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Explain the hormonal regulation of the menstrual cycle.

The menstrual cycle is regulated by hormones. Luteinizing hormone and follicle-stimulating hormone, which are produced by the pituitary gland, promote ovulation and stimulate the ovaries to produce oestrogen and progesterone.

The menstrual cycle lasts about 28 days, although there is some variation. It involves interactions between the pituitary gland in the base of the brain, the follicles in the ovary, and the lining of the uterus. The cycle is normally counted from the beginning of menstruation - due to the lining of the uterus peeling away, with associated loss of blood.

After this stage, FSH (follicle stimulating hormone) together with LH (luteinising hormone), both released from the pituitary, stimulate a follicle in the ovary, causing it to develop so that the ovum (egg) within it matures. This also causes the ovary to release the hormone oestrogen.

The combination of FSH and LH, and oestrogen, has a positive feedback effect, causing the release of more and more oestrogen, FSH and LH. Oestrogen causes the muscle and lining layers of the uterus to grow thicker, in preparation for the possible embryo.

The surge of LH on or about day 14 causes ovulation (release of an egg from the follicle). The ovum enters the oviduct (Fallopian tube) and travels towards the uterus. Along the way, it may or may not meet up with a sperm cell and become fertilised.

The remaining section of the follicle develops into the corpus luteum ("yellow body"), which secretes the hormone progesterone for several days. Progesterone has the effect of maintaining the lining of the uterus, and developing more blood vessels. This would be necessary for the interchange of materials with an embryo developing from a fertilised egg, if present. The combination of oestrogen and progesterone and has a negative feedback effect on the pituitary, stopping the release of FSH and LH.

If the ovum is not fertilised

. Eventual deterioration of the corpus luteum causes progesterone production to stop.

. Falling levels of progesterone and oestrogen cause the uterine lining to shrink and lose blood- menstruation.

. Increased FSH and LH production causes the cycle.

If the ovum is fertilised

The implanted embryo (ball of cells) produces HCG (human chorionic gonadotrophin) which passes into the mother's blood stream and maintains the corpus luteum so that it continues to produce progesterone, causing steady conditions during pregnancy.

HORMONES INVOLVED IN REGULATION

The regulatory system functions through the hormones of hypothalamo-pituitary-ovarian axis. Hormones involved in the regulation of menstrual cycle are:

1. Hypothalamic hormone: GnRH

2. Anterior pituitary hormones: FSH and LH

3. Ovarian hormones: Estrogen and progesterone.

Hypothalamic Hormone – GnRH

GnRH triggers the cyclic changes during menstrual cycle by stimulating secretion of FSH and LH from anterior pituitary. GnRH secretion depends upon two factors:

i. External factors like psychosocial events, which act on hypothalamus via cortex and many other brain centres.

ii. Feedback effects of ovarian changes via ovarian hormones.

Anterior Pituitary Hormones – FSH and LH

FSH and LH modulate the ovarian and uterine changes by acting directly and/or indirectly via ovarian hormones. FSH stimulates the recruitment and growth of immature ovarian follicles. LH triggers ovulation and sustains corpus luteum. Secretion of FSH and LH is under the influence of GnRH.

Ovarian Hormones – Estrogen and Progesterone

Estrogen and progesterone which are secreted by follicle and corpus luteum, show many activities during menstrual cycle. Ovarian follicle secretes large quantity of estrogen and corpus luteum secretes large quantity of progesterone. Estrogen secretion reaches the peak twice in each cycle; once during follicular phase just before ovulation and another one during luteal phase (Fig. 80.4). On the other hand, progesterone is virtually absent during follicular phase till prior to ovulation. But it plays a critical role during luteal phase. Estrogen is responsible for the growth of follicles. Both the steroids act together to produce the changes in uterus, cervix and vagina.Both the ovarian hormones are under the influence of GnRH, which acts via FSH and LH. In addition, the secretion of GnRH, FSH and LH is regulated

by ovarian.

Follicular Phase

1. The biological clock responsible to trigger the cyclic events is the pulsatile secretion of GnRH, at about every 2 hours (due to some mechanism that is not understood clearly)

2. Pulsatile release of GnRH stimulates the secretion of FSH and LH from anterior pituitary

3. LH induces the synthesis of androgens from theca cells of growing follicle

4. FSH promotes aromatase activity in granulosa cells of the follicle resulting in the conversion of androgens into estrogen. It also promotes follicular development

5. Estrogen is responsible for development and growth of graafian follicle. It also stimulates the secretory activities of theca cells

6. Estrogen also exerts a double feedback control on GnRH

i. Initially, when estrogen secretion is moderate, it exerts a negative feedback control on GnRH so that GnRH secretion is inhibited. This leads to decrease in secretion of FSH and LH (negative feedback).

ii. During later period of follicular phase, when a large amount of estrogen is secreted by the maturing follicle, it exerts a positive feedback effect on GnRH secretion. Now, GnRH secretion is increased, resulting in secretion of large quantity of FSH and LH. This in turn, facilitates the growth of graafian follicle.

7. In addition, estrogen shows the following actions:

i. Increases the number of FSH and LH receptors on the granulosa cells of follicles and increases the sensitivity of these cells for FSH and LH.

ii. Facilitates the faster growth of graafian follicle

8. LH is necessary to provide the final touches for the growth of graafian follicle. It stimulates the secretion of estrogen. At the same time, it stimulates the theca cells to secrete progesterone.

Ovulation

LH is important for ovulation. Without LH, ovulation does not occur even with a large quantity of FSH. The need for excessive secretion of LH for ovulation is known as ovulatory surge for LH or luteal surge. Prior to ovulation, a large quantity of LH is secreted due to positive feedback effect of estrogen on GnRH, as mentioned above.

Luteal Phase

Role of LH

Ovarian changes during luteal phase depend mainly on LH.

Luteinizing hormone:

1. Induces development of corpus luteum from the follicle (devoid of ovum) by converting the granulosa cells into lutein cells.

2. Stimulates corpus luteum to secrete progesterone and estrogen

3. Necessary for the maintenance of corpus luteum.

Role of FSH

FSH also plays a role during luteal phase.

Follicle-stimulating hormone:

1. Maintains the secretory activity of corpus luteum.

2. Stimulates lutein cells to secrete inhibin, which in turn inhibits FSH secretion.

If the ovum is not fertilized or if implantation of ovum does not take place, the changes in the level of the hormones produce some effects on corpus luteum which are:

1. Progesterone and estrogen secreted from corpus luteum, inhibit the secretion of FSH and LH from anterior pituitary by negative feedback.

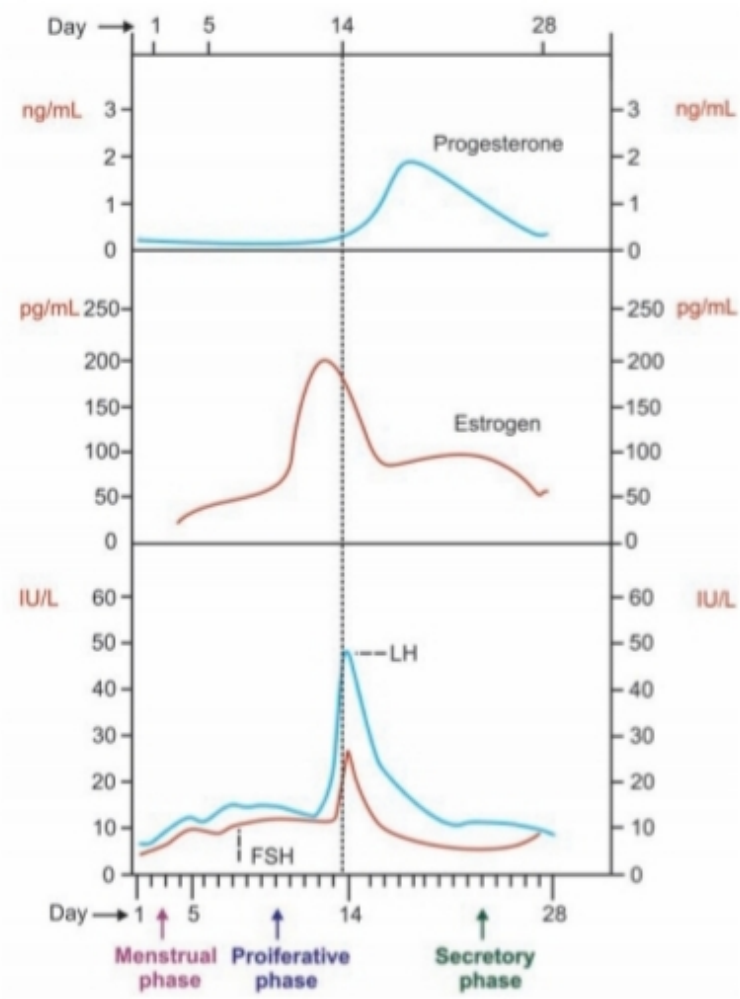
2. Granulosa lutein cells secrete another hormone called inhibin. Inhibin also inhibits the secretion of FSH and LH by negative feedback.

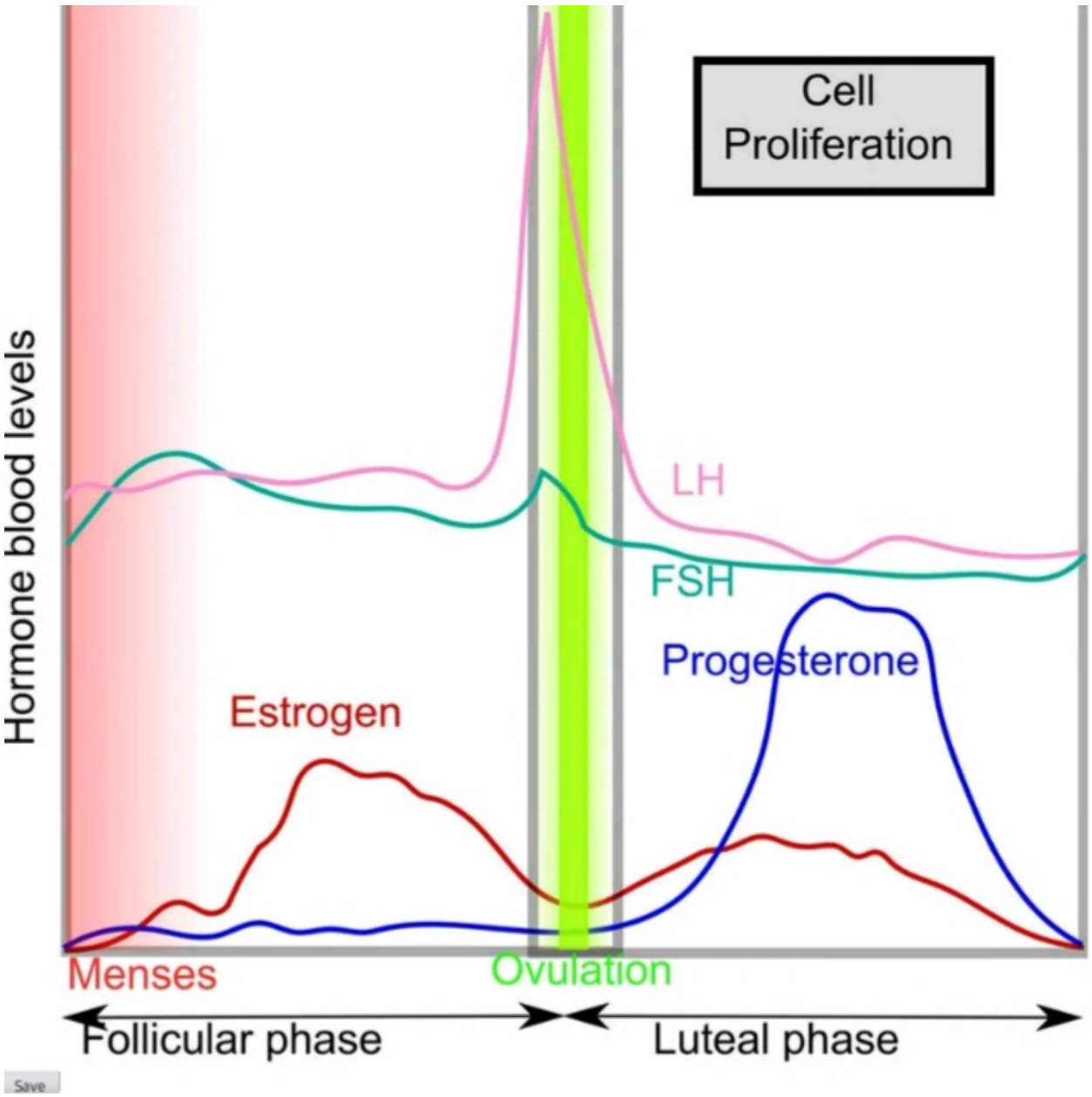
3. In the absence of FSH and LH, the corpus luteum becomes inactive.

4. Finally, the corpus luteum regresses by means of luteolysis; so progesterone and estrogen are not available.

5. Absence of progesterone and estrogen induces the secretion of GnRH from hypothalamus.

6. GnRH stimulates the secretion of FSH and LH from anterior pituitary.


Day
1
5
14
28
ng/mL
3
2
1
0
Progesterone
pg/mL
250
200
150
100
50
0
Estrogen
IU/L
60
50
40
30
20
10
0
LH
FSH
Menstrual phase
Proliferative phase
Secretory phase



2. **Cyclic changes in the breast**

What is normal breast development?

Breast development is a vital part of a woman’s reproduction. Breast development happens in certain stages during a woman's life: first before birth, again at puberty, and later during the childbearing years. Changes also happen to the breasts during the menstrual cycle and when a woman reaches menopause.

When does breast development begin?

Breasts begin to form while the unborn baby is still growing in the mother's uterus. This starts with a thickening in the chest area called the mammary ridge or milk line. By the time a baby girl is born, nipples and the beginnings of the milk-duct system have formed. Breast changes continue to happen over a woman's life. The first thing to develop are lobes, or small subdivisions of breast tissue. Mammary glands develop next and consist of 15 to 24 lobes. Mammary glands are influenced by hormones activated in puberty. Shrinkage (involution) of the milk ducts is the final major change that happens in the breast tissue. The mammary glands slowly start to shrink. This often starts around age 35.

What breast changes happen at puberty?

As a girl approaches her teen years, the first visible signs of breast development begin. When the ovaries start to produce and release (secrete) estrogen, fat in the connective tissue starts to collect. This causes the breasts to enlarge. The duct system also starts to grow. Often these breast changes happen at the same that pubic hair and armpit hair appear. Once ovulation and menstruation begin, the maturing of the breasts begins with the formation of secretory glands at the end of the milk ducts. The breasts and duct system continue to grow and mature, with the development of many glands and lobules. The rate at which breasts grow is different for each young woman.

Female breast developmental stages

Stage 1

Description

Preteen. Only the tip of the nipple is raised.

Stage 2

Description

Buds appear, and breast and nipple are raised. The dark area of skin around the nipple (the areola) gets larger.

Stage 3

Description

Breasts are slightly larger, with glandular breast tissue present.

Stage 4

Description

The areola and nipple become raised and form a second mound above the rest of the breast.

Stage 5

Description

Mature adult breast. The breast becomes rounded and only the nipple is raised.

What cyclical changes happen to the breasts during the menstrual cycle?

Each month, women go through changes in the hormones that make up the normal menstrual cycle. The hormone estrogen is produced by the ovaries in the first half of the menstrual cycle. It stimulates the growth of milk ducts in the breasts. The increasing level of estrogen leads to ovulation halfway through the cycle. Next, the hormone progesterone takes over in the second half of the cycle. It stimulates the formation of the milk glands. These hormones are believed to be responsible for the cyclical changes that many women feel in their breasts just before menstruation. These include swelling, pain, and soreness. During menstruation, many women also have changes in breast texture. Their breasts may feel very lumpy. This is because the glands in the breast are enlarging to get ready for a possible pregnancy. If pregnancy does not happen, thebreasts go back to normal size. Once menstruation starts, the cycle begins again.

What happens to the breasts during pregnancy and milk production?

Many healthcare providers believe the breasts are not fully mature until a woman has given birth and made milk. Breast changes are one of the earliest signs of pregnancy. This is a result of the hormone progesterone. In addition, the dark areas of skin around the nipples (the areolas) begin to swell. This is followed by the rapid swelling of the breasts themselves. Most pregnant women feel soreness down the sides of the breasts, and nipple tingling or soreness. This is because of the growth of the milk duct system and the formation of many more lobules. By the fifth or sixth month of pregnancy, the breasts are fully capable of producing milk. As in puberty, estrogen controls the growth of the ducts, and progesterone controls the growth of the glandular buds. Many other hormones also play vital roles in milk production. These include follicle-stimulating hormone (FSH), luteinizing hormone(LH), prolactin, oxytocin, and human placental lactogen (HPL). Other physical changes happen as well. These include the blood vessels in the breast becoming more visible and the areola getting larger and darker. All of these changes are in preparation for breastfeeding the baby after birth.

What happens to the breasts at menopause?

By the time a woman reaches her late 40s and early 50s, perimenopause is starting or is well underway. At this time, the levels of estrogen and progesterone begin to change. Estrogen levels dramatically decrease. This leads to many of the symptoms commonly linked to menopause. Without estrogen, the breast’s connective tissue becomes dehydrated and is no longer elastic. The breast tissue, which was prepared to make milk, shrinks and loses shape. This leads to the "saggy" breasts associated with women of this age.

Women who are taking hormone therapy may have some of the premenstrual breast symptoms that they had while they were still menstruating, such as soreness and swelling. But if a woman’s breasts were saggy before menopause, this will not change with hormone therapy.

ROLE OF HORMONES IN GROWTH OF MAMMARY GLANDS

Various hormones are involved in the development and growth of breasts at different stages:

1. Estrogen
2. Progesterone
3. Prolactin
4. Placental hormones
5. Other hormones.

1. ESTROGEN

Growth of Ductile System

Estrogen causes growth and branching of duct system; so the normal development of duct system in breasts at puberty depends upon estrogen. Estrogen is also responsible for the accumulation of fat in breasts.

2. PROGESTERONE

Growth of Glandular Tissue

The development of stroma of the mammary glands depends upon progesterone activity. Progesterone also stimulates the development of glandular tissues.

PROLACTIN

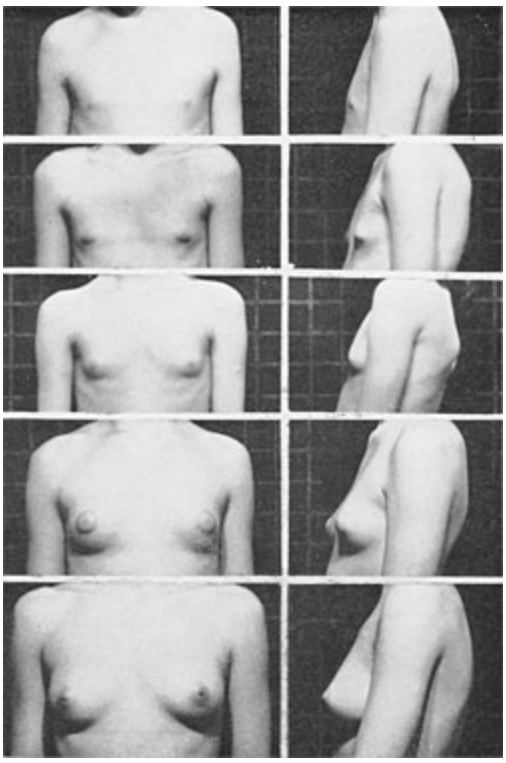
Prolactin is necessary for milk secretion. However, it also plays an important role in growth of mammary glands during pregnancy. Normally, prolactin is inhibited by prolactin-inhibiting hormone secreted from hypothalamus. However, prolactin secretion starts increasing from 5th month of pregnancy. At that time, it acts directly on the mammary glands and causes proliferation of epithelial cells of alveoli.

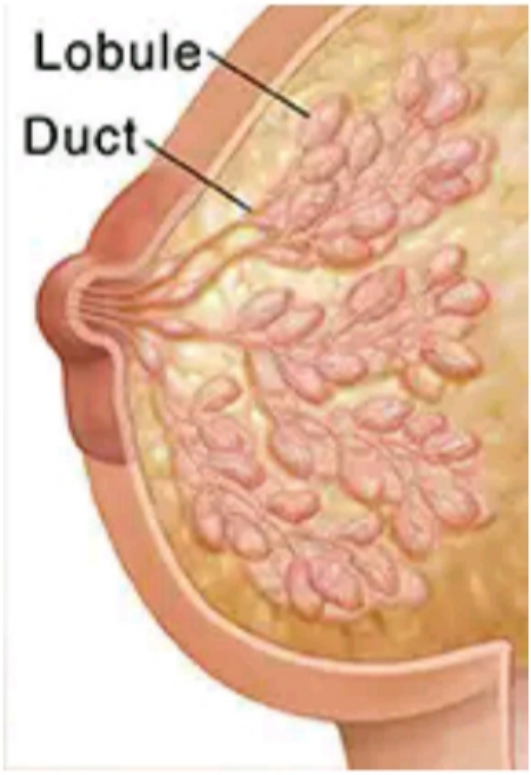
4. PLACENTAL HORMONES

Estrogen and progesterone secreted from placenta are essential for further development of mammary glands during pregnancy. Both the hormones stimulate the proliferation of ducts and glandular cells during pregnancy.

5. OTHER HORMONES

Growth hormone, thyroxine and cortisol enhance the overall growth and development of mammary glands in all stages. Relaxin also facilitates the development of mammary glands. It is secreted by corpus luteum, mammary glands and placenta. Its major function is to facilitate dilatation of cervix during labour.





Cyclic changes in the vaginal

The vaginal epithelium is the inner lining of the vagina consisting of multiple layers of (squamous) cells. The basal membrane provides the support for the first layer of the epithelium-the basal layer. The intermediate layers lie upon the basal layer and the superficial layer is the outermost layer of the epithelium. Anatomists have described the epithelium as consisting of as many as 40 distinct layers. [citation needed] The mucus found on the epithelium is secreted by the cervix and uterus. The rugae of the epithelium create an involuted surface and result in a large surface area that covers 360 cm 3 . This large surface area allows the trans-epithelial absorption of some medications via the vaginal route.

In the course of the reproductive cycle , the vaginal epithelium is subject to normal, cyclic changes, that are influenced by estrogen : with increasing circulating levels of the hormone , there is proliferation of epithelial cells along with an increase in the number of cell layers. As cells proliferate and mature, they undergo partial cornification. Although hormone induced changes occur in the other tissues and organs of the female reproductive system, the vaginal epithelium is more sensitive and its structure is an indicator of estrogen levels. Some Langerhans cells and melanocytes are also present in the epithelium. The epithelium of the ectocervix is contiguous with that of the vagina, possessing the same properties and function. The vaginal epithelium is divided into layers of cells, including the basal cells , the

parabasal cells, the superficial squamous flat cells , and the intermediate cells. The superficial cells exfoliate continuously and basal cells replace the superficial cells that die and slough off from the stratum corneum . Under the stratus corneum is the stratum granulosum and stratum spinosum . The cells of the vaginal epithelium retain a usually high level of glycogen compared to other epithelial tissue in the body. The surface patterns on the cells themselves are circular and arranged in longitudinal rows. The epithelial cells of the uterus possess some of the same characteristics of the vaginal epithelium.

The vagina itself does not contain mucous glands .Though mucus is not produced by the vaginal epithelium, mucus originates from the cervix. The cervical mucus that is located inside the vagina can be used to assess fertility in ovulating women. The Bartholin's glands and Skene's glands located at the entrance of the vagina do produce mucus.

Cyclic variations

During the luteal and follicular phases of the estrous cycle the structure of the vaginal epithelium varies. The number of cell layers vary during the days of the estrous cycle:

Day 10, 22 layers

Days 12-14, 46 layers

Day 19, 32 layers

Day 24, 24 layers

The glycogen levels in the cells is at its highest immediately before ovulation.

VAGINAL CHANGES DURING MENSTRUAL CYCLE

Proliferative Phase

Epithelial cells of vagina are cornified. Estrogen is responsible for this.

Secretory Phase

Vaginal epithelium proliferates due to the actions of progesterone. It is also infiltrated with leukocytes.

These two changes increase the resistance of vagina for infection.

Cyclic changes in the vagina.

	Estrogen	Epithelium	Glycogen	pH	Flora
Newborn	+		+	Acid 4-5	Sterile ↓ Doderlein's bacilli Secretion abundant
Month-old child	–		+	Alkaline >7	Sparse, coccal, and varied flora Secretion scant
Puberty	Appears		– → +	Alkaline ↓ Acid	Sparse, coccal ↓ Rich bacillary
Mature	++		+	Acid 4-5	Doderlein's bacilli Secretion abundant
Postmenopause	+ → –		–	Neutral or alkaline 6 to >7	Varied Dependent on level of circulating estrogen Secretion scant