Origins of Progesterone Therapy

Ray Peat's Newsletter

By the beginning of the 20th century, the idea of extracting regulatory substances from animal tissues was coming into general acceptance in Western medicine. J.A. Lebreton, in Paris, was one of the first to argue for the therapeutic use of an extract of the corpus luteum. Around 1904, C.F. Burnam, of Baltimore, began using corpus luteum of the sow, administered orally, to treat the nervous symptoms associated with menopause or with the menstrual cycle, and also to treat functional amenorrhea, obesity, sterility, and habitual miscarriage. (1912 edition of *New and Nonofficial Remedies*, and *JAMA*, August 31, 1919, 1ix, p. 698.) By the 1920s, tablets of desiccated corpus luteum were generally available, and the daily dosage recommended (representing 6 to 18 grams of fresh tissue) contained a very substantial quantity of progesterone.

The chemical structure of pure cyrstalline progesterone was determined in 1934 (by Butenandt), and within 2 years many publications were reporting the beneficial effects of injections of the purified material. By 1935, animal research was confirming that the therapeutic work previously done with the crude extract had been on the right track. Although the early research showed that progesterone was very beneficial in threatened miscarriage, arthritis, infertility, cancer and functional diseases of the nervous system, interest in this generic, public-domain material faded as the pharmaceutical industry found methods for converting it into proprietary synthetic glucocorticoids, estrogens, and progestins.

Animals are generally more sensitive to progesterone than humans are, and in animals no toxic level has been found, except that in the highest doses it is anesthetic. In humans, even this effect has never been reported in the medical literature, and it is clearly anti-toxic in nature. Besides preventing acute poisoning of many kinds, it also reduces the incidence of birth defects and cancer.

Progesterone, The Protective Substance of Youth

In 1971, I discovered that vitamin E and progesterone work together to sustain efficient production and use of biological energy.[1]

In the mid-1970s, I found that progesterone is the most powerful order-preserving substance (anti-chaotropic) on the cellular level, and that this explains its range of protective actions, from anti-toxic to anti-stress.[2,3]

Around 1980, I discovered that vitamin E, with its crucial effect on the mitochondrial respiratory enzymes, is a uniquely powerful, stable, and biologically compatible solvent for progesterone.[4]

Their intimate association at certain cellular sites requires mutual solubility. This property of mutual affinity extends to all biological areas, meaning that the solution of progesterone in vitamin E can be administered with exceptional efficiency by application to the skin or other membranes, or by ingestion, where normal digestive processes convert it into chylomicrons and distribute it to all tissues, allowing it to escape the tendency of the liver to convert it rapidly to an excretory form, as occurs when progesterone is administered in other forms.

Because of its profound biological compatibility, the progesterone-vitamin E solution permits otherwise impossibly high doses to be given, increasing by as much as 2,000% progesterone's already dramatic effects in a wide range of major biological problems, including epilepsy, habitual miscarriages, auto-immune diseases, and cancer of the uterus, breast, and kidney.

Some Aspects of Basic Progesterone Research

By 1945, Hans Selye had demonstrated that progesterone in itself has the full spectrum of regulatory and anti-stress functions of the adrenal steroids.

A little later, Albert Szent-Gyorgyi showed that progesterone is able to regulate the heart, in a manner similar to digitalis. In the 1970s, I demonstrated that it acts similarly on vascular smooth muscle, regulating its tone and preventing venous pooling of blood, and maintaining normal filling of the heart, opposing shock. The immediate improvement in circulation can have dramatic effects, which include restoration of kidney function, elimination of fluid from the lungs, restoration of sensation in the feet, and healing of gangrenous toes.

It restores normal tone to other smooth muscles, including the gall bladder, urinary bladder, intestine, sphicters, and uterus.

Progesterone's ability to regulate thresholds of cellular excitation operates in nerves, as well as in smooth and cardiac muscle. It sensitizes nerves that regulate respiration, and has been used to treat infant apnea, sleep apnea in adults, and polycythemia vera in men.

In cases of specific progesterone deficiency in men, small doses can cure impotence. It has been used effectively to treat benign prostatic enlargement.

It normalizes fluid pressure, as in bursitis and glaucoma treatment.

It restores many of the functions of aged skin, and is the normal defense against calcium loss from bones.

It is one of the few essential requirements, besides nutrients, for nerve (brain) cell growth and survival. In young people of both sexes, the brain contains more progesterone than other organs do.

It is reasonable that progesterone, the dominant hormone in pregnancy, should have a full range of protective functions to protect the vulnerable organism during its intra-uterine life.

Practical Issues

A typical dose of progesterone/vitamin E, 20 mg/day for 10 consecutive days, costs about $1.00 per month, at the present retail price.

Pharmacists have the authority to compound drugs as they choose, just as physicians can prescribe the formulation they prefer.

Neither progesterone nor vitamin E has any toxicity when used orally.

Under federal law, a prescription is needed for a dosage form of a drug that is potentially harmful. In practice, the very dangerous injectable insulin is always sold without need for a prescription, presumably because its use is conceived as akin to nutrition, providing an essential natural substance to restore a natural function of the body. By analogy with insulin, the infinitely less dangerous progesterone should not require a prescription.

The logcal way to make progesterone/vitamin E available to the public would be to license the patent to a chain of drugstores.

The availability of this effective and economical form of progesterone can hardly be kept secret, because people tell their friends, and patients eventually convince their physicians that it works.

An exclusive licensing agreement would be possible with 10% royalties, based on the retail price, with a guaranteed sales volume, and with lower royalties for larger volumes.

Economic Questions

Because of its absorption by a natural digestive route which distributes it to all of the tissues, progesterone dissolved in vitamin E is almost 100% absorbed when taken orally. Less than 1% is absorbed from some types of suppositories, and less than 5% absorption is typical. Taken orally as a micronized powder, pharmaceutical efficiency is only slightly better.

Most of the valid human research before 1981 used intramuscular injections of progesterone dissolved in vegetable oil and benzyl alcohol. Benzyl alcohol has a high affinity for water, and in contact with the tissue fluid, it leaves the mixture, causing progesterone crystals to form, since vegetable oil is a poor solvent for progesterone. Therapeutic blood levels of progesterone can be achieved by intramuscular injections, but at the cost of leaving toxic debris at the site of injection. Benzyl alcohol is a powerful neuro-toxin, but its harm is reduced by progesterone's anti-toxic action. The cost of the injectable progesterone, and of the injection itself, has been the main factor preventing wider acceptance of this form of progesterone in the United States.

Natural progesterone, and closely related steroids, occur in a wide variety of organisms. Up to the present, the cheapest source of the raw material has been the wild Dioscorea yam of tropical Mexico, but soybeans have also been used as the source of a steroid for production of progesterone. Since the soybean is a major source of vitamin E, the finished product can be made anywhere the bean is produced. Fenugreek, a quick-growing plant, contains the same substance as the Mexican yam, and can also be used as a source of vitamin E.

The chemistry for converting crude diosgenin into pregnenolone, and for converting pregnenolone into progesterone, is very simple, and can be done with little capital, at the site of production of the raw material. Interstate commerce needn't be involved, except for the economy of scale.

Correspondence and Subscriptions
Ray Peat
Ray Peat's Newsletter
P.O. Box 3427
Eugene, Oregon 97403
503-345-9855

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