



## ARTICLE

### **Meat physiology, stress, and degenerative physiology**

The US Department of Agriculture claims that the Pure Food and Drugs Act of 1906 and the Meat Inspection Act of the same year were passed because the food industry demanded them. Ordinary historians believe that Upton Sinclair's 1905 serial publication of his novel about the meat industry, *The Jungle*, caused the public and Theodore Roosevelt to pressure Congress to pass the laws. Sinclair's descriptions of the use of poisonous preservatives and deodorants to disguise the smell of rotten meat angered the public and the president enough to overcome the industry pressure that had kept the US Congress from regulating the commercial food supply long after European governments had begun regulating food production and sales.

Before the government's intervention, it was common practice to soak all kinds of meat in water or chemical solutions to increase their weight. At present, the US Department of Agriculture, through the mass media and funding the training of food technologists and "meat scientists," now takes the position that it is natural for meat to leak water after it is packaged, and says it is perfectly legal for meat producers to soak the meat in water with chemicals until it has increased its weight by 8%. The chemicals, such as trisodium phosphate (in a solution strength as high as 12%), are chosen because they powerfully stimulate swelling and water retention. Considerable amounts of some chemicals, such as sodium citrate, are allowed to add to the weight of the meat. The use of ozone and hydrogen peroxide to deodorize meat causes instantaneous oxidative changes, including lipid peroxidation and protein carbonyl formation, as well as increasing water retention.

Most supermarket meat is now packaged with thick diapers so the buyer won't notice that he is paying for a sizeable amount of pink water. The USDA has an internet site, and consumer hotlines, to inform angry consumers that they are mistaken if they believe that meat shouldn't leak. They explain that meat is now "bred" to contain less fat, and so it contains more water, and that it is simply the leanness of the meat that accounts for its poor flavor.

Before the slaughtered animal is put into the soaking solution to gain a specific amount of weight, the animal has almost always been treated in ways that cause it to go to slaughter in a state of massive edema. Even before the meat is soaked, the animal has been treated to maximize its water retention.

Muscle physiologists and endocrine physiologists know that fatigue, stress and excess estrogen can cause the tissues to swell hugely, increasing their weight and water content without increasing their protein content.

As soon as cheap synthetic estrogens, such as DES, became available in the 1940s, their use in animals was promoted because it was clear that they caused massive water retention. Women who suffer from

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hyperestrogenism always have a problem with water retention, but they have never been known to suffer from over-developed skeletal muscles. In fact, in humans of both sexes, an excess of estrogen has been commonly associated with sarcopenia, muscular dystrophy, and atrophy of the skeletal muscles. Similar observations have been made in a variety of animals. Meat scientists are the only people I know of who have ever referred to estrogen as an anabolic steroid, in the sense of "building muscle."

When it was publicized around 1970 that DES is powerfully carcinogenic, after it had been used for several decades in the meat industry, its use was outlawed, but its illegal use continued and was overlooked by the US government. The Swiss government has rejected meat from a large producer in Kansas because it contained DES. Other estrogens are openly used, and the US government continues to apply pressure to other countries to accept meat exports containing estrogens.

There are many ways to increase the water content of meat, besides feeding estrogen to the animal and soaking the meat after slaughter. Everything that causes water retention and tissue swelling in the living animal, that is, every kind of stress, fatigue, poisoning, malnutrition and injury, will make the animal gain weight, without consuming expensive nutritious food. Crowding, fright, and other suffering increase water retention and accelerate the breakdown of fats and proteins.

The water content of meat shouldn't be increased by any of those methods, not only because it is a form of stealing from the consumer, but because it makes the product toxic and unappetizing, and makes the production process a degrading experience.

Any chemicals, such as estrogen or arsenic, that remain in the meat are of course harmful to the consumer, but the changes they produce in the animals' tissues are the main problem. When grains and soybeans are used for fattening animals, their characteristic fatty acids are present in the meat, and are harmful to the consumer, but their complex degradation products, such as isoprene, acrolein, and isoprostanes, remain, along with the complex changes they induce in every aspect of the tissue. The reactive products of oxidative fat degradation stimulate, among other things, the adaptive/defensive production of polyamines, small molecules derived from amino acids. The polyamines, in turn, can be oxidized, producing highly toxic aldehydes, including acrolein (Sakata, et al., 2003). These molecules stimulate cell multiplication, and alter, at least temporarily, the way the cell's genes function.

An excess of water stimulates cell division, and an important mechanism in producing that effect is the increased production of polyamines by the enzyme ornithine decarboxylase. This enzyme is activated by an excess of water (hypotonicity), by estrogen, and by stress.

Besides stimulating cell division and modifying the cell's state of differentiation (including developmental imprinting), the polyamines also contribute to nerve cell excitation and excitotoxicity. Estrogen and excess water can contribute to nerve cell excitation, for example producing convulsive seizures. The polyamines are increased during seizures, and they can affect the stability of the nerve cells, for example contributing to cocaine's seizure-sensitizing action. Although they tend to block free radicals, they accelerate nerve injury (Yatin, et al., 2001), and can contribute to breakdown of the blood-brain barrier (Wengenack, et al., 2000, Koenig, et al., 1989).

The polyamines are increased in cancers, and therapies to block their

formation are able to stop the growth of various cancers, including prostate, bowel, and breast cancer. Metabolites of the polyamines in the urine appear to be useful as indicators of cancer and other diseases. (In pancreatic cancer, Yamaguchi, et al., 2004; in cervical cancer, Lee, et al., 2003; in adult respiratory stress syndrome, Heffner, et al., 1995.) The quantity of polyamines in the urine of cancer patients has been reported to be 20 times higher than normal (Jiang, 1990). Polyamines in the red blood cells appear to indicate prognosis in prostate cancer (Cipolla, et al., 1990).

The prostaglandins in semen have been suspected to have a role in producing cervical cancer (Fernandez, et al., 1995).

In protein catabolism, one fate of the protein's nitrogen is to be converted to the polyamines, rather than to urea. In plants, at least, these small molecules help cells to balance osmotic stresses.

Adding water to meat, or stressing the animals before slaughter, will increase the meat's content of the polyamines, but the longer the meat is stored, the greater will be the production of reactive oxygen products and polyamines.

The deliberate "aging" of meat is something that the meat scientists often write about, but it has a peculiar history, and is practiced mainly in the English speaking cultures. When a supermarket in Mexico City began selling U.S.-style meat for the American colony, I got some T-bone steaks and cooked them for some of my Mexican friends. The meat wasn't water-logged (it was 1962, and the beef had been grown in Mexico), but it had been aged for the American customers, and though my friends ate the steaks for the sake of politeness, I could see that they found it difficult.

In Mexico, even in the present century, butcher shops often don't have refrigeration, and they don't need it because they sell the meat immediately. The fresh meat tastes fresh. Traditionally, liver is sold only on the day of slaughter, because its high enzyme content causes it to degrade much faster than the muscle meats. When it is fresh, it lacks the characteristic bad taste of liver in the US.

Both the liver and the muscles contain a significant amount of glycogen when they are fresh, if the animal was healthy. At first, the lack of oxygen causes the glycogen to be metabolized into lactic acid, and some fatty acids are liberated from their bound form, producing slight changes in the taste of the meat. But when the glycogen has been depleted, the anaerobic metabolism accelerates the breakdown of proteins and amino acids.

In the absence of oxygen, no carbon dioxide is produced, and the result is that the normal disposition of ammonia from amino acids as urea is blocked, and the polyamines are formed instead. The chemical names of two of the main poly-amines are suggestive of the flavors that they impart to the aging meat: Cadaverine and putrescine. After two or three weeks of aging, there has been extensive breakdown of proteins and fats, with the production of very complex new mixtures of chemicals.

Mexicans, despite their low average income, have a very high per capita consumption of meat, as do several other Latin American countries. Argentina has a per capita meat consumption of nearly a pound a day. There is a lot of theorizing about the role of meat in causing cancer, for example comparing Japan's low mortality from prostate cancer, and their

low meat consumption, with the high prostate cancer mortality in the US, which has a higher meat consumption. But Argentina and Mexico's prostate cancer mortality ranks very favorably with Japan's.

If meat consumption in the US contributes to the very high cancer rate, it clearly isn't the quantity of meat consumed, but rather the quality of the meat.

The polar explorer Vilhjalmur Stefansson was interested in the health effects of a diet based on meat, because of his observation that fresh meat prevented scurvy much more effectively than the fruits and vegetables carried by other polar explorers. He commented on the importance of culture and learning in shaping food preferences:

"In midwinter it occurred to me to philosophize that in our own and foreign lands taste for a mild cheese is somewhat plebeian; it is at least a semi-truth that connoisseurs like their cheeses progressively stronger. The grading applies to meats, as in England where it is common among nobility and gentry to like game and pheasant so high that the average Midwestern American or even Englishman of a lower class, would call them rotten.

"I knew of course that, while it is good form to eat decayed milk products and decayed game, it is very bad form to eat decayed fish. I knew also that the view of our populace that there are likely to be "ptomaines" in decaying fish and in the plebeian meats; but it struck me as an improbable extension of the class-consciousness that ptomaines would avoid the gentleman's food and attack that of a commoner.

"These thoughts led to a summarizing query; If it is almost a mark of social distinction to be able to eat strong cheeses with a straight face and smelly birds with relish, why is it necessarily a low taste to be fond of decaying fish? On that basis of philosophy, though with several qualms, I tried the rotten fish one day, and if memory serves, liked it better than my first taste of Camembert. During the next weeks I became fond of rotten fish."

Since Stefansson's observations nearly a century ago, most Americans have become accustomed to the taste of half-spoiled meat, as part of the process of adapting to an industrial-commercial food system. Tests done by food technologists have found that most Americans prefer the taste of synthetic strawberry flavor in ice cream to the taste of ice cream made with real strawberries. If it took Stefansson only a few weeks to become fond of rotten fish, it isn't surprising that the public would, over a period of many decades, learn to enjoy a diet of stale foods and imitation foods.

Polyamines are increased in stressed and stored vegetables, as in aged meats. This defensive reaction retards tissue aging, and researchers are testing the application of polyamines to fruits to retard their ripening. A plastic surgeon, Vladimir Filatov, discovered that tissue stored in the cold stimulated the healing process when used for tissue reconstruction, such as corneal transplants. He found that stressed plant tissues developed the same tissue stimulants. Another pioneer of tissue transplantation, L.V. Polezhaev, saw that degenerating tissue produced factors that seem to activate stem cells.

Although the diffusion of these stimulating factors from stressed tissues normally functions to accelerate healing and tissue regeneration, under less optimal conditions they are undoubtedly important factors in tissue

degeneration and tumor formation. For example, the bystander effect (contributing to delayed radiation damage, and producing a field of precancerous changes around a cancer), in which substances diffusing from injured tissues damage surrounding cells, involves disturbances in polyamine metabolism.

The direct, optimal effects of the polyamines are protective, but when excessive, prolonged, or without maintained cellular energy, they become harmful.

The expression of genes involves their physical arrangement and accessibility to enzymes and substrates. The negatively charged nucleic acids are associated with positively charged proteins, the histones. The very small positively charged polyamines can powerfully modify the interactions between histones and DNA. In recent years people have begun to speak of the "histone code," as a kind of expansion of the idea of the "genetic code." But the polyamines, produced in response to stress, might be thought of as a complex expansion of the "histone code."

The addition of small molecules, methyl and acetyl groups, to the large molecules can regulate the expression of genes, and these patterns can be passed on transgenerationally, or modified by stress. Barbara McClintock's "controlling factors" were mobile genes that caused the genome to be restructured under the influence of stress. Her discoveries were the same as those made by Trofim Lysenko decades earlier, and like his observations, McClintock's were angrily rejected until the 1980s, when the genetic engineering industry needed some scientific background and natural precedent for their unnatural intervention in the genome.

The brain is extremely different from a malignant tumor, and the derangements produced by stress, by high cortisol and estrogen and an excess of water, are different in the two types of organ (considering the tumor as an ad hoc organ), but the polyamines have central roles in the degenerating brain and in the divergent disorganization of tumors. Their importance in stress physiology is coming to be recognized, along with the meaning of "epigenetic development," in which the influence of the environment becomes central, rather than just a place in which the "genotype" is allowed to passively express its "genetic potential." Every developmental decision involves an evaluation of resources and their optimal marshaling for adaptation. The polyamines are part of the cytoplasm's equipment for controlling the genome. The ratio between the different types of polyamine governs the nature of their regulation of cellular functions.

The old idea, "one is what one eats," has evolved far beyond ideas of simple nutritional adequacy or deprivation, and it's now commonly accepted that many things in foods have fairly direct effects on our brain transmitters and hormones, such as serotonin, dopamine, adrenalin, endorphins, prostaglandins, and other chemicals that affect our behavior and physiology.

In 1957 James McConnell discovered that when flatworms were fed other flatworms that had been trained, their performance was improved by 50%, compared with normal flatworms. Later, similar experiments were done with rats and fish, showing that tissue extracts from trained animals modified the behavior of the untrained animals so that it approximated that of the trained animals. Georges Ungar, who did many experiments with higher animals, demonstrated changes in brain RNA

associated with learning, and he and McConnell believed that proteins and peptides were likely to be the type of substance that transmitted the learning.

A dogmatic belief that "memory molecules" would be unable to penetrate the "blood-brain barrier" allowed most biologists to dismiss their work. Ungar's death, and the hostility of most biologists to their work, have caused their ideas to be nearly forgotten for the last 30 years. Negatively charged molecules such as ordinary proteins tend to be repelled by negative charges on the wall of capillaries, but positively charged molecules spontaneously associate with cellular proteins, and easily penetrate the barrier. Highly positively charged molecules tend to concentrate in the brain (Jonkman, et al., 1983), and people are currently attempting to use the principle to deliver antibodies (which are normally excluded from the brain) therapeutically to the brain by combining them with small positively charged molecules (Herve, et al., 2001). This affinity of the brain for positively charged molecules is gradually being recognized as an important factor in the toxicity of ammonia and guanidine derivatives. As mentioned earlier, even endogenous polyamines can be involved in disruption of the blood-brain barrier.

So, apart from the question of exactly what molecules were responsible for the learning transfer produced by McConnell and Ungar, there should be no doubt that polyamines derived from food can enter tissues, especially the brain. People who eat meat from stressed animals are substantially replicating the experiments of McConnell and Ungar, except that people normally eat a variety of foods, and each type of food will have had slightly different experiences in its last days of life. But the deliberate aging of meat is subjecting it to a standardized stress--two or three weeks of cold storage. Because of the great generality of genetic processes, it wouldn't be surprising if cold storage of vegetables turned out to produce polyamine patterns similar to those of cold storage meats. Air pollution and other stressful growing conditions cause vegetables to have very high levels of polyamines.

Prolonged exposure to certain patterns of polyamines might produce particular syndromes, but the mere fact of increasing the total quantity of polyamines in our diet is likely to increase the incidence of stress-related diseases. Experiments with cells in culture show that added polyamines can produce a variety of extremely harmful changes, but so far, there has been almost no investigation of their specific regulatory functions, of their "code."

Besides rejecting stale foods produced under stressful conditions, there are probably some specific ways that we can protect ourselves from polyamine poisoning.

When the organism is functioning efficiently, its respiration is producing an abundance of carbon dioxide, which protectively modifies many systems and structures. Adequate carbon dioxide protects against fatigue, cellular and vascular leakiness, edema and swelling.

Increasing carbon dioxide will tend to direct ammonia into urea synthesis, and away from the formation of polyamines. Bicarbonate protects against many of the toxic effects of ammonia, and since carbon dioxide spontaneously reacts with amino groups, it probably helps to inactivate exogenous polyamines. This could account for some of the protective effects of carbon dioxide (or high altitude), for example its anti-seizure, anticancer, and antistress effects.



Other things that protect against excessive polyamines are procaine and other local anesthetics (Yuspa, et al., 1980), magnesium, niacin, vitamin A, aspirin, and, in some circumstances, caffeine. Since endotoxin stimulates the formation of polyamines, a diet that doesn't irritate the intestine is important. Tryptophan and methionine contribute to the formation of polyamines, so gelatin, which lacks those amino acids and is soothing to the intestine, should be a regular part of the diet.

Because the polyamines intensify the neurotoxic and carcinogenic effects of estrogen and of polyunsaturated fats, those three types of substance should be considered as a functional unit in making food choices. (Grass-fed organic beef fresh from a local farm would be a reasonable choice.) Unfortunately, the meat industry has maximized all of those dangers, just for the increased weight of their product.

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