mildred Seelig, Adjunct Professor, Pharmacology, New York Medical College, published a review of excess D and cardiovascular, kidney and brain damage in infants and children.[1168] In 1954

physicians in England began seeing hypercalcemia in infants. (too much calcium in the blood) In addition to the D added to milk and cereal parents were giving infants and children cod liver oil or halibut liver oil. Combinations may have reached 3,000-4,000 IU of D a day. Fortification of foods with vitamin D began in 1945 and ended in 1957.

The years from 1945-1953 had increased incidence of renal acidosis, an early symptom of excess vitamin D. In 1954 this shifted to elevated calcium in the blood. In some children, when D was withdrawn, most of the symptoms reversed but not all. Arteries, kidneys, and other soft tissues were damaged by calcium deposits. These children experienced severe health problems, even death in some cases.

What came out of this disaster was recognition that we all have very different tolerances for vitamin D. Nothing has changed. We all have very different tolerances whether to sunlight and to vitamin D. Guessing is dangerous. (and dumb)

American food processors don't fortify with much D. They learned from the Brits that it could be dangerous. Dry cereals, infant formula and cereals, margarine and milk are about the only fortified foods. Fortified milk has rarely tested correctly. Usually the amount of D in milk is too low, under the required 100 IU but sometimes it too high.[889,1169,1170,1171] Fortification is still put forth as a solution to vitamin D deficiency here and in other parts of the world. It just doesn't seem like a very good idea. We are all different in what we need.

There is a move currently under way to reconsider fortification of foods with vitamin D. I consider this very bad science and worse public policy.

SAFE USE OF SUPPLEMENTS

High or Low Dose D?

In The Reverse Effect by Walter A. Herby, MediScience Publishers, 1998, Herby lists 4,921 references showing how often the symptoms of too little and too much of any given nutrient are similar. His advice regarding moderate supplement intake is well founded. His well-documented examples of excess are important reminders to consider the balance of nutrients. His book is a great addition to any health library. An example of the reverse effect, too much vitamin A, and too little vitamin A may cause dry skin. As you've read too little or too much D both seem to contribute to bone loss and heart disease.

A and D are particularly interesting because excess of one or the other may contribute to the reverse effect but also seems to create a relative deficiency of the limited vitamin. Previously mentioned high levels of vitamin A in foods or supplements may create a relative deficiency of D, which is the probable connection between vitamin A intake and increased osteoporosis. [951,955]

Cats or dogs fed liver too frequently or exclusively may suffer from hypervitaminosis A leading to bone and joint abnormalities.[951,1172,1173,1174,1175] Too much and too little vitamins A and D BOTH contribute to bone loss and it is likely the imbalance caused by excess of either would affect other conditions as well.

Supplemental D, Storage and Toxicity

Current medical treatment of vitamin D deficiency uses extremely high doses of D. This has caused some problems.[1176,1177,1178,1179] Clinicians seem to believe high chronic or intermittent doses are necessary to produce appropriate levels of 25(OH)D. The origination of this idea may have arisen from the work of several researchers including Stamp, Davies, Chel and Holick comparing sunlight to vitamin D. These studies are reviewed by Vieth.[53].

The various researchers determined how much 25(OH)D could be produced by a given UV-B exposure. They then gave varying doses of D over various periods of time to see what oral dose was needed to produce the equivalent rise in serum 25(OH)D. The researchers seemed to find 8,000-10,000 IU of D were the daily equivalent of sun exposure.

In Vieth's paper he reviews the doses of vitamin D used in past studies and found to be toxic, which according to accepted definitions means elevated calcium in the blood (elevated serum calcium). In these studies vitamin D, doses ranging from 20,000-600,000 IU, was given once, intermittently, or daily for different periods of

time. The cases of toxicity induced by supplementation produced 25(OH)D values that were extremely elevated reaching values as high as 682 ng/ml. These early studies using over supplementation, producing excess levels of D, are unhelpful, to the patients, and to our understanding vitamin D.

Stamp in 1977 and Davies in 1982 looked at UV light exposure, 25(OH)D and supplemental D. Supplementing with various amounts of vitamin D they looked for the dose that would create levels of 25(OH)D matching UV-B exposure. At the end of the study, however long it may have lasted, levels of 25(OH)D reached levels similar to the sun exposure.

The doses determined by Stamp and Davies were similar, 10,000 IU a day for 28-69 days. None of the study participants showed elevated serum calcium to indicate any toxicity. So far it seems to make sense. Compared to the early highly toxic doses of D these doses appear to be relatively moderate and are even called physiologic by the researchers comparing them to UV light exposure. Based somewhat on this data a number of ongoing studies are utilizing doses of 4,000-10,000 IU of D in research protocols. In completed studies using similar doses serum calcium has remained normal.

At the present time the determination has been made by some researchers that these doses do not result in toxicity and are safe. Long term studies as to what amount of D might be optimal are in progress. Unfortunately long-term studies, studies lasting 3 or more YEARS, are not available to us now.

None of the supplementation studies using the high 'moderate' doses, 2,000 IU or greater, have continued two or three years. Most last 3-6 months, 12 months at most.

The accepted definition of hypervitaminosis D among vitamin D researchers is not based on the level of 25(OH)D but the appearance of elevated serum calcium. As I have cautioned there is evidence that elevated 25(OH)D can, itself, cause damage to cells and tissues.[923,1005] I explained this in the section on hypervitaminosis D from the work of Holmes and Kummerow.

So why am I concerned about the seemingly moderate 'sunlight equivalent' doses of D?

I said understanding storage was really important. When we produce D on our skins it is very rapidly bound to D-binding protein, carried to the liver, and converted to 25(OH)D. When we take D orally from supplements or food something completely different happens.[1049] Vitamin D is fat-soluble. Taken in food or supplements it is absorbed from the gut wall into the lymph system bound to chylomicrons.

Chylomicrons are lipoproteins (fat-protein molecules) that travel from the gut through the lymph carrying things like cholesterol, vitamin A, beta-carotene and vitamin D to where ever they need to go. Some of the D we consume will rapidly transfer to D-binding protein but if the dose is excessive some may be carried to adipose tissue by chylomicrons.[923,1049] About 50% of oral D is bound to D-binding proteins, the rest carried by chylomicrons while 98% of skin produced D is protein bound.[793]

In the storage study high doses of D stored in fat. Brouwer and colleagues fed 1,500 IU of D (cholecalciferol) to rats for just 14 days. They continued to study the rats

for another 88 days. Serum cholecalciferol increased in all rats rapidly reaching a steady state. Fat storage of cholecalciferol and serum levels of 25(OH)D continued to rise for 1-2 days after the supplements were stopped. Half lives of D metabolites and fat stores were serum cholecalciferol 1.4 days; serum 25(OH)D 22.5 days; perirenal fat tissue 97.5 days and adipose tissue 80.9 days.

The study concludes oral vitamin D in high doses rapidly accumulates in fat stores. They fasted rats on days 14-17 and 98-101. As in earlier studies the fat stores of cholecalciferol released very slowly even under fasting conditions.

This process is protective as regards excess D in the serum but it is not an actual 'storage' mechanism releasing D when serum vitamin D drops, unless low serum D happens to be accompanied by fasting. Even under fasting conditions fatty acids are released in preference to cholecalciferol.

This process is very similar to the cycling of toxic chemicals into adipose tissue to protect the body.

GP: When we use supplements of oral vitamin D a large portion of the supplement is immediately diverted to fat storage. It is likely this diversion is even more prominent when high doses of D are used. The rat study lasted only 14 days. Studies using 4,000-10,000 IU of D have lasted less than a year. Continued excess will eventually fill fat stores and serum levels of both cholecalciferol and 25(OH)D will rise. Worse news the filled fat stores will make the job of reducing serum D precede at an excruciatingly slow pace. Studies suggesting oral vitamin D and sunlight dosing can be equivalent, as the studies were designed, are ignoring the evidence of very different metabolic pathways.

Earlier you read about an osteoporosis study using vitamin D and calcium that didn't improve bone mass.[389] Women were given calcium, 1450 mg daily and vitamin D, 400 IU daily or calcium, vitamin D and other nutrients or dietary instruction. Researchers then monitored bone mineral density, 25(OH)D, parathyroid hormone, osteocalcin, and several other markers of bone health over a three-year period.

I suggested in the section on bones the study may have failed because vitamin D levels in many of the participants never reached a level considered adequate by Heaney and others for bone health. But something very interesting did happen over the three years. 25(OH)D increased significantly. At the beginning of the trial only 7 subjects had a D value >30 ng/ml. At the end of three years 39 of 89 had values over 30 ng/ml.

Just 400 IU of D plus calcium or diet advice to increase calcium to 800-1450 mg. raised serum D 47% of participants to bone healthy levels in three years.

These subjects needed more than 400 IU or perhaps some sun. The amount of D in the study wasn't enough to maximize their D during most of the study period, but over time their D slowly rose to levels sufficient for bone. The vitamin D levels rose in the group using a diet emphasizing calcium as well as those taking vitamin D and calcium.

What this might be telling us:

Getting more calcium in our food or from supplements spares 25(OH)D by methods explained in the section on the vitamin D endocrine system.

Oral intake of vitamin D builds up over time. Slowly.

Just 400 IU of D with calcium may be insufficient for many people to raise 25(OH)D above 30ng/ml. as in this study.

Whether our need for D has increased because of sun avoidance has yet to be determined. It is possible the recommended 400 IU might be sufficient if people engaged in regular safe sunning. Only individual testing can confirm this for each individual.

Studies of large populations reduced to a mean won't give a clue to what will happen to you.

Testing and using moderate supplementation or sun suitable to our skin types should adequately supply our individual need for D, safely. But testing must continue over a minimum of three years to ensure both adequacy and safety.

A study of 2,589 postmenopausal women in 18 countries found 64% had 25(OH)D levels below 30 ng/ml.[1180]

Many of us don't get enough D or sunlight. We can sun at noon during the summer months and take a supplement of 400-800 IU of D or a little cod liver oil with adequate calcium, enough but not too much, in the darker parts of the year.

We are the GP, people not patients. Wise use of sunlight and D may help keep us both healthy and happy. For most Americans there is probably, yet to be determined, no need to take high doses of D, ever. If, over time, testing indicates a higher level of vitamin D is needed continued monitoring is important to help determine our individual needs.

There are diseases and conditions that require monitored supplementation or prescription D as a part of medical treatment. Enthusiastic over-supplementation has been discussed before so just a reminder here:

Persons experimenting with high oral dosing of D, 2,000-4,000 IU, have found 25(OH)D levels reach a plateau within the 'safe' range for some time, as long as 2 years, and then may rapidly elevate. Once this point is reached, even after eliminating vitamin D and sunlight, 25(OH)D drops extremely slowly, two cases taking more than a year to return to values under 70 ng/ml.

Serious consequences of taking 3,000 IU of vitamin D daily have occurred in just over one year with bone pain, bone loss, and general malaise with 25(OH)D reaching 110 ng/ml.

Supplements of 2,500-3,000 IU a day did not increase D beyond the upper limit, 60 ng/ml, in two family members until the third year of supplementation when values jumped rapidly to over 120 ng/ml.

For the record none of the individuals experiencing elevations of 25(OH)D tested with elevated serum calcium but all had elevated calcium in the urine. This is an important because some experts discount possible vitamin D excess as long as serum calcium remains normal.

Supplementing Vitamin D

Some of you will need just sunlight and food. Some will need a supplement, possibly ranging from 400-1,000 IU mixed with some sun. Testing is essential to determine what you have, what works, a supplement or sunlight and how this changes summer and winter.

It is my opinion after some 7+ years of experimentation and research use of vitamin D supplements should be kept to a minimum. For most people in the US sunlight is a better and safer source. If it is determined your levels of D are very low, <10 ng/ml, which is considered a clinical deficiency, you may need to enlist the help of your physician and use supplemental vitamin D for a few months eventually reducing your supplementation to the amounts that maintain your 25(OH)D above 40 ng/ml (but below 75 ng/ml).

Guidelines in a physician and patient protocol for supplementation are available from the website http://sunlightd.org.

If your test is between 30-40 ng/ml just increasing calcium, if your intake is low, or adding 400-800 IU to your regular daily diet/supplements may rapidly bring you above 40 ng/ml. If you have light skin use UV-B sun if available, you don't need supplements or supplements may only be needed during the dark months.

Once you have raised your D, if you are using supplements, it is likely you will need to reduce your dose. This is especially true if you initially used more than 1,000-2,000 IU daily to raise your D. Continuously check your 25(OH)D over several years, summer and winter, to see if your sunning or supplementation is enough to maintain year round values.

Information currently available seems to point to 40 ng/ml as an optimum test value for most people. Raising 25(OH)D higher than 40 ng/ml is not likely to increase any of the benefits of vitamin D. The 40-60 ng/ml range allows for higher summer values from sun.

If you raise your D to 60 ng/ml using supplements you will already be at the top of summer values. Going in the sun will further increase your D beyond the upper limit. Don't over shoot your goal. More is not better.

When vitamin D is consumed in food or supplements a significant portion of the dose is shifted to adipose tissue so vitamin D levels may rise slowly. Patience and consistency should provide you with ample D safely. Once you are within range consider skipping sunlight or vitamin D one or two days a week.

For persons with deep color: There is very little information on vitamin D supplementation or use of sunlight to produce vitamin D in people of color. Unless you live in Florida or south Texas a combination of sunlight and vitamin D will probably be necessary.

GP- The sunlightd.org website will have a place to report personal experiences and to get new information. If you cannot access the internet you can send a report of your results, to be included in the next edition of this book, to the address given in the Final Note to the GP.

Supplementing Calcium

Don't consider taking vitamin D without getting sufficient calcium from food, preferred, or supplements. The range of calcium is probably 600-1,200 mg. a day. The Garland's book The Calcium Connection Putnam Publishing Group, 1988, is still available and has great high calcium recipes. See how fast your hair and nails grow. They, your hair and nails, are both great indicators of your calcium and D status.

If you have a severe deficiency, are unsure of what you're doing, have any history of kidney disease or any other diagnosed disease relating to vitamin D or calcium do not try to supplement on your own. Get professional, knowledgeable help. If the healthcare professional you choose suggests high doses of vitamin D, 2,000 IU a day or greater, without frequent testing and monitoring, 'because they know it's safe', find someone else.

Nutrient Ranges (for healthy but low D adults)

Vitamin D and/or sunlight determined by testing.

Calcium- The long term effects of calcium supplementation and its interaction with vitamin D need research clarification. The tendency of some of us to hold on to calcium more than others, the problem of kidney stones, and the interesting relationship between calcium and D make the recommendations below very fuzzy.

Like vitamin D we all need calcium and like D it is probable our genes allow some of us to get by with less than others, or put another way, some of us tolerate higher doses better than others of us; some need more, others need less.

Think food first but do supplement, especially if you are under 29 years of age, to build good bone if dietary calcium is insufficient.

Table 10 Changing Recommendations- RDI and DRI

Age	Recommended Daily Intake 1995	Desirable Reference Intake 1999
Birth – 6 months	400 mg.	500 mg
6-12 months	600 mg.	500 mg until age 4
1-5 years	800 mg	4-8 yrs 800 mg
6-10 years	800-1,200 mg	9-18 yrs. 1,300 mg

Age	Recommended Daily Intake 1995	Desirable Reference Intake 1999
11-24 years	1,200-1,500 mg	
Women 25-50	1,000 mg.	age 19-50 yrs 1,000 mg
Women, pregnant or nursing	1,200-1,500 mg	under 19 1,300 mg 19-50 1,000 mg
Postmenopausal women on HRT	1,000 mg	1,000 mg
Men 25-65 years	1,000 mg	1,000 mg
Men and women over 65 years	1,500-2,000 mg	over 51 yrs. 1,200 mg.
Upper limit of safety	2,000 mg.	2,500 mg 1-over 65 yrs.

The National Institutes of Health Consensus Development Conference 1994 and Dietary Reference Intakes Executive Summary [1181]

Obviously ideas about calcium (and vitamin D) change over time. It's likely we have different needs and most of us aren't _norm'.

There are some questions about some genetic groups needing very little calcium. The altered metabolism in Hispanics, blacks, Inuits and other genetically similar groups may or may not be a concern. As these groups, in their ancestral locations with traditional foods, seemed to have had sufficient vitamin D combined with low calcium intakes, the possible interactions, such as what may happen when rapid excesses if both D and calcium are supplied, remain to be studied.

As the UL is 2,500 mg [1182] you may want to try different amounts and see what seems to work best for you. As with vitamin D, excess calcium, for you, is not beneficial. If you have unusual symptoms physical or psychological do try reducing your dose.

There are researchers who are concerned we may be taking too much calcium and this may contribute to kidney stones but suggest calcium taken with magnesium limits the risks.[565]

Signs to indicate adequate calcium intake include deep sleep, strong nails, normal bone density, fast growing hair and nails, and healthy teeth and gums. Calcium isn't the only nutrient that supports those things but it is a big part.

Dr. Heaney has been studying calcium for many years. Recently he looked at serum levels of 25(OH)D and calcium absorption. He concluded when serum 25(OH)D rose from 20 ng/ml to 35 ng/ml calcium absorption increased by 65%. This is a very big difference.[864]

Heaney looked at calcium absorption in 1990 by how much of a given dose was reflected in serum. Below are his calculations. At that time serum vitamin D was not considered so it is difficult to know what changes would be made to this table based D status. Assuming marginal D (low D has been around for quite a while) in subjects

completing the study below the single dose of 500 mg yielded 145 mg. The new study suggests serum 25(OH)D >34 ng/ml would increase this to 240 mg., almost double.

Table 11 Calcium Absorption

500 mg. calcium-one dose	29% absorption
500 mg. calcium-two doses (250 mg. each)	36% absorption
500 mg. calcium-3 doses (167 mg. each)	40% absorption
2,000 mg- one dose	14% absorption

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

Given Heaney's new data on vitamin D and absorption and his earlier work with divided doses we end up with a new questions yet to be addressed, 'Do higher levels of serum vitamin D alter the requirement for calcium?' We will have to wait for the research.

Smaller amounts of calcium taken more frequently are better absorbed. The amount is more important than the kind of calcium.[1183,1184] If food in not an available source of calcium for you the easiest way to take small amounts throughout the day is by finding and using a children's chewable calcium with magnesium. Find one that tastes good to you.

If you need a calcium supplement choose one that contains magnesium.[404,950,1185] Magnesium is important for teeth, bone and heart health, and helps protects the kidney from excess calcium and kidney stones.[950] A good calcium magnesium combination will have a ratio of calcium:magnesium 2:1.

There are an amazing number of calcium supplements with an even more amazing number of claims. The best calcium and magnesium is one you are able to chew or swallow that provides your daily calcium in increments, not all at once, that you are willing to take every day, and that you can afford.

Vitamin D_2 and Vitamin D_3

When you purchase a vitamin D supplement, or multiple with vitamin D in it, it is either ergocalciferol, which is vitamin D_2 or cholecalciferol, vitamin D_3. There are numerous arguments about whether these two substances are equal to one another. When I say numerous I am not exaggerating. Studying research you get the feeling that lots of information just makes things 'slipperier', not giving much firm ground.

The molecules D_2 and D_3 look different, they are different as they start from similar but not the same molecule, ergosterol and 7-dehydrocholesterol. When they begin traveling through the various pathways of our vitamin D endocrine system they can still be identified as different so that the chemical names are $25(OH)D_2$ or $25(OH)D_3$ and $1,25(OH)_2D_2$ or $1,25(OH)_2D_3$.

You've already learned D_3 is more biologically active in humans.[192] Vitamin supplements of D may be oil based, water based (emulsified), or dry. Over eight years of using D and testing 25(OH)D vitamin D_3 derived from fish liver oil consistently raised 25(OH)D to desired levels.

This is not to say the others won't work, they just didn't work with some people, sometimes. You'll have to test them for yourself. If they work for you, they work. Some will argue toxicity being greater with one type or the other. If you don't over supplement and test regularly there isn't a problem. They do all work in humans.

D_2 is natural. Vitamin D_2 is found in the pollen of the pine species.[1186] It is produced in any number of plants and fungi and consumed by grazing animals.[1187,1188,1189]

Not in any of the literature, but a common experience, is that the _hypo-allergenic' or _dry' vitamin D supplements do not work as well or at all to raise serum 25(OH)D in a significant number of persons. It was explained to me by a product formulator the base used to extract the D (drying agent holding the extracted D) may not release the D in your digestive tract. If you use one of these supplements and your D doesn't change consider using an oil based/derived product.

AND whether you use oil or dry based D make sure to always take it with a meal high in fat. Fat soluble vitamins need bile to absorb and fatty meals stimulate bile production.

Whatever brand or kind of D you choose, get a strength not greater than 1,000 IU. You can always take more if you need it.

Cod liver oil

Cod liver oil contains essential omega-3 fatty acids, vitamin A and vitamin D. The ratio of A to D is probably tolerable in moderate doses. Excessive doses of cod liver oil or newer cod liver oil concentrates must be a concern given our lack of understanding of just what the balance between these two nutrients, A and D, should be. Some cod liver oils have large amounts of vitamin A with little D likely making them a poor choice.

There are some persons who claim cod liver oil is natural and therefore not toxic at any dose. They are wrong. However natural a substance may be, too much is too much. Don't take high doses of D in any form unless specifically prescribed and monitored by a knowledgeable health care professional or you have garnered the knowledge needed to monitor yourself..

Other Nutrients for Health

This is a book on sunlight and vitamin D but as we are very complex systems and things _go together' a great diet will make your use of sunlight or vitamin D even more beneficial.

There are other important nutrients needed to keep us healthy. Your best source will always be whole foods. If you decide to supplement, DON"T over do. More is not better.

A complete multivitamin containing only natural folate and mineral typically will have all or most of the following nutrients and others in 2-8 capsules or tablets a day.

Vitamin A 3,000-5,000 IU

As yet the relationship between vitamins, A and D, are not well understood. The recommended level of vitamin A (not beta-carotene) is 3,000 IU and the upper limit is 10,000 IU. Just 5,000 IU has disturbed bone remodeling in persons who perhaps were D deficient.

Vitamin A can be supplied easily from food by eating liver once a week.

Calcium 400-1,200 mg and Magnesium 400-800 mg

Dark green leafy vegetables, nuts and seeds contain significant amounts of magnesium. So does chocolate, for the record, but this isn't a recommendation.

Iron if you don't eat red meat or liver, are under 35, are female pre-menopausal;

No iron if you eat red meat, liver and wild game; or if you have hemochromatosis.

Trace minerals

Boron, selenium, chromium, and other trace elements. Usually these are in a comprehensive multiple. A diet of whole foods with legumes, whole grains, leafy greens, fresh fruits and vegetables naturally contains trace elements. Dulse or other seaweeds are also excellent additions for trace minerals if tolerated.

Vitamin K 500-1000 mcg (micrograms) This is not potassium, the element K on the periodic chart. This is the vitamin K, which comes as $K_{1,}$ phylloquinone, and $K_{2,}$ menaquinone. German researchers believe the minimum dose is about 900 mcg., ten times the US recommended dietary allowance for bone and heart health.[1190] Vitamin K is a fat-soluble vitamin found in dark green leafy vegetables (and only absorbed if you put oil on your greens) and naturally fermented foods. [1191,1192,1193,1194,1195]

Kaneki, M. 2006 Clin.Calcium 16 1526-1534

[Protective effects of vitamin K against osteoporosis and its pleiotropic actions.]

Vitamin K is a nutrient originally identified as an essential factor for blood coagulation. Recently, vitamin K has emerged as a potential protector against osteoporosis and hepatocarcinoma. Accumulated evidence indicates that subclinical non-hemostatic vitamin K deficiency in extrahepatic tissues, particularly in bone, exists widely in the otherwise healthy adult population. Both vitamin K(1) and K(2) have been shown to exert protective effects against osteoporosis. Moreover, therapeutic potential of vitamin K(2) as an anti-hepatoma drug has been recently highlighted. Most of the new biological functions of vitamin K in bone and hepatoma cells are considered to be attributable to promotion of gamma-carboxylation of glutamic acid residues in vitamin K-dependent proteins, which is shared by both vitamins K(1) and K(2). In contrast, vitamin K(2)-specific, gamma-carboxylation-unrelated functions have also been demonstrated. These functions include stimulation of steroid and xenobiotic receptor (SXR) -mediated transcription and anti-oxidant property. Thus, biological differences between vitamins K(1) and K(2), and a potential involvement of gamma-carboxylation-independent actions in the new roles of vitamin K remain open issues. Molecular bases of coagulation-unrelated pleiotropic actions of vitamin K and its implications in human health deserve further investigations.

Vitamin K, like A, D, E and beta-carotene is fat-soluble and must be consumed with fat. Quality full fat yogurt should contain vitamin K but we don't test for it so it's impossible to know. The Japanese get vitamin K from natto a traditional fermented soy product.[1196] Dark green vegetables have vitamin K but you won't absorb it if you don't eat it with butter or olive oil.[1197] Other sources include liver, butter, and egg yolk.

Exception: People on Coumadin, an anticoagulant, may need to avoid vitamin K unless instructed by their physician though it is now thought K may actually be needed when using Coumadin.[1198,1199,1200]

Vitamin C 1,000-2,000 mg

Vitamin C plays a role in building bone.[420] Tissue (skin) saturation with vitamin C may be UV-B skin protective and definitely keeps skin younger longer. What may not be known by most is that vitamin C is absolutely necessary for the conversion of D2 and D3 to 25(OH)D and further to 1,25(OH)2D[1201,1202,1203,1204] The amount of vitamin C needed daily that seems to assure tissue saturation is 2,000 mg.[1205]

The B vitamins 3-25 mg

Food sources are liver and nutritional yeast.

Folic Acid (methylfolate) and vitamin B-12 special members of the B-complex that may help prevent heart disease. Make sure folic acid is methylfolate. Do NOT use synthetic folic acid found in most supplements and all fortified foods.

Folic Acid as methylfolate or food source 400-800 mcg In liver, nutritional yeast, and dark green leafy vegetables

B-12 500-1,000 mcg. in liver, red meat or egg yolk.

Zinc, other essential minerals and trace elements are important, for building good bones and teeth and for supporting your immune system. Some of all of them should be present in a good multiple. Some of all of them should be present in your food.

Potassium is very important, for bones, muscles, including your heart and to prevent stroke[1206,1207,1208] The best (and safest) source of potassium is always food. Foods high in potassium provide numerous other nutrients that are good for you. Some high potassium foods include orange juice not from concentrate, tomatoes, potatoes with the skin, avocado, and most fruits and vegetables in their whole state. If you steam the veggies the potassium will escape so be sure to incorporate the 'juice'.

Think of these recommendations as a smorgasbord of nutrients providing optimal nutrition to support health while sunning; a smattering of everything, not too much of any one thing.

IT'S BEST TO GET YOUR NUTRIENTS FROM WHOLE REAL FOOD.

It‘s best to get D from the sun.

CHAPTER 9 SAFE D FROM SAFE SUN

Mad dogs and Englishmen go out in the midday sun
The Japanese don't care to, the Chinese wouldn't dare to
Hindus and Argentines sleep firmly from twelve to one
But Englishmen
Detest a Siesta.
Noël Coward (1899–1973), British poet

Safe sun means getting the minimum amount of sun needed to produce your daily D and sun avoidance when insufficient UV-B is present. You'll need to learn what works for you and stick to it. More is not better. The Goldilocks' Principle: Not too much, not too little, just right, for you.

SUNLIGHT

If sun burning always occurs at any exposure level; you are taking a medication causing sun sensitivity; you have a disease aggravated by sunlight; or there has been a prior incidence of skin cancer do not use sunlight to maintain Vitamin D. Use an appropriate vitamin D supplement. Test frequently for the first 3 years.

The Rules

Never expose your skin for longer than needed to produce vitamin D.

Make sure UV-B is present at an intensity that allows rapid production of D without skin damage before you sun.

Use clothing or a total sunblock when spending time in the sun beyond D production.

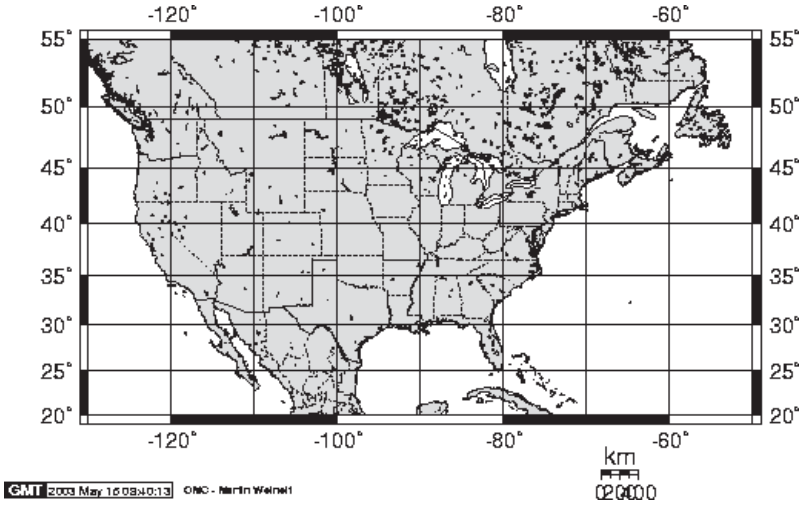
Determine by testing how many 'sun' days a week will maintain your D and keep to the minimum number of days.

See what your 25(OH)D is at end of summer, September, and test during mid-winter to make sure your levels haven't dropped below 35 ng/ml

To use sunlight in lieu of supplementation refer to the skin exposure guide. The guide provides an estimate of the time needed to produce optimal levels of D. These exposure times are probably sufficient for most persons but remember they are calculated on a UV Index that may not reflect actual intensity.

There is never a reason to sun longer than necessary to produce vitamin D.

The guide applies in seasons, latitudes, and altitudes of UV-B production. Please see the latitude and altitude information for UV-B levels or consider a UV-B meter such as Solartech's UV-B Solarmeter®, in the source list at the end of this book. Remember, UV-B does not penetrate glass, smog, fog, some haze, or clouds. UV-B does penetrate water so swimming when UV-B is present counts.



The map shows U.S. latitudes in 5°increments. Latitudes above 30° have insufficient UV-B 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-B sunlight any month of the year, including summer months. These locations depend on dietary sources of vitamin D. Traditional diets would have contained foods providing vitamin D historically but modern diets are likely profoundly insufficient.

Studies show exposure at latitudes 30°-45° may provide optimal amounts of D *for persons with light skin* if exposure is midday, scant clothing, during summer months. [98]

Supplements of D may be necessary in winter unless you migrate south like the birds or make a tropic vacation a mainstay. Your vacation would need to last more than a week. It is probable 3-8 weeks, depending on where you go and your skin type, of carefully calibrated sunning could boost winter levels of D. The time needed to produce daily D in tropical sun would be very short, just minutes in light skin, indicating a need for clothing, shade and/or waterproof sunblock when not sunning for D.

Altitude compensates for degrees of latitude. Each 1,000 ft above sea level increases UV-B by about 8-10%, the equivalent of traveling 60-70 miles, about 1 latitudinal degree, closer to the equator and shortens the time needed to produce vitamin D (and skin damage). Skiing in Vail, Colorado, about 39 degrees north and 8,300 feet in altitude would likely have a UV-B reading similar to Austin, TX., 30 degrees south at an altitude of 500 feet.

As skiers spending time in high altitudes know, high mountain locations shorten the time needed to damage skin.[1209,1210] Part of the greater risk for damage is attributable to the fact that snow greatly intensifies existing UV-B and UV-A. Fresh snow may reflect as much as 94 percent of incoming radiation while snow free land typically reflects about 2-4 percent and ocean surfaces about 5-8 percent.

Knowing your latitude and altitude will help you determine sun exposure. There is an individual dose but only you can determine what that is. Monitor your skin carefully to see how you respond at any given season and location. Over your first summer you will get a good idea of how much sunlight you need to provide optimal D and avoid sun damage.

If you decide to use sun to get D, it is best not to supplement in sunning months. If you continue to use a supplement of D and sun make sure to take that into consideration when you test your end of summer 25(OH)D value.

Skin pigmentation in the lower latitudes generally is darker, allowing for and actually requiring longer exposures to higher intensity UV light. [1156] Persons of Caucasian or Asian heritage, skin Type 1 or 2, need only short periods of daily exposure to benefit from UV-B, 10-30 minutes midday. Clothing and sun avoidance are appropriate when living in latitudes lower than that of your ancestors.

GP If you have light skin get a little midday sun over lots of your body in the warm season. If you have moved closer to the equator than your ancestors alter your behavior and cover up.

Persons of color, i.e., skin type 5 or 6 on the chart, need longer exposure times in higher latitudes (latitude not altitude). Blacks in the U.S. in northern locations or in cities with summer smog may find it impossible to get adequate D from sunlight during any season. [97] Studies show rickets, extreme D deficiency, in Texas, latitude near 30°, in children of African-American and Hispanic origin. [18] Little research has been done regarding dark skins and response to sunlight in the U.S. You will be your own experiment.

UV-B Exposure Guidelines

To get your optimal daily dose of D from sunlight without damaging your skin 70-80% of your skin's surface must be exposed for the length of time equal to the 'pre-erythemal' (before pinkening) dose. This means exposing your skin to midday sun until just before you would experience any changes in skin color (for most of us this is usually pinkness). This 'time before' is somewhat difficult to determine at first. The time needed to reach this dose depends on your skin's color. The chart is a guide. Less is more. This is NOT about tanning.

You may make the mistake of staying too long. If your skin changes color even hours later you overstayed your sunbath. Don't make this mistake often or you will most certainly contribute to skin damage and later skin problems ranging from premature aging to skin cancers. There is no need, *ever*, to tan or produce even a slight change in skin color to get enough UV-B to make D.

For vitamin D to be produced skin exposure must take place when UV-B is present in adequate amounts. This is between 10AM and 2PM during the summer for most of the United States, on cloud and smog free days. Near noon is best. Before 10AM or after 2PM you will get the full brunt of UV-A with minimal UV-B and may experience burning yet produce very little vitamin D.

The more intense the UV-B the less time needed to maximize D production. This is a good thing. It means that if you live in very sunny places like Florida or South Texas you can make lots of D without overexposing your skin most months of the year. In other locations this limits exposure to summer months.

Table 12 UV Index

What does the UV Index mean to me? (Type II light, untanned skin)		
UV Index Midday	Category	Erythema Time
over 9	extreme	less than 15 minutes
7-9	high	about 20 minutes
4-7	medium	about 30 minutes
0-4	low	more than 1 hour
This does not evaluate D production, but gives an approximate _time to skin damage‘ value. When the UV index is over 9, UV-B is extremely strong, producing erythema in type 2 skins in less than 15 minutes. Type 1 skins may need full sun avoidance or as little as 2-10 minutes. Minutes for Types 3 –6 multiply your Type # times UV # minutes. Example: Type 6 X (UV 7) 20 minutes=120 minutes		

For type 1-3 skins sunbathing near noon in temperate zones during summer months will assure enough UV-B to produce D before burning occurs. For skin types 4-

6 UV-B intensity, or lack of it in U.S. latitudes, makes getting D more difficult. For dark skins many parts of the U.S. may not provide adequate UV-B to optimize D at any time of the day or year. Let me know at the website how you fare.

The suggestions and charts are _fuzzy' guides to personal discovery. They are all ESTIMATES and must be proven to be true or not true in your body in your location. Don't blame the chart if you stay too long and get pink. You are learning your individual need and tolerance for UV-B light.

Table 13 Skin Type and D Production

Skin Type	Time Needed for Daily D Production All calculations are for UV Index 8-10
Type 1- Always burns easily, never tans, extremely sun-sensitive skin. Examples: Red-haired, freckles, Celtic, Irish-Scots.	5-7 minutes per side, 10 minutes full body at UV Index 9-10, above 10 less time is needed.
Type 2- Always burns easily, tans minimally, very sun-sensitive skin. Examples: Fair-skinned, fair haired, blue-eyed, Caucasians	10-15 minutes per side, Approx. 20 minutes full body at UV Index 9-10, above 10 less time is needed.
Type 3- Sometimes burns, tans gradually to light brown, sun-sensitive skin. Examples: Darker Caucasians	15-25 minutes per side, 30 minutes full body at UV Index 9-10, above 10 less time is needed.
Type 4- Burns minimally, always tans to moderate brown, minimally sun-sensitive. Examples: Mediterranean type olive skins.	30 minutes per side, 60 minutes full body at UV Index 9-10, above 10 less time is needed.
Type 5- Rarely burns, tans well, sun-insensitive skin. Examples: Middle Eastern, some Hispanics, some Blacks	45 minutes per side, 90 minutes full body at UV Index 9-10, above 10 less time is needed.
Type 6- Never burns, deeply pigmented, sun-insensitive skin. Example: Blacks	60 minutes per side, 120 minutes full body at UV Index 9-10, above 10 less time is needed.

A note about the UV Index- The weather service puts out daily bulletins estimating the UV intensity. Go to http://iwin.nws.noaa.gov/iwin/us/ultraviolet.html.

GP: The difficulty using these ratings is that they do not actually look at the local UV-B but estimate from 'sources' so local clouds or fog or smog may alter how much UV-B is actually available. The UV Index also includes shorter waves of UV-A, which contribute to erythema but don't produce vitamin D.

.

Table 14 Sunning for D with the UV Index

UV Index Check your local paper or online.	Sun Exposure Levels Skin Type 2 Time is for midday exposure Skin Type 1 deduct minutes Skin Types 3 & 4 add minutes	Skin Correction for Skin Types 5-6
0 - 2 (Minimal)	An Index reading of 0 - 2 indicates minimal danger from the sun's UV radiation for the average (Type 2) person. You won't burn. You won't make any D.	No D
3 - 4 (Low) -	An index reading of 3 -4 indicates low risk of harm to the skin from the sun's radiation. It's unlikely you would burn. You won't make D.	No D
5 -6 (Moderate)	An index reading of 5 - 6 indicates some risk of skin damage if exposure continued for hours. At this intensity erythema would occur before adequate D production.	No D
7 -9 (High)	An index reading of 7 - 9 indicates high risk of harm from unprotected exposure to the sun. Time in the sun should be limited during midday (10:00 A.M. - 4:00 P.M.) as skin may burn in as little as 13 - 20 minutes. Enough D would be generated in 10-15 minutes (before burning) in Type 1 or 2 skins	Some D with 60-90 minutes exposure.
10+ (Very High)	An index reading of 10 indicates very high risk of harm from unprotected sun exposure. Between 10:00 A.M. and 4:00 P.M. the length of time to burn may be less than 10 minutes without protection. Enough D would be generated in 5-10 minutes (before erythema) in Type 1 and 2 skins	Some D with 45-60 minutes exposure.
11+ (The Tropics)	Burning is the rule for Type 1 and 2. Clothing and a hat will allow enough incidental UV-B to produce D. Remember the rule- NO pinkening.	Lots of D.

The instructions above, followed carefully, provide the maximum and optimal UV exposure and production of vitamin D. You never need to remain in UV light long enough to damage your skin. Whether this will provide you with all the D you need must be determined by testing your response. Remember that testing is critical. We are all different and our responses, to sunlight or supplements, are unique.

Tropical sun cannot be judged by these values. Remember, only 'mad dogs and Englishmen go out in the noon day sun' *in the tropics*. As little as a few minutes, almost any time of the day, may be needed to produce D in tropical locations in persons with very light skin. More exposure begins damaging skin.

The UV Index: Typical summer midday values	
Location	UV Index
Tropics-Hawaii	13 (extreme)
TX-Florida-Southern California-AZ	10 (extreme)
Washington, D.C.	9 (high)
Massachusetts-NY-Indiana-Wisconsin	9 (high)
Dakotas-Oregon-Maine	8 (high)
Washington State (no clouds or fog)	7 (moderate)
Alaska	5 (moderate)

North Pole	2.3 (low)
The closer to the equator, the higher the UV index; the closer to noon the higher the UVI; the closer to the sun (altitude) the higher the UVI; the closer to June 21 (northern hemisphere) the higher the UVI. Actually all of these variations put us closer to the sun.	

Intentional summer sunning and supplementation should not be mixed and may cause problems, resulting from excess D. When your D is at the upper ranges, 60 ng/ml or more, just a few days in summer sun can rapidly elevate 25(OH)D beyond 70 ng/ml. In supplement trials a number of participants' 25(OH)D levels exceeded high normal values when combining D supplementation and summer sunlight.

A few have found sunlight alters their need for supplementing D very little. This may be because the supplement being used is of low potency, their skin because of age is unable to produce significant D, or their vitamin D endocrine system effectively removes D at a rapid rate.

TEST. This is particularly important in the U.S. where during much of the year, in many locations, UV-B is not present in amounts able to produce D before burning. Depending on latitude sufficient UV-B may be absent 2-3 months each year in San Diego and other cities of similar latitudes to as many as 8 months in Portland, OR, upstate New York, and other locations at higher latitudes or with significant year round cloud cover. While San Diego does have UV-B year round the amount, and therefore vitamin D production, is reduced significantly in mid-winter months and by air pollution during the summer.

The exact amount of sun needed to optimize *your* D won't be determined by a formula. Many and various genes related to vitamin D response, regulate the need for D and response to sunlight. Vitamin D receptor polymorphisms, D-binding proteins, and other genetic variations make a ‗formula' insufficient for our personal needs. The genetic regulators of the vitamin D endocrine system are just beginning to be studied and as yet are poorly understood.[1211]

Tanning Beds or Sunlamps?

Holick and others have studied the use of tanning beds as a source of D.[1212,1213] You can get significant amounts of UV-B from tanning beds and this UV-B does produce vitamin D. How much D would depend on the lights, your skin, and the time spent 'tanning'.

Dermatologists use very strong UV-B and UV-A lights. These lights are licensed medical devices prescribed to treat various skin disorders including psoriasis. Such devices are stringently regulated and only available to licensed physicians. Even though these devices are medical and prescriptive the wisdom of the massive doses seems questionable to me.

I mentioned in the section on excess D, a man receiving narrowband UV-B treatments developed 25(OH)D levels above 120 ng/ml. As some dermatologists have admitted seeing a similar response in other patients, clearly, high levels of D are being produced by treatment with these narrowband UV-B lights. I have yet to see a dermatologist report this in any of the journals and it seems no monitoring of vitamin D, urine or serum calcium is being done in those patients prescribed the UV-B treatments.

These light exposures, both UV-B and PUVA may produce increased cancer incidence in treated patients over time.
(1214,1214,1215,1216,1217,1218,1219,1220,1221,1222,1223,1224,1225,1226)

I find myself wondering about dermatologists. They are the most adamant about the necessity of avoiding sunlight and always using sunscreen and yet prescribe pure UV-A and narrowband UV-B and some really toxic chemicals to treat skin conditions. None that I know of have yet addressed the possible issues of elevated levels of vitamin D from narrowband UV-B therapy.

What is clear is that UV-B lights do produce D in human skin (and according to the ‗naked' section of this book some other interesting things as well). So why not advertise, ‗Get your D here'?

Tanning salons can't say their beds contribute to vitamin D production, at least not in writing. To make a claim about a treatment, such as labeling calcium as able to protect bones, your claim must pass approval of the FDA. Claims for devices also fall under the purview of the FDA. If operators of tanning salons advertised their tanning beds as providing vitamin D it would put tanning beds in the category of medical devices or place salon operators in the position of 'practicing medicine without a license'.

There are a number of other difficulties.

- Tanning beds have varying amounts of UV-B and this amount changes over time as the tanning bed lights age making tanning beds slightly less efficient in producing D. Excess UV-B damages human skin.
- Tanning beds produce UV-A, often advertised as the tanning ray, which may contribute to melanoma and other skin damage such as aging.(1012,1227)
- In a single study tanning beds did raise D but also caused erythema which indicates sun damage.(1212)

There are specific situations when using a tanning bed may be helpful. Tanning salons have helped people with psoriasis.(1228) A woman with Crohn's disease restored levels of D using a tanning bed.(1213) Treatment consisted of 10 minutes exposure 3 times a week wearing a one piece bathing suit. Four weeks of treatment increased her 25(OH)D from 7 ng/ml to 32 ng/ml.

Tanning beds may be effective if used carefully, not to tan, but to get D, perhaps in locations where there isn't much sun or during winter months in other

locations. There is the benefit/risk problem. Whether using a tanning bed or sunlight, monitoring your dose of light and level of D will provide you with valid information about your personal response. You can then use this information throughout your life to maintain your D.

I am not promoting tanning beds. I definitely am not promoting tanning since tanning (or any other excess exposure to UV light) reduces vitamin D.[1229]

The intensity of these beds gives ample opportunity for unwitting abuse. There is a temptation to stay too long in the warm bright light, especially in cold, dark, winter months. If you decide to try a tanning bed for D the lamps used may contain from 2-8% UV-B. The higher the UV-B the shorter your stay but no matter what the type of light DON'T' STAY LONG. Never stay long enough to develop erythema and remember even dark skins may suffer damage from UV light.

(Refresher definition)

> *erythema, def. abnormal redness of the skin resulting from dilation of blood vessels (as in sunburn or inflammation). Erythema may occur during or up to 12 hours following UV exposure.*

Determining what works for you is your job. Just be careful. If you have light skin, especially if your skin has yellow/red undertones, excess UV of any kind must be avoided. Use extreme care whether you are bathing your skin in sunlight, tanning bed light or a home tanning light. That _tanning' in the name is a danger. You don't want to tan, you really don't.

I am NOT promoting the use of sun beds or sun lamps or long stays in summer or tropical sunlight. I am attempting to give factual information on what is needed to produce your own vitamin D.

Home sunlamps made by Sperti have been around for many years and also may be used to produce vitamin D. Older models still sell rapidly on ebay. These small lamps are similar to the lamps used by early researchers and produce intense UV-B light. To generate vitamin D requires placing your skin about 14-15 inches from the light source for some 5-7 minutes (light skin). These lamps will produce erythema and caution is advised. These lamps have an automatic timer to prevent overuse but must still be suggested only with great caution. The Sperti website has information about these lamps and D production. http://www.sperti.com

Photosensitizing Medications-Avoid UV Light (Sun Or Simulated)

Acne Medications
Accutane (Isotretinoin)
Retin-A (Tretinoin)

Antibacterials
Halogenated carbanilides
Halogenated phenols (antibacterials in deodorant bar soaps, antiseptics and cosmetics)
Halogenated salicylanilide
Nalidixic acid
Sulfamethoxazole

Sulfonamides (including Sulfamethoxazole, Sulfisoxazole, Trisulfapyridines)
Trimethoprim

Antibiotics
Achromycin (Tetracycline)
Azulfidine (Sulfasalazine)
Batrim (Sulfamethoxazole-trimethoprim)
Cinobac (Cinoxacin)
Declomycin (Demeclocycline)
Fansidar (Sulfadoxine-pyrimethamine)
Fulvicin-U/F (Griseofulvin)
Gantanol (Sulfamethoxazole)
Gantrisin (Sulfisoxazole)
Minocin (Tetracycline, Minocycline)

NegGram (Nalidixic Acid)

Neotrizine (Sulfacytine)
Renoquid (Sulfacytine)
Rondomycin (Methacycline)
Septra (Sulfamethoxazole-trimethoprim)

Terramycin (Oxytetracycline)
Tetracycline
Thiosulfil (Sulfamethizole)
Vibramycin (Doxycycline)

Anticancer drugs
DTIC-Dome (Dacarbazine)
Efudex (Fluorouracil)
Fluoroplex (Fluorouracil)
Matulane (Procarbazine)
Mexate (Methotrexate)
Velban (Vinblastine)

Antidepressants
Adapin (Doxepin)
Asendin (Amoxapine)
Aventyl HCL (Nortriptyline)
Elavil (Amitriptyline)
Ludiomil (Maprotiline)
Marplan (Isocarboxazid)
Norpramin (Desipramine)
Pamelor (Nortriptyline)
Pertofrane (Desipramine)
Sinequan (Doxepin)
Surmontil (Trimapramine)
Tofranil (Imipramine)
Vivactil (Protriptyline)

Antihistamines
Benadryl, Benylin (Diphenhydramine)
Dimetane (Brompheniramine)
Periactin (Cyproheptadine)

Anti-Inflammatory drugs
Advil, Motrin (Ibuprofen)
Butazolidin (Phenylbutazone)
Clinoril (Sulindac)
Feldene (Piroxicam)
Naprosyn (Naproxen)
Orudis (Ketoprofen)
Rinadyl (Carprofen)

Antiparasitics
Bitin (Bithionol)
Povan (Pyrvinium pamoate)
Quinine

Antipsychotic drugs/Tranquilizers
Compazine (Prochlorperazine)
Haldol (Haloperidol)
Mellaril (Thioridazine)
Navane (Thiothixene)
Permitil (Fluphenazine)
Prolixin (Fluphenazine)
Quide (Piperacetazine)
Stelazine (Trifluoperazine)
Temaril (Trimeprazine)
Teractan (Chlorprothixine)
Thorazine (Chlorpromazine)
Trilafon (Perphenazine)
Vesprin (Triflupromazine)
Antiseizure drugs
Dilantin (Phenytoin)
Paradione (Paramethadione)

Tridione (Trimethadione)

Diuretics
Anhydron (Cyclothiazide)
Aquatensen (Methyclothiazide)
Diamox (Acetazolamide)
Diucardin (Hydroflumethiazide)
Diuril (Chlorothiazide)
Enduron (Methyclothiazide)
Exna (Benzthiazide)
HydroDIURIL (Hydrochlorothiazide)
Hydromox (Quinethazone)
Lasix (Furosemide)
Metahydrin (Trichlormethiazide)
Midamor (Amiloride)
Naturetin (Bendroflumethiazide)
Renese (Polythiazide)
Zaroxolyn (Metolazone)

Hypoglycemics (diabetes)
Diabeta (Glyburide)
Diabinese (Chlorpropamide)
Dymelor (Acetohexamide)
Glucotrol (Glipizide)
Insulase (Chlorpropamide)
Micronase (Glyburide)
Orinase (Tolbutamide)
Tolinase (Tolazamide)

Psoralens
8-Methoxypsoralen
Oxsoralen
Trisoralen

Other Substances
Alpha-hydroxy-Acid (AHA facial peel)
Americaine (Benzocain)
Aralen (Chloroquine Hydrochloride)
Capoten (Captopril)
Cordarone (Amiodarone)
Diethylstilbestrol
Dermoplast (Benzocaine)
Gold salts (Myochrysine, Solganol)
Glycolic acid (facial peel)
Librium (Chlordiazepoxide)
Musk ambrette (in perfumes)
Norpace (Disopyramide)
Oils of bergamot, citron, lavender, lemon, lime, rosemary, sandalwood, cedar and must ambrette (in perfumes and cosmetics)
Oral contraceptives (Estrogen)
PABA (Para-aminobenzoic acid)
Phenergan (Promethazine)
pHisoHex (Hexachlorphene)
Quinidine sulfate and gluconate
Solarcaine (Benzocaine)
Tattoos (Cadmium sulfide)
6-methylcoumarin (in perfumes, shaving lotions, sunscreens)

Photosensitivity puts your skin at risk for sun damage. If you aren‘t sure about a medication or cosmetic, check with your pharmacist. Following acid based facial peels, natural or chemical, a full 7 days must pass before the skin is able to recover its surface and its levels of naturally occurring anti-oxidants so you‘ll be safe in the sun.[1230] If your cosmetics contain these acids (and you use them daily) your skin never recovers its protective outer layer and you must use the strongest sunscreen and/or avoid any sun exposure to your face to protect your skin.

Review and Check List- Just in case you feel more confused than ever.

The simplest way to get D:

- In summer take advantage of midday sun but never longer than needed to make your D.

- Eat foods that contain D, eggs from sunny chickens, fish with the fat and skin, liver on occasion.
- In winter, in the middle and northern states, supplement moderately, not more than 1,000 IU of D daily and check your D in the early spring. If you are at the low end of 40-60 ng/ml you are just right for the season and not too high to begin sunning again in March or April. Rarely some may need 2,000-3,000 IU in winter.
- Stop supplementing D when the UV Index in your area regularly reaches levels greater than 7 if you are intentionally sunning. It is likely 400 IU of D would have little effect on sunlight plus D totals so a multiple with this amount is of no concern.

Exceptions:

- Tropical vacations! REMEMBER: If you are lucky enough to migrate closer to the equator in winter the rules change. Only 'mad dogs and Englishmen go out in the noon day sun' in the tropics. Be wise on any tropical holiday. If you have light skin sun mid-morning or late afternoon. Keep it brief.
- Darker skins may need to supplement year round depending on your current latitude and lifestyle. As you experiment contact me through the website http://sunlightd.org and I will post what you discover. Don't forget to get your daily calcium and magnesium, from food (preferred) or, if necessary, supplements.
- Very light skinned persons or those who must completely avoid UV light because of genetic, medical or medication contraindications. This group would include some of who have history of multiple skin cancers. You know who you are. You really will need someone to help you figure out year round supplementing.

It is my expectation 800-1000 IU of vitamin D with a minimum of 600-800 mg calcium and 300-400 mg magnesium (preferably from your diet) will work for most people in these groups without complications. Check with your physician. Even though he or she may not know about D (buy them this book or the physician protocol) they can order testing to help you monitor to ensure you get enough and not too much.

What about my kids?

Moderate sunning works for infants and children too. The rules are the same, midday, NO erythema. Pediatricians may become apoplectic when hearing this advice but if this happens ask them what they intend to do about vitamin D. Given the huge variables a Recommended Daily Allowance just won‘t do. And giving a standard dose without regular testing is never wise.

Supplements for children in the darker months or when avoiding sun are probably 400-500 IU but could be higher. Some view 1,000 IU appropriate for even very young children. There is just no solid information for children at this time. Studies with infants and children have only considered rickets as a marker of D sufficiency.

Do not give a dose of vitamin D greater than 400-500 IU daily over an extended period of time without working closely with a physician interested in this work willing to test. There are no immediate, obvious symptoms of too much D. Home testing, a

finger prick, is available from http://www.bloodtestathome.com/vitamin_D_test.html Optimal 25(OH)D is the same for children or adults 40-60 ng/ml.

Children need a nutrient dense diet; UN-processed (real) foods. These are the years your child will build a life time of bone and strong, straight, cavity free teeth. Real meat, fish, poultry, eggs and dairy if tolerated with lots of fresh fruits and vegetables are the core components. Whole food including fresh fruits and vegetables are absolute necessities for your child's health.

So is the sun.

If your child is dairy intolerant get and use a children's chewable calcium with magnesium. Look for one that tastes good and has about twice as much calcium as magnesium in each chewable tablet. You and your child can share it.

Testing Protocol for Sunlight and Vitamin D:

Everyone should have a yearly vitamin D test. If you are taking vitamin D currently, continue (but don‘t take any supplements the day before and morning of your test).

When evaluating your test consider any supplementation or regular sun exposure, ie. My D is _____ when I take _____IU of D daily and/or I spend _____ time in the sun.

Figuring out how much sun and D and how they work in combination may take a year or two but it is an important investment in your long term health. It is appropriate for winter levels to be lower than summer levels. Ideally your winter 25(OH)D will not drop below 32 ng/ml, 40 ng/ml may be a better ‚low‘ marker.. (Numbers are fuzzy. If it‘s April and your D is 29 ng/ml step out and enjoy some springtime sun around lunchtime.)

If sun alone is used for D, test to make sure it provides you with enough D. You don't have to worry about excess D from the sunlight available in the U.S. Check at the end of summer to see what the sun is doing for you and at the New Year to see how your summer sun values are holding up.

D Sufficiency Checklist:

- Does my skin type require a small or large amount of sun? If your skin is in the middle, not dark or light, you'll have to experiment.
- Am I in a location where I can get sun to provide D for skin type? and do I have the time midday to 'sun'? If not you will have to supplement. If there is sun you'll have to decide if you'll use it regularly or not.

- Can I get all the D I need from my local sun or do I need supplements during some parts of the year? You'll need to test to determine the amount of supplementation you need and during what parts of the year.
- Is my diet high or low in calcium? Calcium is critical and supplements a must if you can't arrange to regularly eat high calcium meals. The need for calcium is likely genetically programmed and some may need much less than others to maintain normal serum and urinary calcium.
- Do I have any diseases or conditions or am I taking medications that require complete avoidance of sunlight? Check with your physician to make sure and if you must avoid the sun take a supplement..
- Do I have any conditions that might alter the way I use vitamin D?

Bile insufficiency
Gallstones
Gallbladder removed by surgery. (Cholecystectomy.)
Cirrhosis
Kidney disease
Stomach banding or bypass surgery
Celiac disease (gluten-intolerance)
Crohn's disease
IBS- Irritable bowel syndrome
Sarcoidosis
Cancer
Obesity

Testing, Again

Test, test and retest. Whether you use sunlight or vitamin D there is no way to know how you are responding without testing. There is no safe way to supplement without testing if you use a vitamin D supplement greater than 800 IU a day.

The test you want is 25(OH)D also called 25-hydroxyvitamin D. This is the precursor to the active D hormone $1,25(OH)_2D$ that can also be tested but is NOT the test you want. If you find you have elevated 25(OH)D the appropriate action is to lower D as rapidly as possible by avoiding all foods containing D, all supplements containing D and all sunlight or other sources of UV-B light. The process is slow. Retesting may be done every 6-8 weeks.

If you find you need D because your values are too low it's important to test every three or four months the first year and every six months during years two and three. Testing at these intervals will give you the information you need to ensure what you're doing is working. It also makes sure you don't overdo. Vitamin D, even at moderate levels, does build up over time.

There is no clinical data to support 60 ng/ml being better than 40 ng/ml. Moderation is essential. At the present time the strongest indication of benefit to risk remains in the 40-60 ng/ml. range. The low end is just fine.

CHAPTER 10 VITAMIN D AND THE GP

WHO ARE YOU?

As you try out sunlight or vitamin D keep a record. Get a vitamin D test before you start. If sunning record time of day, duration of sunbath, and how much skin you exposed. Make a note if your skin changed color over the next 24 hours after sun exposure or if it ‗felt tender'. Check your 25(OH)D again every three months the first year, every six months the second and third years. As you use diet, supplements, and sun and monitor your levels of vitamin D you will begin to find out who you are in relationship to sunlight and vitamin D.

If you feel ‗overloaded', with sun or supplements, stop and test.

WHERE DO YOU LIVE?

Latitude and Altitude

Where do you live? If you are at any latitude higher than 30° north or south, the temperate zones, 'just getting sun' won't guarantee optimum levels of vitamin D. While higher altitudes help increase access to UV-B mountain living may or may not provide the amount of UV-B you need.

Use the map to help determine your location and possible UV-B. You may find the effort to get D from sunlight just doesn't make sense because of your location, lifestyle or sun sensitivity.

Using a UV-B Meter

Historically D deficiency rickets became epidemic in the cities of England and Germany. City life has a dire affect on access to UV-B. In olden times coal stoves and wood fires made the haze. Today the haze and smog is a mix of often semi-invisible chemicals that create an artificial ozone layer over large cities worldwide. Whatever the cause this layer blocks a significant portion of the UV-B.

Recently a vitamin D seeker measured the UV-B at the beach in Malibu, CA to be 50% of Florida noon but just minutes away on top of a not very tall local mountain, UV-B intensity reached 80% of Florida noon. While altitude played a small role in the difference, ocean haze blocked UV-B at the seashore. Local UV Index readings would not reflect the differences.

The simplest way to determine how much UV-B is available in your sunlight is the use of a UV-B meter. I've found them to be the only sure way to know the availability and intensity of UV-B. With a meter I am able to immediately determine if it's a good day to sun. If the intensity is too low I skip it until another day. If intensity is high my meter lets me calculate the exact amount of time before erythema so I can get my D safely and get out of the sun.

A meter helps determine UV-B vitamin D response because the national weather service UV Index isn't calibrated to UV-B. The Index is calculated with UV-B and shorter wave UV-A. The Index can't give an accurate reading of your location either. The meter or data being used to determine the UVI isn't located in your back yard. Your location may or may not reflect the local UV Index because of clouds, haze, fog or smog.

Meters are a great learning tool. After all the media attention about excess UV-B you will be able to see when UV-B is absent, which is much of the time in latitudes above 30°. UV-B meters are not created equal. See resources for more information.

One of the interesting things you'll learn with a meter is how truly dumb a SPF 45 sunscreen is. Sunscreen SPF only protects the skin from UV-B, not UV-A. Living in northern California at peak midday in June UV-B reaches 80% of Florida noon. This intensity lasts for about two hours. If I would burn in 15 minutes a 45 sunscreen would keep me from burning for 675 minutes. Intense UV-B only lasts for about 240 minutes at most. Light skinned person visiting Hawaii might benefit from a 45 SPF but for most of the United States, 15 will do nicely.…

WHAT DO YOU EAT? WHAT SUPPLEMENTS DO YOU TAKE?

Sunlight or Supplements?

Consider your skin. If it is dark you may discover there is not enough sunlight anywhere near for you to get the D you need. Consider your lifestyle. If you work and your schedule is such you cannot take a noon break to sunbathe or you live in a city with smog or fog where midday sun cannot provide the necessary UV-B or you live in the far north or south (other hemisphere) where UV-B is just not available most of the year any time of day you will need to use supplements to guarantee your body has the D it needs.

Because supplements are not _safe at any dose‘, you can take too much D, testing is absolutely necessary, and not just once but as many times as needed over a number of years to make sure you are getting enough and not too much.

Sunlight	Supplements
Location, is there enough UV-B light	Cost of monitoring to insure safety
Skin Type, too sensitive, too dark for latitude	Remembering to take the supplement
Diseases that cause sun sensitivity	Greater possibility of toxicity
Medications that cause sun sensitivity	Can combine with sunlight = excess D
Prior skin cancer or skin damage	Reaction to the supplement

Table 15 Sunlight or Supplements- Pros/Cons

Maximizing Diet

What we eat makes a difference in how we feel. Crummy food really does make us feel crummy. The Encarta® World English Dictionary says crummy means of little worth, inferior or miserable.

When we eat whole foods they contain all of the 'stuff' someone will try to sell us next year in a pill. Whole foods are foods that are whole and real.

Real foods are foods that are alive or were recently alive and are identifiable as such. This does not include sodas, potato chips, candy, dairy creamer (What is that anyway?), or even health food bars and protein powders. Think about the number of steps between the original food and the item your thinking of eating. The more steps the less real. I am not advocating raw food, or vegetarian or vegan eating. I am suggesting traditional, from scratch cooking and eating suits humans best. You'll find it at every really good restaurant. The best restaurants never serve food from a box or can. Some even keep their own gardens.

Some years ago a young man explained to me that he couldn't buy and eat real food because it didn't come with instructions. I bought him a cookbook. Really good

cookbooks use real food. My mother's cookbooks, the Delineator Cook Book from 1928 and The Boston Cooking-School Cook Book from 1938, are loaded with amazing recipes all using real food. Sally Fallon's Nourishing Traditions New Trends Publishing, Inc., 2001, contains recipes from around the world all using real foods.

Prior to World War II and for a time afterwards food was fresh, frequently grown in the backyard or in small city garden plots. Nearby farms provided produce for the cities. Gardening will always be a great pastime because it provides fresh food, summer sunlight, and exercise.

Prior to the spread of agri-business farming and ‗canning facilities' local fresh produce, often home grown, was 'canned' at home. Canning was a family affair taking a number of days involving preparation of produce, boiling water, and glass jars with rubber gasketed tops, no actual cans. Food was preserved for the long winter. I think one of my favorite recipes must be my mother's dill pickles. My favorite home-canned food from out summer garden was definitely steamy hot stewed tomatoes with melting butter.

Few Americans under 50 are aware of the dramatic changes that have taken place in our food consumption patterns since the 1940s and 50s. Schools in earlier generations taught home economics and young women learned to cook and even to sew. At a time I am unable to pinpoint an idea began circulating that industry could better provide us with not just our clothing but also our food.

Processed foods lack essential nutrients; are often high in processed fat and refined carbohydrates; and are provided everywhere; fast food restaurants, school breakfast and lunch programs, hospital cafeterias, grocery shelves, and gas station mini-marts.

The Western Diet is defined as high in added fat and refined carbohydrates, see processed foods just above. The Western Diet is associated with obesity, hypertension, insulin resistance, diabetes, and cancer. As mentioned this diet seems to increase the need for calcium and vitamin D. Adding D and calcium did correct some of the problems experienced by the test animals.

A better idea would be making a serious attempt to eat more real food. Let go of the processed fats and carbohydrates. You won't miss them when you're eating shrimp with homemade mayonnaise or fresh ripe fruit with coconut milk or oatmeal with real cream and dark maple syrup. Processed foods aren't really satisfying. A little is never enough. Real food is so satisfying it's hard to eat a lot.

I recently visited a store called ―Whole Foods", apparently a part of a large chain. What fascinated me is the small amount of whole foods available. The isles were filled with processed, packaged, canned, bottled, diced and sliced products, not ‗whole food' by my definition.

whole, def.
Including all components without exception; being one unit or constituting the full amount or extent or duration; complete
Including everything
wholly unharmed
Not impaired or diminished in any way

Whole real foods are satisfying because they provide real nutrition. As an example whole sugar cane, with abundant mineral content, does not contribute to tooth decay and contributes to overall mineral balance and trace mineral supplies. [1231] Refined cane sugar depletes minerals by increasing the acid load causing the withdrawal of stores of calcium and potassium and is a major contributor to dental decay.

Nutrients	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

Table 16 Composition of Sugars

Source "Composition of Colombian Foods" – José Gongora y López

Whole grain dark bread, as eaten by our ancestors and in cultures consuming traditional foods, is/was made from whole grain freshly ground the day it is baked contains non-rancid essential fats, vitamins, minerals, proteins, and trace elements, a far richer biochemical composition than modern white bread even when fortified. Refined foods lack many of the nutrients of the original whole food and the added nutrients that government fortification requires replace only a fraction of what has been taken away.

Just adding calcium and D won't compensate for a bad diet but if you just aren't ready to change your bad habits then do think about checking your D and getting extra calcium. It just might help.[150,547,550,593,1232,1233]

As mentioned before, cereals and grains seem to increase the need for D, especially oatmeal, corn, barley, brown rice and whole wheat.[1234,1235] Epidemiological studies of populations consuming high levels of unleavened whole grain breads demonstrate high levels of D deficiency and rickets. Some interesting early studies by Dr. Mellanby showed oatmeal to be the worst cereal offender in contributing to D deficiency, a situation completely reversed if extra vitamin D was added to the diet or the oatmeal was exposed to UV-B light.[1235] Think of it, sunny food☺.

Vegetarian, vegan and macrobiotic diets do not provide sufficient vitamin D. There is a prevalence of rickets and bone disorders within these dietary communities.[41,102,103,104,1236,1237] Sunlight is the only natural source for D if not consuming organ meats, eggs or fish. If you have chosen one of these diets, vegetarian

D is available from most health food stores or if location permits use safe sunning. As the vegetarian D sources are always _dry' D do check to make sure your supplement is working. Make sure to get your D checked regularly. (Kids too.) As long as the diet includes D and incorporates high levels of fruits and vegetables bones stay healthy but if the diet is not well balanced osteoporosis can occur. Strict macrobiotic diets seem to present the most dangers, especially to children.[1238]

Foods That Contain D

All animals, poultry, fish, and reptiles have vitamin D in their flesh and fat. We just have no idea how much. We, means you and me. We have no idea because the USDA and the powers that be don't test. Even if they did test it would only reflect amounts for that animal, at that time. The amount of D in us or in our food is directly proportional to sunlight exposure and/or vitamin D supplements.

Unfortunately animal and poultry supplementation with vitamin D and 25(OH)D, is unregulated and it is therefore possible (but unlikely) excessive amounts could be present in supplemented animals and poultry. Supplements in excess of need will leave residues in the animals flesh and fat and this will be passed on to the consumer.

As yet there are no regulations regarding the use of high doses of vitamin D or 25(OH)D in animal feed.

You need to know if you get any D from food so you can better understand your 25(OH)D test. Most of us get our D from sunlight as little vitamin D is found in typically consumed foods.

- Fortified milk
- Summer cream and butter
- Cold Water Fish, found in the skin and fat under the skin
- Eggs from sunny chickens
- Cod Liver Oil (small amounts and may have high amounts of vitamin A)

Vitamin D Supplements

Available vitamin D supplements include ergocalciferol, fish oil based cholecalciferol (in oil based soft gels) or dry cholecalciferol made by irradiating the precursor D extracted from sheep's wool, lanosterol. Supplements can be purchased at most drugstores or health food stores. These over the counter supplements usually contain 400 IU or 1,000 IU per soft gel or capsule. Some companies have recently made higher dose supplements available. I do not recommend these.

The fish liver oil based vitamin D supplements should say vitamin D on the front of the label but may list a small amount of vitamin A on the back of the label under ingredients. When isolating vitamin D from fish liver oil it is impossible to eliminate all of the vitamin A. *This is not a problem unless you are taking other supplements of A or using topical skin treatments containing retinoids.*

Since 2010 most companies no longer offer vitamin D from fish liver oil. Almost all vitamin D3 in the United States is irradiated lanosterol (sheeps'wool extract). Whichever supplement you choose do test and if you change brands retest because supplement efficacy (how well it works for you) is extremely variable. The supplement strength does not reflect the actual absorption of that amount in your body.

If you determine by testing you need vitamin D see the section on Supplementation. A manual for your physician is available from the sunlightd.org website.

VITAMIN D COMPLICATIONS

Foods That Increase or Decrease Uptake or Utilization

When D was first discovered researchers also discovered ‗anti-calcifying' substances. When animals were low in vitamin D feeding them cereals brought on rickets or made it worse. Oatmeal was the worst but corn, rice, barley and wheat all had an effect which lowered response to vitamin D and calcium. Polished rice and white flour were the least harmful and wheat germ was as damaging as oatmeal. Adding calcium didn't help but increasing vitamin D completely reversed any rachitic factor.[1239]

This relationship has been noted by others in animals[1234,1240,1241] and in macrobiotic children.[105] The effect has been associated with the phytate content of foods.[1242]

Diseases Altering D

Sarcoidosis is a chronic disease afflicting an estimated 10-40 persons per 100,000 in the U.S.. An immune trigger, some believe a cell wall deficient bacteria or other low-grade chronic infection, others simply accept the term autoimmune, causes local cellular inflammation and the formation granulomas. Localized cellular production of calcitriol ($1,25(OH)_2D$, the active hormone vitamin D) in excess of normal sends a message to other hormones which take calcium out of blood and bone and deposit it in the affected tissue or organ. This process also may lead to hypercalcemia, elevated serum calcium. Any tissue or organ may be affected but most

commonly the lung, the lymph nodes, the skin, the eyes or the liver. Other tissues and organs may be involved but less often.[137]

It‘s an interesting disease to help us understand that we all need vitamin D unless we don‘t. This condition does not mean the affected person has sufficient vitamin D nor does it have anything to do with taking too much vitamin D or getting too much sun.

This is the story of an aberrant hormone, in this case vitamin D, for reasons yet to be understood, dissolving bone and hardening vital tissues and organs.

Part of the sarcoidosis treatment requires complete elimination of any source of vitamin D including and especially sunlight. Reducing the amount of pre-D seems to help but does not cure this disease. Other drugs are used to block the immune response but they too treat symptoms and patient and doctor hope for a remission.

Often levels of 25(OH)D will be normal or low if tested when diagnosed with sarcoidosis and only a test for calcitriol will show the problem. During treatment foods with high levels of vitamin D are avoided, including fortified dairy and fatty fish.

This is not a condition to self-treat with vitamins, minerals or other supplements. The condition is appropriately addressed with avoidance of all sources of vitamin D and medical intervention. [1243,1244]

If you suffer from sarcoidosis you might consider the Marshall Protocol. [1245] developed by Trevor Marshall, MD. While this is still considered quite controversial and experimental, many of Marshall‘s patients have seen relief of chronic and acute symptoms. Marshall treats sarcoidosis and some other autoimmune diseases with removal of all vitamin D, avoidance of sunlight, and the use of minocycline. The rational for this treatment and general protocol may be found on the Marshall Protocol site on the web.

I am not promoting the Marshall Protocol but do accept that it is possible low vitamin D might slow or stop progression of some diseases or infectious organisms..

There is no indication long term avoidance of vitamin D is safe or sane.

Xeroderma pigmentosum is an hereditary disease. Skin cells are unable to repair damage from ultraviolet light. The condition is rare. Complete avoidance of ultraviolet light, UV-B and UV-A are critical.[307,1246] The need for or benefit of vitamin D or other nutrients in this condition is unknown. The accepted 25(OH)D in this condition is WELL BELOW newer optimal values. Researchers suggest most who must avoid UV light will benefit from D and all should be tested. [1096,1247,1248,1249,1250,1251]

Gluten intolerance, an hereditary condition causing damage to the gut wall when foods containing gluten are eaten, contributes to multiple deficiencies of many nutrients including vitamin D and calcium.[1252,1253,1254,1255,1256] Avoiding gluten containing foods and maintaining a balanced diet with extra D or sunlight corrects D deficiency. If you are gluten intolerant it is important to keep to the gluten-free diet.

There are no supplements or other treatments that change intolerance to gluten.

Crohn's disease or IBS presents with vitamin D deficiency frequently. [707,709,1213,1257,1258,1259] Make sure to check your D. If the disease is active use sunlight

as your source. It is even more important to make sure vitamin D and calcium are adequate if corticosteroids are being used to treat this autoimmune disease. Corticosteroids alter vitamin D and calcium status and it is important to protect your bones and other cells too.[708,1260]

Bile insufficiency: Insufficient production or stimulation of bile will result in malabsorption of all fat-soluble vitamins because bile is needed to emulsify fats and allow absorption of fatty substances. People who have cholestasis (bile insufficiency), gallstones, or have had their gall bladder removed, called cholecystectomy, frequently end up with deficiencies of the fat soluble vitamins which include vitamins A, D, E and K.[945,946,948,1261,1262,1263,1264]

In the review of D and cholecystectomy levels of 25(OH)D were 20 ng/ml in the controls and 12.9 ng/ml in those having had the surgery.[1265] The study was done an average of 9 years following surgery to determine if deficiencies were present. Taking vitamin D won't always improve D status and in a number of cases this is due to malabsorption.

The use of water miscible pre-emulsified fat soluble vitamins, especially vitamins A and D has a serious potential for hypervitaminosis.[1266] Soy lecithin emulsifies fat similar to the action of bile. (You'll see it listed in the ingredients on your chocolate bar) Lecithin granules will work as effectively as bile. Taking lecithin with (at the same time as) fat-soluble vitamins, A, D, E, K or beta-carotene, emulsifies the nutrients allowing them to be absorbed. Lecithin also provides a source of choline and inositol, both good for your body and brain.

Hypothyroidism: Vitamin D levels in hypothyroid individuals are lower than those in persons with normal thyroid function. Hypothyroidism alters the vitamin D endocrine system. Though many functions are restored after thyroid hormone treatment, responses to vitamin D supplementation remain abnormal. 25(OH)D should be checked in persons being treated for hypothyroidism. If levels are low appropriate supplementation of vitamin D and calcium may be indicated but only after normalization of thyroid hormones.[1267,1268,1269,1270,1271]

This also suggests that in some cases failure to respond to vitamin D supplementation may indicate low thyroid function. A good yearly physical should include tests, TSH, Free T3, and Free T4, as well as vitamin D.

Corticosteroid Treated Diseases: A number of diseases are treated with corticosteroids. These include rheumatic disorders including polymyalgia rheumatica, systemic lupus erythematosis (SLE), asthma, autoimmune diseases including Crohn's disease, myasthenia gravis and autoimmune Addison's Disease. Vitamin D and calcium are important to prevent bone loss and osteoporosis associated with corticosteroid use.[1272,1273,1274,1275,1276,1277,1278,1279,1280,1281]

Kidney Disease: Kidney diseases are very special situations and need medical treatment. Calcium, protein, and vitamin D needs change as kidney disease progresses. What is correct at one point in time may further damage your kidney at another point in time. Make sure your physician has vitamin D knowledge and pays attention to your vitamin D levels. Do not try to treat your condition on your own with vitamins, minerals, herbs, or other supplements. Kidney disease, whatever the cause, is a very

serious condition and needs expert medical support. Do make sure your physician is well versed in how and when to test and use vitamin D and/or its metabolites.

Kidney Stones: The development of kidney stones is associated with excess calcium in the urine and the Western diet.[556,566,1282,1283] Making sure potassium, from fruits and vegetables, not supplements, and magnesium (foods or supplement) are sufficient will help prevent the formation of kidney stones.[559,1284,1285,1286,1287] Fish oil has also proved helpful in normalizing some inflammatory aspects of the propensity to develop nephrolithiasis.[1288] Magnesium, calcium and vitamin B-6 protect the kidney from developing stones.[1284,1285,1289] A rat study showed feeding a semi-purified diet, think processed foods, contributed to kidney stones whereas a whole food diet prevented deposits.[1287]

A FINAL NOTE TO THE GP

GP, I know much of this book seems over referenced and overly technical. I did not do this to make it harder to understand. I needed to present the data that shows just how important sunlight and D are for all of us. To get HMOs and physicians to help maintain D they have to be convinced testing 25(OH)D serves a purpose and that the outcome is worth the investment of time and testing. You need at least some of the technical stuff to know how to maximize D safely.

The guidelines in this book are not designed for persons with a diagnosed disease. If you have any of the diseases listed in this book it is likely having adequate D would be a good thing, but complications relating to medications or other possible complications or interactions require the assistance of a willing, knowledgeable, licensed, medical professional.

Though I have taken every precaution to present the information carefully and conservatively much is yet to be learned about sunlight and D. You may need the support of someone knowledgeable enough to watch out for possible problems along the way. Disease states alter the way we respond to many substances. What works to prevent a disease may actually contribute to complications once the disease is present.
An example: Potassium protects the kidney and higher dietary potassium may help prevent some types of kidney disease but high dietary intake of potassium, once kidney function has declined, can be life threatening.

For the rest of you, it may sound difficult, figuring all this out, but I've done it, learned how to maximize my D, and by the end of the first year I developed a sense of what works for me. My clients have done it. You will too.

Persons regularly monitoring vitamin D found they began to have an intuitive sense of when they needed sunlight or D or calcium. You may develop this sense too. If you experiment, monitor and listen to your body it may tell you when it needs sun and you'll

know from experience, without checking the UV index or a meter, when the UV-B sun you need is present.

Learning how long to stay in the sun, safely, is a bit tricky, especially if you have very light skin. It's fine to under-dose and under-sun while you work out the details. More is not better. A sun meter is fun, a techie toy, to use and does help determine the presence of UV-B and give you an idea of possible 'time to pinken' but the UV Index can work almost as well and is available free everywhere; just remember, the UV Indeex reflects midday sun, always midday, and the UV Index is unreliable if there are clouds or haze..

Testing may be too expensive for some. I am continually working to get testing costs down and/or get funding for free or reduced price testing. Watch the website for information. Access it from a public library if you don't have online access at home or school. Participate. Let me know how you're doing. Problems or complications are the stuff we all deal with every day. I won't be able to answer individual questions but I will post some general questions and answers on the website. If you need individual help and can't find it locally, request a referral or consultation. Working together we will find solutions to getting the sunlight and D we need.

GP this book really is for you.

Contact me through the website http://sunlightd.org or write to:

Krispin Sullivan, CN
938 Wendy Lane
Unit B
Incline Village, NV 89451

http://sunlightd.org
info@sunlightd.org

CHAPTER 11 RESOURCES

TESTING

Your serum 25(OH)D is altered by some foods and calcium intake as well as sun or supplements of vitamin D. As getting enough calcium may boost vitamin D levels wait to test your D until you know you have been getting a minimum of 800 mg of calcium in your supplements and/or diet. If your calcium intake is very low work hard to get calcium (with magnesium and some trace elements) for a month or so before testing.

Remember the young boys in Nigeria. Low 25(OH)D can be a response to low calcium when sources of D are sufficient.

If your physician orders testing at your local lab the test may be called either of the names below:
25(OH)D
25-hydroxyvitamin D

Local testing is available without a physician‘s order from Life Extension Foundation. Cost to members is about $48, for non-members $68. Testing is arranged locally and results provided by mail. Find them online at http://lef.org or order by phone 1-800-544-4440

At home testing for about $60. It is a finger stick, easy but not comfortable for some. http://www.bloodtestathome.com/vitamin_D_test.html

Testing is also available from ZRT Labs. http://www.zrtlab.com in the Health Consumers section or call 866-600-1636 to order. This is a blood spot test you do at home and mail in. The cost is about $135.

Neither LEF or ZRT may be used in New York state. There you must have a prescription from your MD. Time to complain. Let your legislature know you want health freedom.

Do not sun or take any vitamin D or other supplements for a minimum of 24 hours before your test. Go first thing in the morning before you eat or take supplements.

Make sure your physician orders the correct test.
Make sure you don't get the $1,25(OH)_2D$ test unless you specifically request this test for reasons other than monitoring vitamin D status. Labs unfamiliar with testing vitamin D may make a mistake even though you asked for the correct test.

Remember, other than the Life Extension Foundation testing or ZRT Lab your physician must arrange/order your vitamin D test. This is also true if you would like your insurance company or HMO to pay the bill.

There are some states that allow you to request your own tests without a physician (or an order from LEF). I believe Maryland is one of these states. If other sources of testing become available I will post it on the sunlightd.org website

FYI testing: One of the most commonly used tests, many labs and researchers use this, is from DiaSorin, Inc. You can‘t order from them but your lab or physician can.

DiaSorin Inc.
1951 Northwestern Avenue –
P.O. Box 285
Stillwater, MN 55082-0285
Tel: +1.651.439.9710
Fax: +1.651.779.7847
For physicians and labs: http://www.diasorin.com
For patients: http://www.vitamind.com

SUN METERS

The sunlightd.org website will list other meters if they prove useful and will help users correlate the various displays to skin type and sun time. http://sunlightd.org

Solarmeter® Model 6.2 UVB $179.00
Solartech, Inc.
26101 Harbour Pointe Dr N.
Harrison Twp, MI 48045
Business [1](800) 798-3311
Business [1](586) 790-8025
Fax [1](586) 790-8026
Email:: information@solarmeter.com

http://www.solarmeter.com
Very well made, just UV-B, great accuracy. You'll have a real idea of how much UV-B is present.

SafeSun® Personal UV Meter
SafeSun® Classic - US$149/unit +
SafeSun® Sensor - US$109/unit +
Optix Tech Inc.
1050 17th Street, NW, Suite 1150
Washington, DC 20036
toll free: 888-327-6641
phone: 202-737-6641
fax: 202-737-2351
email: info@safesun.com
http://www.safesun.com

The SafeSun meter is very good-looking. It isn't a UV-B meter but based on the erythemal curve which also includes shorter wave UV-A. This makes it less accurate for UV-B/vitamin D but not much and probably some adjustment (in how you read the values, not in the meter) might make it more accurate for UV-B sunning.

CLOTHING

Cotton T-shirts work as the Tibetan study proved, but if you want something more high-tech (doesn't mean it works better) there are a number of companies that make clothing with a known SPF.

SunChasers Swimwear, Inc.
740 Greenville Blvd.
Suite 400, Box 273
Greenville, NC 27858
sales@sun-chasers.com
US & Canada 1.800.232.8106

Sunbarrier Clothing
Telephone 1-604-415-0273
Order Desk 1-800-679-7792
P.O. Box 51, Lake Errock, B.C. Canada,
V5A 4B7
info@sunbarrier.com
Sales: 1-800-679-7792
Customer Support: 1-604-415-0273

Sun Clothing, etc.
(540) 842-4583
http://sunclothingetc.com

Sun-Protective-Clothing.com
Telephone: 1.800.878.9600
Fax: 1.480.991.1036
Email: info@sun-protective-clothing.com
P.O. Box 13102
Scottsdale, AZ 85267-3102

Sun Precautions
2815 Wetmore Avenue
Everett, WA 98201
Telephone 1-800-882-7860
Fax 1-425-303-0836
http://www.sunprecautions.com

Solartex Sun Gear
10605 Anna Marie Dr.
Glen Allen, VA 23060
1-877-476-5789

Coolibar
4206 Park Glen Road
St. Louis Park, MN 55416
Attention: Customer Service
Phone: 1-800-926-6509
Fax: 1-952-922-1455
service@coolibar.com

CHAPTER 12 FOR RESEARCHERS AND PHYSICIANS

STUDIES WAITING TO BE DONE

Vitamin D and light researchers, I hope I have fairly represented a small portion of your work. The opinions expressed are mine as are any errors. Do correct me; I will make any changes in the next edition. Some parts of this book reflect my personal experiences and the experiences of others over a six year period of study, trials, and errors. Throughout this book I mention studies waiting to be done. I thought I'd summarize some of what I would like to see. You are welcome to add to the list.

If any indigenous groups, living and eating as their ancestors did, can be still be isolated- testing of the serum 25(OH)D, PTH, and serum calcium. Both current location and food sources should be similar to ancestral habitats.

Repeated testing of various levels of calcium and vitamin D over a period of time, not less than 3 years.

A trial of extra D plus calcium, for several months, followed by moderate D and calcium supplementation over three years to test for the efficacy of a 'loading dose' and then maintenance.

25(OH)D, serum calcium and PTH of matched women with and without breast cancer (or same tests of any other matched disease/disease free group). Having adequate D does not mean you will not get breast cancer. I have had clients with 25(OH)D exceeding 50 ng/ml who have had the disease.

Testing of foods for vitamin D. I know this may be seasonal but it may also be possible supplementation of animals is altering D year round. Someone needs to check.

Research determining the optimal balance between vitamins A and D or at least what ratio becomes an imbalance.

Testing to determine the differences in vitamin D content of farmed fish and free living fish and testing to determine what parts of the fish provide what amounts of D.

Testing and clear labeling of the UV-A protection of sunblocks. Currently the labels and advertising are extremely misleading. No one in the U.S. needs a 45 sunblock as there isn't that much UV-B anywhere in the U.S. except perhaps Hawaii; but they do need a reliable, INEXPENSIVE, UV-A block.

Testing and reporting of actual amounts of UV-B not 'worst case scenarios'

Trials looking at reversal or prevention of sun damage by replacement of antioxidants destroyed by moderate sun exposure using moderate supplementation or high anti-oxidant foods that include all essential elements.

Trials to better understand the nature of pheomelanin and what may (supplements, food) help protect it from UV damage.

Studies to clearly determine the alterations as found in some blacks and the Inuit, retaining calcium and how that plays into levels of D and calcium need.

Studies to determine the amount of actual sun needed by Asian Indians to maintain D given the rapid breakdown of D within their skin.

Studies to determine what other races/ethnicities have specific requirements or need to avoid specific nutrients such as calcium and sunlight.

As above- Studies looking at genetic markers as indicators of altered need for a nutrient or sunlight rather than just for diagnosis or drug treatment.

I look forward to a broadening of the current model of nutrition and health to encompass the complexities, which include the variables, of our many individual needs. Across the large landscape of latitudes, colors and diets found within these United States a pattern will begin to emerge as we recognize health will never be found in fast foods, drugs, powders, bars, or pills, but in wholesome food, sunlight, family and friends.

ERRORS AND UPDATES

This book is about what is known, what we may have forgotten, and what we have yet to learn about our need for sunlight and vitamin D. Great effort has been taken to accurately communicate the information. There will be mistakes in this work. Forgive me for my failings and unintentional errors. Take the parts that work for you, the parts that feel right and over time prove to be true for you. None yet have all the pieces to the puzzle, the mystery of life.

Some errors will be entirely mine, others may occur because information as reported is later found to be incorrect or because I missed the book, paper or article that would have better served the issue. There is a website, http://sunlightd.org available for posting comments and questions, and if you find an error needing correction, that is the place to report it. It is not a site for vitamin D diagnosis, treatment, arguments, or promotion of any supplement, product, or protocol.

Later editions will reflect research updates and correction of errors.

There is one mistake I have not made. After more than 14 years of working with vitamin D and sunlight I am absolutely sure the only way to utilize sunlight or vitamin D safely is with great care and understanding. Ignoring vitamin D deficiency or insufficiency prevents optimal health. Increasing levels of vitamin D by sunlight, food or supplements may be beneficial or harmful.

The only way to know your current vitamin D status or the outcome of any supplementation by sunlight or vitamin D is to get a vitamin D test. Because vitamin D levels can decline or accumulate over time, testing must be continued over time. Any authority from any source that suggests otherwise is unaware of or ignoring the complexities vitamin D endocrine system.

We are all very different and while there are generalities, we all need D, we can get it from sunlight and/or supplements, the details, who, what, when, where, are much more complex, and individual. Acknowledging biochemical individuality in response to sunlight and vitamin D is critical to our health and longevity.

DEAR DOCTOR

Dear Doctor,

You have purchased this book or it has been given to you so that you may help make the world a happier and healthier place to be. If you only read parts of this book you may miss something important. Please try to make it all the way through and before you discount any of the information at least be willing to read the cited studies.

Many of your patients may need your help to get testing so they may understand their current vitamin D status; and they need you to monitor whatever program they choose, to optimize their D safely. Diasorin, in the Resources, can provide you with information on testing or your local lab or clinic may have facilities to test.

I ask that you to make an effort to provide the most reasonably priced testing, not more than $60, less if you can arrange it. Some of those who need your help most won't have much money or insurance to pay the bill.

People of color, all colors, need your help. The burden of illness is great and sufficient sunlight lacking in many of our largest urban centers.

Seniors need your help. Getting enough D and calcium will keep muscles strong, warding off fractures and perhaps bone loss. Optimizing D frequently relieves back pain. This is no small thing.

When people seek your help they won't be coming as patients to be diagnosed and treated for a disease. They will come as neighbors and friends needing you to help them find D safely in their current life and location. There is information in this book and in the Physician‘s Guide that will allow you provide them with the guidance they need.

If you need more information on treatment protocols, complications, or concerns, phone consultations and written materials are available for licensed professionals.

Krispin Sullivan, CN
938 Wendy Lane
Incline Village, NV 84950

1-775-831-0292
http://sunlightd.org
info@sunlightd.org

Reference List

1. The evolutionary significance of vitamin D, skin pigment, and ultraviolet light Neer, R. M. 1975 Am.J.Phys.Anthropol.
2. Evolutionary biology and pathology of vitamin D Holick, M. F. 1992 J.Nutr.Sci.Vitaminol.(Tokyo)
3. Vitamin D: A millenium perspective Holick, M. F. 2003 J Cell Biochem.
4. Severe myopathy associated with vitamin D deficiency in western New York Prabhala, A., Garg, R., and Dandona, P. 4-24-2000 Arch.Intern.Med.
5. 25-Hydroxyvitamin D levels during breast-feeding with or without maternal or infantile supplementation of vitamin D Ala-Houhala, M. 1985 J.Pediatr.Gastroenterol.Nutr.
6. Persistence of Vitamin D-deficiency rickets in Toronto in the 1990s [see comments] Binet, A. and Kooh, S. W. 1996 Can.J.Public Health
7. Vitamin d deficiency in breast-fed toddlers Biser-Rohrbaugh, A. and Hadley-Miller, N. 2001 J Pediatr.Orthop.
8. Prevalence of vitamin D insufficiency in an adult normal population Chapuy, M. C., Preziosi, P., Maamer, M., Arnaud, S., Galan, P., Hercberg, S., and Meunier, P. J. 1997 Osteoporos.Int.
9. Hypovitaminosis D in a sunny country: relation to lifestyle and bone markers Gannage-Yared, M. H., Chemali, R., Yaacoub, N., and Halaby, G. 2000 J.Bone Miner.Res.
10. [Hypovitaminosis D: a major worldwide public health problem] Gannage-Yared, M. H., Tohme, A., and Halaby, G. 4-7-2001 Presse Med.
11. Nutritional rickets: report of four cases diagnosed at orthopaedic evaluation Kaper, B. P., Romness, M. J., and Urbanek, P. J. 2000 Am.J.Orthop.
12. Plasma 25-hydroxyvitamin D and its determinants in an elderly population sample Jacques, P. F., Felson, D. T., Tucker, K. L., Mahnken, B., Wilson, P. W., Rosenberg, I. H., and Rush, D. 1997 Am.J.Clin.Nutr.
13. [Rickets in Asian immigrants] Lopez, Segura N., Bonet, Alcaina M., and Garcia, Algar O. 2002 An.Esp.Pediatr.

14. Seasonal variation in serum levels of vitamin D metabolites and parathormone in geriatric patients with fractures in Southern Israel Meller, Y., Kestenbaum, R. S., Galinsky, D., and Shany, S. 1986 Isr.J.Med.Sci.
15. Diets and living conditions of Asian boys in Coventry with and without signs of rickets O'Hara-May, J. and Widdowson, E. M. 1976 Br.J.Nutr.
16. Vitamin D status of Saudi men Sedrani, S. H. 1984 Trop.Geogr.Med.
17. Vitamin D status of two groups of elderly in Oslo: living in old people's homes and living in own homes Sem, S. W., Sjoen, R. J., Trygg, K., and Pedersen, J. I. 1987 Compr.Gerontol.[A]
18. Nutritional rickets still afflict children in north Texas Shah, M., Salhab, N., Patterson, D., and Seikaly, M. G. 2000 Tex.Med.
19. 25-Hydroxyvitamin D and total calcium: extraordinarily low plasma concentrations in Saudi mothers and their neonates Taha, S. A., Dost, S. M., and Sedrani, S. H. 1984 Pediatr.Res.
20. [Disease caused by lack of sunlight: rickets and osteomalacia] Wauters, I. M. and van Soesbergen, R. M. 3-20-1999 Ned.Tijdschr.Geneeskd.
21. Cod-liver oil, vitamin D and the fight against rickets [see comments] Wilton, P. 5-1-1995 CMAJ.
22. Vitamin D intake and vitamin D status of Australians Nowson, C. A. and Margerison, C. 8-5-2002 Med.J Aust.
23. Vitamin D deficiency in Iranian mothers and their neonates: a pilot study Bassir, M., Laborie, S., Lapillonne, A., Claris, O., Chappuis, M. C., and Salle, B. L. 2001 Acta Paediatr.
24. Vitamin D deficiency and associated factors in adolescent girls in Beijing Du, X., Greenfield, H., Fraser, D. R., Ge, K., Trube, A., and Wang, Y. 2001 Am J Clin Nutr
25. [Hypovitaminosis D: a veiled diagnosis] Grootjans-Geerts, I. 10-27-2001 Ned.Tijdschr.Geneeskd.
26. Vitamin D deficiency in veiled or dark-skinned pregnant women Grover, S. R. and Morley, R. 9-3-2001 Med.J Aust.
27. Wintertime vitamin D deficiency in male adolescents: effect on parathyroid function and response to vitamin D3 supplements Guillemant, J., Le, H. T., Maria, A., Allemandou, A., Peres, G., and Guillemant, S. 2001 Osteoporos.Int.
28. A high prevalence of hypovitaminosis D in Finnish medical in- and outpatients Kauppinen-Makelin, R., Tahtela, R., Loyttyniemi, E., Karkkainen, J., and Valimaki, M. J. 2001 J Intern.Med.
29. Vitamin D deficiency and bone health in healthy adults in finland: could this be a concern in other parts of Europe? Lamberg-Allardt, C. J., Outila, T. A., Karkkainen, M. U., Rita, H. J., and Valsta, L. M. 2001 J Bone Miner.Res.
30. Vitamin D Deficiency and Secondary Hyperparathyroidism in the Elderly: Consequences for Bone Loss and Fractures and Therapeutic Implications Lips, Paul 8-1-2001 Endocr.Rev.
31. Vitamin D deficiency and insufficiency in Orthodox and non-Orthodox Jewish mothers in Israel Mukamel, M. N., Weisman, Y., Somech, R., Eisenberg, Z., Landman, J., Shapira, I., Spirer, Z., and Jurgenson, U. 2001 Isr.Med.Assoc.J
32. Vitamin D deficiency in mothers of infants with rickets Nozza, J. M. and Rodda, C. P. 9-3-2001 Med.J Aust.
33. [Hypovitaminosis D in postmenopausal women with low bone mineral density] Rodriguez Portales, J. A. 2001 Rev.Med.Chil.
34. Changes in bone and calcium metabolism following hip fracture in elderly patients Sato, Y., Kaji, M., Higuchi, F., Yanagida, I., Oishi, K., and Oizumi, K. 2001 Osteoporos.Int.
35. [Vitamin D deficiency in a multicultural setting] Lips, P. 10-27-2001 Ned.Tijdschr.Geneeskd.
36. Low vitamin D levels in outpatient postmenopausal women from a rheumatology clinic in Madrid, Spain: their relationship with bone mineral density Aguado, P., del Campo, M. T., Garces, M. V., Gonzalez-Casaus, M. L., Bernad, M., Gijon-Banos, J., Martin, Mola E., Torrijos, A., and Martinez, M. E. 2000 Osteoporos.Int.
37. Vitamin D Deficiency Is Implicated in Reduced Serum Albumin Concentrations in Patients With End-Stage Renal Disease Yonemura, K., Fujimoto, T., Fujigaki, Y., and Hishida, A. 2000 Am.J.Kidney Dis.
38. Osteoporosis and vitamin D deficiency in Israel Weisman, Y. 2000 Public Health Rev.
39. Vitamin D deficiency rickets in children: prevalence and need for community education Hartman, J. J. 2000 Orthop.Nurs.
40. Sunlight exposure and vitamin D deficiency in Turkish women Alagol, F., Shihadeh, Y., Boztepe, H., Tanakol, R., Yarman, S., Azizlerli, H., and Sandalci, O. 2000 J.Endocrinol.Invest
41. Dietary intake of vitamin D in premenopausal, healthy vegans was insufficient to maintain concentrations of serum 25-hydroxyvitamin D and intact parathyroid hormone within normal ranges during the winter in Finland Outila, T. A., Karkkainen, M. U., Seppanen, R. H., and Lamberg-Allardt, C. J. 2000 J.Am.Diet.Assoc.
42. [Osteomalacia caused by vitamin D deficiency in a female Tamil immigrant] Paetzold, M., Hintze, G., Menger, H., Bartel-Kuss, S., Jorg, J., and Kobberling, J. 2-15-1993 Med.Klin.

43. Vitamin D metabolism is altered in Asian Indians in the southern United States: a clinical research center study Awumey, E. M., Mitra, D. A., Hollis, B. W., Kumar, R., and Bell, N. H. 1998 J.Clin.Endocrinol.Metab
44. Rickets in black children beyond infancy in Natal Bhimma, R., Pettifor, J. M., Coovadia, H. M., Moodley, M., and Adhikari, M. 1995 S.Afr.Med.J.
45. Vitamin D deficiency in pregnancy is not associated with obstructed labor. A study among Pakistani women in Karachi Brunvand, L., Shah, S. S., Bergstrom, S., and Haug, E. 1998 Acta Obstet.Gynecol.Scand.
46. Commonly recommended daily intake of vitamin D is not sufficient if sunlight exposure is limited Glerup, H., Mikkelsen, K., Poulsen, L., Hass, E., Overbeck, S., Thomsen, J., Charles, P., and Eriksen, E. F. 2000 J.Intern.Med.
47. Vitamin D and bone health Holick, M. F. 1996 J.Nutr.
48. Rickets and deprivation: a Nigerian study Akpede, G. O., Omotara, B. A., and Ambe, J. P. 1999 J.R.Soc.Health
49. Vitamin D deficiency and chronic low back pain in Saudi Arabia Al Faraj, S. and Al Mutairi, K. 1-15-2003 Spine
50. Diet, clothing, sunshine exposure and micronutrient status of Arab infants and young children Dawodu, A., Dawson, K. P., Amirlak, I., Kochiyil, J., Agarwal, M., and Badrinath, P. 2001 Ann.Trop.Paediatr.
51. Vitamin D deficiency in veiled Kuwaiti women el Sonbaty, M. R. and Abdul-Ghaffar, N. U. 1996 Eur.J.Clin.Nutr.
52. Efficacy and safety of vitamin D(3) intake exceeding the lowest observed adverse effect level Vieth, R., Chan, P. C., and MacFarlane, G. D. 2001 Am.J.Clin.Nutr.
53. Vitamin D supplementation, 25-hydroxyvitamin D concentrations, and safety [see comments] Vieth, R. 1999 Am.J.Clin.Nutr.
54. Vitamin D Nutrition and Its Potential Health Benefits for Bone, Cancer, and Other Conditions Vieth, R. 12-1-2001 Journal of Nutritional & Environmental Medicine
55. Vitamin D insufficiency in a population of healthy western Canadians Rucker, D., Allan, J. A., Fick, G. H., and Hanley, D. A. 6-11-2002 CMAJ.
56. Gains in bone mineral density with resolution of vitamin D intoxication Adams, J. S. and Lee, G. 8-1-1997 Ann.Intern.Med.
57. Serum 25-hydroxyvitamin D3 levels are elevated in South Indian patients with ischemic heart disease Rajasree, S., Rajpal, K., Kartha, C. C., Sarma, P. S., Kutty, V. R., Iyer, C. S., and Girija, G. 2001 Eur.J Epidemiol.
58. The vitamin D status of elderly Americans Holmes, R. P. and Kummerow, F. A. 1983 Am.J Clin Nutr
59. Additive risk factors in atherosclerosis Kummerow, F. A., Cho, B. H., Huang, W. Y., Imai, H., Kamio, A., Deutsch, M. J., and Hooper, W. M. 1976 Am.J.Clin.Nutr.
60. Nutrition imbalance and angiotoxins as dietary risk factors in coronary heart disease Kummerow, F. A. 1979 Am.J.Clin.Nutr.
61. Ultrastructure of cardiovascular lesions induced by hypervitaminosis D and its withdrawal Taura, S., Taura, M., Imai, H., Kummerow, F. A., Tokuyasu, K., and Cho, S. B. 1978 Paroi.Arterielle.
62. Do we really need > or = 100 microg vitamin D/d, and is it safe for all of us? Muskiet, F. A., Dijck-Brouwer, D. A., van, der, V, and Schaafsma, A. 2001 Am.J Clin Nutr
63. Maternal and postnatal vitamin D ingestion influences rat aortic structure, function and elastin content Norman, P., Moss, I., Sian, M., Gosling, M., and Powell, J. 8-1-2002 Cardiovasc.Res.
64. Vitamin D deficiency: a concern in pregnant Asian women Alfaham, M., Woodhead, S., Pask, G., and Davies, D. 1995 Br.J.Nutr.
65. Biochemical evidence of vitamin D deficiency in pregnant Asian women Bashir, T., Macdonald, H. N., and Peacock, M. 1981 J Hum.Nutr
66. The nutrient intakes of pregnant and lactating mothers of good socio- economic status in Cambridge, UK: some implications for recommended daily allowances of minor nutrients Black, A. E., Wiles, S. J., and Paul, A. A. 1986 Br.J.Nutr.
67. Vitamin D-deficient rats produce reduced quantities of a nutritionally adequate milk Brommage, R. and DeLuca, H. F. 1984 Am.J.Physiol
68. Vitamin D deficiency and fetal growth Brunvand, L., Quigstad, E., Urdal, P., and Haug, E. 7-5-1996 Early Hum.Dev.
69. Maternal vitamin D intake and mineral metabolism in mothers and their newborn infants Cockburn, F., Belton, N. R., Purvis, R. J., Giles, M. M., Brown, J. K., Turner, T. L., Wilkinson, E. M., Forfar, J. O., Barrie, W. J., McKay, G. S., and Pocock, S. J. 7-5-1980 Br.Med.J.
70. [Placental vitamin D: synthesis, regulation, and clinical implications] Cravioto, C. 2000 Rev.Invest Clin
71. Vitamin D deficiency in pregnant and breast-feeding women and their infants Daaboul, J., Sanderson, S., Kristensen, K., and Kitson, H. 1997 J.Perinatol.

72. Vitamin D supplementation during pregnancy: effect on neonatal calcium homeostasis Delvin, E. E., Salle, B. L., Glorieux, F. H., Adeleine, P., and David, L. S. 1986 J.Pediatr.
73. [Vitamin D: implications for health and pregnancy] Diaz, L., Carino, C., and Mendez, I. 2001 Rev.Invest Clin
74. Folate, vitamin D, and iron intakes are low among pregnant Finnish women Erkkola, M., Karppinen, M., Jarvinen, A., Knip, M., and Virtanen, S. M. 1998 Eur.J.Clin.Nutr.
75. High prevalence of vitamin D deficiency among Ethiopian women immigrants to Israel: exacerbation during pregnancy and lactation [see comments] Fogelman, Y., Rakover, Y., and Luboshitzky, R. 1995 Isr.J.Med.Sci.
76. Perinatal vitamin D and calcium status of northern Canadian mothers and their newborn infants Waiters, B., Godel, J. C., and Basu, T. K. 1999 J.Am.Coll.Nutr.
77. Patterns of treated non-melanoma skin cancer in Queensland--the region with the highest incidence rates in the world Stenbeck, K. D., Balanda, K. P., Williams, M. J., Ring, I. T., MacLennan, R., Chick, J. E., and Morton, A. P. 11-5-1990 Med.J.Aust.
78. Intake of vitamin D and risk of type 1 diabetes: a birth-cohort study Hypponen, E., Laara, E., Reunanen, A., Jarvelin, M. R., and Virtanen, S. M. 11-3-2001 Lancet
79. Prevention of rickets and vitamin D deficiency: new guidelines for vitamin D intake Gartner, L. M. and Greer, F. R. 2003 Pediatrics
80. Nutritional vitamin D deficiency rickets in Sudanese children el Hag, A. I. and Karrar, Z. A. 1995 Ann.Trop.Paediatr.
81. The effect of darkness on vitamin D in adults Fairney, A., Fry, J., and Lipscomb, A. 1979 Postgrad.Med.J
82. Vitamin D deficiency and secondary hyperparathyroidism: clinical and biochemical associations in older non-institutionalised Southern Tasmanians Inderjeeth, C. A., Nicklason, F., Al Lahham, Y., Greenaway, T. M., Jones, G., Parameswaran, V. V., and David, R. 2000 Aust.N.Z.J.Med.
83. Do North American women need supplemental vitamin D during pregnancy or lactation? Specker, B. L. 1994 Am.J.Clin.Nutr.
84. Calcinosis and metastatic calcification due to vitamin D intoxication. A case report and review Allen, S. H. and Shah, J. H. 1992 Horm.Res.
85. Nephrocalcinosis due to vitamin D intoxication Besbas, N., Oner, A., Akhan, O., Saatci, U., Bakkaloglu, A., and Topaloglu, R. 1989 Turk.J.Pediatr.
86. Vitamin D intoxication associated with an over-the-counter supplement Koutkia, P., Chen, T. C., and Holick, M. F. 7-5-2001 N.Engl.J Med.
87. The steroid hormone of sunlight soltriol (vitamin D) as a seasonal regulator of biological activities and photoperiodic rhythms Stumpf, W. E. and Privette, T. H. 1991 J.Steroid Biochem.Mol.Biol.
88. Genomic actions of 1,25-dihydroxyvitamin D3 Whitfield, G. K., Hsieh, J. C., Jurutka, P. W., Selznick, S. H., Haussler, C. A., MacDonald, P. N., and Haussler, M. R. 1995 J Nutr
89. Vitamin D receptors in breast cancer cells Buras, R. R., Schumaker, L. M., Davoodi, F., Brenner, R. V., Shabahang, M., Nauta, R. J., and Evans, S. R. 1994 Breast Cancer Res.Treat.
90. Vitamin D and genomic stability Chatterjee, M. 4-18-2001 Mutat Res
91. The vitamin D hormone and its nuclear receptor: molecular actions and disease states Haussler, M. R., Haussler, C. A., Jurutka, P. W., Thompson, P. D., Hsieh, J. C., Remus, L. S., Selznick, S. H., and Whitfield, G. K. 1997 J.Endocrinol.
92. The impact of atmospheric pollution on vitamin D status of infants and toddlers in Delhi, India Agarwal, K. S., Mughal, M. Z., Upadhyay, P., Berry, J. L., Mawer, E. B., and Puliyel, J. M. 2002 Arch.Dis.Child
93. Hypovitaminosis D prevalence and determinants among African American and white women of reproductive age: third National Health and Nutrition Examination Survey, 1988-1994 Nesby-O'Dell, S., Scanlon, K. S., Cogswell, M. E., Gillespie, C., Hollis, B. W., Looker, A. C., Allen, C., Doughertly, C., Gunter, E. W., and Bowman, B. A. 2002 Am.J.Clin.Nutr.
94. [Nutritional rickets. An old disease with new relevance] Brunvand, L. and Nordshus, T. 5-20-1996 Tidsskr.Nor Laegeforen.
95. An outbreak of vitamin D deficiency rickets in a susceptible population Bachrach, S., Fisher, J., and Parks, J. S. 1979 Pediatrics
96. Nutritional rickets in African American breast-fed infants Kreiter, S. R., Schwartz, R. P., Kirkman, H. N., Jr., Charlton, P. A., Calikoglu, A. S., and Davenport, M. L. 2000 J.Pediatr.
97. Photosynthesis of vitamin D in the skin: effect of environmental and life-style variables Holick, M. F. 1987 Fed.Proc.
98. Influence of season and latitude on the cutaneous synthesis of vitamin D3: exposure to winter sunlight in Boston and Edmonton will not promote vitamin D3 synthesis in human skin Webb, A. R., Kline, L., and Holick, M. F. 1988 J.Clin.Endocrinol.Metab

99. [Vitamin D deficiency among pregnant women from Pakistan. How best to prevent it?] Brunvand, L., Henriksen, C., and Haug, E. 5-20-1996 Tidsskr.Nor Laegeforen.
100. Vitamin D status in different subgroups of British Asians Hunt, S. P., O'Riordan, J. L., Windo, J., and Truswell, A. S. 12-4-1976 Br.Med.J.
101. [Vitamin D status of children and adolescents of African and Asian diplomats in Germany] Koch, H. C. and Burmeister, W. 1993 Klin.Padiatr.
102. Vitamin D deficiency rickets and vitamin B12 deficiency in vegetarian children Hellebostad, M., Markestad, T., and Seeger, Halvorsen K. 1985 Acta Paediatr.Scand.
103. American Academy of Pediatrics. Committee on Nutrition. Nutritional aspects of vegeterianism, health foods, and fad diets 1977 Pediatrics
104. Plasma 25-hydroxyvitamin-D-levels during pregnancy in Caucasians and in vegetarian and non-vegetarian Asians Dent, C. E. and Gupta, M. M. 11-29-1975 Lancet
105. Macrobiotic nutrition and child health: results of a population-based, mixed-longitudinal cohort study in The Netherlands Dagnelie, P. C. and van Staveren, W. A. 1994 Am.J.Clin.Nutr.
106. Properties of human milk and their relationship with maternal nutrition Emmett, P. M. and Rogers, I. S. 10-29-1997 Early Hum.Dev.
107. Nutritional rickets Feldman, K. W., Marcuse, E. K., and Springer, D. A. 1990 Am.Fam.Physician
108. Nutritional rickets among breast-fed black and Alaska Native children [see comments] Gessner, B. D., deSchweinitz, E., Petersen, K. M., and Lewandowski, C. 1997 Alaska Med.
109. Fatty acid composition of mature breast milk according to the mothers diet during pregnancy Moya, M., Juste, M., Cortes, E., and Carratala, F. 2000 Adv.Exp.Med.Biol
110. Nutritional aspects of calcium and vitamin D from infancy to adolescence Saggese, G. and Igli, Baroncelli G. 1995 Ann.Ist.Super.Sanita
111. Fat-Soluble Vitamins in the Maternal Diet, Influence of Cod Liver Oil Supplementation and Impact of the Maternal Diet on Human Milk Composition Olafsdottir, A. S., Wagner, K. H., Thorsdottir, I., and Elmadfa, I. 2001 Ann.Nutr Metab
112. Vitamin D--soltriol the heliogenic steroid hormone: somatotrophic activator and modulator. Discoveries from histochemical studies lead to new concepts Stumpf, W. E. 1988 Histochemistry
113. Vitamin D (soltriol), light, and reproduction Stumpf, W. E. and Denny, M. E. 1989 Am.J.Obstet.Gynecol.
114. Some observations on the influence of vitamin D metabolites when added to the diet of commercial laying hens Harms, R. H., Bootwalla, S. M., Woodward, S. A., Wilson, H. R., and Untawale, G. A. 1990 Poult.Sci.
115. Fat-soluble vitamin nutrition for dairy cattle Herdt, T. H. and Stowe, H. D. 1991 Vet.Clin.North Am.Food Anim Pract.
116. Reduced fecundity of vitamin D deficient rats Hickie, J. P., Lavigne, D. M., and Woodward, W. D. 1983 Comp Biochem.Physiol A
117. [Vitamin D and reproduction in Wistar rats] Kayser, J., Sabel, A., and Lavollay, J. 12-17-1979 C.R.Seances Acad Sci D.
118. [Influence of the biological activity of substances on the puerperal period and fertility of cows] Konstantinov, P. 1975 Vet.Med.Nauki
119. 1,25-Dihydroxyvitamin D3 restores fertility of vitamin D-deficient female rats Kwiecinksi, G. G., Petrie, G. I., and DeLuca, H. F. 1989 Am.J.Physiol
120. Vitamin D is necessary for reproductive functions of the male rat Kwiecinski, G. G., Petrie, G. I., and DeLuca, H. F. 1989 J Nutr
121. 25-hydroxycholecalciferol in poultry nutrition Soares, J. H., Jr., Kerr, J. M., and Gray, R. W. 1995 Poult.Sci.
122. Influences of calcium intake and vitamin D supplementation on reproductive performance of dairy cows Ward, G., Marion, G. B., Campbell, C. W., and Dunham, J. R. 1971 J Dairy Sci
123. Effect of vitamin D on testicular CaBP28K expression and serum testosterone in chickens Inpanbutr, N., Reiswig, J. D., Bacon, W. L., Slemons, R. D., and Iacopino, A. M. 1996 Biol.Reprod.
124. Vitamin D is an important factor in estrogen biosynthesis of both female and male gonads Kinuta, K., Tanaka, H., Moriwake, T., Aya, K., Kato, S., and Seino, Y. 2000 Endocrinology
125. Vitamin D and calcium dysregulation in the polycystic ovarian syndrome Thys-Jacobs, S., Donovan, D., Papadopoulos, A., Sarrel, P., and Bilezikian, J. P. 1999 Steroids
126. Low serum 25-hydroxyvitamin D concentrations are associated with insulin resistance and obesity in women with polycystic ovary syndrome Hahn, S., Haselhorst, U., Tan, S., Quadbeck, B., Schmidt, M., Roesler, S., Kimmig, R., Mann, K., and Janssen, O. E. 2006 Exp.Clin.Endocrinol.Diabetes
127. Serum parathyroid hormone concentrations are increased in women with polycystic ovary syndrome Panidis, D., Balaris, C., Farmakiotis, D., Rousso, D., Kourtis, A., Balaris, V., Katsikis, I., Zournatzi, V., and amanti-Kandarakis, E. 2005 Clin.Chem.
128. Influence of Ultraviolet Irradiation Upon Excretion of Sex hormones in the Male Myerson, A. and Neustadt, R. 1939 Endocrinology

129. On the hypophysis as the regulator of gonadal rhythm Marshall, F. H. A. 1938 Les Hormones Sexuelles
130. Bright Light Exposure Increases Male Hormone Yoong, I and Youngstedt, S 2003 Neurosci.Lett.
131. Effects of transdermal testosterone on bone and muscle in older men with low bioavailable testosterone levels Kenny, A. M., Prestwood, K. M., Gruman, C. A., Marcello, K. M., and Raisz, L. G. 2001 J Gerontol.A Biol.Sci.Med.Sci.
132. Evidence for an interaction of insulin and sex steroids in the regulation of vitamin D metabolism in the rat Nyomba, B. L., Bouillon, R., and De Moor, P. 1987 J.Endocrinol.
133. Elevation of serum 25-hydroxycalciferol levels in androgen-treated and ultraviolet-irradiated rats Ohata, M., Sakagami, Y., and Fujita, T. 1977 Endocrinol.Jpn.
134. Hypovitaminosis D Myopathy Without Biochemical Signs of Osteomalacic Bone Involvement Glerup, H., Mikkelsen, K., Poulsen, L., Hass, E., Overbeck, S., Andersen, H., Charles, P., and Eriksen, E. F. 2000 Calcif.Tissue Int.
135. Muscle weakness in intensive care patients: initial manifestation of vitamin D deficiency Rimaniol, J. M., Authier, F. J., and Chariot, P. 1994 Intensive Care Med.
136. Does calcitriol therapy improve muscle function in uremic patients Wanic-Kossowska, M., Grzegorzewska, A., Plotast, H., and Bombicki, K. 1996 Perit.Dial.Int.
137. Environmental factors that influence the cutaneous production of vitamin D Holick, M. F. 1995 Am.J Clin Nutr
138. Aging decreases the capacity of human skin to produce vitamin D3 MacLaughlin, J. and Holick, M. F. 1985 J Clin Invest
139. At what time should one go out in the sun? Moan, J., Dahlback, A., and Porojnicu, A. C. 2008 Adv.Exp.Med.Biol.
140. Ultraviolet exposure scenarios: risks of erythema from recommendations on cutaneous vitamin D synthesis Webb, A. R. and Engelsen, O. 2008 Adv.Exp.Med.Biol.
141. Optimizing solar UV-radiation exposures for vitamin D3: comparing global and diffuse spectral UV radiation Turnbull, D. J. and Parisi, A. V. 2008 Radiat.Res.
142. [The photobiology of vitamin D--a topic of renewed focus] Moan, J. and Porojnicu, A. C. 4-6-2006 Tidsskr.Nor Laegeforen.
143. Vitamin D -vs- Erythema: Efficts of Solar Angle & Artificial Sources Sayre, R. M., Dowdy, J. C., Shephard, R. J., Sadiq, I., Baqer, A., and Kollias, N. 1998
144. Vitamin D in an ecological context Bjorn, L. O. and Wang, T. 2000 Int.J.Circumpolar.Health
145. Season, latitude, and ability of sunlight to promote synthesis of vitamin D3 in skin 1989 Nutr.Rev.
146. Health promotion when the 'vaccine' does not work Wortman, J. 2006 Health Promot.J.Austr.
147. Impact of recent increase in incidence on future diabetes burden: U.S., 2005-2050 Narayan, K. M., Boyle, J. P., Geiss, L. S., Saaddine, J. B., and Thompson, T. J. 2006 Diabetes Care
148. Projection of diabetes burden through 2050: impact of changing demography and disease prevalence in the U.S Boyle, J. P., Honeycutt, A. A., Narayan, K. M., Hoerger, T. J., Geiss, L. S., Chen, H., and Thompson, T. J. 2001 Diabetes Care
149. High-carbohydrate, low-fat diet? Negative Garg, A. and Grundy, S. M. 1992 Hosp.Pract.(Off Ed)
150. Diet, diabetes, hypertension and blacks Gaskin, R. 1999 Ethn.Dis.
151. Should NIDDM patients be on high-carbohydrate, low-fat diets? Affirmative Stacpoole, P. W. 1992 Hosp.Pract.(Off Ed)
152. Cardiovascular disease: a historic perspective Smith, D. 2000 Jpn.J Vet.Res.
153. Hyperhomocysteinemia and cobalamin deficiency in young Asian Indians in the United States Carmel, R., Mallidi, P. V., Vinarskiy, S., Brar, S., and Frouhar, Z. 2002 Am.J Hematol.
154. Moderate folate depletion increases plasma homocysteine and decreases lymphocyte DNA methylation in postmenopausal women Jacob, R. A., Gretz, D. M., Taylor, P. C., James, S. J., Pogribny, I. P., Miller, B. J., Henning, S. M., and Swendseid, M. E. 1998 J.Nutr.
155. Folate supplementation inhibits intimal hyperplasia induced by a high-homocysteine diet in a rat carotid endarterectomy model Smith, T. P., Cruz, C. P., Brown, A. T., Eidt, J. F., and Moursi, M. M. 2001 J Vasc.Surg.
156. Nutritional and metabolic aspects of stroke prevention Spence, J. D. 2003 Adv.Neurol.
157. Treatment of hyperhomocysteinemia with folic acid and vitamins B12 and B6 attenuates thrombin generation Undas, A., Domagala, T. B., Jankowski, M., and Szczeklik, A. 9-15-1999 Thromb.Res.
158. The emergence of cardiovascular disease during urbanisation of Africans Vorster, H. H. 2002 Public Health Nutr
159. [Nutrition in the prevention of ischemic heart disease] Ginter, E. 1989 Bratisl.Lek.Listy
160. Epidemiology of cardiovascular diseases in Europe Kromhout, D. 2001 Public Health Nutr
161. Diet and cardiovascular diseases Kromhout, D. 2001 J Nutr Health Aging

162. Vitamin D and ischaemic heart disease Lund, B., Badskjaer, J., Lund, B., and Soerensen, O. H. 1978 Horm.Metab Res.
163. Sunlight, cholesterol and coronary heart disease Grimes, D. S., Hindle, E., and Dyer, T. 1996 QJM.
164. Calcium from dairy products, vitamin D intake, and blood pressure: the Tromso study Jorde, R. and Bonaa, K. H. 2000 Am.J.Clin.Nutr.
165. Hypothesis: Correction of low vitamin D status among Arab women will prevent heart failure and improve cardiac function in established heart failure Saadi, H. F., Kazzam, E., Ghurbana, B. A., and Nicholls, M. G. 7-5-2006 Eur.J.Heart Fail.
166. Macro- and micronutrients in African-Americans with heart failure Bhattacharya, S. K., Ahokas, R. A., Carbone, L. D., Newman, K. P., Gerling, I. C., Sun, Y., and Weber, K. T. 2006 Heart Fail.Rev.
167. Cutaneous malignant melanoma, sun exposure, and sunscreen use: epidemiological evidence Bastuji-Garin, S. and Diepgen, T. L. 2002 Br.J.Dermatol.
168. Sunscreen isn't enough Diffey, B. 11-15-2001 J.Photochem.Photobiol.B
169. Changes in ultraviolet absorbance and hence in protective efficacy against lipid peroxidation of organic sunscreens after UVA irradiation Damiani, E., Rosati, L., Castagna, R., Carloni, P., and Greci, L. 3-1-2006 J.Photochem.Photobiol.B.
170. The effect of sunscreen on skin elastase activity induced by ultraviolet-A irradiation Tsukahara, K., Moriwaki, S., Hotta, M., Fujimura, T., Sugiyama-Nakagiri, Y., Sugawara, S., Kitahara, T., and Takema, Y. 2005 Biol.Pharm.Bull.
171. A review of sunscreens and their adverse reactions Pustisek, N., Lipozencic, J., and Ljubojevic, S. 2005 Acta Dermatovenerol.Croat.
172. Geographic variation in breast cancer mortality in the United States: a hypothesis involving exposure to solar radiation Garland, F. C., Garland, C. F., Gorham, E. D., and Young, J. F. 1990 Prev.Med.
173. Sunlight, vitamin D, and ovarian cancer mortality rates in US women Lefkowitz, E. S. and Garland, C. F. 1994 Int.J.Epidemiol.
174. Enamel hypoplasia of the teeth associated with neonatal tetany: a manifestation of maternal vitamin-D deficiency Purvis, R. J., Barrie, W. J., MacKay, G. S., Wilkinson, E. M., Cockburn, F., and Belton, N. R. 10-13-1973 Lancet
175. Factors affecting newborn bone mineral content: in utero effects on newborn bone mineralization Namgung, R. and Tsang, R. C. 2000 Proc.Nutr.Soc.
176. Low total body bone mineral content and high bone resorption in Korean winter-born versus summer-born newborn infants [see comments] Namgung, R., Tsang, R. C., Lee, C., Han, D. G., Ho, M. L., and Sierra, R. I. 1998 J.Pediatr.
177. Improving vitamin D levels in pregnancy and breastfeeding Hairon, N. 1-8-2008 Nurs.Times
178. Maternal vitamin D deficiency associated with neonatal hypocalcaemic convulsions Camadoo, L., Tibbott, R., and Isaza, F. 2007 Nutr.J.
179. Vitamin D-deficiency rickets among children in Canada Ward, L. M., Gaboury, I., Ladhani, M., and Zlotkin, S. 7-17-2007 CMAJ.
180. Vitamin D: the secosteroid hormone and human reproduction Perez-Lopez, F. R. 2007 Gynecol.Endocrinol.
181. Who needs vitamin supplements? More, J. 2007 J.Fam.Health Care
182. Eating for pregnancy and breast-feeding Theobald, H. E. 2007 J.Fam.Health Care
183. How practice meets guidelines: evaluation of nutrition counselling in Finnish well-women and well-baby clinics Huurre, A., Laitinen, K., Hoppu, U., and Isolauri, E. 2006 Acta Paediatr.
184. [Vitamin deficiencies in breastfed children due to maternal dietary deficiency] Kollee, L. A. 3-4-2006 Ned.Tijdschr.Geneeskd.
185. [Seizures in foreign newborns due to maternal vitamin-D deficiency] Visser, H. K. 4-23-2005 Ned.Tijdschr.Geneeskd.
186. 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.
187. In utero dietary exposures and risk of islet autoimmunity in children Fronczak, C. M., Baron, A. E., Chase, H. P., Ross, C., Brady, H. L., Hoffman, M., Eisenbarth, G. S., Rewers, M., and Norris, J. M. 2003 Diabetes Care
188. Malaria: burden of disease Guinovart, C., Navia, M. M., Tanner, M., and Alonso, P. L. 2006 Curr.Mol.Med.
189. Nutrition and Physical Degeneration Price, W. A. 1989
190. Nomenclature Committee of IUB (NC-IUB) and IUB-IUPAC Joint Commission on Biochemical Nomenclature (JCBN): Newsletter 1983 1-1-1983 Biochem.J
191. Normal and abnormal regulation of 1,25-(OH)2D synthesis Breslau, N. A. 1988 Am.J.Med.Sci.
192. Evidence that vitamin D3 increases serum 25-hydroxyvitamin D more efficiently than does vitamin D2 Trang, H. M., Cole, D. E., Rubin, L. A., Pierratos, A., Siu, S., and Vieth, R. 1998 Am.J.Clin.Nutr.
193. Vitamin D2 in vertebrate evolution Hay, A. W. and Watson, G. 1977 Comp Biochem.Physiol [B]

194. Relative biopotency of dietary ergocalciferol and cholecalciferol and the role of and requirement for vitamin D in rainbow trout (Salmo gairdneri) Barnett, B. J., Cho, C. Y., and Slinger, S. J. 1982 J.Nutr.
195. Evidence that discrimination against ergocalciferol by the chick is the result of enhanced metabolic clearance rates for its mono- and dihydroxylated metabolites Hoy, D., Ramberg, C., and Horst, R. 5-1-1988
196. [Comparative antirachitic activity of vitamins D2 and D3 in the body of chicks] Valinietse, M. I. and Bauman, V. K. 1981 Prikl.Biokhim.Mikrobiol.
197. Cutaneous photosynthesis of vitamin D: an evolutionary highly-conserved endocrine system that protects against environmental hazards including UV-radiation and microbial infections Tremezaygues, L., Sticherling, M., Pfohler, C., Friedrich, M., Meineke, V., Seifert, M., Tilgen, W., and Reichrath, J. 2006 Anticancer Res.
198. Association of UV index, latitude, and melanoma incidence in nonwhite populations--US Surveillance, Epidemiology, and End Results (SEER) Program, 1992 to 2001 Eide, M. J. and Weinstock, M. A. 2005 Arch.Dermatol.
199. Immunological responses to ultraviolet light B radiation in Black individuals Matsuoka, L. Y., McConnachie, P., Wortsman, J., and Holick, M. F. 1999 Life Sci.
200. Effect of season and vitamin D supplementation on plasma concentrations of 25-hydroxyvitamin D in Norwegian infants Markestad, T. 1983 Acta Paediatr.Scand.
201. Breast cancer: hormones and other risk factors Hulka, B. S. and Moorman, P. G. 6-15-2002 Maturitas
202. Estrogen Plus Progestin and the Incidence of Dementia and Mild Cognitive Impairment in Postmenopausal Women: The Women's Health Initiative Memory Study: A Randomized Controlled Trial Shumaker, Sally A., Legault, Claudine, Thal, Leon, Wallace, Robert B., Ockene, Judith K., Hendrix, Susan L., Jones, Beverly N., III, Assaf, Annlouise R., Jackson, Rebecca D., Morley Kotchen, Jane, Wassertheil-Smoller, Sylvia, and Wactawski-Wende, Jean 5-28-2003 JAMA
203. The cutaneous photosynthesis of previtamin D3: a unique photoendocrine system Holick, M. F. 1981 J.Invest Dermatol.
204. [Pyridoxine toxicity] Komiyama, A. 2000 Ryoikibetsu.Shokogun.Shirizu.
205. Effects of pyridoxine neurotoxicity on a distribution of calcitonin gene-related peptide binding sites Bellibas, S. E., Guidobono, F., Bettica, P., Netti, C., and Pecile, A. 1997 Pol.J.Pharmacol.
206. Pyridoxine megavitaminosis: an analysis of the early changes induced with massive doses of vitamin B6 in rat primary sensory neurons Krinke, G., Naylor, D. C., and Skorpil, V. 1985 J.Neuropathol.Exp.Neurol.
207. Hypervitaminosis D and premature aging: lessons learned from Fgf23 and Klotho mutant mice Razzaque, M. S. and Lanske, B. 2006 Trends Mol.Med.
208. The acute and chronic toxic effects of vitamin A Penniston, K. L. and Tanumihardjo, S. A. 2006 Am.J.Clin.Nutr.
209. Hypervitaminosis A-induced liver fibrosis: stellate cell activation and daily dose consumption Nollevaux, M. C., Guiot, Y., Horsmans, Y., Leclercq, I., Rahier, J., Geubel, A. P., and Sempoux, C. 2006 Liver Int.
210. Subclinical hypervitaminosis A in rat: measurements of bone mineral density (BMD) do not reveal adverse skeletal changes Lind, P. M., Johansson, S., Ronn, M., and Melhus, H. 1-5-2006 Chem.Biol.Interact.
211. Hypervitaminosis A resulting in DNA aberration in fetal transgenic mice (Muta Mouse) Inomata, T., Kiuchi, A., Yoshida, T., Hisamatsu, S., Takizawa, A., Kashiwazaki, N., Akahori, F., and Ninomiya, H. 9-5-2005 Mutat.Res.
212. Hypercalcaemia in two dogs caused by excessive dietary supplementation of vitamin D Mellanby, R. J., Mee, A. P., Berry, J. L., and Herrtage, M. E. 2005 J.Small Anim Pract.
213. Polar hysteria: an expression of hypervitaminosis A O'Donnell, J. 2004 Am.J.Ther.
214. Risk of hypervitaminosis D from prolonged feeding of high vitamin D premature infant formula Nako, Y., Tomomasa, T., and Morikawa, A. 2004 Pediatr.Int.
215. Is vitamin A consumption a risk factor for osteoporotic fracture? Barker, M. E. and Blumsohn, A. 2003 Proc.Nutr.Soc.
216. Vitamin A and infancy. Biochemical, functional, and clinical aspects Perrotta, S., Nobili, B., Rossi, F., Di, Pinto D., Cucciolla, V., Borriello, A., Oliva, A., and Della, Ragione F. 2003 Vitam.Horm.
217. Hypervitaminosis A and fractures Lips, P. 1-23-2003 N.Engl.J.Med.
218. A review of the biochemistry, metabolism and clinical benefits of thiamin(e) and its derivatives Lonsdale, D. 2006 Evid.Based.Complement Alternat.Med.
219. Effects of excess pantothenic acid administration on the other water-soluble vitamin metabolisms in rats Shibata, K., Takahashi, C., Fukuwatari, T., and Sasaki, R. 2005 J.Nutr.Sci.Vitaminol.(Tokyo)
220. Tissue minerals of magnesium-deficient rats with thiamine deficiency and excess Itokawa, Y. 1987 Magnesium
221. Copper toxicity, oxidative stress, and antioxidant nutrients Gaetke, L. M. and Chow, C. K. 7-15-2003 Toxicology

222. Chronic copper poisoning in sheep resulting from free-choice, trace-mineral-salt ingestion KOWALCZYK, T., POPE, A. L., and SORENSEN, D. K. 8-1-1962 J.Am.Vet.Med.Assoc.
223. Zinc requirements and the risks and benefits of zinc supplementation Maret, W. and Sandstead, H. H. 2006 J.Trace Elem.Med.Biol.
224. 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.
225. How safe are folic acid supplements? Campbell, N. R. 8-12-1996 Arch.Intern.Med.
226. Comparative effectiveness of vitamin D3 and dietary vitamin E on peroxidation of lipids and enzymes of the hepatic antioxidant system in Sprague--Dawley rats Sardar, S., Chakraborty, A., and Chatterjee, M. 1996 Int.J.Vitam.Nutr.Res.
227. Vitamin D is a membrane antioxidant. Ability to inhibit iron-dependent lipid peroxidation in liposomes compared to cholesterol, ergosterol and tamoxifen and relevance to anticancer action Wiseman, H. 7-12-1993 FEBS Lett.
228. Inadequate vitamin D status: does it contribute to the disorders comprising syndrome 'X'? [published erratum appears in Br J Nutr 1998 Dec;80(6):585] Boucher, B. J. 1998 Br.J.Nutr.
229. Modulatory role of 1,25 dihydroxyvitamin D3 on pancreatic islet insulin release via the cyclic AMP pathway in the rat Bourlon, P. M., Faure-Dussert, A., and Billaudel, B. 1997 Br.J.Pharmacol.
230. Vitamin D3 deficiency and alterations of glucose metabolism in rat endocrine pancreas Billaudel, B., Barakat, L., and Faure-Dussert, A. 1998 Diabetes Metab
231. Influence of vitamin D3 deficiency and 1,25 dihydroxyvitamin D3 on de novo insulin biosynthesis in the islets of the rat endocrine pancreas Bourlon, P. M., Billaudel, B., and Faure-Dussert, A. 1999 J.Endocrinol.
232. Vitamin D, glucose tolerance and insulinaemia in elderly men [published erratum appears in Diabetologia 1997 Jul;40(7):870] Baynes, K. C., Boucher, B. J., Feskens, E. J., and Kromhout, D. 1997 Diabetologia
233. Nutritional status in persons with and without senile cataract: blood vitamin and mineral levels Jacques, P. F., Hartz, S. C., Chylack, L. T., Jr., McGandy, R. B., and Sadowski, J. A. 1988 Am J Clin Nutr
234. Redefining vitamin D insufficiency Malabanan, A., Veronikis, I. E., and Holick, M. F. 3-14-1998 Lancet
235. Vitamin D deficiency: a culprit in metabolic bone disease Hofeldt, F. D. 1993 Prog.Food Nutr.Sci.
236. Vitamin D and bone health in the elderly Parfitt, A. M., Gallagher, J. C., Heaney, R. P., Johnston, C. C., Neer, R., and Whedon, G. D. 1982 Am.J.Clin.Nutr.
237. Lower serum 25-hydroxyvitamin D is associated with increased bone resorption markers and lower bone density at the proximal femur in normal females: a population-based study Scharla, S. H., Scheidt-Nave, C., Leidig, G., Woitge, H., Wuster, C., Seibel, M. J., and Ziegler, R. 1996 Exp.Clin.Endocrinol.Diabetes
238. Subclinical vitamin D deficiency in neonates: definition and response to vitamin D supplements Zeghoud, F., Vervel, C., Guillozo, H., Walrant-Debray, O., Boutignon, H., and Garabedian, M. 1997 Am.J.Clin.Nutr.
239. Latitude and ischaemic heart disease [letter] Segall, J. J. 5-20-1989 Lancet
240. Latitude and heart disease [letter] Williams, F. L. and Lloyd, O. L. 5-13-1989 Lancet
241. Regulation of adiposity by dietary calcium Zemel, M. B., Shi, H., Greer, B., Dirienzo, D., and Zemel, P. C. 2000 FASEB J.
242. Four amino acid changes are associated with the Aldh3a1 locus polymorphism in mice which may be responsible for corneal sensitivity to ultraviolet light Shiao, T., Tran, P., Siegel, D., Lee, J., and Vasiliou, V. 1999 Pharmacogenetics
243. Regulation of adiposity and obesity risk by dietary calcium: mechanisms and implications Zemel, M. B. 2002 J.Am.Coll.Nutr.
244. 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
245. Stimulation of ultraviolet-induced carcinogenesis by 1,3-Bis(2-chloroethyl)-1-nitrosourea Epstein, J. H. 1979 Cancer Res.
246. 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.
247. Regulation of TNF-alpha release from bone marrow-derived macrophages by vitamin D [published erratum appears in J Cell Biochem 1994 Nov;56(3):426] Abu-Amer, Y. and Bar-Shavit, Z. 1994 J.Cell Biochem.
248. Vitamin D and autoimmunity: is vitamin D status an environmental factor affecting autoimmune disease prevalence? Cantorna, M. T. 2000 Proc.Soc.Exp.Biol.Med.
249. Reduced 25-hydroxyvitamin D levels in primary Sjogren's syndrome. Correlations to disease manifestations Bang, B., Asmussen, K., Sorensen, O. H., and Oxholm, P. 1999 Scand.J.Rheumatol.
250. Dietary vitamin D intake in patients with Crohn's disease Vogelsang, H., Klamert, M., Resch, H., and Ferenci, P. 1995 Wien.Klin.Wochenschr.
251. [Vitamin D deficiency. Easy to diagnose, often overlooked (see comments)] Glerup, H. and Eriksen, E. F. 4-26-1999 Ugeskr.Laeger

252. Normalization of serum calcium restores fertility in vitamin D-deficient male rats Uhland, A. M., Kwiecinski, G. G., and DeLuca, H. F. 1992 J.Nutr.
253. Vitamin D and calcium in menstrual migraine Thys-Jacobs, S. 1994 Headache
254. An ecologic study of dietary and solar ultraviolet-B links to breast carcinoma mortality rates Grant, W. B. 1-1-2002 Cancer
255. Geographic patterns of prostate cancer mortality. Evidence for a protective effect of ultraviolet radiation Hanchette, C. L. and Schwartz, G. G. 12-15-1992 Cancer
256. In colorectal carcinoma patients, serum vitamin D levels vary according to stage of the carcinoma Niv, Y., Sperber, A. D., Figer, A., Igael, D., Shany, S., Fraser, G., and Schwartz, B. 8-1-1999 Cancer
257. Vitamin D and prostate cancer Tuohimaa, P., Lyakhovich, A., Aksenov, N., Pennanen, P., Syvala, H., Lou, Y. R., Ahonen, M., Hasan, T., Pasanen, P., Blauer, M., Manninen, T., Miettinen, S., Vilja, P., and Ylikomi, T. 2001 J Steroid Biochem.Mol.Biol.
258. Calcium and vitamin D. Diagnostics and therapeutics Holick, M. F. 2000 Clin.Lab Med.
259. Vitamin D and breast cancer risk: the NHANES I Epidemiologic follow-up study, 1971-1975 to 1992. National Health and Nutrition Examination Survey John, E. M., Schwartz, G. G., Dreon, D. M., and Koo, J. 1999 Cancer Epidemiol.Biomarkers Prev.
260. Vitamin D and prostate cancer: biologic interactions and clinical potentials Miller, G. J. 1998 Cancer Metastasis Rev.
261. Vitamin D increases expression of the tyrosine hydroxylase gene in adrenal medullary cells Puchacz, E., Stumpf, W. E., Stachowiak, E. K., and Stachowiak, M. K. 1996 Brain Res.Mol.Brain Res.
262. The adrenal: a new target organ of the calciotropic hormone 1,25- dihydroxyvitamin D3 Clark, S. A., Stumpf, W. E., Bishop, C. W., DeLuca, H. F., Park, D. H., and Joh, T. H. 1986 Cell Tissue Res.
263. 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
264. Insulin secretion after oral calcium load Fujita, T., Sakagami, Y., Tomita, T., Okamoto, Y., and Oku, H. 1978 Endocrinol.Jpn.
265. [Effects of calcium supplementation using AAACa or milk on nocturnal bone resorption in young women] Ohgitani, S., Fujii, Y., and Fujita, T. 1997 Nippon Ronen Igakkai Zasshi
266. Fall of blood ionized calcium on watching a provocative TV program and its prevention by active absorbable algal calcium (AAA Ca) Fujita, T., Ohgitani, S., and Nomura, M. 1999 J.Bone Miner.Metab
267. High prevalence of vitamin D deficiency and reduced bone mass in elderly women with Alzheimer's disease Sato, Y., Asoh, T., and Oizumi, K. 1998 Bone
268. High prevalence of vitamin D deficiency and reduced bone mass in Parkinson's disease Sato, Y., Kikuyama, M., and Oizumi, K. 1997 Neurology
269. Calcium absorption, endogenous excretion, and endocrine changes during and after long-term bed rest LeBlanc, A., Schneider, V., Spector, E., Evans, H., Rowe, R., Lane, H., Demers, L., and Lipton, A. 1995 Bone
270. Effect of immobilization on vitamin D status and bone mass in chronically hospitalized disabled stroke patients Sato, Y., Kuno, H., Asoh, T., Honda, Y., and Oizumi, K. 1999 Age Ageing
271. Prenatal Nutritional Deformities and Disease Types Price, W. A. 1989
272. [The effect of deficiency of selected bioelements on hyperactivity in children with certain specified mental disorders] Starobrat-Hermelin, B. 1998 Ann.Acad.Med.Stetin.
273. Vitamin D and the immune system Amento, E. P. 1987 Steroids
274. Effects of specific nutrients on the immune response. Selected clinical applications Corman, L. C. 1985 Med.Clin.North Am.
275. Vitamins and the regulation of the immune response Long, K. Z. and Santos, J. I. 1999 Pediatr.Infect.Dis.J.
276. 1,25-Dihydroxyvitamin D3 as a natural regulator of human immune functions Muller, K. and Bendtzen, K. 1996 J.Investig.Dermatol.Symp.Proc.
277. Sun protection factor measurement of sunscreens is dependent on minimal erythema dose Damian, D. L., Halliday, G. M., and Stc, Barnetson R. 1999 Br.J.Dermatol.
278. Do sunlight and vitamin D reduce the likelihood of colon cancer? Garland, C. F. and Garland, F. C. 1980 Int.J.Epidemiol.
279. Effect of calcium intake on serum levels of 25-hydroxyvitamin D3 Berlin, T. and Bjorkhem, I. 1988 Eur.J.Clin.Invest
280. Vitamin D metabolism in chronic childhood hypoparathyroidism: evidence for a direct regulatory effect of calcium Carpenter, T. O., Insogna, K. L., Boulware, S. D., and Mitnick, M. A. 1990 J.Pediatr.
281. Hyperproliferation and defects in epithelial polarity upon conditional ablation of alpha-catenin in skin Vasioukhin, V., Bauer, C., Degenstein, L., Wise, B., and Fuchs, E. 2-23-2001 Cell
282. Vitamin D influences gap junctional communication in C3H/10T 1/2 murine fibroblast cells Stahl, W., Nicolai, S., Hanusch, M., and Sies, H. 9-19-1994 FEBS Lett.

283. Evidence supporting the role of vitamin D in reducing the risk of cancer Grant, W. B. and Garland, C. F. 2002 J.Intern.Med.
284. Beneficial effects of sun exposure on cancer mortality Ainsleigh, H. G. 1993 Prev.Med.
285. Calcium, vitamin D, sunshine exposure, dairy products and colon cancer risk (United States) Kampman, E., Slattery, M. L., Caan, B., and Potter, J. D. 2000 Cancer Causes Control
286. Can colon cancer incidence and death rates be reduced with calcium and vitamin D? Garland, C. F., Garland, F. C., and Gorham, E. D. 1991 Am.J.Clin.Nutr.
287. Research on the probable cause of an outbreak of field rickets in turkeys Huff, W. E., Huff, G. R., Clark, F. D., Moore, P. A., Jr., Rath, N. C., Balog, J. M., Barnes, D. M., Erf, G. F., and Beers, K. W. 1999 Poult.Sci.
288. Sunlight and mortality from breast, ovarian, colon, prostate, and non-melanoma skin cancer: a composite death certificate based case-control study Freedman, D. M., Dosemeci, M., and McGlynn, K. 2002 Occup.Environ.Med.
289. Sunlight--can it prevent as well as cause cancer? [see comments] Studzinski, G. P. and Moore, D. C. 9-15-1995 Cancer Res.
290. Vitamin D adequacy: a possible relationship to breast cancer Newmark, H. L. 1994 Adv.Exp.Med.Biol.
291. Epidemiology of malignant melanoma: intermittent or total accumulated exposure to the sun? Armstrong, B. K. 1988 J.Dermatol.Surg.Oncol.
292. Sun exposure and skin cancer Armstrong, B. K., Kricker, A., and English, D. R. 1997 Australas.J.Dermatol.
293. A role for photoproducts of vitamin D in the etiology of cutaneous melanoma? Braun, M. M. and Tucker, M. A. 1997 Med.Hypotheses
294. Cutaneous melanoma in relation to intermittent and constant sun exposure--the Western Canada Melanoma Study Elwood, J. M., Gallagher, R. P., Hill, G. B., and Pearson, J. C. 4-15-1985 Int.J.Cancer
295. Conversion of vitamin D3 to 1alpha,25-dihydroxyvitamin D3 in human skin equivalents Lehmann, B., Rudolph, T., Pietzsch, J., and Meurer, M. 2000 Exp.Dermatol.
296. Vitamin D and systemic cancer: is this relevant to malignant melanoma? Osborne, J. E. and Hutchinson, P. E. 2002 Br.J.Dermatol.
297. Vitamin D insufficiency in south-east Queensland McGrath, J. J., Kimlin, M. G., Saha, S., Eyles, D. W., and Parisi, A. V. 2-5-2001 Med.J.Aust.
298. Differential apoptotic response of human melanoma cells to 1 alpha,25-dihydroxyvitamin D3 and its analogues Danielsson, C., Fehsel, K., Polly, P., and Carlberg, C. 1998 Cell Death.Differ.
299. Positive and negative interaction of 1,25-dihydroxyvitamin D3 and the retinoid CD437 in the induction of human melanoma cell apoptosis Danielsson, C., Torma, H., Vahlquist, A., and Carlberg, C. 5-5-1999 Int.J Cancer
300. The relationship between the vitamin D system and cancer DeLuca, H. F. and Ostrem, V. 1986 Adv.Exp.Med.Biol.
301. Skin cancer and ultraviolet-B radiation under the Antarctic ozone hole: southern Chile, 1987-2000 Abarca, J. F. and Casiccia, C. C. 2002 Photodermatol.Photoimmunol.Photomed.
302. Effects of solar radiation on cutaneous detoxification pathways Afaq, F. and Mukhtar, H. 2001 J.Photochem.Photobiol.B
303. Incidence of skin cancers and precancerous lesions in Japanese--risk factors and prevention Araki, K., Nagano, T., Ueda, M., Washio, F., Watanabe, S., Yamaguchi, N., and Ichihashi, M. 1999 J.Epidemiol.
304. The epidemiology of UV induced skin cancer Armstrong, B. K. and Kricker, A. 2001 J.Photochem.Photobiol.B
305. UV-induced cutaneous photobiology Beissert, S. and Granstein, R. D. 1996 Crit Rev.Biochem.Mol.Biol.
306. An approach towards understanding the genesis of sunlight-induced skin cancer Chatterjee, S. N., Agarwal, S., and Bose, B. 1990 Indian J Biochem.Biophys.
307. UV damage, DNA repair and skin carcinogenesis Cleaver, J. E. and Crowley, E. 4-1-2002 Front Biosci.
308. Action spectrum for photocarcinogenesis de Gruijl, F. R. 1995 Recent Results Cancer Res.
309. [Adverse effects of sunlight on the skin] de Gruijl, F. R. 3-21-1998 Ned.Tijdschr.Geneeskd.
310. Skin cancer and solar UV radiation de Gruijl, F. R. 1999 Eur.J.Cancer
311. The mutagenic effect of ultraviolet-A1 on human skin demonstrated by sequencing the p53 gene in single keratinocytes Persson, A. E., Edstrom, D. W., Backvall, H., Lundeberg, J., Ponten, F., Ros, A. M., and Williams, C. 2002 Photodermatol.Photoimmunol.Photomed.
312. Environmental factors in nonmelanoma and melanoma skin cancer Woodhead, A. D., Setlow, R. B., and Tanaka, M. 1999 J.Epidemiol.
313. Photochemoprevention by botanical antioxidants Afaq, F. and Mukhtar, H. 2002 Skin Pharmacol.Appl.Skin Physiol
314. Cutaneous photochemoprotection by green tea: a brief review Ahmad, N. and Mukhtar, H. 2001 Skin Pharmacol.Appl.Skin Physiol

315. Dietary factors in the prevention and treatment of nonmelanoma skin cancer and melanoma Bialy, T. L., Rothe, M. J., and Grant-Kels, J. M. 2002 Dermatol.Surg.
316. Protective effect of topically applied olive oil against photocarcinogenesis following UVB exposure of mice Budiyanto, A., Ahmed, N. U., Wu, A., Bito, T., Nikaido, O., Osawa, T., Ueda, M., and Ichihashi, M. 2000 Carcinogenesis
317. Preventive effect of antioxidant on ultraviolet-induced skin cancer in mice Ichihashi, M., Ahmed, N. U., Budiyanto, A., Wu, A., Bito, T., Ueda, M., and Osawa, T. 2000 J Dermatol.Sci
318. Photoprotective actions of topically applied vitamin E Krol, E. S., Kramer-Stickland, K. A., and Liebler, D. C. 2000 Drug Metab Rev.
319. Prevention of ultraviolet radiation-induced suppression of contact hypersensitivity by Aloe vera gel components Lee, C. K., Han, S. S., Shin, Y. K., Chung, M. H., Park, Y. I., Lee, S. K., and Kim, Y. S. 1999 Int.J Immunopharmacol.
320. 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.
321. Postadministration protective effect of magnesium-L-ascorbyl-phosphate on the development of UVB-induced cutaneous damage in mice Kobayashi, S., Takehana, M., Kanke, M., Itoh, S., and Ogata, E. 1998 Photochem.Photobiol.
322. Antioxidant nutrients protect against UVB-induced oxidative damage to DNA of mouse keratinocytes in culture Stewart, M. S., Cameron, G. S., and Pence, B. C. 1996 J Invest Dermatol.
323. The effect of a vitamin A acetate diet on ultraviolet radiation-induced immune suppression as measured by contact hypersensitivity in mice Sailstad, D. M., Boykin, E. H., Slade, R., Doerfler, D. L., and Selgrade, M. K. 2000 Photochem.Photobiol.
324. Skin, sun, and vitamin A: from aging to cancer Saurat, J. H. 2001 J.Dermatol.
325. Photoimmune suppression and photocarcinogenesis Ullrich, S. E. 3-1-2002 Front Biosci.
326. Intermittent oral disodium pamidronate in established osteoporosis: a 2 year double-masked placebo-controlled study of efficacy and safety Ryan, P. J., Blake, G. M., Davie, M., Haddaway, M., Gibson, T., and Fogelman, I. 2000 Osteoporos.Int.
327. UVA-induced immune suppression through an oxidative pathway Iwai, I., Hatao, M., Naganuma, M., Kumano, Y., and Ichihashi, M. 1999 J Invest Dermatol.
328. Calcium and Vitamin D are Effective in Preventing Fractures in Elderly People by Reversing Senile Secondary Hyperparathyroidism Meunier, P. J. 1998 Osteoporos.Int.
329. The immune system in ultraviolet carcinogenesis Nishigori, C., Yarosh, D. B., Donawho, C., and Kripke, M. L. 1996 J Investig.Dermatol.Symp.Proc.
330. Biologically effective doses of sunlight for immune suppression at various latitudes and their relationship to changes in stratospheric ozone De Fabo, E. C., Noonan, F. P., and Frederick, J. E. 1990 Photochem.Photobiol.
331. Immunosuppression by factors released from UV-irradiated epidermal cells: selective effects on the generation of contact and delayed hypersensitivity after exposure to UVA or UVB radiation Kim, T. Y., Kripke, M. L., and Ullrich, S. E. 1990 J Invest Dermatol.
332. Effects of ultraviolet radiation on the immune system in humans Morison, W. L. 1989 Photochem.Photobiol.
333. Mechanism of immune suppression by ultraviolet irradiation in vivo. I. Evidence for the existence of a unique photoreceptor in skin and its role in photoimmunology De Fabo, E. C. and Noonan, F. P. 7-1-1983 J Exp.Med.
334. Ultraviolet radiation, resistance to infectious diseases, and vaccination responses Sleijffers, A., Garssen, J., and van Loveren, H. 2002 Methods
335. Effects of ultraviolet exposure on the immune system Garssen, J. and van, Loveren H. 2001 Crit Rev.Immunol.
336. Dose response for UV-induced immune suppression in people of color: differences based on erythemal reactivity rather than skin pigmentation Selgrade, M. K., Smith, M. V., Oberhelman-Bragg, L. J., LeVee, G. J., Koren, H. S., and Cooper, K. D. 2001 Photochem.Photobiol.
337. Suberythemal UV-Irradiation Increases Immunological Capacity in Children with Frequent Cold Krause, R., Kuhn, G, Pose, M, Dobberke, J, Chen, T. C., Holick, M. F., Renz, H, and Buhring, M. 1999
338. Vitamin D, thyroid hormones and muscle mass influence natural killer (NK) innate immunity in healthy nonagenarians and centenarians [published erratum appears in Clin Exp Immunol 1999 Jul;117(1):206] 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.
339. Reduced susceptibility to peroxidation of erythrocyte plasma membranes from centenarians Rabini, R. A., Moretti, N., Staffolani, R., Salvolini, E., Nanetti, L., Franceschi, C., and Mazzanti, L. 2002 Exp.Gerontol.

340. Muscle strength in the elderly: its relation to vitamin D metabolites [see comments] Bischoff, H. A., Stahelin, H. B., Urscheler, N., Ehrsam, R., Vonthein, R., Perrig-Chiello, P., Tyndall, A., and Theiler, R. 1999 Arch.Phys.Med.Rehabil.
341. Relationship between muscle strength and vitamin D metabolites: are there therapeutic possibilities in the elderly? Bischoff, H. A., Stahelin, H. B., Tyndall, A., and Theiler, R. 2000 Z.Rheumatol.
342. Non-genomic signal transduction pathway of vitamin D in muscle de Boland, A. R. and Boland, R. L. 1994 Cell Signal.
343. Neuromuscular and psychomotor function in elderly subjects who fall and the relationship with vitamin D status Dhesi, J. K., Bearne, L. M., Moniz, C., Hurley, M. V., Jackson, S. H., Swift, C. G., and Allain, T. J. 2002 J Bone Miner.Res.
344. Vitamin D and muscle function Pfeifer, M., Begerow, B., and Minne, H. W. 2002 Osteoporos.Int.
345. Muscle strength, functional mobility and vitamin D in older women Verhaar, H. J., Samson, M. M., Jansen, P. A., de Vreede, P. L., Manten, J. W., and Duursma, S. A. 2000 Aging (Milano.)
346. Relation Between Vitamin D, Physical Performance, and Disability in Elderly Persons Zamboni, M., Zoico, E., Tosoni, P., Zivelonghi, A., Bortolani, A., Maggi, S., Di, Francesco, V, and Bosello, O. 1-1-2002 J Gerontol.A Biol.Sci.Med.Sci.
347. The biological activity of 25-hydroxycholecalciferol and 1,25-- dihydroxycholecalciferol for rainbow trout (Salmo gairdneri) Barnett, B. J., Jones, G., Cho, C. Y., and Slinger, S. J. 1982 J.Nutr.
348. Ultraviolet light may contribute to geographic and racial blood pressure differences [see comments] Rostand, S. G. 1997 Hypertension
349. Ultraviolet B and blood pressure Krause, R., Buhring, M., Hopfenmuller, W., Holick, M. F., and Sharma, A. M. 8-29-1998 Lancet
350. [Importance of the wave length and dose in the protective action of ultraviolet irradiations in experimental renal hypertension] Baronenko, V. A. 1974 Vopr.Kurortol.Fizioter.Lech.Fiz Kult.
351. [Heliotherapy in hypertensive disease] Gavrikov, N. A. 1971 Vopr.Kurortol.Fizioter.Lech.Fiz Kult.
352. [High altitude climate, its curative and pathogenic influence on hypertension depending on meteorological and helio-geophysical factors] Aliev, M. A. 1966 Kardiologiia.
353. The protective role of Langerhans' cells and sunlight in multiple sclerosis Dumas, M. and Jauberteau-Marchan, M. O. 2000 Med.Hypotheses
354. Mortality from multiple sclerosis and exposure to residential and occupational solar radiation: a case-control study based on death certificates Freedman, D. M., Dosemeci, M., and Alavanja, M. C. 2000 Occup.Environ.Med.
355. Possible effects of sunlight on human lymphocytes Green, M. H., Petit-Frere, C., Clingen, P. H., Bentham, G., Cole, J., and Arlett, C. F. 1999 J.Epidemiol.
356. On the causes of multiple sclerosis Hutter, C. 1993 Med.Hypotheses
357. Multiple sclerosis: sunlight, diet, immunology and aetiology Hutter, C. D. and Laing, P. 1996 Med.Hypotheses
358. Climate, diffused solar radiation and multiple sclerosis Laborde, J. M., Dando, W. A., and Teetzen, M. L. 1988 Soc.Sci.Med.
359. Geographical considerations in multiple sclerosis Leibowitz, U., Sharon, D., and Alter, M. 1967 Brain
360. Multiple sclerosis and the Canadian climate Neutel, C. I. 1980 J.Chronic.Dis.
361. Epidemiology of multiple sclerosis in U.S. veterans: 2. Latitude, climate and the risk of multiple sclerosis Norman, J. E., Jr., Kurtzke, J. F., and Beebe, G. W. 1983 J.Chronic.Dis.
362. [Geographic distribution of multiple sclerosis and comparison with geophysical values] Resch, J. 1995 Soz.Praventivmed.
363. The low incidence of multiple sclerosis in areas near the equator may be due to ultraviolet light induced suppressor cells to melanocyte antigens Sharpe, R. J. 1986 Med.Hypotheses
364. Sudden death in multiple sclerosis associated with sun exposure: a report of two cases Avis, S. P. and Pryse-Phillips, W. E. 1995 Can.J.Neurol.Sci.
365. A fatal case of sun exposure in a multiple sclerosis patient Harbison, J. W., Calabrese, V. P., and Edlich, R. F. 1989 J.Emerg.Med.
366. Vitamin D in the Treatment of Osteoporosis Fujita, T 2002
367. Vitamin D status and its adequacy in healthy Danish perimenopausal women: relationships to dietary intake, sun exposure and serum parathyroid hormone Brot, C., Vestergaard, P., Kolthoff, N., Gram, J., Hermann, A. P., and Sorensen, O. H. 2001 Br.J Nutr
368. Vitamin d status and bone mineral density of veiled and unveiled Turkish women Guzel, R., Kozanoglu, E., Guler-Uysal, F., Soyupak, S., and Sarpel, T. 2001 J Womens Health Gend.Based.Med.
369. Calcium and vitamin D supplements reduce tooth loss in the elderly Krall, E. A., Wehler, C., Garcia, R. I., Harris, S. S., and Dawson-Hughes, B. 10-15-2001 Am J Med.

370. [Prevalence of hypovitaminosis D in elderly institutionalized residents: influence of a sustitutive treatment] Larrosa, M., Gratacos, J., Vaqueiro, M., Prat, M., Campos, F., and Roque, M. 11-17-2001 Med.Clin (Barc.)
371. Relation between vitamin D insufficiency, bone density, and bone metabolism in healthy postmenopausal women Mezquita-Raya, P., Munoz-Torres, M., Luna, J. D., Luna, V., Lopez-Rodriguez, F., Torres-Vela, E., and Escobar-Jimenez, F. 2001 J Bone Miner.Res.
372. Vitamin D status, trunk muscle strength, body sway, falls, and fractures among 237 postmenopausal women with osteoporosis Pfeifer, M., Begerow, B., Minne, H. W., Schlotthauer, T., Pospeschill, M., Scholz, M., Lazarescu, A. D., and Pollahne, W. 2001 Exp.Clin Endocrinol.Diabetes
373. Serum 25-hydroxyvitamin D concentrations and related dietary factors in Nakamura, K., Nashimoto, M., Hori, Y., and Yamamoto, M. 2000 Am.J.Clin.Nutr.
374. Relationships between bone mineral density, serum vitamin D metabolites and calcium:phosphorus intake in healthy perimenopausal women Brot, C., Jorgensen, N., Madsen, O. R., Jensen, L. B., and Sorensen, O. H. 1999 J.Intern.Med.
375. Vitamin D and its Metabolites in the Treatment of Osteoporosis Burckhardt, P. and Lamy, O. 1998 Osteoporos.Int.
376. Effect of Calcium and Vitamin D Supplementation on Bone Density in Men and Women 65 Years of Age or Older Dawson-Hughes, Bess, Harris, Susan S., Krall, Elizabeth A., and Dallal, Gerard E. 9-4-1997 N.Engl.J.Med.
377. The vitamin D story: a collaborative effort of basic science and clinical medicine DeLuca, H. F. 3-1-1988 FASEB J.
378. Hip fracture in elderly men: the importance of subclinical vitamin D deficiency and hypogonadism Diamond, T., Smerdely, P., Kormas, N., Sekel, R., Vu, T., and Day, P. 8-3-1998 Med.J.Aust.
379. Bone changes and aortic calcification in aging inhabitants of mountain versus seacoast communities in the Kii Peninsula Fujita, T., Okamoto, Y., Sakagami, Y., Ota, K., and Ohata, M. 1984 J.Am.Geriatr.Soc.
380. Calcium and vitamin D nutrition and bone disease of the elderly Gennari, C. 2001 Public Health Nutr
381. Bone mineral density of the spine and femur in healthy Saudi females: relation to vitamin D status, pregnancy, and lactation Ghannam, N. N., Hammami, M. M., Bakheet, S. M., and Khan, B. A. 1999 Calcif.Tissue Int.
382. Nutritional aspects of hip fractures Bonjour, J. P., Schurch, M. A., and Rizzoli, R. 1996 Bone
383. Age-related (type II) femoral neck osteoporosis in men: biochemical evidence for both hypovitaminos Boonen, S., Vanderschueren, D., Cheng, X. G., Verbeke, G., Dequeker, J., Geusens, P., Broos, P., and Bouillon, R. 1997 J.Bone Miner.Res.
384. Factors associated with hip fracture occurrence in old age. Implications in the postsurgical management Boonen, S., Broos, P., and Haentjens, P. 1999 Acta Chir Belg.
385. Vitamin D status of patients with femoral neck fractures Brown, I. R., Bakowska, A., and Millard, P. H. 1976 Age Ageing
386. Vitamin D3 and calcium to prevent hip fractures in the elderly women Chapuy, M. C., Arlot, M. E., Duboeuf, F., Brun, J., Crouzet, B., Arnaud, S., Delmas, P. D., and Meunier, P. J. 12-3-1992 N.Engl.J.Med.
387. Risk factors for longitudinal bone loss in elderly men and women: the Framingham Osteoporosis Study [In Process Citation] Hannan, M. T., Felson, D. T., Dawson-Hughes, B., Tucker, K. L., Cupples, L. A., Wilson, P. W., and Kiel, D. P. 2000 J.Bone Miner.Res.
388. The Epidemiology of Osteoporosis in Asia Lau, EMC 1997
389. Long-term effects of nutrient intervention on markers of bone remodeling and calciotropic hormones in late-postmenopausal women Jensen, C., Holloway, L., Block, G., Spiller, G., Gildengorin, G., Gunderson, E., Butterfield, G., and Marcus, R. 2002 Am.J Clin Nutr
390. Human serum 25-hydroxycholecalciferol response to extended oral dosing with cholecalciferol Heaney, R. P., Davies, K. M., Chen, T. C., Holick, M. F., and Barger-Lux, M. J. 2003 Am.J Clin Nutr
391. Vitamin D--the steroid hormone prescription for every patient Plotnikoff, G. A. 2003 Minn.Med.
392. [In Process Citation] Gaspard, U., van den, Brule F., Pintiaux, A., and Foidart, J. M. 2002 Rev.Med.Liege
393. Induced hyperproliferation in epithelial cells of mouse prostate by a Western-style diet Xue, L., Yang, K., Newmark, H., and Lipkin, M. 1997 Carcinogenesis
394. Role of vitamin D, its metabolites, and analogs in the management of osteoporosis Bikle, D. D. 1994 Rheum.Dis.Clin.North Am.
395. A review of clinical trials of therapies for osteoporosis using fracture as an end point Blank, R. D. and Bockman, R. S. 1999 J.Clin.Densitom.
396. Therapeutic uses of vitamin D analogues Brown, A. J. 2001 Am.J Kidney Dis.
397. [Hypervitaminosis D. Review of fifteen cases] Castello, F., Callis, L., Nieto, J. L., and Vilaplana, E. 1979 An.Esp.Pediatr.
398. [Vitamin D poisoning in infants: a preventable cause of hypercalciuria and nephrocalcinosis] Hoppe, B., Gnehm, H., Wopmann, M., Neuhaus, T., Willi, U., and Leumann, E. 2-22-1992 Schweiz Med Wochenschr

399. Effects of hypervitaminosis A on the bone and mineral metabolism of the rat Hough, S., Avioli, L. V., Muir, H., Gelderblom, D., Jenkins, G., Kurasi, H., Slatopolsky, E., Bergfeld, M. A., and Teitelbaum, S. L. 1988 Endocrinology
400. Endocrine and physical determinants of bone mass in late postmenopause Albanese, C. V., Civitelli, R., Tibollo, F. G., Masciangelo, R., and Mango, D. 1996 Exp.Clin.Endocrinol.Diabetes
401. Markers of bone remodeling in the elderly subject: effects of vitamin D insufficiency and its correction Brazier, M., Kamel, S., Maamer, M., Agbomson, F., Elesper, I., Garabedian, M., Desmet, G., and Sebert, J. L. 1995 J.Bone Miner.Res.
402. The effect of vitamin K supplementation on circulating osteocalcin (bone Gla protein) and urinary calcium excretion Knapen, M. H., Hamulyak, K., and Vermeer, C. 12-15-1989 Ann Intern.Med.
403. Calcium and vitamin D supplementation increases spinal BMD in healthy, postmenopausal women Baeksgaard, L., Andersen, K. P., and Hyldstrup, L. 1998 Osteoporos.Int.
404. The role of nutrition in osteoporosis Bunker, V. W. 1994 Br.J.Biomed.Sci.
405. [Osteoporosis and nutrition] Burckhardt, P. 1998 Ther.Umsch.
406. Treatment options for osteoporosis Khosla, S. and Riggs, B. L. 1995 Mayo Clin.Proc.
407. Vitamin D supplementation in postmenopausal black women Kyriakidou-Himonas, M., Aloia, J. F., and Yeh, J. K. 1999 J.Clin.Endocrinol.Metab
408. The roles of calcium and vitamin D in the prevention of osteoporosis Reid, I. R. 1998 Endocrinol.Metab Clin.North Am.
409. Biochemical Aspects of Osteoporosis Woo, J, Lau, EMC, and Swaminathan, R. 1997
410. Effect of an intermittent weekly dose of human parathyroid hormone (1- 34) on osteoporosis: a randomized double-masked prospective study using three dose levels Fujita, T., Inoue, T., Morii, H., Morita, R., Norimatsu, H., Orimo, H., Takahashi, H. E., Yamamoto, K., and Fukunaga, M. 1999 Osteoporos.Int.
411. Two years of treatment with recombinant human growth hormone increases bone mineral density in men with idiopathic osteoporosis Gillberg, P., Mallmin, H., Petren-Mallmin, M., Ljunghall, S., and Nilsson, A. G. 2002 J Clin Endocrinol.Metab
412. Effect of low-dose of recombinant human growth hormone on bone metabolism in elderly women with osteoporosis Sugimoto, T., Kaji, H., Nakaoka, D., Yamauchi, M., Yano, S., Sugishita, T., Baylink, D. J., Mohan, S., and Chihara, K. 2002 Eur.J Endocrinol.
413. The Importance of Growth Hormone (GH) and GH Secretagogues for Bone Mass and Density Svensson, J. 2002 Curr.Pharm.Des
414. The use of estrogen, DHEA, and diosgenin in a sustained delivery setting as a novel treatment approach for osteoporosis in the ovariectomized adult rat model Higdon, K., Scott, A., Tucci, M., Benghuzzi, H., Tsao, A., Puckett, A., Cason, Z., and Hughes, J. 2001 Biomed.Sci Instrum.
415. 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.
416. 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.
417. [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., and . 1995 Nippon Ronen Igakkai Zasshi
418. Bone health: the role of micronutrients New, S. A. 1999 Br.Med.Bull.
419. Osteoporosis: current approaches and future prospects in diagnosis, pathogenesis, and management Raisz, L. G. 1999 J.Bone Miner.Metab
420. The role of vitamins in the prevention of osteoporosis--a brief status report Weber, P. 1999 Int.J.Vitam.Nutr.Res.
421. Nutritional factors in causation of osteoporosis Heaney, R. P. 1988 Ann Chir Gynaecol.
422. Osteoporosis in postmenopausal women Renner, R. P., Boucher, L. J., and Kaufman, H. W. 1984 J.Prosthet.Dent.
423. The role of trace minerals in osteoporosis Saltman, P. D. and Strause, L. G. 1993 J.Am.Coll.Nutr.
424. The role of trace minerals in the pathogenesis of postmenopausal osteoporosis and a new effect of calcitonin Gur, A., Colpan, L., Nas, K., Cevik, R., Sarac, J., Erdogan, F., and Duz, M. Z. 2002 J Bone Miner.Metab
425. Zinc deficiency exaggerates diabetic osteoporosis Fushimi, H., Inoue, T., Yamada, Y., Horie, H., Kameyama, M., Inoue, K., Minami, T., and Okazaki, Y. 1993 Diabetes Res.Clin.Pract.
426. Studies on the relationship between boron and magnesium which possibly affects the formation and maintenance of bones Nielsen, F. H. 1990 Magnes.Trace Elem.
427. The relationship between boron and magnesium status and bone mineral density in the human: a review Volpe, S. L., Taper, L. J., and Meacham, S. 1993 Magnes.Res.

428. The effect of nutrient intake on bone mineral status in young adults: the Northern Ireland young hearts project Neville, C. E., Robson, P. J., Murray, L. J., Strain, J. J., Twisk, J., Gallagher, A. M., McGuinness, M., Cran, G. W., Ralston, S. H., and Boreham, C. A. 2002 Calcif.Tissue Int.
429. [Vitamin D supplementation in pregnancy: a necessity. Committee for Nutrition] 1995 Arch.Pediatr.
430. Age considerations in nutrient needs for bone health Miller, G. D., Groziak, S. M., and Dirienzo, D. 1996 J.Am.Coll.Nutr.
431. Nutrition in bone health revisited: a story beyond calcium Ilich, J. Z. and Kerstetter, J. E. 2000 J Am.Coll.Nutr
432. Improved mineral balance and skeletal metabolism in postmenopausal women treated with potassium bicarbonate Sebastian, A., Harris, S. T., Ottaway, J. H., Todd, K. M., and Morris, R. C., Jr. 6-23-1994 N Engl.J Med.
433. Vitamin D deficiency and severe hyperparathyroidism Jonard, S., Gauthier-Morgenstern, M., Douillard, C., Leteurtre, E., Nocaudie, M., Leroy, X., Proye, C., Marchandise, X., Wemeau, J. L., and Vantyghem, M. C. 2002 Ann Endocrinol.(Paris)
434. Effect of vitamin D nutrition on parathyroid adenoma weight: pathogenetic and clinical implications Rao, D. S., Honasoge, M., Divine, G. W., Phillips, E. R., Lee, M. W., Ansari, M. R., Talpos, G. B., and Parfitt, A. M. 2000 J.Clin.Endocrinol.Metab
435. Role of vitamin D and calcium nutrition in disease expression and parathyroid tumor growth in primary hyperparathyroidism: a global perspective Rao, D. S., Agarwal, G., Talpos, G. B., Phillips, E. R., Bandeira, F., Mishra, S. K., and Mithal, A. 2002 J Bone Miner.Res.
436. Biochemical effects of a calcium supplement in postmenopausal women with primary hyperparathyroidism Horowitz, M., Wishart, J. M., Need, A. G., Morris, H. A., and Nordin, B. E. 1994 Horm.Metab Res.
437. Vitamin D status in primary hyperparathyroidism in India Harinarayan, C. V., Gupta, N., and Kochupillai, N. 1995 Clin.Endocrinol.(Oxf)
438. Decrease in vitamin D receptor and calcium-sensing receptor in highly proliferative parathyroid adenomas Yano, S., Sugimoto, T., Tsukamoto, T., Chihara, K., Kobayashi, A., Kitazawa, S., Maeda, S., and Kitazawa, R. 2003 Eur.J Endocrinol.
439. Reduced parathyroid vitamin D receptor messenger ribonucleic acid levels in primary and secondary hyperparathyroidism Carling, T., Rastad, J., Szabo, E., Westin, G., and Akerstrom, G. 2000 J.Clin.Endocrinol.Metab
440. Pathophysiology of primary hyperparathyroidism [In Process Citation] Hellman, P., Carling, T., Rask, L., and Akerstrom, G. 2000 Histol.Histopathol.
441. Regulation of parathyroid vitamin d receptor expression by extracellular calcium Garfia, B., Canadillas, S., Canalejo, A., Luque, F., Siendones, E., Quesada, M., Almaden, Y., Aguilera-Tejero, E., and Rodriguez, M. 2002 J Am.Soc.Nephrol.
442. Distinct, tissue-specific regulation of vitamin D receptor in the intestine, kidney, and skin by dietary calcium and vitamin D Zineb, R., Zhor, B., Odile, W., and Marthe, R. R. 1998 Endocrinology
443. Vitamin D and Bone Health in Postmenopausal Women Malabanan, A. O. and Holick, M. F. 2003 J Womens Health (Larchmt.)
444. Assessment of vitamin D and calcium status in healthy adult Austrians Kudlacek, S., Schneider, B., Peterlik, M., Leb, G., Klaushofer, K., Weber, K., Woloszczuk, W., and Willvonseder, R. 2003 Eur.J Clin Invest
445. [Osteoporosis as a lifestyle-related disease] Hata, M., Miyao, M., and Mizuno, Y. 2003 Nippon Rinsho
446. A very high incidence of low 25 hydroxy-vitamin D serum concentration in a French population of patients with primary hyperparathyroidism Boudou, P., Ibrahim, F., Cormier, C., Sarfati, E., and Souberbielle, J. C. 2006 J.Endocrinol.Invest
447. Vitamin D status of 51-75-year-old Irish women: its determinants and impact on biochemical indices of bone turnover Hill, T. R., O'Brien, M. M., Lamberg-Allardt, C., Jakobsen, J., Kiely, M., Flynn, A., and Cashman, K. D. 2006 Public Health Nutr.
448. [Fortification of food with vitamin D is a reasonable approach to fracture prophylaxis] Lips, P. 5-27-2006 Ned.Tijdschr.Geneeskd.
449. Prevalence of vitamin D inadequacy in patients attending a metabolic bone clinic in Medway Ryan, P. and Dixon, T. 2006 Curr.Med.Res.Opin.
450. Vitamin D status among patients with hip fracture and elderly control subjects in Yekaterinburg, Russia Bakhtiyarova, S., Lesnyak, O., Kyznesova, N., Blankenstein, M. A., and Lips, P. 2006 Osteoporos.Int.
451. [The common occurrence of osteoarthritis and osteoporosis and the value of markers of bone turnover] Drees, P., Decking, J., Ghezel-Ahmadi, V., Delank, K. S., Wilhelm, B., and Eckardt, A. 2005 Z.Rheumatol.
452. [Prevalence of secondary hyperparathyroidism (SHPT) and causal factors in adult population in Reykjavik area] Karlsson, S. L., Indridason, O. S., Franzson, L., and Sigurdsson, G. 2005 Laeknabladid.
453. The relationship of vitamin D status to bone mineral density in an Italian population of postmenopausal women Malavolta, N., Pratelli, L., Frigato, M., Mule, R., Mascia, M. L., and Gnudi, S. 2005 Osteoporos.Int.

454. Vitamin D intake and status in Irish postmenopausal women Hill, T., Collins, A., O'Brien, M., Kiely, M., Flynn, A., and Cashman, K. D. 2005 Eur.J.Clin.Nutr.
455. Racial/ethnic considerations in making recommendations for vitamin D for adult and elderly men and women wson-Hughes, B. 2004 Am.J.Clin.Nutr.
456. Failure to normalize parathyroid hormone during treatment of vitamin D deficiency in Asian patients Peacey, S. R., Wright, D., and Harries, M. J. 2004 Clin.Endocrinol.(Oxf)
457. Which circulating level of 25-hydroxyvitamin D is appropriate? Lips, P. 2004 J.Steroid Biochem.Mol.Biol.
458. Vitamin D insufficiency in Greenlanders on a westernized fare: ethnic differences in calcitropic hormones between Greenlanders and Danes Rejnmark, L., Jorgensen, M. E., Pedersen, M. B., Hansen, J. C., Heickendorff, L., Lauridsen, A. L., Mulvad, G., Siggaard, C., Skjoldborg, H., Sorensen, T. B., Pedersen, E. B., and Mosekilde, L. 2004 Calcif.Tissue Int.
459. Older people in China and the United Kingdom differ in the relationships among parathyroid hormone, vitamin D, and bone mineral status Yan, L., Zhou, B., Wang, X., D'Ath, S., Laidlaw, A., Laskey, M. A., and Prentice, A. 2003 Bone
460. Association of low 25-hydroxyvitamin D concentrations with elevated parathyroid hormone concentrations and low cortical bone density in early pubertal and prepubertal Finnish girls Cheng, S., Tylavsky, F., Kroger, H., Karkkainen, M., Lyytikainen, A., Koistinen, A., Mahonen, A., Alen, M., Halleen, J., Vaananen, K., and Lamberg-Allardt, C. 2003 Am.J.Clin.Nutr.
461. Prevalence of hypovitaminosis D in elderly women in Italy: clinical consequences and risk factors Isaia, G., Giorgino, R., Rini, G. B., Bevilacqua, M., Maugeri, D., and Adami, S. 2003 Osteoporos.Int.
462. In a population study, can parathyroid hormone aid the definition of adequate vitamin D status? A study of people aged 65 years and over from the British National Diet and Nutrition Survey Bates, C. J., Carter, G. D., Mishra, G. D., O'Shea, D., Jones, J., and Prentice, A. 2003 Osteoporos.Int.
463. Hyperparthyroidism in elderly osteopenic women Albertazzi, P., Steel, S. A., Purdie, D. W., Gurney, E., Atkin, S. L., and Robertson, W. S. 12-10-2002 Maturitas
464. The association between parathyroid hormone, vitamin D and bone mineral density in 70-year-old Icelandic women Sigurdsson, G., Franzson, L., Steingrimsdottir, L., and Sigvaldason, H. 2000 Osteoporos.Int.
465. Vitamin D status, parathyroid function and femoral bone density in an elderly Swedish population living at home Melin, A. L., Wilske, J., Ringertz, H., and Saaf, M. 1999 Aging (Milano.)
466. High prevalence of hypovitaminosis D among free-living postmenopausal women referred to an osteoporosis outpatient clinic in northern Italy for initial screening Bettica, P., Bevilacqua, M., Vago, T., and Norbiato, G. 1999 Osteoporos.Int.
467. [Vitamin D deficiency. Easy to diagnose, often overlooked] Glerup, H. and Eriksen, E. F. 4-26-1999 Ugeskr.Laeger
468. Ultraviolet irradiation corrects vitamin D deficiency and suppresses secondary hyperparathyroidism in the elderly Chel, V. G., Ooms, M. E., Popp-Snijders, C., Pavel, S., Schothorst, A. A., Meulemans, C. C., and Lips, P. 1998 J.Bone Miner.Res.
469. Vitamin D status, parathyroid hormone and sunlight in Turkish, Moroccan and Caucasian children in The Netherlands Meulmeester, J. F., van den, Berg H., Wedel, M., Boshuis, P. G., Hulshof, K. F., and Luyken, R. 1990 Eur.J.Clin.Nutr.
470. Vitamin D status of elderly people in Spain Quesada, J. M., Jans, I., Benito, P., Jimenez, J. A., and Bouillon, R. 1989 Age Ageing
471. Serum levels of vitamin D metabolites in the elderly Aksnes, L., Rodland, O., Odegaard, O. R., Bakke, K. J., and Aarskog, D. 1989 Acta Endocrinol.(Copenh)
472. Studies on the relationship between vitamin D3 status and urinary excretion of calcium in healthy subjects: effects of increased levels of 25-hydroxyvitamin D3 Berlin, T., Emtestam, L., and Bjorkhem, I. 1986 Scand.J.Clin.Lab Invest
473. Resolution of vitamin D insufficiency in osteopenic patients results in rapid recovery of bone mineral density Adams, J. S., Kantorovich, V., Wu, C., Javanbakht, M., and Hollis, B. W. 1999 J.Clin.Endocrinol.Metab
474. [Severe vitamin D deficiency osteomalacia by coincidence of multiple risk factors] Batge, B., Struck, J., Klein, H. H., and Brinckmann, J. 6-16-2000 Dtsch.Med.Wochenschr.
475. Vitamin D and the parathyroid Beckerman, P. and Silver, J. 1999 Am.J Med.Sci
476. [The importance of vitamins "A" and "D" to teeth and gingiva] 1965 Bol.Dent.Urug.
477. The effect of diets deficient in calcium or phosphorus in the presence and absence of supplements of vitamin D on the incisor teeth and bone of adult rats Ferguson, H. W. and Hartles, R. L. 1966 Arch.Oral Biol.
478. Influence of microelements on the morphology of the teeth Moller, I. J. 1967 J.Dent.Res.
479. Effects of vitamin D on developing bones and teeth Toverud, S. U., Ramp, W. K., Crenshaw, M. A., Gonnerman, W. A., and Mechanic, G. L. 1973 N.C.Dent.J
480. Interaction of vitamin A deficiency and excess fluoride in calcification of rat bones and teeth Harris, S. S. and Navia, J. M. 1984 Acta Vitaminol.Enzymol.

481. The cellular and extracellular distribution of osteocalcin and dentin phosphoprotein in teeth of vitamin D-deficient rats Berdal, A., Gorter, de Vries, I, Hotton, D., Cuisinier-Gleizes, P., and Mathieu, H. 1991 J.Biol.Buccale
482. Growth factors in bones and teeth Finkelman, R. D. 1992 J.Calif.Dent.Assoc.
483. Delay of natural bone loss by higher intakes of specific minerals and vitamins Schaafsma, A., de Vries, P. J., and Saris, W. H. 2001 Crit Rev.Food Sci Nutr
484. The Influence of Diet on the Structure of Teeth Mellanby, May 1928 Physiol Rev
485. An Experimental Study of the Influence of Diet on Tooth Formation Mellanby, May 1918 Lancet
486. Effect of Diet on Structure of Teeth: Interrelationship Between Calcium and Other Food Factors Mellanby, May 1923 British Dental Journal
487. Influence of Light in Relation to Diet on Formation of Teeth Mellanby, May 1924 British Dental Journal
488. The Effect of Diet on the Resistance of Teeth to Caries Mellanby, May 1923
489. The Structure of Human Teeth in Relation to Caries Mellanby, May 1927 British Dental Journal
490. Primitive Control of Dental Caries Price, W. A. 1989
491. Scanning electron microscopy of the influence of dietary calcium and vitamin D-deficiency on periodontium in the adult rats Golebiewska, M. and Bielaczyc, A. 1997 Rocz.Akad.Med.Bialymst.
492. Ultrastructural changes of a tooth root in young rats fed a low calcium and vitamin D-deficient diet Bielaczyc, A. and Golebiewska, M. 1997 Rocz.Akad.Med.Bialymst.
493. Histology and microradiography of early post-natal molar tooth development in vitamin-D deficient rats Berdal, A., Balmain, N., Cuisinier-Gleizes, P., and Mathieu, H. 1987 Arch.Oral Biol.
494. Effect of hypocalcemic state on enamel formation in rat maxillary incisors Ranggard, L. and Noren, J. G. 1994 Scand.J.Dent.Res.
495. The mouth as an indicator of internal nutritional problems Dreizen, S. 1989 Pediatrician.
496. Dietary factors related to preservation of oral and skeletal bone mass in women Faine, M. P. 1995 J.Prosthet.Dent.
497. Increased risk of tooth loss is related to bone loss at the whole body, hip, and spine Krall, E. A., Garcia, R. I., and Dawson-Hughes, B. 1996 Calcif.Tissue Int.
498. [Correction of mineral and protein metabolism by anabolic preparations and vitamin D2 in rats with dental caries] Rudenko, M. M., Levitskii, A. P., Putintsev, N. I., and Genesina, T. I. 1989 Fiziol.Zh.
499. Baby-bottle tooth decay: are we on the right track? Smith, P. J. and Moffatt, M. E. 1998 Int.J Circumpolar.Health
500. Plasma 25-hydroxyvitamin D in growing kittens is related to dietary intake of cholecalciferol Morris, J. G., Earle, K. E., and Anderson, P. A. 1999 J.Nutr.
501. Dietary vitamin D dependence of cat and dog due to inadequate cutaneous synthesis of vitamin D How, K. L., Hazewinkel, H. A., and Mol, J. A. 1994 Gen.Comp Endocrinol.
502. Photosynthesis of vitamin D in the skin of dogs cats and rats How, K. L., Hazewinkel, H. A., and Mol, J. A. 1995 Vet.Q.
503. Dental Hard Tissues; Evidence based management of dental caries. Wilding, R. J. C. 2000
504. The effect of vitamin D deficiency on secretion of saliva by rat parotid gland in vivo Glijer, B., Peterfy, C., and Tenenhouse, A. 1985 J Physiol
505. The parotid gland: a new target organ for vitamin D action Goodwin, D., Noff, D., and Edelstein, S. 3-1-1978 Biochim.Biophys.Acta
506. Vitamin D-mediated decrease of Ca2+-pump activity in the rat parotid gland Hayakawa, M., Aoki, H., Terao, N., Abiko, Y., and Takiguchi, H. 1983 Int.J Biochem.
507. Vitamin D receptors in isolated rat parotid gland acinar cells Peterfy, C. and Tenenhouse, A. 10-11-1982 Biochim.Biophys.Acta
508. Vitamin D and parotid gland function in the rat Peterfy, C., Tenenhouse, A., and Yu, E. 1988 J Physiol
509. [Arteriosclerosis and osteoporosis (editorial)] Laroche, M. 1-20-1996 Presse Med.
510. Relationship between tooth loss and electrocardiographic abnormalities in octogenarians Takata, Y., Ansai, T., Matsumura, K., Awano, S., Hamasaki, T., Sonoki, K., Kusaba, A., Akifusa, S., and Takehara, T. 2001 J Dent.Res.
511. Periodontal disease: link to cardiovascular disease Loesche, W. J. 2000 Compend.Contin.Educ.Dent.
512. Possible explanations for the tooth loss and cardiovascular disease relationship Joshipura, K. J., Douglass, C. W., and Willett, W. C. 1998 Ann Periodontol.
513. Comparative epidemiology of multiple sclerosis and dental caries Craelius, W. 1978 J.Epidemiol.Community Health
514. Calbindin-D9k. A vitamin-D-dependent, calcium-binding protein in mineralized tissues Balmain, N. 1991 Clin.Orthop.
515. [Influence of nutrition on bones and dentition] Bramstedt, F. and Maiwald, L. 1970 Internist (Berl)

516. [The metabolism of vitamin D and its significance for bone and dental tissues] Holmberg, I. 1974 Odontol.Foren.Tidskr.
517. Enamel defects in primary and permanent teeth of children born prematurely Aine, L., Backstrom, M. C., Maki, R., Kuusela, A. L., Koivisto, A. M., Ikonen, R. S., and Maki, M. 2000 J Oral Pathol.Med.
518. Dental changes in hypervitaminosis D Giunta, J. L. 1998 Oral Surg.Oral Med.Oral Pathol.Oral Radiol.Endod.
519. The etiology of enamel hypoplasia: a unifying concept Nikiforuk, G. and Fraser, D. 1981 J.Pediatr.
520. Persisting vitamin D deficiency in the Asian adolescent O'Hare, A. E., Uttley, W. S., Belton, N. R., Westwood, A., Levin, S. D., and Anderson, F. 1984 Arch.Dis.Child
521. The relationship between dietary intake and the number of teeth in elderly Japanese subjects Yoshihara, A., Watanabe, R., Nishimuta, M., Hanada, N., and Miyazaki, H. 2005 Gerodontology.
522. Association between serum concentrations of 25-hydroxyvitamin D and gingival inflammation Dietrich, T., Nunn, M., wson-Hughes, B., and Bischoff-Ferrari, H. A. 2005 Am.J.Clin.Nutr.
523. Prevalence of caries among preschool-aged children in a northern Manitoba community Schroth, R. J., Smith, P. J., Whalen, J. C., Lekic, C., and Moffatt, M. E. 2005 J.Can.Dent.Assoc.
524. Dental alveolar bone defects related to Vitamin D and calcium status Davideau, J. L., Lezot, F., Kato, S., Bailleul-Forestier, I., and Berdal, A. 2004 J.Steroid Biochem.Mol.Biol.
525. Diagnosis and management of unusual dental abscesses in children Seow, W. K. 2003 Aust.Dent.J.
526. Effect of vitamin D and calcium on periodontitis Hildebolt, C. F. 2005 J.Periodontol.
527. Osteoporosis and its implications for dental patients Edwards, B. J. and Migliorati, C. A. 2008 J.Am.Dent.Assoc.
528. Bone health and oral health Kaye, E. K. 2007 J.Am.Dent.Assoc.
529. Association between serum concentrations of 25-hydroxyvitamin D3 and periodontal disease in the US population Dietrich, T., Joshipura, K. J., wson-Hughes, B., and Bischoff-Ferrari, H. A. 2004 Am.J.Clin.Nutr.
530. The periodontal-systemic connection: implications for treatment of patients with osteoporosis and periodontal disease Krall, E. A. 2001 Ann.Periodontol.
531. Osteoporosis and the risk of tooth loss Krall, E. A. 2006 Clin.Calcium
532. Experimental Evidence Demonstrating the Influence of a Special Dietetic Factor on the Development of the Teeth and Jaws 1920 Lancet
533. Inter-relationships of calcium, phosphorus and vitamin D in the bones and teeth of the rat Leaver, A. G. 1971 Clin.Orthop.Relat Res.
534. Biochemical composition and electrolyte balance of "unstimulated" whole human saliva [In Process Citation] Rehak, N. N., Cecco, S. A., and Csako, G. 2000 Clin.Chem.Lab Med.
535. Response of rat salivary glands to mastication of pelleted vitamin A-deficient diet Horn, V. J., Redman, R. S., and Ambudkar, I. S. 1996 Arch.Oral Biol.
536. Trace elements in saliva and dental caries in young adults Borella, P., Fantuzzi, G., and Aggazzotti, G. 8-22-1994 Sci.Total Environ.
537. Identification of zinc proteins in rat parotid saliva Etzel, K. R., Hempel, J. D., and Koepsel, R. R. 1997 Arch.Oral Biol.
538. Efficacy of exogenous oral zinc in treatment of patients with carbonic anhydrase VI deficiency Henkin, R. I., Martin, B. M., and Agarwal, R. P. 1999 Am.J Med.Sci.
539. Effects of protein deficiency and diet consistency on the parotid gland and parotid saliva of rats Johnson, D. A., Lopez, H., and Navia, J. M. 1995 J Dent.Res.
540. [The chemical element content of mixed unstimulated saliva in periodontal diseases] Zaichk, V. E. and Bagirov, ShT 1994 Stomatologiia (Mosk)
541. Studies on the presence of 25-hydroxyvitamin D in human saliva Trafford, D. J. and Makin, H. L. 3-28-1983 Clin Chim.Acta
542. Hypovitaminosis D in medical inpatients [see comments] Thomas, M. K., Lloyd-Jones, D. M., Thadhani, R. I., Shaw, A. C., Deraska, D. J., Kitch, B. T., Vamvakas, E. C., Dick, I. M., Prince, R. L., and Finkelstein, J. S. 3-19-1998 N.Engl.J.Med.
543. Relation of dietary intake and serum levels of vitamin D to progression of osteoarthritis of the knee among participants in the Framingham Study McAlindon, T. E., Felson, D. T., Zhang, Y., Hannan, M. T., Aliabadi, P., Weissman, B., Rush, D., Wilson, P. W., and Jacques, P. 9-1-1996 Ann.Intern.Med.
544. Vitamins and arthritis. The roles of vitamins A, C, D, and E Sowers, M. and Lachance, L. 1999 Rheum.Dis.Clin.North Am.
545. Serum vitamin D levels and incident changes of radiographic hip osteoarthritis: a longitudinal study. Study of Osteoporotic Fractures Research Group Lane, N., Gore, L., Cummings, S., Hochberg, M., Scott, J., Williams, E., and Nevitt, M. 5-1-1999 Arthritis Rheum
546. Colonic hyperplasia and hyperproliferation induced by a nutritional stress diet with four components of Western-style diet Newmark, H. L., Lipkin, M., and Maheshwari, N. 3-21-1990 J.Natl.Cancer Inst.

547. Calcium, vitamin D, and colon cancer Newmark, H. L. and Lipkin, M. 4-1-1992 Cancer Res.
548. Hyperplasia, hyperproliferation and decreased migration rate of colonic epithelial cells in mice fed a diet deficient in vitamin D Sadava, D., Remer, T., and Petersen, K. 1996 Biol.Cell
549. Epithelial cell hyperproliferation induced in the exocrine pancreas of mice by a western-style diet Xue, L., Yang, K., Newmark, H., Leung, D., and Lipkin, M. 11-6-1996 J.Natl.Cancer Inst.
550. A Western-style diet induces benign and malignant neoplasms in the colon of normal C57Bl/6 mice Newmark, H. L., Yang, K., Lipkin, M., Kopelovich, L., Liu, Y., Fan, K., and Shinozaki, H. 2001 Carcinogenesis
551. Effects of vitamin A deficiency on cell proliferation and morphology of trachea of the hamster Chopra, D. P., Cooney, R. A., and Taylor, G. W. 1990 Cell Tissue Kinet.
552. Vitamin A regulates proliferation and differentiation of human prostatic epithelial cells Peehl, D. M., Wong, S. T., and Stamey, T. A. 1993 Prostate
553. Prevention of lens damage associated with cigarette smoke exposure in rats by alpha-tocopherol (vitamin E) treatment Avunduk, A. M., Yardimci, S., Avunduk, M. C., Kurnaz, L., Aydin, A., Kockar, M. C., Delibasi, T., and Dayanir, V. 1999 Invest Ophthalmol.Vis.Sci.
554. Acid/alkaline ash diets: time for assessment and change Dwyer, J., Foulkes, E., Evans, M., and Ausman, L. 1985 J Am.Diet.Assoc.
555. [Osteoporosis diet] Morselli, B., Neuenschwander, B., Perrelet, R., and Lippuner, K. 2000 Ther.Umsch.
556. Neutralization of Western diet inhibits bone resorption independently of K intake and reduces cortisol secretion in humans Maurer, M., Riesen, W., Muser, J., Hulter, H. N., and Krapf, R. 2003 Am.J Physiol Renal Physiol
557. A review of the role of acid-base balance in amino acid nutrition Patience, J. F. 1990 J Anim Sci
558. Differing effects of supplemental KCl and KHCO3: pathophysiological and clinical implications Morris, R. C., Jr., Schmidlin, O., Tanaka, M., Forman, A., Frassetto, L., and Sebastian, A. 1999 Semin.Nephrol.
559. Prevention of spinal bone loss by potassium citrate in cases of calcium urolithiasis Pak, C. Y., Peterson, R. D., and Poindexter, J. 2002 J Urol.
560. [Renal acidification mechanism disorders in patients with osteoporosis] Sanchez, A. and Libman, J. 1995 Medicina (B Aires)
561. 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
562. Potassium, magnesium, and fruit and vegetable intakes are associated with greater bone mineral density in elderly men and women Tucker, K. L., Hannan, M. T., Chen, H., Cupples, L. A., Wilson, P. W., and Kiel, D. P. 1999 Am.J Clin Nutr
563. Acid-base balance affects dietary choice in cats Cook, N. E., Rogers, Q. R., and Morris, J. G. 1996 Appetite
564. Genetic hypercalciuric stone-forming rats Bushinsky, D. A. 1999 Curr.Opin.Nephrol.Hypertens.
565. Dietary calcium and mineral/vitamin supplementation: a controversial problem Celotti, F. and Bignamini, A. 1999 J.Int.Med.Res.
566. Metabolic and endocrine effects of metabolic acidosis in humans Wiederkehr, M. and Krapf, R. 3-10-2001 Swiss.Med.Wkly.
567. Dietary vitamin D and calcium and risk of colorectal cancer: a 19-year prospective study in men Garland, C., Shekelle, R. B., Barrett-Connor, E., Criqui, M. H., Rossof, A. H., and Paul, O. 2-9-1985 Lancet
568. Effect of a calcium-enriched diet on the colonic epithelial hyperproliferation induced by N-methyl-N'-nitro-N-nitrosoguanidine in rats on a low calcium and fat diet Reshef, R., Rozen, P., Fireman, Z., Fine, N., Barzilai, M., Shasha, S. M., and Shkolnik, T. 3-15-1990 Cancer Res.
569. Vitamin D and its metabolites inhibit cell proliferation in human rectal mucosa and a colon cancer cell line Thomas, M. G., Tebbutt, S., and Williamson, R. C. 1992 Gut
570. Calcium, vitamin D, dairy foods, and the occurrence of colorectal adenomas among men and women in two prospective studies Kampman, E., Giovannucci, E., van, 't, V, Rimm, E., Stampfer, M. J., Colditz, G. A., Kok, F. J., and Willett, W. C. 1-1-1994 Am.J.Epidemiol.
571. Calcium and vitamin D: possible protective agents against colorectal cancer? Kleibeuker, J. H., Van der, Meer R., and de Vries, E. G. 1995 Eur.J.Cancer
572. Calcium and the prevention of colon cancer Lipkin, M. and Newmark, H. 1995 J Cell Biochem.Suppl
573. Relationship between vitamin and calcium supplement use and colon cancer White, E., Shannon, J. S., and Patterson, R. E. 1997 Cancer Epidemiol.Biomarkers Prev.
574. The association of calcium and vitamin D, and colon and rectal cancer in Wisconsin women Marcus, P. M. and Newcomb, P. A. 1998 Int.J.Epidemiol.
575. Calcium and vitamin D. Their potential roles in colon and breast cancer prevention Garland, C. F., Garland, F. C., and Gorham, E. D. 1999 Ann.N.Y.Acad.Sci.

576. Colorectal cancer in the Faroe Islands--a setting for the study of the role of diet Dalberg, J., Jacobsen, O., Nielsen, N. H., Steig, B. A., and Storm, H. H. 1999 J Epidemiol.Biostat.
577. Vitamin D, calcium and prevention of breast cancer: a review Lipkin, M. and Newmark, H. L. 1999 J.Am.Coll.Nutr.
578. Sunlight and breast cancer incidence in the USSR Gorham, E. D., Garland, F. C., and Garland, C. F. 1990 Int.J.Epidemiol.
579. Evidence from randomised trials on the long-term effects of hormone replacement therapy Beral, V., Banks, E., and Reeves, G. 9-21-2002 Lancet
580. Increase in Breast Cancer Incidence in Middle-aged Women during the 1990s Prehn, A., Clarke, C., Topol, B., Glaser, S., and West, D. 2002 Ann.Epidemiol.
581. Efficacy of Vitamin D compounds to modulate estrogen receptor negative breast cancer growth and invasion Flanagan, L., Packman, K., Juba, B., O'Neill, S., Tenniswood, M., and Welsh, J. 2003 J Steroid Biochem.Mol.Biol
582. Chemoprevention of mammary carcinogenesis by 1alpha-hydroxyvitamin D5, a synthetic analog of Vitamin D Mehta, R. G., Hussain, E. A., Mehta, R. R., and Das Gupta, T. K. 2003 Mutat.Res.
583. Interactions of vitamin D analogue CB1093, TNFalpha and ceramide on breast cancer cell apoptosis Pirianov, G. and Colston, K. W. 2-14-2001 Mol.Cell Endocrinol.
584. Interaction of vitamin D analogs with signaling pathways leading to active cell death in breast cancer cells Pirianov, G. and Colston, K. W. 3-1-2001 Steroids
585. Induction of differentiation by 1alpha-hydroxyvitamin D(5) in T47D human breast cancer cells and its interaction with vitamin D receptors Lazzaro, G., Agadir, A., Qing, W., Poria, M., Mehta, R. R., Moriarty, R. M., Das Gupta, T. K., Zhang, X. K., and Mehta, R. G. 2000 Eur.J.Cancer
586. Association between low levels of 1,25-dihydroxyvitamin D and breast cancer risk Janowsky, E. C., Lester, G. E., Weinberg, C. R., Millikan, R. C., Schildkraut, J. M., Garrett, P. A., and Hulka, B. S. 1999 Public Health Nutr
587. [Germany is not a "vitamin deficient country": reports of vitamin deficiency cases in Germany cause insecurity in consumers] 2003 Kinderkrankenschwester.
588. Epidemiology of vitamins A, E, D and C in rural villages in Finland: biochemical, nutritional and socioeconomical aspects Parviainen, M. T., Kumpusalo, E., Halonen, P., Neittaanmaki, L., and Pekkarinen, H. 1992 Int.J.Vitam.Nutr.Res.
589. Effect of heavy alcohol consumption on serum concentrations of fat- soluble vitamins and selenium Bjorneboe, G. A., Johnsen, J., Bjorneboe, A., Morland, J., and Drevon, C. A. 1987 Alcohol Alcohol
590. Deranged vitamin D metabolism but normal bone mineral density in Finnish noncirrhotic male alcoholics Laitinen, K., Valimaki, M., Lamberg-Allardt, C., Kivisaari, L., Lalla, M., Karkkainen, M., and Ylikahri, R. 1990 Alcohol Clin.Exp.Res.
591. Vitamin D3 binding activity during leukemic cell differentiation Feldman, J., Federico, M. H., Sonohara, S., Katayama, M. L., Koike, M. A., Roela, R. A., da Silva, M. R., and Brentani, M. M. 1993 Leuk.Res.
592. [Vitamin D] Miyaura, C. and Suda, T. 1993 Nippon Rinsho
593. Influence of dietary calcium and vitamin D on diet-induced epithelial cell hyperproliferation in mice Xue, L., Lipkin, M., Newmark, H., and Wang, J. 1-20-1999 J.Natl.Cancer Inst.
594. Risk factors for clinical benign prostatic hyperplasia in a community-based population of healthy aging men Meigs, J. B., Mohr, B., Barry, M. J., Collins, M. M., and McKinlay, J. B. 2001 J Clin Epidemiol.
595. Vitamin D inhibition of prostate adenocarcinoma growth and metastasis in the Dunning rat prostate model system Getzenberg, R. H., Light, B. W., Lapco, P. E., Konety, B. R., Nangia, A. K., Acierno, J. S., Dhir, R., Shurin, Z., Day, R. S., Trump, D. L., and Johnson, C. S. 1997 Urology
596. Exposure to ultraviolet radiation: association with susceptibility and age at presentation with prostate cancer Luscombe, C. J., Fryer, A. A., French, M. E., Liu, S., Saxby, M. F., Jones, P. W., and Strange, R. C. 8-25-2001 Lancet
597. Is vitamin D deficiency a risk factor for prostate cancer? (Hypothesis) Schwartz, G. G. and Hulka, B. S. 1990 Anticancer Res.
598. Heterogeneity in genetic susceptibility to prostate cancer Cussenot, O. and Valeri, A. 2001
599. How is individual risk for prostate cancer assessed? Giovannucci, E. 1996 Hematol.Oncol.Clin.North Am.
600. Racial variation in prostate cancer incidence and in hormonal system markers among male health professionals Platz, E. A., Rimm, E. B., Willett, W. C., Kantoff, P. W., and Giovannucci, E. 12-20-2000 J Natl.Cancer Inst.
601. Prostate cancer and prediagnostic levels of serum vitamin D metabolites (Maryland, United States) Braun, M. M., Helzlsouer, K. J., Hollis, B. W., and Comstock, G. W. 1995 Cancer Causes Control
602. [Diet probably plays an important role in the development of prostatic cancer] Damber, J. E. 8-9-2000 Lakartidningen

603. Vitamin D in the prevention and treatment of prostate cancer Konety, B. R., Johnson, C. S., Trump, D. L., and Getzenberg, R. H. 1999 Semin.Urol.Oncol.
604. Vitamin D and prostate cancer risk Peehl, D. M. 1999 Eur.Urol.
605. [Molecular effects of vitamin D on cell cycle and oncogenesis] Schmidt, J., Wittenhagen, P., and Horder, M. 7-20-1998 Ugeskr.Laeger
606. Serum vitamin D concentration and prostate cancer risk: a nested case-control study Ahn, J., Peters, U., Albanes, D., Purdue, M. P., Abnet, C. C., Chatterjee, N., Horst, R. L., Hollis, B. W., Huang, W. Y., Shikany, J. M., and Hayes, R. B. 6-4-2008 J.Natl.Cancer Inst.
607. Links between genetic and environmental factors and prostate cancer risk Ekman, P., Gronberg, H., Matsuyama, H., Kivineva, M., Bergerheim, U. S., and Li, C. 6-1-1999 Prostate
608. Diet, nutrition and prostate cancer Giles, G. and Ireland, P. 1997 Int.J.Cancer
609. Vitamin A and apoptosis in prostate cancer Zhang, X. K. 2002 Endocr.Relat Cancer
610. [Risk factors of prostate cancer--a matched case-control study] Wei, Q., Tang, X., Yang, Y., Zhan, Y., and Yin, H. 1994 Hua Xi.Yi.Ke.Da.Xue.Xue.Bao.
611. Inhibition and reversal by beta-retinoic acid of hyperplasia induced in cultured mouse prostate tissue by 3-methylcholanthrene or N-methyl-N'-nitro-N-nitrosoguanidine Chopra, D. P. and Wilkoff, L. J. 1976 J Natl.Cancer Inst.
612. Dress up for sun protection/creation of public awareness Cesarini, P. 2002 Recent Results Cancer Res.
613. Vitamin D and serotonin in winter Partonen, T. 1998 Med.Hypotheses
614. Vitamin D3 enhances mood in healthy subjects during winter Lansdowne, A. T. and Provost, S. C. 1998 Psychopharmacology (Berl)
615. Chronic vitamin D deficiency in the weanling rat alters catecholamine metabolism in the cortex Baksi, S. N. and Hughes, M. J. 6-24-1982 Brain Res.
616. Calcium and monoamine regulation: role of vitamin D nutrition Brion, F. and Dupuis, Y. 1980 Can.J.Physiol Pharmacol.
617. Vitamin D Hormone Confers Neuroprotection in Parallel with Downregulation of L-Type Calcium Channel Expression in Hippocampal Neurons Brewer, L. D., Thibault, V., Chen, K. C., Langub, M. C., Landfield, P. W., and Porter, N. M. 1-1-2001 J.Neurosci.
618. Calretinin-containing axons and neurons are resistant to an intrastriatal 6-hydroxydopamine lesion Tsuboi, K., Kimber, T. A., and Shults, C. W. 6-2-2000 Brain Res.
619. Effect of 1,25-dihydroxyvitamin D(3) on cultured mesencephalic dopaminergic neurons to the combined toxicity caused by L-buthionine sulfoximine and 1-methyl-4-phenylpyridine Shinpo, K., Kikuchi, S., Sasaki, H., Moriwaka, F., and Tashiro, K. 11-1-2000 J.Neurosci.Res.
620. Diabetes in British South Asians: nature, nurture, and culture [letter] Boucher, B. 1997 Diabet.Med.
621. Glucose intolerance and impairment of insulin secretion in relation to vitamin D deficiency in east London Asians Boucher, B. J., Mannan, N., Noonan, K., Hales, C. N., and Evans, S. J. 1995 Diabetologia
622. Role of cellular calcium metabolism in abnormal glucose metabolism and diabetic hypertension Levy, J., Zemel, M. B., and Sowers, J. R. 12-8-1989 Am.J.Med.
623. Insulin resistance, carbohydrate metabolism, and hypertension Sowers, J. R., Standley, P. R., Ram, J. L., Zemel, M. B., and Resnick, L. M. 1991 Am.J.Hypertens.
624. Calcium modulation of hypertension and obesity: mechanisms and implications Zemel, M. B. 2001 J.Am.Coll.Nutr.
625. Nutritional and endocrine modulation of intracellular calcium: implications in obesity, insulin resistance and hypertension Zemel, M. B. 1998 Mol.Cell Biochem.
626. Insulin resistance vs. hyperinsulinemia in hypertension: insulin regulation of Ca2+ transport and Ca(2+)-regulation of insulin sensitivity Zemel, M. B. 1995 J.Nutr.
627. Calcium is essential in normalizing intolerance to glucose that accompanies vitamin D depletion in vivo Beaulieu, C., Kestekian, R., Havrankova, J., and Gascon-Barre, M. 1993 Diabetes
628. Vitamin D receptor gene polymorphisms influence insulin secretion in Bangladeshi Asians Hitman, G. A., Mannan, N., McDermott, M. F., Aganna, E., Ogunkolade, B. W., Hales, C. N., and Boucher, B. J. 1998 Diabetes
629. Effects of seasonality on blood ionized calcium in early neonatal periods Zheng Ming-Ci, Zhou Lu Sheng, and Zheng Guo Feng 1993 Asia Pacific J Clin Nutr
630. Vitamin D status and bone histomorphometry in gross obesity Compston, J. E., Vedi, S., Ledger, J. E., Webb, A., Gazet, J. C., and Pilkington, T. R. 1981 Am.J.Clin.Nutr.
631. Low circulating vitamin D in obesity Liel, Y., Ulmer, E., Shary, J., Hollis, B. W., and Bell, N. H. 1988 Calcif.Tissue Int.
632. Vitamin D Deficiency in the Morbidly Obese Buffington, C., Walker, B., Cowan, G. S., Jr., and Scruggs, D. 1993 Obes.Surg.

633. Unchanged hypovitaminosis D and secondary hyperparathyroidism in morbid obesity after bariatric surgery Ybarra, J., Sanchez-Hernandez, J., Gich, I., De, Leiva A., Rius, X., Rodriguez-Espinosa, J., and Perez, A. 2005 Obes.Surg.
634. [Comparisons of bioavailability of various calcium salts. Utilization incisor dentin in parathyroidectomized rats] Matsumoto, S., Arai, M., Yamaguchi, M., Togari, A., Ohira, T., Takei, H., and Kohsaka, M. 1989 Aichi.Gakuin.Daigaku Shigakkai.Shi
635. Minerals and trace elements in milk Flynn, A. 1992 Adv.Food Nutr Res.
636. Improving bone health to optimise calcium metabolism in the dairy cow Bhanugopan, M. S., Rankin, A., Hyde, M. L., Fraser, D. R., and McNeil, D. M. 2004 Asia Pac.J.Clin.Nutr.
637. Effects of potassium citrate supplementation on bone metabolism Marangella, M., Di, Stefano M., Casalis, S., Berutti, S., D'Amelio, P., and Isaia, G. C. 2004 Calcif.Tissue Int.
638. Effects of increased consumption of fluid milk on energy and nutrient intake, body weight, and cardiovascular risk factors in healthy older adults Barr, S. I., McCarron, D. A., Heaney, R. P., Dawson-Hughes, B., Berga, S. L., Stern, J. S., and Oparil, S. 2000 J Am.Diet.Assoc.
639. Some non-traditional aspects on the regulation of glucose assimilation in the small intestine Ozols, A. 1993 Comp Biochem.Physiol Comp Physiol
640. Interactions between zinc, vitamins A and D and hormones in the regulation of growth Bunce, G. E. 1994 Adv.Exp.Med.Biol.
641. [Alterations of calcium, magnesium, and zinc in essential hypertension:their relation to the renin-angiotensin-aldosterone system] Garcia Zozaya, J. L. and Padilla, Viloria M. 1997 Invest Clin.
642. Sunscreens suppress cutaneous vitamin D3 synthesis Matsuoka, L. Y., Ide, L., Wortsman, J., MacLaughlin, J. A., and Holick, M. F. 1987 J.Clin.Endocrinol.Metab.
643. Vitamin D concentrations in Asian children living in England. Limited vitamin D intake and use of sunscreens may lead to rickets [letter; comment] [see comments] Zlotkin, S. 5-22-1999 BMJ
644. Retinoic acid and vitamin D(3) powerfully inhibit in vitro leptin secretion by human adipose tissue Menendez, C., Lage, M., Peino, R., Baldelli, R., Concheiro, P., Dieguez, C., and Casanueva, F. F. 2001 J Endocrinol.
645. The possibility of active form of vitamins A and D as suppressors on adipocyte development via ligand-dependent transcriptional regulators Kawada, T., Kamei, Y., and Sugimoto, E. 1996 Int.J Obes.Relat Metab Disord.
646. n-3 Essential fatty acids decrease weight gain in genetically obese mice Cunnane, S. C., McAdoo, K. R., and Horrobin, D. F. 1986 Br.J Nutr
647. Changes of vitamin D3 serum concentrations at the onset of immune-mediated type 1 (insulin-dependent) diabetes mellitus Baumgartl, H. J., Standl, E., Schmidt-Gayk, H., Kolb, H. J., Janka, H. U., and Ziegler, A. G. 1991 Diabetes Res.
648. Vitamin D supplement in early childhood and risk for Type I (insulin- dependent) diabetes mellitus. The EURODIAB Substudy 2 Study Group 1999 Diabetologia
649. [Secondary osteoporosis and its treatment--diabetes mellitus] Kumeda, Y., Inaba, M., and Nishizawa, Y. 1998 Nippon Rinsho
650. Bone demineralization and impaired mineral metabolism in insulin- dependent diabetes mellitus. A possible role of magnesium deficiency Saggese, G., Bertelloni, S., Baroncelli, G. I., Federico, G., Calisti, L., and Fusaro, C. 1989 Helv.Paediatr.Acta
651. Serum 25-hydroxyvitamin D3 levels decreased in impaired glucose tolerance and diabetes mellitus Scragg, R., Holdaway, I., Singh, V., Metcalf, P., Baker, J., and Dryson, E. 1995 Diabetes Res.Clin.Pract.
652. The effects of high dietary calcium on salt-induced hypertension in rats Adegunloye, B. J. and Sofola, O. A. 1996 Afr.J.Med.Med.Sci.
653. The role of calcium intake in preventing bone fragility, hypertension, and certain cancers Barger-Lux, M. J. and Heaney, R. P. 1994 J.Nutr.
654. Dietary calcium supplementation restores pressure natriuresis responses in Dahl-S rats Butler, T. V., Cameron, J., and Kirchner, K. A. 1995 Am.J.Hypertens.
655. Calcium paradox: consequences of calcium deficiency manifested by a wide variety of diseases [In Process Citation] Fujita, T. 2000 J.Bone Miner.Metab
656. Relationship between vitamin D3 and the peripheral circulation in moderate arterial primary hypertension Duprez, D., De Buyzere, M., De Backer, T., and Clement, D. 1994 Blood Press
657. Calcemic response to parathyroid hormone in spontaneously hypertensive rats: role of calcitriol Hsu, C. H., Patel, S., and Young, E. W. 1987 J.Lab Clin.Med.
658. Relation between low calcium intake, parathyroid hormone, and blood pressure Jorde, R., Sundsfjord, J., Haug, E., and Bonaa, K. H. 2000 Hypertension
659. The vitamin D/parathyroid hormone axis in the pathogenesis of hypertension and insulin resistance in uremia Mak, R. H. and Wong, J. H. 1992 Miner.Electrolyte Metab

660. Disturbed calcium metabolism in subjects with elevated diastolic blood pressure [see comments] Reichel, H., Liebethal, R., Hense, H. W., Schmidt-Gayk, H., and Ritz, E. 1992 Clin.Investig.
661. Involvement of parathyroid hormone (PTH) in genetic models of hypertension Schleiffer, R. 1992 J.Endocrinol.Invest
662. Regulation of parathyroid hormone and vitamin D in essential hypertension Young, E. W., Morris, C. D., Holcomb, S., McMillan, G., and McCarron, D. A. 1995 Am.J.Hypertens.
663. Parathyroid hormone and vitamin D levels are independently associated with calcific aortic stenosis Linhartova, K., Veselka, J., Sterbakova, G., Racek, J., Topolcan, O., and Cerbak, R. 2008 Circ.J.
664. Vitamin D and autoimmune disease Ginanjar, E., Sumariyono, Setiati, S., and Setiyohadi, B. 2007 Acta Med.Indones.
665. [Calcium and blood pressure] Simonetti, G. and Mohaupt, M. 2007 Ther.Umsch.
666. Vitamin D and disease prevention with special reference to cardiovascular disease Zittermann, A. 2006 Prog.Biophys.Mol.Biol.
667. Serum 25-hydroxycholecalciferol concentration in newly detected hypertension Scragg, R., Holdaway, I., Singh, V., Metcalf, P., Baker, J., and Dryson, E. 1995 Am.J.Hypertens.
668. Single-dose cholecalciferol suppresses the winter increase in parathyroid hormone concentrations in healthy older men and women: a randomized trial Khaw, K. T., Scragg, R., and Murphy, S. 1994 Am.J.Clin.Nutr.
669. Ultraviolet light may contribute to geographic and racial blood pressure differences Rostand, S. G. 1997 Hypertension
670. Vitamin D deficiency in UK Asian families: activating a new concern Shaw, N. J. and Pal, B. R. 2002 Arch.Dis.Child
671. Putative susceptibility markers of coronary artery disease: association between VDR genotype, smoking, and aromatic DNA adduct levels in human right atrial tissue Van Schooten, F. J., Hirvonen, A., Maas, L. M., De Mol, B. A., Kleinjans, J. C., Bell, D. A., and Durrer, J. D. 1998 FASEB J.
672. Active serum vitamin D levels are inversely correlated with coronary calcification Watson, K. E., Abrolat, M. L., Malone, L. L., Hoeg, J. M., Doherty, T., Detrano, R., and Demer, L. L. 9-16-1997 Circulation
673. Congestive heart failure caused by vitamin D deficiency? Brunvand, L., Haga, P., Tangsrud, S. E., and Haug, E. 1995 Acta Paediatr.
674. Beard calcium concentration as a marker for coronary heart disease as affected by supplementation with micronutrients including selenium MacPherson, A., Balint, J., and Bacso, J. 1995 Analyst
675. Effects of dietary vitamin D deficiency on the cardiovascular system De, Novellis, V, Loffreda, A., Vitagliano, S., Stella, L., Lampa, E., Filippelli, W., Vacca, C., Guarino, V., and Rossi, F. 1994 Res.Commun.Chem.Pathol.Pharmacol.
676. Effect of vitamin D deficiency and 1,25-dihydroxyvitamin D3 on rat heart metabolism Stio, M., Lunghi, B., Iantomasi, T., Vincenzini, M. T., and Treves, C. 1994 J.Mol.Cell Cardiol.
677. Regulation of myosin isozyme expression by vitamin D3 deficiency and 1,25-dihydroxyvitamin D3 in the rat heart O'Connell, T. D., Weishaar, R. E., and Simpson, R. U. 1994 Endocrinology
678. [Neonatal cardiac failure secondary to hypocalcemia caused by maternal vitamin D deficiency] Memmi, I., Brauner, R., Sidi, D., Sauvion, S., Souberbielle, J. C., and Garabedian, M. 1993 Arch.Fr.Pediatr.
679. [A severe form of vitamin D deficiency with hypocalcemic cardiomyopathy] Yaseen, H., Maragnes, P., Gandon-Laloum, S., Bensaid, P., N'Guyen, B., Ricaud, D., and Lecacheux, C. 1993 Pediatrie.
680. Plasma 25-hydroxyvitamin D3 and its relation to physical activity and other heart disease risk factors in the general population Scragg, R., Holdaway, I., Jackson, R., and Lim, T. 1992 Ann.Epidemiol.
681. Vitamin D independence of small calcium-binding proteins in nonclassical target tissues Walters, M. R., Bruns, M. E., Carter, R. M., and Riggle, P. C. 1991 Am.J.Physiol
682. Involvement of vitamin D3 with cardiovascular function. III. Effects on physical and morphological properties Weishaar, R. E., Kim, S. N., Saunders, D. E., and Simpson, R. U. 1990 Am.J.Physiol
683. Effect of ethane-I-hydroxy-I, I-diphosphonate on arterial calcinosis induced by hypervitaminosis D: a morphologic investigation Kingma, J. G., Jr. and Roy, P. E. 1990 J.Exp.Pathol.(Oxford)
684. [Congestive heart failure in rickets caused by vitamin D deficiency] Gillor, A., Groneck, P., Kaiser, J., and Schmitz-Stolbrink, A. 1989 Monatsschr.Kinderheilkd.
685. Ultrastructural study of hypervitaminosis D induced arterial calcification in Wistar rats Kingma, J. G., Jr. and Roy, P. E. 1988 Artery
686. Case report. Congestive heart failure complicating the hungry bone syndrome Falko, J. M., Bush, C. A., Tzagournis, M., and Thomas, F. B. 1976 Am.J.Med.Sci.
687. Letter: Ischaemic heart disease, vitamins D and A, and magnesium Seelig, M. S. 9-13-1975 Br.Med.J.
688. Vitamin D in preventive medicine: are we ignoring the evidence? Zittermann, A. 2003 Br.J Nutr
689. Bone mass, vitamin D deficiency, and hyperparathyroidism in congestive heart failure [see comments] Shane, E., Mancini, D., Aaronson, K., Silverberg, S. J., Seibel, M. J., Addesso, V., and McMahon, D. J. 1997 Am.J.Med.

690. Congestive heart failure is associated with the rate of bone loss Nishio, K., Mukae, S., Aoki, S., Itoh, S., Konno, N., Ozawa, K., Satoh, R., and Katagiri, T. 2003 J Intern.Med.
691. Myocardial infarction is inversely associated with plasma 25-hydroxyvitamin D3 levels: a community-based study Scragg, R., Jackson, R., Holdaway, I. M., Lim, T., and Beaglehole, R. 1990 Int.J.Epidemiol.
692. Tolerance of weanling pigs for dietary vitamin A and D Blair, R., Burton, B. A., Doige, C. E., Halstead, A. C., and Newsome, F. E. 1989 Int.J.Vitam.Nutr.Res.
693. The effects of calcium and vitamin D on blood pressure in conscious sheep Tresham, J. J., McGuire, P., Coghlan, J. P., Whitworth, J. A., and Scoggins, B. A. 1988 Clin.Exp.Hypertens.[A]
694. Pathogenesis of heart myofibril lesion in experimental vitamin D-induced cardionecrosis Walentynowicz, O. and Wrzolkowa, T. 1995 Exp.Mol.Pathol.
695. Hypothesis: etiology of atherosclerosis and osteoporosis: are imbalances in the calciferol endocrine system implicated? Moon, J., Bandy, B., and Davison, A. J. 1992 J.Am.Coll.Nutr.
696. [Structural-functional changes in plasma lipoproteins during vitamin D- deficient rickets in children] Antonenko, L. V., Kholodova, IuD, Apukhovskaia, L. I., Voziian, P. A., Solodova, E. V., and Kvashnina, L. V. 1990 Ukr.Biokhim.Zh.
697. Vitamin D Supplement Use and the Risk of Coronary Heart Disease Mortality in Older Women Varosy, P. D., Ensrud, K. E., Browner, W. S., Stone, K. L., Reid, I. R., Hillier, T, and Cummings, S. 4-23-2002
698. Immunomodulatory effects of 1,25-dihydroxyvitamin D3 Casteels, K., Bouillon, R., Waer, M., and Mathieu, C. 1995 Curr.Opin.Nephrol.Hypertens.
699. Vitamin D: its role and uses in immunology DeLuca, H. F. and Cantorna, M. T. 2001 FASEB J.
700. Mechanisms and functions of vitamin D DeLuca, H. F. and Zierold, C. 1998 Nutr.Rev.
701. Prolongation of allograft survival by 1,25-dihydroxyvitamin D3 Hullett, D. A., Cantorna, M. T., Redaelli, C., Humpal-Winter, J., Hayes, C. E., Sollinger, H. W., and DeLuca, H. F. 10-15-1998 Transplantation
702. [Polyglandular autoimmune syndrome] Inaba, M. and Morii, H. 1995 Nippon Rinsho
703. Prevention of autoimmune diabetes in NOD mice by 1,25 dihydroxyvitamin D3 Mathieu, C., Waer, M., Laureys, J., Rutgeerts, O., and Bouillon, R. 1994 Diabetologia
704. [Vitamin D and the immune system] Thomasset, M. 1994 Pathol.Biol.(Paris)
705. Dietary calcium is a major factor in 1,25-dihydroxycholecalciferol suppression of experimental autoimmune encephalomyelitis in mice Cantorna, M. T., Humpal-Winter, J., and DeLuca, H. F. 1999 J.Nutr.
706. Vitamin D receptor gene polymorphism: association with Crohn's disease susceptibility Simmons, J. D., Mullighan, C., Welsh, K. I., and Jewell, D. P. 2000 Gut
707. Regulators of calcium homeostasis and bone mineral density in patients with Crohn's disease Andreassen, H., Rix, M., Brot, C., and Eskildsen, P. 1998 Scand.J.Gastroenterol.
708. Altered bone metabolism in inflammatory bowel disease [see comments] Bischoff, S. C., Herrmann, A., Goke, M., Manns, M. P., von zur, Muhlen A., and Brabant, G. 1997 Am.J.Gastroenterol.
709. Bones and Crohn's: problems and solutions Buchman, A. L. 1999 Inflamm.Bowel.Dis.
710. [Bone demineralization in Crohn's disease, its diagnosis, therapy and prevention] Kocian, J. and Kocianova, J. 8-30-1999 Cas.Lek.Cesk.
711. Does immunosuppressive ultraviolet radiation explain the latitude gradient for multiple sclerosis? McMichael, A. J. and Hall, A. J. 1997 Epidemiology
712. Multiple sclerosis: decreased relapse rate through dietary supplementation with calcium, magnesium and vitamin D Goldberg, P., Fleming, M. C., and Picard, E. H. 1986 Med.Hypotheses
713. Vitamin D: a natural inhibitor of multiple sclerosis Hayes, C. E. 2000 Proc.Nutr.Soc.
714. Vitamin D and multiple sclerosis Hayes, C. E., Cantorna, M. T., and DeLuca, H. F. 1997 Proc.Soc.Exp.Biol.Med.
715. High prevalence of vitamin D deficiency and reduced bone mass in multiple sclerosis Nieves, J., Cosman, F., Herbert, J., Shen, V., and Lindsay, R. 1994 Neurology
716. Cytokine profile in patients with multiple sclerosis following vitamin D supplementation Mahon, B. D., Gordon, S. A., Cruz, J., Cosman, F., and Cantorna, M. T. 2003 J Neuroimmunol.
717. Vitamin D and its role in immunology: multiple sclerosis, and inflammatory bowel disease Cantorna, M. T. 2006 Prog.Biophys.Mol.Biol.
718. The role of vitamin D in corticosteroid-induced osteoporosis: a meta- analytic approach [see comments] Amin, S., LaValley, M. P., Simms, R. W., and Felson, D. T. 1999 Arthritis Rheum.
719. Vitamin D compounds: activity against microbes and cancer Gombart, A. F., Luong, Q. T., and Koeffler, H. P. 2006 Anticancer Res.
720. Vitamin d receptor agonists, cancer and the immune system: an intricate relationship Adorini, L., Daniel, K. C., and Penna, G. 2006 Curr.Top.Med.Chem.
721. Steroid-induced osteoporosis in systemic lupus erythematosus Cunnane, G. and Lane, N. E. 2000 Rheum.Dis.Clin.North Am.

722. [Bone density and 25-OH vitamin D serum level in patients with systemic lupus erythematosus] Becker, A., Fischer, R., and Schneider, M. 2001 Z.Rheumatol.
723. Osteoporosis in systemic lupus erythematosus: prevention and treatment Sen, D. and Keen, R. W. 2001 Lupus
724. Vitamin D3 metabolism in patients with rheumatic diseases: low serum levels of 25-hydroxyvitamin D3 in patients with systemic lupus erythematosus Muller, K., Kriegbaum, N. J., Baslund, B., Sorensen, O. H., Thymann, M., and Bentzen, K. 1995 Clin.Rheumatol.
725. Vitamin D levels in women with systemic lupus erythematosus and fibromyalgia Huisman, A. M., White, K. P., Algra, A., Harth, M., Vieth, R., Jacobs, J. W., Bijlsma, J. W., and Bell, D. A. 2001 J.Rheumatol.
726. Systemic lupus erythematosus and related disorders of childhood Arkachaisri, T. and Lehman, T. J. 1999 Curr.Opin.Rheumatol.
727. Effects of nutritional supplementation on bone mineral status of children with rheumatic diseases receiving corticosteroid therapy Warady, B. D., Lindsley, C. B., Robinson, F. G., and Lukert, B. P. 1994 J.Rheumatol.
728. Osteoporosis prevention in myasthenia gravis: a reminder Lewis, S. J. and Smith, P. E. 2001 Acta Neurol.Scand.
729. Calcium and vitamin D for corticosteroid-induced osteoporosis Homik, J., Suarez-Almazor, M. E., Shea, B., Cranney, A., Wells, G., and Tugwell, P. 2000 Cochrane.Database.Syst.Rev.
730. Do diets rich in polyunsaturated fatty acids affect disease activity in rheumatoid arthritis? Darlington, L. G. 1988 Ann.Rheum.Dis.
731. Effect of cod liver oil on symptoms of rheumatoid arthritis Gruenwald, J., Graubaum, H. J., and Harde, A. 2002 Adv.Ther.
732. Serum calcium levels in rheumatoid arthritis Scott, D. L., Farr, M., Hawkins, C. F., Wilkinson, R., and Bold, A. M. 1981 Ann.Rheum.Dis.
733. [Disorders of calcium and phosphorus metabolism in rheumatoid arthritis] Ota, K. and Uezu, A. 1982 Nippon Rinsho
734. Metabolic bone disease among in-patients with rheumatoid arthritis Wordsworth, B. P., Vipond, S., Woods, C. G., and Mowat, A. G. 1984 Br.J.Rheumatol.
735. Osteoporosis in rheumatoid arthritis Jones, S. M. and Bhalla, A. K. 1993 Clin.Exp.Rheumatol.
736. Low serum vitamin D metabolites in women with rheumatoid arthritis Kroger, H., Penttila, I. M., and Alhava, E. M. 1993 Scand.J.Rheumatol.
737. [Vitamin D metabolites in rheumatoid arthritis: findings--hypotheses-- consequences] Hein, G. and Oelzner, P. 2000 Z.Rheumatol.
738. [Are there effective dietary recommendations for patients with rheumatoid arthritis?] Keysser, G. 2001 Z.Rheumatol.
739. Vitamin D intake is inversely associated with rheumatoid arthritis: results from the Iowa Women's Health Study Merlino, L. A., Curtis, J., Mikuls, T. R., Cerhan, J. R., Criswell, L. A., and Saag, K. G. 2004 Arthritis Rheum.
740. Eroded enamel lesion remineralization by saliva as a possible factor in the site-specificity of human dental erosion Amaechi, B. T. and Higham, S. M. 2001 Arch.Oral Biol
741. Abnormal vitamin D3 metabolism in patients with primary Sjogren's syndrome Muller, K., Oxholm, P., Sorensen, O. H., Thymann, M., Hoier-Madsen, M., and Bendtzen, K. 1990 Ann Rheum.Dis.
742. Regulation of cutaneous previtamin D3 photosynthesis in man: skin pigment is not an essential regulator Holick, M. F., MacLaughlin, J. A., and Doppelt, S. H. 2-6-1981 Science.
743. Environmental factors in the etiology of type 1 diabetes Akerblom, H. K., Vaarala, O., Hyoty, H., Ilonen, J., and Knip, M. 5-30-2002 Am.J Med.Genet.
744. Variations in the vitamin D-binding protein (Gc locus) are associated with oral glucose tolerance in nondiabetic Pima Indians Baier, L. J., Dobberfuhl, A. M., Pratley, R. E., Hanson, R. L., and Bogardus, C. 1998 J.Clin.Endocrinol.Metab
745. Ethnic differences in the association between body mass index and hypertension Colin, Bell A., Adair, L. S., and Popkin, B. M. 2-15-2002 Am.J Epidemiol.
746. Erythrocyte cation metabolism in salt-sensitive hypertensive blacks as affected by dietary sodium and calcium Zemel, M. B., Kraniak, J., Standley, P. R., and Sowers, J. R. 1988 Am.J Hypertens.
747. Health status of African Americans Dreeben, O. 2001 J Health Soc.Policy
748. Serum testosterone levels in African-American and white men undergoing prostate biopsy Kubricht, W. S., III, Williams, B. J., Whatley, T., Pinckard, P., and Eastham, J. A. 1999 Urology
749. Serum testosterone levels in healthy young black and white men Ross, R., Bernstein, L., Judd, H., Hanisch, R., Pike, M., and Henderson, B. 1986 J Natl.Cancer Inst.
750. Differences in mineral homeostasis, volumetric bone mass and femoral neck axis length in black and white South African women Daniels, E. D., Pettifor, J. M., Schnitzler, C. M., Moodley, G. P., and Zachen, D. 1997 Osteoporos.Int.

751. The effect of ethnic group on appendicular bone mass in children Patel, D. N., Pettifor, J. M., Becker, P. J., Grieve, C., and Leschner, K. 1992 J Bone Miner.Res.
752. Low bone mineral content is common but osteoporotic fractures are rare in elderly rural Gambian women Aspray, T. J., Prentice, A., Cole, T. J., Sawo, Y., Reeve, J., and Francis, R. M. 1996 J Bone Miner.Res.
753. Comparative skeletal mass and radial bone mineral content in black and white women Cohn, S. H., Abesamis, C., Yasumura, S., Aloia, J. F., Zanzi, I., and Ellis, K. J. 1977 Metabolism
754. Rarity of colorectal adenomas in the African black population [see comments] Segal, I. 1998 Eur.J.Cancer Prev.
755. Human calcium absorption from whole-wheat products Weaver, C. M., Heaney, R. P., Martin, B. R., and Fitzsimmons, M. L. 1991 J Nutr
756. Hypertension in east Africans and others of African descent: a review Mbaya, V. B. 1998 East Afr.Med.J.
757. Cardiovascular reactivity in Black South-African males of different age groups: the influence of urbanization van Rooyen, J. M., Huisman, H. W., Eloff, F. C., Laubscher, P. J., Malan, L., Steyn, H. S., and Malan, N. T. 2002 Ethn.Dis.
758. Benign prostatic hyperplasia and prostate carcinoma in native Africans Dawam, D., Rafindadi, A. H., and Kalayi, G. D. 2000 BJU.Int.
759. Increased incidence of prostate cancer in Nigerians Ogunbiyi, J. O. and Shittu, O. B. 1999 J Natl.Med.Assoc.
760. Characterization of prostatic carcinoma among blacks: a continuation report Jackson, M. A., Ahluwalia, B. S., Herson, J., Heshmat, M. Y., Jackson, A. G., Jones, G. W., Kapoor, S. K., Kennedy, J., Kovi, J., Lucas, A. O., Nkposong, E. O., Olisa, E., and Williams, A. O. 1977 Cancer Treat.Rep.
761. The changing pattern of prostate cancer in Nigerians: current status in the southeastern states Ekwere, P. D. and Egbe, S. N. 2002 J Natl.Med.Assoc.
762. A prospective study of intake of fish and marine fatty acids and prostate cancer Augustsson, K., Michaud, D. S., Rimm, E. B., Leitzmann, M. F., Stampfer, M. J., Willett, W. C., and Giovannucci, E. 2003 Cancer Epidemiol.Biomarkers Prev.
763. Fatty fish consumption and risk of prostate cancer Terry, P., Lichtenstein, P., Feychting, M., Ahlbom, A., and Wolk, A. 6-2-2001 Lancet
764. Prostate cancer risk and consumption of fish oils: a dietary biomarker-based case-control study Norrish, A. E., Skeaff, C. M., Arribas, G. L., Sharpe, S. J., and Jackson, R. T. 1999 Br.J Cancer
765. Nutritional aspects of vitamin D and its metabolites in Japanese children and adults Kobayashi, T. 1999 J.Bone Miner.Metab
766. Dietary factors and risk of prostate cancer in Poland. Results of case-control study Pawlega, J., Rachtan, J., and Dyba, T. 1996 Neoplasma
767. Molecular epidemiology of vitamin D receptor gene variants Zmuda, J. M., Cauley, J. A., and Ferrell, R. E. 2000 Epidemiol.Rev.
768. The evolution of human skin coloration Jablonski, N. G. and Chaplin, G. 2000 J.Hum.Evol.
769. Epidemiology of malignant melanoma of the skin in South Africa Rippey, J. J. and Rippey, E. 4-14-1984 S.Afr.Med.J.
770. Basal cell carcinoma in North American blacks. Clinical and histopathologic study of 26 patients Abreo, F. and Sanusi, I. D. 1991 J Am.Acad Dermatol.
771. Skin cancer in blacks in the United States Halder, R. M. and Bang, K. M. 1988 Dermatol.Clin
772. Cancer of the skin in blacks. I. A review of 163 black patients with cutaneous squamous cell carcinoma Mora, R. G. and Perniciaro, C. 1981 J Am.Acad Dermatol.
773. Vitamin D metabolism in polar vertebrates Griffiths, P. and Fairney, A. 1988 Comp Biochem.Physiol B
774. Contribution of Selected Traditional and Market Foods to the Diet of Nunavik Inuit Women Blanchet, C., Dewailly, E., Ayotte, P., Bruneau, S., Receveur, O., and Holub, B. J. 2000 Can.J Diet.Pract.Res.
775. Stimulation of human melanocytes by vitamin D3 possibly mediates skin pigmentation after sun exposure Tomita, Y., Torinuki, W., and Tagami, H. 1988 J Invest Dermatol.
776. The distribution and storage of vitamin D and its metabolites in human tissues Mawer, E. B., Backhouse, J., Holman, C. A., Lumb, G. A., and Stanbury, S. W. 1972 Clin.Sci.
777. Vitamin D metabolism in the hooded seal (Cystophora cristata) Keiver, K. M., Draper, H. H., and Ronald, K. 1988 J Nutr
778. Minnesota rickets. Need for a policy change to support vitamin D supplementation Eugster, E. A., Sane, K. S., and Brown, D. M. 1996 Minn.Med.
779. Low birth-weight infants: the continuing ethnic disparity and the interaction of biology and environment Fuller, K. E. 2000 Ethn.Dis.
780. A preliminary report of vitamin D and calcium metabolism in older African Americans Perry, H. M., III, Miller, D. K., Morley, J. E., Horowitz, M., Kaiser, F. E., Perry, H. M., Jr., Jensen, J., Bentley, J., Boyd, S., and Kraenzle, D. 1993 J.Am.Geriatr.Soc.

781. The effects of vitamin D insufficiency in patients with primary hyperparathyroidism Silverberg, S. J., Shane, E., Dempster, D. W., and Bilezikian, J. P. 1999 Am.J.Med.
782. Vitamin D deficiency and aging: implications for general health and osteoporosis Eriksen, E. F. and Glerup, H. 2002 Biogerontology.
783. Ethnic and genetic differences in bone mass: a review with a hereditary vs environmental perspective Pollitzer, W. S. and Anderson, J. J. 1989 Am.J Clin Nutr
784. Greater secretion of growth hormone in black than in white men: possible factor in greater bone mineral density--a clinical research center study Wright, N. M., Renault, J., Willi, S., Veldhuis, J. D., Pandey, J. P., Gordon, L., Key, L. L., and Bell, N. H. 1995 J Clin Endocrinol.Metab
785. Osteoporosis and African American women Bohannon, A. D. 1999 J.Womens Health Gend.Based.Med.
786. Aging and bone metabolism in African American and Caucasian women Perry, H. M., III, Horowitz, M., Morley, J. E., Fleming, S., Jensen, J., Caccione, P., Miller, D. K., Kaiser, F. E., and Sundarum, M. 1996 J.Clin.Endocrinol.Metab
787. 25-Hydroxyvitamin D3 reverses alteration of the vitamin D-endocrine system in blacks Bell, N. H. 1995 Am.J Med.
788. [The factors of individual sensitivity to ultraviolet radiation] Strzhizhovskii, A. D. 1998 Usp.Fiziol.Nauk
789. Sun protection behaviors among African Americans Hall, H. I. and Rogers, J. D. 1999 Ethn.Dis.
790. Case-control study of factors associated with nutritional rickets in Nigerian children Thacher, T. D., Fischer, P. R., Pettifor, J. M., Lawson, J. O., Isichei, C. O., and Chan, G. M. 2000 J Pediatr.
791. Etiology of rickets in Nigerian children Oginni, L. M., Worsfold, M., Oyelami, O. A., Sharp, C. A., Powell, D. E., and Davie, M. W. 1996 J Pediatr.
792. Absence of vitamin D deficiency in young Nigerian children Pfitzner, M. A., Thacher, T. D., Pettifor, J. M., Zoakah, A. I., Lawson, J. O., Isichei, C. O., and Fischer, P. R. 1998 J.Pediatr.
793. McCollum Award Lecture, 1994: vitamin D--new horizons for the 21st century Holick, M. F. 1994 Am.J.Clin.Nutr.
794. Calcium, vitamin D, and parathyroid hormone status in young white and black women: association with racial differences in bone mass Meier, D. E., Luckey, M. M., Wallenstein, S., Clemens, T. L., Orwoll, E. S., and Waslien, C. I. 1991 J Clin Endocrinol.Metab
795. Rickets in Nigerian children: a consequence of calcium malnutrition Okonofua, F., Gill, D. S., Alabi, Z. O., Thomas, M., Bell, J. L., and Dandona, P. 1991 Metabolism
796. Appendicular bone mass in children with a high prevalence of low dietary calcium intakes Pettifor, J. M. and Moodley, G. P. 1997 J Bone Miner.Res.
797. [Bone density in 20 black African young adults of the Bantu race is identical to that in subjects of white race] Bileckot, R., Audran, M., Masson, C., Ntsiba, H., Simon, P., and Renier, J. C. 11-30-1991 Rev.Rhum.Mal Osteoartic.
798. Cortical bone mass in Nigerian children: an anthropometric assessment Odita, J. C. 1994 Skeletal Radiol.
799. Ethnic and genetic differences in susceptibility to osteoporotic fractures Anderson, J. J. and Pollitzer, W. S. 1994 Adv.Nutr Res.
800. Growth hormone secretion and bone mineral density in prepubertal black and white boys Wright, N. M., Papadea, N., Veldhuis, J. D., and Bell, N. H. 2002 Calcif.Tissue Int.
801. Low levels of serum calcidiol in an African population compared to a North European population Feleke, Y., Abdulkadir, J., Mshana, R., Mekbib, T. A., Brunvand, L., Berg, J. P., and Falch, J. A. 1999 Eur.J.Endocrinol.
802. Improved Cholecalciferol Nutrition in Rats Is Noncalcemic, Suppresses Parathyroid Hormone and Increases Responsiveness to 1,25-Dihydroxycholecalciferol Vieth, Reinhold, Milojevic, Susan, and Peltekova, Vanya 3-1-2000 J.Nutr.
803. Altered cation transport in non-insulin-dependent diabetic hypertension: effects of dietary calcium Zemel, M. B., Bedford, B. A., Zemel, P. C., Marwah, O., and Sowers, J. R. 1988 J Hypertens.Suppl
804. A comparison of calcium, vitamin D, or both for nutritional rickets in Nigerian children [see comments] Thacher, T. D., Fischer, P. R., Pettifor, J. M., Lawson, J. O., Isichei, C. O., Reading, J. C., and Chan, G. M. 8-19-1999 N.Engl.J.Med.
805. Racial pigmentation and the cutaneous synthesis of vitamin D [see comments] Matsuoka, L. Y., Wortsman, J., Haddad, J. G., Kolm, P., and Hollis, B. W. 1991 Arch.Dermatol.
806. Alteration of vitamin D metabolism in Mexican-Americans Reasner, C. A., Dunn, J. F., Fetchick, D. A., Liel, Y., Hollis, B. W., Epstein, S., Shary, J., Mundy, G. R., and Bell, N. H. 1990 J Bone Miner.Res.
807. Vitamin D receptor genotype and breast cancer in Latinas (United States) Ingles, S. A., Garcia, D. G., Wang, W., Nieters, A., Henderson, B. E., Kolonel, L. N., Haile, R. W., and Coetzee, G. A. 2000 Cancer Causes Control

808. Alteration of vitamin D metabolism in Mexican-Americans [see comments] Reasner, C. A., Dunn, J. F., Fetchick, D. A., Liel, Y., Hollis, B. W., Epstein, S., Shary, J., Mundy, G. R., and Bell, N. H. 1990 J.Bone Miner.Res.
809. Obesity and the metabolic syndrome Keller, K. B. and Lemberg, L. 2003 Am.J Crit Care
810. Cardiovascular disease risk factors among older black, Mexican-American, and white women and men: an analysis of NHANES III, 1988-1994. Third National Health and Nutrition Examination Survey Sundquist, J., Winkleby, M. A., and Pudaric, S. 2001 J Am.Geriatr.Soc.
811. Serum calcium in Greenland Eskimos Jeppesen, B. B. and Harvald, B. 1983 Acta Med.Scand.
812. Adaptation of Inuit children to a low-calcium diet Sellers, E. A., Sharma, A., and Rodd, C. 4-29-2003 CMAJ.
813. Vitamin-D-deficient rickets in Manitoba, 1972-84 Haworth, J. C. and Dilling, L. A. 2-1-1986 CMAJ.
814. Causes, treatment and prevention of early childhood caries: a microbiologic perspective Berkowitz, R. J. 2003 J Can.Dent.Assoc.
815. Low incidence of cardiovascular disease among the Inuit-what is the evidence? Bjerregaard, P., Kue, Young T., and Hegele, R. A. 2003 Atherosclerosis
816. Health expectancy in Greenland Iburg, K. M., Bronnum-Hansen, H., and Bjerregaard, P. 2001 Scand.J Public Health
817. Health status of American Indians/Alaska Natives: general patterns of mortality Mahoney, M. C. and Michalek, A. M. 1998 Fam.Med.
818. The health status of American Indians and Alaska Natives: 2. Lessons for cancer educators Mahoney, M. C. and Michalek, A. M. 1999 J Cancer Educ.
819. Dietary change and obesity associated with glucose intolerance in Alaska Natives Murphy, N. J., Schraer, C. D., Thiele, M. C., Boyko, E. J., Bulkow, L. R., Doty, B. J., and Lanier, A. P. 1995 J Am.Diet.Assoc.
820. Prevalence and severity of dental caries among American Indians and Alaska Natives Niendorff, W. J. and Jones, C. M. 2000 J Public Health Dent.
821. Rheumatic diseases in North America's indigenous peoples Peschken, C. A. and Esdaile, J. M. 1999 Semin.Arthritis Rheum.
822. Body fat distribution and other cardiac risk factors among circumpolar Inuit and nGanasan Rode, A. and Shephard, R. J. 1995 Arctic Med.Res.
823. Hypertension and diabetes among Siberian Yupik Eskimos of St. Lawrence Island, Alaska Schraer, C. D., Ebbesson, S. O., Boyko, E., Nobmann, E., Adler, A., and Cohen, J. 1996 Public Health Rep.
824. Diabetes complications and mortality among Alaska Natives: 8 years of observation Schraer, C. D., Adler, A. I., Mayer, A. M., Halderson, K. R., and Trimble, B. A. 1997 Diabetes Care
825. Periodontal disease in American Indians and Alaska Natives Skrepcinski, F. B. and Niendorff, W. J. 2000 J Public Health Dent.
826. One year in an Alaskan arthritis clinic Templin, D. 1999 Int.J Circumpolar.Health
827. High age-adjusted prevalence of Parkinson's disease among Inuits in Greenland Wermuth, L., Pakkenberg, H., and Jeune, B. 5-14-2002 Neurology
828. Type 2 diabetes mellitus in Canada's first nations: status of an epidemic in progress Young, T. K., Reading, J., Elias, B., and O'Neil, J. D. 9-5-2000 CMAJ.
829. Heart disease and its related risk factors in Asian Indians Uppaluri, C. R. 2002 Ethn.Dis.
830. Cardiovascular risk factors in ethnic minority women aged < or =30 years Palaniappan, L., Anthony, M. N., Mahesh, C., Elliott, M., Killeen, A., Giacherio, D., and Rubenfire, M. 3-1-2002 Am.J Cardiol.
831. Coronary heart disease and its risk factors in first-generation immigrant Asian Indians to the United States of America Enas, E. A., Garg, A., Davidson, M. A., Nair, V. M., Huet, B. A., and Yusuf, S. 1996 Indian Heart J
832. Epidemiology of type II diabetes: an international perspective Songer, T. J. and Zimmet, P. Z. 1995 Pharmacoeconomics.
833. A study on Asian Indian and American vegetarians: indications of a racial predisposition to glucose intolerance Scholfield, D. J., Behall, K. M., Bhathena, S. J., Kelsay, J., Reiser, S., and Revett, K. R. 1987 Am.J Clin Nutr
834. The effect of Gc genotype on fasting insulin level in Dogrib Indians Szathmary, E. J. 1987 Hum.Genet.
835. Nutritional status of children of Mexican-American migrant families Larson, L. B., Dodds, J. M., Massoth, D. M., and Chase, H. P. 1974 J.Am.Diet.Assoc.
836. Are elderly Asians in Britain at a high risk of vitamin D deficiency and osteomalacia? Solanki, T., Hyatt, R. H., Kemm, J. R., Hughes, E. A., and Cowan, R. A. 1995 Age Ageing
837. Long-term vitamin D3 supplementation may have adverse effects on serum lipids during postmenopausal hormone replacement therapy Heikkinen, A. M., Tuppurainen, M. T., Niskanen, L., Komulainen, M., Penttila, I., and Saarikoski, S. 1997 Eur.J.Endocrinol.

838. The relevance of the women's health initiative results on combined hormone replacement therapy in clinical practice Lemay, A. 2002 J Obstet.Gynaecol.Can.
839. The changing view of hormone replacement therapy Vogel, R. A. 2003 Rev.Cardiovasc.Med.
840. Hormone replacement therapy, cardiovascular and cerebrovascular disease Teede, H. J. 2003 Best.Pract.Res.Clin Endocrinol.Metab
841. Hormone Replacement Therapy for Primary and Secondary Prevention of Heart Disease Shah, S. H. and Alexander, K. P. 2003 Curr.Treat.Options.Cardiovasc.Med.
842. The paths to the discovery of vitamins A and D McCollum, E. V. 1967 J Nutr
843. The history of vitamin research. Selected aspects Morton, R. A. 1968 Int.Z.Vitaminforsch.
844. Vitamins: essential dietary constituents discovered Sharman, I. M. 1977 Endeavour
845. Some legacies of nutrition pioneer E. V. McCollum Davis, D. R. 1979 Trans.Kans.Acad.Sci.
846. Vitamine--vitamin. The early years of discovery Rosenfeld, L. 1997 Clin.Chem.
847. Historical Aspects DeLuca, H. 1979
848. The History of Rickets Hess, A 1929
849. Vitamin D resistant rickets of a young adult patient. A review and case report Pliskin, M. E., Brown, A. M., Baden, E. E., and Kimball, H. G. 1975 J.Oral Med.
850. Vitamin D status in hospitalized black children under 2 years of age Sochett, E. B., Pettifor, J. M., Moodley, G., and Pentopoulos, M. 6-29-1985 S.Afr.Med.J.
851. Nutritional rickets in breast-fed infants Cosgrove, L. and Dietrich, A. 1985 J.Fam.Pract.
852. Prevention of rickets in Asian children: assessment of the Glasgow campaign Dunnigan, M. G., Glekin, B. M., Henderson, J. B., McIntosh, W. B., Sumner, D., and Sutherland, G. R. 7-27-1985 Br.Med.J.(Clin.Res.Ed)
853. Rickets in very low birthweight infants. Influence of supplementation with vitamin D, phosphorus and calcium Lindroth, M., Westgren, U., and Laurin, S. 1986 Acta Paediatr.Scand.
854. Vitamin D deficiency rickets. A report on three cases Kruger, D. M., Lyne, E. D., and Kleerekoper, M. 1987 Clin.Orthop.
855. Etiology of rickets in Egyptian children Lawson, D. E., Cole, T. J., Salem, S. I., Galal, O. M., el Meligy, R., Abdel-Azim, S., Paul, A. A., and el Husseini, S. 1987 Hum.Nutr.Clin.Nutr.
856. Osteomalacia of the mother--rickets of the newborn Park, W., Paust, H., Kaufmann, H. J., and Offermann, G. 1987 Eur.J.Pediatr.
857. Serum concentrations of vitamin D metabolites in rachitic Libyan children Elzouki, A. Y., Markestad, T., Elgarrah, M., Elhoni, N., and Aksnes, L. 1989 J.Pediatr.Gastroenterol.Nutr.
858. [Deficiency rickets: the current situation in France and Algeria] Garabedian, M. and Ben Mekhbi, H. 1989 Pediatrie.
859. Vitamin-D-deficiency rickets in Kuwait: the prevalence of a preventable disease Lubani, M. M., al Shab, T. S., al Saleh, Q. A., Sharda, D. C., Quattawi, S. A., Ahmed, S. A., Moussa, M. A., and Reavey, P. C. 1989 Ann.Trop.Paediatr.
860. The biochemistry and physiology of vitamin D Nicolaysen, R. and Eeg-Larsen, N. 1953
861. Recommendations for vitamin A supplementation Ross, D. A. 2002 J Nutr
862. The influence of function on the lime requirements of animals. Steenbock, H. and Hart, E. B. 1913 J Biol Chem
863. An investigation of sources of variation in calcium absorption efficiency [published erratum appears in J Clin Endocrinol Metab 1995 Jul;80(7):2068] Barger-Lux, M. J., Heaney, R. P., Lanspa, S. J., Healy, J. C., and DeLuca, H. F. 1995 J.Clin.Endocrinol.Metab
864. Calcium Absorption Varies within the Reference Range for Serum 25-Hydroxyvitamin D Heaney, R. P., Dowell, M. S., Hale, C. A., and Bendich, A. 2003 J Am.Coll.Nutr
865. The role of carotenoids and retinoids in gap junctional communication Stahl, W. and Sies, H. 1998 Int.J Vitam.Nutr Res.
866. Stimulation by 1,25-dihydroxyvitamin D3 of insulin receptor expression and insulin responsiveness for glucose transport in U-937 human promonocytic cells Maestro, B., Campion, J., Davila, N., and Calle, C. 2000 Endocr.J
867. Overproduction of insulin in the chromium-deficient rat Striffler, J. S., Polansky, M. M., and Anderson, R. A. 1999 Metabolism
868. Low vitamin K intake effects on glucose tolerance in rats Sakamoto, N., Wakabayashi, I., and Sakamoto, K. 1999 Int.J Vitam.Nutr Res.
869. Biotin supplementation improves glucose and insulin tolerances in genetically diabetic KK mice Reddi, A., DeAngelis, B., Frank, O., Lasker, N., and Baker, H. 1988 Life Sci
870. Vitamin D sites and mechanisms of action: a histochemical perspective. Reflections on the utility of autoradiography and cytopharmacology for drug targeting Stumpf, W. E. 1995 Histochem.Cell Biol
871. Vitamin D: recent advances DeLuca, H. F. and Schnoes, H. K. 1983 Annu.Rev.Biochem.
872. Extrarenal production of calcitriol Dusso, A., Brown, A., and Slatopolsky, E. 1994 Semin.Nephrol.

873. Human prostate cells synthesize 1,25-dihydroxyvitamin D3 from 25- hydroxyvitamin D3 Schwartz, G. G., Whitlatch, L. W., Chen, T. C., Lokeshwar, B. L., and Holick, M. F. 1998 Cancer Epidemiol.Biomarkers Prev.
874. 1alpha-Hydroxylase and the action of vitamin D Hewison, M., Zehnder, D., Bland, R., and Stewart, P. M. 2000 J.Mol.Endocrinol.
875. Extrarenal expression of 25-hydroxyvitamin d(3)-1 alpha-hydroxylase Zehnder, D., Bland, R., Williams, M. C., McNinch, R. W., Howie, A. J., Stewart, P. M., and Hewison, M. 2001 J.Clin.Endocrinol.Metab
876. Vitamin D metabolism in human prostate cells: implications for prostate cancer chemoprevention by vitamin D Flanagan, J. N., Young, M. V., Persons, K. S., Wang, L., Mathieu, J. S., Whitlatch, L. W., Holick, M. F., and Chen, T. C. 2006 Anticancer Res.
877. Mechanism of vitamin D receptor action Demay, M. B. 2006 Ann.N.Y.Acad.Sci.
878. Vitamin D endocrine system and the genetic susceptibility to diabetes, obesity and vascular disease. A review of evidence Reis, A. F., Hauache, O. M., and Velho, G. 2005 Diabetes Metab
879. The Vitamin D endocrine system of the gut--its possible role in colorectal cancer prevention Cross, H. S., Bises, G., Lechner, D., Manhardt, T., and Kallay, E. 2005 J.Steroid Biochem.Mol.Biol.
880. Vitamin D and skin cancer: a problem in gene regulation Bikle, D. D., Oda, Y., and Xie, Z. 2005 J.Steroid Biochem.Mol.Biol.
881. Regulation of gene Expression by 1alpha,25-dihydroxyvitamin D3 and Its analog EB1089 under growth-inhibitory conditions in squamous carcinoma Cells Akutsu, N., Lin, R., Bastien, Y., Bestawros, A., Enepekides, D. J., Black, M. J., and White, J. H. 2001 Mol.Endocrinol.
882. The in vitro evaluation of 25-hydroxyvitamin D3 and 19-nor-1alpha,25- dihydroxyvitamin D2 as therapeutic agents for prostate cancer Chen, T. C., Schwartz, G. G., Burnstein, K. L., Lokeshwar, B. L., and Holick, M. F. 2000 Clin.Cancer Res.
883. Relative sparing of calretinin containing neurons in the substantia nigra of 6-OHDA treated rat Parkinsonian model Kim, B. G., Shin, D. H., Jeon, G. S., Seo, J. H., Kim, Y. W., Jeon, B. S., and Cho, S. S. 2-7-2000 Brain Res.
884. Vitamin D deficiency found in the diet of the elderly in South Carolina Ryan, C. and Lui, J. H. 1993 J.S.C.Med.Assoc.
885. Elevation of blood vitamin D2 levels does not impede the release of vitamin D3 from the skin Matsuoka, L. Y., Wortsman, J., Haddad, J. G., and Hollis, B. W. 1992 Metabolism
886. Osteopathy and resistance to vitamin D toxicity in mice null for vitamin D binding protein Safadi, F. F., Thornton, P., Magiera, H., Hollis, B. W., Gentile, M., Haddad, J. G., Liebhaber, S. A., and Cooke, N. E. 1999 J.Clin.Invest
887. Vitamin D-binding protein prevents vitamin D deficiency and presents vitamin D for its renal activation Berg, J. P. 1999 Eur.J Endocrinol.
888. Metabolism of cholecalciferol in vitamin D intoxicated chicks Ratzkowski, C., Fine, N., and Edelstein, S. 6-1-1982 Isr J Med Sci
889. Hypervitaminosis D associated with drinking milk [see comments] Jacobus, C. H., Holick, M. F., Shao, Q., Chen, T. C., Holm, I. A., Kolodny, J. M., Fuleihan, G. E., and Seely, E. W. 4-30-1992 N.Engl.J.Med.
890. 1,25-dihydroxyvitamin D3 receptor is upregulated in aortic smooth muscle cells during hypervitaminosis D Rajasree, S., Umashankar, P. R., Lal, A. V., Sarma, P. S., and Kartha, C. C. 3-1-2002 Life Sci.
891. Serum levels of free 1,25-dihydroxyvitamin D in vitamin D toxicity Pettifor, J. M., Bikle, D. D., Cavaleros, M., Zachen, D., Kamdar, M. C., and Ross, F. P. 4-1-1995 Ann Intern.Med.
892. Plasma concentrations of vitamin D3 and its metabolites in the rat as influenced by vitamin D3 or 25-hydroxyvitamin D3 intakes Shephard, R. M. and DeLuca, H. F. 1980 Arch.Biochem.Biophys.
893. Relations between vitamin D and fatty acid binding properties of vitamin D-binding protein Calvo, M. and Ena, J. M. 8-30-1989 Biochem.Biophys.Res.Commun.
894. Structure function analysis of vitamin D analogs with C-ring modifications Bouillon, R., Allewaert, K., van Leeuwen, J. P., Tan, B. K., Xiang, D. Z., De Clercq, P., Vandewalle, M., Pols, H. A., Bos, M. P., and Van Baelen, H. 2-15-1992 J.Biol.Chem.
895. Linoleic acid esterified in low density lipoprotein serves as substrate for increased arachidonic acid synthesis in differentiating monocytic cells Hrboticky, N., Sellmayer, A., Yeo, Y., Pietsch, A., and Weber, P. C. 8-16-1996 Biochim.Biophys.Acta
896. Inhibition of Western-diet induced hyperproliferation and hyperplasia in mouse colon by two sources of calcium Richter, F., Newmark, H. L., Richter, A., Leung, D., and Lipkin, M. 1995 Carcinogenesis
897. Effect of vitamin D deficiency on lipid composition and calcium transport in basolateral membrane vesicles from chick intestine Alisio, A., Canas, F., de Bronia, D. H., Pereira, R., and Tolosa, de Talamoni 1997 Biochem.Mol.Biol.Int.

898. Polyunsaturated fatty acid enrichment increases ultraviolet A-induced lipid peroxidation in NCTC 2544 human keratinocytes Quiec, D., Maziere, C., Santus, R., Andre, P., Redziniak, G., Chevy, F., Wolf, C., Driss, F., Dubertret, L., and Maziere, J. C. 1995 J Invest Dermatol.
899. Regulation of matrix vesicle metabolism by vitamin D metabolites Boyan, B. D., Schwartz, Z., Swain, L. D., Bonewald, L. F., and Khare, A. 1989 Connect.Tissue Res.
900. Vitamin D receptors: not just in the nucleus anymore Fleet, J. C. 1999 Nutr.Rev.
901. Molecular mechanism of transcriptional control by nuclear vitamin receptors Kato, S. 2000 Br.J Nutr
902. Retinoic acid--a player that rules the game of life and death in neutrophils Mehta, K. 2002 Indian J Exp.Biol
903. Anticancer activity and mechanism of action of retinoids in oral and pharyngeal cancer Klaassen, I. and Braakhuis, B. J. 2002 Oral Oncol.
904. Investigation of the elemental distribution in iliac crests of female New Zealand rabbits using NAA Zhang, Y., Li, D., Zhuang, G., Cheng, F., Zhang, G., Wang, Z., and Xia, J. 2002 Biol Trace Elem.Res.
905. Beta-carotene inhibits growth of human colon carcinoma cells in vitro by induction of apoptosis Briviba, K., Schnabele, K., Schwertle, E., Blockhaus, M., and Rechkemmer, G. 2001 Biol Chem
906. Retinoids, apoptosis and cancer Simoni, D. and Tolomeo, M. 2001 Curr.Pharm.Des
907. Apoptosis induction of POS canine osteosarcoma cells by vitamin D and retinoids Barroga, E. F., Kadosawa, T., Asano, K., Okumura, M., and Fujinaga, T. 1998 J Vet.Med.Sci.
908. Gene regulation by vitamin D3 Carlberg, C. and Polly, P. 1998 Crit Rev.Eukaryot.Gene Expr.
909. Vitamin D and prostate cancer Polek, T. C. and Weigel, N. L. 2002 J.Androl
910. Interaction between estrogen and vitamin D-endocrine system: a potential addition to the unitary model of osteoporosis [letter; comment] Liel, Y., Shany, S., and Schwartz, B. 1998 J.Bone Miner.Res.
911. Steroid hormone receptor expression and action in bone Bland, R. 2000 Clin.Sci.(Colch.)
912. Modulation of intestinal vitamin D receptor by ovariectomy, estrogen and growth hormone Chen, C., Noland, K. A., and Kalu, D. N. 12-15-1997 Mech.Ageing Dev.
913. DIFFERENTIAL REGULATION OF GROWTH PLATE CHONDROCYTES BY 1alpha,25-(OH)(2)D(3) AND 24R,25-(OH)(2)D(3) INVOLVES CELL-MATURATION-SPECIFIC MEMBRANE-RECEPTOR-ACTIVATED PHOSPHOLIPID METABOLISM Boyan, B. D., Sylvia, V. L., Dean, D. D., Del Toro, F., and Schwartz, Z. 2002 Crit Rev.Oral Biol Med.
914. Vitamin D receptor is not required for the rapid actions of 1,25-dihydroxyvitamin D3 to increase intracellular calcium and activate protein kinase C in mouse osteoblasts Wali, R. K., Kong, J., Sitrin, M. D., Bissonnette, M., and Li, Y. C. 3-1-2003 J Cell Biochem.
915. Update on biological actions of 1alpha,25(OH)(2)-vitamin D(3) (rapid effects) and 24R,25(OH)(2)-vitamin D(3) Norman, A. W., Okamura, W. H., Bishop, J. E., and Henry, H. L. 11-29-2002 Mol.Cell Endocrinol.
916. Expression of plasma membrane calcium pump mRNA in rat intestine: effect of age and 1,25-dihydroxyvitamin D Armbrecht, H. J., Boltz, M. A., and Wongsurawat, N. 10-12-1994 Biochim.Biophys.Acta
917. Effect of vitamin D depletion on calcium transport by the luminal and basolateral membranes of the proximal and distal nephrons Bouhtiauy, I., Lajeunesse, D., and Brunette, M. G. 1993 Endocrinology
918. Identification of a membrane receptor for 1,25-dihydroxyvitamin D3 which mediates rapid activation of protein kinase C Nemere, I., Schwartz, Z., Pedrozo, H., Sylvia, V. L., Dean, D. D., and Boyan, B. D. 1998 J Bone Miner.Res.
919. Vitamin D -- induced changes in the renal membrane ATPase system Shamoo, A. E. and Bronner, F. 6-2-1975 Calcif.Tissue Res.
920. Amelioration of osteopenia and hypovitaminosis D by 1alpha- hydroxyvitamin D3 in elderly patients with Parkinson's disease Sato, Y., Manabe, S., Kuno, H., and Oizumi, K. 1999 J.Neurol.Neurosurg.Psychiatry
921. Phosphate/calcium alterations in the first stages of Alzheimer's disease: implications for etiology and pathogenesis Landfield, P. W., Applegate, M. D., Schmitzer-Osborne, S. E., and Naylor, C. E. 1991 J.Neurol.Sci.
922. Angiotoxicity in swine of a moderate excess of dietary vitamin D3 Toda, T., Ito, M., Toda, Y., Smith, T., and Kummerow, F. 1985 Food Chem.Toxicol.
923. The relationship of adequate and excessive intake of vitamin D to health and disease Holmes, R. P. and Kummerow, F. A. 1983 J.Am.Coll.Nutr.
924. Wintertime vitamin D insufficiency is common in young Canadian women, and their vitamin D intake does not prevent it Vieth, R., Cole, D. E., Hawker, G. A., Trang, H. M., and Rubin, L. A. 2001 Eur.J Clin Nutr
925. Healthy elderly French women living at home have secondary hyperparathyroidism and high bone turnover in winter. EPIDOS Study Group Chapuy, M. C., Schott, A. M., Garnero, P., Hans, D., Delmas, P. D., and Meunier, P. J. 1996 J.Clin.Endocrinol.Metab
926. [Winter serum levels of 25-hydroxy-vitamin D in Ushuaia and Buenos Aires] Oliveri, M. B., Ladizesky, M., Somoza, J., Martinez, L., and Mautalen, C. 1990 Medicina (B Aires)

927. [Determination of 25-hydroxyvitamin D serum levels and its seasonal variations in healthy young people] Aguirre, C., Depix, M. S., and Pumarino, H. 1996 Rev.Med.Chil.
928. Components of 25-hydroxyvitamin D in serum of young children in upper midwestern United States Arnaud, S. B., Matthusen, M., Gilkinson, J. B., and Goldsmith, R. S. 1977 Am.J.Clin.Nutr.
929. Serum 25(OH)D3 and ultraviolet exposure of residents in an old people's home in Germany Barth, J., Gerlach, B., Knuschke, P., and Lehmann, B. 1992 Photodermatol.Photoimmunol.Photomed.
930. Vitamin D: seasonal and regional differences in preschool children in Great Britain [published erratum appears in Eur J Clin Nutr 1999 Jul;53(7):584] Davies, P. S., Bates, C. J., Cole, T. J., Prentice, A., and Clarke, P. C. 1999 Eur.J.Clin.Nutr.
931. Hypovitaminosis D in healthy schoolchildren El Hajj, Fuleihan G., Nabulsi, M., Choucair, M., Salamoun, M., Hajj, Shahine C., Kizirian, A., and Tannous, R. 2001 Pediatrics
932. Effects of above average summer sun exposure on serum 25-hydroxyvitamin D and calcium absorption Barger-Lux, M. J. and Heaney, R. P. 2002 J.Clin.Endocrinol.Metab.
933. [The long term correction of vitamin D deficiency: comparison between different treatments with vitamin D in clinical practice.] Rossini, M., Viapiana, O., Gatti, D., James, G., Girardello, S., and Adami, S. 2005 Minerva Med.
934. Vitamin D supplementation in the elderly: review of safety and effectiveness of different regimes Byrne, P. M., Freaney, R., and McKenna, M. J. 1995 Calcif.Tissue Int.
935. Vitamin D supplementation in pregnancy: a controlled trial of two methods Mallet, E., Gugi, B., Brunelle, P., Henocq, A., Basuyau, J. P., and Lemeur, H. 1986 Obstet.Gynecol.
936. Vitamin D prophylaxis during infancy: comparison of the long-term effects of three intermittent doses (15, 5, or 2.5 mg) on 25- hydroxyvitamin D concentrations Zeghoud, F., Ben Mekhbi, H., Djeghri, N., and Garabedian, M. 1994 Am.J.Clin.Nutr.
937. High-dose vitamin D therapy: indications, benefits and hazards Davies, M. 1989 Int.J Vitam.Nutr Res.Suppl
938. 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
939. Factors influencing the conversion of carotenoids to retinol: bioavailability to bioconversion to bioefficacy Tanumihardjo, S. A. 2002 Int.J Vitam.Nutr Res.
940. Causes of severe visual impairment and blindness in children in schools for the blind in Ethiopia Kello, A. B. and Gilbert, C. 2003 Br.J Ophthalmol.
941. Vitamin A deficiency in Nigeria Rabiu, M. M. and Kyari, F. 2002 Niger.J Med.
942. Assessment and control of vitamin A deficiency disorders Ramakrishnan, U. and Darnton-Hill, I. 2002 J Nutr
943. Vitamin A for preventing secondary infections in children with measles--a systematic review D'Souza, R. M. and D'Souza, R. 2002 J Trop.Pediatr.
944. Vitamin A for treating measles in children D'Souza, R. M. and D'Souza, R. 2002 Cochrane.Database.Syst.Rev.
945. Fat-soluble vitamin nutriture in primary biliary cirrhosis Kaplan, M. M., Elta, G. H., Furie, B., Sadowski, J. A., and Russell, R. M. 1988 Gastroenterology
946. Plasma vitamin K1 level is decreased in primary biliary cirrhosis Kowdley, K. V., Emond, M. J., Sadowski, J. A., and Kaplan, M. M. 1997 Am J Gastroenterol.
947. [Hepatobiliary and pancreatic disorders as risk factors for fat-soluble vitamin deficiencies] Shirahata, A. 1999 Nippon Rinsho
948. Malabsorption of liposoluble vitamins in a child with bile acid deficiency Vanderpas, J. B., Koopman, B. J., Cadranel, S., Vandenbergen, C., Rickaert, F., Quenon, M., Wolthers, B. G., Brauherz, G., Vertongen, F., and Tondeur, M. 1987 J.Pediatr.Gastroenterol.Nutr.
949. Alpha-Tocopherol and beta-carotene supplements and lung cancer incidence in the alpha-tocopherol, beta-carotene cancer prevention study: effects of base-line characteristics and study compliance Albanes, D., Heinonen, O. P., Taylor, P. R., Virtamo, J., Edwards, B. K., Rautalahti, M., Hartman, A. M., Palmgren, J., Freedman, L. S., Haapakoski, J., Barrett, M. J., Pietinen, P., Malila, N., Tala, E., Liippo, K., Salomaa, E. R., Tangrea, J. A., Teppo, L., Askin, F. B., Taskinen, E., Erozan, Y., Greenwald, P., and Huttunen, J. K. 11-6-1996 J Natl.Cancer Inst.
950. A complementary approach to urolithiasis prevention Anderson, R. A. 2002 World J Urol.
951. Hypervitaminosis A and bone Binkley, N. and Krueger, D. 2000 Nutr Rev.
952. Vitamin A intake and hip fractures among postmenopausal women Feskanich, D., Singh, V., Willett, W. C., and Colditz, G. A. 1-2-2002 JAMA
953. Excessive dietary intake of vitamin A is associated with reduced bone mineral density and increased risk for hip fracture Melhus, H., Michaelsson, K., Kindmark, A., Bergstrom, R., Holmberg, L., Mallmin, H., Wolk, A., and Ljunghall, S. 11-15-1998 Ann Intern.Med.

954. Excess retinol intake may explain the high incidence of osteoporosis in northern Europe Whiting, S. J. and Lemke, B. 1999 Nutr Rev.
955. 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.
956. New understanding of the molecular mechanism of receptor-mediated genomic actions of the vitamin D hormone Haussler, M. R., Jurutka, P. W., Hsieh, J. C., Thompson, P. D., Selznick, S. H., Haussler, C. A., and Whitfield, G. K. 1995 Bone
957. New insight into the structure and functions of the vitamin D receptor MacDonald, P. N., Dowd, D. R., and Haussler, M. R. 1994 Semin.Nephrol.
958. Vitamin D-retinoid association: molecular basis and clinical applications Carlberg, C. and Saurat, J. H. 1996 J Investig.Dermatol.Symp.Proc.
959. The interaction of dietary vitamin A and vitamin D related to skeletal development in the turkey poult Metz, A. L., Walser, M. M., and Olson, W. G. 1985 J.Nutr.
960. Hypervitaminosis A in the dog Cho, D. Y., Frey, R. A., Guffy, M. M., and Leipold, H. W. 1975 Am J Vet.Res.
961. Interactions of vitamins A, D3, E, and K in the diet of broiler chicks Abawi, F. G. and Sullivan, T. W. 1989 Poult.Sci.
962. The influence of vitamin A on the utilization and amelioration of toxicity of cholecalciferol, 25-hydroxycholecalciferol, and 1,25 dihydroxycholecalciferol in young broiler chickens Aburto, A., Edwards, H. M., Jr., and Britton, W. M. 1998 Poult.Sci
963. Excess dietary vitamin A in the growing chick: effect of fat source and vitamin D Veltmann, J. R., Jr., Jensen, L. S., and Rowland, G. N. 1986 Poult.Sci.
964. Hypervitaminosis A and calcium-regulating hormones in the rat Frankel, T. L., Seshadri, M. S., McDowall, D. B., and Cornish, C. J. 1986 J Nutr
965. Retinoic acid action on D3 hypervitaminosis Callari, D., Garra, M. L., and Billitteri, A. 6-30-1986 Boll.Soc.Ital.Biol.Sper.
966. Vitamin A antagonizes the action of vitamin D in rats Rohde, C. M., Manatt, M., Clagett-Dame, M., and DeLuca, H. F. 1999 J Nutr
967. Vitamin A antagonizes calcium response to vitamin D in man Johansson, S. and Melhus, H. 2001 J Bone Miner.Res.
968. [Diagnosis of hypovitaminosis A and nutritional anemia status in the population of Vale do Jequitinhonha, Minas Gerais, Brazil] Araujo, R. L., Araujo, M. B., Sieiro, R. O., Machado, R. D., and Leite, B. V. 1986 Arch.Latinoam.Nutr
969. 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
970. Blindness in the tropics Narita, A. S. and Taylor, H. R. 1993 Med.J Aust.
971. Evaluation of vitamin A deficiency in the Yelimane Circle of Mali, west Africa Perkins, A. L. 1994 Trop.Doct.
972. Childhood blindness due to vitamin A deficiency in India: regional variations Rahi, J. S., Sripathi, S., Gilbert, C. E., and Foster, A. 1995 Arch.Dis.Child
973. Risk factors for vitamin A deficiency in rural areas of the Philippines Rosen, D. S., Sloan, N. L., del Rosario, A., and de la Paz, T. C. 1994 J Trop.Pediatr.
974. Serum vitamin A levels of preschool children in a Nigerian rural community Uzoechina, O. N. and Okoro, B. A. 1994 Ann Trop.Paediatr.
975. Severe vitamin A deficiency in a rural village in the Hararge region of Ethiopia Wolde-Gebriel, Z., Gebru, H., Fisseha, T., and West, C. E. 1993 Eur.J Clin Nutr
976. Blindness and low vision in Jimma Zone, Ethopia: results of a population-based survey Zerihun, N. and Mabey, D. 1997 Ophthalmic Epidemiol.
977. Causes of blindness in children attending four schools for the blind in Thailand and the Philippines. A comparison between urban and rural blind school populations Gilbert, C. and Foster, A. 1993 Int.Ophthalmol.
978. A prevalence study of xerophthalmia in the Philippines: implications for supplementation strategies Klemm, R. D., Villate, E. E., Tuason, C. S., Bayugo, G., and Mendoza, O. M. 1993 Southeast Asian J Trop.Med.Public Health
979. UV treatment of uraemic pruritus reduces the vitamin A content of the skin Berne, B., Vahlquist, A., Fischer, T., Danielson, B. G., and Berne, C. 1984 Eur.J Clin Invest
980. Oxidative stress-independent depletion of epidermal vitamin A by UVA Sorg, O., Tran, C., Carraux, P., Didierjean, L., Falson, F., and Saurat, J. H. 2002 J Invest Dermatol.
981. Plant sources of vitamin A and human nutriture: how much is still too little? Solomons, N. W. 1999 Nutr Rev.

982. [Serum carotenoids and vitamin A in melanodermic and albino subjects in Cameroon] Aquaron, R., le Francois, P., Kamdem, L., and Gueguen, R. 1978 Int.J Vitam.Nutr Res.
983. Influence of palm oil (Elaesis guineensis) on health Ebong, P. E., Owu, D. U., and Isong, E. U. 1999 Plant Foods Hum.Nutr
984. Modulation of ultraviolet light-induced oxidative stress in mice skin related to dietary vitamin A and selenium intake Savoure, N., Maudet, M., Nicol, M., Pelissier, M. A., Albrecht, R., Briand, G., and Combre, A. 1996 Int.J Vitam.Nutr Res.
985. Cutaneous vitamins A and E in the context of ultraviolet- or chemically-induced oxidative stress Sorg, O., Tran, C., and Saurat, J. H. 2001 Skin Pharmacol.Appl.Skin Physiol
986. Vitamin A status and metabolism of cutaneous polyamines in the hairless mouse after UV irradiation: action of beta-carotene and astaxanthin Savoure, N., Briand, G., Amory-Touz, M. C., Combre, A., Maudet, M., and Nicol, M. 1995 Int.J Vitam.Nutr Res.
987. Vitamin D metabolite concentrations in vitamin D deficiency. Are calcitriol levels normal Chesney, R. W., Zimmerman, J., Hamstra, A., DeLuca, H. F., and Mazees, R. B. 1981 Am.J Dis.Child
988. Comparison of commercially available (125)I-based RIA methods for the determination of circulating 25-hydroxyvitamin D Hollis, B. W. 2000 Clin Chem
989. Vitamin D: a hormone for all seasons--how much is enough? Morris, H. A. 2005 Clin.Biochem.Rev.
990. Parathyroid hormone may be a cancer promoter - an explanation for the decrease in cancer risk associated with ultraviolet light, calcium, and vitamin D McCarty, M. F. 2000 Med.Hypotheses
991. Seasonal deficiency of vitamin D in children: a potential target for osteoporosis-preventing strategies? Docio, S., Riancho, J. A., Perez, A., Olmos, J. M., Amado, J. A., and Gonzalez-Macias, J. 1998 J Bone Miner.Res.
992. The effect of high or low dietary calcium on bone and calcium homeostasis in young male rats Persson, P., Gagnemo-Persson, R., and Hakanson, R. 1993 Calcif.Tissue Int.
993. Fat soluble vitamins in blood and tissues of free-ranging and captive rhinoceros Clauss, M., Jessup, D. A., Norkus, E. B., Chen, T. C., Holick, M. F., Streich, W. J., and Dierenfeld, E. S. 2002 J Wildl.Dis.
994. Vitamin D and intact PTH status in patients with hip fracture Sakuma, M., Endo, N., Oinuma, T., Hayami, T., Endo, E., Yazawa, T., Watanabe, K., and Watanabe, S. 7-28-2006 Osteoporos.Int.
995. Vitamin D status and secondary hyperparathyroidism: The importance of 25-hydroxyvitamin D cut-off levels Gomez-Alonso, C., Naves-Diaz, M. L., Fernandez-Martin, J. L., Diaz-Lopez, J. B., Fernandez-Coto, M. T., and Cannata-Andia, J. B. 2003 Kidney Int.Suppl
996. [Accidental vitamin D poisoning in an infant] Ailal, F., Slaoui, B., Lasry, F., and Dehbi, F. 1998 Med.Trop.(Mars.)
997. [Review of 15 cases of hypervitaminosis D] Castello, F., Callis, L., Vilaplana, E., and Fortuny, G. 1977 Bol.Med.Hosp.Infant Mex.
998. Vitamin D poisoning by table sugar Vieth, R., Pinto, T. R., Reen, B. S., and Wong, M. M. 2-23-2002 Lancet
999. Calcium requirement and calcium therapy Nordin, B. E., Horsman, A., Marshall, D. H., Simpson, M., and Waterhouse, G. M. 1979 Clin.Orthop.
1000. Vitamin D is not directly necessary for bone growth and mineralization Underwood, J. and DeLuca, H. 6-1-1984 Am J Physiol
1001. Age-related arterial calcification in rats Kieffer, P., Robert, A., Capdeville-Atkinson, C., Atkinson, J., and Lartaud-Idjouadiene, I. 5-5-2000 Life Sci.
1002. The effect of vitamin D status on cutaneous sterologenesis in vivo and in vitro Feingold, K. R., Williams, M. L., Pillai, S., Menon, G. K., Halloran, B. P., Bikle, D. D., and Elias, P. M. 9-14-1987 Biochim.Biophys.Acta
1003. [Vitamins and metals: possible hazards for humans (published erratum appears in Schweiz Med Wochenschr 1996 Jun 8;126(23):1042)] Ballmer, P. E. 4-13-1996 Schweiz.Med.Wochenschr.
1004. Vitamin D toxicity complicating the treatment of senile, postmenopausal, and glucocorticoid-induced osteoporosis. Four case reports and a critical commentary on the use of vitamin D in these disorders Schwartzman, M. S. and Franck, W. A. 1987 Am.J.Med.
1005. 25-Hydroxysterols increase the permeability of liposomes to Ca2+ and other cations Holmes, R. P. and Yoss, N. L. 2-29-1984 Biochim.Biophys.Acta
1006. The role of altered [Ca2+]i regulation in apoptosis, oncosis, and necrosis Trump, B. F. and Berezesky, I. K. 10-11-1996 Biochim.Biophys.Acta
1007. The mechanisms of calcium-mediated cell injury and cell death [correcgted] Trump, B. F. and Berezesky, I. K. 1996 New Horiz.
1008. Solar ultraviolet radiation effects on biological systems Diffey, B. L. 1991 Phys.Med.Biol.
1009. Modern approaches to photoprotection DeBuys, H. V., Levy, S. B., Murray, J. C., Madey, D. L., and Pinnell, S. R. 2000 Dermatol.Clin.
1010. Ultraviolet Light Blunt, K. and Cowan, R. 1930

1011. Solar considerations in the development of cutaneous melanoma Loggie, B. W. and Eddy, J. A. 1988 Semin.Oncol.
1012. [Is UV-A a cause of malignant melanoma?] Moan, J. 3-20-1994 Tidsskr.Nor Laegeforen.
1013. An estimation of biological hazards due to solar radiation [In Process Citation] Parisi, A. V. and Wong, J. C. 2000 J.Photochem.Photobiol.B
1014. Wavelengths effective in induction of malignant melanoma Setlow, R. B., Grist, E., Thompson, K., and Woodhead, A. D. 7-15-1993 Proc.Natl.Acad.Sci.U.S.A
1015. [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
1016. 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.
1017. 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
1018. Age dependent increase of elastase type protease activity in mouse skin. Effect of UV-irradiation Labat-Robert, J., Fourtanier, A., Boyer-Lafargue, B., and Robert, L. 2000 J Photochem.Photobiol.B
1019. [The role of free radicals in the UV-induced skin damage. Photo-aging] Emri, G., Horkay, I., and Remenyik, E. 4-23-2006 Orv.Hetil.
1020. UVA radiation impairs phenotypic and functional maturation of human dermal dendritic cells Furio, L., Berthier-Vergnes, O., Ducarre, B., Schmitt, D., and Peguet-Navarro, J. 2005 J.Invest Dermatol.
1021. Chronic UVA irradiation of human HaCaT keratinocytes induces malignant transformation associated with acquired apoptotic resistance He, Y. Y., Pi, J., Huang, J. L., Diwan, B. A., Waalkes, M. P., and Chignell, C. F. 6-22-2006 Oncogene.
1022. Sunscreen use and intentional exposure to ultraviolet A and B radiation: a double blind randomized trial using personal dosimeters Autier, P., Dore, J. F., Reis, A. C., Grivegnee, A., Ollivaud, L., Truchetet, F., Chamoun, E., Rotmensz, N., Severi, G., and Cesarini, J. P. 2000 Br.J.Cancer
1023. Time spent outdoors and seasonal variation in serum concentrations of 25-hydroxyvitamin D in Korean women Kim, J. H. and Moon, S. J. 2000 Int.J Food Sci.Nutr
1024. Comparison of oral 25-hydroxycholecalciferol, vitamin D, and ultraviolet light as determinants of circulating 25-hydroxyvitamin D Stamp, T. C., Haddad, J. G., and Twigg, C. A. 6-25-1977 Lancet.
1025. Prevalence and significance of low 25-hydroxyvitamin D concentrations in healthy subjects in delhi [In Process Citation] Goswami, R., Gupta, N., Goswami, D., Marwaha, R. K., Tandon, N., and Kochupillai, N. 2000 Am.J.Clin.Nutr.
1026. Biologically effective ultraviolet radiation: surface measurements in the United States, 1974 to 1985 Scotto, J., Cotton, G., Urbach, F., Berger, D., and Fears, T. 2-12-1988 Science
1027. Climate change, ozone depletion and the impact on ultraviolet exposure of human skin Diffey, B. 1-7-2004 Phys.Med.Biol.
1028. Children at risk from ozone air pollution--United States, 1991-1993 4-28-1995 MMWR Morb.Mortal.Wkly.Rep.
1029. Acid haze air pollution and breast and colon cancer mortality in 20 Canadian cities Gorham, E. D., Garland, C. F., and Garland, F. C. 1989 Can.J Public Health
1030. The regulation and role of epidermal lipid synthesis Feingold, K. R. 1991 Adv.Lipid Res.
1031. Induced melanin reduces mutations and cell killing in mouse melanoma Li, W. and Hill, H. Z. 1997 Photochem.Photobiol.
1032. Melanin content of cultured human melanocytes and UV-induced cytotoxicity De Leeuw, S. M., Smit, N. P., Van Veldhoven, M., Pennings, E. M., Pavel, S., Simons, J. W., and Schothorst, A. A. 8-30-2001 J Photochem.Photobiol.B
1033. Mutagenicity of melanin from human red hair Harsanyi, Z. P., Post, P. W., Brinkmann, J. P., Chedekel, M. R., and Deibel, R. M. 3-15-1980 Experientia
1034. (Pheo)melanin photosensitizes UVA-induced DNA damage in cultured human melanocytes Wenczl, E., Van der Schans, G. P., Roza, L., Kolb, R. M., Timmerman, A. J., Smit, N. P., Pavel, S., and Schothorst, A. A. 1998 J.Invest Dermatol.
1035. The melanocortin-1 receptor: red hair and beyond Schaffer, J. V. and Bolognia, J. L. 2001 Arch.Dermatol.
1036. Human melanocortin 1 receptor variants, receptor function and melanocyte response to UV radiation Scott, M. C., Wakamatsu, K., Ito, S., Kadekaro, A. L., Kobayashi, N., Groden, J., Kavanagh, R., Takakuwa, T., Virador, V., Hearing, V. J., and Abdel-Malek, Z. A. 6-1-2002 J Cell Sci
1037. Pheomelanin as well as eumelanin is present in human epidermis Thody, A. J., Higgins, E. M., Wakamatsu, K., Ito, S., Burchill, S. A., and Marks, J. M. 1991 J Invest Dermatol.
1038. Vitamin D nutrition increases skin tyrosinase response to exposure to ultraviolet radiation Pavlovitch, J. H., Rizk, M., and Balsan, S. 1982 Mol.Cell Endocrinol.

1039. [Effect of vitamin D on skin metabolism (author's transl)] Pavlovitch, J. H., Rizk, M., Delecluse, C., and Balsan, S. 1981 Ann Endocrinol.(Paris)
1040. Hormonal effects of vitamin D3 on epidermal melanocytes Abdel-Malek, Z. A., Ross, R., Trinkle, L., Swope, V., Pike, J. W., and Nordlund, J. J. 1988 J Cell Physiol
1041. The human melanocyte as a particular target for UVA radiation and an endpoint for photoprotection assessment Marrot, L., Belaidi, J. P., Meunier, J. R., Perez, P., and Agapakis-Causse, C. 1999 Photochem.Photobiol.
1042. Skin types and epidermal photosynthesis of vitamin D3 Matsuoka, L. Y., Wortsman, J., Haddad, J. G., and Hollis, B. W. 1990 J.Am.Acad.Dermatol.
1043. Racial pigmentation and the cutaneous synthesis of vitamin D Matsuoka, L. Y., Wortsman, J., Haddad, J. G., Kolm, P., and Hollis, B. W. 1991 Arch.Dermatol.
1044. Current update and trends in melanin pigmentation and melanin biology Jimbow, K. 1995 Keio J Med.
1045. In vivo threshold for cutaneous synthesis of vitamin D3 Matsuoka, L. Y., Wortsman, J., Haddad, J. G., and Hollis, B. W. 1989 J.Lab Clin.Med.
1046. Suntanning and cutaneous synthesis of vitamin D3 Matsuoka, L. Y., Wortsman, J., and Hollis, B. W. 1990 J.Lab Clin.Med.
1047. Structural and functional changes of normal aging skin Fenske, N. A. and Lober, C. W. 1986 J.Am.Acad.Dermatol.
1048. Skin as the site of vitamin D synthesis and target tissue for 1,25-dihydroxyvitamin D3. Use of calcitriol (1,25-dihydroxyvitamin D3) for treatment of psoriasis Holick, M. F., Smith, E., and Pincus, S. 1987 Arch.Dermatol.
1049. Human plasma transport of vitamin D after its endogenous synthesis Haddad, J. G., Matsuoka, L. Y., Hollis, B. W., Hu, Y. Z., and Wortsman, J. 1993 J.Clin.Invest
1050. Results of photopatch testing in Rotterdam during a 10-year period Bakkum, R. S. and Heule, F. 2002 Br.J.Dermatol.
1051. 7 years experience of photopatch testing with sunscreen allergens in Sweden Berne, B. and Ros, A. M. 1998 Contact Dermatitis
1052. Results of evaluation of 203 patients for photosensitivity in a 7.3-year period Fotiades, J., Soter, N. A., and Lim, H. W. 1995 J Am.Acad Dermatol.
1053. Sunscreen sensitization: a 5-year study Journe, F., Marguery, M. C., Rakotondrazafy, J., El Sayed, F., and Bazex, J. 1999 Acta Derm.Venereol.
1054. Chronic sunscreen use decreases circulating concentrations of 25- hydroxyvitamin D. A preliminary study Matsuoka, L. Y., Wortsman, J., Hanifan, N., and Holick, M. F. 1988 Arch.Dermatol.
1055. Early persistent UVA-pigmentation: ultrastructural and morphometric analyses Ryckmanns, F., Schmoeckel, C., Plewig, G., and Braun-Falco, O. 1987 Arch.Dermatol.Res.
1056. The carcinogenic risks of modern tanning equipment: is UV-A safer than UV-B? van Weelden, H., de Gruijl, F. R., van der Putte, S. C., Toonstra, J., and van der Leun, J. C. 1988 Arch.Dermatol.Res.
1057. Ultraviolet radiation and cataract development in the U.S. Virgin Islands Anduze, A. L. 1993 J Cataract Refract.Surg.
1058. The significance of ultraviolet radiation for eye diseases. A review with comments on the efficacy of UV-blocking contact lenses Bergmanson, J. P. and Soderberg, P. G. 1995 Ophthalmic Physiol Opt.
1059. Ultraviolet light exposure and risk of posterior subcapsular cataracts Bochow, T. W., West, S. K., Azar, A., Munoz, B., Sommer, A., and Taylor, H. R. 1989 Arch.Ophthalmol.
1060. Risk factors for age-related cortical, nuclear, and posterior subcapsular cataracts. The Italian-American Cataract Study Group 3-15-1991 Am.J.Epidemiol.
1061. Ascorbic acid and the eye lens Varma, S. D. and Richards, R. D. 1988 Ophthalmic Res.
1062. Prevention of cataracts by nutritional and metabolic antioxidants Varma, S. D., Devamanoharan, P. S., and Morris, S. M. 1995 Crit Rev.Food Sci Nutr
1063. Scientific basis for medical therapy of cataracts by antioxidants Varma, S. D. 1991 Am.J Clin Nutr
1064. Superoxide dismutase of the eye: relative functions of superoxide dismutase and catalase in protecting the ocular lens from oxidative damage Bhuyan, K. C. and Bhuyan, D. K. 8-3-1978 Biochim.Biophys.Acta
1065. Vitamin D analogues Brown, A. J. 1998 Am.J.Kidney Dis.
1066. Nutritional factors in cataract Bunce, G. E., Kinoshita, J., and Horwitz, J. 1990 Annu.Rev.Nutr
1067. A prospective study of carotenoid and vitamin A intakes and risk of cataract extraction in US women Chasan-Taber, L., Willett, W. C., Seddon, J. M., Stampfer, M. J., Rosner, B., Colditz, G. A., Speizer, F. E., and Hankinson, S. E. 1999 Am.J Clin Nutr
1068. Vitamin C supplements and the risk of age-related cataract: a population-based prospective cohort study in women Rautiainen, S., Lindblad, B. E., Morgenstern, R., and Wolk, A. 2010 Am.J.Clin.Nutr.

1069. Blood levels of vitamin C, carotenoids and retinol are inversely associated with cataract in a North Indian population Dherani, M., Murthy, G. V., Gupta, S. K., Young, I. S., Maraini, G., Camparini, M., Price, G. M., John, N., Chakravarthy, U., and Fletcher, A. E. 2008 Invest Ophthalmol.Vis.Sci.
1070. Age-related nuclear cataract-oxidation is the key Truscott, R. J. 2005 Exp.Eye Res.
1071. Protective effect of ascorbate against oxidative stress in the mouse lens Hegde, K. R. and Varma, S. D. 1-5-2004 Biochim.Biophys.Acta
1072. 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.
1073. Relationship in humans between ascorbic acid consumption and levels of total and reduced ascorbic acid in lens, aqueous humor, and plasma Taylor, A., Jacques, P. F., Nadler, D., Morrow, F., Sulsky, S. I., and Shepard, D. 1991 Curr.Eye Res.
1074. Associations between nutrition and cataract Taylor, A. 1989 Nutr.Rev.
1075. Delay of UV-induced eye lens protein damage in guinea pigs by dietary ascorbate Blondin, J., Baragi, V., Schwartz, E., Sadowski, J. A., and Taylor, A. 1986 J.Free Radic.Biol.Med.
1076. Ultraviolet radiation and the eye: an epidemiologic study Taylor, H. R. 1989 Trans.Am.Ophthalmol.Soc.
1077. SEER Cancer Statistics Review, 1975-2000 2003
1078. Light and immunomodulation Roberts, J. E. 2000 Ann N Y Acad Sci
1079. Ultraviolet light depletes surface markers of Langerhans cells Aberer, W., Schuler, G., Stingl, G., Honigsmann, H., and Wolff, K. 1981 J Invest Dermatol.
1080. Experimental ultraviolet photocarcinogenesis: wavelength interactions and time-dose relationships Forbes, P. D., Davies, R. E., and Urbach, F. 1978 Natl.Cancer Inst.Monogr
1081. [Modification of alpha-MSH by UVA irradiation of the skin] Holzmann, H., Altmeyer, P., Stohr, L., and Chilf, G. N. 1983 Hautarzt
1082. Ultraviolet radiation A-induced precursors of cutaneous melanoma in Monodelphis domestica Ley, R. D. 9-1-1997 Cancer Res.
1083. Stability of DNA in mammalian cells irradiated with near-uv light (uv-a) Lonn, U. 1984 Radiat.Res.
1084. An estimation of biological hazards due to solar radiation Parisi, A. V. and Wong, J. C. 2000 J Photochem.Photobiol.B
1085. Cutaneous malignant melanoma and sun exposure. Recent developments in epidemiology Katsambas, A. and Nicolaidou, E. 1996 Arch.Dermatol.
1086. UVB-induced conversion of 7-dehydrocholesterol to 1alpha,25-dihydroxyvitamin D3 in an in vitro human skin equivalent model Lehmann, B., Genehr, T., Knuschke, P., Pietzsch, J., and Meurer, M. 2001 J Invest Dermatol.
1087. Demonstration of UVB-induced synthesis of 1alpha,25-dihydroxyvitamin D(3) (calcitriol) in human skin by microdialysis Lehmann, B., Sauter, W., Knuschke, P., Dressler, S., and Meurer, M. 2003 Arch.Dermatol.Res.
1088. The Epidermal Vitamin D System Segaert, S., De Haes, P., and Bouillon, R. 2002
1089. A novel pathway for hormonally active calcitriol Lehmann, B., Knuschke, P., and Meurer, M. 2000 Horm.Res.
1090. Occupational sunlight exposure and melanoma in the U.S. Navy Garland, F. C., White, M. R., Garland, C. F., Shaw, E., and Gorham, E. D. 1990 Arch.Environ.Health
1091. Regulation of melanin synthesis of B16 mouse melanoma cells by 1 alpha, 25-dihydroxyvitamin D3 and retinoic acid Hosoi, J., Abe, E., Suda, T., and Kuroki, T. 1985 Cancer Res.
1092. Use of vitamins A and D in chemoprevention and therapy of cancer: control of nuclear receptor expression and function. Vitamins, cancer and receptors Niles, R. 1-1-1995 Adv Exp Med Biol
1093. Use of topical sunscreen for the evaluation of regional synthesis of vitamin D3 Matsuoka, L. Y., Wortsman, J., and Hollis, B. W. 1990 J.Am.Acad.Dermatol.
1094. Clinically prescribed sunscreen (sun protection factor 15) does not decrease serum vitamin D concentration sufficiently either to induce changes in parathyroid function or in metabolic markers Farrerons, J., Barnadas, M., Rodriguez, J., Renau, A., Yoldi, B., Lopez-Navidad, A., and Moragas, J. 1998 Br.J.Dermatol.
1095. The effect of regular sunscreen use on vitamin D levels in an Australian population. Results of a randomized controlled trial [see comments] Marks, R., Foley, P. A., Jolley, D., Knight, K. R., Harrison, J., and Thompson, S. C. 1995 Arch.Dermatol.
1096. Normal vitamin D levels can be maintained despite rigorous photoprotection: six years' experience with xeroderma pigmentosum [see comments] Sollitto, R. B., Kraemer, K. H., and DiGiovanna, J. J. 1997 J.Am.Acad.Dermatol.
1097. Role of clothes in sun protection Gambichler, T., Altmeyer, P., and Hoffmann, K. 2002 Recent Results Cancer Res.
1098. Photoprotection and prevention of melanoma Marks, R. 1999 Eur.J.Dermatol.

1099. Clothing prevents ultraviolet-B radiation-dependent photosynthesis of vitamin D3 Matsuoka, L. Y., Wortsman, J., Dannenberg, M. J., Hollis, B. W., Lu, Z., and Holick, M. F. 1992 J Clin Endocrinol.Metab
1100. Sun protection with clothing Diffey, B. L. 2001 Br.J.Dermatol.
1101. Rising trends in melanoma. An hypothesis concerning sunscreen effectiveness Garland, C. F., Garland, F. C., and Gorham, E. D. 1993 Ann.Epidemiol.
1102. Why ultraviolet protection with clothing makes sense Kaskel, P. 2001 Br.J.Dermatol.
1103. Protection against UV photocarcinogenesis by fabric materials Menter, J. M., Hollins, T. D., Sayre, R. M., Etemadi, A. A., Willis, I., and Hughes, S. N. 1994 J.Am.Acad.Dermatol.
1104. The historical aspects of sunscreens Urbach, F. 11-15-2001 J.Photochem.Photobiol.B
1105. Should you pay $75 to block the sun? For most of us, a regular t-shirt is enough Comarow, A. 8-9-1999 US.News World Rep.
1106. Report of 19 cases of photoallergic contact dermatitis to sunscreens seen at the Skin and Cancer Foundation Cook, N. and Freeman, S. 2001 Australas.J.Dermatol.
1107. Photoallergic contact dermatitis due to combined UVB (4-methylbenzylidene camphor/octyl methoxycinnamate) and UVA (benzophenone-3/butyl methoxydibenzoylmethane) absorber sensitization Schmidt, T., Ring, J., and Abeck, D. 1998 Dermatology
1108. In vitro and in vivo estrogenicity of UV screens Schlumpf, M., Cotton, B., Conscience, M., Haller, V., Steinmann, B., and Lichtensteiger, W. 2001 Environ.Health Perspect.
1109. Methylparaben potentiates UV-induced damage of skin keratinocytes Handa, O., Kokura, S., Adachi, S., Takagi, T., Naito, Y., Tanigawa, T., Yoshida, N., and Yoshikawa, T. 7-28-2006 Toxicology.
1110. Swimming and the risk of cutaneous melanoma Nelemans, P. J., Rampen, F. H., Groenendal, H., Kiemeney, L. A., Ruiter, D. J., and Verbeek, A. L. 1994 Melanoma Res.
1111. Formation of disinfection by-products in chlorinated swimming pool water Kim, H., Shim, J., and Lee, S. 2002 Chemosphere.
1112. Evaluation of dermal and respiratory chloroform exposure in humans Levesque, B., Ayotte, P., LeBlanc, A., Dewailly, E., Prud'homme, D., Lavoie, R., Allaire, S., and Levallois, P. 1994 Environ.Health Perspect.
1113. Free residual chlorine in bathing water reduces the water-holding capacity of the stratum corneum in atopic skin Seki, T., Morimatsu, S., Nagahori, H., and Morohashi, M. 2003 J.Dermatol.
1114. Occupational asthma caused by chloramines in indoor swimming-pool air Thickett, K. M., McCoach, J. S., Gerber, J. M., Sadhra, S., and Burge, P. S. 2002 Eur.Respir.J.
1115. Initiation of rapid, P53-dependent growth arrest in cultured human skin fibroblasts by reactive chlorine species Vile, G. F., Rothwell, L. A., and Kettle, A. J. 5-1-2000 Arch.Biochem.Biophys.
1116. Dermal uptake of chloroform and haloketones during bathing Xu, X. and Weisel, C. P. 2005 J.Expo.Anal.Environ.Epidemiol.
1117. A feasibility study of cumulative risk assessment methods for drinking water disinfection by-product mixtures Teuschler, L. K., Rice, G. E., Wilkes, C. R., Lipscomb, J. C., and Power, F. W. 4-23-2004 J.Toxicol.Environ.Health A.
1118. Percutaneous absorption of trihalomethanes, haloacetic acids, and haloketones Xu, X., Mariano, T. M., Laskin, J. D., and Weisel, C. P. 10-1-2002 Toxicol.Appl.Pharmacol.
1119. 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.
1120. 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.
1121. UV radiation and cancer prevention: what is the evidence? Krause, R., Matulla-Nolte, B., Essers, M., Brown, A., and Hopfenmuller, W. 2006 Anticancer Res.
1122. Modulation of UV-light-induced skin inflammation by D-alpha-tocopherol and L-ascorbic acid: a clinical study using solar simulated radiation Fuchs, J. and Kern, H. 1998 Free Radic.Biol Med.
1123. Topical L-ascorbic acid: percutaneous absorption studies Pinnell, S. R., Yang, H., Omar, M., Monteiro-Riviere, N., DeBuys, H. V., Walker, L. C., Wang, Y., and Levine, M. 2001 Dermatol.Surg.
1124. Ultraviolet irradiation of human skin causes functional vitamin A deficiency, preventable by all-trans retinoic acid pre-treatment Wang, Z., Boudjelal, M., Kang, S., Voorhees, J. J., and Fisher, G. J. 1999 Nat.Med.
1125. The importance of vitamin A in nutrition Dawson, M. I. 2000 Curr.Pharm.Des
1126. Intervention studies on cancer [see comments] Young, K. J. and Lee, P. N. 1999 Eur.J.Cancer Prev.
1127. Vitamin A and carotene in animal nutrition Bondi, A. and Sklan, D. 1984 Prog.Food Nutr Sci
1128. Vitamin A status and nutritional intake of carotenoids of preschool children in Ijaye Orile community in Nigeria Oso, O. O., Abiodun, P. O., Omotade, O. O., and Oyewole, D. 2003 J Trop.Pediatr.

1129. Effect of supplementation with beta-carotene and vitamin A on lung nutrient levels Redlich, C. A., Blaner, W. S., Van Bennekum, A. M., Chung, J. S., Clever, S. L., Holm, C. T., and Cullen, M. R. 1998 Cancer Epidemiol.Biomarkers Prev.
1130. Plant sources of provitamin A and human nutriture Solomons, N. W. and Bulux, J. 1993 Nutr Rev.
1131. [Prevention of ultraviolet ray damage: external and internal sunscreens] Grundmann, J. U. and Gollnick, H. 1999 Ther.Umsch.
1132. Supplementation with beta-carotene or a similar amount of mixed carotenoids protects humans from UV-induced erythema Heinrich, U., Gartner, C., Wiebusch, M., Eichler, O., Sies, H., Tronnier, H., and Stahl, W. 2003 J Nutr
1133. Effect of eicosapentaenoic acid, an omega-3 polyunsaturated fatty acid, on UVR-related cancer risk in humans. An assessment of early genotoxic markers Rhodes, L. E., Shahbakhti, H., Azurdia, R. M., Moison, R. M., Steenwinkel, M. J., Homburg, M. I., Dean, M. P., McArdle, F., Beijersbergen van Henegouwen, G. M., Epe, B., and Vink, A. A. 2003 Carcinogenesis
1134. n-6 Polyunsaturated fatty acids increase skin but not cervical cancer in human papillomavirus 16 transgenic mice Qi, M., Chen, D., Liu, K., and Auborn, K. J. 1-15-2002 Cancer Res.
1135. In vitro and in vivo effects of beta-carotene on rat epidermal lipoxygenases Lomnitski, L., Grossman, S., Bergman, M., Sofer, Y., and Sklan, D. 1997 Int.J Vitam.Nutr Res.
1136. 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.
1137. Telomere length of the skin in association with chronological aging and photoaging Sugimoto, M., Yamashita, R., and Ueda, M. 2006 J.Dermatol.Sci.
1138. 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
1139. Ultraviolet B-induced DNA damage in human epidermis is modified by the antioxidants ascorbic acid and D-alpha-tocopherol Placzek, M., Gaube, S., Kerkmann, U., Gilbertz, K. P., Herzinger, T., Haen, E., and Przybilla, B. 2005 J.Invest Dermatol.
1140. UV light increases vitamin C uptake by bovine lens epithelial cells Corti, A., Ferrari, S. M., Lazzarotti, A., Del, Corso A., Mura, U., Casini, A. F., and Paolicchi, A. 8-6-2004 Mol.Vis.
1141. Topical ascorbic acid on photoaged skin. Clinical, topographical and ultrastructural evaluation: double-blind study vs. placebo Humbert, P. G., Haftek, M., Creidi, P., Lapiere, C., Nusgens, B., Richard, A., Schmitt, D., Rougier, A., and Zahouani, H. 2003 Exp.Dermatol.
1142. 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., Righele, F., Tomasello, F., Caffieri, S., and Beijersbergen van Henegouwen, G. M. 2003 Photochem.Photobiol.
1143. Molecular analysis of the chemoprotective effects of topical sunscreen and vitamin C in preventing UV-induced and reactive oxygen species-induced DNA damage, respectively, using the PCR inhibition methodology Jenkins, G. J., Stephens, L. A., Masnavi, N., and Parry, J. M. 2002 Anticancer Res.
1144. UVR-induced oxidative stress in human skin in vivo: effects of oral vitamin C supplementation McArdle, F., Rhodes, L. E., Parslew, R., Jack, C. I., Friedmann, P. S., and Jackson, M. J. 11-15-2002 Free Radic.Biol.Med.
1145. Effect of ascorbic acid on incidence of spontaneous mammary tumors and UV-light-induced skin tumors in mice Pauling, L. 1991 Am.J.Clin.Nutr.
1146. Effects of intake of L-ascorbic acid on the incidence of dermal neoplasms induced in mice by ultraviolet light Dunham, W. B., Zuckerkandl, E., Reynolds, R., Willoughby, R., Marcuson, R., Barth, R., and Pauling, L. 1982 Proc.Natl.Acad.Sci.U.S.A
1147. 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.
1148. Protective effects of topical antioxidants in humans Dreher, F. and Maibach, H. 2001 Curr.Probl.Dermatol.
1149. Green tea polyphenolic antioxidants and skin photoprotection (Review) Katiyar, S. K. and Elmets, C. A. 2001 Int.J.Oncol.
1150. Treatment of silymarin, a plant flavonoid, prevents ultraviolet light-induced immune suppression and oxidative stress in mouse skin Katiyar, S. K. 2002 Int.J Oncol.
1151. Green Tea Polyphenols Induce Differentiation and Proliferation in Epidermal Keratinocytes Hsu, S. D., Bollag, W. B., Lewis, J., Huang, Q., Singh, B., Sharawy, M., Yamamoto, T., and Schuster, G. 3-27-2003 J Pharmacol.Exp.Ther.
1152. Flavonoid antioxidant silymarin and skin cancer Singh, R. P. and Agarwal, R. 2002 Antioxid.Redox.Signal.
1153. Antioxidants modulate acute solar ultraviolet radiation-induced NF-kappa-B activation in a human keratinocyte cell line Saliou, C., Kitazawa, M., McLaughlin, L., Yang, J. P., Lodge, J. K., Tetsuka, T., Iwasaki, K., Cillard, J., Okamoto, T., and Packer, L. 1999 Free Radic.Biol Med.

1154. Skin cancer chemopreventive effects of a flavonoid antioxidant silymarin are mediated via impairment of receptor tyrosine kinase signaling and perturbation in cell cycle progression Ahmad, N., Gali, H., Javed, S., and Agarwal, R. 6-18-1998 Biochem.Biophys.Res.Commun.
1155. Ultraviolet B radiation-induced DNA lesions in mouse epidermis: an assessment using a novel 32P-postlabelling technique Chatterjee, M. L., Agarwal, R., and Mukhtar, H. 12-13-1996 Biochem.Biophys.Res.Commun.
1156. Sunlight, season, skin pigmentation, vitamin D, and 25-hydroxyvitamin D: integral components of the vitamin D endocrine system [editorial; comment] [see comments] Norman, A. W. 1998 Am.J.Clin.Nutr.
1157. Vitamin A as an anti-inflammatory agent Reifen, R. 2002 Proc.Nutr Soc.
1158. Effects of zinc histidine and zinc sulfate on natural human keratinocytes Deters, A., Schnetz, E., Schmidt, M., and Hensel, A. 2003 Forsch.Komplementarmed.Klass.Naturheilkd.
1159. Skin and mucosal manifestations in vitamin deficiency Barthelemy, H., Chouvet, B., and Cambazard, F. 1986 J Am.Acad Dermatol.
1160. Effects of vitamin C on dark circles of the lower eyelids: quantitative evaluation using image analysis and echogram Ohshima, H., Mizukoshi, K., Oyobikawa, M., Matsumoto, K., Takiwaki, H., Kanto, H., and Itoh, M. 2009 Skin Res.Technol.
1161. 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.
1162. [Vitamin C] Valdes, F. 2006 Actas Dermosifiliogr.
1163. Biological role of vitamin C in keratinocytes Catani, M. V., Savini, I., Rossi, A., Melino, G., and Avigliano, L. 2005 Nutr.Rev.
1164. Dietary fish oil reduces basal and ultraviolet B-generated PGE2 levels in skin and increases the threshold to provocation of polymorphic light eruption Rhodes, L. E., Durham, B. H., Fraser, W. D., and Friedmann, P. S. 1995 J Invest Dermatol.
1165. Keloids in rural black South Africans. Part 3: a lipid model for the prevention and treatment of keloid formations Louw, L. 2000 Prostaglandins Leukot.Essent.Fatty Acids
1166. Dietary eicosapentaenoic acid prevents systemic immunosuppression in mice induced by UVB radiation Moison, R. M. and Beijersbergen van Henegouwen, G. M. 2001 Radiat.Res.
1167. Vitamin D: balancing cutaneous and systemic considerations Fuller, K. E. and Casparian, J. M. 2001 South.Med.J
1168. Vitamin D and cardiovascular, renal, and brain damage in infancy and childhood Seelig, M. S. 9-26-1969 Ann.N.Y.Acad.Sci.
1169. An outbreak of hypervitaminosis D associated with the overfortification of milk from a home-delivery dairy Blank, S., Scanlon, K. S., Sinks, T. H., Lett, S., and Falk, H. 1995 Am.J.Public Health
1170. The vitamin D content of fortified milk and infant formula [see comments] Holick, M. F., Shao, Q., Liu, W. W., and Chen, T. C. 4-30-1992 N.Engl.J.Med.
1171. Fluid milk vitamin fortification compliance in New York State Murphy, S. C., Whited, L. J., Rosenberry, L. C., Hammond, B. H., Bandler, D. K., and Boor, K. J. 2001 J Dairy Sci
1172. Nutrition and bone disease in the dog and cat Bennett, D. 4-17-1976 Vet.Rec.
1173. Hypervitaminosis A in a cat Goldman, A. L. 6-15-1992 J Am.Vet.Med.Assoc.
1174. Fatal soft tissue calcification in suckling puppies Howerth, E. W. 1983 J S.Afr.Vet.Assoc.
1175. [Experimental study of hyperostosis induced by hypervitaminosis A] Ishizawa, N. 1992 Nippon Seikeigeka Gakkai Zasshi
1176. Concentration of 25-hydroxyvitamin D in serum of infants under the intermittent high-dose vitamin D3 prophylactic treatment Pietrek, J., Otto-Buczkowska, E., Kokot, F., Karpiel, R., and Cekanski, A. 1980 Arch.Immunol.Ther.Exp.(Warsz.)
1177. The osteodystrophy of hypervitaminosis D: a metabolic study Davies, M., Mawer, E. B., and Freemont, A. J. 1986 Q.J.Med.
1178. [Normal radiologic anatomic variants and X-ray findings of hypervitaminosis D of the ulna, radius and carpal bones in children] Jiang, Y. 1990 Zhonghua Yi.Xue.Za Zhi.
1179. Hypervitaminosis D after prolonged feeding with a premature formula Nako, Y., Fukushima, N., Tomomasa, T., Nagashima, K., and Kuroume, T. 1993 Pediatrics
1180. Risk factors for vitamin D inadequacy among women with osteoporosis: an international epidemiological study Rizzoli, R., Eisman, J. A., Norquist, J., Ljunggren, O., Krishnarajah, G., Lim, S. K., and Chandler, J. 2006 Int.J.Clin.Pract.
1181. **DRI: Dietary Reference IntakesFor Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride Tables** 1999 National Academy Press
1182. Calcium nutrition and bone health in the elderly Heaney, R. P., Gallagher, J. C., Johnston, C. C., Neer, R., Parfitt, A. M., and Whedon, G. D. 1982 Am.J Clin Nutr

1183. The effect of calcium gluconate and other calcium supplements as a dietary calcium source on magnesium absorption in rats Chonan, O., Takahashi, R., Yasui, H., and Watanuki, M. 1997 Int.J.Vitam.Nutr.Res.
1184. Absorbability and cost effectiveness in calcium supplementation Heaney, R. P., Dowell, S. D., Bierman, J., Hale, C. A., and Bendich, A. 2001 J Am.Coll.Nutr
1185. Disturbances of vitamin D metabolism and action during clinical and experimental magnesium deficiency Carpenter, T. O. 1988 Magnes.Res.
1186. Vitamin D and its metabolites in the pollen of pine. Part 5: Steroid hormones in the pollen of pine species Saden-Krehula, M. and Tajic, M. 1987 Pharmazie
1187. Vitamin D in an ecological context [In Process Citation] Bjorn, L. O. and Wang, T. 2000 Int.J.Circumpolar.Health
1188. Calcinosis-calcinogenic plants Mello, J. R. 2003 Toxicon
1189. Bioactive phytochemicals with emphasis on dietary practices Krishnaswamy, K. and Raghuramulu, N. 1998 Indian J Med.Res.
1190. 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.
1191. The vitamin K-dependent carboxylase Berkner, K. L. 2000 J Nutr
1192. A high phylloquinone intake is required to achieve maximal osteocalcin gamma-carboxylation Binkley, N. C., Krueger, D. C., Kawahara, T. N., Engelke, J. A., Chappell, R. J., and Suttie, J. W. 2002 Am.J Clin Nutr
1193. Vitamin K1 Supplementation Retards Bone Loss in Postmenopausal Women Between 50 and 60 Years of Age Braam, L. A., Knapen, M. H., Geusens, P., Brouns, F., Hamulyak, K., Gerichhausen, M. J., and Vermeer, C. 4-3-2003 Calcif.Tissue Int.
1194. Strategies for skeletal health in the elderly Eastell, R. and Lambert, H. 2002 Proc.Nutr Soc.
1195. Effect of food composition on vitamin K absorption in human volunteers Gijsbers, B. L., Jie, K. S., and Vermeer, C. 1996 Br.J Nutr
1196. Japanese fermented soybean food as the major determinant of the large geographic difference in circulating levels of vitamin K2: possible implications for hip-fracture risk Kaneki, M., Hedges, S. J., Hosoi, T., Fujiwara, S., Lyons, A., Crean, S. J., Ishida, N., Nakagawa, M., Takechi, M., Sano, Y., Mizuno, Y., Hoshino, S., Miyao, M., Inoue, S., Horiki, K., Shiraki, M., Ouchi, Y., and Orimo, H. 2001 Nutrition
1197. Determination of phylloquinone and menaquinones in food. Effect of food matrix on circulating vitamin K concentrations Schurgers, L. J. and Vermeer, C. 2000 Haemostasis
1198. Vitamin K-dependent Proteins, Warfarin, and Vascular Calcification Danziger, J. 5-21-2008 Clin.J.Am.Soc.Nephrol.
1199. Does adding vitamin K to warfarin improve anticoagulation control? 2008 J.Fam.Pract.
1200. Vitamin K and bone health in adult humans Bugel, S. 2008 Vitam.Horm.
1201. Ascorbic acid effects on vitamin D hormone metabolism and binding in guinea pigs Sergeev, I. N., Arkhapchev, Y. P., and Spirichev, V. B. 1990 J.Nutr.
1202. [Effect of ascorbic acid on 25-hydroxyvitamin D3 metabolism in the kidneys and 1,25-dihydroxyvitamin D3 reception in the small intestine mucosa of guinea pigs] Sergeev, I. N., Arkhapchev, IuP, Kim, R. K., Kodentsova, V. M., and Spirichev, V. B. 1987 Biokhimiia.
1203. Ascorbate increases the 1,25 dihydroxyvitamin D3-induced monocytic differentiation of HL-60 cells Quesada, J. M., Lopez-Lluch, G., Buron, M. I., Alcain, F. J., Borrego, F., Velde, J. P., Blanco, I., Bouillon, R., and Navas, P. 1996 Calcif.Tissue Int.
1204. The importance of vitamin C for hydroxylation of vitamin D3 to 1,25(OH)2D3 in man Cantatore, F. P., Loperfido, M. C., Magli, D. M., Mancini, L., and Carrozzo, M. 1991 Clin.Rheumatol.
1205. 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.
1206. Predictive and preventive pathology of cardiovascular diseases Yamori, Y. 1989 Acta Pathol.Jpn.
1207. Potential role of potassium as a determinant of morbidity and mortality in patients with systemic hypertension and congestive heart failure Packer, M. 3-6-1990 Am.J Cardiol.
1208. The decline in stroke mortality. An epidemiologic perspective Klag, M. J. and Whelton, P. K. 1993 Ann Epidemiol.
1209. Sun safety behaviours of alpine skiers and snowboarders in the western United States Buller, D. B., Andersen, P. A., and Walkosz, B. 1998 Cancer Prev.Control
1210. Ultraviolet radiation in alpine skiing: magnitude of exposure and importance of regular protection Rigel, E. G., Lebwohl, M. G., Rigel, A. C., and Rigel, D. S. 2003 Arch.Dermatol.
1211. Influence of vitamin D deficiency and vitamin D receptor polymorphisms on tuberculosis among Gujarati Asians in west London: a case-control study Wilkinson, R. J., Llewelyn, M., Toossi, Z., Patel, P., Pasvol, G., Lalvani, A., Wright, D., Latif, M., and Davidson, R. N. 2000 Lancet

1212. Tanning, protection against sunburn and vitamin D formation with a UV-A 'sun-bed' Devgun, M. S., Johnson, B. E., and Paterson, C. R. 1982 Br.J Dermatol.
1213. Treatment of vitamin D deficiency due to Crohn's disease with tanning bed ultraviolet B radiation Koutkia, P., Lu, Z., Chen, T. C., and Holick, M. F. 2001 Gastroenterology
1214. Response of psoriasis to sunbed treatment: comparison of conventional ultraviolet A lamps with new higher ultraviolet B-emitting lamps Das, S., Lloyd, J. J., Walshaw, D., Diffey, B. L., and Farr, P. M. 2002 Br.J.Dermatol.
1215. High frequency of ultraviolet mutations at the INK4a-ARF locus in squamous cell carcinomas from psoralen-plus-ultraviolet-A-treated psoriasis patients Kreimer-Erlacher, H., Seidl, H., Back, B., Cerroni, L., Kerl, H., and Wolf, P. 2003 J.Invest Dermatol.
1216. High levels of ultraviolet B exposure increase the risk of non-melanoma skin cancer in psoralen and ultraviolet A-treated patients Lim, J. L. and Stern, R. S. 2005 J.Invest Dermatol.
1217. Consensus workshop on the toxic effects of long-term PUVA therapy Morison, W. L., Baughman, R. D., Day, R. M., Forbes, P. D., Hoenigsmann, H., Krueger, G. G., Lebwohl, M., Lew, R., Naldi, L., Parrish, J. A., Piepkorn, M., Stern, R. S., Weinstein, G. D., and Whitmore, S. E. 1998 Arch.Dermatol.
1218. The increased risk of skin cancer is persistent after discontinuation of psoralen+ultraviolet A: a cohort study Nijsten, T. E. and Stern, R. S. 2003 J.Invest Dermatol.
1219. Treatment with UV-B for psoriasis and nonmelanoma skin cancer: a systematic review of the literature Pasker-de Jong, P. C., Wielink, G., van, der, V, and van der Wilt, G. J. 1999 Arch.Dermatol.
1220. UVB doses in maintenance psoriasis phototherapy versus solar UVB exposure Schothorst, A. A., Slaper, H., Schouten, R., and Suurmond, D. 1985 Photodermatol.
1221. Ultraviolet exposure as the main initiator of p53 mutations in basal cell carcinomas from psoralen and ultraviolet A-treated patients with psoriasis Seidl, H., Kreimer-Erlacher, H., Back, B., Soyer, H. P., Hofler, G., Kerl, H., and Wolf, P. 2001 J.Invest Dermatol.
1222. Skin carcinoma in patients with psoriasis treated with topical tar and artificial ultraviolet radiation Stern, R. S., Zierler, S., and Parrish, J. A. 4-5-1980 Lancet
1223. Risks of cancer associated with long-term exposure to PUVA in humans: current status--1991 Stern, R. S. 1992 Blood Cells
1224. The carcinogenic risk of treatments for severe psoriasis. Photochemotherapy Follow-up Study Stern, R. S. and Laird, N. 6-1-1994 Cancer
1225. Malignant melanoma in patients treated for psoriasis with methoxsalen (psoralen) and ultraviolet A radiation (PUVA). The PUVA Follow-Up Study Stern, R. S., Nichols, K. T., and Vakeva, L. H. 4-10-1997 N.Engl.J.Med.
1226. Oral psoralen and ultraviolet-A light (PUVA) treatment of psoriasis and persistent risk of nonmelanoma skin cancer. PUVA Follow-up Study Stern, R. S., Liebman, E. J., and Vakeva, L. 9-2-1998 J.Natl.Cancer Inst.
1227. Do tanning lamps cause melanoma? An epidemiologic assessment Swerdlow, A. J. and Weinstock, M. A. 1998 J.Am.Acad.Dermatol.
1228. Alternative therapies commonly used within a population of patients with psoriasis Fleischer, A. B., Jr., Feldman, S. R., Rapp, S. R., Reboussin, D. M., Exum, M. L., and Clark, A. R. 1996 Cutis
1229. Increased skin pigment reduces the capacity of skin to synthesise vitamin D3 Clemens, T. L., Adams, J. S., Henderson, S. L., and Holick, M. F. 1-9-1982 Lancet.
1230. Topical glycolic acid enhances photodamage by ultraviolet light Kaidbey, K., Sutherland, B., Bennett, P., Wamer, W. G., Barton, C., Dennis, D., and Kornhauser, A. 2003 Photodermatol.Photoimmunol.Photomed.
1231. Relationship between habits and dental health among rural Tanzanian children Normark, S. and Mosha, H. J. 1989 Community Dent.Oral Epidemiol.
1232. Development of hypertension in a rat model of diet-induced obesity Dobrian, A. D., Davies, M. J., Prewitt, R. L., and Lauterio, T. J. 2000 Hypertension
1233. Western-type diets induce insulin resistance and hyperinsulinemia in LDL receptor-deficient mice but do not increase aortic atherosclerosis compared with normoinsulinemic mice in which similar plasma cholesterol levels are achieved by a fructose-rich diet Merat, S., Casanada, F., Sutphin, M., Palinski, W., and Reaven, P. D. 1999 Arterioscler.Thromb.Vasc.Biol.
1234. Variable rachitogenic effects of grain and alleviation by extraction or supplementation with vitamin D, fat and antibiotics MacAuliffe, T., Pietraszek, A., and McGinnis, J. 1976 Poult.Sci.
1235. The Effect of Different Foods on Calcium and Phosphorus Metabolism Blunt, K. and Cowan, R. 1930
1236. Blunted seasonal variation in serum 25-hydroxy vitamin D and increased risk of osteomalacia in vegetarian London Asians Finch, P. J., Ang, L., Colston, K. W., Nisbet, J., and Maxwell, J. D. 1992 Eur.J Clin Nutr
1237. Low serum 25-hydroxyvitamin D concentrations and secondary hyperparathyroidism in middle-aged white strict vegetarians Lamberg-Allardt, C., Karkkainen, M., Seppanen, R., and Bistrom, H. 1993 Am.J.Clin.Nutr.

1238. Multiple nutritional deficiencies in infants from a strict vegetarian community Zmora, E., Gorodischer, R., and Bar-Ziv, J. 1979 Am.J Dis.Child
1239. Effect of Foods on Metabolism Blunt, K. and Cowen, E. W. 1930
1240. The effect of grain component of the diet on the response of turkey poults to vitamin D3 and penicillin MacAuliffe, T., Pietraszek, A., and McGinnis, J. 1976 Poult.Sci.
1241. The role of cereals in the aetiology of nutritional rickets: the lesson of the Irish National Nutrition Survey 1943-8 Robertson, I., Ford, J. A., McIntosh, W. B., and Dunnigan, M. G. 1981 Br.J Nutr
1242. Nutritional significance of phytic acid and phytase Pallauf, J. and Rimbach, G. 1997 Arch.Tierernahr.
1243. Biochemical indicators of disordered vitamin D and calcium homeostasis in sarcoidosis Adams, J. S., Gacad, M. A., Anders, A., Endres, D. B., and Sharma, O. P. 1986 Sarcoidosis.
1244. Vitamin D metabolite-mediated hypercalcemia Adams, J. S. 1989 Endocrinol.Metab Clin.North Am.
1245. Sarcoidosis succumbs to antibiotics--implications for autoimmune disease Marshall, T. G. and Marshall, F. E. 2004 Autoimmun.Rev.
1246. Xeroderma pigmentosum Lambert, W. C., Kuo, H. R., and Lambert, M. W. 1995 Dermatol.Clin
1247. Ichthyosiform erythroderma with rickets: report of five cases Sethuraman, G., Khaitan, B. K., Dash, S. S., Chandramohan, K., Sharma, V. K., Kabra, M., Verma, K. K., Goswami, R., and Thulkar, S. 2008 Br.J.Dermatol.
1248. Sunlight, skin cancer and vitamin D: What are the conclusions of recent findings that protection against solar ultraviolet (UV) radiation causes 25-hydroxyvitamin D deficiency in solid organ-transplant recipients, xeroderma pigmentosum, and other risk groups? Reichrath, J. 2007 J.Steroid Biochem.Mol.Biol.
1249. Evidence of a marked 25-hydroxyvitamin D deficiency in patients with congenital ichthyosis Ingen-Housz-Oro, S., Boudou, P., Bergot, C., Ibrahim, F., Souberbielle, J. C., Dubertret, L., and Blanchet-Bardon, C. 2006 J.Eur.Acad.Dermatol.Venereol.
1250. Rickets in xeroderma pigmentosum Raza, N., Ejaz, A., and Hussain, S. 2005 J.Coll.Physicians Surg.Pak.
1251. A plea for the analysis of Vitamin-D levels in patients under photoprotection, including patients with xeroderma pigmentosum (XP) and basal cell nevus syndrome (BCNS) Querings, K. and Reichrath, J. 2004 Cancer Causes Control
1252. Bone and celiac disease Bianchi, M. L. and Bardella, M. T. 2002 Calcif.Tissue Int.
1253. Osteomalacia and celiac disease: response to 25-hydroxyvitamin D Hepner, G. W., Jowsey, J., Arnaud, C., Gordon, S., Black, J., Roginsky, M., Moo, H. F., and Young, J. F. 1978 Am.J.Med.
1254. Bone remodeling indices and secondary hyperparathyroidism in celiac disease [see comments] Keaveny, A. P., Freaney, R., McKenna, M. J., Masterson, J., and O'Donoghue, D. P. 1996 Am.J.Gastroenterol.
1255. Celiac disease as a cause of transient hypocalcemia and hypovitaminosis D in a 13 year-old girl Rakover, Y., Hager, H., Nussinson, E., and Luboshitzky, R. 1994 J.Pediatr.Endocrinol.
1256. Reversal of osteopenia with diet in adult coeliac disease Valdimarsson, T., Lofman, O., Toss, G., and Strom, M. 1996 Gut
1257. Caries risk in patients with Crohn's disease: a pilot study Bevenius, J. 1988 Oral Surg.Oral Med.Oral Pathol.
1258. Bone disease in vitamin D-deficient patients with Crohn's disease Vogelsang, H., Ferenci, P., Woloszczuk, W., Resch, H., Herold, C., Frotz, S., and Gangl, A. 1989 Dig.Dis.Sci.
1259. A 2008 panorama on osteoporosis and inflammatory bowel disease Sapone, N., Pellicano, R., Simondi, D., Sguazzini, C., Reggiani, S., Terzi, E., Rizzetto, M., and Astegiano, M. 2008 Minerva Med.
1260. Treatment of Crohn's disease Hoffmann, J. C. and Zeitz, M. 2000 Hepatogastroenterology
1261. Fat-soluble vitamin deficiency in infants and children Argao, E. A. and Heubi, J. E. 1993 Curr.Opin.Pediatr.
1262. Hypocalcemia as the initial manifestation of occult cholestatic liver disease Clark, J. H. and Hudson, S. D. 1992 Clin.Pediatr.(Phila)
1263. Bone disease in chronic childhood cholestasis. I. Vitamin D absorption and metabolism Heubi, J. E., Hollis, B. W., Specker, B., and Tsang, R. C. 1989 Hepatology
1264. The role of magnesium in the pathogenesis of bone disease in childhood cholestatic liver disease: a preliminary report Heubi, J. E., Higgins, J. V., Argao, E. A., Sierra, R. I., and Specker, B. L. 1997 J.Pediatr.Gastroenterol.Nutr.
1265. Calcium/phosphate/vitamin D homeostasis and bone mass in patients after gastrectomy, vagotomy, and cholecystectomy Marcinowska-Suchowierska, E. B., Talalaj, M. J., Wlodarcyzk, A. W., Bielecki, K., Zawadzki, J. J., and Brzozowski, R. 1995 World J.Surg.
1266. Water-miscible, emulsified, and solid forms of retinol supplements are more toxic than oil-based preparations Myhre, A. M., Carlsen, M. H., Bohn, S. K., Wold, H. L., Laake, P., and Blomhoff, R. 2003 Am.J.Clin.Nutr.
1267. Effect of vitamin D3 loading and thyroid hormone replacement therapy on the decreased serum 25-hydroxyvitamin D level in patients with hypothyroidism Barsony, J., Lakatos, P., Foldes, J., and Feher, T. 1986 Acta Endocrinol.(Copenh)
1268. Mineral and bone metabolism in thyroid disease: a review Auwerx, J. and Bouillon, R. 1986 Q.J Med.

1269. Hypercalcaemia induced by increased thyroxine substitution in a patient treated with dihydrotachysterol Hallengren, B., Spjuth, J., and Dymling, J. F. 1984 Acta Endocrinol.(Copenh)
1270. Thyroid function and bone turnover Bijlsma, J. W., Duursma, S. A., Roelofs, J. M., and der Kinderen, P. J. 1983 Acta Endocrinol.(Copenh)
1271. Influence of thyroid function on the serum concentration of 1,25-dihydroxyvitamin D3 Bouillon, R., Muls, E., and De Moor, P. 1980 J Clin Endocrinol.Metab
1272. Improving trends in glucocorticoid-induced osteoporosis management: 2002 to 2006 Mohammad, A., Ryan, J. G., Ralph, N., Ryan, C., and O'Connell, P. G. 2007 Clin.Exp.Rheumatol.
1273. Vitamin D insufficiency underlies unexpected hypocalcemia following high dose glucocorticoid therapy Kinoshita, Y., Masuoka, K., Miyakoshi, S., Taniguchi, S., and Takeuchi, Y. 2008 Bone
1274. [Calcium and vitamin D preparations in steroid osteoporosis in patients with rheumatoid arthritis] Bazhenov, A. N., Plesovskaia, I. V., and Iliushina, L. V. 2007 Ter.Arkh.
1275. [Glucocorticoid induced osteoporosis] Lange, U. and Muller-Ladner, U. 2007 Orthopade
1276. [Secondary osteoporosis. Glucocorticoid induced osteoporosis in childhood : prophylaxis and treatment] Tanaka, H. 2007 Clin.Calcium
1277. Osteoporosis: integrating biomarkers and other diagnostic correlates into the management of bone fragility McCormick, R. K. 2007 Altern.Med.Rev.
1278. Glucocorticoid-induced osteoporosis: pathophysiology and therapy Canalis, E., Mazziotti, G., Giustina, A., and Bilezikian, J. P. 2007 Osteoporos.Int.
1279. Prevention and treatment of glucocorticoid-induced osteoporosis Curtis, J. R. and Saag, K. G. 2007 Curr.Osteoporos.Rep.
1280. Glucocorticoid-induced osteoporosis: a systematic review and cost-utility analysis Kanis, J. A., Stevenson, M., McCloskey, E. V., Davis, S., and Lloyd-Jones, M. 2007 Health Technol.Assess.
1281. Glucocorticoid-induced osteoporosis: mechanisms and therapeutic approach Devogelaer, J. P. 2006 Rheum.Dis.Clin.North Am.
1282. Hypercalciuria Audran, M. and Legrand, E. 2000 Joint Bone Spine
1283. Renal acidification defects in patients with recurrent calcium nephrolithiasis Tessitore, N., Ortalda, V., Fabris, A., D'Angelo, A., Rugiu, C., Oldrizzi, L., Lupo, A., Valvo, E., Gammaro, L., and Loschiavo, C. 1985 Nephron
1284. The role of calcium in the prevention of kidney stones Heller, H. J. 1999 J.Am.Coll.Nutr.
1285. Citrate and renal calculi: an update Pak, C. Y. 1994 Miner.Electrolyte Metab
1286. Nephrolithiasis: acute management and prevention Wasserstein, A. G. 1998 Dis.Mon.
1287. Effect of diet and intranephronic calculosis on bone modeling and parathyroid volume in rats Woodard, J. C. and Jee, W. S. 1984 J.Nutr.
1288. Plasma phospholipid arachidonic acid content and calcium metabolism in idiopathic calcium nephrolithiasis Baggio, B., Budakovic, A., Nassuato, M. A., Vezzoli, G., Manzato, E., Luisetto, G., and Zaninotto, M. 2000 Kidney Int.
1289. "Nutritional insurance" supplementation and corticosteroid toxicity McCarty, M. F. 1982 Med.Hypotheses