

Progestin: Synthetic Progesterone ^[1]

By: Butler, Aliya Sheraden, Seward Keywords: [Contraception](#) ^[2] [Reproduction](#) ^[3]

Progestin is a synthetic form of [progesterone](#) ^[4], a naturally occurring [hormone](#) ^[5], which plays an important role in the female reproductive cycle. During the 1950s two types of [progestin](#) ^[6] that were later used in [birth control](#) ^[7] pills were created, [norethindrone](#) ^[8] and [norethynodrel](#) ^[9]. In 1951 [Carl Djerassi](#) ^[10] developed [norethindrone](#) ^[8] at [Syntex](#) ^[11], SA Laboratories located in Mexico City, receiving a patent on 1 May 1956. In 1953 [Frank Colton](#) ^[12] developed [norethynodrel](#) ^[9] at G.D. Searle and Company Laboratories located in Chicago, receiving a patent on 29 November 1955. These two types of synthetic [progesterone](#) ^[4] are important to the history of [embryology](#) ^[13] as part of the [birth control movement](#) ^[14], because they facilitated the development and creation of the [birth control](#) ^[7] pill, which changed the way people viewed [birth control](#) ^[7] and revolutionized women's [birth control](#) ^[7] methods.

During the 1940s there was a strong desire among chemists and pharmaceutical companies to develop synthetic steroids because of advances in basic knowledge of [hormones](#) ^[15] and [endocrinology](#) ^[16]. Also, the development and commercial success of cortisone, a steroid used for the treatment of arthritis, encouraged the exploration of steroids for treatment of other medical problems. It was believed that [sex hormones](#) ^[17] in particular would hold great potential for possible treatments. The steroid research programs of commercial laboratories at this time focused on simply creating synthetic steroids and then supplying them to researchers and physicians to discover and develop uses for them.

Djerassi was the first to develop a synthetic [progestin](#) ^[6] known as [norethindrone](#) ^[8]. He had long been interested in steroids and came to [Syntex](#) ^[11] because of the opportunity to focus on steroid synthesis. [Russell Marker](#) ^[18], who also worked at [Syntex](#) ^[11], had discovered in 1943 that [progestin](#) ^[6] could be synthesized in large quantities from diosgenin, a steroid found in Mexican yams, through a process known as "marker degradation." Although this work was not directly related to Djerassi's development of [norethindrone](#) ^[8], it established [Syntex](#) ^[11] as a major site for [hormone](#) ^[5] research and production, facilitating Djerassi's later work.

At the same time, [Frank Colton](#) ^[12] developed [norethynodrel](#) ^[9] at G. D. Searle and Company in Chicago. Norethynodrel is a potent, orally active [progestin](#) ^[6] that differs from [norethindrone](#) ^[8] only in the location of one of its carbon double bonds. Both synthetic progestins, [norethindrone](#) ^[8] and [norethynodrel](#) ^[9], function in [birth control](#) ^[7] by elevating [progesterone](#) ^[4] levels and preventing [ovulation](#) ^[19], mimicking the conditions during [pregnancy](#) ^[20]. Norethindrone was considered to induce more masculine tendencies and was prescribed to women who had problems such as tender breasts prior to [menstruation](#) ^[21]. Norethynodrel was considered to have more feminizing tendencies and was prescribed to women who had problems with acne.

Neither Djerassi nor Colton had intended for the compounds to be used in [birth control](#) ^[7] pills, assuming instead that they would be used to treat gynecological disorders such as irregular menstrual cycles and [endometriosis](#) ^[22], which causes painful [menstruation](#) ^[21] and [infertility](#) ^[23]. However, both Searle and [Syntex](#) ^[11], unaware of Gregory Pincus' research agenda, had supplied samples of their compounds to him at the Worcester Foundation, where Pincus and others were actively developing a hormonal [birth control](#) ^[7] pill. In October 1955 at the Fifth International Conference on Planned Parenthood, Pincus reported that based on tests in rats, the two compounds [norethindrone](#) ^[8] and [norethynodrel](#) ^[9] were the most promising for use in a [birth control](#) ^[7] pill based on their ability to prevent [ovulation](#) ^[19]. These findings were also published in *Endocrinology* and *Science*.

Ultimately [norethynodrel](#) ^[9] was chosen for use in [Enovid](#) ^[24], the first hormonal [birth control](#) ^[7] pill, which was marketed in 1960. This selection was because of Pincus' ties to Searle through his past consulting work, as well as Searle's enthusiasm for the [birth control](#) ^[7] pill. On the other hand, [Syntex](#) ^[11] laboratories was associated with Parke-Davis Pharmaceuticals, who were reluctant to produce a [birth control](#) ^[7] pill due to concern over religious and moral backlash. In 1962, [norethindrone](#) ^[8] was marketed by Ortho, a division of Johnson and Johnson, as the [birth control](#) ^[7] pill [Ortho-Novum](#) ^[25]. Despite initial hesitation in selling [birth control](#) ^[7], in 1964 Parke-Davis gained rights to [norethindrone](#) ^[8] acetate, a derivative of [norethindrone](#) ^[8], from [Syntex](#) ^[11], giving [Syntex](#) ^[11] a large share of the [birth control](#) ^[7] market.

By 1969 there were twenty-two different brands of pills marketed in the US, and they differed by the amounts of [progestin](#) ^[6] and [estrogen](#) ^[26] they contained. At this time the most commonly used [progestin](#) ^[6] was still [norethindrone](#) ^[8]. [Enovid](#) ^[24] had contained very large doses of [norethynodrel](#) ^[9] and some [estrogen](#) ^[26], but due to the side effects from such large doses of [hormones](#) ^[15], it was no longer prescribed as an oral contraceptive. [Ortho-Novum](#) ^[25] was still used in 1969 because it contained much smaller doses of [hormones](#) ^[15] and did not have the same side effects.

The creation of [progestin](#) ^[6] is important to understanding and controlling development because of the role it played in the development of the hormonal [birth control](#) ^[7] pill. Although this was not its intended purpose, [progestin](#) ^[6] and [synthetic estrogen](#)

^[27] (specifically ethinyl [estradiol](#) ^[28]) are essential components of the [birth control](#) ^[7] pill and other [birth control](#) ^[7] technologies, such as Plan B.

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Progestin is a synthetic form of progesterone, a naturally occurring hormone, which plays an important role in the female reproductive cycle. During the 1950s two types of progestin that were later used in birth control pills were created, norethindrone and norethynodrel. In 1951 Carl Djerassi developed norethindrone at Syntex, S.A. laboratories located in Mexico City, receiving a patent on 1 May 1956. In 1953 Frank Colton developed norethynodrel at G.D. Searle and Company laboratories located in Chicago, receiving a patent on 29 November 1955. These two types of synthetic progesterone are important to the history of embryology because they facilitated the development and creation of the birth control pill, which changed the way people viewed birth control and revolutionized women's birth control methods.

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