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QUESTION
I expect more on the physiology of lactation and details on the physiology of pregnancy in a normal woman.

1.
PHYSIOLOGY OF LACTATION
Lactation means synthesis, secretion and ejection of milk. Lactation involves two processes:
A. Milk secretion
B. Milk ejection.
MILK SECRETION
Synthesis of milk by alveolar epithelium and its passage through the duct system is called milk secretion.
Milk secretion occurs in two phases:
1. Initiation of milk secretion or lactogenesis
2. Maintenance of milk secretion or galactopoiesis.
1. Initiation of Milk Secretion or Lactogenesis
Although small amount of milk secretion occurs at later months of pregnancy, a free flow of milk occurs only after the delivery of the child. The milk, which is secreted initially before parturition is called colostrum.
Colostrum is lemon yellow in color and it is rich in protein (particularly globulins) and salts. But its sugar content is low. It contains almost all the components of milk except fat.
Role of hormones in lactogenesis
Prolactin is responsible for lactogenesis. During pregnancy, particularly in later months, large quantity of prolactin is secreted. But the activity of this hormone is suppressed by estrogen and progesterone secreted by placenta. Because of this, lactation is prevented during pregnancy.
Immediately after the delivery of the baby and expulsion of placenta, there is sudden loss of estrogen and progesterone. Now, the prolactin is free to exert its action on breasts and to promote lactogenesis.
2. Maintenance of Milk Secretion or Galactopoiesis
Galactopoiesis depends upon the hormones like growth hormone, thyroxine and cortisol, which are essential for continuous supply of glucose, amino acids, fatty acids, calcium and other substances necessary for the milk production
Role of hypothalamus in galactopoiesis
Galactopoiesis occurs till 7 to 9 months after delivery of child provided feeding the baby with mother's milk is continued till then. In fact, the milk production is continued only if feeding the baby is continued. Suckling of nipple by the baby is responsible for continuous milk production.
When the baby suckles, the impulses from touch receptors around the nipple stimulate hypothalamus. It is suggested that hypothalamus releases some prolactin-releasing factors, which cause the prolactin secretion from anterior pituitary. Prolactin acts on glandular tissues and

maintains the functional activity of breast for subsequent nursing.

MILK EJECTION

Milk ejection is the discharge of milk from mammary gland. It depends upon suckling exerted by the baby and on contractile mechanism in breast, which expels milk from alveoli into the ducts.

Milk ejection is a reflex phenomenon. It is called milk ejection reflex or milk let-down reflex. It is a neuroendocrine reflex.

EFFECT OF LACTATION ON MENSTRUAL CYCLE

Woman who nurses her child regularly does not have menstrual cycle for about 24 to 30 weeks after delivery.

It is because, regular nursing the baby stimulates prolactin secretion continuously. Prolactin inhibits GnRH secretion resulting in suppression of gonadotropin secretion. In the absence of gonadotropin, the ovaries become inactive and ovulation does not occur.

When the frequency of nursing the baby decreases (after about 24 weeks) the secretion of GnRH and gonadotropins starts slowly. When sufficient quantity of gonadotropins is secreted, the menstrual cycle starts.

BREAST MILK

Breast or human milk forms the primary source of nutrition for infants.

COMPOSITION

Breast milk contains about 88.5% of water and 11.5% of solids. Important solids are lactose, lactalbumin, iron, vitamins A and D and minerals.

ADVANTAGES OF BREAST MILK

Breast milk is always considered superior to animal milk (cow milk or goat milk) because it consists of sufficient quantity of all the substances necessary for infants like iron, vitamins and minerals.

Besides nourishment of infant, the breast milk also provides several antibodies, which help the infant resist the infection by lethal bacteria. Even some neutrophils and macrophages are secreted in milk. These phagocytic cells protect the infant by destroying microbes in the infant's body.

DISADVANTAGES OF ANIMAL MILK

1. It causes irritation of GI tract and anemia.
2. Excess proteins and fats in animal milk are difficult to digest and absorb by the infants.
3. High content of casein is harder to digest resulting in GI bleeding and anemia
4. High concentrations of sodium and potassium in animal milk causes overstraining of immature kidneys in infants.
5. Low iron content in animal milk develops iron deficiency anemia.
6. It has low content of vitamins and essential fatty acids.

2. PHYSIOLOGY OF PREGNANCY

Ovum is released from graafian follicle of
ovary into the abdominal cavity at the time of ovulation.

From abdominal cavity, ovum enters fallopian tube through the fimbriated end. Entry of ovum is facilitated by movement of cilia present in the inner surface of fimbriated end.

Ovum of matured follicle in the ovary is in primary oocyte stage with diploid number (23 pairs) of chromosomes. Just before ovulation, meiotic division takes place in the ovum.

Primary oocyte divides into a secondary oocyte and a first polar body. First polar body is expelled

out. Secondary oocyte contains only 23 chromosomes (haploid). Remaining 23 chromosomes are lost in the expelled first polar body.

Thus, when the ovum is released into abdominal cavity during ovulation, it is in the secondary oocyte stage with haploid number of chromosomes.

FERTILIZATION OF THE OVUM

Fertilization refers to fusion (union) of male and female gametes (sperm and ovum) to form a new offspring.

If sexual intercourse occurs at ovulation time and semen is ejaculated in the vagina, the sperms travel through the vagina and uterus to reach the fallopian tube. Sperms reach the ovarian end of fallopian tube within 30 to 60 minutes.

Movement of the sperm through uterus is facilitated by the anti-peristaltic contractions of uterine muscles. Uterine contractions are induced by oxytocin, which is secreted from posterior pituitary by neuroendocrine reflex during sexual intercourse (Chapter 66). Uterine contractions are also facilitated by prostaglandin (PGE2) present in male seminal fluid.

Among 200 to 300 millions of sperms entering female genital tract, only a few thousand sperms reach the spot near the ovum. Among these few thousand sperms, only one succeeds in fertilizing the ovum.

During fertilization, the sperm enters the ovum by penetrating the multiple layers of granulosa cells known as corona radiata present around the ovum. It is facilitated by hyaluronidase and proteolytic enzymes present in acrosome of sperm. Proteolytic enzymes from acrosome of the successful sperm diffuse through the structures of zona pellucida and inactivate the other sperms entering the ovum.

Penetrating movement of sperm is enabled by a protein called Casper present in the tail portion of the sperm. It is a tunnel-shaped protein and forms the ion channel for entry of calcium into sperm cell.

Immediately after fertilization, ovum, which is in secondary oocyte stage, divides into a matured ovum and a second polar body. Second polar body is expelled. Nucleus of matured ovum becomes female pronucleus with 23 chromosomes, which include 22 autosomes and one sex chromosome called X chromosome.

Simultaneously, head of sperm swells and becomes male pronucleus. Then 23 chromosomes of the sperm and 23 chromosomes of ovum arrange themselves to reform the 23 pairs of chromosomes in the fertilized ovum.

SEX CHROMOSOMES AND SEX DETERMINATION

SEX CHROMOSOMES

All the dividing cells in the body have 23 pairs of chromosomes. Among the 23 pairs, 22 pairs are called somatic chromosomes or autosomes. Remaining one pair of chromosomes is called sex chromosomes. Sex chromosomes are X and Y chromosomes.

SEX DETERMINATION

Sex chromosomes are responsible for sex determination. During fertilization of ovum, 23 chromosomes from ovum and 23 chromosomes from the sperm unite together to form the 23 pairs (46) of chromosomes in the fertilized ovum. Now, sex determination occurs. Ovum contains the X

chromosome. Sperm has either X chromosome or Y chromosome. When the ovum is fertilized by a sperm with X chromosome, the child will be female with XX chromosome. And, if the ovum is fertilized by a sperm
with Y chromosome, the sex of the child will be male with XY chromosome. So, the sex of the child depends upon the male partner.

IMPLANTATION

Implantation is the process by which the fertilized ovum called zygote implants (fixes itself or gets attached) in the endometrial lining of uterus.

After the fertilization, the ovum is known as zygote. Zygote takes 3 to 5 days to reach the uterine cavity from fallopian tube. While travelling through the fallopian tube, the zygote receives its nutrition from the secretions of fallopian tube.

After reaching the uterus, the developing zygote remains freely in the uterine cavity for 2 to 4 days before it is implanted. Thus, it takes about 1 week for implantation after the day of fertilization. During the stay in uterine cavity before implantation, the zygote receives its nutrition from the secretions of endometrium, which is known as uterine milk.

Just before implantation, the zygote develops into morula and then the implantation starts. A layer of spherical cells called trophoblast cells is formed around morula. Trophoblast cells release proteolytic enzymes over the surface of endometrium. These enzymes digest the cells of the endometrium. Now, morula moves through the digested part of endometrium and implants itself.

DEVELOPMENT OF PLACENTA AND EMBRYO

Already uterus is prepared by progesterone secreted from the corpus luteum during secretory phase of menstrual cycle. After implantation, placenta develops between morula and endometrium.

When implantation occurs, there is further increase in the thickness of endometrium because of continuous secretion of progesterone from corpus luteum. At this stage, the endometrial stromal cells are called decidual cells and the endometrium at the implanted area is called decidua.

Now the trophoblastic cells of morula develop into cords, which are attached with decidual portion of endometrium. Blood capillaries grow into these cords from the blood vessels of the newly formed embryo. At about 16th day after fertilization, heart of embryo starts pumping the blood into the trophoblastic cords.

At the same time, blood sinusoids develop around the trophoblastic cords. These sinusoids receive blood from blood from the mother.

Trophoblastic cells form some vascular projections into which fetal capillaries grow. These vascular projec- tions become placental villi.

Thus, the final form of placenta has got the fetal part and the maternal part.

Fetal part of placenta contains the two umbilical arteries, which carry fetal blood to the placental villi through the capillaries. The blood returns back to fetus through umbilical vein. Maternal part of placenta is formed by uterine arteries through which blood flows into sinusoids that surround the villi. The blood returns back to mother’s body through uterine vein.

MATERNAL CHANGES DURING PREGNANCY

During pregnancy, the changes are noticed in various organs, body weight, the metabolic activities and func- tional status of different physiological systems in the mother.

STRUCTURAL CHANGES

Various structural changes are noticed in the primary sex organs, accessory sex organs and in the mammary glands during pregnancy.

1. Ovaries

ii. Size

Size of the uterus also increases due to:

a. Hyperplasia (increase in number of cells) of myometrium.

b. Hypertrophy (increase in size of the cells) of myometrium.

c. Growth of fetus.

iii. Shape

The shape of non-pregnant uterus is pyriform. As the fetus grows, at the 12th week of pregnancy, it becomes globular. Then, once again it becomes pyriform gradually.

iv. Weight

Non-pregnant uterus weighs about 30 to 50g. The weight increases as the pregnancy advances. At the end of pregnancy, the uterine weight increases to about 1,000 to 1,200 g.

v. Histological changes

Endometrium shows formation of decidua, which is the bed for the fertilized ovum during the initial stages of pregnancy. Later, by the end of 3 months, three layers of decidua are formed:

a. Decidua basalis, which is the maternal part

b. Decidua capsularis that surrounds fetal sac

c. Decidua parietalis, which lines rest of uterine wall.

After the 3rd month, the decidua capsularis and parietalis fuse together.

3. Vagina

Vagina increases in size and its color changes to violet due to increased blood supply. There is deposition of glycogen in the epithelial cells.

4. Cervix

In cervix, the number of glands, blood supply and mucus secretion increase. The tough cervix becomes soft and it is closed by mucus plug.

5. Fallopian Tube

The number of epithelial cells and blood supply increase in fallopian tubes.

6. **Mammary Glands**

Size of the mammary glands increases because of development of new ducts and alveoli, deposition of fat and increased vascularization. Pigmentation of nipple and areola occurs.

INCREASE IN BODY WEIGHT

Average weight gained by the body during pregnancy is about 12 kg. Approximate weight of various structures, which adds to the weight gain:

Fetus:3.5kg

Amniotic fluid:2.0kg

Placenta:1.5kg

Increase in maternal body weight:5.0kg

If problem prenatal care is not taken, the body weight increases greatly by about 20g to 30g.

METABOLIC CHANGES

The metabolic activities are accelerated in the body due to increased secretion of various hormones like thyroxine, cortisol and sex hormones.

1. Basal Metabolic Rate

Increase in the secretion of various hormones especially thyroxine increases the basal metabolic rate by about 15% in the later stages of pregnancy.

2. Protein Metabolism

The anabolism of proteins increases during pregnancy. Positive nitrogen balance occurs. The deposition of proteins increases in the uterus.

3. Carbohydrate Metabolism

Blood glucose level increases leading to glucosuria. Ketosis develops either due to less food or more vomiting. Because of all these reasons, there is hyperplasia of beta cells of islets of Langerhans in pancreas leading to increase in secretion of insulin. Inspite of this, there is possibility of developing diabetes in pregnancy or latent diabetes after delivery.

4. Lipid Metabolism

During pregnancy, there is deposition of about 3 to 4 kg of fat in the maternal body. It also increases the blood cholesterol level and ketosis.

5. Water and Mineral Metabolism

Estrogen and progesterone are secreted by corpus luteum in the first trimester and by placenta later. These hormones increase the retention of sodium and water. Secretion of aldosterone increases during pregnancy. Aldosterone in turn increases the reabsorption of sodium from renal tubules. Apart from water and sodium retention, there is retention of calcium and phosphorus. Calcium and phosphorus are necessary for the growing fetus.

CHANGES IN PHYSIOLOGICAL SYSTEMS

1. Blood

The blood volume increases by about 20% or about 1 L. This increase is mainly because of increase in plasma volume. It causes hemodilution. Because of great demand for iron by the fetus, the mother usually develops anemia. It can be rectified by proper prenatal care and iron replacement.

2. Cardiovascular System Cardiac output

Generally, cardiac output increases by about 30% in the first trimester. After the 3rd month, cardiac output starts decreasing and reaches almost the normal level in the later stages of pregnancy.

- **Blood pressure**

Arterial blood pressure remains unchanged during the first trimester. During the second trimester, there is a slight decrease in blood pressure. It is due to the diversion of blood to uterine sinuses. And, hypertension develops if proper prenatal care is not taken.

- **Pre-eclampsia**

Pre-eclampsia is the hypertensive disorder of pregnancy. It is otherwise known as toxemia of pregnancy. About 3% to 4% of the pregnant women suffer from this. It usually occurs during last trimester of pregnancy.

Cause for hypertension

1. Release of vasoconstrictor substances from placenta.
2. Hypersecretion of adrenal hormones and other hormones, which cause vasoconstriction.
3. Development of autoimmune processes induced by the presence of placenta or fetus.

Other symptoms associated with hypertension

1. Decreased blood flow to kidney and thickening of glomerular capillary membrane, leading to reduc- tion in GFR and urinary output
2. Retention of sodium and water
3. Decreased urinary output along with retention of
sodium and water results in increased extracellular
fluid volume and edema
4. Excretion of proteins through urine.

Eclampsia

Eclampsia is the serious condition of pre-ecclampsia characterized by severe vascular spasm, dangerous hypertension and convulsive muscular contractions almost like seizures. It occurs just before, during or immediately after delivery. It leads to death, if timely treatment is not given.

Features of eclampsia

1. Spasm of blood vessels
2. Very severe hypertension
3. Renal failure
4. Liver failure
5. Heart failure
6. Convulsions
7. Coma.

Treatment for eclampsia

Treatment should be immediate. It includes administration of quick acting vasodilator drugs or termination of pregnancy.

3. Respiratory System

Overall activity of respiratory system increases slightly. Tidal volume, pulmonary ventilation and oxygen utilization are increased.

4. Excretory System

Renal blood flow and GFR increase resulting in increase in urine formation. It is because of increase in fluid intake and the increased excretory products from fetus. The urine becomes diluted with the specific gravity of 1,025. In the first trimester, the frequency of micturition increases because of the pressure exerted by the uterus on bladder.

5. Digestive System

During the initial stages of pregnancy, the morning sickness occurs in mother. It involves nausea, vomiting and giddiness. This is because of the hormonal imbal- ance. The motility of GI tract decreases by progesterone and constipation is common. Indigestion and hypo chlorhydria (decrease in the amount of hydrochloric acid in gastric juice) also occur.

6. Endocrine System

i. Anterior pituitary

During pregnancy, the size of anterior pituitary increases by about 50%. And secretion of corticotropin, thyrotropin

and prolactin increases. However, the secretion of FSH and LH decreases very much. It is because of negative feedback control by estrogen and progesterone, which are continuously secreted from corpus luteum initially and placenta later on.

ii. Adrenal cortex

There is moderate increase in secretion of cortisol, which helps in the mobilization of amino acids from the mother ' s tissues to the fetus. Aldosterone secretion also increases. It reaches the maximum at the end of pregnancy. Along with estrogen and progesterone, aldosterone is responsible for the retention of water and sodium.

iii. Thyroid gland

The size and the secretory activity of thyroid gland increase during pregnancy. The increased secretion of thyroxine helps in the preparation of mammary glands for lactation. It is also responsible for increase in basal metabolic rate.

iv. Parathyroid glands

Parathyroid glands also show an increase in the size and secretory activity. Parathormone is responsible for maintenance of calcium level in mother's blood in spite of loss of large amount of calcium to fetus.

7. Nervous System

There is general excitement of nervous system during pregnancy. It leads to the psychological imbalance such as change in the

GESTATION PERIOD

Gestation period refers to the pregnancy period. The average gestation period is about 280 days or 40 weeks from the date of last menstrual period (LMP). Traditionally, it is calculated as 10 lunar months. However, in terms of modern calendar it is calculated as 9 months and 7 days. If the menstrual cycle is normal 28 day cycle, the fertilization of ovum by the sperm occurs on 14th day after LMP. Thus the actual duration of human pregnancy is 280 – 14 = 266 days. If the pregnancy ends before 28th week, it is referred as miscarriage. If the pregnancy ends before 37th week, then it is considered as premature labor.

PARTURITION

Parturition is the expulsion or delivery of the fetus from the mother's body. It occurs at the end of pregnancy. The process by which the delivery of fetus occurs is called labor. It involves various activities such as contraction of uterus, dilatation of cervix and opening of vaginal canal.

BRAXTON HICKS CONTRACTIONS

Braxton Hicks contractions are the weak, irregular, short and usually painless uterine contractions, which start after 6th week of pregnancy. These contractions are named after the British doctor, John Braxton Hicks who discovered them in 1872. It is suggested that these contractions do not induce cervical dilatation but may cause softening of cervix. Often called the practice contractions, Braxton Hicks contractions help the uterus practice for upcoming labor. Sometimes these

contractions cause discomfort.

Braxton Hicks contractions are triggered by several factors such as:

1. Touching the abdomen
2. Movement of fetus in uterus
3. Physical activity
4. Sexual intercourse
5. Dehydration.

FALSE LABOR CONTRACTIONS

While nearing the time of delivery, the Braxton Hicks contractions become intense and are called false labor contractions. The false labor contractions are believed to help cervical dilatation.

STAGES OF PARTURITION

Parturition occurs in three stages:

First Stage

First, the strong uterine contractions called labor con tractions commence. Labor contractions arise from fundus of uterus and move downwards so that the head of fetus is pushed against cervix. It results in dilatation of cervix and opening of vaginal canal. Exact cause for the onset of labor is not known. This stage extends for a variable period of time.

Second Stage

In this stage, the fetus is delivered out from uterus through cervix and vaginal canal. This stage lasts for about 1 hour.

Third Stage

During this stage, the placenta is detached from the decidua and is expelled out from uterus. It occurs within 10 to 15 minutes after the delivery of the child.

MECHANISM OF LABOR

The slow and weak contractions of uterus commence at about a month before parturition. Later, the contractions gradually obtain strength and finally are converted into labor contractions at the time of labor. Exact cause for the onset of labor contractions is not known. It is strongly believed that the labor contractions are induced by the signal from fetus. And during labor, reflexes from uterus and cervix produce the powerful uterine contractions. Thus, uterus and cervix play an important role in labor. Many hormones are also involved during parturition.

ROLE OF UTERUS

Once started, the uterine contractions cause the development of more and more strong contractions. That is, the irritation of uterine muscle during initial contraction leads to further reflex contractions. It is called positive feedback mechanism. It plays an important role, not only in producing more number of uterine contractions but also the contractions to become more and more powerful.

ROLE OF CERVIX

Cervix also plays an important role in increasing the strength of uterine contractions. When the

head of fetus is forced against the cervix during the first stage of labor, the cervix stretches. It causes stimulation of muscles of cervix, which in turn results in reflex contractions of uterus.

ROLE OF HORMONES

Hormones involved in the process of parturition:

Maternal Hormones

1. Oxytocin
2. Prostaglandins
3. Cortisol
4. Catecholamines
5. Relaxin.

Fetal Hormones

1. Oxytocin
2. Cortisol
3. Prostaglandins.

Placental Hormones

1. Estrogen
2. Progesterone
3. Prostaglandins.

Estrogen

somatic nerve fibers and result in the release of a large quantity of oxytocin, which enhances labor. The release of more amount of oxytocin occurs due to positive feedback.

Relaxin

Relaxin is secreted from maternal ovary (corpus luteum) during the initial period of pregnancy. It is secreted in large quantity at the time of labor by placenta and mammary glands.

Relaxin:

i.Helps labor by softening the cervix and loosening the ligaments of symphysis pubis, so that the dilatation of cervix occurs

ii.Increases the number of receptors for oxytocin in the myometrium

iii.Simultaneously suppresses the inhibitory action of progesterone on uterine contraction so that the uterus starts contracting

iv. Facilitates the development of mammary
glands.

Prostaglandins

In recent times, prostaglandins are considered to play a vital role in labor. Prostaglandins particularly PGE2 facilitate labor by increasing the force of uterine contractions. The prostaglandins are secreted from uterine tissues, fetal membranes and placenta. Their concentration is increased in maternal blood and amniotic fluid at the time of labor.

Prostaglandins increase the force of uterine contractions by elevating the intracellular concentration of calcium ions in the uterine muscles.

Catecholamines

It is believed that the circulating adrenaline and nor- adrenaline also might increase the uterine

contraction through alpha adrenergic receptors.

Cortisol

At the time of labor, hypothalamus releases large quan- tity of corticotropin-releasing hormone, which increases the release of cortisol from the adrenal cortex. Cortisol enhances the uterine contraction and plays an important role in helping the mother to withstand the stress during labor.

Estrogen is continuously secreted along with proges- terone throughout the gestation period. However, in the later period, the quantity of estrogen released is much greater than that of progesterone.

Estrogen:

i. Increases the force of uterine contractions

ii. Increases the number of oxytocin receptors in uterine wall

iii. Accelerates the synthesis of prostaglandin from uterus.

Progesterone

Progesterone plays an important role in labor indirectly by its sudden withdrawal at the end of pregnancy.

Throughout the period of gestation, progesterone suppresses uterine contractions. It also inhibits the synthesis of prostaglandin (PGE2), which is necessary for uterine contraction. Progesterone inhibits prostaglandin synthesis by inhibiting the release of the enzyme phospholipase A, which is essential for prostaglandin synthesis.

Sudden decrease in progesterone secretion at the end of gestation period increases the uterine contractions and PGE2 synthesis.

Oxytocin:

i. Causes contraction of smooth muscle of uterus

and enhances labor. During the later stages of pregnancy, the number of receptors for oxytocin increases in the wall of uterus by the influence of estrogen. Because of this, the uterus becomes more sensitive to oxytocin.

ii. Stimulates the release of prostaglandins in the decidua.

Oxytocin is released in large quantity during labor. It is due to neuroendocrine reflex. During the movement of fetus through cervix, the receptors on the cervix are stimulated and start discharging a large number of impulses. Impulses are carried to hypothalamus