Gelatin, stress, longevity

From the original article in 2009. Author: Ray Peat.

The main bulk of an animal's body consists of water, protein, fat and bones. Fat tissue and bone are metabolically more quiescent than the protein-water systems. During stress or starvation, or even hibernation, animals lose lean mass faster than fat.

The amino acids that constitute protein have many hormone-like functions in their free state. When our glucose (glycogen) stores have been depleted, we convert our own tissue into free amino acids, some of which are used to produce new glucose. The amino acids cysteine and tryptophan, released in large quantities during stress, have antimetabolic (thyroid-suppressing) and, eventually, toxic effects. Hypothyroidism itself increases the catabolic turnover of protein, even though general metabolism is slowed.

Other amino acids act as nerve-modifiers ("transmitters"), causing, for example, excitation or inhibition.

Some of these amino acids, such as glycine, have a very broad range of cell-protective actions.

Their physical properties, rather than their use for production of energy or other metabolic function, are responsible for their important cytoprotective actions.

Gelatin (the cooked form of collagen) makes up about 50% of the protein in an animal, but a much smaller percentage in the more active tissues, such as brain, muscle, and liver. 35% of the amino acids in gelatin are glycine, 11% alanine, and 21% proline and hydroxyproline.

In the industrialized societies, the consumption of gelatin has decreased, relative to the foods that contain an inappropriately high proportion of the antimetabolic amino acids, especially tryptophan and cysteine.

The degenerative and inflammatory diseases can often be corrected by the use of gelatin-rich foods.

I usually think about something for a long time before I get around to integrating it into my life, sometimes because old habits have to be changed, but usually because our social organization is set up to do things in conventional ways. Our foods reflect our social organization, enforced by laws and rules. When I first went to Mexico to study, many traditional foods were still available even in the city--fried pig skin, served crisp or boiled with a sauce, blood tacos, cartilaginous parts of various animals, chicken-foot soup, crustaceans, insects, etc. Later, when I studied biochemistry, I realized that each part of an organism has a characteristic chemistry and special nutritional value. I knew of Weston Price's research on traditional diets, and his argument that the degenerative "diseases of civilization" were produced by the simplified diets that are characteristic of the highly industrialized societies.

As I began to study endocrinology, I realized that there were some radical misconceptions behind the ideas of "scientific nutrition." I. P. Pavlov, who had studied nutritional physiology because it constituted the animal's closest interactions with its environment, was motivated by a desire to understand life in its totality, including consciousness. But western nutritionists were nearly all committed to an ideology that forced them to think in terms of "essential factors for growth," leading to ideas such as "minimum daily requirement" for each nutrient. Bodily bulk (especially body length) was the criterion, not the experienced quality of life. And there has been no scarcity of evidence showing that rapid bodily growth has its drawbacks (e.g., Miller, et al., 2002, "Big mice die young").

One of the brightest of the genetically oriented nutritionists, Roger Williams, used the idea of genetic individuality to explain that the popular idea of a species-wide standard diet couldn't be applied to exceptional individuals, and that disease was often the result of the mismatch between special nutritional requirements and a "standard" diet. Linus Pauling's concept of orthomolecular medicine was a restatement of Williams' principle for the general scientific community.

But still, the emphasis was on the match between a specific chemical and the ***genetic constitution*** of the organism. Pavlov's idea of the "trophic" actions of nerves was discarded, and the rest of his work was relegated to a crudely caricatured branch of psychology. His therapeutic recommendation of beef broth for many ailments was ignored as having nothing to do with the caricatured "Pavlovism."

If nerves are intimately involved in the processes of nutrition and development, the effects of nutrients on the nerves and their development should have a central place in nutritional research. Our appetites reflect our biochemical needs, and our "unconditional reflexes" are likely to be wiser than the theories that are based simply on the amount of weight a young animal gains on a particular diet.

When I began teaching endocrinology, some of my students didn't want to hear about anything except "lock and key" endocrinology, in which "a hormone" signals certain cells that have a suitable receptor for that hormone. But the studies of Hans Selye and Albert Szent-Gyorgyi made it clear that Pavlov's global, holistic approach to the organism in its environment was the soundest scientific basis for physiology, including endocrinology. A cell's response to a hormone depended on the state of the cell. Nutrients and metabolites and hormones and neurotransmitters all modify the cell's sensitivity to its surroundings. The assumptions of "molecular biology," as generally understood, are fundamentally mistaken.

The idea of fixed requirements for specific nutrients, and especially the idea that rapid physical growth was the way to

determine the essentiality of a substance, led to a monstrous distortion of the official dietary recommendations. Business, industry, government, and the health professions collaborated in the propagation of an ideology about nutrition that misrepresented the nature of the living organism.

Most studies of the nutritional requirements for protein have been done for the agricultural industries, and so have been designed to find the cheapest way to get the maximum growth in the shortest time. The industry isn't interested in the longevity, intelligence, or happiness of their pigs, chickens, and lambs. The industry has used chemical growth stimulants in combination with the foods that support rapid growth at least expense. Antibiotics and arsenic and polyunsaturated fatty acids have become part of our national food supply because they produce rapid weight gain in young animals.

The amino acids in proteins have been defined as “essential” on the basis of their contribution to growth, ignoring their role in producing long life, good brain development, and good health. The amino acid and protein requirements during aging have hardly been studied, except in rats, whose short life-span makes such studies fairly easy. The few studies that have been done indicate that the requirements for tryptophan and cysteine become very low in adulthood.

Although Clive McKay's studies of life extension through caloric restriction were done in the 1930s, only a few studies have been done to find out which nutrients' restriction contributes most to extending the life span. Restricting toxic heavy metals, without restricting calories, produces about the same life-extending effect as caloric restriction. **Restricting only tryptophan, or only cysteine, produces a greater extension of the life span than achieved in most of the studies of caloric restriction.** How great would be the life-span extension if both tryptophan and cysteine were restricted at the same time?

Both tryptophan and cysteine inhibit thyroid function and mitochondrial energy production, and have other effects that decrease the ability to withstand stress. Tryptophan is the precursor to serotonin, which causes inflammation, immunodepression, and generally the same changes seen in aging. Histidine is another amino acid precursor to a mediator of inflammation, histamine**;** would the restriction of histidine in the diet have a longevity promoting effect, too?

It happens that gelatin is a protein which contains no tryptophan, and only small amounts of cysteine, methionine, and histidine. Using gelatin as a major dietary protein is an easy way to restrict the amino acids that are associated with many of the problems of aging.

The main amino acids in gelatin are glycine and proline**;** alanine is also present in significant quantity. Glycine and proline are responsible for the unusual fibrous property of collagen.

An animal's body, apart from fat and water, is mostly protein, and about half of the protein in the body is collagen (which is the native, uncooked form of gelatin). Its name is derived from its traditional use as glue. It is responsible for the structural toughness of mature animal bodies.

When cells are stressed, they form extra collagen, but they can also dissolve it, to allow for tissue remodeling and growth. Invasive cancers over-produce this kind of enzyme, destroying the extracellular matrix which is needed for normal cellular differentiation and function. When collagen is broken down, it releases factors that promote wound healing and suppress tumor invasiveness. (Pasco, et al., 2003) Glycine itself is one of the factors promoting wound healing and tumor inhibition.

It has a wide range of antitumor actions, including the inhibition of new blood vessel formation (angiogenesis), and it has shown protective activity in liver cancer and melanoma. Since glycine is non-toxic (if the kidneys are working, since any amino acid will contribute to the production of ammonia), this kind of chemotherapy can be pleasant.

When we eat animal proteins in the traditional ways (for example, eating fish head soup, as well as the muscles, or “head-cheese” as well as pork chops, and chicken-foot soup as well as drumsticks), we assimilate a large amount of glycine and gelatin. This whole-animal balance of amino acids supports all sorts of biological process, including a balanced growth of children's tissues and organs.

When only the muscle meats are eaten, the amino acid balance entering our blood stream is the same as that produced by extreme stress, when cortisol excess causes our muscles to be broken down to provide energy and material for repair. The formation of serotonin is increased by the excess tryptophan in muscle, and serotonin stimulates the formation of more cortisol, while the tryptophan itself, along with the excess muscle-derived cysteine, suppresses the thyroid function.

A generous supply of glycine/gelatin, against a balanced background of amino acids, has a great variety of antistress actions. Glycine is recognized as an “inhibitory” neurotransmitter, and promotes natural sleep. Used as a supplement, it has helped to promote recovery from strokes and seizures, and to improve learning and memory. But in every type of cell, it apparently has the same kind of quieting, protective antistress action. The range of injuries produced by an excess of tryptophan and serotonin seems to be prevented or corrected by a generous supply of glycine. Fibrosis, free radical damage, inflammation, cell death from ATP depletion or calcium overload, mitochondrial damage, diabetes, etc., can be prevented or alleviated by glycine.

Some types of cell damage are prevented almost as well by alanine and proline as by glycine, so the use of gelatin, rather than glycine, is preferable, especially when the gelatin is associated with its normal biochemicals. For example, skin is a rich source of steroid hormones, and cartilage contains “Mead acid,” which is itself antiinflammatory.

The other well-studied inhibitory neurotransmitter is GABA, so it's significant that GABA (gamma amino butyric acid) is a close analog of glycine (alpha amino acetic acid). A synthetic molecule structurally similar to those natural inhibitory “transmitters,” beta amino propanoic acid, has some of the protective effects of glycine and GABA. The other molecules in the series, at least up to epsilon amino caproic acid, have some of the same antiinvasive, antiinflammatory, anti-angiogenic, properties. Alanine and proline, with cell-protecting actions, have the same basic composition, carbon (CH_2 or CH) atoms

separating acid and amino groups. Even the amino acids in which the lipophilic carbon atoms extend out in a branched side-chain, valine, leucine, and isoleucine, have some of the antiseizure (inhibitory) action (Skeie, et al., 1992, 1994) of GABA and glycine. Tests done with one, or a few, of the relatively lipophilic (aliphatic) amino acids prevent seizures, while the "balanced" mixtures of amino acids permit seizures; unfortunately, results of this sort haven't led researchers to question the idea of "balance" that developed within the setting of agricultural research.

The similarity between the structures and actions of glycine and GABA suggest that their "receptors" are similar, if not identical. For years, it has been known that progesterone and pregnenolone act on the GABA receptor, to reinforce the protective, inhibitory effects of GABA. Estrogen has the opposite effect, inhibiting GABA's action. Since GABA opposes estrogen and inhibits the growth of breast cancer, it wouldn't be surprising if glycine, alanine, etc., did the same.

Recent research shows that progesterone and its metabolites also act on the "glycine receptor," increasing inhibition, and that the "phytoestrogen," genistein, antagonizes the inhibitory effect of glycine.

The inhibitory systems are opposed by excitatory systems, especially by the excitatory amino acid system, activated by glutamic and aspartic acid. Progesterone and estrogen act on that system, too, decreasing and increasing excitation, respectively.

I have previously discussed the arguments for viewing progesterone as a "cardinal adsorbent" (as in Ling and Fu, 1987, 1988, Ling, et al., 1984, a steroid alters glycine's influence on the cell's electrical behavior) which increases the lipophilic, fat-loving property of the cytoplasm, and estrogen as having the opposite action, increasing the water-loving hydrophilic quality of the cytoplasm. If we think of the proteins known as the GABA and glycine receptors as having some regions in which the basic amine of lysine associates with the acidic group of aspartic or glutamic acid, then the action of glycine, or other amino acids would be to introduce additional lipophilic carbon atoms into those regions (with the amino acids' polar ends pairing with their opposites on the protein), where the cardinal adsorbents exert their influence.

Generally, biologists seem puzzled by such facts, because they don't fit into the "lock and key" model of molecular biology. But I think they make the organism easier to understand, since these constellations of facts illustrate simple and general physical principles. They suggest the idea that estrogen and progesterone and glycine, GABA, etc., will be active in any functioning cell, at a suitable concentration. It was this kind of thinking in terms of general physical principles that led Szent-Gyorgyi to investigate the effects of estrogen and progesterone on heart physiology. The old characterization of estrogen and progesterone as "sex" and "pregnancy" hormones acting on a few tissues through specific receptors never had a good basis in evidence, but the accumulated evidence has now made those ideas impossible for an informed person to accept. (Progesterone increases the heart's pumping efficiency, and estrogen is antagonistic, and can produce cardiac arrhythmia.)

In the context of the excitatory actions of estrogen, and the inhibitory action of glycine, it would be reasonable to think of glycine as one of the antiestrogenic substances. Another type of amino acid, taurine, is structurally similar to glycine (and to beta amino propanoic acid, and to GABA), and it can be thought of as antiestrogenic in this context. The specific kinds of excitation produced by estrogen that relate to reproduction occur against a background of very generalized cellular excitation, that includes increased sensitivity of sensory nerves, increased activity of motor nerves, changes in the EEG, and, if the estrogen effect is very high, epilepsy, tetany, or psychosis.

Glycine's inhibitory effects appear to oppose estrogen's actions generally, in sensory and motor nerves, in regulating angiogenesis, and in modulating the cytokines and "chemokines" that are involved in so many inflammatory and degenerative diseases, especially tumor necrosis factor (TNF), nitric oxide (NO), and prostaglandins. Exposure to estrogen early in life can affect the health in adulthood, and so can an early deficiency of glycine. The degenerative diseases can begin in the earliest years of life, but because aging, like growth, is a developmental process, it's never too late to start the corrective process.

One of estrogen's "excitatory" effects is to cause lipolysis, the release of fatty acids from storage fat; it directs the conversion of glucose into fat in the liver, so that the free fatty acids in the circulation remain chronically high under its influence. The free fatty acids inhibit the oxidation of glucose for energy, creating insulin resistance, the condition that normally increases with aging, and that can lead to hyperglycemia and "diabetes."

Gelatin and glycine have recently been reported to facilitate the action of insulin in lowering blood sugar and alleviating diabetes. Gelatin has been used successfully to treat diabetes for over 100 years (A. Guerard, Ann Hygiene 36, 5, 1871; H. Brat, Deut. Med. Wochenschrift 28 (No. 2), 21, 1902). Glycine inhibits lipolysis (another antiexcitatory, "antiestrogenic" effect), and this in itself will make insulin more effective, and help to prevent hyperglycemia. (A gelatin-rich diet can also lower the serum triglycerides.) Since persistent lipolysis and insulin resistance, along with a generalized inflammatory state, are involved in a great variety of diseases, especially in the degenerative diseases, it's reasonable to consider using glycine/gelatin for almost any chronic problem. (Chicken foot soup has been used in several cultures for a variety of ailments; chicken foot powder has been advocated as a stimulant for spinal cord regeneration--Harry Robertson's method was stopped by the FDA).

Although Hans Selye observed as early as the 1930s that stress causes internal bleeding (in lungs, adrenals, thymus, intestine, salivary and tear glands, etc.), the medical establishment, which has the opportunity to see it after surgery, burns or other trauma, and following strokes and head injuries, prefers to explain it by "stomach hyperacidity," as if it were limited to the stomach and duodenum. And the spontaneous bruising, and easy bruising, that is experienced by millions of women, especially with the premenstrual syndrome, and nose bleeds, and scleral bleeding, purpura senilis, urinary bleeding, bleeding gums, and many other kinds of "spontaneous" or stress related bleeding, are treated by main-line medicine as if they had no particular physiological significance.

Stress is an energy problem, that leads to the series of hormonal and metabolic reactions that I have often written about--

lipolysis, glycolysis, increased serotonin, cortisol, estrogen, prolactin, leaky capillaries, protein catabolism, etc. The capillaries are among the first tissues to be damaged by stress.

Although Selye showed that estrogen treatment mimics shock and stress, and that progesterone prevents the stress reaction, the effects of these hormones on the circulatory system have never been treated systematically. Katherina Dalton observed that progesterone treatment prevented the spontaneous bruising of the premenstrual syndrome; Soderwall observed that estrogen caused enlargement of the adrenals, sometimes with hemorrhage and necrosis; old female animals often have bleeding in the adrenals (Dhom, et al., 1981). Strangely, estrogen's induction of uterine bleeding has been compartmentalized, as if the endometrial blood vessels didn't follow the same rules as vessels elsewhere in the body. Both estrogen and cortisol are known to cause clotting disorders and to increase capillary fragility, but these steroids have been elevated to the realm of billion dollar drug products, beyond the reach of ordinary physiological thinking. Other stress-released substances that are entangled in the drug market (tryptophan, serotonin, nitric oxide, and unsaturated fats, for example) are similarly exempt from consideration as factors in circulatory, neoplastic, and degenerative diseases.

At the time Selye was observing stress-induced bleeding, standard medicine was putting gelatin to use--orally, subcutaneously, and intravenously--to control bleeding. Since ancient times, it had been used to stop bleeding by applying it to wounds, and this had finally been incorporated into medical practice.

The 1936 Cyclopedia of Medicine (G.M. Piersol, editor, volume 6) mentions the use of gelatin solution to quickly control nosebleeds, excessive menstrual bleeding, bleeding ulcers (using three doses of 18 grams as a 10% solution during one day), and bleeding from hemorrhoids and the lower bowel, and hemorrhage from the bladder. But since Selye's work relating the thrombohemorrhagic syndromes to stress wasn't known at that time, gelatin was thought of as a useful drug, rather than as having potentially far-reaching physiological effects, antagonizing some of the agents of stress-induced tissue damage.

Skin cells and nerve cells and many other cells are “electrically” stabilized by glycine, and this effect is currently being described in terms of a “chloride current.” A variety of mechanisms have been proposed for the protective effects of some of the amino acids, based on their use as energy or for other metabolic purpose, but there is evidence that glycine and alanine act protectively without being metabolized, simply by their physical properties.

A small dose of glycine taken shortly after suffering a stroke was found to accelerate recovery, preventing the spreading of injury through its inhibitory and antiinflammatory actions. Its nerve-stabilizing action, increasing the amount of stimulation required to activate nerves, is protective in epilepsy, too. This effect is important in the regulation of sleep, breathing, and heart rhythm.

Glycine's antispastic activity has been used to alleviate the muscle spasms of multiple sclerosis. It is thought to moderate some of the symptoms of schizophrenia.

A recent publication shows that glycine alleviates colitis; but the use of gelatin, especially in the form of a concentrated gelatinous beef broth, for colitis, dysentery, ulcers, celiac disease, and other diseases of the digestive system, goes far back in medical history. Pavlov's observation of its effectiveness in stimulating the secretion of digestive juices occurred because the stimulating value of broth was already recognized.

Although I pointed out a long time ago the antithyroid effects of excessive cysteine and tryptophan from eating only the muscle meats, and have been recommending gelatinous broth at bedtime to stop nocturnal stress, it took me many years to begin to experiment with large amounts of gelatin in my diet. Focusing on the various toxic effects of tryptophan and cysteine, I decided that using commercial gelatin, instead of broth, would be helpful for the experiment. For years I hadn't slept through a whole night without waking, and I was in the habit of having some juice or a little thyroid to help me go back to sleep. The first time I had several grams of gelatin just before bedtime, I slept without interruption for about 9 hours. I mentioned this effect to some friends, and later they told me that friends and relatives of theirs had recovered from long-standing pain problems (arthritic and rheumatic and possibly neurological) in just a few days after taking 10 or 15 grams of gelatin each day.

For a long time, gelatin's therapeutic effect in arthritis was assumed to result from its use in repairing the cartilage or other connective tissues around joints, simply because those tissues contain so much collagen. (Marketers suggest that eating cartilage or gelatin will build cartilage or other collagenous tissue.) Some of the consumed gelatin does get incorporated into the joint cartilage, but that is a slow process, and the relief of pain and inflammation is likely to be almost immediate, resembling the antiinflammatory effect of cortisol or aspirin.

Inflammation produces fibrosis, because stress, hypoxia, and inadequate supply of glucose stimulate the fibroblasts to produce increased amounts of collagen. In lungs, kidneys, liver, and other tissues, glycine protects against fibrosis, the opposite of what the traditional view would suggest.

Since excess tryptophan is known to produce muscle pain, myositis, even muscular dystrophy, gelatin is an appropriate food for helping to correct those problems, simply because of its lack of tryptophan. (Again, the popular nutritional idea of amino acids as simply building blocks for tissues is exactly wrong--muscle protein can exacerbate muscle disease.) All of the conditions involving excess prolactin, serotonin, and cortisol (autism, postpartum and premenstrual problems, Cushing's disease, "diabetes," impotence, etc.) should benefit from reduced consumption of tryptophan. But the specifically antiinflammatory amino acids in gelatin also antagonize the excitatory effects of the tryptophan-serotonin-estrogen-prolactin system.

In some of the older studies, therapeutic results improved when the daily gelatin was increased. Since 30 grams of glycine was commonly used for treating muscular dystrophy and myasthenia gravis, a daily intake of 100 grams of gelatin wouldn't seem unreasonable, and some people find that quantities in that range help to decrease fatigue. For a growing child, though, such a large amount of refined gelatin would tend to displace other important foods. The National Academy of Sciences

recently reviewed the requirements for working adults (male and female soldiers, in particular), and suggested that 100 grams of balanced protein was needed for efficient work. For adults, a large part of that could be in the form of gelatin.

If a person eats a large serving of meat, it's probably helpful to have 5 or 10 grams of gelatin at approximately the same time, so that the amino acids enter the blood stream in balance.

Asian grocery stores are likely to sell some of the traditional gelatin-rich foods, such as prepared pig skin and ears and tails, and chicken feet.

Although the prepared powdered gelatin doesn't require any cooking, dissolving it in hot water makes it digest a little more quickly. It can be incorporated into custards, mousses, ice cream, soups, sauces, cheese cake, pies, etc., or mixed with fruit juices to make desserts or (with juice concentrate) candies.

Although pure glycine has its place as a useful and remarkably safe drug, it shouldn't be thought of as a food, because manufactured products are always likely to contain peculiar contaminants.

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"In recent years, evidence has mounted in favor of the antiinflammatory, immunomodulatory and cytoprotective effects of the simplest amino acid L-glycine." "Glycine protects against shock caused by hemorrhage, endotoxin and sepsis, prevents ischemia/reperfusion and cold storage/reperfusion injury to a variety of tissues and organs including liver, kidney, heart, intestine and skeletal muscle, and diminishes liver and renal injury caused by hepatic and renal toxicants and drugs. Glycine also protects against peptidoglycan polysaccharide-induced arthritis..." and inhibits gastric secretion "....and protects the gastric mucosa against chemically and stress-induced ulcers. Glycine appears to exert several protective effects, including antiinflammatory, immunomodulatory and direct cytoprotective actions. Glycine acts on inflammatory cells such as macrophages to suppress activation of transcription factors and the formation of free radicals and inflammatory cytokines. In the plasma membrane, glycine appears to activate a chloride channel that stabilizes or hyperpolarizes the plasma membrane potential. As a consequence, ... opening of ... calcium channels and the resulting increases in intracellular calcium ions are suppressed, which may account for the immunomodulatory and antiinflammatory effects of glycine. Lastly, glycine blocks the opening of relatively non-specific pores in the plasma membrane that occurs as the penultimate event leading to necrotic cell death."

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