Physiology Team 439

MED439
KING SAUD UNIVERSITY

Revised & Approved

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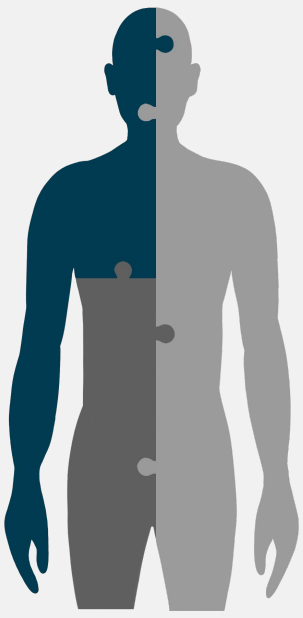


Physiology of Pregnancy

Objectives:

- Describe fertilization and the implantation of the blastocyst in the uterus.
- Recognize the development and the normal physiology of the placenta.
- Describe the physiological functions of placental hormones during pregnancy.
- Explain the physiological response of mother's body to pregnancy.

Color index:

- Important.
- Girls slide only.
- Boys slide only.
- Dr's note.
- Extra information.

Editing File

Introduction*

- **How many sperms in the ejaculated semen?** 35-200 million sperms per ml of semen, usually 2-5 ml of semen is ejaculated. On average, half a billion sperms are deposited in the vagina, and only few thousands make it to the fallopian tubes.
- **In which stage the ova is after ovulation?** Secondary oocyte, arrested at metaphase of meiosis II.
- **What is the % of ovulated ova that can reach fallopian tube?** Around 98%.
- **Can the ova that is released from the right ovary reaches the left fallopian tube?** Yes. some women who only had one ovary and only one remaining fallopian tube (on the contralateral side) had several children with ease. Ova are released into the abdominal cavity and are then picked up by the fimbriae of the fallopian tube which are equipped with cilia that beat inwards towards the uterus thereby reinforcing this "hooking" process.
- **What are the factors that help the ovulated ova to reach the fallopian tube?**
  1- The cilia of the fallopian tubes beat towards the uterus. 2- Fluid. 3- Muscles lining the fallopian tube.
- **Is there any obstacles?** Yes, the irregularity of fallopian tube lining impedes the movements of the fertilized ovum, and the isthmus remain tonically constricted until progesterone causes its relaxation around three days after ovulation.
- **What are the factors that help the sperm to travel in the female genital tract?** Sperm motility through its flagella, PGs from the semen and oxytocin released from the female during orgasm can initiate antiperistaltic contractions that help propel sperm into the ovum, oocytes release certain chemicals that attract sperm through olfactory receptors and other factors.
- **Is there any obstacles?** Acidity of vaginal fluids, thick cervical mucus, possible antigenicity due to the occasional WBC infiltration of vagina and cervix, the barriers around ovum itself (zona pellucida and corona radiata)
- **How does the ova survive in the fallopian tube?** Secretion of peg cells of the fallopian tubes nourishes the ovum, the ovum is also protected by thick outer layer of glycoproteins (zona pellucida) and granulosa cells (corona radiata).

Fertilization

If the ovum becomes fertilized by a sperm, a new sequence of events called gestation or pregnancy takes place, and the fertilized ovum eventually develops into a full-term fetus.

- After ejaculation, sperms reach ampulla of fallopian tube within 30-60 min (By the action of Prostaglandins from seminal vesicles and oxytocin). These hormones causes pulsatile contraction and relaxation of the uterus inducing negative pressure resulting in suction power inside the uterus
- Sperm penetrate corona radiata and zona pellucida (hyaluronidase & proteolytic enzymes). The enzymes (released from acrosomal vesicles) digest the cell wall until the sperm reaches zona pellucida
- Sperm binds to ZP3 on zona pellucida.
- Oocyte divides to form mature ovum (female pronucleus 23 unpaired chromosomes.)
- Head of sperm swells (male pronucleus 23 unpaired chromosomes).
- Fertilized ovum (zygote) contains 23 pairs of chromosomes.
- The 23 chromosomes of the male and female pronuclei align themselves to re-form a complete complement of 46 chromosomes.
- Sperm nucleus entry causes a reaction causing calcium release from the granules > blocks the receptors which prevents polyspermy. Polyspermy causes malformations that lead to abortion

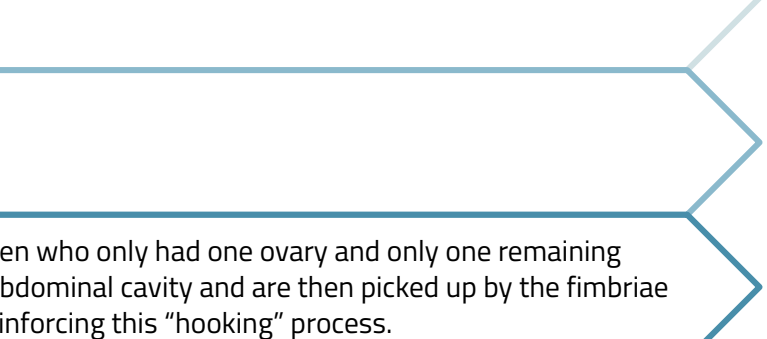


Figure 6.1a

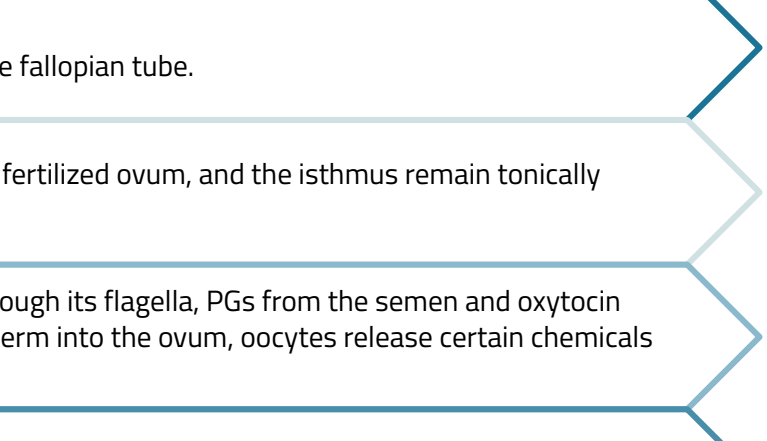


Figure 6.1b (Important)

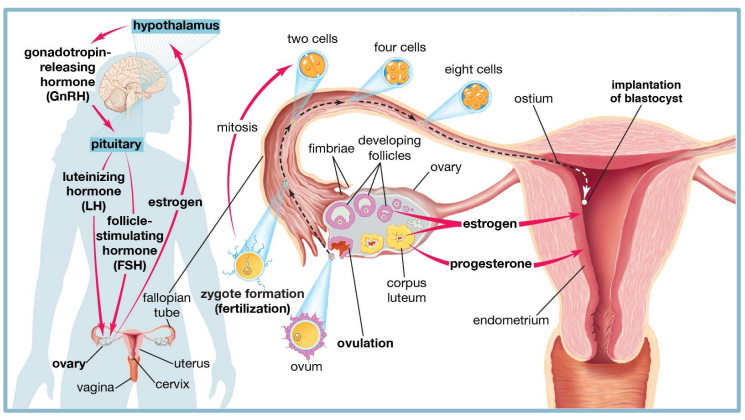


Figure 6.2a

Cleavage

- Following fertilization, the zygote undergoes several mitotic divisions inside the zona pellucida (overall size does not change).
- First cleavage yields a 2 celled embryo, each cell is called a blastomere and is totipotent. Totipotent : has the full potential to become or develop into anything
- Divisions continue rapidly until the 32 cell stage (morula).

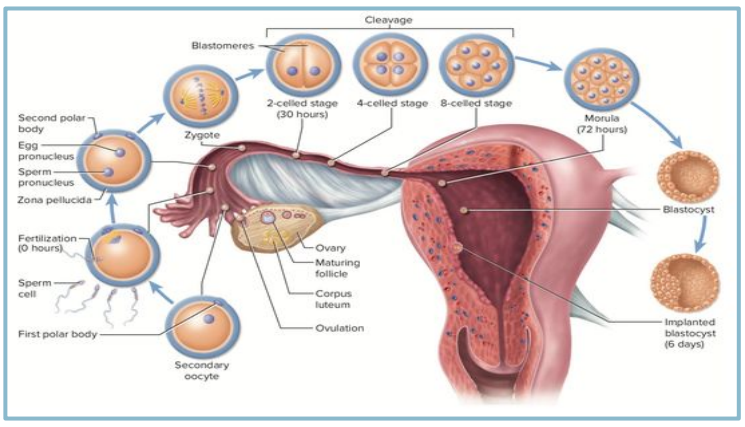


Figure 6.2b

Figure 6.1a:
Normal sperm count is from 300-500 million sperms. Less than 20 million sperms indicates infertility.

Transport of Fertilized Ovum and Implantation

Zygote begins to divide as it travels through oviduct. The zygote reaches the uterine cavity 3-5 days after fertilization.

Transport: fluid current + action of cilia + weak contractions of the fallopian tube.(estrogen, PGs)

Delayed transport allows cell division to occur before the dividing ovum enters the uterus.

Isthmus (last two centimeters) relaxes under effect of progesterone.
Isthmus is usually contracted

Blastocyst ~100 cells, enters the uterus. Implants into lining of uterus.
Nutrition of blastocysts (secretory cells in fallopian tubes)

Implantation occurs 5-7 days after Fertilization.

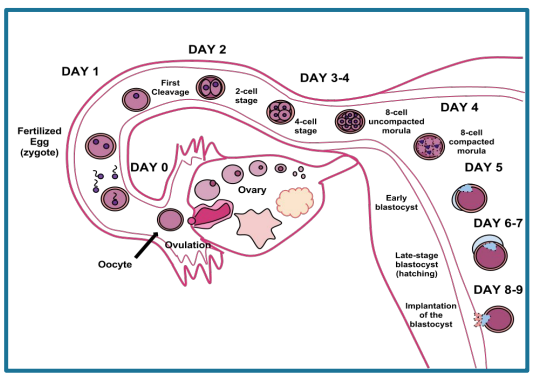


Figure 6.3a

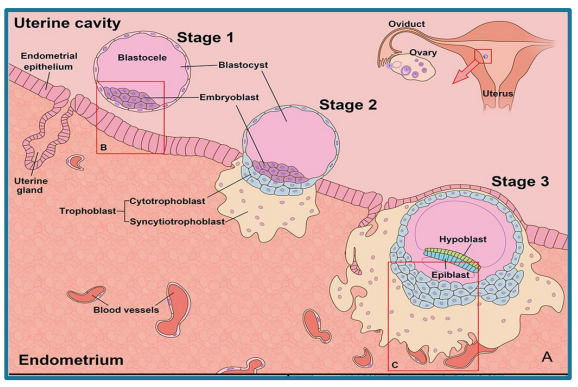


Figure 6.3b

Figure 6.3a:
The cells are dividing and compacted on each other preserving the cell size until there is a cavity formed called the blastocoele then the cell is called blastocyst. At this stage it becomes ready for implantation..
Inner cell mass gives rise to the fetus while the trophoblast (the surface cells) give rise to extraembryonic structures including placenta.

Figure 6.3b:
The embryonic pole will release enzymes that digest the endometrial epithelium and it will become decidua under the influence of progesterone.
The trophoblastic cords project into the endometrial epithelium in villous like structures with intervillous space and connects with the vascularity of the mother (feto-maternal circulation)

Placenta

	Functions	Characteristics of Placenta
1	Respiration	❖ Trophoblastic cords from blastocyst.
2	Nutrition	❖ Blood capillaries grow in the cords.
3	Excretion	❖ 21 days after fertilization, blood starts to be pumped by fetal heart into the capillaries.
4	Endocrine	❖ Maternal blood sinuses develop around the trophoblastic cords.
5	Protection	❖ More and more trophoblast projections develop (placental villi).

Placental Permeability and Membrane Diffusion Conductance*

- In the **early** months of pregnancy, the placental membrane is still thick and the surface area is small because it is not fully developed and grown.
- In **later** pregnancy, the permeability increases because of thinning of the membrane diffusion layers and because the surface area expands many times over.

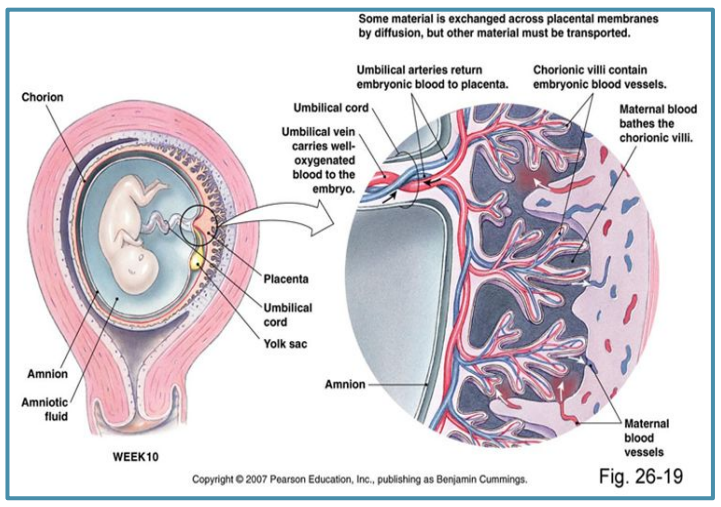


Figure 6.4a

Figure 6.4b

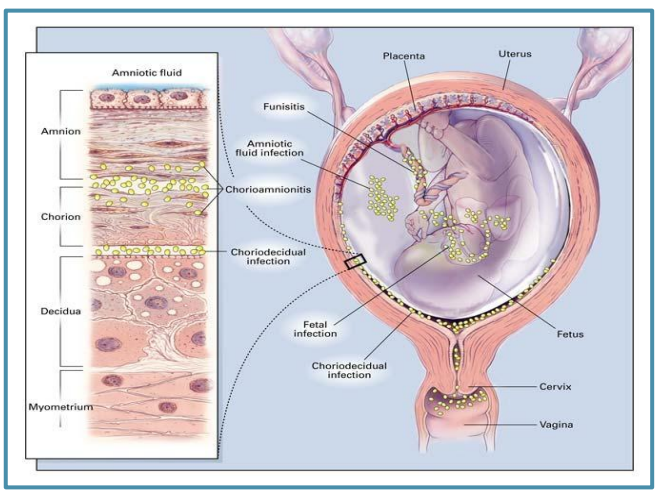


Figure 6.4a:
The placenta is connected by umbilical cord which contains:
One vein احمر
Two arteries ازرق

- The most dangerous period in pregnancy is organogenesis which extends from 2nd week until the 8th week so we make sure that the mother is away from anything that could harm the fetus development of organs during this stage.

Important Factors Facilitating Delivery of Oxygen to The Fetal Tissues (Respiration)

❑ Diffusion of oxygen through the placental membrane:*

- PCO_2 is **2-3** mm Hg higher in fetal than maternal blood.
- Dissolved O_2 in mother's blood passes to fetal blood by **simple diffusion.**
- The mean partial pressure of oxygen (PO_2) of the mother's blood in the placental sinuses is about **50** mm Hg, and the mean PO_2 in the fetal blood after it becomes oxygenated in the placenta is about **30** mm Hg.
- **50** mm Hg (M) – **30** mm Hg (F) = **20** mm Hg (mean pressure gradient).

❑ There are <u>three</u> reasons why this low PO_2 is sufficient to deliver O_2 to the fetal tissues:

- Hemoglobin of the fetus.
- High fetal hemoglobin concentration (16-17 g/dl) and it's about 50% greater than that of mother. **So fetus uses oxygen first.**
- The Bohr effect

Physiologically the fetus respires before the mother; he gets the nutritional requirements from breathing before the mother does.
Why? Because of the gradient , Hb (the concentration also), bohr effect.

❑ Hemoglobin of the fetus:

- Fetal hemoglobin (**HbF**).
- Fetal hemoglobin (HbF) concentration is about **50%** greater than that of the mother (HbA).
- At the low PO_2 levels in fetal blood, the fetal hemoglobin can carry 20 to 50% more oxygen than maternal hemoglobin. (HbF has a **higher** oxygen carrying capacity than HbA)[2].

Double Bohr Effect

High pH in fetal blood (alkaline).

Low pH in mother's blood (acidic).

❑ Important shifts of the dissociation curves take place in the placenta:*

1. The maternal blood gains CO_2, the pH falls and the curve shifts to the right releasing additional oxygen.
2. On the fetal side of the placenta CO_2 is lost, the pH rises and the curve shifts to the **left** allowing additional oxygen uptake.
3. These changes cause the capacity of fetal blood to combine with O_2 to increase, and maternal blood to decrease, which forces more O_2 from the maternal blood while enhancing oxygen uptake by the fetal blood.*

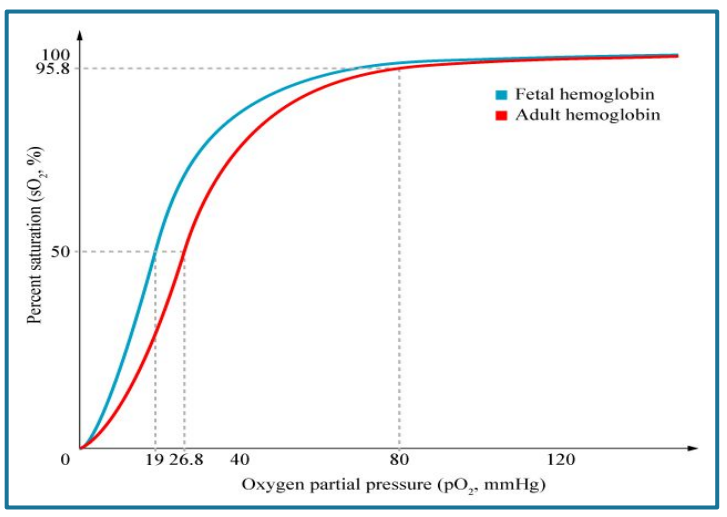


Figure 6.5a

❑ Other Factors:*

- ❖ High maternal intervillous blood flow (almost double the fetal placental flow).
- ❖ High fetal cardiac output (120-170 BPM).
- ❖ The fetal metabolic acidosis-which shifts the curve to the right and thus aids delivery of oxygen to the tissues.

Placental flow -> مرتين
Maternal flow -> ٤ مرات

<u>Notes:</u>
- Acidosis is caused because the tissues of the fetus are metabolizing and the lungs aren't working to expel the CO2 out > Co2 accumulates leading to metabolic acidosis
- Acidity will cause O2 release from the mothers hb and the fetus will gain that O2

Nutrition

01 Fetus uses mainly glucose for nutrition so the trophoblast cells in placental villi transport glucose by carrier molecules; GLUT-1 (facilitated diffusion). GLUT-3 Male doctor

02 Fatty acids diffuse due to high solubility in cell membrane (more slowly than glucose).

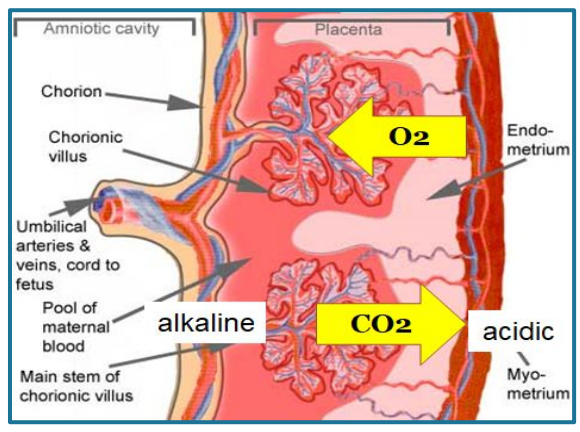
03 The placenta actively transports all amino acids, with fetal concentrations exceeding maternal levels.

04 K^+, Na^+ and Cl^- diffuse from maternal to fetal blood.

Excretion

1	Excretory products of the fetus diffuse through the placental membrane to maternal blood to be excreted with the waste products of the mother: Urea, uric acid and creatinine.
2	Higher conc. of excretory products in fetal blood ensures continuous diffusion of these substances to the maternal blood.

Figure 6.6a



Placenta as an Endocrine Organ

	Characteristics	Functions
Estrogen	❖ Steroid hormone. ❖ Secreted by syncytial trophoblast cells. ❖ Towards the end of pregnancy it reaches **30×**. ❖ Derived from weak androgen (DHEA) released from maternal & fetal adrenal cortex. The reason for the increase in the end is because the fetal adrenal cortex is matured and an extra pathway has been created	❖ Enlargement of uterus, breast & external genitalia. ❖ Relaxation of pelvic ligaments in preparation for labor. ❖ Activation of the uterus (gap junctions) **Functions mentioned elsewhere in the lecture:** ❖ Increases blood volume of pregnant woman. It increases at the end also to prepare for labour, to terminate pregnancy.
Progesterone	❖ Steroid hormone. ❖ Secreted by syncytial trophoblast cells. ❖ Towards the end of pregnancy it reaches **10×**. ❖ Derived from cholesterol.	❖ Provides nutrition to developing embryo (uterine secretory phase). ❖ Development of decidual cells. ❖ Inhibits the contractility of the uterus. ❖ Development of breast lobules and alveoli. **Functions mentioned elsewhere in the lecture:** ❖ Increases the sensitivity of respiratory center to CO_2
Relaxin	❖ Polypeptide. ❖ Secreted by corpus luteum and placenta.	❖ Relaxation of symphysis pubic ligament (weak). ❖ Softens the cervix at delivery.
Human Chorionic Gonadotropin (hCG)	❖ Glycoprotein. ❖ Secreted by syncytial trophoblast cells. Used for pregnancy test. Appears in blood 1-2 weeks after fertilization, while in urine it appears 2-3 weeks after fertilization IMP MCQ	❖ **Most important function is to maintain corpus luteum (↑estrogen & progesterone) till 13-17 weeks of gestation.** ❖ Exerts interstitial (Leyding) cell-stimulating effect on testes of these male fetus (growth of male sex organs). **Functions mentioned elsewhere in the lecture:** ❖ TSH-like activity to increase thyroxine production.
Human Chorionic Somatomammotropin or Human Placental Lactogen (hPL)	❖ Protein hormone. ❖ Secreted by placenta around **5th** gestational week.	❖ **Breast development. (hPL facilitates mammogenesis)** ❖ Weak growth hormone's action. Masculinization effect, enlarged nose ❖ Inhibits insulin sensitivity = ↓ glucose utilization. (gestational diabetes) ❖ Promotes release of fatty acids.

Physiological Adaptation to Pregnancy

	Changes
Maternal Endocrine System	❖ **Anterior pituitary gland enlargement (50%):** - Release of ACTH, **TSH and PL increase.** - FSH and LH almost totally suppressed. ❖ **Adrenal gland:** - Increase glucocorticoids secretion (mobilize AA). - Increase aldosterone (retain fluid)/(reabsorb excess Na). ❖ **Thyroid gland enlargement (50%):** - Increase thyroxine production (hCG). Physiological goiter ❖ **Parathyroid gland enlargement:** - Increase PTH secretion (maintains normal Ca^{+2}).
Different Organs	❖ **Increase in uterine size (50 gm to 1100 gm).** ❖ **The breasts double in size.** ❖ **The vagina enlarges.** ❖ **Development of edema and acne.** ❖ **Masculine or acromegalic features.** ❖ **Weight gain 10-12 kg (last 2 trimesters).** - Increase appetite. - Removal of food by fetus. - Hormonal effect.
Circulatory System	❖ **Increase in cardiac output (30-40%) by 27th weeks.** ❖ **Increase in blood flow through the placenta.** Leading to hypotension ❖ **Increase in maternal blood volume (30%) due to:** - **Increase aldosterone and estrogen (↑ ECF).** - Increase activity of the bone marrow (↑ RBCs 40%). - They will have physiological anemia despite the increase in rbcs لان السوائل كثير
Respiration	❖ **Increase in O_2 consumption (20%):** - Increase BMR. - Increase in body size. ❖ **Growing uterus presses upwards (restriction)** ❖ **Increase in respiratory rate (RR).** ❖ **Progesterone ↑ sensitivity of respiratory centers to CO_2.** ❖ **Increase in minute ventilation (Tidal Volume x Respiratory Rate) by 50% and a decrease in arterial PCO_2 to several millimeters.**
Metabolism & Kidney Function	❖ **Increase basal metabolic rate (15%).** ❖ **Increase in daily requirements for:** - Iron. - Phosphates. - Calcium. - Vitamins: vitamin D (Ca^{+2} absorption). ❖ **The renal tubules' reabsorptive capacity for Na, Cl, and water is increased as much as 50%.** ❖ **The renal blood flow and GFR increase up to 50%.** ❖ **Normal pregnant woman accumulates only about 5 pounds (2.27Kg) of extra water and salt.**

A Special Thanks to Team 438

MCQ & SAQ:

Q1: After ejctulation, how long does it take the sperm to reach the fallopian tubes?

A. 10-30 minutes
B. 30-60 minutes
C. 60-80 minutes
D. 80-90 minutes

Q2: All of the following are functions of the placenta EXCEPT:

A. Nutrition
B. Respiration
C. Exocrine
D. Endocrine

Q3: The mean PO_2 in fetal blood after it gets oxygenated in the placenta is?

A. 20 mm Hg
B. 50 mm Hg
C. 30 mm Hg
D. 40 mm Hg

Q4: The maternal blood .... CO_2, the pH .... and the curve shifts to the right releasing additional oxygen.

A. Falls, Falls
B. Grains , Falls
C. Gains , Gains
D. Falls, Gains

Q5: What is the main function of human chorionic gonadotropin?

A. Maintains corpus luteum
B. Degrades theca interna cells
C. Secretes estrogen and progesterone
D. Thyroxine production

Q6: During pregnancy, all of the following hormones increase EXCEPT:

A. Prolactin
B. ACTH
C. PTH
D. FSH

answer key:
1: B
2: C
3: C
4: B
5: A
6: D

1- What are the functions of the human placental lactogen hormone?

2- Why is the low PO_2 sufficient to deliver O_2 to the fetal tissues?

3- Explain the process of Implantation.

A1:
- Breast development.
- Weak growth hormone's action. Masculinization effect, enlarged nose
- Inhibits insulin sensitivity = ↓ glucose utilization.
- Promotes release of fatty acids.

A2:
- High fetal hemoglobin concentration and the bohr effect.

A3:
- Slide 4

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