Progestin

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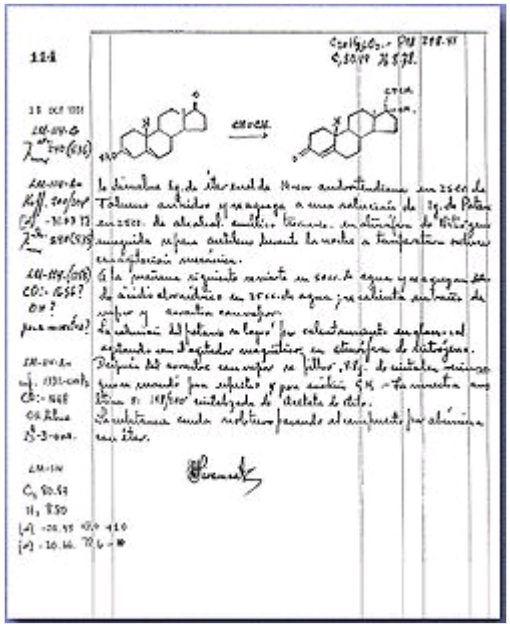
A **progestin** is a synthetic[1] progestogen that has progestinic effects similar to progesterone. [2] The two most common uses of progestins are for hormonal contraception (either alone or with an estrogen), and to prevent endometrial hyperplasia from unopposed estrogen in hormone replacement therapy. Progestins are also used to treat secondary amenorrhea, dysfunctional uterine bleeding and endometriosis, and as palliative treatment of endometrial cancer, renal cell carcinoma, breast cancer, and prostate cancer. High-dose megestrol acetate is used to treat anorexia, cachexia, and AIDS-related wasting. Progesterone (or sometimes the progestin dydrogesterone or 17α-hydroxyprogesterone caproate) is used for luteal support in IVF protocols, questionably for treatment of recurrent pregnancy loss, and for prevention of preterm birth in pregnant women with a history of at least one spontaneous preterm birth.[3] They are also used in judicial chemical castration of sex offenders as well as a treatment options for those suffering from paraphilia.



Co-inventor Luis E. Miramontes's signed laboratory notebook. October 15, 1951

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History

The recognition of progesterone's ability to suppress ovulation during pregnancy spawned a search for a similar hormone that could bypass the problems associated with administering progesterone (low bioavailability when administered orally and local irritation and pain when continually administered parenterally) and, at the same time, serve the purpose of controlling ovulation. The many synthetic hormones that resulted are known as progestins.

The first orally active progestin, ethisterone (pregneninolone, 17α-ethynyltestosterone), the 17α-ethynyl analog of testosterone, synthesized in 1938 by Hans Herloff Inhoffen, Willy Logemann, Walter Hohlweg and Arthur Serini at Schering AG in Berlin, was marketed in Germany in 1939 as *Proluton C* and by Schering in the U.S. in 1945 as *Pranone*[4][5][6][7][8]

A more potent orally active progestin, norethisterone (norethindrone, 19-nor-17α-ethynyltestosterone), the 19-nor analog of ethisterone, synthesized in 1951 by Carl Djerassi, Luis Miramontes, and George Rosenkranz at Syntex in Mexico City, was marketed by Parke-Davis in the U.S. in 1957 as *Norlutin*, and was used as the

progestin in some of the first oral contraceptives (*Ortho-Novum*, *Norinyl*, etc.) in the early 1960s.[5][5][6][7][8][9]

Norethynodrel, an isomer of norethisterone, was synthesized in 1952 by Frank B. Colton at Searle in Skokie, Illinois and used as the progestin in *Enovid*, marketed in the U.S. in 1957 and approved as the first oral contraceptive in 1960.[5][6][7][8][10]

Examples

Some examples of progestins that have been used in hormonal contraceptives are norethynodrel (Enovid), norethindrone (many brand names, most notably Ortho-Novum and Ovcon) norgestimate (Ortho Tricyclen, Ortho-Cyclen), norgestrel, levonorgestrel (Alesse, Trivora-28, Plan B, Mirena), medroxyprogesterone (Provera, Depo-Provera), desogestrel, etonogestrel (Implanon), and drospirenone (Yasmin, Yasminelle, YAZ).

Sometimes progestins are classified by *generation*:

- First (estrane): norethindrone, norethynodrel,[11] norethindrone acetate, ethynodiol diacetate
- Second (gonane): levonorgestrel, norethisterone,[12] norgestrel
- Third (gonane): desogestrel, gestodene, norgestimate, drospirenone[12]
- Fourth: dienogest, drospirenone, nestorone, nomegestrol acetate and trimegestone[13]

Tanaproget is a non-steroidal progestin.

Methods of progestin-based contraception

It has been found that the most effective method of hormonal contraception is with a combination of estrogen and progestin. This can be done in a monophasic, biphasic, or triphasic manner. In the monophasic method, both an estrogen and a progestin are administered for 20 or 21 days and stopped for a 7- or 8-day period that includes the 5-day menstrual period. Sometimes, a 28-day regimen that includes 6 or 7 inert tablets is used. Newer biphasic and triphasic methods are now used to more closely simulate the normal menstrual cycle. Yet another method is to administer a small dose of progestin only (no estrogen) in order to decrease certain risks associated with administering estrogen, but a major side-effect is irregular bleeding usually observed during the first 18 months of such therapy.

Alternatively, it can be delivered by intra-muscular injection every several months.

See also

List of steroid abbreviations

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