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**QUESTION - BRIEFLY EXPLAIN THE CYCLIC CHANGES IN ANY TWO OF THE FOLLOWING**

1. Cervix
2. Vagina
3. Breasts
4. **CYCLIC CHANGES IN THE CERVIX**

The cervix is a cylinder-shaped neck of tissue that connects the vagina and uterus. Located at the lowermost portion of the uterus, the cervix is composed primarily of fibromuscular tissue. There are two main portions of the cervix:

* The part of the cervix that can be seen from inside the vagina during a gynecologic examination is known as the ectocervix. An opening in the center of the ectocervix, known as the external os, opens to allow passage between the uterus and vagina.
* The endocervix, or endocervical canal, is a tunnel through the cervix, from the external os into the uterus.

The overlapping border between the endocervix and ectocervix is called the transformation zone. The cervix produces cervical mucus that changes in consistency during the menstrual cycle to prevent or promote pregnancy. During childbirth, the cervix dilates widely to allow the baby to pass through. During menstruation, the cervix opens a small amount to permit passage of menstrual flow.

**Anatomical Structure**

The cervix is composed of two regions; the ectocervix and the endocervical canal.

* The ectocervix is the portion of the cervix that projects into the vagina. It is lined by stratified squamous non-keratinized epithelium. The opening in the ectocervix, the external os, marks the transition from the ectocervix to the endocervical canal.
* The endocervical canal (or endocervix) is the more proximal, and ‘inner’ part of the cervix. It is lined by a mucus-secreting simple columnar epithelium. The endocervical canal ends, and the uterine cavity begins, at a narrowing called the internal os.

**Functions**

The cervix performs two main functions:

* It facilitates the passage of sperm into the uterine cavity. This is achieved via dilation of the external and internal os.
* Maintains sterility of the upper female reproductive tract. The cervix, and all structures superior to it, are sterile. This ultimately protects the uterine cavity and the upper genital tract by preventing bacterial invasion. This environment is maintained by the frequent shedding of the endometrium, thick cervical mucus and a narrow external os.

**Vascular Supply and Lymphatics**

The blood supply to the uterus is through the uterine artery. Venous drainage is through a plexus in the broad ligament that drains into the uterine veins.

Lymphatic drainage of the uterus is through the iliac, sacral, aortic and inguinal lymph nodes.



**The cyclic change in the cervix**

Thirty parous ewes were divided into six groups and sacrificed on day 0 (first day of estrus), 1, 2, 10, 15 or 16 of the estrous cycle. The cervices were removed immediately and processed for examination with the scanning electron microscope. Observation of the tissues reveals that the surface of the cervix is highly convoluted, which results in the formation of numerous folds or crypts. Two forms of columnar epithelial cells, a ciliated and a non-ciliated cell with microvilli, line the luminal surface of the cervix in the day 10, luteal-phase ewes. However, on day 15, 2 days before estrus, the non-ciliated cells differentiate into two morphologically distinct types of secretory cells. One type forms when the apex of the non-ciliated cell dilates outward into the lumen of the cervix. Concurrent with apical enlargement, the microvilli are lost and the limiting cell membrane becomes smooth. The other type of cell is characterized by only a slight apical swelling. Consequently, remnants of microvilli along with secretory granules can be observed on the limiting membrane of this cell. Both cells release a particulate component, which is believed to be a precursor of mucus, into the lumen of the cervix. These particles undergo a series of morphological transformations to form a fibrillary layer, generally referred to as 'cervical mucus', that covers the epithelial surface at estrus. One to 2 days following the onset of estrus, the fibers become more closely associated with amorphous material that begins to coagulate, thereby revealing the underlying ciliated and non-ciliated cells that characterize the cervix of the luteal-phage ewe.

**The cyclic change in the cervical mucus**

Papers surveying the fate of spermatozoa in the various regions of the woman's reproductive tract and correlating the cycle of mucus with other cyclic sexual phenomena led to a study on some practical problems associated with variations in cervical mucus. Samples were aspirated from the normal external os of sterile, amenorrheic, pregnant, and menopausal women. Stilbestrol therapy definitely affected the character of cervical mucus in sterile and menopausal women changing it from acid and impenetrable to alkaline and readily penetrable. Upon discontinuation of stilbestrol, the mucus returned to an impenetrable acid. 14 cervical mucus specimens from pregnant women were observed. In all instances mucus was slightly penetrable but the pH varied from 4.5 to 7.5 making superfetation an unlikely possibility. 20 menopausal preestrogenic therapy patients had scant or moderate viscid or crumbly cervical mucus with a pH of 4.5. Mucus was impenetrable to semen in each case. Estrogen therapy noticeably altered the mucus. These observations indicate that determination of mucus responses will be more exact and simple than the vaginal smear technique.

1. **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**

Preteen. Only the tip of the nipple is raised.

* **Stage 2**

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

* **Stage 3**

Breasts are slightly larger, with glandular breast tissue present.

* **Stage 4**

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

* **Stage 5**

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

**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:

* Estrogen
* Progesterone
* Prolactin
* Placental hormones
* Other hormones.

**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.

**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.

**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.

**OTHER HORMONES**

Growth hormone, thyroxine and cortisol enhance the overall growth and development of mammary glands in all stages. Relaxing 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 CHANGE THAT HAPPEN TO THE BREAST DURING 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, the breasts go back to normal size. Once menstruation starts, the cycle begins again.



**EXPLAIN ANY ONE OF THE FOLLOWING**

1. MENSTRUAL CYCLE
2. HORMONAL REGULATION OF THE MENTSRUAL CYCLE

**MENSTRUAL CYCLE**

Menstruation is bleeding from the vagina that happens about once a month, as a normal part of the menstrual cycle. It is also known as having a period.

During this cycle, your hormones make the lining of the uterus become thicker, getting ready in case of pregnancy. Hormones also cause an egg to be released from an ovary, which is known as ovulation. If you don’t become pregnant, your periods start about two weeks after you ovulate. The lining of the uterus falls away and, along with some blood, flows out through the vagina. Periods can be light or heavy, and the blood can range from bright red to dark brown. You might also notice small clots.

Medically, menstruation (also termed period or bleeding) is the process in a woman of discharging blood and other materials from the lining of the uterus at about one monthly interval from puberty until menopause, except during pregnancy. This discharging process lasts about 3-5 days.

**Signs and symptoms of menstruation**

Beside the bleeding, other signs and symptoms of menstruation may include headache, acne, bloating, pains in the low abdomen, tiredness, mood changes, food cravings, breast soreness, and diarrhea.

**When a menstruation begins and when it ends**

The menstrual cycle is the hormonal driven cycle; Day 1 is the first day of your period (bleeding) while day 14 is the approximate day you ovulate and if an egg is not fertilized, hormone levels eventually drop and at about day 25; the egg begins to dissolve and the cycle begins again with the period at about day 30. Menstruation begins day 1 and normally ends days 3-5 of the menstrual cycle.

**How long a period last?**

The menstrual cycle is the hormonal driven cycle. Day 1 is the first day of your period (bleeding) while day 14 is the approximate day you ovulate and if an egg is not fertilized, hormone levels eventually drop and at about day 25. The egg then begins to dissolve and the cycle begins again with the period at about day 30.

Most periods vary somewhat, the flow may be light, moderate or heavy and can vary in length from about 2 to 7 days; with age, the cycle usually shortens and becomes more regular.

**Treatment for pain and other symptoms caused by menstruation**

Treatment for the causes of menstrual pain depend on what the cause is, and may include birth control pills, heavy or prolonged periods, IUDs, noninflammatory steroid drugs (NSAIDs), for example, ibuprofen (Advil), aspirin, naproxen (Aleve), and other-the-counter pain (OTC) medications to relive pain and cramping.

Women should change the pad/tampon before it becomes soaked with blood (about every 4 to 8 hours); follow directions on the box to help avoid TSS (toxic shock syndrome), a potentially deadly disease. Call your doctor or other health professional if you have any abnormalities in your period, for example, excessive bleeding, no periods, severe pain, fever with tampon use, sudden irregularities, and other problems.

**When do girls start their period?**

Girls have their first period during puberty. Most often that is around the age 12 or 13 years old, but girls can start menstruating as young as 9, or as late as 16.

Bleeding. When you menstruate, your body sheds the lining of the uterus (womb). Menstrual blood flows from the uterus through the small opening in the cervix and passes out of the body through the vagina. Most menstrual periods last from 3 to 5 days.

**How long periods last**

Menstruation affects every woman, but the experience can differ between women. When periods (menstruations) come regularly, this is called the menstrual cycle. Having regular menstrual cycles is a sign that important parts of your body are working normally. The menstrual cycle provides important body chemicals, called hormones, to keep you healthy. It also prepares your body for pregnancy each month. A cycle is counted from the first day of 1 period to the first day of the next period. The average menstrual cycle is 28 days long. Cycles can range anywhere from 21 to 35 days in adults and from 21 to 45 days in young teens. The rise and fall of levels of hormones during the month control the menstrual cycle.

**Signs and symptoms of menstruation**

Some women get symptoms leading up to and during menstruation, for example, cramps or pains low in the abdomen, bloating or swelling in the abdomen, constipation before your period, diarrhea when your period starts, acne, tiredness, and mood changes.

**When periods stops**

Women usually have periods until menopause. Menopause occurs between the ages of 45 and 55, usually around age 50. Menopause means that a woman is no longer ovulating (producing eggs) or having periods and can no longer get pregnant. Like menstruation, menopause can vary from woman to woman and these changes may occur over several years.

For the first few years after menstruation begins, longer cycles are common. A woman's cycle tends to shorten and become more regular with age. Most of the time, periods will be in the range of 21 to 35 days apart.

Periods stop during pregnancy, and often while you are breastfeeding. Some women find their periods stop for a time because of long-term illness, low body weight, stress, lots of strenuous exercise and hormone problems. Some medications, such as contraceptives, might stop your period. This can be helpful for some women, especially if their periods are heavy or painful. Sometimes after stopping the pill or other contraceptive, it can take a while for your periods to come back. Periods stop altogether when women reach menopause - the average age is 51-52.

**If the ovum is not fertilized**

* 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 fertilized**

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:

* Hypothalamic hormone: GnRH
* Anterior pituitary hormones: FSH and LH
* 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:

* External factors like psychosocial events, which act on hypothalamus via cortex and many other brain centres.
* 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. 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.
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
* 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).
* 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.
1. In addition, estrogen shows the following actions:
* 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.
* Facilitates the faster growth of graafian follicle
1. 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:

* Induces development of corpus luteum from the follicle (devoid of ovum) by converting the granulosa cells into lutein cells.
* Stimulates corpus luteum to secrete progesterone and estrogen
* Necessary for the maintenance of corpus luteum.

**Role of FSH**

FSH also plays a role during luteal phase.

**Follicle-stimulating hormone**:

* Maintains the secretory activity of corpus luteum.
* 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:

* Progesterone and estrogen secreted from corpus luteum, inhibit the secretion of FSH and LH from anterior pituitary by negative feedback.
* Granulosa lutein cells secrete another hormone called inhibin. Inhibin also inhibits the secretion of FSH and LH by negative feedback.
* In the absence of FSH and LH, the corpus luteum becomes inactive.
* Finally, the corpus luteum regresses by means of luteolysis; so progesterone and estrogen are not available.
* Absence of progesterone and estrogen induces the secretion of GnRH from hypothalamus.
* GnRH stimulates the secretion of FSH and LH from anterior pituitary.



