the FELIX Letter
A COMMENTARY ON NUTRITION
No. 87 1996

CYANOGENIC GLYCOSIDES: LEAVE 'EM OR LOVE 'EM?

At the end of a six-year prospective mortality study in which almost 700,000 men and women reported on their aspirin use, the researchers said the risk of death from colon cancer among persons using aspirin 16 or more times per month was approximately half that of nonusers [*New Eng J Med,* Dec 5, 1991, 1593-6].

Before you reach for the aspirin bottle, let's view things from a little-explored perspective. Aspirin (acetyl salicylic acid) is in the benzene ring "family" of organic, i.e., carbon-based substances. The benzene molecule-- a hexagon of six atoms of carbon, each attached to a hydrogen--forms the basis for much of our world's petroleum and industrial substances, and exists widely in the plant world.

The salicylic acid portion of aspirin is designated *hydroxybenzoic acid*, or *hydroxybenzaldehyde.* In traditional herbal medicine, willow bark containing salicylic acid was used (still is) to relieve fever, pain, and inflammation. A French chemist isolated salicylic acid from the bark and by 1852 it was being produced synthetically. By 1899, chemists had attached an acetic acid molecule (as in vinegar) to make it less irritating and--lo! modern aspirin was born.

Well, folks, guess which plant substances--commonly ingested by animals, birds and humans in a state of nature--release a benzaldehyde or benzoic acid molecule similar to salicylic acid? Sure enough, my favorite "orphan" plants, those bearing the cyanogenic glucosides (also known as cyanogenetic glycosides or nitrilosides).

Cyanogenic glucosides are compounds capable of liberating cyanide (HCN). They're found in more than 1,000 species of plants, many of them edible. When eaten, all nitrilosides release **HCN** and **glucose,** and many release **benzaldehyde**. Examples include almond, apple, apricot, cherry, peach, pear, plum, quince, elderberry, flax, and sorghum.

All creatures, including ourselves, normally detoxify cyanide by combining it with sulfur (provided by sulfur-bearing amino acids in protein), to form *thiocyanate.*

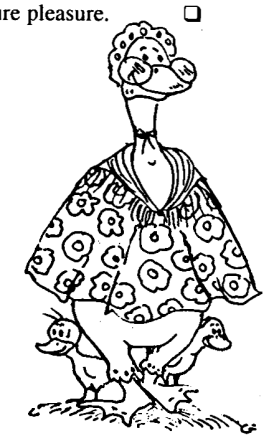
What am I driving at? Merely that nature put into tasty plant foods substances that may not only relieve aches 'n pains, but may also protect against cancer.

For instance, *flaxseed* is showing up as a cancer fighter in current research. The yew tree from which the new ovarian cancer fighter, taxol, is made is in the *Taxus* species which contain cyanogenic glucosides. Japanese and Norwegian scientists have been investigating benzaldehyde derivatives in *figs* for anticancer effects. And, as described in *FL#86,* there's very encouraging work being done with isothiocyanates and thiocyanates, found in the broccoli family.

Yet cyanogenic glucosides (CGs) as a whole continue to be viewed solely as toxins and potential menaces to people and grazing animals. I've yet to find a textbook that says CGs may be responsible for easing the severity of malaria by sabotaging the growth of the *Plasmodium falciparum* parasite; that CGs play a role in ameliorating sickle cell anemia; that CGs may have some natural function in blood pressure regulation via thiocyanate. Nor that they may help prevent cancer.

CGs only do these things, however, after we eat them! I'm sticking to my 3 to 4 apricot kernels a day; a tablespoon of ground flaxseed several times a week; lots of broccoli and cabbage; "hash browns" made of grated cassava (manioc or yuca); apple and pear seeds (the white parts only) along with the fruit; wild blackberries in season (I'd gather huckleberries and blueberries, too, if they grew out here, which they don't. I have to buy 'em); mung bean sprouts, lentils, chick peas, buckwheat, millet; and cookies, crackers, and pancakes from sorghum flour!

Aspirin gives me a belly-ache but eating this stuff is pure pleasure. ❑



BLOOD PRESSURE NEWS

The good effects of regular exercise in relieving modest hypertension are well known, but doctors at Veterans Affairs Medical Center, Washington DC, discovered it afforded solid benefits in *severe* hypertension as well. African-American men were chosen for the study because they suffer more from high blood pressure than any other U.S. racial group. All (aged 35 to 76) received blood pressure medication because of their initially high diastolic pressure (at least 110 mm mercury; normal is around 80 mm). In addition, they suffered from enlarged left ventricle of the heart caused by chronic high blood pressure. Half of the group did 3-day a week aerobic exercises (stationary cycling), gradually increasing in intensity and length until the men were cycling 20-60 minutes per session. After 16 weeks, blood pressure medication was reduced gradually in those whose diastolic pressure had dropped to below 90 mm.

At the end of 32 weeks, diastolic pressure had decreased more in the exercise group, and stayed down even with less medication. Moreover, there was a significant reduction of the enlarged left ventricle of the heart in the exercising men, but not in the non-exercisers. All in all, a satisfying outcome for researchers and exercisers. [*New Eng J Med,* Nov. 30, 1995, 1462-7.]

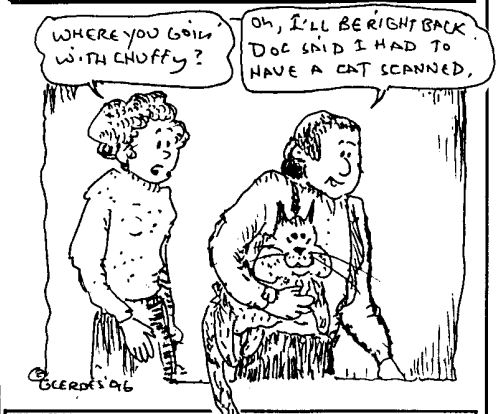
Potassium & Pressure

In an outpatient double-blind clinical trial in the Bay area, 91 men and women with moderate hypertension (at least 90 mm diastolic pressure) were treated for 16 weeks with either potassium bicarbonate, potassium chloride, or placebo. Those on hypertension medication were taken off it before the study began.

Only potassium bicarbonate significantly lowered both systolic and diastolic pressure in the group as a whole.

The African-Americans in the trial who got potassium bicarbonate had much greater than average drops in diastolic blood pressure. But unlike the group as a whole, African-Americans who were given potassium chloride had a big drop in systolic pressure. Researchers speculate that this strong response to both forms of potassium might mean their regular diet was low in the mineral. Could it also mean that African-Americans have higher potassium requirements?

As described in *FLs 52 & 53*, I keep handy a dry mixture of 1 part potassium bicarbonate to 1-2 parts sodium bicarbonate in a tightly sealed glass jar, and take 1/2 teaspoon in water or soda whenever I need an alkalizer to help digestion, ease allergies, or fight off a cold or flu. I'm now glad to learn it may lower blood pressure too! Even though potassium bicarbonate is sold to bakeries as a leavening agent, here in the Bay area it doesn't seem to be available to the public. Alka Seltzer Gold contains potassium bicarbonate, sodium bicarbonate, citric acid, and no aspirin--in case anyone feels like experimenting! ❑



SUNLIGHT, VITAMIN D, OR BOTH?

Felix Letter readers, scattered as they are mostly over U.S. and Canada, vary widely in opportunities for basking in warm, golden rays. How much vitamin D do we need, and how much is too much? *FL#85* dealt with a Canadian physician's clinical observations on deficits of vitamin D and calcium as prime causes of "energy starvation" in the body's cells. The curtailing of cellular power incites a host of malfunctions, Dr. Carl Reich of Calgary said. In his many years of practice he saw improvement in a variety of disorders only after his patients first replenished their dietary vitamin D and calcium.

There seems, however, to be some justification for medical wariness about vitamin D supplementation. Nature meant us to make our own, as all animals and birds do, by allowing ultraviolet B (UV-B) rays of sunlight to energize cholesterol-derived molecules in our skin, forming "previtamin D_3." In the tropical birthplace of our species the danger would be from too much sunlight--unlike Canada! Evolution provided protective melanin, i.e darker skin, as one answer. *The other is a marvelous biomechanism that permits only a safe amount of previtamin D_3 to be made in the skin.* The previtamin then enters the circulation and is transformed by liver and kidneys into the active form (1,25-dihydroxyvitamin D, mercifully known as calcitriol), which behaves as a true hormone. **"This is the likely explanation for why there are no reported cases of vitamin D intoxication from chronic excessive overexposure to sun-light,"** writes Michael Holick, Ph.D., M.D. [*Am J Clin Nutr,* Oct 1994].

Hypervitaminosis D, or vitamin D intoxication, caused by over-supplementation results in *dumping of calcium into tissues.* Vitamin D's main job is to maintain proper levels of ionized calcium and phosphorus in the blood. It does this by (**a**) increasing the small intestine's ability to absorb dietary calcium and phosphorus; and (**b**) stimulating withdrawal of calcium and phosphorus from our bones. Longterm overdosing with vitamin D can force bones to relinquish too much calcium, leading to "hypercalcemia," i.e., abnormally high levels of calcium in the blood. This can be a prelude to harmful calcification of "soft" tissues--renal, cardiovascular, even brain.

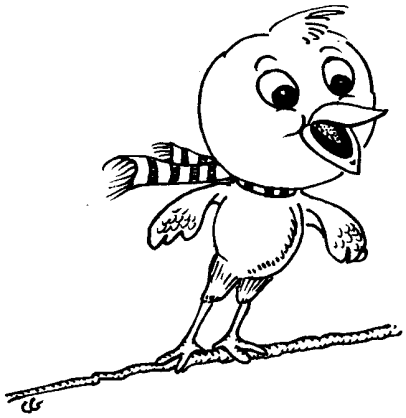
The vitamin's reputation for toxicity has to do mostly with problems in infants and young children. After WWII, there was a sudden rise in Great Britain in hospital admissions of sick infants who had abnormally high blood and tissue levels of calcium. This was a time of intensified vitamin D fortification of dried milk and cereals. Many mothers also were giving their kids high-vitamin D cod liver oil. A baby consuming 1-1/2 pints of milk, one ounce of cereal, and one teaspoon cod liver oil a day easily got 3000 to 4000 IU (International Units) of the vitamin.

The RDA in the U.S. for vitamin D is, and has been for many years, 300 IU for infants up to six months, and 400 IU afterwards. (Studies show these amounts are more than enough to prevent rickets.) In other words, many British babies were getting ten times the known safe amounts.

The cases of hypervitaminosis D involved several hundred children between1953 and 1955. The result was the banning of vitamin D fortification of milk in Great Britain. "This drastic measure, however, has unfortunately led to a high incidence of rickets and osteomalacia [bone softening in adults] in that country." [Claire H. Jacobus, Michael F. Holick, et al., *New Eng J Med,* April 30, 1992.] Cases rarely crop up in the United States, even though milk has been fortified with 400 IU per quart since the 1930s.* Researchers suggest some infants may be abnormally sensitive to the vitamin, for reasons not yet understood. Nevertheless, vitamin D intoxication is rare. The cases make scary reading in medical journals, but their incidence, fortunately, is low.

* Between 1988-91, 8 patients in Massachusetts suffered the "unusual occurrence" of vitamin D intoxication. The only source was milk, since none took supplements. Further sleuthing revealed the milk all came from one dairy. Investigation uncovered criminal carelessness in the dairy's fortification methods. Amounts differed widely from batch to batch, ranging from a low of 42 IU vitamin D_3 per quart ***to a high of 232,565 IU.*** The wonder is there were only 8 patients! [Jacobus, Holick, et al., *New Eng J Med,* April 30, 1992.]

Still, the watchword for supplementing little ones is *caution*. Far better to exploit available sunlight! Exposure to UV-B light during the sunnier months for 10-30 minutes several times a week may provide the baby with enough vitamin D stores to carry it through winter--*depending, of course, on the latitude, how long the winters are, how much UV-B light is available, how free of smog the air is, etc.* Glass or plastic windows absorb UV light, preventing it from reaching us. *Darker-skinned babies need much longer UV-B exposure time than light-skinned ones to make all the vitamin D they need;* in northern latitudes they may require supplements for many months.



Breast-fed youngsters in northern latitudes may benefit from supplemental vitamin D in winter, since breast milk is low in the vitamin--suggesting our species evolved in climates where dietary sources--even mother's milk--took second place to ample sunlight! Infants in the U.S. and Canada on formula or regular milk will be supplemented automatically, although amounts of vitamin D in milk have often been found to be less than the stated 400 IU per quart.

For all ages, the best way to get vitamin D is to *make* it, by baring face, arms, legs, or other body parts to sunlight. If you live in Calgary, though, your chances are slim for making enough during the summer to last you the rest of the year. In Florida, no problem! Supplementation is a logical option for folks who seldom are outdoors, and/or live in northern latitudes, and/or don't drink milk. Many are allergic to milk. (Recently I learned I'm allergic to all dairy and have been feeling extra bouncy since I quit.)

The few natural unfortified food sources are fatty fish, e.g. sardines, salmon, mackerel, herring, 300 to 900 IU per 3-1/2 oz; one egg yolk 30 IU; 3-1/2 oz chicken liver 67 IU.

The older we get and the thinner our skin, the less we're able to make vitamin D. In sunny low-latitudes this may not matter unless we never go outdoors, but the evidence is that older folks in higher latitudes tend to be at risk. Dr. Holick writes:[1] "The elderly population...have a decreased capacity to produce vitamin D in their skin. In addition,

they are likely to heed the warnings about the damaging effects of sunlight and use a sunscreen and wear more clothing, thus preventing the cutaneous synthesis of vitamin D." The net effect is demineralization of bones and more hip fractures.

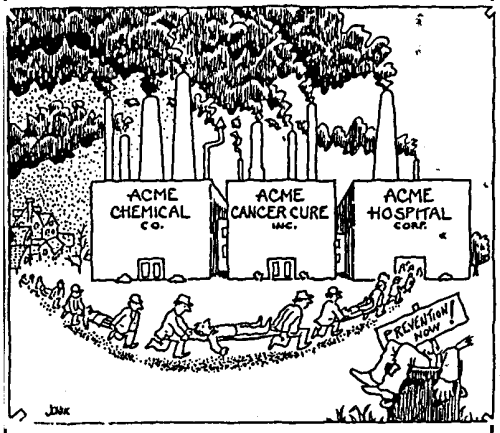
Holick, a professor at Boston U.'s School of Medicine, recommends that *in the spring, summer, and fall, Boston's elderly population should try to get 5 to 30 minutes of exposure to sunlight in the morning or late afternoon 2-3 days a week, when the rays are not so damaging to the skin.* Afterwards, he suggests they apply a sunscreen with a sun protective factor of at least 8.

Like Carl Reich, he believes supplements may be important for older folks. "It has been estimated that in both the United States and Great Britain approximately 30-40% of elderly patients with hip fractures are vitamin D-insufficient or vitamin D-deficient....There is mounting evidence that the RDA of 5 micrograms [200 IU] is much too low for elderly people and for people not exposed to sunlight...It is likely that the true vitamin D requirement in the absence of any exposure to sunlight is closer to 15 micrograms [600 IU] a day."

Currently, there's further incentive to maintain optimal vitamin D status. It seems the vitamin has receptors in an unexpected number of tissues where its roles are not yet understood, but one of them may be *to stop abnormal overgrowth, i.e., cell proliferation.* Dr. Holick describes trials using a prescribed form of the active vitamin D, calcitriol, on the skins of patients afflicted with psoriasis, a "hyperproliferative" skin disorder. Of 84 subjects, 91% "showed either complete or almost complete clearing and 9% demonstrated slight improvement of their lesions." [*Am J Clin Nutr,* Oct 1994.]

Although researchers Holmes and Kummerow warned in 1983 that chronic longterm ingestion of "moderately excessive" doses of vitamin D possibly could lead to heart and kidney damage, they acknowledged that hard evidence was scanty. [*J Am Coll Nutr*, 2; 173-199.] More recently, P.E. Norman et al. speculated that vitamin D overdosing may play a role in the development of "abdominal aortic aneurysm"--dilatation and weakness in the main abdominal artery [*Medical Hypotheses,* 1995: 45; 17-20]. Dr. Holick, however, is less concerned with toxicity, and more with deficiency, especially in older folks. Let's not be afraid of supplementation, say, 400-1,000 IU, when it's called for. Dr. Reich and neighbors at latitude 51° in Calgary will need more supplement days than I will in sunny Berkeley, close to the 38th parallel. The darker the skin, the more UV-B exposure adults require, just as with infants. Let's tap into benign solar forces! ❑

[1]Michael F. Holick, "Vitamin D" in *Modern Nutrition in Health & Disease, 8th ed.,* editors Shils, Olson, & Shike, 1994. pp 308-325.

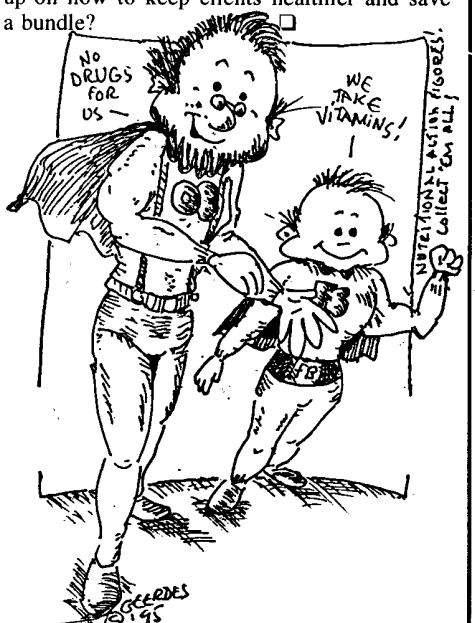


THE A.M.A. IS NOT AMUSED!

The Pacific Northwest is taking the lead in making alternative health therapies respectable--and available. In January, Washington state began requiring health insurers to cover treatments such as acupuncture, massage therapy, and other licensed natural health care. Seattle is planning the country's first tax-supported natural health clinic, which Bastyr University, a naturopathic school, will help to run. The clinic expects to put these treatments within reach of low-income folks.

Although nothing quite so splendid is happening in our state, acupuncture, biofeedback, and other nontraditional therapies were consolidated this past October into a new Alternative Medicine Clinic at Kaiser Permanente's medical center in Vallejo, 20-some miles north of Oakland. Also, Kaiser Permanente researchers in Oakland are getting set for their first-ever clinical study of an ancient herbal remedy: *dong quai* will be tested on 72 ladies for its effects on menopausal discomforts.

D'you suppose HMOs and insurers are wising up on how to keep clients healthier and save a bundle? ❑



It's ***CAPTAIN OAT BRAN*** and ***FLAX BOY***
Fighting the neverending battle against the forces of Corporate Constipation!

FLAXSEED GOES BIGTIME

Canada, the largest grower of flax in the world, began to look seriously only about ten years ago at flax's commercial potential as *human* food for this hemisphere. Up until then only Europe was interested in edible flax oil, to be blended with soy and other oils for margarine production; Germany bought tons of flaxseed for popular breads and bakery goods. Most of the Canadian flaxseed was pressed for worldwide *industrial* use as 'linseed' oil, to be incorporated into products like paint, linoleum, and inks, while some of the pressed 'cake' was sold for livestock feed.

On the other hand, China, another big flax producer, has pressed the seeds for centuries to use as a food oil. Clearly, they've known something Western science didn't pick up on until a few years ago!

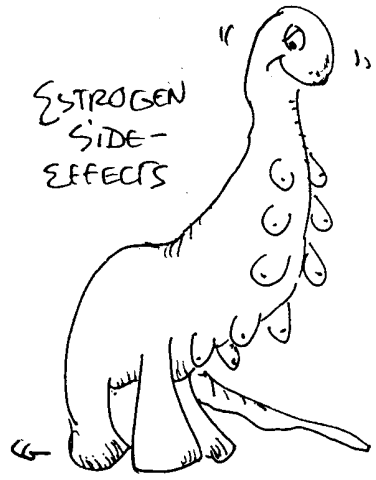
Flaxseed in Human Nutrition, edited by University of Toronto professors Stephen Cunnane and Lilian Thompson, does a superb job of helping the western world to catch up. (1995, AOCS Press, P.O. Box 3489, Champaign, IL 61826.) The seed contains about 25% protein and 40% oil. ***About 45 to 60% of the oil's fatty acids are alpha-linolenic (essential omega-3);*** 20-25% monounsaturated oleic; 15% linoleic, the essential omega-6. The super-rich supply of alpha-linolenic acid (ALA) makes it unique among seeds (only perilla and hemp seeds match it and they're not commercially available in western countries), giving us the chance to fill our omega-3 (w3) reservoirs while at the same time supplying decent amounts of essential w6.

Even though in 1930 the husband and wife team of Burr and Burr found both w6 linoleic acid (LA) and w3 ALA to be essential to growth and health, most researchers until very, very recently were convinced w6 LA was the 'only show in town'. So entrenched was this conviction that a big push still exists among Canada's flax growers to breed species with very low ALA seed content--this, of course, to provide an oil that won't oxidize and turn rancid easily, as normal flax oil does. But what's the point? The supermarkets already are loaded with low ALA seed oils!

As we've pointed out in many *FL* issues, ALA may be the only form of w3 that strict vegetarians get from their food, hence the only source of longer-chain, ultrapoly-unsaturated w3s, e.g., EPA and DHA, which the body can make from ALA. EPA, in turn, can be transformed into prostaglandins that control anti-inflammatory and anti-thrombotic functions. DHA is especially important in neural tissues such as the brain and retina of the eye.

Interestingly, ALA is oxidized by the body much faster than w6 LA, disappearing from stored body fat very quickly. It's not all just used up as body fuel, though. After ALA was

injected into infant rats, the carbons of its 18-carbon molecules showed up rapidly in brain lipids--not only as DHA, but as cholesterol and other fatty acids that were needed for the developing brain. That's one reason why human babies did better after ALA (usually from soybean oil) was added to most infant formula to make it a bit more like mother's breast milk. (The next step--I hope!--is adding w3 DHA, and w6 GLA and arachidonic acid to formula, as several European or Japanese companies have done.)



The book reports that an ALA-rich Mediterranean diet, consumed over a 2-year period, resulted in a *70% reduction in cardiovascular death* compared to a control group. In another trial involving thousands of middle-aged American men at high risk for heart disease, *deaths from coronary artery disease and other cardiovascular ailments were "inversely related" to ALA intakes,* i.e., the higher the intake, the fewer the deaths, and vice-versa--as was mortality from all causes.

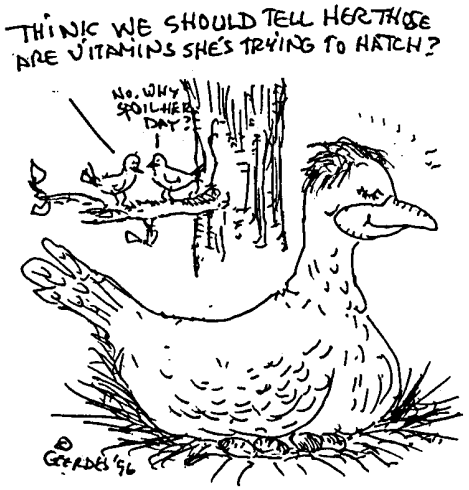
In the same study, *cancer deaths decreased when the ratio of ALA intake to LA intake increased.* In another study involving women with breast cancer, low levels of ALA in breast adipose tissue were associated with a higher risk of lymph node involvement and metastasis to other tissues.

Which brings us to another "good-news molecule" in flaxseed: *lignan.* Plant lignan found in fibrous foods is somewhat related to lignin, the woody part of plants; plants make them by a similar process. *Mammalian lignans* are made *from plant lignans* by normal bacterial flora in the colon. Scores of high lignan foods, e.g., seaweeds, beans, cereals, and cereal brans, are capable of promoting mammalian lignans, but *flaxseed is the champion of them all, producing several hundred times more* than the others.

What's good about making lots of mammalian lignans? *High levels in people are associated with low rates of breast and colon cancer.* Animal studies show protective effects of flaxseed on both mammary and colon carcinogenesis, according to Dr. Thompson.

The chapter titled "Flaxseed, Lignans, and Sex Hormones" explains how mammalian lignans inhibit cell proliferation of estrogen-dependent breast cancer cells. *Flaxseed intake also may promote an increased ratio of progesterone to estrogen,* fewer non-ovulating menstrual cycles, and a longer luteal phase. A longer (progesterone-dominated) luteal phase of the menstrual cycle cuts down on excess estrogen stimulation of breast and uterine tissues that tends to promotes cell proliferation.

Flaxseed is unique in other ways. It's rich in viscous fiber which soaks up water to form a mucilage *that helps to regulate blood glucose,* which is especially useful for diabetics. The fiber also has a *cholesterol-lowering effect.*



We come to the nitty-gritty now: flaxseed's cyanogenic glucosides (CGs)--those nasty cyanide-spewing molecules! A doctor from British Columbia wrote me to ask if his use of raw ground flaxseed was safe, referring to comments by "a dietician here in Vancouver who claims that flax should be cooked before eating because it contains cyagenic [sic] toxins. Have you ever heard of this?"

Yes, indeed, sir, I've heard almost nothing but!--beginning with every nutrition and toxicology professor *and* textbook when I was an undergrad at UCB in the late '70s. (See "Cyanogenic Glycosides" above.) Even Drs. Cunnane and Thompson and the book's other enlightened contributors take an orthodox stance, decrying these compounds as unfortunate blots on flaxseed's fair name. I say it's time for rethinking. Sure, an overload of CGs will do people and animals harm, and standards for safe intakes must be followed, there's no question about that. My beef is with a granite mindset that shuts out all intelligent speculation on why these supposedly wretched molecules have existed for millenia in favorite foods of humans, beasts, and birds; and why populations of wild creatures as well as pre-industrial people somehow have managed to derive maximum good and minimum harm from them!

All creatures including ourselves have active mechanisms in place (in liver, kidneys, thyroid) for detoxifying cyanide (HCN). The product of detoxification, thiocyanate, is present normally in plasma, saliva, and urine. We're long overdue for a big research push on this molecule, which was used medically in the 1930s and '40s for migraine headaches, high blood pressure, and as a bactericide to fight dysentery. Today, a number of anthropologists, biochemists, and doctors say it reduces sickling crises and anemia in persons who have homozygous genes for sickle cell. It's my unhumble opinion that flaxseed's growing rep as a cancer fighter may stem not just from its ALA and lignan content but also from its cyanogenic glucosides and the thiocyanate they cause us to make. Consumption of 50 grams of flaxmeal daily produced slightly higher plasma thiocyanate levels than before in volunteers and no toxicity, Dr. David Jenkins writes in his chapter on incorporating flaxseed into cereal foods. He's optimistic about the practicality of widespread use of flaxseed in all sorts of popular food products in the future, seeing no toxicity danger at normal levels of consumption. I say go for it!

The book's Introduction by Dr. Andrew Judd is a concise, elegant review of flax's unique role in the play of historical and cultural forces since the first recorded use of woven linen some 9000 years ago. Yes, that's another use for *Linum usitatissimum,* the flax plant. ❑

A wondrous look at nutrition and evolution, *The Driving Force* by Dr. Michael Crawford and David Marsh, is now in paperback, retitled ***NUTRITION & EVOLUTION,*** available from Keats Publishing Inc., Box 876, New Canaan, CT. Ordering tel: 1-800-858-7014.

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