



*Physiology Team 431*  
*Reproductive Block*

*Lecture 6*  
*Physiology of pregnancy*

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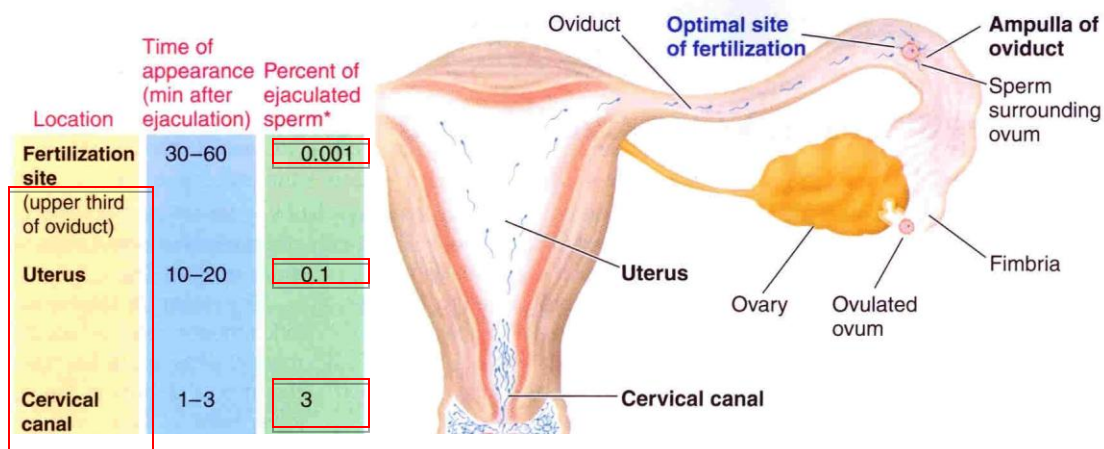
# Physiology of pregnancy

Red=important  
 Pink= female doctor's notes  
 Green=males  
 Blue=extra information

## Objectives:

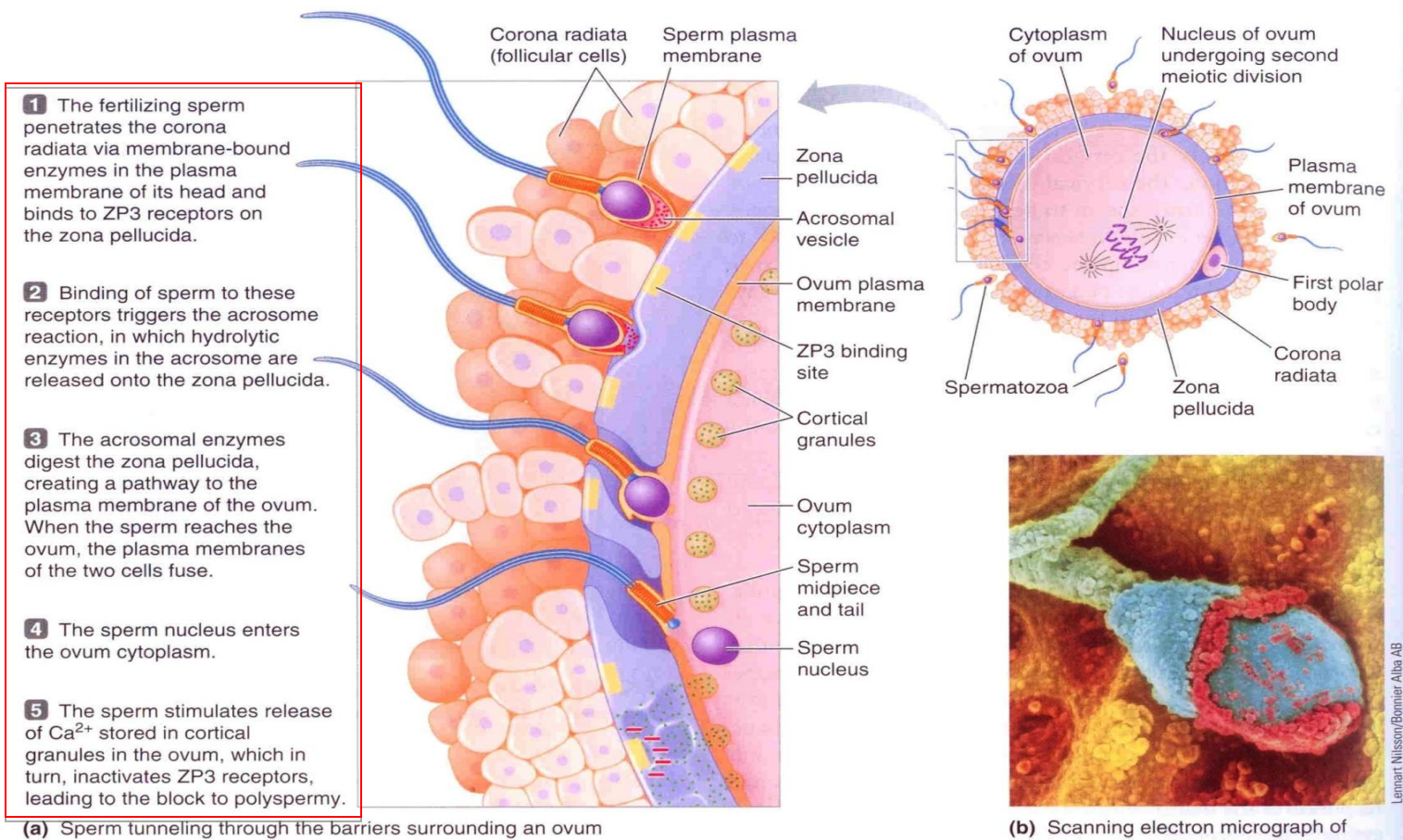
- Fertilization
- Development and function of the placenta
- Placenta as an endocrine organ
- Physiological functions of placental hormones
- Maternal adaptation to pregnancy

## ❖ Fertilization:



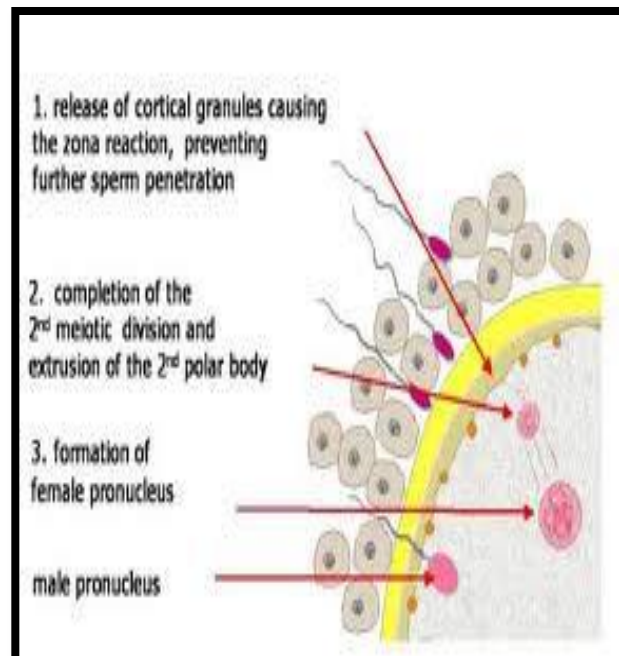
After entering of sperm in cervix, the cervix produces secretions that filter immature and immotile sperms. Only 3% pass and reach the cervical canal out of 200-300 million sperms per ejaculation. So in order for fertilization to happen, at least 20 million sperms must enter per ejaculation.





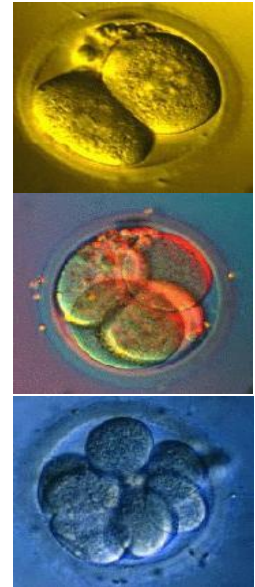
● **FIGURE 20-25 Process of fertilization.**

- After ejaculation sperms reach ampulla of fallopian tube within 30-60 min (uterine contractions)
- Sperm penetrate corona radiata and zona pellucida (hyaluronidase)( the head's enzyme) (see picture "a" for details)
- Oocyte divides to form **mature ovum** (female pronucleus **23 unpaired** chromosomes) + **2<sup>nd</sup> polar body** → by **2<sup>nd</sup> meiotic** division
- Head of sperm swells (male pronucleus **23 unpaired** chromosomes)
- Fertilized ovum (zygote) contain **23 paired** chromosomes = **46 chromosomes**



## ❖ Zygote cleavage:

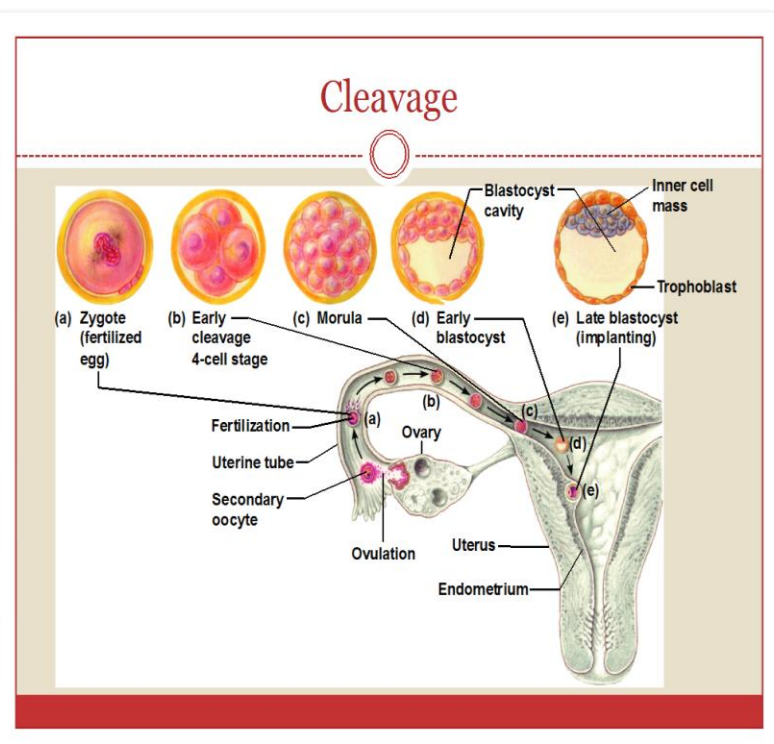
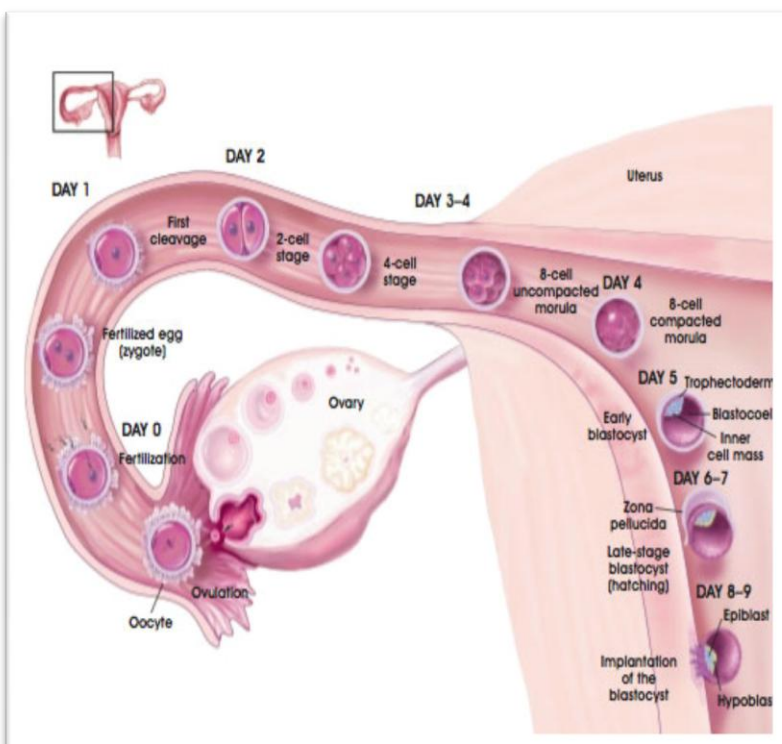
- Following fertilization the zygote undergoes several **mitotic** divisions inside the zona pellucida (overall **size does not change**).
- 1<sup>st</sup> cleavage yields a 2 celled embryo, (Each cell is called a blastomere and is **totipotent\***)
- Divisions continue rapidly **until the 32 cell stage**



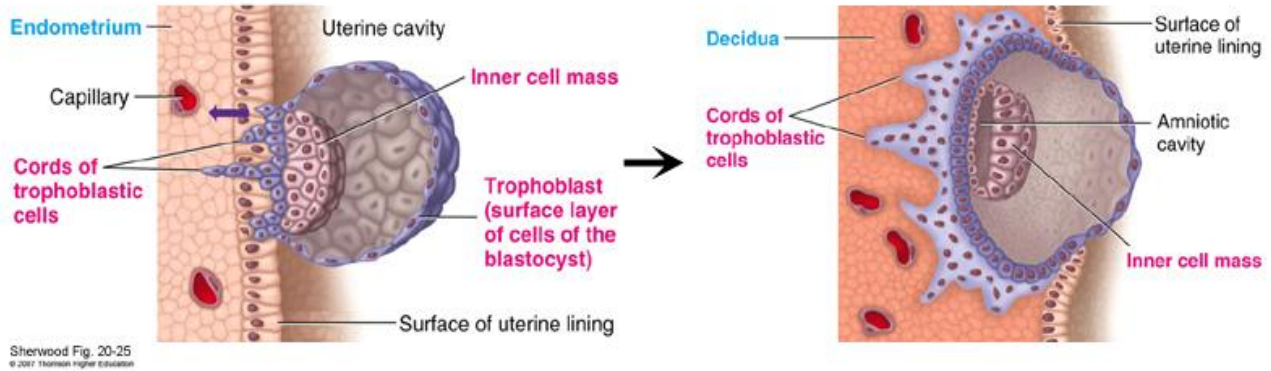
\*totipotent: a stem cell that can produce all types of differentiated cells, including extra-embryonic tissues

## ❖ Traveling (transport of fertilized ovum):

- Zygote begins to divide as it travels through oviduct
- After fertilization **3-5 days** till zygote reach uterine cavity
- Transport: fluid current + action of cilia + weak contractions of the fallopian tube
- Isthmus (last 2cm) **relaxes under effect of progesterone** (to allow passage of morula to uterine cavity) **before 3<sup>rd</sup> day it is narrow**
- Delayed transport allows cell division
- **Blastocyst (100 cells)** enters the uterus (**blastocyst's cavity enlarges until the cells form a plate**)
- Implants into lining of uterus







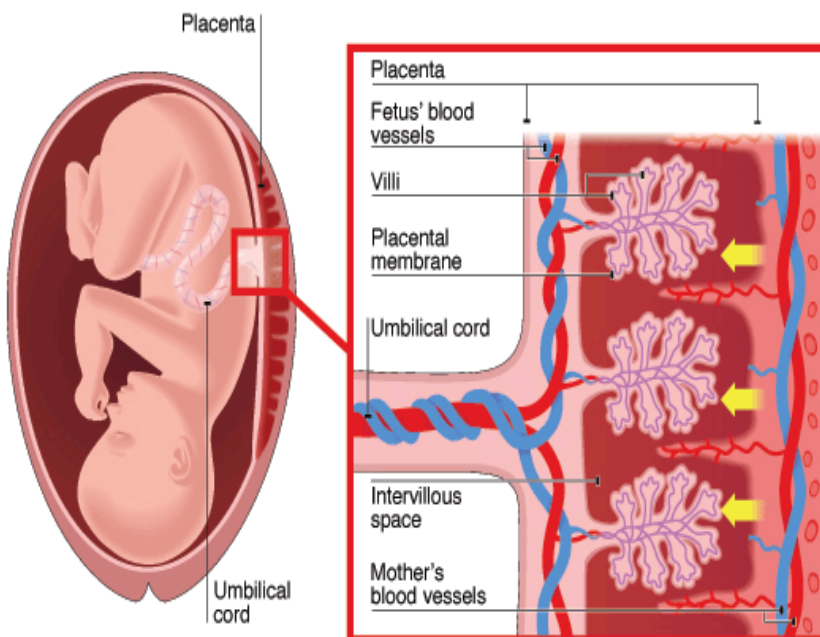
Implantation needs prepared uterine endometrium by hormones (e.g progesterone from corpus luteum).

After implantation the blastocyst sends primary trophoblastic cords (chorionic villi). Then the blastocyst enters deep inside the endometrial lining and is covered. Later it projects again and forms the fetus.

More and more cells called cytotrophoblasts and other cells fuse together to form what looks like one cell with many nuclei (syncytiotrophoblast= syncytium)

### ❖ placenta:

- Trophoblastic cords from blastocyst
- Blood capillaries grow in the cords
- **21 days after fertilization blood** start to be pumped by fetal heart into the capillaries
- Maternal blood sinuses develop around the trophoblastic cords (to facilitate material transport)
- More and more trophoblast projections develop (placental villi)



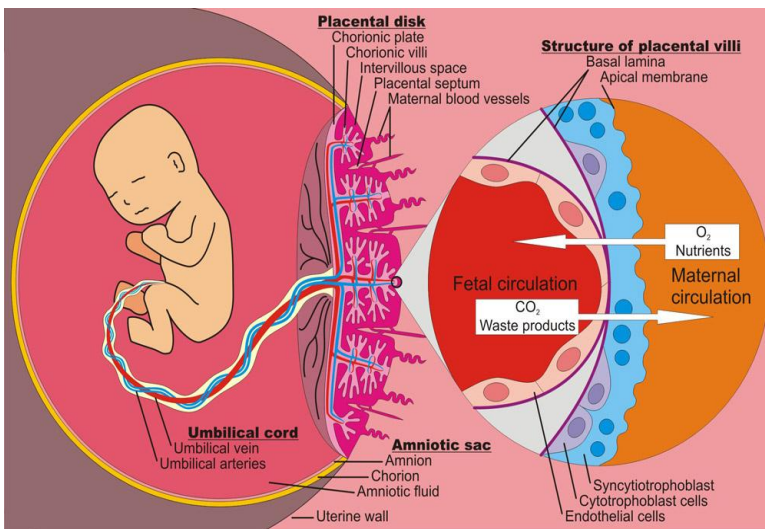
Primary, secondary and tertiary villi are surrounded by maternal blood. The mother's artery will be eroded and start delivering blood in intervillous spaces.

In the umbilical cord, the arteries (in blue) carry CO<sub>2</sub> and waste products from fetus to mother while the vein (in red) carries O<sub>2</sub> and nutrients from mother's blood to fetus. (The opposite of normal blood circulation)

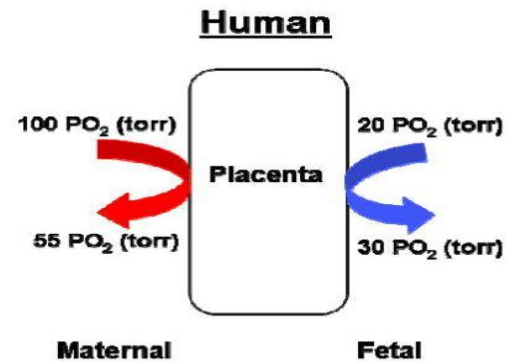
○ Functions of placenta:

- Major function:
  - Respiration
  - Nutrition
  - Excretion
- Endocrine
- Protection

❖ Respiration:



The wall of the villi is very thin to allow diffusion of O<sub>2</sub> and CO<sub>2</sub>



- PCO<sub>2</sub> is 2-3 mm Hg **higher in fetal** than maternal blood (because the fetus can't breathe from his lungs so he can't get rid of CO<sub>2</sub>)
  - Dissolved O<sub>2</sub> in mother's blood passes to fetal blood by **simple diffusion**  
 PO<sub>2</sub> 50 mm Hg (M) - 30 mm Hg (F) = 20 mmHg → (PO<sub>2</sub> = 100 mm Hg once it leaves the mother's heart then declines to 50-55 when it reaches the placenta)
    - At low PO<sub>2</sub> = 50, HbF carry 20-50% more O<sub>2</sub> than HbA (HbF has a **higher oxygen carrying capacity** than HbA)
    - HbF **concentration is 50% higher** than HbA in mother
- Remember: HgF is the main hemoglobin in Fetus and HgA is the main hemoglobin in Adult

## ❖ Continue respiration:

### ○ Double Bohr effect

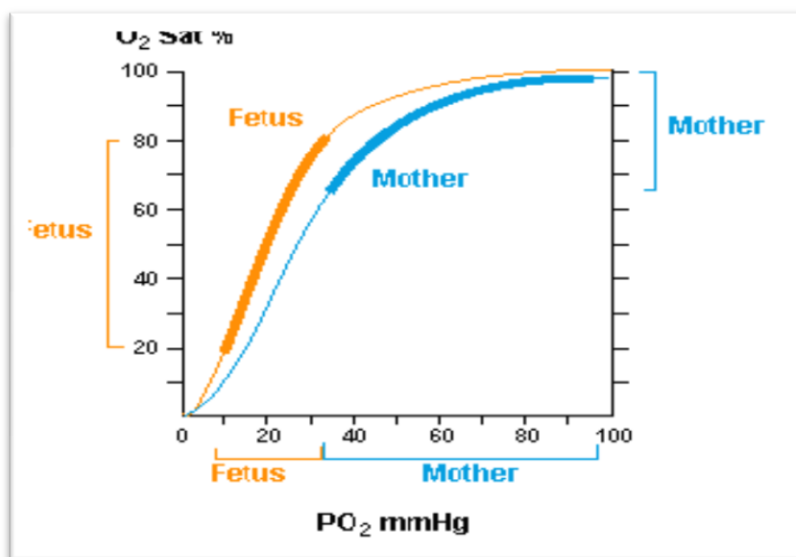
Low pH in mother's blood (acidic) (due to CO<sub>2</sub> from fetus)

High pH in fetal blood (alkaline) (loss of CO<sub>2</sub>)

} This is only in placenta only (outside the fetus)

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

- The **maternal blood** gains CO<sub>2</sub>, the pH falls and the **curve shifts to the right** releasing additional oxygen.
- On the **fetal side** of the placenta CO<sub>2</sub> is lost, the pH rises and the **curve shifts to the left** allowing additional **oxygen uptake**.



{ This curve shows that at low PO<sub>2</sub> the affinity to O<sub>2</sub> is higher in fetus }

## Important factors facilitate delivery of oxygen to the fetal tissues:

- High maternal intervillous blood flow (almost double the fetal placental flow) (which cause hypotension)
- High fetal haemoglobin (16 - 17 g/dl) (Hb of mother is (11-12 g/dl))
- High fetal cardiac output (his HR= 120-160 while the mother's= 60-80)
- The **fetal metabolic acidosis** which shifts the curve to the right and thus aids delivery of oxygen to the tissues. (inside the fetus (near tissues))

## ❖ Nutrition:

- Fetus uses mainly glucose for nutrition so the trophoblast cells in placental villi transport **glucose by carrier molecules; GLUT (facilitated diffusion)**
- **Fatty acids diffuse** due to high solubility in cell membrane (**more slowly** than glucose)
- The placenta **actively transports** all **amino acids**, with fetal concentrations exceeding maternal levels. (**amino acids are important for the rapid growth of tissue**)
- K<sup>+</sup>, Na<sup>+</sup> and Cl<sup>-</sup> diffuses from maternal to fetal blood
- **Epithelial cells at the lining of endometrium transform into desidual cells which contain lots of nutrients until the development of placenta**

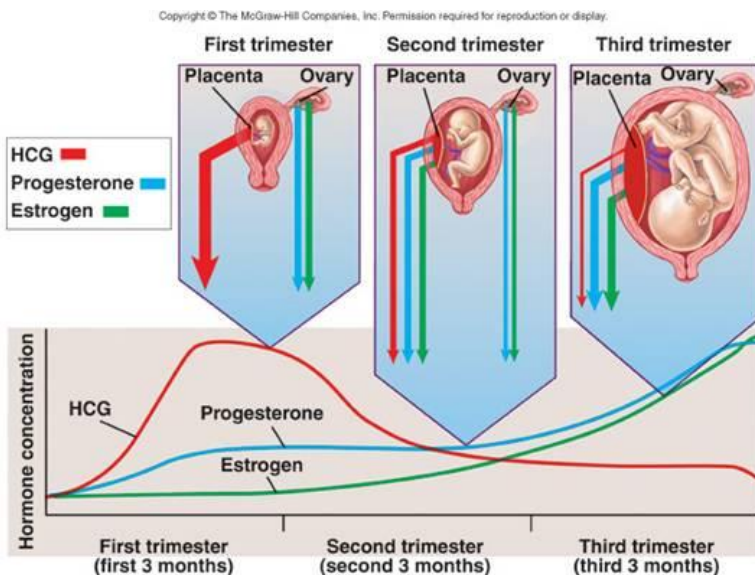
## ❖ Excretion:

Excretory products of the fetus diffuse through placental membrane to maternal blood to be excreted with waste products of the mother

Urea, uric acid and creatinine

Higher conc. Of excretory products in fetal blood insures continuous diffusion of these substances to the maternal blood

## ❖ Endocrine:



- Human Chorionic Gonadotropin (hCG)  
Glycoprotein  
**Most important function is to maintain corpus luteum (↑ estrogen & progesterone) till 13-17 weeks of gestation**  
Exerts interstitial (**Leydig**) **cell-stimulating** effect on testes of the male fetus (growth of male sex organs) (**produce testosterone**)  
**HCG is used in pregnancy detecting tests.**

### 1<sup>st</sup> trimester:

- HCG is high, that could be the reason of nausea and vomiting.
- Estrogen and progesterone are produced from corpus luteum.

### 2<sup>nd</sup> trimester:

- HCG levels decrease. Estrogen and progesterone are mainly released from syncytiotrophoblasts and still released from corpus luteum.

### 3<sup>rd</sup> trimester:

the placenta secretes tiny amount of HCG and mainly estrogen and progesterone (their highest levels), once progesterone decreases labor starts.



- Estrogen

Steroid hormone

Secreted by syncytial trophoblast cells

Towards end of pregnancy reaches 30×

Derived from weak androgen (DHEA) released from maternal & fetal adrenals

- Functions in the mother

Enlargement of uterus, breast & external genitalia

Relaxation of pelvic ligaments in preparation to labor

Activation of the uterus (gap junctions) (gap junctions are important for the spread of contraction)

- Progesterone

Steroid hormone

Secreted by syncytial trophoblast cells

Towards end of pregnancy reaches 10×

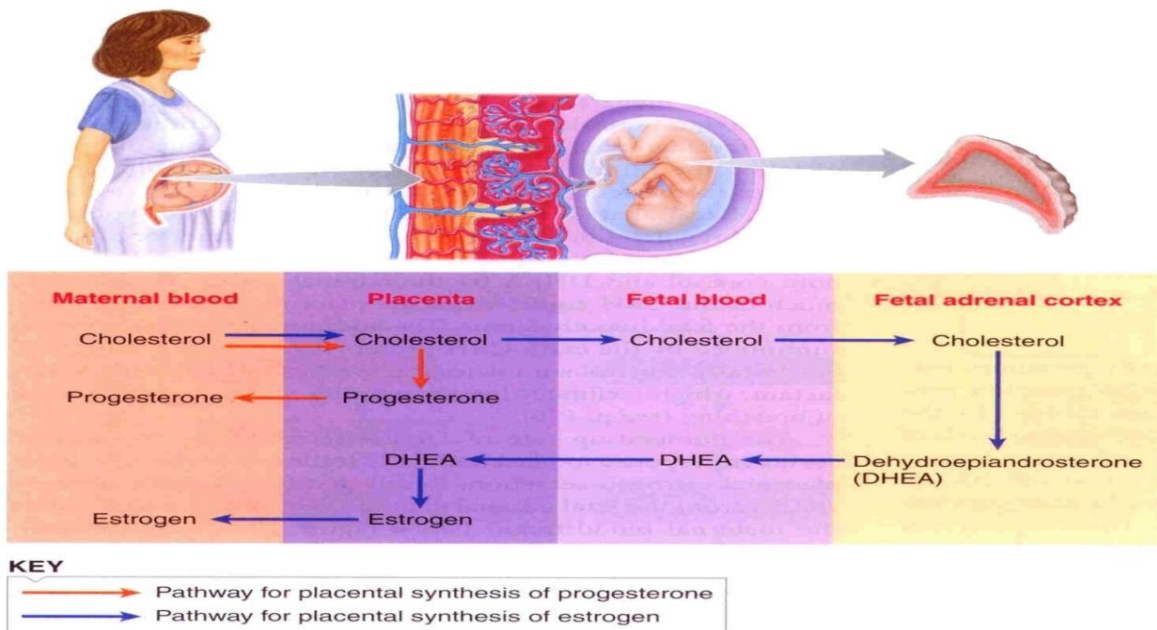
Derived directly from cholesterol

- Functions in the mother

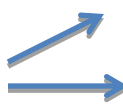
Provides nutrition to developing embryo

Development of decidual cells

Inhibit the contractility of the uterus



• **FIGURE 20-31 Secretion of estrogen and progesterone by the placenta.** The placenta secretes increasing quantities of progesterone and estrogen into the maternal blood after the first trimester. The placenta itself can convert cholesterol into progesterone (orange pathway) but lacks some of the enzymes necessary to convert cholesterol into estrogen. However, the placenta can convert DHEA derived from cholesterol in the fetal adrenal cortex into estrogen when DHEA reaches the placenta by means of the fetal blood (blue pathway).

- Human Chorionic Somatomamotropin 
    - Protein hormone
    - Secreted by placenta around 5<sup>th</sup> gestational week
    - Functions in the mother
      - Breast development (hPL) = human placental lactogen (similar to prolactin)
      - Weak growth hormone action
      - Inhibit insulin sensitivity = ↓ glucose utilization
      - Promote release of fatty acids
- Somato= body ( growth hormone)  
Mamo= affecting mammary glands
- } GH actions

- Relaxin
    - Polypeptide
    - Secreted by corpus luteum and placenta
    - Functions in the mother
      - Relaxation of symphysis pubic ligament (weak)
      - Softens the cervix at delivery (for dilatation)
- } To allow fetus delivery

### ❖ Physiological adaptation to pregnancy:

#### Changes in maternal endocrine system:

- Anterior pituitary gland enlargement (50%)
  - Release of ACTH, TSH and PL increase
  - FSH and LH almost totally suppressed (because of the negative feedback from estrogen & progesterone)
- Adrenal gland
  - Increase glucocorticoids secretion (mobilize aa)
  - Increase aldosterone (retain fluid)
- Thyroid gland enlargement (50%)
  - Increase thyroxine production (hCG) (physiological goiter sometimes)
- Parathyroid gland enlargement
  - Increase PTH secretion (maintain normal Ca<sup>+2</sup>) (by bone resorption, for the fetus)

### 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 and progesterone)
- Masculine or acromegalic features (GH)
- Weight gain 10-12 kg (last 2 trimesters)

Increase appetite

Removal of food by fetus

Hormonal effect

### Changes in metabolism:

- Increase basal metabolic rate (15%) (TH)
- Increase in daily requirements for
  - Iron
  - Phosphates
  - Calcium
  - Vitamins
    - Vitamin D (Ca<sup>+2</sup> absorption)

### Changes in circulatory system:

- Increase in COP( cardiac output) (30-40%) by 27 weeks (due to enlarged placenta and it's withdrawal of mother's blood)
- Increase in blood flow through the placenta
- Increase in maternal blood volume (30%) due to
  - Increase aldosterone and estrogen (↑ ECF)
  - Increase activity of the bone marrow (↑ RBCs)

Blood volume increase because of fluid retention and formation of RBCs but the fluid is relatively more than the RBCs so this cause physiological anemia

### Changes in respiration:

- Increase in O<sub>2</sub> consumption (20%)
  - Increase BMR
  - Increase in body size
- Growing uterus presses upwards (restriction of lungs)
- Increase in RR= respiratory rate
- Increase in minute ventilation(TV× RR) by 50% (TV=tidal volume)
  - Progesterone ↑ sensitivity of RC to CO<sub>2</sub> (RC=respiratory center)



# Questions

- 1-What is the receptor responsible for sperms in the oocyte?
  - a) Zp1
  - b) Zp2
  - c) Zp3
  - d) Spermceptor
  
- 2- at which days does the fertilized ovum reach the uterine cavity?
  - a) 1-3
  - b) 3-5
  - c) 6-7
  - d) 8-10
  
- 3- the pH of the fetal blood in placenta is?
  - a) high
  - b) low
  - c) Normal
  - d) Variable
  
- 4- hormone that is used to detect pregnancy?
  - a) GH
  - b) TH
  - c) HSG
  - d) HCG
  
- 5- amino acids are transported to fetus through which of the followings?
  - a) Gap junctions
  - b) Simple diffusion
  - c) Active transport
  - d) Passive transport

Answers: c,b,a,d,c