

FURTHER DEVELOPMENT 14.3: THE MENSTRUAL CYCLE

The center of the menstrual cycle is the relationship between two hormonally induced processes: the release of an oocyte from the ovary followed by the formation of the corpus luteum, and the shedding and regeneration of the uterine tissue that can catch and nurture the embryo. The first day of vaginal bleeding is considered to be day 1 of the menstrual cycle. This bleeding represents the sloughing off of endometrial tissue and blood vessels that would have aided the implantation of the blastocyst. In the first part of the cycle (called the **proliferative or follicular phase**), the pituitary starts secreting increasingly large amounts of **follicle stimulating hormone (FSH)**. Any maturing follicles that have reached a certain stage of development respond to this hormone with further growth and cellular proliferation. FSH also induces the formation of **luteinizing hormone (LH)** receptors on the granulosa cells. Shortly after this period of initial follicle growth, the pituitary begins secreting LH. In response to LH, the meiotic block is broken. The nuclear membranes of competent oocytes break down, and the chromosomes assemble to finish the first meiotic division. It is at this stage that the egg will be ovulated.

The two gonadotropins, FSH and LH, acting together, cause the follicle cells to produce increasing amounts of estrogen, which has at least five major activities in regulating the further progression of the menstrual cycle:

1. It causes the uterine endometrium to begin its proliferation and to become enriched with blood vessels.
2. It causes the cervical mucus to thin, thereby permitting sperm to enter the inner portions of the reproductive tract.
3. It causes an increase in the number of FSH receptors on the granulosa cells of the mature follicles while causing the pituitary to lower its FSH production. It also stimulates the granulosa cells to secrete the peptide hormone inhibin, which also suppresses pituitary FSH secretion.
4. At low concentrations, it inhibits LH production, but at high concentrations, it stimulates it.
5. At very high concentrations and over long durations, estrogen interacts with the hypothalamus, causing it to secrete gonadotropin-releasing hormone.

As estrogen levels increase as a result of follicular production, FSH levels decline. LH levels, however, continue to rise as more estrogen is secreted. As estrogen continues to be made (days 7-10), the granulosa cells continue to grow.

Starting on day 10, estrogen secretion rises sharply. This rise is followed at midcycle by an enormous surge of LH and a smaller burst of FSH. Experiments with female monkeys have shown that exposure of the hypothalamus to greater than 200 picograms of estrogen per milliliter of blood for more than 50 hours results in hypothalamic secretion of gonadotropin-releasing hormone. This factor causes the subsequent release of FSH and LH from the pituitary. Within 10 to 12 hours after the gonadotropin peak, the egg is ovulated (Garcia et al. 1981).

Following ovulation, the **luteal phase** of the menstrual cycle begins. The remaining cells of the ruptured follicle, under the continued influence of LH, become the **corpus luteum**. (They are able to respond to this LH because the surge in FSH stimulates them to develop even more LH receptors.) The corpus luteum secretes some estrogen, but its predominant secretion is progesterone. This steroid hormone circulates to the uterus, where it completes the job of preparing the uterine tissue for blastocyst implantation, stimulating the growth of the uterine wall and its blood vessels. Blocking the progesterone receptor with the synthetic steroid mifepristone (RU486) stops the uterine wall from thickening and prevents the implantation of a blastocyst¹ (Couzin et al. 1986; Greb et al. 1999). Progesterone is also necessary for regulating the immune system so that the mother's immune cells don't attack the embryo. Progesterone induces the stromal cells of the uterus to produce interleukin-15, a compound that matures the **uterine natural killer cells**. These cells block the mother's immune response against the embryo, and they help remodel the spiral arteries of the uterus (which temporarily supply blood to the endometrium during the luteal phase) so that the blastocyst will find a nutrient-rich environment when it arrives (Diaz-Hernández et al 2021). The period of time between days 20-24 of the menstrual cycle is considered the "window of implantation" for the best chances of pregnancy (Cha et al 2012)

¹ This is why RU486 is used for postconception birth control. RU486 is thought to compete for the progesterone receptor inside the nucleus. RU486 can bind to the progesterone site in the receptor, and the receptor-RU486 complex appears to form heterodimers with the normal progesterone-carrying progesterone receptor. When this RU486-progesterone complex binds to progesterone-responsive enhancer elements on the DNA, transcription from these sites is inhibited (Vegeto et al. 1992; Spitz and Bardin 1993).

Progesterone also inhibits the production of FSH, thereby preventing the maturation of any more follicles and ova. (For this reason, a combination of estrogen and progesterone has been used in birth control pills. The growth and maturation of new ova are prevented as long as FSH is inhibited.) If the ovum is not fertilized, the corpus luteum degenerates, progesterone secretion ceases, and the uterine wall is sloughed off. With the decline in serum progesterone levels, the pituitary secretes FSH again, and the cycle is repeated. However, if fertilization occurs, the trophoblast secretes a new hormone, **chorionic gonadotropin**², which causes the corpus luteum to remain active and serum progesterone levels to remain high.

Thus, the menstrual cycle enables the periodic maturation and ovulation of human eggs and allows the uterus to periodically develop into an organ capable of catching a blastocyst and nurturing a developing organism for 37 weeks.

Scientists speak: A review of the menstrual cycle by the Khan Academy

<https://www.youtube.com/watch?v=K0mWhPj7eYQ>

<https://www.youtube.com/watch?v=uA7Xny276sk>

All the material on this website is protected by copyright. It may not be reproduced in any form without permission from the copyright holder.

© 2023 Oxford University Press |

² This is the protein that is usually measured in home pregnancy kits and can reach detectable levels about ten days after fertilization.