

# Progesterone Deceptions

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From the [original article](#) in 2007. Author: [Ray Peat](#).

In the 1930s, it was demonstrated that estrogen, even in small doses, produced abortions, and that when it is given early enough, even a very small dose will prevent implantation of the fertilized embryo. Progesterone was known, by the early 1940s, to protect against the many toxic effects of estrogen, including abortion, but it was also known as nature's contraceptive, since it can prevent pregnancy without harmful side-effects, by different mechanisms, including prevention of sperm entry into the uterus. That is, progesterone prevents the miscarriages which result from excess estrogen (1,2), but if used before intercourse, it prevents conception, and thus is a true contraceptive, while estrogen is an abortifacient, not a contraceptive.

In the 1950s, there was a search for chemicals which would prevent ovulation. According to Carl Djerassi (), drug companies were extremely reluctant to risk a religious backlash against their other products, and so hesitated to market contraceptives. Obviously, the induction of monthly abortions would have been even harder to sell.

According to Djerassi (3), "Until the middle 1940s it was assumed that progesterone's biological activity was extremely specific and that almost any alteration of the molecule would diminish or abolish its activity." This would obviously discourage interest from the drug companies, who could patent a substance which they had chemically modified, but could not patent a simple natural substance. However, many substances--even non-steroidal chemicals--were known to have estrogenic action. (4)

By 1942, Hans Selye had demonstrated that natural steroids retain their activity when administered orally. But every drug company with a steroid patent had an obvious interest in having the public believe that there is a reason that the natural steroids cannot be conveniently used. The doctrine that natural steroids are destroyed by stomach acid appeared, was promoted, and was accepted--without any supporting evidence. In the manufacture of progesterone, the precursor steroid is boiled in hydrochloric acid to free it from its glucose residue. No one seriously believed that stomach acid hurts progesterone, except the public--and the doctors, who had seen the claim in their medical journals, and had heard it from drug salesmen.

The myth stopped the use of the cheap tablets of progesterone, as tablets of the synthetic "progestins" came on the market, at a much higher price. Doctors who insisted on using real progesterone were forced to buy it in an injectable form. As a result, solubility became an issue. Progesterone is extremely insoluble in water, and, though it is vastly more soluble in vegetable oil than in water, it does not stay in solution at room temperature even at the low concentration of 1 part in 1000 parts of a typical vegetable oil.

When people speak of an allergy to progesterone (or even to penicillin) they generally are not aware of the presence of a very toxic solvent.(5) For a time, progesterone was often sold dissolved in benzyl benzoate. The Physician's Desk Reference warned of possible allergic reactions to progesterone. Now, it is supposedly sold dissolved in vegetable oil, with about 10% benzyl alcohol as--supposedly--a "bacteriostatic agent."

Bacteriostatic water contains 0.9% to 1.9% benzyl alcohol, and can irreversibly harm nerves. (6,7) Its use in hospitals killed thousands of babies. Awareness of benzyl alcohol's toxicity goes back to 1918 at least; it was proposed as an effective insecticide, and was found to be toxic to many animal systems. The safe systemic dose (7) is exceeded with an injection of 150 mg. of progesterone, yet the local concentration is far higher. It can cause a severe reaction even when used at a lower concentration, in bacteriostatic water. (5)

Other alcohols, including ethanol, have been used as solvents, but since they (ethanol even more than benzyl alcohol) have an affinity for water, the solution decomposes in contact with tissue water.

In spite of the toxicity of the vehicle, several beneficial effects can be obtained with injected progesterone, in serious conditions such as epilepsy or cancer of the breast or uterus. Many researchers have commented on the very obvious difficulty of giving very large amounts of progesterone. (8) My comparisons of oral progesterone in tocopherol with other forms and methods of administration show a roughly similar efficiency for oral and inject progesterone, and about 1/20 the effect for suppositories. Crystals of progesterone are visible in the suppositories I have examined, and this material is obviously wasted.

An old theory of vitamin E's mechanism of action in improving fertility was that it spares progesterone.(9) It is established that some of the effects of vitamin E and progesterone are similar, for example, both prevent oxygen waste and appear to improve mitochondrial coupling of phosphorylation with respiration. I suspected that if they actually both work at the same mitochondrial site, then they must have a high mutual solubility.

Knowing the long-standing problem of administering large doses of progesterone without a toxic solvent, I applied for and was granted a patent for the composition of progesterone in tocopherol. One of my reasons for publishing in the form of patents is that I have had many years of experience in having my discoveries taken up by others without acknowledgment, if they are compatible with conventional prejudices. Typically, an editor rejects a paper, and then a few months later publishes a very similar paper by someone else. My dissertation research, which established that an estrogen excess kills the embryo by suffocation, and that progesterone protects the embryo by promoting the delivery of both oxygen and glucose, didn't strike a responsive chord in the journals which are heavily influenced by funds from the drug industry.

According to a consultant for a major medical journal, the idea "...of dissolving progesterone, a fat soluble steroid hormone, in vitamin E which is then incorporated into chylomicrons absorbed via the lymphatics, and thus avoids the liver on the so called first pass... ..is so simple it is amazing that the pharmaceutical companies have not jumped on it." (A more sophisticated

writer might have said "...stomped on it.")

In the powder form, direct and intimate contact with a mucous membrane allows lipid phase to lipid phase transfer of progesterone molecules. Instead of by-passing the liver, much of the progesterone is picked up in the portal circulation, where a major part of it is glucuronidated, and made water soluble for prompt excretion.

Since this glucuronide form cross-reacts to some extent with the ordinary progesterone in the assay process, and since 50% of the ordinary free progesterone is carried inside the red blood cells (10,11), and 50% is associated with proteins in the plasma, while the glucuronide hardly enters the red blood cells at all, it is better to judge by clinical efficacy when comparing different oral forms. My comparisons show several times higher potency in the tocopherol composition than in powder form.

Since progesterone's use as a drug antedates the 1938 law requiring special federal approval, its legal status is similar to that of thyroid hormone. Unfortunately, for both thyroid and progesterone, there is a tendency to cut corners for the sake of a bigger profit margin.

For example, steroid acetates are generally a little cheaper than the simple natural steroid. Some people assume that an acetate or butyrate can be substituted for the steroid itself. This can cause dangerous reactions.

Medroxyprogesterone acetate is considered a progestin (though it is not supportive of gestation), because it modifies the uterus in approximately the way progesterone does, but it is luteolytic, and lowers the ovaries' production of progesterone while progesterone itself has a positive effect on the corpus luteum, stimulating progesterone synthesis. Defining "progestin" in a narrow way allows many synthetics to be sold as progestogens, though some of them are strongly estrogenic, allowing them to function as contraceptives--it is odd that contraceptives and agents which suppress progesterone synthesis should be officially called "supportive of pregnancy." It is probably partly the acetate group in the medroxyprogesterone acetate molecule which makes it bind firmly to receptors, yet causes it to block the enzymes which would normally be involved in progesterone metabolism. (I think testosterone, even, might be a safer progestin than medroxyprogesterone acetate.) Pregnenolone acetate similarly blocks the enzymes which normally metabolize pregnenolone. (12) In aspirin, it has been found that it is the acetyl group which (by a free radical action) blocks an enzyme involved in prostaglandin synthesis.

If the category called "progestogens" or "progestins" is to be defined on the basis of a single tissue reaction, then it is possible to classify progesterone with the toxic synthetic substances, but then it becomes highly deceptive to imply that progesterone is *just* a progestin, or that it has any of the *other properties* of the toxic synthetics, but this continues to be done. The warnings about "progestins causing birth defects," for example, cause epileptic women to use conventional anti-seizure drugs (all of which cause birth defects) during pregnancy, and to avoid natural progesterone, which generally could control their seizures. Thus, a false message attached to progesterone creates precisely the harm it claims to want to prevent. In my communications with the regulatory agencies, I have concluded that their attempts to deceive are too blatant to ascribe to incompetence. Whether it's the Forest Service the FDA, the principle is the same: The regulatory agencies have been captured by the regulated industries.

Another place to cut costs is in the tocopherol. Tocopherol acetate does have vitamin E activity, but since it is only about half as efficiently absorbed as the simple tocopherol (13), it is a mistake to save a few dollars an ounce, at the expense of losing half of the therapeutic effect. People who have compared natural progesterone in natural tocopherols with other compositions have insisted that the other compositions must not contain progesterone.

The taste of natural vitamin E is stronger than that of the synthetic forms, but since the mixture is absorbed by any tissue it contacts, including various parts of the bowel, it can be taken in a capsule. If a small amount of olive oil is used with it, absorption through the skin is very rapid. Many women use it vaginally, spread onto a diaphragm, to hold it in contact with the membranes. The efficiency of absorption by all routes is so high that patients should be warned against its anesthetic effect, until their dosage requirement is known approximately. Some physicians prefer concentrations higher than 10%, but the risk of accidental drunkenness or anesthesia is higher with the stronger solutions.

It is an indication of the tocopherol solution's high availability that medical researchers such as Roy Hertz (8), who thought they were administering maximal doses by combining injections with suppositories, never mentioned the problem of an anesthetic effect from an overdose. Similarly, it is evidence of the extremely poor availability of the micropulverized progesterone that the researchers have administered hundreds of milligrams per day, without mentioning the symptoms of an overdose. Because of the difficulties involved in scientifically studying the clinical effectiveness of various formulations, I think the most practical way of evaluating the effectiveness of different progesterone formulations is to measure the amount extractable from the red blood cells, a few hours after the peak serum level has been reached. This will reasonably reflect the amounts reaching brain cells, adrenal glands, and the various other cells on which progesterone has its therapeutic action.

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