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**THE CYCLIC CHANGES IN:**

**a)CERVIX**

The cervix is typically open during menstruation, which allows menstrual blood and uterine tissues to leave the woman’s body.

 During menstrual bleeding, the cervix is normally low and slighty open to allow the blood to flow out. After menstruation the stops, the cervix remains low and hard and the opening to the uterus (uterine os)remains closed.As ovulation approaches, the cervix rises up to the top of the vagina and becomes softer and moister.At the height hat it blends in with the vaginal walls. of ovulation the cervix is really soft that sometimes may seem to disappear because it becomes so soft

The hormone estrogen is responsible for changes throughout a woman’s cycle.

**CHANGES IN CERVIX DURING MENSTRUAL CYCLE** :Mucus membrane of the cervix also shows cyclic changes during different phases of menstrual cycle.

**Proliferative Phase:** During proliferative phase, the mucus membrane of cervix becomes thinner and more alkaline due to the influence of estrogen. It helps in the survival and motility of spermatozoa.

**Secretory Phase:** During secretory phase, the mucus membrane of cervix becomes more thick and adhesive because of actions of progesterone.

**b)VAGINA**

  **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.

 Aroung mid cycle, when the estrogen is highest vaginal tiisues becomes thicker and fuller

2a) **Menstrual cycle**

 Menstrual cycle is defined as cyclic events that take place in a rhythmic fashion during the reproductive period of a woman’s life. Menstrual cycle starts at the age of 12 to 15 years, which marks the onset of puberty. The commencement of menstrual cycle is called menarche. Menstrual cycle ceases at the age of 45 to 50 years. Permanent cessation of menstrual cycle in old age is called menopause.

** DURATION OF MENSTRUAL CYCLE**: Duration of menstrual cycle is usually 28 days. But, under physiological conditions, it may vary between 20 and 40 days.

  **CHANGES DURING MENSTRUAL CYCLE**: During each menstrual cycle, series of changes occur in ovary and accessory sex organs. These changes are divided into 4 groups:

 1. Ovarian changes

 2. Uterine changes

3. Vaginal changes

 4. Changes in cervix.

 1**) OVARIAN CHANGES**

Changes in the ovary during each menstrual cycle occur in two phases **(Ovulation** occurs in between these two phases):

 A. Follicular phase

 B. Luteal phase.

 A) Follicular phase :Follicular phase extends from the 5th day of the cycle until the time of ovulation, which takes place on 14th day. Maturation of ovum with development of ovarian follicles takes place during this phase.

Ovarian Follicles Ovarian follicles are glandular structures present in the cortex of ovary. Each follicle consists of the ovum surrounded by epithelial cells, namely granulosa cells. The follicles gradually grow into a matured follicle through various stages:

1. Primordial follicle

2. Primary follicle

 3. Vesicular follicle

 4. Matured follicle or graafian follicle.

1. Primordial Follicle:At the time of puberty, both the ovaries contain about 400,000 primordial follicles. Diameter of the primordial follicle is about 15 to 20 µ and that of ovum is about 10 µ. Each primordial follicle has an ovum, which is incompletely surrounded by the granulosa cells. These cells provide nutrition to the ovum during childhood. Granulosa cells also secrete the oocyte maturation inhibiting factor, which keeps ovum in the immature stage. All the ova present in the ovaries are formed before birth. No new ovum is developed after birth. At the onset of puberty, under the influence of FSH and LH the primordial follicles start growing through various stages.

2. Primary Follicle: Primordial follicle becomes the primary follicle, when ovum is completely surrounded by the granulosa cells. During this stage, the follicle and the ovum increase in size. The follicle is not covered by a definite connective tissue capsule.

Changes taking place during development of primary follicle

i.Proliferation of granulosa cells and increase in size of the follicle

 ii. Increase in size of the ovum

iii. Onset of formation of connective tissue capsule around the follicle. Primary follicles develop into vesicular follicles.

3. Vesicular Follicle.

Changes taking place during the development of vesicular follicle

i.Changes in granulosa cells

ii. Changes in ovum

iii. Formation of capsule.

i. Changes in granulosa cells :

a. First, the proliferation of granulosa cells occurs

 b. A cavity called follicular cavity or antrum is formed in between the granulosa cells

 c. Antrum is filled with a serous fluid called the liquor folliculi

 d. With continuous proliferation of granulosa cells, the follicle increases in size

e. Antrum with its fluid also increases in size

 f. Ovum is pushed to one side and it is surrounded by granulosa cells, which forms the germ hill or cumulus oophorus

 g. Granulosa cells, which line the antrum form membrana granulosa

 h. Cells of germ hill become columnar and form corona radiata.

 ii. Changes in ovum:

 a. First, the ovum increases in size and its diameter increases to 100 to 150 µ

 b. Nucleus becomes larger and vesicular

 c. Cytoplasm becomes granular

 d. Thick membrane is formed around the ovum, which is called zona pellucida

e. A narrow cleft appears between ovum and zona pellucida. This cleft is called perivitelline space.

iii. Formation of capsule: Spindle cells from the stroma of ovarian cortex are modified and form a covering sheath around the follicle. The covering sheath is known as follicular sheath or theca folliculi. Theca folliculi divides into two layers:

 a. Theca interna

 b. Theca externa.

a. Theca interna :Theca interna is the inner vascular layer with loose connective tissue. This layer also contains special type of epithelial cells with lipid granules and some delicate collagen fibers. Epithelial cells become secretory in nature and start secreting the female sex hormones, especially estrogen. Hormones are released into the fluid of antrum.

b. Theca externa: Theca externa is the outer layer of follicular capsule and consists of thickly packed fibers and spindleshaped cells. After about 7th day of menstrual cycle, one of the vesicular follicles outgrows others and becomes the dominant follicle. It develops further to form graafian follicle. Other vesicular follicles degenerate and become atretic by means of apoptosis.

4.Graafia Follicle: Graafian follicle is the matured ovarian follicle with maturing ovum

Changes taking place during the development of graafian follicle:

i.Size of the follicle increases to about 10 to 12 mm. It extends through the whole thickness of ovarian cortex

ii. At one point, the follicle encroaches upon tunica albuginea and protrudes upon surface of the ovary. This protrusion is called stigma. At the stigma, the tunica albuginea becomes thin iii. Follicular cavity becomes larger and distended with fluid

 iv. Ovum attains maximum size

v. Zona pellucida becomes thick

 vi. Corona radiata becomes prominent

 vii. Small spaces filled with fluid appear between the cells of germ hill, outside the corona radiata. These spaces weaken the attachment of the ovum to the follicular wall

viii. Theca interna becomes prominent. Its thickness becomes double with the formation of rich capillary network

 ix. On the 14th day of menstrual cycle, graafian follicle is ready for the process of ovulation.



 **Diagram of the graafian follicle**

 **OVULATION** :Ovulation is the process by which the graafian follicle ruptures with consequent discharge of ovum into the abdominal cavity. It is influenced by LH. Ovulation occurs on 14th day of menstrual cycle in a normal cycle of 28 days. The ovum enters the fallopian tube.

 Stages of ovulation

 1. Rupture of graafian follicles takes place at the stigma

 2. Follicular fluid oozes out

3. Germ hillock is freed from wall

4. Ovum is expelled out into the abdominal cavity along with some amount of fluid and granulosa cells 5. From abdominal cavity, the ovum enters the fallopian tube through the fimbriated end. Ovum becomes haploid before or during ovulation by the formation of polar bodies. After ovulation, the ovum is viable only for 24 to 48 hours. So it must be fertilized within that time. Fertilized ovum is called zygote. Zygote moves from fallopian tube and reaches the uterus on 3rd day after ovulation. It is implanted in the uterine wall on 6th or 7th day.

**If fertilization does not occur,** ovum degenerates. Generally, only one ovum is released from one of the ovaries.

B) LUTEAL PHASE: Luteal phase extends between 15th and 28th day of menstrual cycle. During this phase, corpus luteum is developed and hence this phase is called luteal phase (Fig. 80.2).

Corpus Luteum Corpus luteum is a glandular yellow body, developed from the ruptured graafian follicle after the release of ovum. It is also called yellow body.

**Functions of Corpus Luteum**

1. Secretion of hormones Corpus luteum acts as a temporary endocrine gland. It secretes large quantity of progesterone and small amount of estrogen. Granulosa lutein cells secrete progesterone and theca lutein cells secrete estrogen. LH influences the secretion of these two hormones.

2. Maintenance of pregnancy If pregnancy occurs, corpus luteum remains active for about 3 months, i.e. until placenta develops. Hormones secreted by corpus luteum during this period maintain the pregnancy.

 Abortion occurs if corpus luteum becomes inactive or removed before third month of pregnancy, i.e. before placenta starts secreting the hormones

 2) **UTERINE CHANGES DURING MENSTRUAL CYCLE**

During each menstrual cycle, along with ovarian changes, uterine changes also occur simultaneously. Uterine changes occur in three phases:

1. Menstrual phase

 2. Proliferative phase

 3. Secretory phase

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  MENSTRUAL PHASE(also called menses, emmenia or catamenia): After ovulation, if pregnancy does not occur, the thickened endometrium is shed or desquamated. This desquamated endometrium is expelled out through vagina along with blood and tissue fluid. Two days before the onset of bleeding, that is on 26th or 27th day of the previous cycle, there is a sudden reduction in the release of estrogen and progesterone from ovary. Decreased level of these two hormones is responsible for menstruation.

Changes in Endometrium during Menstrual Phase

i.Lack of estrogen and progesterone causes sudden involution of endometrium

 ii. It leads to reduction in the thickness of endometrium, up to 65% of original thickness

 iii. During the next 24 hours, the tortuous blood vessels in the endometrium undergo severe constriction.

vi. Outer layer of the necrotic endometrium is separated and passes out along with blood

 PROLIFERATIVE PHASE: Proliferative phase extends usually from 5th to 14th day of menstruation. It corresponds to the follicular phase of ovarian cycle. At the end of menstrual phase, only a thin layer (1 mm) of endometrium remains, as most of the endometrial stroma is desquamated.

Changes in Endometrium during Proliferative Phase

i.Endometrial cells proliferate rapidly

 ii. Epithelium reappears on the surface of endometrium within the first 4 to 7 days

 iii. Uterine glands start developing within the endometrial stroma

 iv. Blood vessels appear in the stroma v. Proliferation of endometrial cells occurs continuously, so that the endometrium reaches the thickness of 3 to 4 mm at the end of proliferative phase. All these uterine changes during proliferative phase occur because of the influence of estrogen released from ovary. On 14th day, ovulation occurs under the influence of LH. This is followed by secretory phase.

  SECRETORY PHASE Secretory phase extends between 15th and 28th day of the menstrual cycle, i.e. between the day of ovulation and the day when menstruation of next cycle commences.

Changes in Endometrium during Secretory Phase

i.Endometrial glands become more tortuous.

 ii. Cytoplasm of stromal cells increases because of the deposition of glycogen and lipids

iii. Many new blood vessels appear within endometrial stroma. Blood vessels also become tortuous

iv. Blood supply to endometrium increases

v. Thickness of endometrium increases up to 6 mm.

Actually, secretory phase is the preparatory period, during which the uterus is prepared for implantation of ovum. All these uterine changes during secretory phase occur due to the influence of estrogen and progesterone. Estrogen is responsible for repair of damaged endometrium and growth of the glands. Progesterone is responsible for further growth of these structures and secretory activities in the endometrium.

 If a fertilized ovum is implanted during this phase and if the implanted ovum starts developing into a fetus, then further changes occur in the uterus for the survival of the developing fetus. If the implanted ovum is unfertilized or if pregnancy does not occur, menstruation occurs after this phase and a new cycle begins.

 3)**CHANGES IN CERVIX AND VAGINA DURING MENSTRUAL CYCLE**

 Mucus membrane of the cervix also shows cyclic changes during different phases of menstrual cycle.

Proliferative Phase During proliferative phase, the mucus membrane of cervix becomes thinner and more alkaline due to the influence of estrogen. It helps in the survival and motility of spermatozoa

Secretory Phase During secretory phase, the mucus membrane of cervix becomes more thick and adhesive because of actions of progesterone.

 4)**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.

**HORMONAL REGULATION OF MENSTRUAL CYCLE**

 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 centers

 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.

 The diagram below shows hormonal level during menstrual cycle, LH = Luteinizing hormones, FSH = Follicle-stimulating hormone;

 