the FELIX Letter
A COMMENTARY ON NUTRITION
No. 97 1998

ALL DOPED UP!

On October 25, 1972, Candace Pert, a 26-year-old mother, wife, and doctoral candidate in the pharmacology department of Johns Hopkins University, made medical history. The hunches and passion driving her lab experiments finally extracted the proof she needed that special *"opiate receptors"* for molecules like morphine, opium, and heroin *actually existed in the brain.* This could mean only only one thing: *the brain must make its own opiates* to fit these receptors. The reverberations of this discovery set off a feverish research scramble on several continents, and less than three years later scientists in Scotland triumphantly announced they had isolated and determined the structure of the brain's very own "morphine" -- an opioid molecule that fits the brain's opiate receptor and has the same effect as the drug. They named it *enkephalin,* but soon after, the term *endorphin* [for endogenous, i.e., body-made, morphine], devised by U.S. researchers, came into common usage.

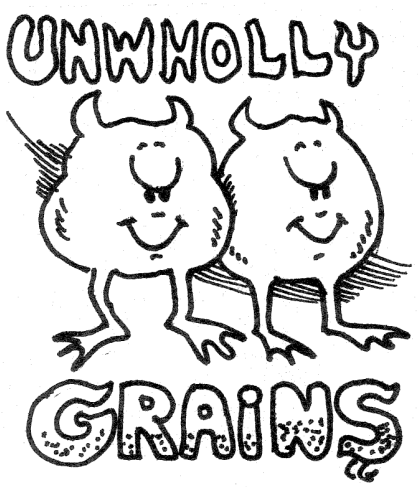
In *MOLECULES of EMOTION* (Scribner, 1997), Candace Pert, Ph.D., tells the story of this turning point and its ramifications in neuroscience as well as in her own life. Until then, the brain and nervous system had been viewed solely as an *electrical* network made up of nerve cells (neurons) with their axons and dendrites, plus neurotransmitters to convey messages by making the jump "from one neuron to another, across the little moat known as the *synaptic cleft.*" The explosion of research that followed her discovery led to recognition of a *second* nervous system, every bit as powerful as the electrical one and, in fact, more ancient in terms of evolution because it existed in living creatures long before they had neurons, or even brains!

Our "Information Molecules"

This second nervous system, more chemical than electrical, uses *receptors* and *ligands* to govern us. Receptors, now known to exist not just in our brain but in many organs and tissues, are large protein molecules the body makes out of amino acids "strung together in crumpled chains, looking something like beaded necklaces that have folded in on themselves." They hover in our cell membranes, waiting for their own special 'soul mates,' i.e., ligands, to diffuse through fluids around each cell and latch on, or bind, to them. Each 'mating' of a receptor-ligand sends a message to the cell, revving up any number and kinds of activities. "In short, the life of the cell, what it's up to at any moment, is determined by which receptors are on its surface, and whether those receptors are occupied by ligands or not," Dr. Pert writes.

The ligands we make -- much smaller than receptors -- can be one of three chemical types: *neurotransmitters* such as acetylcholine, norepinephrine, and serotonin; *steroids*, such as testosterone, progesterone, and cortisol -- all derived in the body from cholesterol; and the largest category (about 95% of all ligands) -- ***peptides***, i.e., strings of amino acids in various formulations, depending on which receptors they're designed to fit.

She writes: "In the wake of discoveries in the 1980s, these receptors and their ligands have come to be seen as 'information molecules' -- the basic units of a language used by cells throughout the organism to communicate across systems such as the endocrine, neurological, gastrointestinal, and even the immune system." (This stuff is still so new, let alone revolutionary, that I'm having to replace a bunch of my fairly recent [*expensive!*] physiology and medical textbooks because, alas, they're clueless.)



Good Endorphins & Bad Exorphins

Along with a multitude of receptors and ligands that have been or are still being identified, we know the body can make its own "feel good" opioid peptides, and that our opioid receptors not only bind enthusiastically with these homemade endorphins, but with [highly addictive] morphine, opium, and heroin (also with a nonaddictive *opiate antagonist,* naloxone, that's used in treating addicts because it latches on to the receptors and nullifies opiate drug effects). That's where the bad stuff begins. (I'm confining myself to one small negative aspect of the receptor-ligand story. Pert's panoramic work, in contrast, explores with plausible optimism the usefulness of peptide ligands--the "molecules of emotion"-- as agents of healing.)

Exorphins & Childhood Autism

We come to the troublemakers: **exorphins**. That's the term now used for exogenous [derived outside of the body], typically ***food-derived*** opioid peptide ligands, in contrast to the endogenous [self-made] endorphins or enkephalins. Sadly, the driving force behind several scientists' work was the need to explore the role exorphins played in their own autistic children's disorder. Autism is a heartbreaker. Until Dr. Bernard Rimland* and other dedicated workers subdued the psychoanalytic 'experts' by piling up solid physiological evidence of brain dysfunction, well into the 1970s the dazed parents of these often beautiful babies and toddlers were still being pummeled with the 'interpretation' that mothers had brought on the tragedy by being 'rejecting' and 'cold' to their infants! In fact, autistic babies often seem to reject their *mothers*; they may appear indifferent to, or even alarmed by cuddling, baby-talk, etc. As children, they use language oddly or not at all, display intense interest in objects but none in people, sleep poorly, resist new learning -- the list is long and painful.

Because autism and childhood schizophrenia share some similarities, researchers wondered if ***gluten*** -- a complex mixture of proteins in the grains mainly of wheat, rye, and

barley -- might be exacerbating symptoms in autistic children as it does in many schizophrenics. Although not embraced by mainstream psychiatrists, the gluten-schizophrenia connection appears to be a valid one, as shown by a number of experiments where hospital patients improved, some dramatically, on glutenfree diets. This work began long before scientists had evidence of endorphins/enkephalins. Then in the late '70s, the breakthrough happened: *opioid peptides were found that were derived from food proteins.* (Zioudrou C. et al., *J. Biol Chem* 1979;254:2446-9). After that, studies piled up pointing unerringly to gluten as a main source. When gluten is only partially digested, certain peptides -- protein fragments that are not fully broken down into their individual amino acids -- are released. Should these peptides enter the bloodstream from the gut *they can commandeer the brain's opioid receptors and act like opioids. Now we can call them exorphins.*

*Bernard Rimland, Ph.D., who pioneered the shift towards a biochemical and nutritional research and treatment focus, is director of the non-profit Autism Research Institute [ARI] and editor of its great quarterly *Autism Research Review International,* in which scientists, doctors, and parents -- and, on occasion, recovered autistic patients! -- share experiences and new treatment info. U.S. subscriptions for a year are $18 in the U.S. and $20 (U.S. funds) outside U.S. His adult son, Mark Rimland, was one of the autistic savants with whom Dustin Hoffman worked in preparing for his role as an autistic savant in the Academy Award winning film *Rain Man.* Mark's exquisite paintings are available on note cards that can be purchased from ARI. His artistic talent was not discovered until he was 21! Autism Research Institute, 4182 Adams Ave., San Diego CA 92116.

What does this have to do with autism?

It appears many autistic children have abnormally permeable mucous membranes in their intestines -- so-called "leaky gut" -- allowing ready escape of incompletely digested protein fragments into the bloodstream. Abnormal amounts of exorphins are detected in their urine, as well as in cerebrospinal fluid which bathes the brain.

How do exorphins affect these children?

Karl-L. Reichelt, M.D., Ph.D., and his pediatric research group in Oslo, Norway[1] wanted to see what would happen if exorphin-making foods were removed or restricted. They kept tabs on 19 autistic youngsters, 3 to 17 years old, for one year during which both gluten and casein-containing foods were restricted. (Yes, cow's milk protein is another exorphin source for some children.)

The research group found the year-end reports of teachers and parents to be remarkable. In a majority of the kids, "the dominant changes...are increased social contact, decreased stereotypy, an end to self-mutilation like head banging, and a decrease in 'dreamy state' periods. Alimentary problems generally improved dramatically. Normal sleep gradually replaced the fitful and sleepless states, and general ability to learn increased rapidly....An unexpected benefit was fewer epileptic episodes in 3 out of 4 patients with EEG-confirmed epilepsy..." Along with this formal study, anecdotal reports by parents in many countries indicate their autistic kids do lots better on glutenfree diets.

Exorphins are Us???

Now there's growing interest in what these exorphins may be doing to the rest of us. Clinicians are finding "leaky gut syndrome" to be somewhat common, certainly not confined to autistic persons. A number of factors (poor digestion, loss of protective nutrients, chronic unrelieved stress, overgrowth of the wrong bacteria and yeasts in the gut, too much alcohol, overconsumption of allergenic foods, etc.) can contribute to this abnormal permeability of the mucosal lining of a person's small intestine. This allows incompletely digested food molecules -- and that's what exorphins are -- to get in the bloodstream. But exorphins are unique *because they specifically can latch on to our brain's opioid receptors.* That does at least two things we know of. (1) It knocks the natural endorphins, which have many known and as yet unknown benign effects, off the receptors so we're deprived of their activity; and (2) it substitutes exorphins, which are not benign, yet are powerfully addictive!

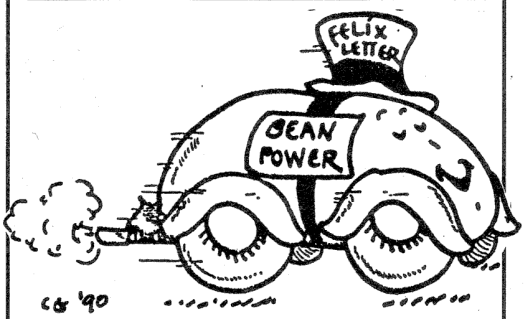
[1] Karl-L. Reichelt et al., "Gluten, milk proteins and autism: Dietary intervention effects on behavior and peptide secretion." *J of Applied Nutrition,* vol. 42, No. 1, 1990, pp 1-11.

The Way It Used To Be

Here's the crux of the matter. A typical day's meals and snacks for a majority of us now include many of these foods: breads, bagels, biscuits, crackers, cakes, cookies, dry cereals, pastas, baby foods -- all usually made with wheat flour, all widely available without much home preparation. All high-gluten. We accept this not only as normal, but as American as apple pie.

It comes as a shock to kids today to learn that a hundred or so years ago, if Mom didn't bake the stuff, or make the pasta, there wasn't any to eat! People here and in Europe got most of their carbos from home-grown beans, corn, rice, squash and root vegetables (potatoes, yams, parsnips, carrots, turnips) -- *all non-gluten.* Cakes, cookies, etc., were only for special occasions. My papa grew up poor in a little *shtetl* in the Ukraine, the last of seven children. Their foods were cabbage, potatoes, herring, buckwheat (*kashe*), millet cereal -- all non-gluten. Heavy dark rye bread was the only gluten staple. For the Sabbath his widowed mother baked a *challeh* (braided wheat bread), but only when she had enough money to buy the flour.

Also, many of the world's people until a hundred or so years ago didn't grow or import wheat, rye, or barley. Starchy staples, depending on climate and availability, were such *nongluten* foods as yams, potatoes, sweet potatoes, squash, manioc (cassava), taro, coconut, chestnuts, acorns, peas, beans, rice, corn, quinoa, buckwheat, and millet. Non-gluten fare was the natural heritage for *all* Native Americans, from Alaska to South America, all Caribbean native people, all Pacific Islanders, Filipinos, Japanese, and most Africans.



Gluten Glut!!

So now everybody lives in a Gluten-Dominant World that all accept as the norm. Slowly and grudgingly, however, medical science is beginning to peer at a phenomenon called gluten intolerance, the symptoms of which sometimes look as if they may cover the whole spectrum of mental and physical ailments. (We're talking, for starters, about bowel dysfunction, 'leaky gut,' high blood pressure, arthritis, neuralgias, infertility, epilepsy, cancerous lymphoma, kidney disease, skin rashes, *depression*, maybe even Down's Syndrome, let alone schizophrenia!)

Folks with true gluten intolerance, or celiac disease, have to avoid all gluten foods -- there's no other remedy.

But what about the rest of us who are not celiacs but merely caught up in the late 20th century's glorious gorging on gluten? Could there be consequences we're not fully aware of? (I'm not talking here about obesity, diabetes, etc.) Could we be setting ourselves up for incomplete digestion, simply out of sheer overload, of gluten's *very* complex proteins? *Could **exorphins** be escaping from our gut, leaky or not, into the blood circulation? Could we be **addicted** to gluten because of the way these exorphins affect our brain and nervous system?*

Our Own Natural Feel-Good System

Since Dr. Pert's initial detection of opiate receptors in the brain, an era of discovery began that's still in full swing. Neuroscientists are hunting down receptors for innumerable kinds of ligands all over the body, along the spinal cord (related, perhaps, to ancient Hindu *chakras,* or energy centers!), on internal organs, in the immune system, even on the skin.

Naturally, there's great interest in tracking down what specifically sets off our endorphins, since they're such big players in the body's feel-good network. Sexual orgasm is known to release endorphins, as is exercising to the point of sweating. Endorphins are nature's painkillers, many times more powerful than morphine. Conscious, controlled breathing of the kind employed by yogis of the East and by women in labor who are trained, e.g., in Lamaze technique, definitely can relieve pain, causing release of many peptides, including endorphins, from an area of the brain known to be filled with opiate receptors.

The new science of neuropeptides and their ligands still is in its infancy "as neuroscientists attempt to trace the precise connections among all the parts of the body," Pert writes. "Each of us has his or her own natural pharmacopoeia -- the very finest drugstore available at the cheapest cost -- to produce all the drugs we ever need to run our bodymind in precisely the way it was designed to run over centuries of evolution." The implications of her research are "that all exogenous drugs are potentially harmful to the system, not only as disrupters of the natural balance of the feedback loops involving many systems and organs, but because of the changes that happen at the level of the receptor."

Nullifying our Natural Endorphins

When we take in exogenous "'feel-good' ligands (e.g., alcohol, marijuana, cocaine, Valium, Librium), she says they compete for receptors with the natural ligands, oftentimes flooding the receptors, which then signal a decrease in natural peptide secretion. All such drugs "can alter the natural flow of your own feel-good peptides, and so, biochemically, there is no difference between legal and illegal ones."

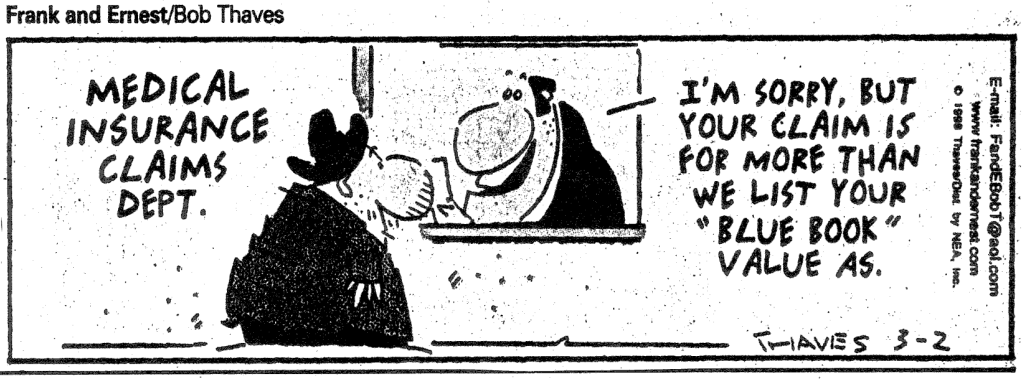
Here's a question that needs exploring related to today's humongous gluten intake; I certainly don't know the answer: If exorphins are taking over and knocking off natural endorphins from brain receptors, do we then not only lose the effects of the soothing and energizing endorphins, ***but instead depend on the kick we get from exorphins which can form when we gorge on gluten?***

An interesting effect when exorphin-making foods were taken out of the diet of the autistic kids in the Oslo experiment was an actual *worsening* of behavior in most of them during the first weeks: restlessness, agitation, anxiety, palpitations, diarrhea, sleep problems, etc. The doctors didn't comment on the cause, but a logical interpretation would be *they were suffering from drug withdrawal* --the drug being exorphins!

When their systems finally were freed of exorphins, is it possible the big improvements seen in these kids' well-being and behavior came about in some measure because normal feel-good endorphins were freer to bind to receptors?

Is the kick we get from eating gluten night and day depriving us of ***real*** well-being from home-made endorphins? We may have to go through withdrawal for a few weeks to find out! I suspect it'll be worth it. ❐

Frank and Ernest/Bob Thaves



YOU STARTED IT ALL, ADELLE DAVIS!

I don't know about the drug stores in your neighborhoods, but during one of my rare shopping forays I was amazed at how hugely both the independents and the chains have expanded their *supplement* sections here in the East Bay. I suspect, despite ominous grumbles issued routinely by medical experts about the perils of vitamin overdose, that people increasingly have been taking such matters into their own hands. After all, when someone's best friend who's 75 tells them her arthritis really got better after she took "you know, the stuff everyone's talking about -- glucosamine sulfate and chondroitin sulfate!"* folks pay attention, especially if *they've* had a few touchy joints for ten years and all their doctor ever does is tell them it's degenerative arthritis, "incurable at your age," and to keep taking nonsteroidal painkillers.

But we're dealing with a newer phenomenon here: a canny awareness on the part of the pharmaceutical industry that 'there's gold in them thar hills,' i.e., people [many doctors, too] are increasingly disillusioned with dependence on medical drugs and turning for succor to vitamins and herbal supplements -- thus, the Big Boys' new ploy: 'If you can't lick 'em, join 'em!'

Be prepared any day now, folks, to be blanketed coast to coast with media sweet-talk about "nutraceuticals" -- the market term for everything from vitamins to high-omega-3-eggs. As a matter of fact, friends sent me an article from the December 1997 *Reader's Digest,* "Herbs That Heal," that had me reeling. That bastion of conservatism has gone over to ***our*** side, extolling the virtues, e.g., of *St. John's Wort* for depression, *pycnogenol and grapeseed extracts* as antioxidants, *echinacea* when you feel a cold or flu coming on, *zinc* for all sorts of reasons, *selenium* to reduce cancer risk, and -- hold on to your hats -- ***omega-3 fatty acids*** because they're "essential to cardiovascular health and normal brain development....Low levels...also may be linked to depression and learning disabilities, and in the future, omega supplements may be involved in the prevention of these disorders."

Pinch me, I'm dreaming!!

Uh-Oh!

A clue as to what may be motivating the drug companies (besides simple greed) is the April 15 *S.F. Chronicle's* front page story, headlined very boldly: **"Warning on Deadly Drug Side Effects. Study says medications kill over 100,000 a year."** The study by Dr. Bruce Pomeranz in that week's *JAMA* says these deaths are *not* the ones due to mistakes by doctors in prescribing or administering drugs, nor to errors made by patients in using them. Rather, drug reactions occur because *"virtually all medications can have bad side effects in some people, even when taken in proper doses."* [Emphasis mine. How right you are, Dr. Candace Pert!)

The *Chronicle* story continues: "The Food and Drug Administration, which asks doctors to report adverse drug reactions, received notice of only 3,500 such deaths in 1994. And that number is not comprehensive because the reporting is voluntary."

The research, based on 39 studies in U.S. hospitals from 1966 to 1996, led to an estimate of 76,000 to 137,000 deaths a year from these (non-error-type) adverse drug reactions. Even using the lowest estimate, that makes it the *sixth leading cause of death in the U.S.*

Need I remind us this has been going on all through the years the AMA and its experts have continued to send alarms about the horrors of *vitamin* overdose?

*Here's an aside on unexpected health rewards from chondroitin sulfate (CSA) which, along with glucosamine sulfate or glucosamine HCl, is helping many people actually *heal* arthritic joints [see *FL#93*], something aspirin and other NSAIDs can't do. Veterinarians find these natural substances effective in animal patients, too. By chance, I was looking up something in Ronald S. Smith's *Nutrition, Hypertension & Cardiovascular Disease* (1989, Lyncean Press, Portland OR,) and learned that CSA, orally or intravenously, has been found in animal experiments to be protective against *atherosclerosis.* "It also has antithrombogenic [anti-abnormal blood clotting] properties and it inhibits calcification [in blood vessels]." Clinical trials by Lester Morrison, M.D., in the 1950s and '60s using oral CSA with (human) heart patients showed good protective effects. Smith says we should be eating *gristle,* along with muscle meat, when we're chomping on meat and poultry, because that's where natural cartilage ingredients like CSA abound. (I say chew the soft gristly ends of chicken bones -- dogs always do!) He says there's vegetarian CSA derived from red seaweed, described in Morrison's book, *Dr. Morrison's Heart Saver Program* (St. Martin's Press, New York, 1983).

Makes perfect sense, doesn't it, that a natural substance [our body makes it, too], employed as a dietary supplement to reverse a destructive, inflammatory process in the *joints,* will also be good for the *arteries*? Mother Nature seems to work that way. ❐

Omega 3 Oils by Donald O. Rudin, M.D. and me (Avery Publishing Group, 1996) may yet turn out to be mainstream, what with all the burgeoning nutraceutical hoopla. I'm proud of the book: it's a sound, readable, well-referenced guide to understanding the "good fats," what they do in our bodies and brains, how to use them wisely to get healthy and/or stay that way. If your book or health food store doesn't have it, tell them they're behind the times! You can also order it from Omega Nutrition's catalog, 1-800/661-3529, or from Avery, 800/548-5757 or 516/741-2155.

Illustrations by the late Clay Geerdes and other artists as noted.

THE FELIX LETTER, P.O. Box 7094, Berkeley CA 94707, has been published independently, irregularly, and improvidently by Clara Felix since 1981, supported by subscription. Descriptive list of back issues plus sample, $1. Subscriptions US & Canada: $12 six issues; $22 for 12 issues. US funds only.