## Circumcision

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discourage circumcision and to refuse to perform it.

Physicians today have a unique historic opportunity to correct the mistakes of the past by realigning medical practice with ethics and the principles of human rights. Every individual has a right to the body he or she was born with. Physicians have a duty to protect this right and to uphold the first tenet of the Hippocratic oath "First, Do No Harm."

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## Preserving the Tissues

# Osteoporosis and the Skin

by Ray Peat, PhD

While I was working on my dissertation, around 1970, the opposition between stress-injury and energetic resistance became increasingly apparent to me. Estrogen (like X-irradiation, aging, or trauma) called up the cortisone response, and other factors, especially progesterone and thyroid, and allowed the organism to restore itself in ways that neutralized the cortisone response. Therefore, when I saw that the estrogen-like processes became more and more dominant after middle-age, it was natural to think of progesterone and thyroid as the main factors that should be replaced. This is why in 1975 I described menopause as resembling Cushing's syndrome, which is caused by a toxic excess of cortisol. Osteoporosis, hot flashes, insomnia, and mood disorders are caused by cortisol, and so I tried using progesterone and thyroid – the anticortisol factors – for those conditions. The results were so profound that I began to study the general implications for health, and to try to understand the mechanisms so that prevention might replace treatment.

Several people who had been abandoned as hopeless terminal cases – with "epileptic brain damage," inflammatory degeneration of hip and thigh bones, diabetic gangrene, senility – recovered their health within a few days, and went on with their lives in productive and pleasant ways.

I knew that intense and frequent epileptic seizures cause the exhaustion and death of brain cells. A 52 year-old woman had been having seizures for over 15 years. Her neurologist gave her a mental exam every year, and considered her to be hopelessly demented. After using progesterone for a few days, she functioned normally. After about a year, she returned to graduate school at the University of Oregon, and got a master's degree with straight A's.

A 79 year-old woman had had artificial hip joints implanted when she was in her fifties, but her bones had weakened to the point that no further surgical repair was possible. She settled her affairs, and didn't expect to get out of bed again. After using progesterone topically and orally, after two weeks she was able to get out of bed and return to her normal activities. At the age of 85, she went camping on the beach in Mexico, and travelled to Scotland.

An 82-year old man was agitated and confused, and was apparently suffering from senile dementia. After being given progesterone and pregnenolone for a few days, his mind became clear, and he returned to work on scientific projects he had begun decades earlier. A squamous cell cancer on his lip regressed, and never bothered him again.

A 60 year-old woman had "osteoporosis" (shrinking) of the jaw bone that was causing her teeth to loosen. After applying progesterone solution to her gums daily for a few months, her teeth became firm.

When bones had almost disappeared from X-rays, yet became firm and functional within a few weeks, it was obvious that regeneration had taken place. But when brains went in a very short time, from imbecility or idiocy to intellectual productivity, I could only guess what might be happening to the cells. But I got a useful perspective on the mechanism of progesterone's action by seeing some recoveries that were even faster than those I have mentioned.

In animal experiments, I knew that estrogen causes cells to take up water within a few minutes after it reaches the tissue, and that this is at least partly the result of its interfering with the availability of oxygen. Within 40 minutes of administering a large dose of estrogen, the lungs become extremely inefficient at oxygenating the blood. This involves a sudden thickening of the alveolar membranes and the walls of capillaries, simply by taking up water. So, when I saw bulging veins disappear a few minutes after women took progesterone, along with a sudden lifting of extreme depression, I guessed that their circulation had become more efficient, and that better oxygenation had changed their mood.

Then, I repeatedly saw physical changes in other people that were visible

within an hour, and that involved a sudden movement of water out of edematous tissues. In many people with damaged joint cartilage (confirmed by various types of examination, including arthroscopy), the joints became mobile in an hour, and by the next day, the defect no longer existed. A man who was purple from emphysema changed color within a few hours, and within a few days was going to work. The bulging eyes of exophthalmic Graves' disease receded into their sockets noticeably within an hour, and were normal the next day. Simply increasing the circulation couldn't have done those things. Opposing estrogen's edema-promoting action was involved, but I couldn't imagine any mechanism that could explain such rapid movement of water from the swollen tissue into the bloodstream.

One of estrogen's effects is to lower the amount of albumin in the blood. Estrogen causes the liver to synthesize less albumin, partly by causing the messenger RNA to be destabilized and degraded. (Iron can have some similar effects on liver RNA.) When there isn't enough albumin in the blood, water moves from the blood into the tissues, causing edema. (Premenstrually, edema might seem to be just a nuisance, but it can eventually become a serious problem, with aging or pregnancy, for example.) Albumin binds oily substances, and its conformation seems to be opened when it binds them. Progesterone is known to adsorb strongly to proteins – it has been called a "cardinal adsorbant," meaning that it can bind in ways that cause the protein's adsorptive capacity to change. I believe that progesterone and pregnenolone oppose estrogen in many ways, but the amazing speed with which they can cause major structural changes in the soft tissues convinces me that one of their first sites of action is the albumin molecule, causing its conformation to open in such a way that it is able to more strongly bind water molecules. This physical change in albumin would change the blood's osmotic/oncotic pressure, causing water to flow into capillaries. As the edema is reduced, oxygenation is more efficient, because the pathway for oxygen diffusion becomes shorter.

Albumin has been described as a first line of defense against toxins, since it binds them until the liver is able to degrade them chemically. Progesterone, pregnenolone, and cholesterol are known to increase the organism's resistance to a great variety of toxins. (Selye coined the name "catatoxic steroids" to describe steroids of this type.) If these steroids bind to albumin in a way that opens the protein to increase its binding capacity, that single process could explain the "catatoxic" effect, as well as the anti-edema effect.

When the blood is unable to retain its normal amount of water because of insufficient albumin/sodium, the blood volume is reduced as the tissues become water-logged. This causes the hematocrit (the proportion of cells in a volume of blood) to rise, and this increased packing of red blood cells causes the blood to become more viscous. (Knisely studied this phenomenon in a great variety of sicknesses.) Increased viscosity and slower flow decrease the blood's ability to deliver oxygen and nutrients to the tissues, including the blood vessel walls, modifying their tone. Slower flow, even without any changes in the fibrin fibrinogen system itself, increases the formation of clots.

This description of progesterone's immediate action is intended to take some of the mystery out of its dramatic effects, but it isn't intended to argue against any of its actions within cells. It serves to give a general picture of how progesterone can systematically reduce stress and its harmful consequences, just by making blood circulation more efficient.

At first I most often used progesterone dissolved in olive oil to stop the stress-induced processes of deterioration, with a high protein diet to support the processes of repair. Now, I have added a variety of other techniques.

There always seems to be a rough balance between tissue regeneration and tissue degeneration, with growth and repair occurring when the equilibrium shifts in one direction, and with atrophy or degeneration occurring when the balance shifts in the other direction. If we can understand the mechanisms of atrophy, and how to retard or to block tissue destruction, then we can restore the balance to a degree which might allow regeneration to occur, even if we don't clearly understand the mechanisms of growth.

Skin and bones are such different types of tissue that it will be useful to start with them, because if we can see similar processes of degeneration or regeneration in them, then the chances are good that the same processes will occur in other tissues too. Bone is a relatively stable tissue, while skin is a tissue whose cells divide rapidly.

It is common medical knowledge that cortisone and related glucocorticoid-type hormones cause skin to atrophy, becoming thinner. Using topical applications of a synthetic derivative of cortisone, C. M. Papa and A M. Kligman showed that the atrophy extended to the pigment cells, reducing their size and eliminating most of their dendritic branches. They also found that estrogen caused the skin to become thinner. The other steroids they tested, progesterone, testosterone, and pregnenolone, acted in the opposite direction, making aged and atrophied skin thicker and more regular. They also made the pigment cells larger, and increased their branching.[1]

Since these hormones were already known to have protective actions against cortisone and estrogen, these results were not too surprising, though they did directly contradict the claims of people who made estrogen-containing cosmetics.

Since progesterone and pregnenolone do not cause healthy, young skin to thicken, their effect in damaged skin is probably partly to replace the deficiency of that type of steroid which occurs with aging, and to offset the damaging effects of the catabolic hormones, whose influence does not decrease with age.[2]

Many years ago it was found that in old age a woman's estrogens were increased relative to the 17-keto steroids adrenal androgens. Later, it was found that the conversion of androgen to estrogen increases with age in both men and women, and that this occurs largely in fat cells. Several years ago, P. K. Siiteri found that low thyroid modified the enzymes of fat cells in a way that would tend to increase the conversion of androgen to estrogen. More recently, it was found that adding progesterone to the enzymes had the opposite effect of aging and hypothyroidism, protecting the androgen from conversion to estrogen. These researchers (C. J. Newton and colleagues, of London) concluded that the decreased output of progesterone after the menopause might account for the increased production of estrogen.[3] Since progesterone declines in aging men, too, this could account for the same process in men.[2]

Vitamin A's effect on the skin opposes that of estrogen.[4] There are several mechanisms that could account for this. Vitamin A is used in the formation of steroids, and since the skin is a major site of steroid metabolism, vitamin A might help to maintain the level of the anti-catabolic steroids. A deficiency of vitamin A causes excessive release of the lysosomal enzymes, acid hydrolases, resulting in tissue catabolism.[5] Also, vitamin A is necessary for the proper differentiation of cells in skin and other membranes. A deficiency tends to cause an increased rate

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of cell division, with the production of abnormal cells, and a substitution of keratinized cells for other types. Estrogen also promotes keratinization and speeds cell division. A deficiency of vitamin A can cause leukoplakia in the mouth and on the cervix of the uterus; although this is considered "pre-cancerous," I have found it to be very easily reversible, as I have discussed elsewhere.[6] I suspect that the intracellular fiber, keratin, is produced when a cell can't afford to do anything more complex. Adequate vitamin A speeds protein synthesis,[7] and allows it to be used more efficiently.

Prolactin (which is promoted by estrogen, and inhibited by progesterone) increases with stress and with age. It probably affects every tissue, but it seems to have its greatest effects on the secretory membranes. It is known to have strong effects on the kidney, gut and skin (sweat and oil glands, hair follicles, and feathers in birds), and on the gills of fish. Its involvement with milk production suggests that it might mobilize calcium from bones, and in fact it does contribute to osteoporosis. This was foreseen by G. Bourne, in his book on the metabolism of hard tissues, when he suggested that estrogen, acting through the pituitary, might be expected to promote osteoporosis.

Since reading Bourne's book, I have doubted that it was rational to use estrogen to prevent osteoporosis, especially when it is known to be carcinogenic and when the ratio of estrogen to androgens and progesterone increases after menopause. Now that several publications have appeared clearly showing that estrogen increases prolactin, that prolactin increases with aging, and that prolactin contributes to osteoporosis, the postmenopausal use of estrogen is worse than dubious. But this was exactly when the pharmaceutical companies needed help in continuing to sell their profitable estrogens, and this was exactly the time when the FDA came out with its official approval of estrogen for preventing osteoporosis.[8]

Some doctors combine estrogen with testosterone, and this is much safer and more likely to keep the bones healthy. But since testosterone, like estrogen and cortisone, causes the thymus gland to atrophy, it is not a very good idea for chronic use, even if it doesn't cause masculinization. The other anti-estrogens, which are present at high levels in young women, include progesterone and DHEA. I have seen several publications which I think would justify the use of physiological amounts of DHEA to prevent or to treat osteoporosis,[9] and a few which support the use of progesterone.[10,11] My own observations on their use in osteoporosis have been presented many times at alternative medical conferences since the 1970s, but the main-line medical journals and conferences have declined to accept my reports, even when they advertise that all papers submitted will be presented in some form; many physicians believe that they are being presented with a fair sampling of the work being done in endocrinology, when in fact they are being given intensive advertising sessions.

Since it is known that cortisol causes bone loss, and it is widely accepted that progesterone has an "antiglucocorticoid" action, it is reasonable to think that progesterone should protect against bone loss, and that it is a progesterone deficiency after menopause which is a major factor in the development of osteoporosis. In the first edition of *Nutrition for Women* (1975) I pointed this out, in comparing menopause to Cushing's disease. Nencioni and Polvani more recently made observations which support this mechanism, in which progesterone "exerts a protective effect," by blocking the corticosteroid receptors. They observed "that the process of rapid bone resorption starts before the onset of amenorrhea and the abrupt fall in the estrogen levels and coincides with decline in progesterone secretion."[11]

By improving blood circulation and oxygenation of the tissues, progesterone and pregnenolone will decrease the need for the body to produce cortisol. Pregnenolone acts in the brain to decrease the basal secretion of ACTH. This protective effect is more basic than that achieved by blocking the cortisol receptors.

The early tests of the toxicity of vitamin A used cartilage in tissue culture. The same enzymes which are released by a deficiency of vitamin A are released by a large excess, causing dissolution of the cartilage. Other studies showed that a vitamin A deficiency caused similar changes in both bone and cartilage. Although much vitamin A is consumed in the production of progesterone, these studies show a direct effect of the vitamin on tissue stability. Although I believe that a vitamin A supplement will offer considerable protection against osteoporosis (and also against aging of the skin), it is important to remember that excessive vitamin A inhibits the thyroid, and that there is less risk of toxicity when vitamin E is supplemented too. I think many of the headaches currently associated with vitamin A use are the result of a preservative in the capsules (probably a sulfite), since some people who react to the vitamin in capsule form don't react when they use a specially ordered bulk form prepared without preservatives.

Things which damage skin and bones also damage other tissues, and things which protect them also protect other tissues. The protective factors include hormones (thyroid, DHEA, progesterone, and pregnenolone), vitamins A and E, and minerals – including magnesium, calcium, and sodium. Sodium spares magnesium, and helps to make albumin function in regulating blood and tissue water content. Under some conditions, sodium can act as an antioxidant. Since the unsaturated oils (and their prostaglandin derivatives) decrease respiration, cause stress to be more harmful, and have some specific effects that promote aging of skin, bones, and other tissues, the use of coconut oil is especially important. I think its use is one of the factors that prevents osteoporosis in tropical countries.

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