the FELIX Letter

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A COMMENTARY ON NUTRITION

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SICKLE CELL ANEMIA: AN OPTIMISTIC VIEW

I knew a young African-American who joined the company where I worked about ten years ago. He was smart, full of engaging humor, and we all thought he had a bright future with the firm.....until he began taking one long sick leave after another. He had inherited sickle cell genes from both parents. I finally understood the sadness beneath his bonhomie. From childhood on, painful sickling crises would land him in the hospital many times a year. He didn't get the promotion he wanted. I left soon after to write my book and lost touch.

In the late '70s, as an undergraduate at UC Berkeley I had researched the ailment, which is found almost exclusively in blacks. The severe type involves a double set of genes for faulty hemoglobin. "Hemoglobin S" forces the person's red blood cells to become sharp and sickle-shaped instead of disk-like and pliable. The stiffened corpuscles don't circulate well in the blood, can't supply enough oxygen to tissues and are too fragile to survive long. Severe anemia is common. For infants and young children, pneumonia is a recurring threat. Sickled cells may plug up small blood vessels anywhere in a person's body, bringing on crippling pain and damage to tissues. [That's what kept sending my young friend back to the hospital.) The heart and lungs can be compromised, and there's a high risk of stroke. Altogether, a miserable disease to inherit!

But it's different in Africa. My first clue was Robert G. Houston's paper in *The American J. of Clinical Nutrition* of November 1973. Although large numbers of blacks in Africa carry homozygous (double) genes for sickle cell anemia, he said they resisted its morbid effects a whole lot better than blacks in the United States did. I was intrigued. Why the difference?

He said the answer lay in diet. *Native Africans traditionally ate certain plant foods that actually protected their red blood cells from sickling.* Cyanogenetic glycosides [cyanogens for short; sometimes called nitrilosides; see *FL* #69] were abundant in African diet, but seldom eaten in the U.S.

Cyanogens are plants that contain cyanide. Sounds scary, because we know cyanide can kill. However, our clever body employs efficient mechanisms to defuse small amounts of cyanide derived from the foods we eat. For instance, it attaches cyanide to a molecule of sulfur, producing nonlethal *thiocyanate* .]We get sulfur from sulfur-bearing amino acids in protein foods; "thio" is derived from the Greek word for sulfur.] In what seems like a miraculous biochemical feat, thiocyanate and other metabolites of cyanide are able to interact with hemoglobin S in red blood cells, *changing it so that the cells stay permanently unsickled.*

Normally, everyone has some thiocyanate in his or her blood, but Houston said typical levels in African blacks were as much as forty times higher than in African-Americans! Anyone who has the homozygous sickle cell gene but maintains high thiocyanate levels, he suggested, ***stands a good chance of sharply reducing the numbers of red blood cells undergoing sickling.*** This would explain the fewer disabling symptoms and milder nature of the disease in Africa, in contrast to its intensity in the U.S.

Anthropologist Fatimah Linda C. Jackson of the University of Florida supports this theory, based on her field work in Liberia in West Africa (*Am. J. Human Biology,* 2:521-532, 1990). She saw large numbers of villagers who had the hemoglobin S gene but didn't seem to suffer severe sickling illness with it. She thinks "cyanogen-rich cassava" may be the key foodstuff that keeps sickle cell disease under control. Cassava, also called manioc, was imported 400 years ago from South America. It grows luxuriantly, its starchy roots providing satisfying calories. The typical method of preparing the roots---pounding, crushing, and cooking---gets most of the cyanide out. ***Enough is left, however, to insure high blood levels of thiocyanate in the people who consume it, apparently protecting whoever has the sickling genes from the kind of devastating outcomes seen in the U.S.***

A Connection to Malaria

Here in the northern hemisphere we don't worry much about 'tropical' malaria, but it's been only 75 years since the control of this disease finally put an end to its ravages in southern United States and southern Europe. Malaria is ***still*** the biggest killer and cause of chronic disability in most of the world's population.

Believe it or not, sickle cell disease provides protection against malaria! The misshapen blood cells create a lousy, inhospitable environment for any malaria parasites entering a person's bloodstream (via the bite of infected mosquitoes), interfering with the parasites' life cycles and cutting down their numbers. With fewer of them thriving in the host, the disease follows a milder course.

Professor Jackson thinks there are two ways cyanogen-rich diets protect people in malaria-ridden countries. First, the diet allows carriers of sickle-cell genes to lead essentially normal lives, free of both severe sickling illness ***and*** frequent, prolonged malaria attacks. In other words, they can grow up, marry, and pass on the genes to their children! To Jackson, that explains why as many as 20 percent of the people in certain parts of Liberia carry (homozygous) hemoglobin S genes.

But there's a newer theory, borne out by her field studies, explaining

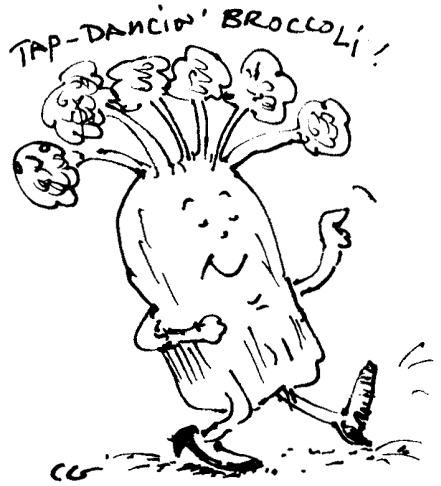
a possible *second* way that people who consume lots of cyanide-yielding foodstuffs year round can ward off the worst aspects of malaria. Cyanide and its metabolites (e.g., cyanate and thiocyanate) actually may *bind with important proteins in the malaria parasite (Plasmodium falciparum)* itself, hindering the critter's growth and development!

So, between preventing malaria parasites in the blood from running amuck, and keeping red blood cells from sickling, the cyanogenic plant foods may yet qualify as the Mother Theresas of medicinal victuals!

By the way, cassava (manioc) is only one of many edible foods which, because of their cyanide and/or thiocyanate content, can elevate a person's thiocyanate levels. **Yams, sweet potatoes, sorghum grain, millet, lima and other beans, chick peas, bamboo (including sprouts), and sugar cane all qualify.** They happen to form a big part of the diet of many black Africans. I've read medical reports of blacks *in the West Indies* who also rely heavily on these foods and cassava. They, too, have high rates of sickle cell genes with little evidence of disabling illness.

Here are more eatables that can raise blood levels of thiocyanate: **blackberries, boysenberries, raspberries, huckleberries, mung bean sprouts, alfalfa sprouts, lentils, collard greens, cabbage, broccoli, kale, buckwheat, apple seeds, apricot kernels, and flaxseed.**

We're talking about tasty, nourishing foods. What's to stop sickle cell sufferers in the U.S. from making such edibles the backbone of everyday eating? If health workers can provide the nudge to get the ball rolling, I'm hoping patients and their families will see enough results to spread the word. No quick fixes promised, just steady changes for the better, in the long term. ❑❑



MARGARINE POLITICS

More big-time corroboration on the "Say 'No!' to margarine" story hit the headlines this spring. Medical evidence is busting out all over on the harm *trans* fats do to people's cardiovascular systems. *Trans* are the technologically distorted fats that abound in margarine and other partially hardened fats, and in the tons of commercial foods prepared with them.

It looks so bad even the American Heart Association *almost* had second thoughts about giving the usual thumbs up to margarine.

Almost, but not quite. At the AHA annual epidemiology meeting last March, Dr. Alberto Ascherio of the Harvard School of Public Health in Boston described the newest heart study in which they had singled out the effects of *trans* fats. More than 500 men and women participated, 239 of whom had had heart attacks. Those whose diets were highest in "funny fats" had more than *twice* the heart attack risk of men and women with the lowest intake. Dr. Ascherio is convinced from his own and others' research that *trans* fats are dangerous. He told the AHA meeting, "We have enough evidence to recommend the elimination of margarine and reduce as much as possible the consumption of hydrogenated fats."

But the AHA is holding firm. The association said it revises its recommendations when definitive new information becomes available and that "no such change. . .is indicated at this time."

I stick by my 1984 *FL* #19 statement: "While margarines and shortenings may come in handy for greasing sled runners, ***they are by no means safe to eat.***"

Meanwhile, Ascherio suggests olive oil as a substitute for margarine. Makes sense. People in the Mediterranean area cook with it, smear it on bread, and don't have a lot of heart trouble. That's been true for thousands of years, so I feel comfortable with his recommendation. (Hydrogenation of oils to make margarine, etc. was invented in the early 1900's. The subsequent explosion in heart disease and cancer doesn't say much for its safety.)

For those who enjoy a little butter (*little* is the operative word), "Better Butter" is a homemade mix of two sticks (1/2 lb.) of melted butter and 3/4 cup salad oil, stirred well and transferred to a covered dish in the fridge. I use any good oil on hand, or any mixture: canola, flaxseed, olive, walnut, etc. After it firms up in the fridge, it spreads easily and the lovely butter flavor *always* dominates.

Reader S. S. of Oakland offers this to microwave users: "I avoid a messy pan and waste by putting the butter in an open glass storage dish in the microwave--you can see through the door when it's melted." After mixing the oil with the melted butter, she covers the dish, and puts it in the fridge. "Glass storage dishes with blue plastic covers" are her favorites. ❑❑

DIABETES & INSULIN RESISTANCE

Maturity-onset diabetes is high on the list of plagues that're mowing people down too early in life. In individuals with the ailment, blood sugar levels can skyrocket, leading to all manner of health snafus. The affliction wasn't common until a few generations ago. Oftentimes it goes hand in hand with obesity, another phenomenon that's blossoming in modern times.

Two hormones made by the pancreas—insulin and glucagon—have much to do with maintaining blood sugar (glucose) at good levels. While not everything is known about how insulin works, when secreted into the bloodstream it apparently prods the body's cells into picking up glucose and amino acids from the circulating blood. (Glucose and amino acids are what starches, sugars, and proteins in foods ultimately become after they're digested.) Insulin makes it possible for these simple molecules to move from the bloodstream into our cells, where they're used to make protein, muscle, and energy to run our inner mechanisms.

In the much rarer form of diabetes, usually seen in children and adolescents, known as 'juvenile diabetes,' daily injections of insulin are needed because the pancreas can't make enough. Many persons with maturity-onset diabetes, on the other hand, make insulin *but their muscle cells have become*

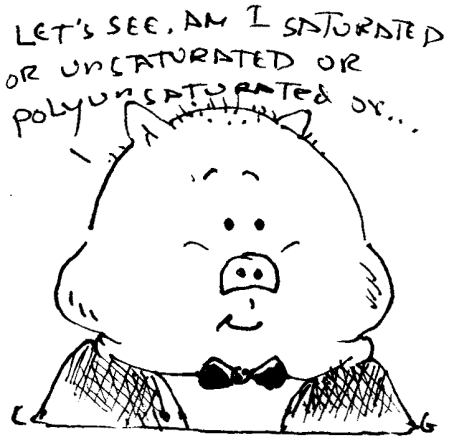
resistant to it. Even in the presence of high circulating levels of insulin, muscle cells don't pull in enough glucose and amino acids from the blood. The sugar overload then ends up spilling out in the urine. Chronically high blood sugar also triggers mechanisms leading to too much fat in the blood. Vessels clogged with fats provide poor circulation and are susceptible to atherosclerosis.

While a juvenile-onset diabetic usually is underweight and a maturity-onset diabetic overweight, both can suffer from serious *muscle wasting,* because not enough amino acids--the building blocks of protein--are getting into their muscle tissues.

Australian researchers have been working on the idea that the *fatty-acid composition of a person's cell membranes* might be one key to understanding insulin resistance. Earlier, other scientists proved that more *poly-unsaturated* fatty acids (in cell cultures) made cell membranes more flexible and responsive to insulin. When cell membranes were high in *saturated* fats, they got stiff and responded poorly to insulin.

Hmm.....interesting. The Australians' next step was finding out what would happen not just in cultured cells but in living creatures. Sure enough, *rats became insulin resistant on a high saturated fat diet.* When enough Omega-3 fatty acids were added to the animals' rations, DHA (the most polyunsaturated of all) began to show up in cell membranes in muscle. At that point, *the rats' muscle cells regained sensitivity to insulin .*

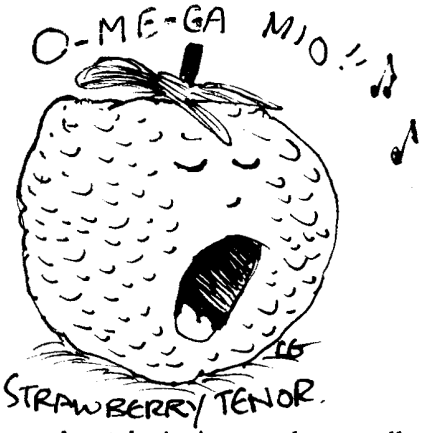
So, the next logical step for the Aussie group was to analyze fatty acids in people, to see if they could spot a similar connection. Okay, you guessed it: The more polyunsaturated fatty acids there are in an individual's cell membranes, the more responsive to insulin the cells become. Especially valuable for this are the longer chain, highly unsaturated fatty acids, from both the Omega-6 and Omega-3 families of essential fats. [*New Eng. J. Medicine,* Jan. 28, 1993, M. Borkman et al., pp 238-244.]



Diabetics aren't the only ones who suffer from insulin resistance. The problem is seen often, for example, in *obese* individuals. It's also not uncommon in those who suffer from *hypertension, high blood fats (hyper-lipidemia), or coronary artery disease.*

The Aussie scientists ask a good question: Is it possible that "abnormalities in the fatty-acid composition of membranes" are a factor in the above disorders, and that all of them are linked to insulin resistance?

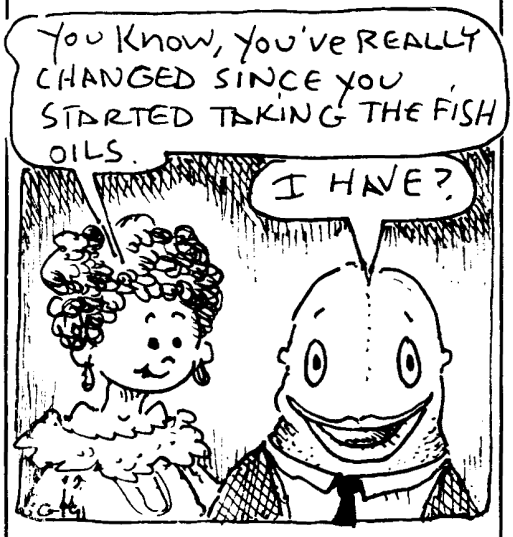
[*A Felix Letter aside:* Except for smart folks who eat a lot of fish and seafood, people in the U.S. get far too few Omega-3's for the balance that's needed in membranes. Typically, they load up daily with too many Omega-6's from margarine, salad dressing, and fried food, adding a plethora of *trans* fats from margarine and packaged stuff. *Trans* fats are listed deceptively on food labels as "unsaturated," but behave like saturated ones. With that unholy combination, average cell membranes don't stand a chance!]



From paleontologists' research, as well as studies of the world's few remaining hunter-gatherer peoples, we've learned the foods eaten by early humans gave them plenty of polyunsaturated Omega-3 and Omega-6 fats. Saturated animal fats were hard to find. (Wild game has infinitely less fat than modern domesticated animals, much of it polyunsaturated.) Fish and shellfish supplied super-polyunsaturated Omega-3's. Troublesome machine-made *trans* fats [see *FL* Nos. 69 & 55] weren't even a gleam in some pre-technologist's eye!

All we really have to remember is,*we become the fats that we eat.* Cell membranes everywhere in the body must renew themselves constantly. We can synthesize all the saturated and monounsaturated fats the body needs (plus plenty it doesn't!) from sugars, starches, and any old fats. *But we're able to make polyunsaturated fats for healthy tissues and organs only from poly-unsaturated Omega-3 and Omega-6 fats in our foodstuffs.*

It doesn't matter what age we are: when the bloodstream ships the right nutrients to our cell membranes, they acquire a new lease on life. I get a kick out of knowing that one of life's lasting pleasures -- good food -- affords us unending remodeling opportunities! ❑



FLAXSEED LONG AGO

Writer and ex-dancer Shyrle Hacker, who'll be 83 this year, grew up in rough mining country in Northern Nevada. She tells me her father used flaxseed on anything that needed a poultice, even snakebite! "Whenever I got something in my eye, my mother would put in a single flaxseed and tell me to roll my eye around. The little gelatinous seed would come out in the corner and take out any foreign object with it."

And medical researcher Dr. Artemis Simopoulostold me in her recent letter: "The ancient Greeks in making bread included linseed flour along with wheat and barley. In fact, Pliny refers to that."

❑❑

A GOOD START IN LIFE

British researcher Dr. Michael A. Crawford says modern medicine has witnessed a rapid reduction in numbers of babies dying at birth, but doesn't have enough answers yet as to why so many are being born with *handicaps* , such as cerebral palsy, poor cognitive ability, mental retardation, poor vision, and retinopathy (disorder of the retina of the eye). The effect on families and the cost to society continue to be devastating. *The highest incidence*

happens in infants of very low birth weight, those less than 3.3 pounds (1.5 kg). Out of a thousand of these tiny ones born, usually prematurely, *more than 200 will be handicapped.*

Too much oxygen used to be considered the major cause of retinopathy in preterm infants. Just the opposite-- too *little* oxygen at birth-- was thought to be the main reason for handicaps like cerebral palsy. Both assumptions are now being questioned. Crawford says the common denominator in these defects is that, in addition to their association with low birth weight, they occur ***when the brain is developing,***

The cells that become the fetus's brain and neural tissues begin dividing and growing even before the mother knows she is pregnant, Crawford said, addressing an international symposium on lipids in The Netherlands last year. (*Am. J. Clinical Nutrition,* May 1993.) ***Individual responsibility for the development of the unborn baby's brain rests with the mother,*** he emphasized. The nutrients in her bloodstream are the only sources for building all neural tissues. When the placenta develops, it "literally pumps selected nutrients into the growing fetus. At this stage, the fetal brain is consuming 70% of the dietary energy fed to it by the mother, to meet the demands for its prodigious rate of growth."

All nutrients are needed in force, **but the dominant polyunsaturated fats required for cerebral lipids are Omega-6 arachidonic acid (AA) and Omega-3 DHA.** Experiments show that chickens born with deficits of both vitamin E and Omega-3 fatty acids *become very susceptible to brain hemorrhage soon after hatching.*

Bleeding into the brain occurs in a large proportion of preterm infants. Sometimes it may repair, but in other cases it causes inflammation and damage leading to cerebral palsy and other disorders. Is there a connection to the nutrient deficits that make chicks so vulnerable to brain hemorrhage? Crawford thinks so.

Normally, during the last three months of fetal life, the brain and the network of blood vessels serving it undergo a huge growth spurt. The placenta works overtime, pumping in premium nutrients, including the long-chain polyunsaturated Omega-6 and Omega-3 fatty acids.

The crucial fact, Crawford says, is the good evidence that a baby born prematurely "is denied the substantial supply of AA and DHA that it otherwise would have received if it had remained as a fetus fed by the placenta. . . .Both these fatty acids are key components of neural and vascular membranes. . . Deficits of these fatty acids, induced by prematurity, would be expected to lead to the loss of membrane integrity manifested by hemolysis and hemorrhage."

A logical preventive approach to these tragedies, Crawford says, is to use every means possible to reduce the numbers of preterm births and tiny birth-weight infants. Basic to prenatal care is good maternal nutrition. Among 513 low-income mothers in London's East end, his research group found ominously low intakes of several vitamins, minerals, and fatty acids by mothers who gave birth to low birth-weight infants compared with moms who produced babies of optimum weight. As a matter of fact, of 44 nutrients tested in their diets, their intake of 43 of them was less than that of the mothers of the normal-weight newborns!

Still, Crawfords points out, no matter how good we get at developing ways to decrease the incidence of preterm births and too-small babies, "we will not prevent all of it nor will we prevent all neuro-developmental disorders. So the question arises, what do we do with the baby born premature or small and hence at high risk of developing some form of disorder after birth?"

We're back to infant formulas again! (See *FL* #69.) Crawford feels strongly that the long-chain polyunsaturated fats, especially AA and DHA, **added to formula,** would be beneficial in preventing bleeding into the brain. Very large amounts of DHA also are needed for normal development of brain synapses and photoreceptor membranes in the retina of the eye. *Thus, AA and DHA are important "in preventing retinopathy and blindness and encouraging full cognitive development."*

Breast milk of well-nourished mothers contains AA and DHA. ***Formula doesn't have any.*** Every encouragement should be given to provide mother's milk to preterm and tiny babies. One recent report claimed that, eight years later, kids who had gotten breast milk as premature newborns were smarter than the preemies who got formula! All tests show that even in full term infants given formula, blood levels of AA and DHA keep dropping below those of breast-fed babies. The danger of formulas lacking these fatty acids is that preterm infants already suffer a deficit of nutritional building blocks, because they were expelled too soon from the womb!

As long ago as 1977, Crawford and A.G. Hassam had recommended that long-chain EFAs [essential fatty acids] be included in formulas. Today, he says, manufacturers of formulas "take into account current information about fetal protein, mineral, and vitamin requirements. However, the one feature they have wrong is the essential fatty acid component. They do not provide the long-chain EFAs. . . .***The case that has to be justified is not the case of putting the long-chain EFAs into substitutes for human milk. The case that must be justified is leaving them out. On the evidence, their omission cannot be justified."***

A smart-aleck kid of mine said that if AA and DHA came from gasoline instead of foods, the big oil companies would manage to get them into baby formula pronto! What a cynic. ❑❑

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