Adaptive substance, creative regeneration: Mainstream science, repression, and creativity

From the original article in 2008. Author: Ray Peat.

> **"I intend to show you how neo-Darwinism has been invalidated within science itself, as an explanation of how life on earth has evolved and is evolving. It is nevertheless still perpetrated by the academic establishment, if only because it serves so well to promote genetic engineering, a technology that has the potential to destroy all life on earth. Furthermore, neo-Darwinism reinforces a worldview that undermines all moral values and prevents us from the necessary shift to holistic, ecological sciences that can truly regenerate the earth and revitalize the human spirit."**
> Mae-Wan Ho http://www.i-sis.org.uk/paris.php

More than 50 years have been wasted in one of the most important and fundamental branches of science and medicine, for reasons that are highly ideological and political. Rather than studying the regeneration of organs and tissues, and recognizing its obvious importance in healing as well as in understanding the nature of life, much of the last century was devoted to the defamation of the researchers who were making real process in the field. Despite many demonstrations that regeneration can occur in adult mammals, students were taught that it happens only in lower vertebrates. I think it's important to look closely at the ideology responsible for this great loss.

Warburg and Szent-Gyorgyi, in thinking about cancer, emphasized that growth is the primordial function of all cells, and that the differentiated functions of complex organisms involve restraints of that primitive function, imposed by a system that has developed through time.

Seen with this orientation, regeneration is the spontaneous result of the disappearance of restraint. The reproduction of a whole plant from a twig, or clone, was a process known for thousands of years. Any part of the plant contains the information needed for making a whole plant. More than thirty years ago, cells from a tumor were added to the cells of a normal embryo, and the animal that matured from the embryo-tumor mix was normal, and had traits of both lineages, showing that the tumor cells had retained the genetic information of a complete healthy organism, and just needed a different environment in which to realize their full potential.

One of the currents of medical thinking, from classical times through Paracelsus to homeopathy and naturopathy, has been a confidence in the capacity of the organism to heal itself. But "modern" medicine has arrogated to itself the "healing power," with terrible results, mitigated only by their occasional reluctant acceptance of fragments of sane organismic thinking, such as recognizing the importance of nutrition, or of keeping sewage out of the drinking water. Research into methods to support the organism's natural restorative powers has been ridiculed and suppressed.

We are immersed in the propaganda of modern medicine, and part of that propaganda involves the confabulation of a history of science that supports their practice and their ideology. The real history of science won't be found in science textbooks.

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Mainstream medical treatments are based on some fundamentally absurd scientific ideas. The advent of experimental animal cloning and the industrialization of genetic engineering have undercut the most important biological doctrines of the 20th century, but the processes of critical thinking haven't made headway against most of the traditional medical stereotypes. Cloning shows that all cells are potential "stem cells," but this fact co-exists with the Hayflick doctrine, that says, essentially, that no cell is a stem cell.

The ideology of culturally significant "intellectuals"--scientists, professors, neurobiologists, linguists, philosophers, oncologists, geneticists--in the US is deeply influenced by the dualism and mechanistic materialism of Rene DesCartes.

The denial that animals can think or understand language, the claim that babies or animals don't feel pain, or that heart cells and brain cells can't divide, or that somatic cells lack the genetic capacity to be cloned, or that they are intrinsically mortal, limited to a maximum of 50 cell divisions--these absurdities of 20th century biology and medicine all resulted from an abject commitment to the mechanistic doctrine of matter and life promoted or invented by DesCartes.

I doubt that DesCartes really invented anything, because, by the evidence of his writing, he wasn't an intelligent man, but he placed himself politically in such a way that his arguments were acceptable to many influential people, and they continue to be acceptable to authoritarian and elitist factions even today.

In the 16th and 17th century the cultures of England, Holland, and France were increasingly dominated by business interests. People who had money to invest wanted to see the world as an orderly, predictable place, and they found that many of the ideas of the ancient Greeks were useful. Mathematics was needed to calculate interest rates, insurance premiums, and, for the military, the trajectories of missiles. In an orderly world, allowance for a little random variation helped to save the perfection of the general rule.

In this environment, theological thinking began retrenching its doctrine, to make it more acceptable to the increasingly powerful commercial people. The clockwork universe of DesCartes' time, in which a perfect world that operated according to perfect natural laws had been divinely created, gradually became theologically acceptable during the 18th and 19th centuries. In the 18th century, the Deists were the most famous embodiment of the idea, and then in the 19th century their place was taken by the Catastrophists, who claimed that the fossils which seemed to show evolutionary change of species actually represented species that had been created along with those now existing, but that had been destroyed by catastrophes, such as Noah's flood. By the end of the 19th century, the president of an American university recognized that theological compromises could prevent his undergraduates from rejecting religion entirely, and forbade sermons against evolution.

There were many biologists who insisted that evolution of new species was analogous to the development of an individual, and that both revealed an adaptive capacity of the living substance. In this view, the adaptive growth of an individual in a new environment revealed novel solutions to new problems, and showed an innate inventiveness and intelligence in the process of growth and adaptation. The appearance of new species was thought to represent the same sorts of adaptive processes.

Erasmus Darwin (grandfather of Charles) was an evolutionist of this sort, but because of political and theological pressure, he kept relatively quiet about his beliefs. There was an underground culture, in which an evolutionary view of the world was accepted, but these views were seldom published, because of increasingly stringent censorship. Because of censorship, poetry, letters, and diaries, rather than academic and scholarly works, give us the true picture of 18th century and early 19th century scientific culture.

The scientists who wanted their work to be acceptable to those in power found ways to work with the Cartesian mechanical view of the world, building on the Deists' compromise, which had succeeded in removing the supernatural from nature. As the fossil evidence of evolution became inescapable, around the time of Charles Darwin's work, those who wanted to bring evolution into the mainstream of culture found that the Catastrophism of the creationists could be adapted to their purposes, with only slight modification.

The doctrine of Thomas Malthus, who argued that war, famine, and disease were beneficial for those who survived, by decreasing the competition for limited resources, became a near equivalent to the catastrophic floods that the creationists had invoked to explain the geological record that contained evidence of many extinct animals. **The doctrine of Malthus, like that of the Catastrophists, made loss, deletion, and destruction into a central device for explaining the history of the world.**

Both of the Darwins had accepted the idea that many biological changes were adaptive, rather than random, but the new practical compromise doctrine introduced the idea that changes were just "random variations." The essentially mechanical nature of the world was preserved, because "chance" occurrences could be dealt with, and didn't involve anything supernatural. **The function of the environment wasn't to add anything to life (that would have been to assert that there were creative powers other than those of the Creator), but simply to eliminate the inferior individuals that appeared as the result of random changes.**

Gregor Mendel applied the principle of chance to explaining the inheritance of certain traits, and showed that "traits" were passed on unchanged, even when they weren't visible. His ideas were published and were acceptable to the scientific mainstream of his time. Traits were determined by "factors" that were passed on, unchanged, from parents, and biological variation was explained by varied mixing of factors which in themselves were unaffected by the organism or the environment. Genetic determinism was safely compatible with creationism.

Shortly after Mendel's death, August Weismann began a campaign to put a stop to the claims of those who, like the Darwins and Lamarck, saw adaptive development of organisms as an essential part of the evolution of species.

Weismann was essentially a propagandist, and his first fame was the result of "disproving" Lamarck by cutting the tails off more than 1500 mice, and observing that their offspring were born with tails. The reason the inheritance of acquired traits was impossible, he said, was that the "germ line" was perfectly isolated from the rest of the organism. The differentiated tissues of the body were produced by the selective loss of information from the nuclei of cells in the embryo. The cells of the germ line were immortal and contained all the information needed to produce an organism, but no other cell of the organism was complete.

Complexity was produced by deletion, and this was the basis for arguing that, if even the development of an individual was nothing but a passive unfolding of inherited properties, much like unpacking a trunkful of clothes, then there could be no adaptively acquired traits, and certainly no inheritance of something which didn't exist. Changes in an individual were simply accidents, such as having a tail amputated, and so the whole issue of the origin of complexity was safely left to a primordial creation.

Weismann and his arguments were famous in Europe and the US, and formed the background for the ideas known as neo-Darwinism. His "isolation of the germ line" was the earliest version of the Central Dogma of molecular biology, namely, that information flows only from DNA to RNA to protein. His doctrine, of complexification through deletion, is the epitome of the greatest dogma of modern times, expressed in doctrines from Catastrophism through the second law of thermodynamics and the theory of the Big Bang, down to Hayflick's Doctrine of the mortality of somatic cells. All these are consequences of the Cartesian and Deistic separation of intelligence from matter.

Regeneration is one of the most vivid examples of the intelligence of living substance.

Given a natural tendency of cells to multiply, the interesting thing about regenerative healing is the question of why the new growth of tissue sometimes differentiates to fit appropriately into its surroundings, but sometimes fails to differentiate, becoming a tumor.

With aging, the regenerative process declines, and the process of tissue rebuilding slows. Against a background of reduced regenerative ability, tissue growth sometimes produces tumors, rather than renewed healthy tissue. When tumors are grafted onto the amputated tail stump of a salamander, which has good regenerative ability, the tumor is transformed into a tail, by its envirornment, or morphogenic field. The "cancer problem" is essentially the problem of understanding the organizing forces of the organism. The aging problem is another aspect of the same problem.

Traditionally, biologists had studied anatomy, physiology, embryology or development, and taxonomy or the classification of organisms. The growth of knowedge early in the 20th century was suddenly seeming to confirm the physiological, adaptive view of organisms that Lamarck had held. C.M. Child, Joseph Needham, Alexander Gurwitsch, and L.V. Polezhaev were demonstrating the primacy of a formative process in biology. Polezhaev and Vladimir Filatov were studying practical means of stimulating regeneration as a medical technique.

Until the beginning of the second world war, the study of regeneration and the pattern-forming processes in embryology were the liveliest parts of biological research. Gestalt psychology was being developed at the same time, with a similar emphasis on patterns and wholes.

But Weismannism and neo-Darwinism, largely embodied in the person of the geneticist T.H. Morgan, deliberately set out to kill that line of biological research. Gestalt psychology was similarly eliminated by the Behaviorists.

One of Morgan's closest associates, his student and colleague A.H. Sturtevant, said that "Morgan's objectives, what he was trying to get at in general in his biological work was to produce mechanistic interpretations of biological phenomena. One of the things that irritated him most was any suggestion of purpose in biological interpretation. He always had some reservations about the idea of natural selection, because it seemed to him to open the door to interpretations of biological phenomena in terms of purpose. He could be talked into the conclusion that there was nothing that wasn't strictly mechanistic about this interpretation, but he never liked it. And you had to talk him into it again every few months." (Sturtevant, A. H., *Genetics, Vol. 159,* 1-5, September 2001, Copyright 2001, Reminiscences of T. H. Morgan.)

Whatever his motives, Morgan was known to have prevented his students (including C.M. Child) from publishing work that supported a holistic view of the organism. After Morgan's death, there was an intense and widespread campaign to suppress any approach to biology other than the "new synthesis," neo-Darwinism, with its doctrine of mechanistic genetic determinism and its doctrine of random variation. A developmental biologist, J.M. Opitz (1985), commented that **"in one of the most astounding developments in Western scientific history, the gradient-field, or epimorphic field concept, as embodied in normal ontogeny and as studied by experimental embryologists, seems to have simply vanished from the intellectual patrimony of Western biologists."**

Formative processes are necessarily multidimensional, and that makes calculation and analysis very complex. To a great extent, the geneticists were motivated to study bacterial genes, rather than vertebrate embryos, by the principle that motivated the drunk to look for his car keys under the street lamp, even though that wasn't where he lost them, because the light made it easier to look there.

Bacteria are easy to study because they lack the complexity that makes it hard to study an embryo or an animal. The language used in genetics textbooks shows not only that bacteria are treated by geneticists as if they were one or two dimensional, but that the concepts developed for bacterial genetics have been extrapolated to use in describing complex organisms: "**Genes interact** to establish the body axis in Drosophila. Homeotic **Genes control** pattern formation along the anterior-posterior body axis." (*Essentials of Genetics,* M. Cummings and W. Klug, Prentice Hall, 2004.)

One of the basic distinctions in embryology is in the way the cells divide after the egg is fertilized. Oysters and earthworms have spiral cleavage, sea urchins and people have radial cleavage. Several decades ago an experimenter was transferring a nucleus from an egg of an animal with radial cleavage, I think a sea urchin, into the enucleated egg of a snail, with spiral cleavage. The nucleus transplanted across such a great difference in phyla didn't sustain maturation of the animal, but it did permit development to proceed for several rounds of cell division, and the pattern of cell division, or cleavage, and embryonic development always followed the pattern of the phylum to which the egg cytoplasm belonged, never the pattern of the phylum from which the nucleus was derived. The genes in the nucleus, obviously, weren't directing the basic pattern formation of the embryo.

One-dimensional bacterial genetics can be used to "explain" multidimensional systems, but it can't be expected to make useful predictions.

The idea of complexity, or of multidimensionality, has often been analyzed in terms of "fields," by analogy with a magnetic field, as some property, or properties, that extend beyond any individual part, giving some coherence to the parts. Lamarck was concerned with understanding ensembles of particles and cells, but in his time electricity and heat were the only principles that physics provided that helped to illuminate the nature of living organisms. At the end of the 19th century, though, the physicist J.C. Bose was noticing that all of the properties of life that had interested Lamarck and Buffon--irritability, sensation, contraction, memory, etc.--had their close analogs in non-living substances. Bose, who invented the radio detector that was the core of Marconi's apparatus, found that, in the presence of an electromagnetic field, particles of a substance, such as finely powdered metal filings, cohered into a unified whole. An otherwise invisible, undetectable "field" which in Lamarck's time might have been known as one of the "subtle fluids," was able to organize a myriad of inert particles into a unified whole.

In the early 1920s, Bungenberg de Jong and A.I. Oparin showed how solutions of organic substances could spontaneously organize themselves into complex systems, with differentiated parts. A Russian embryologist, Alexander Gurwitsch, found that the parts of an organ or embryo could exert their stimulating or organizing influence on other cells even through a piece of glass, and by using different types of filter, he identified ultraweak ultraviolet rays as a medium of communication between cells. F.-A. Popp and others are currently studying the integrating functions of ultraweak light signals. Guenter Albrecht-Buehler (who has an interesting website called Cell Intelligence) is investigating the role of pulsed infrared signals in cell communication.

Electrical fields produced by cells, tissues, and organisms have been shown to influence cellular metabolism and physiology, and to influence growth patterns. Closely associated with cellular electrical fields are fields or gradients of pH and osmolarity, and all of these fields are known to affect the activity of enzymes, and so to create environments or fields of particular chemical concentrations.

A phenomenon that was well known in the 1930s, when developmental fields were still a familiar part of scientific discussion, was the "cancer field." Before a cancer developed in a particular area, the area showed progessive changes, away from normal function and structure, toward the cancer physiology.

In the embryonic state, damaged tissues regenerate quickly. The metabolism of an embryo or fetus is highly oxidative, converting glucose rapidly to carbon dioxide and water. Both carbon dioxide and water are important regulators of cellular metabolism and function, and the concentrations of both of them decrease systematically with maturity and aging. Both are involved with the most basic aspects of cellular sensitivity, responsiveness, and organization.

To resume the scientific tradition that has "simply vanished," I think we have to recover our ability to think about organisms generally, leaving aside as many of the concepts of genetics as possible (such as "gene," "operon," "receptor"; "the gene" has never been more than an ideological artifact), because they so often falsify the most important issues. The organization of tissues and organs, and their functional properties, should be the focus of attention, as they were for Lamarck around 1800, and for Johanes Muller, who in 1840 saw cancer as a problem on the level of tissue, rather than cells. For Lamarck, sensitivity and movement were the essential properties of the living substance, and J. C. Bose showed reasons for believing that the characteristics of life were built on related properties of matter itself.

Sensitivity, the ability to respond appropriately to the environment, is probably a missing factor in the development of a tumor. The ability to become quiescent, to quietly participate in the ensemble of cells, is an essential feature of the sensitivity and responsiveness of the cells of complex organisms. The factors that support organized appropriate functioning are the factors that help cells to inhibit the excitatory state. If the keys of an accordion or organ didn't spring back after the musician pressed them, the instrument would be unplayable. In extreme physiological states, such as epilepsy or malignant hyperthermia, nerves or muscles become incapable of relaxing. Insomnia and muscle cramps are milder degrees of a defective relaxation process. Excitoxicity and inflammation describe less generalized cases of a similar process, in which there is an imbalance between excitation and the restorative ability to stop the excitation. Prolonged excitation, resulting in excessive fatigue, can cause a cell to disintegrate, in the process of cell death called apoptosis, "falling away."

In the experiments of Polezhaev and Filatov, the products of cell disintegration were found to stimulate the birth of new cells (possibly by blocking a signal that restrains cell division). This process has been found in every organ that has been examined appropriately. It amounts to a "streaming regeneration" of the organism, analogous to the progressive creation of Lamarck's view. G. Zajicek has demonstrated an orderly "streaming" renewal in several organs, and even the oocytes (which in the Weismannian dogma were formed at a very early stage during embryonic development, and were perfectly isolated from the cells of the mature body) have recently been shown to be continually regenerated in adult ovaries.

"Stem" cells turn out to be ubiquitous, and the failure of regeneration and restoration seems to be situational. In the 1950s a magazine article described the regeneration of a finger-tip when the wound was kept enclosed. Decades later, friends (one a child, the other a man in his forties) had accidental amputations of a finger-tip, down to the cuticle so that no visible nail remained. The boy's mother fitted his finger with the tube from a ballpoint pen, and the man used an aluminum cigar tube as his "bandage." Within a few weeks, their fingers had regenerated to their normal shape and length. I think the closed environment allows the healing tissues to be exposed to a high concentration of carbon dioxide, in equilibrium with the carbon dioxide in the capillaries, and to a humid atmosphere, regulated by the osmotic or vapor pressure of the living tissues.

Under ordinary conditions, the creation of cells and the dissolution of cells should be exactly balanced. The coordination of these processes requires a high degree of coherence in the organism.

Simple increase of water in the vicinity of a cell increases its tendency to multiply, as well as its excitability, and hypertonicity restrains cell division, and reduces excitability. Carbon dioxide, besides helping proteins to release water, appears to increase the ability of proteins and cells to respond to morphogenetic fields. Carbon dioxide is the most universal agent of relaxation, restoration, and preservation of the ability of cells to respond to signals. Progesterone is another very general agent of restorative inhibition.

The study of regeneration and "stem cells" is helping to illuminate the general process of aging, and to provide very practical solutions for specific degenerative diseases, as well as providing a context for more appropriate treatment of traumatic tissue injury.

In aging, the growth and regenerative processes are slowed. There is some evidence that even cell death is slower in old age, at least in some tissues. Since animals with the highest metabolic rate live the longest, the slowing rate of metabolism during aging probably accounts for those changes in the rate of cell renewal. The continually streaming regeneration of tissues is part of the adaptive process, and it is probably intensified by stress.

The ability to sleep deeply decreases in old age, as a generalized inflammatory, excitatory state of stress develops. With progressive weakening of restorative cellular relaxation (inhibition), cells become more susceptible to disintegration. It's well established that bone loss occurs almost entirely during the night, and since the catabolic hormones generally affect soft tissues as well as bones, the atrophy of soft tissues ("sarcopenia") of aging is also probably a process that occurs mostly during the night. Mediators of inflammation are at their highest during the night (Cutolo and Masi, 2005). But during the period of growth, the length of bones seems to increase mostly during the night (Noonan, et al., 2004). My interpretation of this is that the stress of darkness accelerates biological processes, whether the process is mainly constructive or mainly destructive.

The effect of light supports efficient oxidative energy production, which supports the protective inhibitory processes, by increasing ATP and CO_2, and decreases the inflammatory mediators that intensify stress. If organized cellular luminescence is required for a proper balance, then the random luminescence produced by lipid peroxidation (which may be more intense at night--Diaz-Munoz, et al., 1985), might be an important factor in disrupting the balanced streaming of regeneration. Free radicals, whatever their source, absorb a broad spectrum of radiation, and would block luminous signals of all frequencies. Isoprene, produced mainly at night (Cailleux and Allain, 1989), is another ultraviolet absorber that might account for nocturnal regulatory disorders.

The age pigment, lipofuscin, is known to contribute to degenerative diseases, but the nature of its toxicity has never been established. Its absorptive and fluorescent properties would be very likely to interfere with mitogenetic and morphogenetic radiation. Polyunsaturated fats are the main component of lipofuscin, and these fats in themselves can absorb ultraviolet light. When those fats are present in the skin, exposure to ultraviolet light accelerates the aging of the skin. Free fatty acids often increase during the night, under the influence of hormones such as adrenaline and growth hormone.

A single night of poor sleep probably causes significant anatomical damage to the streaming cellular systems that will be repaired over the next few days if a high level of energy metabolism can be combined with a sufficient amount of deep sleep. The things that optimize energy and sleep form the background for supporting the restorative processes. Salt, glycine, carbon dioxide, progesterone, thyroid hormone and sugar all contribute to preserving the organism's energetic reserves by reducing inappropriate excitation.

Lamarck's idea that organs developed or regressed according to their use or disuse was often attacked by followers of the Weismann-Morgan genetic dogma. In their view, the influence of the environment was limited to either preventing or permitting the realization of "the genetic potential." Once that predefined potential had been unfolded, the finite and mortal nature of the somatic cells didn't allow for any significant changes, except for depletion and death. One of the high points of Weismannian biology came with the publication of an article in Science, around 1970, that proposed to explain learning in terms of the lifelong loss of brain cells, beginning in humans around the age of 18 months, with a daily loss of 100,000 cells, which would record experience by selective deletion, the way punching holes in cards had been used to enter data into computers. I was present to witness "world class biologists" taking that idea very seriously.

As Sturtevant mentioned in the quotation above, T.H. Morgan couldn't accept any attribution of purposefulness to organisms. In his genetic dogma, changes were only random, and people who denied that were denounced as "teleological" (or metaphysical) thinkers. Changes occurred by deletion, not by meaningful addition.

One of Pavlov's students, P.K. Anokhin, developed the concept of the Functional System in the 1930s, to explain the purposive behavior of animals. In the 1950s, Anokhin integrated the endocrinology of stress and adaptation into the concept, and F.Z. Meerson continued the work, concentrating on the metabolic and structural changes that protect the heart during stress. The simplest view of the conditional reflex involves the adaptation of an animal to an external signal, identifying it as the occasion for a particular action. Analyzing the Functional System starts with the need of the animal, for example for food, and examines the processes that are involved in satisfying that need, including nerve cells, a sense of hunger, knowledge of what things are edible, the muscles needed to get the food, and the digestive apparatus for assimilating it.

When an understanding of stress physiology is combined with the idea of functional systems, the adaptive meaning of the use or disuse of certain organs is given a concrete basis. Cortisol mobilizes amino acids from muscles that are idle, and makes them available for the synthesis of proteins in the muscles, nerves, or glands that are activated in adapting to the stress. The London taxi drivers whose hippocampus grows as they learn the locations of the streets are very good examples of the processes described by Meerson, Anokhin, and Lamarck, in which the use of an organ in meeting a need contributes to the development of that organ. The balance between growth and regression is shifted during adaptive behavior.

Exercise physiologists, without mentioning functional systems, have recently discovered some principles that extend the discoveries of Meerson and Anokhin. They found that "concentric" contraction, that is, causing the muscle to contract against resistance, improves the muscle's function, without injuring it. (Walking up a mountain causes concentric contractions to dominate in the leg muscles. Walking down the mountain injures the muscles, by stretching them, forcing them to elongate while bearing a load; they call that eccentric contraction.) Old people, who had extensively damaged mitochondrial DNA, were given a program of concentric exercise, and as their muscles adapted to the new activity, their mitochondrial DNA was found to have become normal.

There are probably the equivalents of constructive "concentric" activity and destructively stressful "eccentric" activity in the brain. For example, "rote learning" is analogous to eccentric muscle contraction, and learning by asking questions is "concentric." "No bird soars too high, if he soars with his own wings." Any activity that seems "programmed" probably stifles cellular energy and cellular intelligence.

When activity is meaningful, and is seen to be meeting a felt need, the catabolic and anabolic systems support and strengthen the components of the functional system that has been activated. Everything we do has an influence on the streaming renewal of the adaptive living substance.

There are many therapeutic techniques that could be improved by organized research, for example, investigating the interactions of increasing carbon dioxide, reducing atmospheric pressure, supplementing combinations of salt and other minerals, balancing amino acids and sugars, and varying light exposure and types of activity. The dramatic results that have occasionally been demonstrated (and then suppressed and forgotten) are just a hint of the possibilities.

If we keep our thoughts on the living substance, the pervasive ideologies lose their oppressive power.

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Brain Res. 1977 Mar 4;123(1):137-45. **Daily variations of various parameters of serotonin metabolism in the rat brain. II. Circadian variations in serum and cerebral tryptophan levels: lack of correlation with 5-HT turnover.** Hery F, Chouvet G, Kan JP, Pujol JF, Glowinski J. Rats submitted to regular 12 h cycles of light and darkness for three weeks were sacrificed at various times of the day. 5-HT, 5-HIAA and tryptophan levels were estimated in the fronto-parietal cerebral cortex. Tyrosine and free and total tryptophan levels in serum were estimated in parallel. Significant circadian variations in 5-HT and 5-HIAA levels were found in cerebral tissues. The peaks of 5-HIAA levels were dectected during the lignt and dark periods respectively, the maximal fluctuations being seen between 17.00 h and 21.00 h, two times separating the light off. Important significant circadian variations in free and total **serum tryptophan** levels were also observed**. In both cases, the maximal levels were found during the middle of the dark phase** after the peak of 5-HIAA levels. The circadian rhythm of tyrosine levels in serum was in opposite phase with that of tryptophan (free or total). The diurnal changes in tryptophan content in cerebral tissues seemed thus related to those found in serum. Taking in consideration results obtained in previous studies 16,17 carried out in

similar experimental conditions, it was concluded that the parallel increase in serum free tryptophan and in tissues 5-HIAA levels seen during the night were not related to a stimulation of 5-HT turnover. Indeed 5-HT synthesis is minimal at this time16.

Kryukov V.I. **An attention model based on the principle of dominanta // *Proceedings in Nonlinear Science. Neurocomputers and Attention. I: Neurobiology, Synchronization, and Chaos.*** 1989. Ed. by A.Y. Holden and V.I. Kryukov, pp. 319-351.

Endocrinol Exp. 1976 Jun;10(2):131-7. **Diurnal variation in the effect of melatonin on plasma and muscle free fatty acid levels in the pigeon.** John TM, George JC. Pigeons maintained on standard diet and held under 12 h daily photo-period in a controlled environmental room, were given intravenous injections of melatonin. A low dose (1.25 mg/kg body weight) of melatonin when given in the middle of the scotophase, produced a significant increase in plasma FFA when estimated at 20 min and 90 min post-injection, whereas no significant change was seen with injections given in the middle of the photophase. No significant change in muscle FFA level was obtained either during the photophase or the scotophase when estimated at 90 min postinjection. **With a higher dose (5 mg/kg body weight) of melatonin given in the scotophase, on the other hand, a significant increase in both plasma as well as muscle FFA levels was obtained at 90 min post-injection but there was no effect on plasma FFA at 20 min or 90 min** post-injection in the photophase and at 20 min in the scotophase. It is concluded that **melatonin has a lipid mobilizing action in the pigeon when administered during the scotophase.**

Exp Brain Res. 2001 Feb;136(3):313-20. **Enhanced neurogenesis after transient global ischemia in the dentate gyrus of the rat.** Kee NJ, Preston E, Wojtowicz JM. "Certain insults such as epileptic seizures and ischemia are known to enhance the rate of neuronal production. We analyzed this phenomenon using the temporary occlusion of the two carotid arteries combined with arterial hypotension as a method to induce ischemia in rats. We measured the rate of cell production and their state of differentiation with a mitotic indicator, bromodeoxyuridine (BrdU), in combination with the immunohistochemical detection of neuronal markers. One week after the ischemic episode, the cell production in dentate gyrus was increased two- to threefold more than the basal level seen in control animals. **Two weeks after ischemia, over 60% of these cells became young neurons as determined by colabeling with BrdU and a cytoplasmic protein (CRMP-4) involved in axonal guidance during development. Five weeks after the ischemia, over 60% of new neurons expressed calbindin, a calcium-binding protein normally expressed in mature granule neurons.** In addition to more cells being generated, a greater proportion of all new cells remained in the differentiated but not fully mature state during the 2- to 5-week period after ischemia." "The results support the hypothesis that survival of dentate gyrus after ischemia is linked with enhanced neurogenesis. Additional physiological stimulation after ischemia may be exploited to stimulate maturation of new neurons and to offer new therapeutic strategies for promoting recovery of neuronal circuitry in the injured brain."

Am J Cardiol. 1998 Dec 17;82(12A):24U-28U; discussion 39U-41U. **Clinical profiles of plain versus sustained-release niacin (Niaspan) and the physiologic rationale for nighttime dosing.** Knopp RH. Niacin is the oldest and most versatile agent in use for the treatment of dyslipidemia. It has beneficial effects on low-density lipoprotein cholesterol; high-density lipoprotein cholesterol; the apolipoproteins B and A-I constituting these fractions; triglyceride; and lipoprotein(a). Together, these benefits lead to a diminished incidence of coronary artery disease among niacin users. The chief constraints against niacin use have been flushing, gastrointestinal discomfort, and metabolic effects including hepatotoxicity. Time-release niacin has been developed in part to limit flushing, and now a nighttime formulation (Niaspan) has been developed that assists in containing this untoward effect. In a pivotal metabolic study, bed-time administration of 1.5 g time-release niacin was shown to have the same beneficial effects as 1.5 g plain niacin in 3 divided doses and to be well tolerated. **Previous studies suggest that bedtime niacin administration diminishes lipolysis and release of free fatty acids** to the liver; this, in turn, leads to an abolition of the usual diurnal increase in plasma triglyceride, which may result in diminished formation and secretion of triglyceride in the very-low-density lipoprotein fraction.

J Pediatr Orthop. 2004 Nov-Dec;24(6):726-31. **Growing pains: are they due to increased growth during recumbency as documented in a lamb model?** Noonan KJ, Farnum CE, Leiferman EM, Lampl M, Markel MD, Wilsman NJ.

Cell Tissue Kinet. 1977 Nov;10(6):557-68. **Circadian rhythms of presumptive stem cells in three different epithelia of the mouse.** Potten CS, Al-Barwari SE, Hume WJ, Searle J.

Physiol Res. 1995;44(4):249-56. **Circadian and circaannual oscillations of tissue lipoperoxides in rats.** Solar P, Toth G, Smajda B, Ahlers I, Ahlersova E. Circadian and circaannual oscillations of tissue lipid peroxides (LPO) were studied in young male Wistar rats. The concentration of malondialdehyde, one of LPO degradation products, was measured at 3-h intervals during 24 hours in rats, adapted to light:dark 12:12 h regimen in the course of the year. LPO in the liver, thymus and bone marrow oscillated rhythmically in the course of the day and year. Circadian oscillations in all tissues were two-peaked, with zeniths at various times of the light and dark parts of the day. In the liver and thymus, **the highest mesors were found during the winter**, in the bone marrow during the spring. The same holds for amplitude values, with the exception of the bone marrow which exhibited the highest values during the summer. The reason for the LPO oscillations is probably resulting from the changing ratio of pro- and anti-oxidative capacities in various tissues during the day and the year.

Biofizika. 1976 Jul-Aug;21(4):688-91. **[Circadian rhythms of ultraweak chemiluminescence of bean roots]** Sul'tsman FM, Petrusevich IuM, Tarusov BN. Circadian rhythms of ultra-weak chemoluminescence of bean roots were investigated. It was found that under periodical change of light and darkness and without subsequent illumination a periodical change of spontaneous chemoluminescence of bean roots was observed. (The study of antiradical activity of the substances extracted from the root showed the dependence of this activity on illumination conditions.

Ukr Biokhim Zh. 1977 Sep-Oct;49(5):64-9. [Effect of "carbostimulin", vitamin D 3 and their mixture on bone tissue regeneration] [Article in Ukrainian] Taran TT, Guly MF, Mykhajlovskyj VO, Dvornykova PD, Fanak MM, Vorobjov NA. "Healing of the bone injury in rabbits was studied as affected by carbostimulin and its mixture with vitamin D3. Some biochemical indexes: the content of sialic acids, calcium and citric acid in blood serum of the animals, intensity of 14C incorporation from NaH14CO3 into the regenerated bone tissue and its proteins as well as histological studies, data, evidence for a positive effect of the mentioned preparations on the bone substance regeneration in the animals under experiment."

Biofizika. 1961;6(4):490-2. **[Study on ultra-weak spontaneous luminescence of animal cells.]** Tarusov BN, Polivoda AI, Zhuravlev AI.

Biofizika. 1961;6(4):83-5. **Study of the faint spontaneous luminescence of animal cells.** Tarusov BN, Polivoda AI, Zhuravlev AI.

Vopr Med Khim. 1977 May-Jun;(3):375-81. **[Free fatty acids and cholesterol as possible participants in lipid oxidation radical reactions in animal tissues]** [Article in Russian] Terekhova SF, Burlakova EB, Elizarova TI. Alterations in concentration of free fatty acids, free cholesterol, native antioxidants as well as in the antioxidative activity were studied in lipids of mice liver tissue and small intestinal mucosa. The intensity of free radical reactions in lipids of animal tissues was affected directly by administration of synthetic inhibitors of the reactions. The inverse correlation was observed between the alteration in concentrations of native antioxidants and free fatty acids as well as between the antioxidative activity of lipids and amount of free cholesterol in them. **Free fatty acids appears to be the constant participants in the system of free radical oxidation of lipids, while cholesterol can center the system under distinct level of these reactions intensity.**

Ukhtomsky A.A. ***Dominanta as factor of behavior // Collected works.*** Leningrad, 1950. Vol.1, pp.293-315.

Biofizika. 1974 Mar-Apr;19(2):295-9. **[Formation of pigments of lipid nature in animal tissues during neoplastic growth and irradiation]** Vertushkov VT, Ivanov II, Tarusov BN.

Biofizika. 1967 Jul-Aug;12(4):739-41. **[Antioxidative activity of blood serum fractions during malignant degeneration studied by inhibition of chemiluminescence]** Zakarian AE, Tarusov BN.

Biofizika. 1966;11(5):919-21. **[Inhibition of chemiluminescence of the blood plasma in malignant growth]** [Article in Russian] Zakarian AE, Tarusov BN.