Si sel à diviser peu besoin de surrénales

le sel ultra important Pour recharger les surrénales

Prog régularise le niveau de sodium

Ray Peat's Newsletter

Le stress ultime c'est le Shock. Pour pas mourir il faut ↑ énergie

Recharging the System

Adelle Davis wrote about the importance of increased salt intake in adrenal failure, and animal experimenters have demonstrated that with adequate sodium and sugar, animals can function normally without their adrenals. Hans Selye demonstrated that progesterone supplements keep animals healthy for their entire life after their adrenals have been removed. Among its many effects, progesterone regulates the levels of sodium and glucose.

Progesterone is both an antistress hormone and an antishock hormone; shock is the state that occurs when our defenses are down, and stress is just a little higher on the scale of resistance, and neither will occur when our resources are adequate. In any bad biological situation, estrogen is likely to accumulate, interfering with energy production, causing blood to pool in the legs, causing water retention and sodium loss.

> "The essence" of shock "seems to be a relative disappearance of blood from the heart and great vessels, so that the heart has not sufficient fluid on which to contract. Much used to be written about 'the mystery of the lost blood.'" W. Boyd, A Text-Book of Pathology, 1943.

Thyroid, progesterone, protein, and salt are powerful defenses against all sorts of stress-associated symptoms, including hot flashes, insomnia, cramps, PMS, edema, toxemia of pregnancy, low-birth-weight babies, epilepsy, heart diseases, hypertension, strokes, migraine, inflammatory diseases, hypoglycemia, fatigue and depression. The first approach to an appropriate diet would be to use **at least** a quart of milk and a quart of orange juice daily, well salted chicken broth, and frequent snacks, especially salty foods. I have written before about the importance of fruit and protein in balancing the hormones, and how adequate energy prevents stress, but I haven't talked about sodium's central biological role in sustaining our energy, and the mechanisms behind these effects of diet and hormones..

Shock is the most extreme stress-state there is, and it can shift gradually into death, as energy production ceases. Things that can bring an individual out of shock are so intimately connected with our energy production that we should understand how to use them routinely.

In shock, G. W. Crile showed that many systems, ranging from the molecular level to the nervous level, are involved, and he introduced methods of anesthesia that reduced shock. He imagined the organism--and each cell--as something like an electrical battery: The liver and the brain formed the poles of the organism-battery, and the nucleus and cytoplasm formed the cell's "poles." Exhaustion and shock, he believed, in some way "discharged" the organism's energy, causing changes in every cell.

> "The use of CO_2 for synthetic purposes by the mammalian cell is now being studied in detail; it has already taken on tremendous significance since it completely reverses the hitherto firmly accepted view that CO_2 is merely a waste product of animal metabolism. R. Levine, "Carbohydrate Metabolism," in Diseases of Metabolism, G.G. Duncan, ed., 1964.

I suspect that Crile's work on the physiology of excitement, exhaustion, and shock made Hans Selye's work on stress and adaptation "less unacceptable" to the scientific establishment than it

Shock state = l'humain n'a plus de défense

thy + prot + Prog + sel Protège contre le stress

Pour traiter le shock: Sodium, Glucose, ATP injectable, antago de morphine Naloxone

would have been without Crile's disturbing precedent. Crile warned about the shock-promoting action of morphine, and influenced the way surgery was done, but unfortunately shock is still too often thought of in a mechanical way, as something that happens to the circulatory system, and the various subsequent discoveries about treating shock have seemed too mysterious or too implausible to gain general acceptance. In the absence of a unifying picture of the organism, treatments are likely to be evaluated in terms of a fragmented aspect of the organism, and if they don't mechanically fit into that system in an obvious way, they are dismissed.

I have written previously about several dramatically effective treatments for shock that were developed in the last fifty years--for example, intravenous ATP, concentrated solutions of sodium chloride or glucose, and the morphine/endorphin-blocker, naloxone. Theoretical reasons have kept some of these techniques from being used as widely as would be appropriate, but gradually the success of the methods is forcing some people to rethink their theories.

A simple newer view of the organism's energy is being developed, and early acceptance of this new view will make it possible to approach treatment in a way that is both integrated and specific.

Although Crile and Selye were famous for their studies of the acute effects of noxious conditions, both were interested in the long-term, cumulative effects. Crile was more explicit about the general evolutionary implications of his discoveries.

One of the least scientific aspects of conventional "evolutionary thinking" is the thought that if an organism has or does something, that thing or behavior must have "survival value." People apply evolutionary explanations in a carefree way, feeling that an explanation without factual support is better than leaving something unexplained.

Shock, inflammation, aging and death have been proposed to "have survival value," because of this totalitarian view of genetics. Couldn't it be that organisms simply aren't perfect, and that some things are just systematically screwed up? That is, an organism has a certain strength, resistance, or adaptive capacity, but if it finds itself in conditions that are too difficult, then processes that never did anything to aid survival might develop, as several individually valid defensive maneuvers start to interfere with each other. "Advance" and "retreat," eat and expel, for example, are processes that have to be functionally separated; if coordination is lost, new but confused processes will emerge. On the cellular level, excitotoxicity is an example of the loss of coordination.

In 1950 Selye, and in 1953, Rees, pointed out the similarities of estrogen's effects to the physiology of stress and shock. Hundreds of studies have confirmed the details of estrogen's actions on the circulatory system, respiration, and metabolism. Since we have the genes needed for making estrogen, it might seem that there is reason to argue that shock "has a genetic basis," but the mistake occurs when that phraseology is extended to claim that "genes for (something which produces) shock prove that shock has survival value." Estrogen's survival value exists only in the context of a whole organism with multiple ways for limiting estrogen's destabilizing actions. Estrogen's harmful effects occur when our systems for opposing it fail.

Recently, there has been a dispute about the reason for the evolution of menstruation among

> Cramps, insomnia, shock, heart attacks, and many other problems could be seen as consequences of a general energy problem, if it weren't for a few dogmatically fixed ideas that are held in place by academic/bureaucratic defensiveness and arrogance. "Membranes" and "membrane pumps" are more important than (other people's) life to these dogmatists.

primates. The argument began when Margie Profet proposed that it is an anti-infective defense mechanism, a "cleansing" procedure. Culturally, this strikes me as primarily a reaction against the archaic doctrine of the "unclean" menses, and scientifically, it is hard to imagine that opening blood vessels and bathing the membranes in blood would be an anti-infective strategy; in fact, infections such as gonorrhea and chlamydia are more likely to occur after menstruation, and blood is an exceedingly good growth medium for germs. Her

response to that observation was that the prevalence of diseases such as AIDS, cholera, and tuberculosis "doesn't mean that the immune system didn't evolve to fight pathogens." I think she is wrong on both issues, the reason for evolving menstruation and the reason for evolving our immune system.*

If we can see menstruation as a side effect of the adaptations we have for producing large brains, without its own special "menstruation genes," we should also be able to see a phenomenon such as shock as something which is not biologically so useful that we "evolved" it in the sense of selecting for "shock genes." (Stumbling is a consequence of walking, and the biological point of interest is the walking, not the stumbling; any interest that stumbling has, is as a "boundary" of the ability to walk.)

My point is to suggest that shock is simply a negative thing, a failure of protective systems, a biological screw-up resulting from the same sort of inadequacy of resources that produces "excitotoxicity." *The fact that shock-like features can be seen in the hormonal effects of estrogen, and in the "normal" process of aging, leads to the thought that the body which can control the effects of estrogen should also be able to control the shock reaction and the aging process, if given the appropriate kinds of support.* Estrogen creates a bias toward cellular "excitotoxicity," since it promotes excitation while limiting energy production. Our body controls estrogen's effects by decreasing excitation while increasing efficient energy production.

The several effective methods of preventing death from shock can give us insight into this general process of the failure of life, and so into the nature of life itself.

The average biology professor is just about as unsophisticated as the average television-viewer about water in organisms--how it got there, why it stays there, what it does. The typical biologist maintains the conventional view of the cell by changing the subject whenever a fact conflicts with a doctrine. The history of the "cell membrane" shows how this mental process has worked.

At first, an oily coat was thought to account for the different composition of the watery solutions around cells, and inside cells. Then "membrane pumps" were introduced to explain the differences, because too many facts were inconsistent with the simple membrane idea. Proteins were found and identified as the pumps. Then it turned out that pumps would require energy that cells couldn't (and needn't) provide, and many ways were devised to explain the minimal energy needed to maintain the composition of cell water. But the "pump-proteins"--calcium-ATP-ase, sodium/potassium ATPase, etc.—are proteins that really exist, though their functions are much more interesting than "pumping." An important context for thinking about these ATPases is that the contractile protein of muscle (myosin) is a calcium-dependent ATPase.

The habit of biochemists has been to think of enzymes as the soluble proteins that could be extracted from cells in a watery solution, and to ignore the insoluble residue, which contained the ATPases. Now, much of the residue has been resurrected for biochemistry, under the name of "membrane proteins." The "ghost" of the red blood cell, after it has been shocked into losing its hemoglobin, is a popular lab preparation that biochemists like to call a "membrane," though the term is grossly misleading. Szent-Gyorgyi, Gilbert Ling, and a few physically conscious biologists spoke of these relatively insoluble proteins as structural proteins.

In 1968 or '69, I had been reading the previous 50 years of research on cell physiology, and I saw that for 20 years, Gilbert Ling had been almost alone in offering a view of the cell that was physically possible. He had solved the problems of ionic regulation in ways that physical chemists could accept, but biologists were proceeding as if his solutions to their problems didn't exist. I wrote to him, to see if I, as a newcomer to "science," was missing something. He said that I just didn't understand what "science" was; it was a matter of money, prestige, and influence, with little concern for what was true.

It has been calculated that the substances which are distributed unequally between cells and

the surrounding fluid would require 15 times as much energy as the cells can produce, if their distribution had to be maintained by pumps, but it has also been demonstrated that cells can remain almost at equilibrium, when their energy production is completely blocked by poisons. **Something maintains the ions and other solutes in their unequal distribution between the inside and outside of the cell, but it doesn't take energy to do it. This is why cells have been compared to ion-exchange resins, which also have the ability to passively select certain ions while excluding others.** People who have examined the atom-by-atom physics of how an ion-pump might work have demonstrated the silliness of the idea. Ion-exchange granules selectively bind certain ions that reach them by passive diffusion, and similar near-equilibrium processes can account for the ion gradients maintained by cells. The interesting difference in cells (compared to ion-exchange resins) is that their physical near-equilibrium is closely balanced with chemical processes, which are also much closer to equilibrium than conventional schemes imagine.

From observing the retarded relaxation of muscles in hypothyroidism, it is clear that low energy makes relaxation difficult.

Szent-Gyorgyi showed that muscle in rigor mortis softened when placed in ATP solution.

The failing heart becomes stiff.

Stretching a muscle increases its ATP.

Increasing the concentration of sodium, ATP, carbon dioxide, ... in the cell's environment increases its ATP content.

Filling the heart stretches it, increasing its ability to beat.

Understanding the silliness of the "pump" idea demystifies the membrane idea, and then a person can begin to think about how cells really work.

Stimulated, active cells expend energy. Besides doing measurable work, such as contraction, they release a measurable amount of heat, at the moment of responding to stimulation. Surprisingly, stimulated nerves have been observed to absorb heat immediately after releasing it, in a "refrigerator-like" process that coincides with their electrical repolarization. No one was able to explain this on the basis of membranes and pumps, since the pumps should be releasing their heat *after stimulation and during repolarization.*

I have thought of this in terms of Kelvin's idea of increased surface area leading to decreased temperature. What we need, in order to understand the way energy can be used in reestablishing the cell's resting condition without releasing heat, might be the idea that physical processes (the change of protein conformation and water structure) are intimately integrated with chemical equilibria.

Around 1970, a famous English researcher was in Eugene lecturing about his theory that the famous "high energy bond of ATP" (14 kcal, I think he said) could be used to explain muscle contraction. I had just read an old paper by one of my professors, Sidney Bernhard, which showed that its bond energy wasn't nearly so high. When I asked Bernhard why "everyone talks about ATP's high-energy bond," he just said "everyone doesn't."

When ATP breaks down it absorbs water, and when it is synthesized, water is released. In a water-free environment, the equilibrium favors the formation of ATP. The chemical activity of water in cells is lower than it is in ordinary water. Given the right (anhydrous) environment, ATP will form spontaneously. As the reactants form ATP and give up water, energy is (at least theoretically) absorbed by the chemical bond. In the abstract, this shows that the formation of ATP and the absorption of energy could be caused by factors that control the activity or availability of water. The protein-ATP complex is one of those water-regulating factors.

The abstract idea that ATP could be formed spontaneously by a "relaxing" cell (recovering from stimulation) goes against the idea that a "cell is a motor and ATP is the fuel." Some people have argued that the contraction occurs first, causing ATP to be split, rather than the reverse. Other examples of enzyme activation support this view, that the contraction or activation is a physical process, like releasing a spring. In the contracted

or activated state, sodium is able to enter the cell momentarily, and the presence of sodium seems to allow the ATP to be reformed. **These differences might seem subtle, but they have made an all-or-none difference in the minds of medical people deciding on therapies and diets.**

This picture of a cell as a loaded spring, or as analogous to the ion exchanger in a water-softener, is the sort of image I have in mind when I speak of "charging the system."

Several researchers have demonstrated that intravenous injections of ATP prevent death from shock, that shock depletes the ATP of the cells, and that depleted cells absorb ATP much more readily than normal cells that don't lack it. All of the biologists and biochemists (at Oregon's Institute for Molecular Biology) that I mentioned this to said it was impossible, "because ATP is highly ionized and can't cross the cell membrane."

Even when a general idea is clear and consistent with the facts, if it opposes the dominant view it needs some experiments that can hardly be understood without it.

Liver ATP is increased as a result of increasing blood sodium. An increase of only about 15% in the blood sodium, for example, caused the cells' ATP to nearly double. [R. L. Veech, et al., "Relationship of free cytoplasmic pyrophosphate to liver glucose content and total pyrophosphate to cytoplasmic phosphorylation potential," FEBS Lett. 117, K65-72, 1980.]

Sodium is an "extracellular" ion, one that binds water to itself so strongly that it is excluded from the cell under normal conditions, in which the water is dominated by the cell's structural molecules. It is only when the cell is stimulated or fatigued that it absorbs larger amounts of sodium, and the fatigued cell also absorbs an excess of water. The textbooks say "water follows sodium," but the physical reality is that sodium also follows (free) water, and that it tends to be excluded from the water of cells. **Increasing the sodium in the environment of a water-logged cell will tend to dehydrate the cell.**

This experiment, using sodium to increase ATP (especially when we remember that ATP is an effective treatment for shock) shows how hypertonic sodium might rescue a shock victim, increasing circulatory efficiency, helping to increase blood volume, restoring the cell's electrical and chemical resting state, and possibly regulating intracellular pH. [G.. B. Haycock, "The influence of sodium on growth in infancy," Pediatr. Nephrol. 7(6), 871-875, 1993.] The increasing blood volume is a "mechanical" effect that helps to make the use of hypertonic sodium culturally more acceptable, but it is really secondary to the other effects of sodium. The first water to be restored to the serum is that contained in red blood cells and the swollen endothelium. *Capillaries and small blood vessels that have been obstructed by swollen endothelial cells allow free passage of the blood, and the increased water lowers the blood's viscosity, improving its ability to deliver oxygen and glucose.* Brain swelling is reduced, and consciousness is restored. Glucose metabolism is also improved under these conditions.

Sodium causes the ATPase to produce ATP, rather than consuming it. (P.J. Garrahan and I. M. Glynn, "The incorporation of inorganic phosphate into adenosine triphosphate by reversal of the sodium pump," J. Physiol. 192, 237-256, 1967.; P. A. Dibrov, et al., "A study on Na+-coupled oxidative phosphorylation: ATP formation supported by artificially imposed delta pNa and delta pK in Vibrio alginolyticus cells," J. Bioenerg. Biomembr. 21(3), 347-357, 1989.)

The membrane-pump theory says that the cell *consumes* ATP to expel the sodium which enters, and increased external sodium increases its likelihood of entering the cell, but in reality increased external sodium causes more ATP to be produced. **The precise balance of ions seems to make the difference between consumption or production of ATP.** [L. Plesner, et al., "[32P]ATP synthesis in steady state from [32P]Pi and ADP by Na+/K+-ATPase from ox brain and pig kidney. Activation by K+," Biochim. Biophys. Acta 1040(2), 167-174, 1990.]

Remembering that the muscle protein is an ATPase, there is a situation that I think is analogous. When a muscle is stretched, it forms ATP, rather than consuming it. This could be the result of a slight change in the physical state of the water and small changes in chemical affinities produced

Sodium act anti-adrenaline ↑ glucose down cell ↑ choles

by the changes in protein conformation. Before this effect of stretch on ATP synthesis was directly observed, Starling's law of the heart recognized that the force of contraction increased with the initial length of the muscle fiber. Simply increasing blood volume increases the effectiveness of the heart contraction. Szent-Gyorgyi described a related process (the "staircase" phenomenon) as "function building structure, structure producing function."

Sodium is required for cells to absorb glucose and amino acids. I have recommended salty foods at bedtime to promote sleep, because of sodium's recognized anti-adrenalin effect. There are some complicated ways of thinking about its effect on adrenalin, as there are for explaining its thermogenic effect, but the simple fact that it is needed for absorbing glucose can explain its ability to lower adrenalin (since adrenalin rises when glucose is needed) and to increase heat production.

In the fetus and the newborn baby, sodium promotes growth. Progesterone, sodium and glucose are often limiting factors in the growth of the baby's brain; when they are deficient, cells die instead of growing.

The fact is that sodium energizes. It helps to remove calcium from the cell, to produce ATP, and to promote absorption of glucose and amino acids. The fear many physicians have of injecting hypertonic sodium chloride is odd, in the light of the knowledge that has accumulated in recent decades. Chloride isn't always the ideal anion, but more elaborate preparation is needed for providing the ideal ionic solution.

Carbon dioxide is powerfully involved in the regulation of both sodium and calcium, as well as in respiration and energy production.

It tends to relax both nerves and muscles. It is apparently one of the essential factors in preventing edema. [For example, in the cornea; M. V. Riley, et al., 1995.]

ATP and CO2 both bind to hemoglobin, regulating its affinity for oxygen. The way in which they bind to this protein indicates that they will bind to many other intracellular proteins, similarly regulating the functions of those proteins.

The elimination of water from the environment in which ATP is formed or decomposed favors its formation, and in this environment ATP doesn't contain its reputed "high energy bonds," but it still has its strong affinity for binding to proteins. Sodium binds water to itself, and it is this feature that leads to its exclusion from the normal cell. CO2, when it is in water, especially with the carbonic anhydrase enzymes, combines with water. As it is formed in the mitochondria, this means that it will carry water (as well as calcium and sodium) out into the cytoplasm, and out of the cell.

In many situations, including brain hypoxia, carbon dioxide is the decisive protective factor.

Low thyroid function involves reduced formation of carbon dioxide, and the body fluids don't retain as much sodium as in normal individuals. Both urine and sweat tend to contain abnormally high sodium concentration in hypothyroidism. Because CO2 is central to the regulation of pH, and hydrogen ion excretion (acid urine) is one mechanism involved in sodium retention, the CO2 deficiency of hypothyroidism is probably closely connected with the inability to retain adequate sodium.

The body fluids are actually hypotonic in hypothyroidism.

If hypertonic sodium energizes, then the low-sodium hypoosmotic fluids of hypothyroidism de-energize.

Low-thyroid cells are also unable to retain magnesium efficiently, and a magnesium deficiency prevents muscle relaxation, wasting energy. Adequate sodium prevents urinary magnesium loss.

Hypothyroidism tends to cause hypoglycemia, and the lack of glucose (even if it is because the glucose in the blood can't be absorbed because of insufficient sodium) causes elevation of adrenalin. Hypertonic sodium given intravenously lowers the amount of adrenalin in the blood, just as the thyroid hormone does.

Hypothyroidism also causes an imbalance between the antiestrogenic antishock hormones, progesterone and pregnenolone, and proshock estrogen.

The close integration of physical and chemical processes when those processes are near

equilibrium is the fact or the principle that is lacking in the doctrine that the cell is like a collection of motors, fueled by ATP. If you can imagine a Chevrolet that at times creates gasoline while absorbing heat, then the simile would be acceptable. The inappropriateness of the mental image of a cell with pumps and motors leads to the treatment of shock with things that produce shock, of heart failure with things that produce heart failure, and of aging with things that accelerate aging.

NOTE: *The estrogen dominance which is needed to start the reproductive cycle, with cell proliferation in the endometrium, breast, and pituitary, is not otherwise useful to the organism, and is controlled and opposed during pregnancy by a constantly rising production of progesterone. The state of estrogen dominance is essentially unstable. P. T. Ellison, emphasizing the "energy hungry brains" of primates, explains the need for the massive endometrial growth in primates, and Strassman observes that endometrial regression occurs in all mammals. These are important points. Their failure to point out that estrogen has many undesirable systemic effects very likely results from the cultural context that has been created by the estrogen-promoting pharmaceutical industry.

The group of processes that we call the immune system is so deeply integrated with everything else in the organism that to talk about "the reason for evolving it" is as misleading as to talk about "the reason" for evolving certain pigmentations–black feathers, for example, are mechanically stronger than white ones, selection of foxes for domesticability changes their fur pigmentation and their voice, selection for egg laying somehow produces suppression of feather pigmentation, etc., yet people like to talk about protective coloration, because an easy connection can be made between that and genetic selection. Being an organism is a problem whose solution may require inventive use of internal and external resources; chromosomes are internal resources, not clusters of traits.

The ideology that sees the organism as a sum of traits, each with its gene, has been a failure in providing understanding about how an organism comes to exist.

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