Estrogen and the Menstrual Cycle in Humans

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Estrogen is the primary sex hormone in women and it functions during the reproductive menstrual cycle. Women have three major types of estrogen: estrone, estradiol, and estriol, which bind to and activate receptors within the body. Researchers discovered the three types of estrogen over a period of seven years, contributing to more detailed descriptions of the menstrual cycle. Each type of estrogen molecule contains a slightly different arrangement or number of atoms that in turn causes some of the estrogens to be more active than others. The different types of estrogen peak and wane throughout women's reproductive cycles, from normal menstruation to pregnancy to the cessation of menstruation (menopause). As scientists better explained the effects of estrogens, they used that information to develop oral contraceptives to control pregnancy, to map the menstrual cycle, and to create hormone therapies to regulate abnormal levels of estrogen.

The estrogens (estradiol, estrone, and estriol) are a group of biologically active steroid hormones. As signaling molecules, estradiol, estrone, and estriol bind to receptor molecules in cells to signal specific changes to occur within the body. The estrogens each attach to receptor molecules with a specific fit, like how one puzzle piece connects to another. Some of the estrogen molecules function during the menstrual cycle, leading to changes in tissue thickness and menstrual bleeding. All three of the estrogen molecules are similar in chemical structure and constituents. The similarities of the different estrogens arise because some estrogen molecules are derivatives of the other, meaning that one estrogen can lead to the creation of another. Each estrogen molecule contains a similar base structure and varies minutely with the addition or elimination of specifically bound atoms, called functional groups. Researchers used the different functional groups to isolate and distinguish estradiol, estrone, and estriol from one another.

In the 1920s, researchers debated about what item in the female body produced most of the estrogen, then called the primary ovarian hormone, during menstrual cycles. Some researchers said that the corpora lutea, which forms on the ovaries after egg release, contained and produced the needed amount of estrogen to complete the menstrual cycle. However, researchers Edward Adelbert Doisy and Edgar Allen hypothesized that the ovarian follicles primarily produced the levels of estrogen needed to complete the cycle. In 1923 at Washington University in St. Louis, Missouri, Allen and Doisy isolated estrogen from ovarian follicle extracts and showed its effect in test animals. Their results showed that the ovarian follicles primarily produced estrogen during the reproductive cycle. That discovery enabled future researchers to outline the follicular phase, the phase in the menstrual cycle that includes egg development, to also include estrogen production in the ovarian follicles.

Later researchers showed that the increase in estrogen levels led to the production of another hormone, the luteinizing hormone, which leads to the release of eggs from ovaries.

The three kinds of estrogen—estradiol, estrone, and estriol—were discovered over time, with estrone being discovered first. In 1929, researchers Doisy, Clement D. Veler, and Sidney Thayer isolated pure crystalized estrone in the Laboratory of Biological Chemistry at the St. Louis University School of Medicine in St. Louis. The three researchers isolated estrone from the urine of pregnant women using distillation, a method that uses boiling point differences to evaporate one liquid from another; and extraction, the removal of one substance from another. At the Institute of Chemistry in Göttingen, Germany, Adolf Frederick Johann Butenandt also isolated estrone around the same time, receiving the Nobel Prize for Chemistry in 1939 for that achievement.

In addition to estrone, Doisy also isolated estriol from hundreds of gallons of urine from pregnant women in 1930, discovering a second estrogen. In 1936, Doisy alongside researchers Donald W. MacCorquodale and Stanley S. Thayer isolated the third type of estrogen, estradiol, from pig ovaries. Estradiol was later found in humans. The structure of estradiol is similar to estrone, but instead of the double bonded oxygen atom, the molecule contains a single bonded oxygen atom. The isolation of estradiol, the estrogen most involved in the reproductive menstrual cycle, enabled researchers to create hormone therapies and oral contraceptives. Doisy also researched Vitamin K, for which he went on to win the Nobel Prize in Physiology or Medicine in 1943.

Later, researchers used Doisy's methods to create hormone therapies for women who lacked proper levels of estrogen. Researchers could cause changes in the menstrual cycle, as they had the ability to give women estradiol, the most biologically active estrogen hormone that predominates during the menstrual cycle.

In 1946 in New York City, New York, physicians Hans Wiesbader and William Filler demonstrated their ability to induce changes in the menstrual cycle when they gave lab made (synthetic) estradiol to women with problems arising from menopause. In the mid twentieth century, researchers synthesized estradiol, like molecules from other products, creating compounds like ethinyl estradiol, which caused the same reactions within the body as natural estradiol. Wiesbader and Filler sought to help women...
Estradiol functions during the menstrual cycle. The drop in
progesterone levels during the luteal phase are high and, together with
estradiol, cause the endometrium to thicken to provide nutrients and a place for adhesion if an
egg is fertilized and becomes an embryo. The increase in levels ofestradiol and progesterone also causes the milk ducts in the breasts to dilate and become larger, resulting in swelling and possible breast soreness prior to the onset of menstruation. If an embryo implants to the endometrium, the corpus luteum functions until the placenta, which nourishes the fetus, develops to take over hormone production in the twelfth or thirteenth weeks of pregnancy. If a fertilized egg does not implant, the corpus luteum degrades around ten days after its initial development and stops secreting progesterone. The luteal phase ends right before the beginning of the next menstrual period or before the onset of pregnancy. The follicular phase occurs next, starting the menstrual cycle all over again.

Estradiol functions during the menstrual cycle. The drop in estradiol levels during the follicular phase causes the endometrium layer of the uterus to shed, beginning menstruation. In the later ovulatory phase, the dominant ovarian follicle produces estrogen and progesterone. The menstrual cycle begins anew if the recently produced egg remains unfertilized or if a fertilized egg does not implant to the uterus. In humans, each menstrual cycle lasts for approximately twenty-eight days but typically varies between individuals, as some women have longer cycles and others have shorter cycles. Professionals quantify each cycle's length by measuring the time in days that it spans from beginning to end. The monthly cycle starts on day one with normal menstruation and ends around day twenty-eight, just before the onset of the next menstruation, if a fertilized egg has not implanted. If a fertilized egg implants to the uterine wall, the menstrual cycle stops and pregnancy begins. In humans, four regulating hormones control the menstrual cycle by initiating and ending a series of stepwise phases. The four hormones include luteinizing hormone, follicle stimulating hormone, progesterone, and estrogen. The phases that make up the menstrual cycle include the follicular phase, the ovulatory phase, and the luteal phase.
Estradiol [6], which increases luteinizing hormone [11] levels, rupturing the ovarian follicle, which releases an egg [6]. The corpus luteum during the final luteal phase produces the hormone [6] estradiol [8] in increasing amounts, which then thickens the endometrium [19], enabling the menstrual cycle to start over again. During pregnancy [7], the placenta [28] produces more estradiol than estradiol [8]. Making estradiol the dominant estrogen [4] measured in blood concentration levels. Estrone increases in concentration and is produced more than estradiol [8] when a woman enters menopause, when menstruation [6] and the menstrual cycle stop.

Sources


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