Ovarian and endometrial cycles and their hormonal control:

Changing hormone levels during the menstrual cycle.
Follicular” Phase of the Ovarian Cycle:

Throughout childhood, the granulosa cells (GC) are believed to provide nourishment for the ovum and to secrete an oocyte maturation-inhibiting factor (OMIF) that keeps the ovum suspended in its primordial state in the prophase stage of meiotic division.

At puberty, when FSH and LH from the anterior pituitary gland begin to be secreted in significant quantities, the ovaries, together with some of the follicles within them, begin to grow and increase in size, these follicles are known as primary follicles. Each month FSH will stimulate the growth of 6 to 12 primary follicles, leading to still larger follicles called vesicular follicles or antral follicles. The antrum will be formed in between the GC filled by follicular fluid; the ovum will be pushed to one side and surrounded by cumulus oophorus and corona radiate cells. The ovum will be surrounded by the zona pellucida and the perivetilline space will be formed. The follicle acquire an additional spindle cells derived from the ovary interstitium collect in several layers outside the granulosa cells, giving rise to a second mass of cells called the theca cells. These are arranged into two layers 1. Theca interna, have the ability to secrete steroid sex hormones (estrogen and progesterone). 2. The theca externa, which becomes the capsule of the developing follicle. E secreted in moderate amount in the early follicular phase, which causes negative feedback effect on the GnRH secretion, FSH and LH.

After the 7th day of menstruation one of the vesicular follicles outgrows others and becomes the dominant follicle. The Remainder Undergo Atresia. This accelerated growth is caused by the following: (1) Estrogen is secreted into the follicle and causes the GC to form increasing numbers of FSH receptors and will become more sensitive to FSH. Then after E causes a positive feedback effect, (2) the pituitary FSH and the estrogens combine to promote LH receptors on the original GC, thus allowing LH stimulation to occur in addition to FSH stimulation and creating an even more rapid increase in follicular secretion. These events bring the LH surge which triggers the final maturation of the ovum and ovulation.
The dominant follicle reaches a diameter of 1 to 1.5 centimeters at the time of ovulation and is called the **mature or Graafian follicle**. The ova resume meiosis II and become haploid (secondary oocyte) and polar body will be formed; meiosis will be arrested in metaphase II.

![Diagram of the ovary and follicle](image)

**Ovulation**

Ovulation in a woman who has a normal 28-day sexual cycle occurs 14 days after the onset of menstruation. Shortly before ovulation, the protruding outer wall of the follicle swells rapidly, and a small area in the center of the follicular capsule, called the stigma will appear. In addition proteolytic enzymes from lysosomes & prostaglandins are secreted into the follicular tissues. These two effects cause discharge of the ovum. This absolutely under Surge of LH (the ova will be viable for 24 hours or so, so it must be fertilized within this time). The expelled ova will reach the abdominal cavity and will be trapped by the fimbrial ends of the fallopian tubes, where the fertilization occurs, and the fertilized ovum (zygot) will be transported into the uterus (3rd day after ovulation) where it will be implanted (7th day).

The LH also has a specific effect on the granulosa and theca cells, converting them mainly to progesterone-secreting cells (Corpus luteum).
How a female can predict her ovulation:

1. Basal Body temperature chart.

2. Ovulation kit (LH).

3. The cervical mucus (spermberkeit and ferning).

4. Midcycle pain (Mittelschmerz (German: "middle pain") is a medical term for "ovulation pain" or "midcycle pain". About 20% of women experience it).

Corpus Luteum—"Luteal" Phase of the Ovarian Cycle

During the first few hours after expulsion of the ovum from the follicle, the remaining granulosa and theca interna cells change rapidly into lutein cells. They enlarge in diameter two or more times and become filled with lipid inclusions that give them a yellowish appearance. This process is called luteinization, and the total mass of cells together is called the corpus luteum. The GC in the corpus luteum develop extensive intracellular smooth endoplasmic reticula that form large amounts of progesterone and little estrogen and another hormone called inhibin; these will feed back to the anterior pituitary and inhibit (if no fertilization) the release of FSH and LH (negative feedback effect). As a consequence there will be drop of sex hormone and the corpus luteum begins to involute and eventually loses its secretory function as well as its yellowish color, becoming the corpus albicans; during the ensuing few weeks, this is replaced by connective tissue. IF the ovum is fertilized: the corpus luteum (corpus luteum gravidarum) persist and secret increasing amount of estrogen until the fourth month of pregnancy where the placenta will take the job and corpus luteum will be degenerated.
Figure demonstrates Hormonal Feedback mechanism of ovarian cycle. Continuous arrow indicate stimulatory effect, dashed arrow is inhibitory effect.

Involuion of the Corpus Luteum cause sudden cessation of secretion of estrogen, progesterone, and inhibin which removes the feedback inhibition of the anterior pituitary gland, allowing it to begin secreting increasing amounts of FSH and LH again. The period between the ovulation and the next cycle is usually 14 days, so any change in the period occurs in the first half of the cycle (i.e. proliferative phase is variable between women).

**Monthly Endometrial Cycle and Menstruation:**

The endometrium is a mirror of the hormonal changes of the ovary it goes through:

1. Proliferative phase (2) secretory phase and (3) desquamation (menstruation).

**Proliferative Phase (Estrogen Phase) of the Endometrial Cycle:**

Under the influence of estrogens, Endometrial proliferate rapidly, the endometrium increases greatly in thickness, owing to increasing numbers of stromal cells and to progressive growth of the endometrial glands and new blood
vessels into the endometrium. At the time of ovulation, the endometrium is 3 to 5 millimeters in thickness.

The endometrial glands, especially those of the cervical region, secrete thin, stringy mucus. The mucus strings actually align themselves along the length of the cervical canal, forming channels that help guide sperm in the proper direction from the vagina into the uterus.

**Secretory Phase (Progestational Phase) of the Endometrial Cycle:**

Progesterone causes marked swelling and secretory development of the endometrium. The glands increase in tortuosity; an excess of secretory substances accumulates in the glandular epithelial cells. Also, the cytoplasm of the stromal cells increases; lipid and glycogen deposits increase and the blood supply to the endometrium further increases in proportion to the developing secretory activity, with the blood vessels becoming highly tortuous.

The whole purpose of all these endometrial changes is to produce a highly secretory endometrium that contains large amounts of stored nutrients to provide appropriate conditions for implantation of a fertilized ovum, called “uterine milk”. The endometrium becomes receptive to implantation at midluteal phase, just as the corpus luteum progesterone and estrogen production reaches its highest level.

**If the ovum is not fertilized,** about 2 days before the end of the monthly cycle, the corpus luteum in the ovary suddenly involutes, and the ovarian hormones (estrogens and progesterone) decrease to low levels of secretion. During the 24 hours preceding the onset of menstruation, the tortuous blood vessels of the mucosal layers of the endometrium become vasoconstrictor types of prostaglandins that are present in abundance at this time initiate necrosis in the endometrium, especially of the blood vessels. Gradually, the necrotic outer layers of the endometrium separate from the superficial layers of the endometrium. The mass of desquamated tissue and blood in the uterine cavity, plus contractile effects of prostaglandins or other substances in the
decaying desquamate, all acting together, initiate uterine contractions that expel the uterine contents.

During normal menstruation, approximately **40 milliliters of blood** and an additional 35 milliliters of serous fluid are lost. **Fibrinolysin** is released and the menstrual blood is usually non-clotted. The presence of clots during menstruation is often clinical evidence of uterine pathology. During menstruation, tremendous numbers of **leukocytes** are released along with the **necrotic material** and blood. As a result of these leukocytes and possibly other factors, the uterus is highly resistant to infection during menstruation.

**APPLEID PHYSIOLOGY:**

Menstrual symptoms:

These are unpleasant symptom with discomfort. These are due to hormonal withdrawals, leading to cramps in uterine muscle before or during menstruation. Common symptom: abdominal pain, dysmenorrhea, headache, irritability depression, migraine, and occasional nausea and vomiting.

Premenstrual syndrome:

Symptom appear due to salt and water retention caused by estrogen. Mood swing, Anxiety, irritability, emotional instability, headache, depression, constipation, abdominal cramp and bloating.

**Menstrual Abnormalities**

anovulatory cycles: common during puberty and before menopause or may be due to hormonal imbalance or oral contraceptive use.

Amenorrhea (primary, secondary) absence of menstruation.

Menorrhagia: excess menstrual bleeding

Hypomenorrhea: decreased menstrual bleeding

Metrorrhagia: intermenstrual bleeding.
Dysmenorrhea (PG): pain associated with mense.

Birth control:

Contraceptive “pills” used for the control of fertility consist of some combination of synthetic estrogens and synthetic progestins. The drug is usually begun in the early stages of the monthly cycle and continued beyond the time that ovulation would normally occur. Then the drug is stopped, allowing menstruation to occur and a new cycle to begin. Their mode of action by inhibition of follicular maturation and ovulation and the cycle become anovulatory.

Nursing stimulates prolactin secretion, and evidence suggests that prolactin inhibits GnRH secretion, inhibits the action of GnRH on the pituitary, and antagonizes the action of gonadotropins on the ovaries. Ovulation is inhibited, and the ovaries are inactive, so estrogen and progesterone output falls to low levels. Consequently, only 5–10% of women become pregnant again during the suckling period, and nursing has long been known to be an important, if only partly effective, method of birth control. Furthermore, almost 50% of the cycles in the first 6 months after resumption of menses are anovulatory.