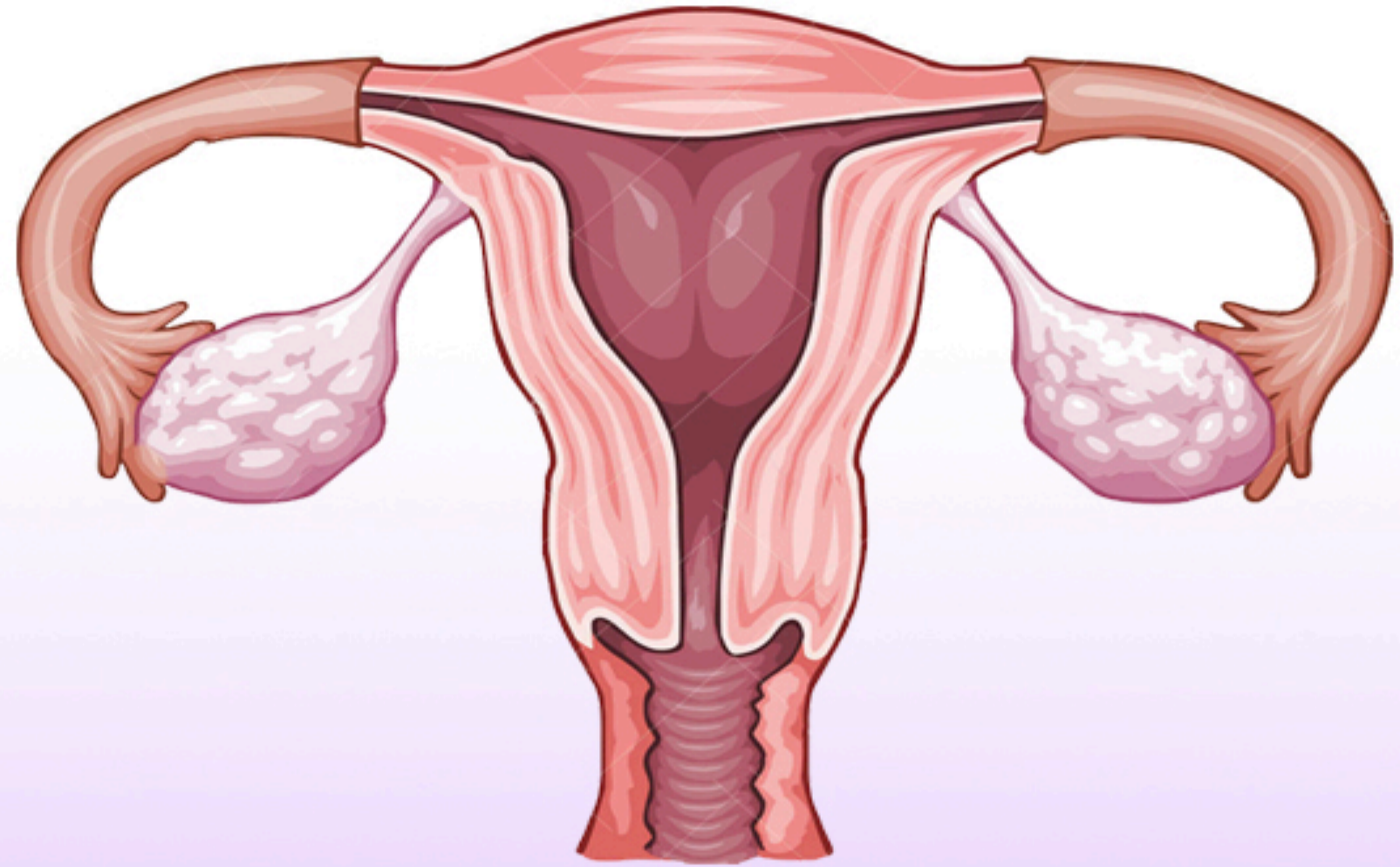




Physiology team



Lecture6:

Physiology of Pregnancy



Sources:

- ✓ Dr.Mohammed Alotaibi slides
- ✓ Guyton: chapter 82

Objectives

- i. Describe fertilization
- ii. Recognize the development and the function of the placenta
- iii. Recognize the placenta as an endocrine organ
- iv. Describe the physiological functions of placental hormones
- v. Explain the mother's physiological response to pregnancy



Abbreviations

HPL	Human placental lactogen
DHEA	dehydroepiandrosterone and 16-hydroxy-dehydroepiandrosterone,

i. Describe fertilization

After ejaculation, sperms reach **ampulla** of fallopian tube within 30-60 min *(PG and OT actions)

⌘ Fertilization :

1 The fertilizing sperm penetrates the corona radiata via membrane-bound enzymes in the plasma membrane of its head and binds to **ZP3** receptors on the zona pellucida.

2 Binding of sperm to these receptors triggers the acrosome reaction, in which hydrolytic enzymes in the acrosome are released onto the zona pellucida.

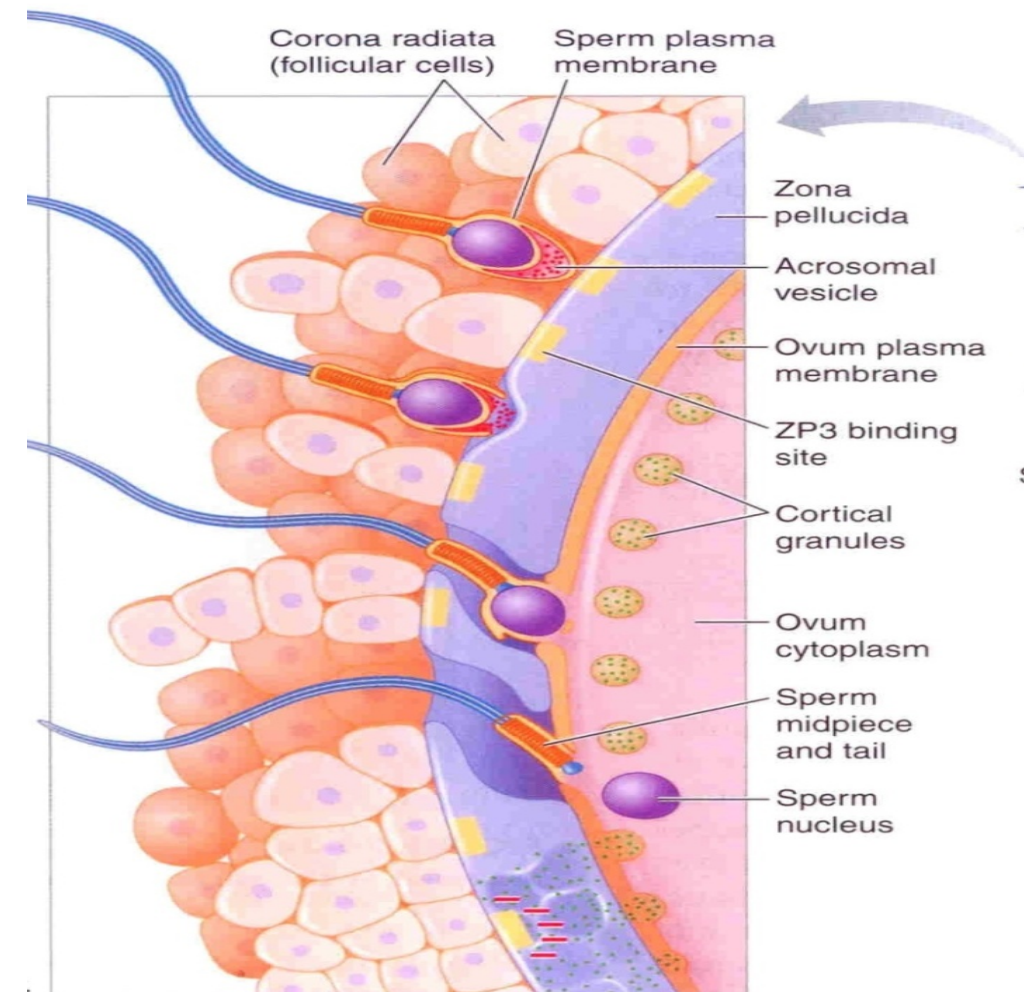
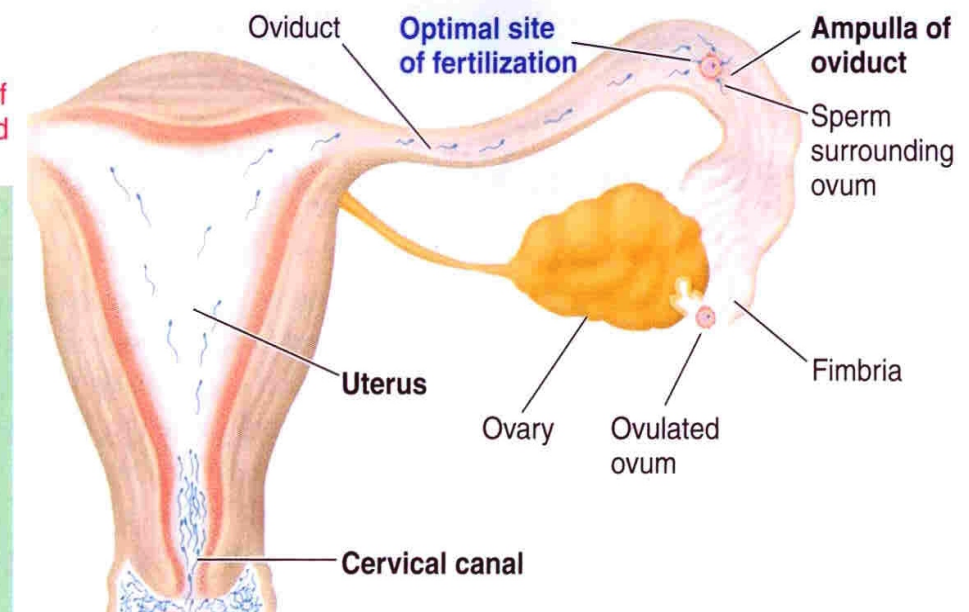
3 The acrosomal enzymes digest the zona pellucida, creating a pathway to the plasma membrane of the ovum. When the sperm reaches the ovum, the plasma membranes of the two cells fuse.

4 The sperm nucleus enters the ovum cytoplasm.

5 The sperm stimulates release of Ca^{2+} stored in cortical granules in the ovum, which in turn, inactivates ZP3 receptors, leading to the block to polyspermy.

- Only the head of the sperm enters the ovum
- The ovum still in the secondary oocyte stage of development .
- Keep in mind the name of the receptor and its location

Location	Time of appearance (min after ejaculation)	Percent of ejaculated sperm*
Fertilization site (upper third of oviduct)	30-60	0.001
Uterus	10-20	0.1
Cervical canal	1-3	3



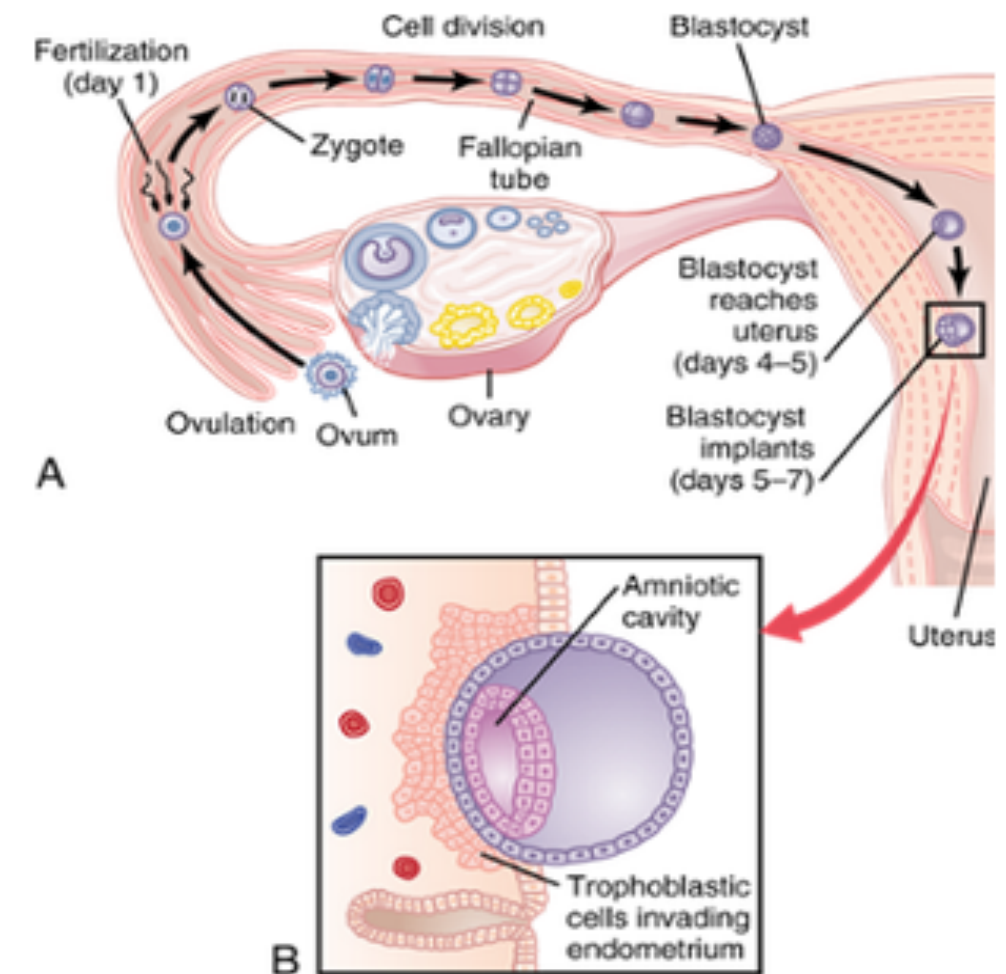
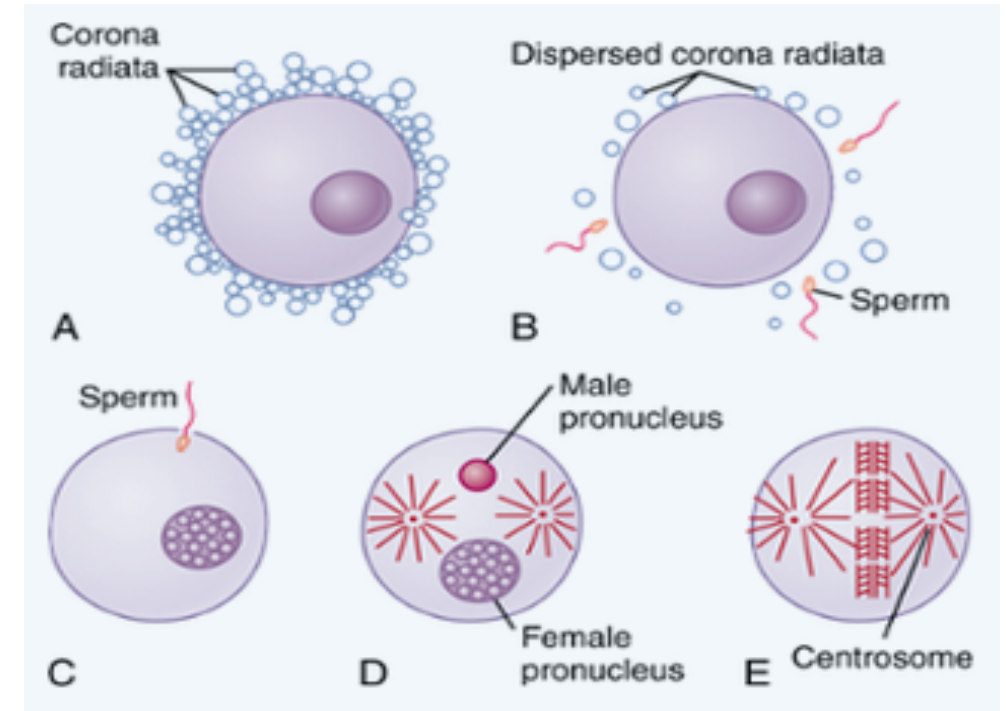
PG = prostaglandins in the male seminal fluid .
OT = oxytocin released by post.pituitary of the female

⌘ Fertilization :

- ✓ Sperm penetrates **corona radiata and zona pellucida (ZP3 receptors)** (hyaluronidase)
- ✓ **Completion of 2nd meiotic division .**
- ✓ Oocyte divides to form **mature ovum (female pronucleus 23 unpaired chr) + 2nd polar body**
- ✓ Head of sperm swells (**male pronucleus 23 unpaired chr**)
- ✓ Fertilized ovum (zygote) contains 23 paired chr

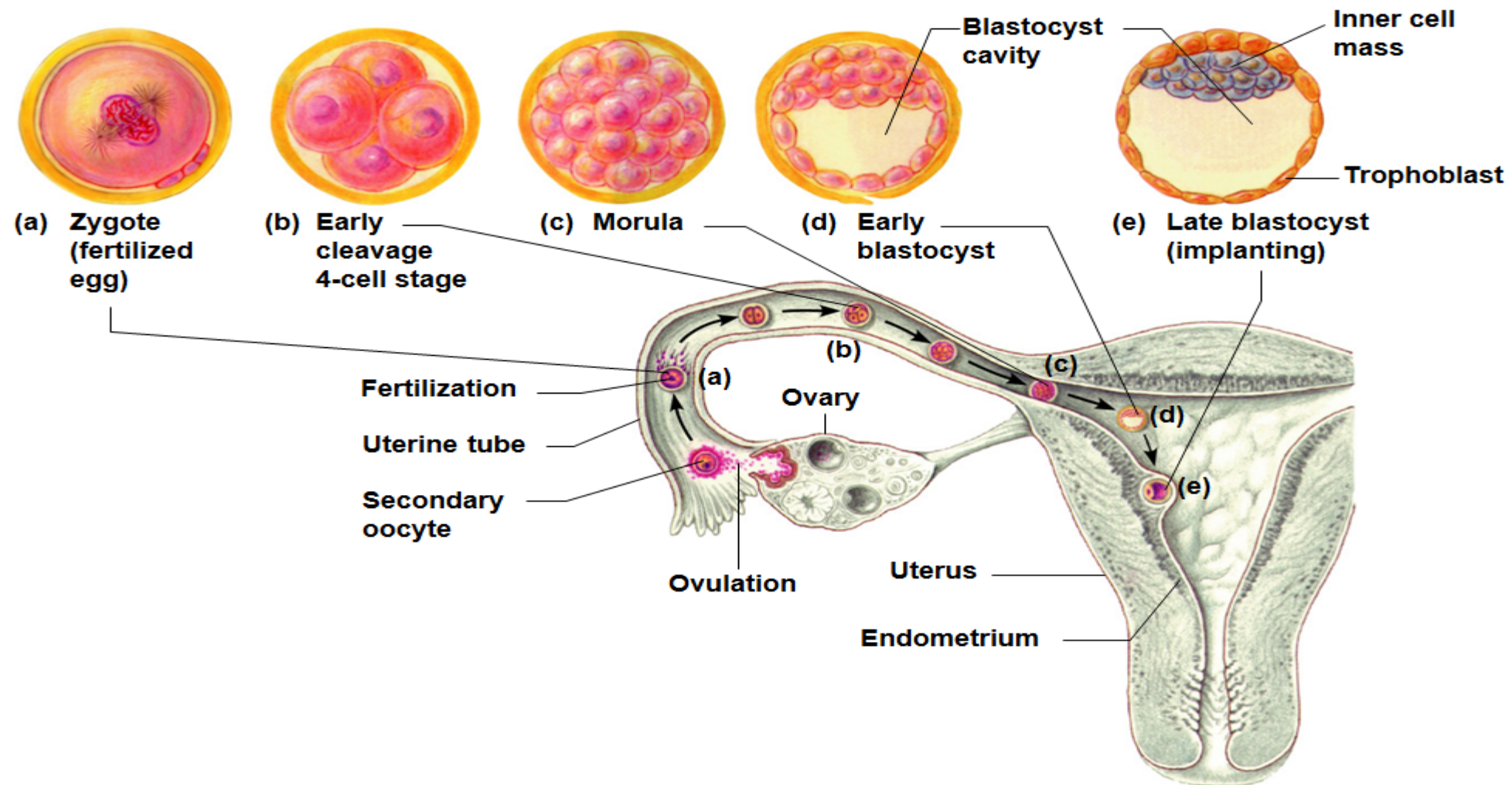
⌘ Transport of fertilized ovum :

- ✓ **Traveling of the fertilized ovum from the fallopian tube in to the cavity of the uterus takes from 3 to 5 days .**
- ✓ This transport is effected mainly by :
 - Fluid current in the tube
 - Action of the ciliated epithelium
 - Week contractions of the fallopian tube
- ✓ **Isthmus (last 2cm) relaxes under effect of progesterone**
(the rapid secretion of progesterone by the corpus luteum first promotes increasing progesterone receptors on the fallopian tube smooth muscle cells then the progesterone activates the receptors → relaxation of the isthmus which allows entry of the ovum into the uterus)
- ✓ This delayed transport of fertilized ovum allows several stages of cell division to occur → blastocyte wit about 100 cells enters the uterus .



⌘ Cleavage:

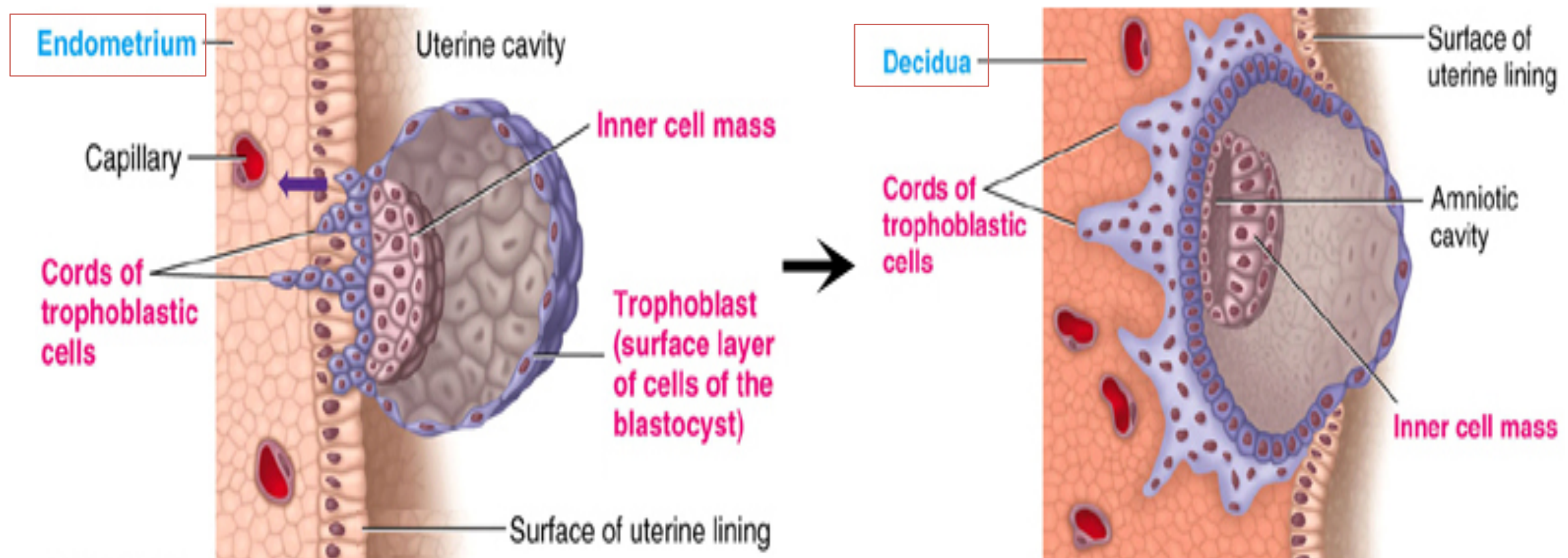
- ✓ Following fertilization, the zygote undergoes several mitotic divisions inside the zona pellucida (**overall size does not change**).
- ✓ 1st cleavage yields a 2 celled embryo,
 - each cell is called a blastomere and is *totipotent*
- ✓ Divisions continue rapidly **until the 32 cell stage**



You don't have to remember the cells names

⌘ Implantation :

- ✓ implantation occurs in 1 week after fertilization .
- ✓ before implantation the blastocyst obtains its nutrition from uterine endometrial secretion called **uterine milk**
- ✓ Trophoblastic cords from blastocyst
- ✓ Blood capillaries grow in the cords
- ✓ 21 days after fertilization, blood starts to be pumped by fetal heart into the capillaries
- ✓ Maternal blood sinuses develop around the trophoblastic cords
- ✓ More and more trophoblast projections develop (placental villi)
- ✓ Endometrium become decidua.



<https://youtu.be/rL0P3OzEwO4>

ii. Recognize the development and the function of the placenta

Placenta

It is the primary site for exchange of gases and nutrients between the mother and the fetus.
Formed at the

Functions

- ① Respiration
- ② Nutrition
- ③ Excretion

- ④ Endocrine
- ⑤ Protection

① Respiration

❖ Important factors facilitating delivery of oxygen to the fetal tissues

- ✓ The mean PO_2 of the mother's blood = 50 mm Hg, and the mean PO_2 in the fetal blood = 30 mm Hg. Therefore, the mean pressure gradient for diffusion of oxygen through the placental membrane is about 20 mm Hg.
- ✓ The dissolved oxygen in the blood of the large maternal sinuses passes into the fetal blood **by simple diffusion**

SO HOW IT IS POSSIBLE FOR A FETUS TO OBTAIN SUFFICIENT OXYGEN?

1. High fetus haemoglobin (HbF)(16 - 17 g/dl) which has high affinity for O_2 than mother's haemoglobin (HbA) Figure 6- 1
2. Haemoglobin concentration of fetal blood is about 50 % greater than that of the mother → Enhancing the amount of oxygen transported to the fetal tissues.
3. Double Bohr effect (hemoglobin can carry more oxygen at a low PCO_2 than it can at a high PCO_2) Figure 6- 2
 - ✓ Loss of the carbon dioxide makes the fetal blood more alkaline (**High pH**)
 - ✓ the increased carbon dioxide in the maternal blood makes it more acidic (**Low pH**)

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

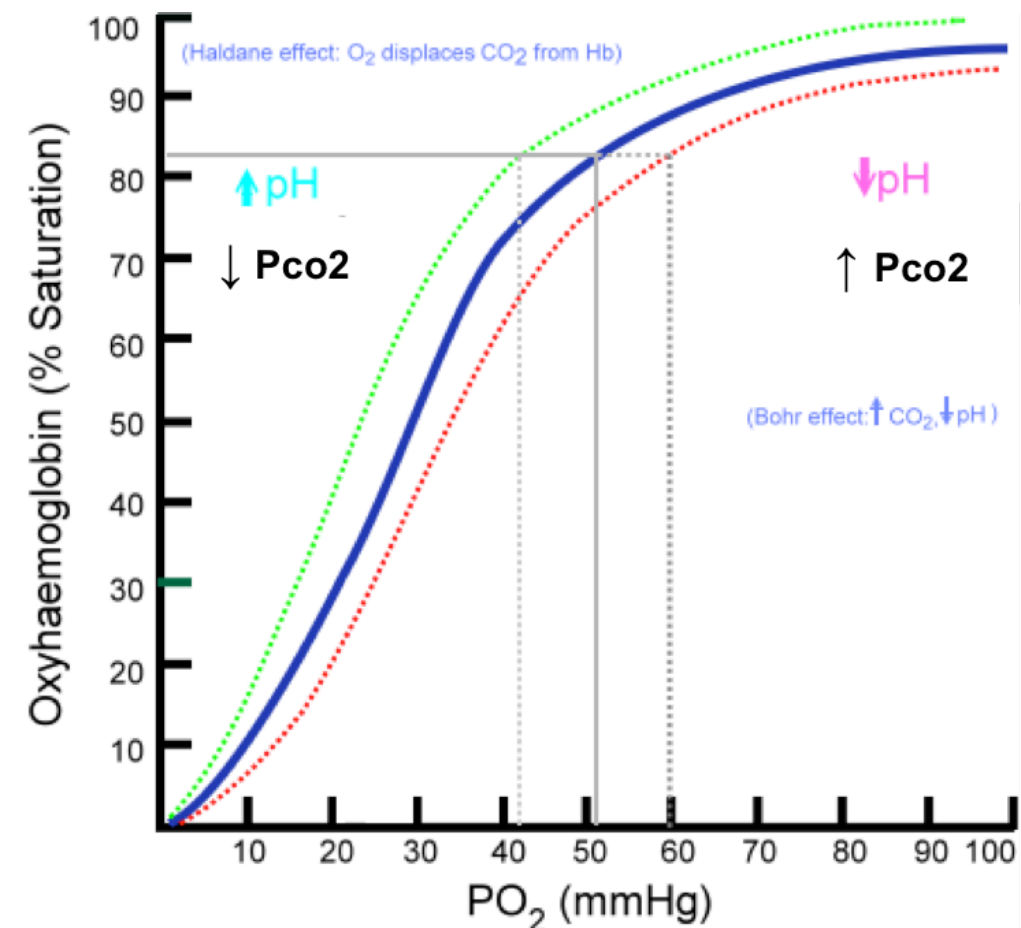
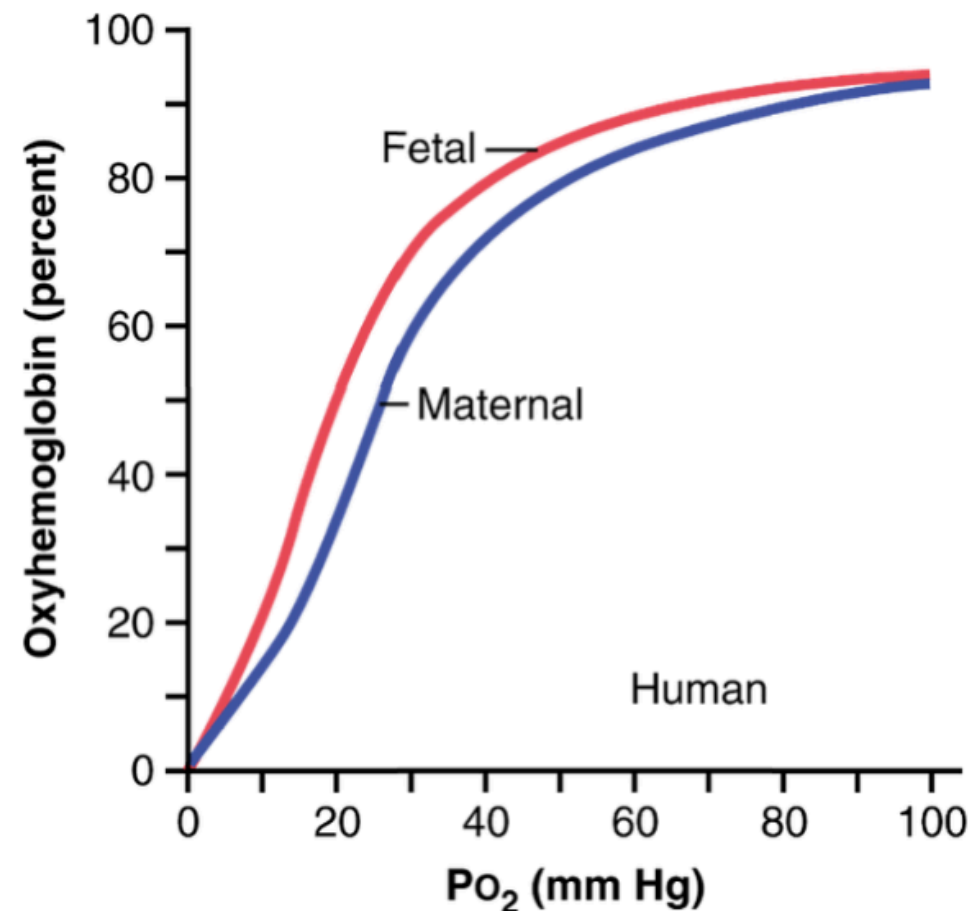


Figure 6- 1 Oxygen-hemoglobin dissociation curves for maternal and fetal blood, showing that fetal blood can carry a greater quantity of oxygen than can maternal blood for a given blood PO_2

fetal hemoglobin is shifted to the left of that for maternal hemoglobin

Figure 6- 2

- ✓ The maternal blood gains CO_2 → the pH falls (acidic) → the curve shifts to the right releasing additional oxygen.
- ✓ On the fetal side of the placenta CO_2 is lost ¹ → the pH rises (alkaline) → the curve shifts to the left allowing additional oxygen uptake.

NOTE The PCO_2 of the fetal blood is 2 to 3 mm Hg higher than that of the maternal blood

② Nutrition

nutrient	Transporte
glucose (Main)	trophoblast cells lining the placental villi provide for facilitated diffusion of glucose through the placental membrane. the glucose is transported by carrier molecules (GLUT) in the trophoblast cells of the membrane.
Fatty acids	diffuse due to high solubility in cell membrane (more slowly than glucose)
ketone bodies and potassium, sodium, and chloride ions	diffuse with relative ease from the maternal blood into the fetal blood.

③ Excretion

- ✓ Excretory products of the fetus diffuse through the placental membrane to maternal blood to be excreted with the waste products of the mother
- ✓ These include the nonprotein nitrogens such as urea, uric acid, and creatinine.
- ✓ higher concentrations of the excretory products in the fetal blood than in the maternal blood, there is continual diffusion of these substances from the fetal blood to the maternal blood.

- iii. Recognize the placenta as an endocrine organ
- iv. Describe the physiological functions of placental hormones

④ Endocrine Figure 6- 3

	Human Chorionic Gonadotropin (hCG) ¹	Estrogen	Progesterone	Human Chorionic Somatomamotropin or (hPL)	Relaxin
	Glycoprotein	Steroid hormone		Protein hormone	Polypeptide
Secreted by	syncytial trophoblast into the fluids of the mother.	Derived from weak androgen (DHEA) released from maternal & fetal adrenals cortex → transported by the blood to the placenta → converted by the trophoblast cells to estrogens	Derived from cholesterol → Secreted by syncytial trophoblast cells	The placenta around 5 th gestational week	Secreted by corpus luteum and placenta
Function	<ul style="list-style-type: none"> ✓ maintain corpus luteum (↑estrogen & progesterone) till 13-17 weeks of gestation ✓ Exerts interstitial (Leyding) cell-stimulating effect on testes resulting in the production of testosterone in male fetuses (growth of male sex organs) 	<ul style="list-style-type: none"> ✓ Enlargement of uterus, breast & external genitalia ✓ Relaxation of pelvic ligaments in preparation for labor ✓ Activation of the uterus (gap junctions) 	<ul style="list-style-type: none"> ✓ Provides nutrition to developing embryo (uterine secretory phase) ✓ Development of decidual cells ✓ Inhibits the contractility of the uterus 	<ul style="list-style-type: none"> ✓ Breast development ✓ Weak growth hormone's action ✓ Inhibits insulin sensitivity = ↓ glucose utilization ✓ Promotes release of fatty acids 	<ul style="list-style-type: none"> ✓ Relaxation of symphysis pubic ligament (weak) ✓ Softens the cervix at delivery

1. Also used for monitoring of pregnancy (pregnancy test)

- iii. Recognize the placenta as an endocrine organ
- iv. Describe the physiological functions of placental hormones

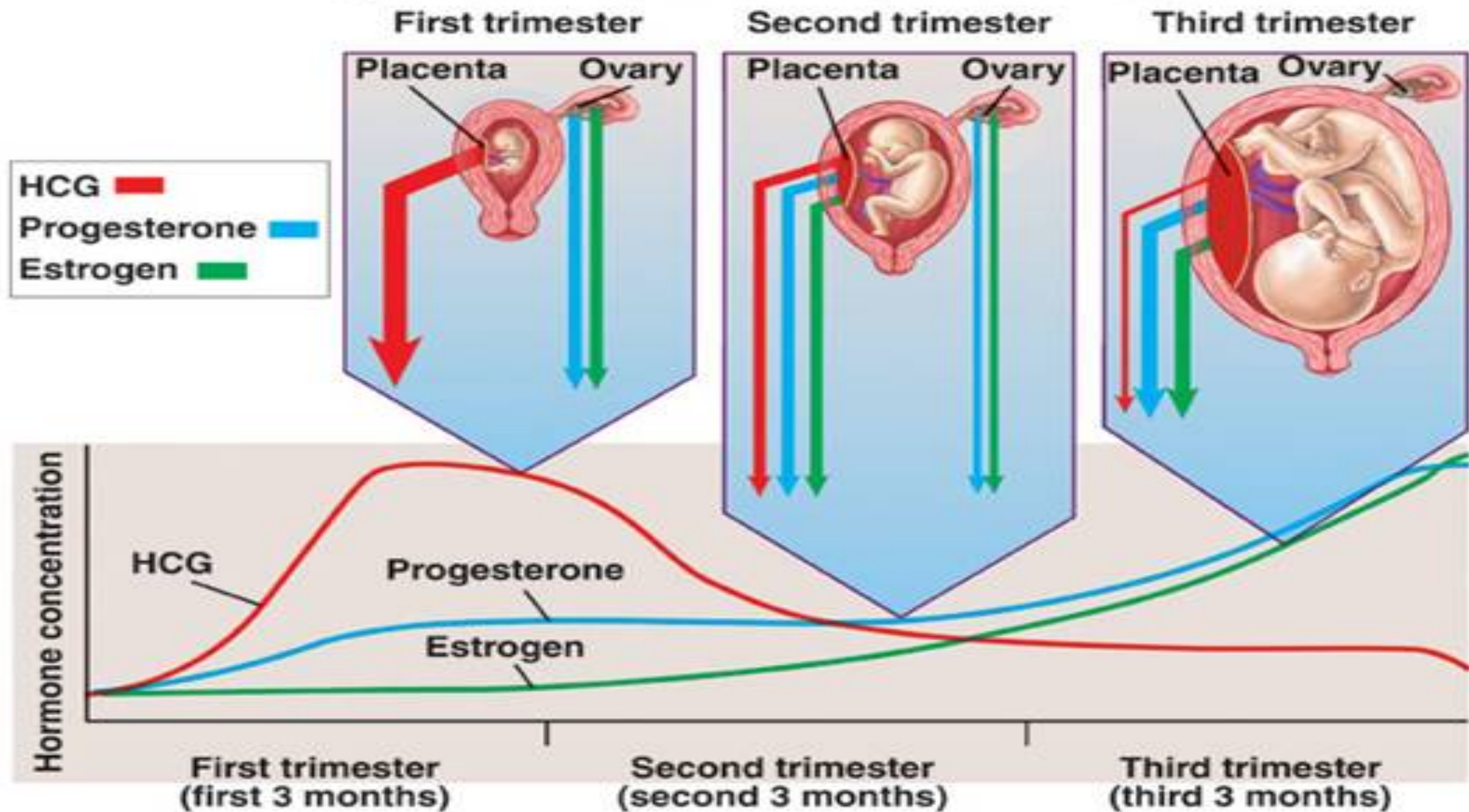


Figure 6- 3 Rates of secretion of estrogens and progesterone, and concentration of human chorionic gonadotropin at different stages of pregnancy.



v. Explain the mother's physiological response to pregnancy

Changes in maternal endocrine system

- Anterior pituitary gland enlargement (50%)
 - Release of ACTH, TSH and PL
 - FSH and LH almost totally suppressed
- Adrenal gland → Increase glucocorticoids secretion (mobilize Amino Acids) & aldosterone (retain fluid)
- Thyroid gland enlargement (50%) → Increase thyroxine production (hCG)
- Parathyroid gland enlargement → Increase PTH secretion (maintain normal Ca^{+2})

Changes in different organs

- Increase in uterine size (50 gm to 1100 gm)
- The breasts double in size
- The vagina enlarges
- Development of edema and acne (due to estrogen)

- Masculine or acromegalic features
- Weight gain 10-12 kg (last 2 trimesters)
 - Increase appetite
 - ✓ Removal of food by fetus
 - ✓ Hormonal effect

Metabolism and kidney function during pregnancy

- Increase basal metabolic rate (15%)
- Increase in daily requirements for (Iron, Phosphates, Calcium and Vitamins - vitamin D (Ca^{+2} absorption)
- The renal tubules' reabsorptive capacity for sodium, chloride, 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 of extra water and salt.



v. Explain the mother's physiological response to pregnancy

Changes in circulatory system

- Increase in Cardiac Output (30-40%) by 27th weeks
- Increase in blood flow through the placenta
- Increase in maternal blood volume (30%) due to
 - Increase aldosterone and estrogen (\uparrow ECF)
 - Increase activity of the bone marrow (\uparrow RBCs)

Changes in respiration

- Increase in O_2 consumption (20%)
 - Increase BMR
 - Increase in body size
- Increase in respiratory rate (RR)
- Progesterone \uparrow sensitivity of RC to CO_2
- Increase in minute ventilation by 50% and a decrease in arterial PCO_2 to several millimeters

Summary

F. Pregnancy (Figure 7-20)

- is characterized by steadily increasing levels of estrogen and progesterone, which maintain the endometrium for the fetus, suppress ovarian follicular function (by inhibiting FSH and LH secretion), and stimulate development of the breasts.

1. Fertilization

- If **fertilization** occurs, the corpus luteum is rescued from regression by **human chorionic gonadotropin (HCG)**, which is produced by the placenta.

2. First trimester

- The corpus luteum (stimulated by **HCG**) is responsible for the production of estradiol and progesterone.
- Peak levels of HCG occur at gestational week 9 and then decline.

3. Second and third trimesters

- **Progesterone** is produced by the placenta.
- **Estrogens** are produced by the interplay of the **fetal adrenal gland** and the placenta. The fetal adrenal gland synthesizes dehydroepiandrosterone-sulfate (DHEA-S), which is then hydroxylated in the fetal liver. These intermediates are transferred to the placenta,

Summary

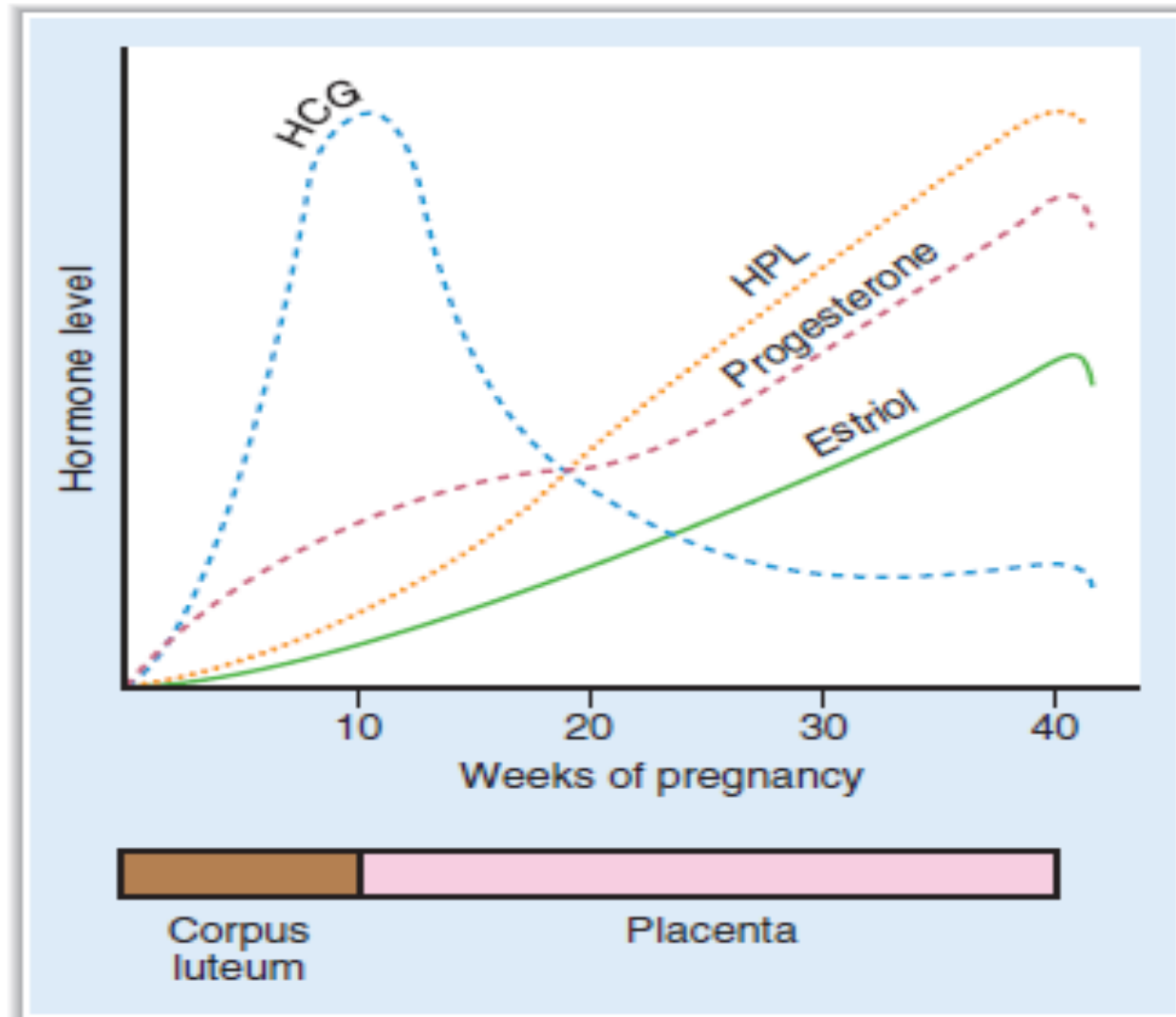


FIGURE 7-20 Hormone levels during pregnancy. HCG = human chorionic gonadotropin; HPL = human placental lactogen.

where enzymes remove sulfate and aromatize to estrogens. **The major placental estrogen is estriol.**

- **Human placental lactogen** is produced throughout pregnancy. Its actions are similar to those of growth hormone and prolactin.

4. Parturition

- Throughout pregnancy, progesterone increases the threshold for uterine contraction.
- Near term, the estrogen/progesterone ratio increases, which makes the uterus more sensitive to contractile stimuli.
- **The initiating event in parturition is unknown.** (Although oxytocin is a powerful stimulant of uterine contractions, blood levels of oxytocin do not change before labor.)

MCOQs

1) The ZP3 receptors located in ?

- A. Corona radiata .
- B. Zona pellucida .
- C. Ovum cytoplasm

2) When the sperm bind to Cortical granules it will star release ?

- A. Ca^{+2}
- B. Na^{+}
- C. K^{+}

3) How long take the travelling of the Zygote from ampulla to uterus ?

- A. 1 Day.
- B. 3-5 Days.
- C. 4-d Days.

4) When the fetal heart starts to pump the blood into the capillaries ?

- A. 19 Days after fertilization .
- B. 21 Days after implantation .
- C. 21 Days after fertilization.

5) Which of the following factor facilitate delivery of oxygen to the fetal tissues?

- A. High fetus haemoglobin (HbF)
- B. Mother $pO_2 >$ fetus pO_2 .
- C. A & B .

6) Where we can find more PCO_2 ?

- A. In placenta .
- B. In maternal blood.
- C. In both the same.

7) The Functions of Human placental lactogen (hPL) ?

- A. Provides nutrition to developing embryo
- B. Inhibits insulin sensitivity .
- C. Maintain corpus luteum .

8) Why maternal blood volume increase ?

- A. Increase aldosterone and estrogen (\uparrow ECF)
- B. Increase activity of the bone marrow (\uparrow RBCs)
- C. A & B

1	2	3	4	5	6	7	8
B	A	B	C	C	A	B	C



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