

Reproductive Physiology

Lecture 6

Physiology of Pregnancy



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Objectives



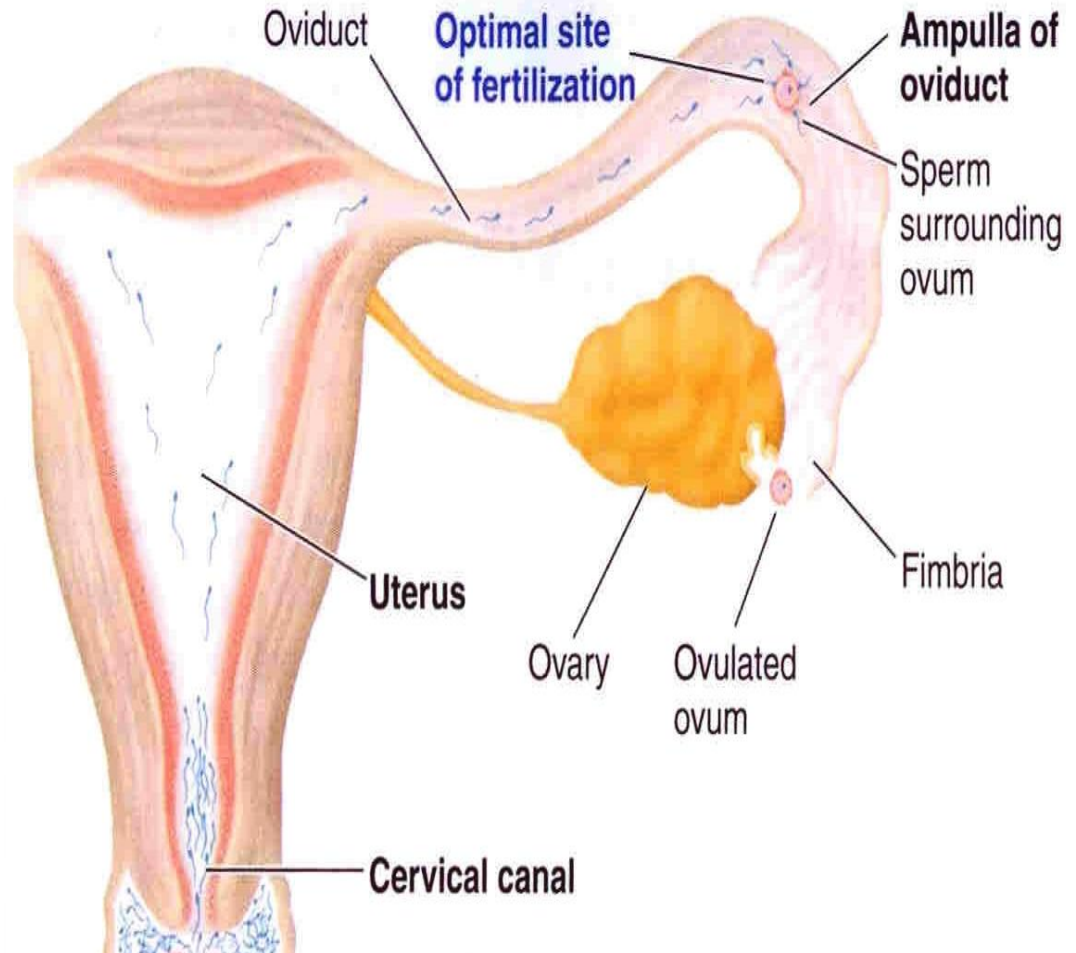
By the end of this lecture, you should be able to:

- Describe fertilization
- Recognize the development and the function of the placenta
- Recognize the placenta as an endocrine organ
- Describe the physiological functions of placental hormones
- Understand the maternal adaptation to pregnancy

Fertilization



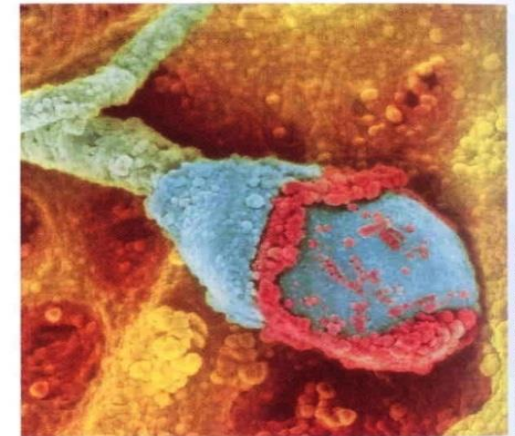
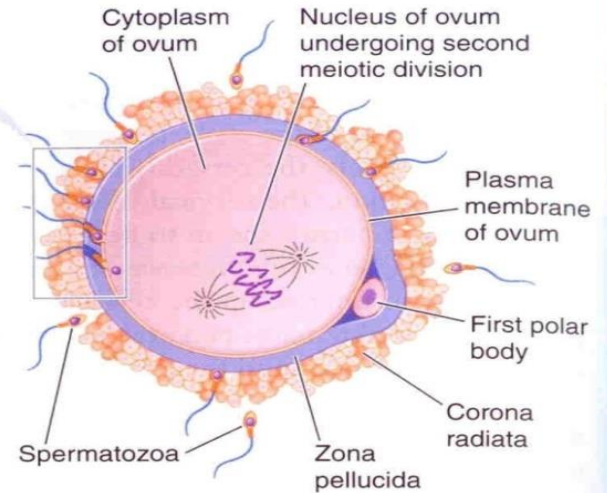
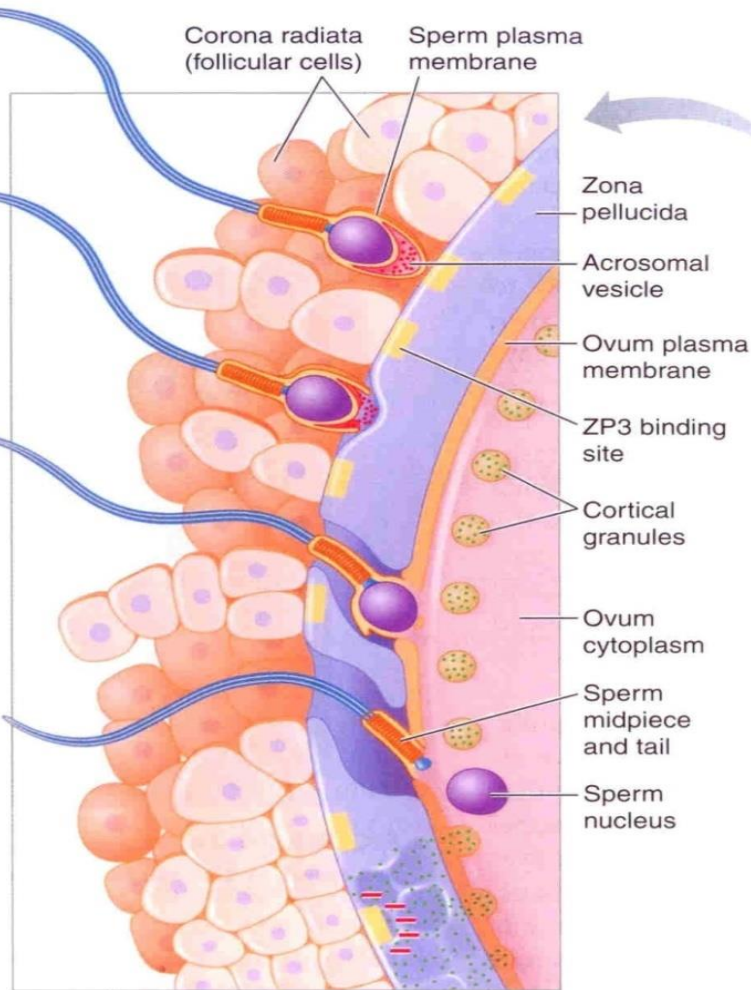
Location	Time of appearance (min after ejaculation)	Percent of ejaculated sperm*
Fertilization site (upper third of oviduct)	30-60	0.001
Uterus	10-20	0.1
Cervical canal	1-3	3



Fertilization



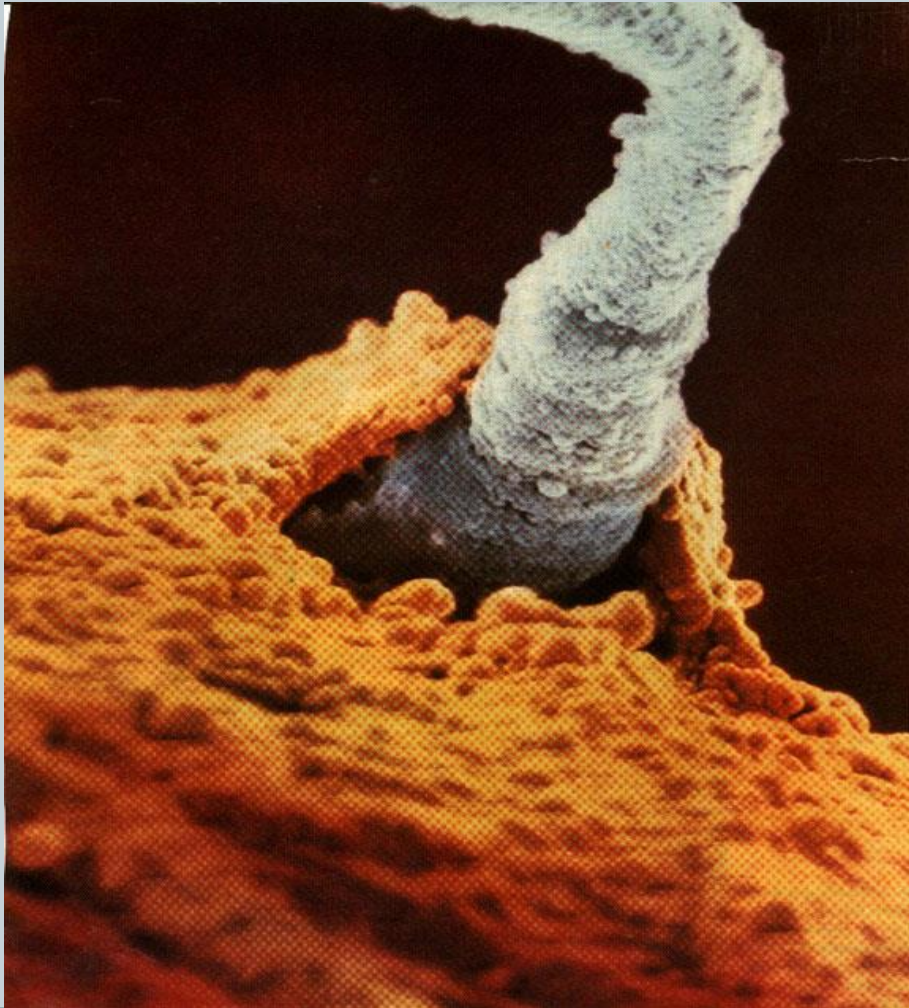
- 1** The fertilizing sperm penetrates the corona radiata via membrane-bound enzymes in the plasma membrane of its head and binds to ZP3 receptors on the zona pellucida.
- 2** Binding of sperm to these receptors triggers the acrosome reaction, in which hydrolytic enzymes in the acrosome are released 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.



(a) Sperm tunneling through the barriers surrounding an ovum

(b) Scanning electron micrograph of spermatozoon with acrosomal enzymes (in red) exposed after acrosomal reaction

Fertilization



Fertilization

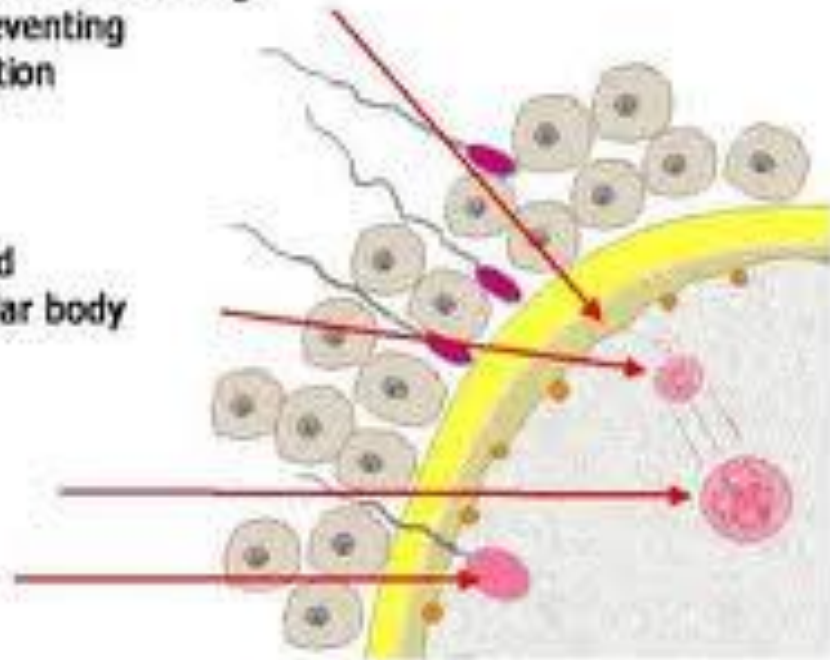


1. release of cortical granules causing the zona reaction, preventing further sperm penetration

2. completion of the 2nd meiotic division and extrusion of the 2nd polar body

3. formation of female pronucleus

male pronucleus



Fertilization

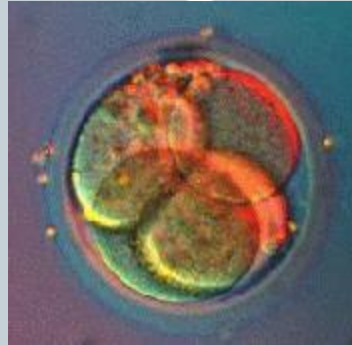


- After ejaculation, sperms reach **ampulla** of fallopian tube within 30-60 min
- Sperm penetrates *corona radiata* and *zona pellucida* (hyaluronidase)
- Oocyte divides to form **mature ovum** (female pronucleus 23 unpaired chr) + 2nd polar body
- Head of sperm swells (male pronucleus 23 unpaired chr)
- Fertilized ovum (zygote) contain 23 paired chr

Zygote



Cleavage

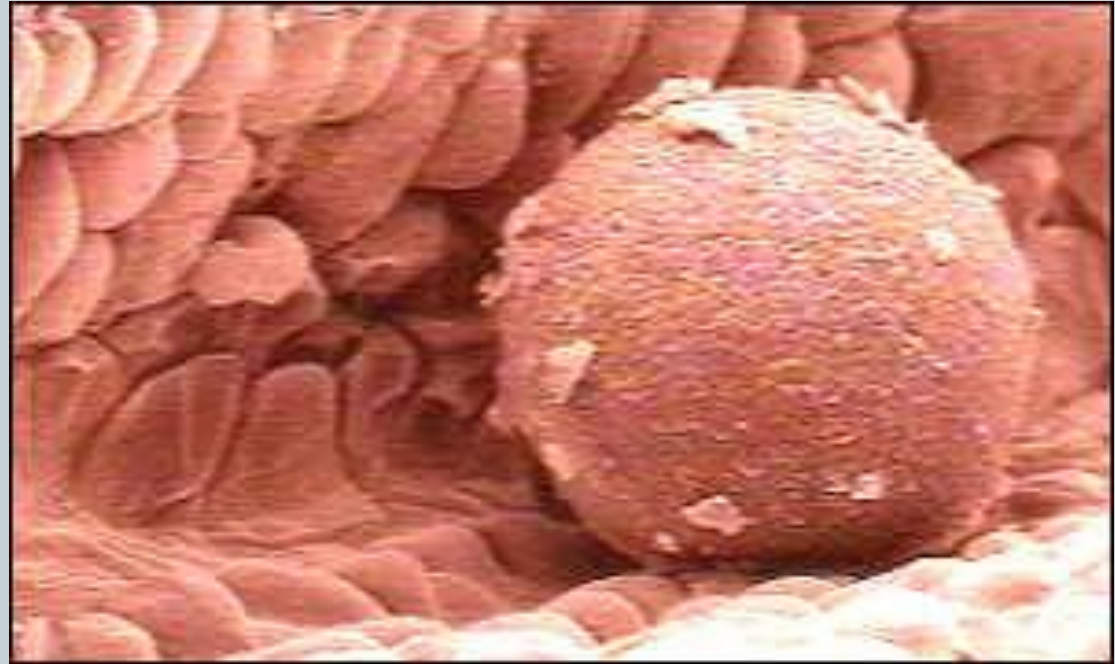


- Following fertilization, the zygote undergoes several mitotic divisions inside the zona pellucida (overall size does not change).
- 1st cleavage yields a 2 celled embryo,
 - each cell is called a **blastomere** and is *totipotent*
- Divisions continue rapidly until the 32 cell stage

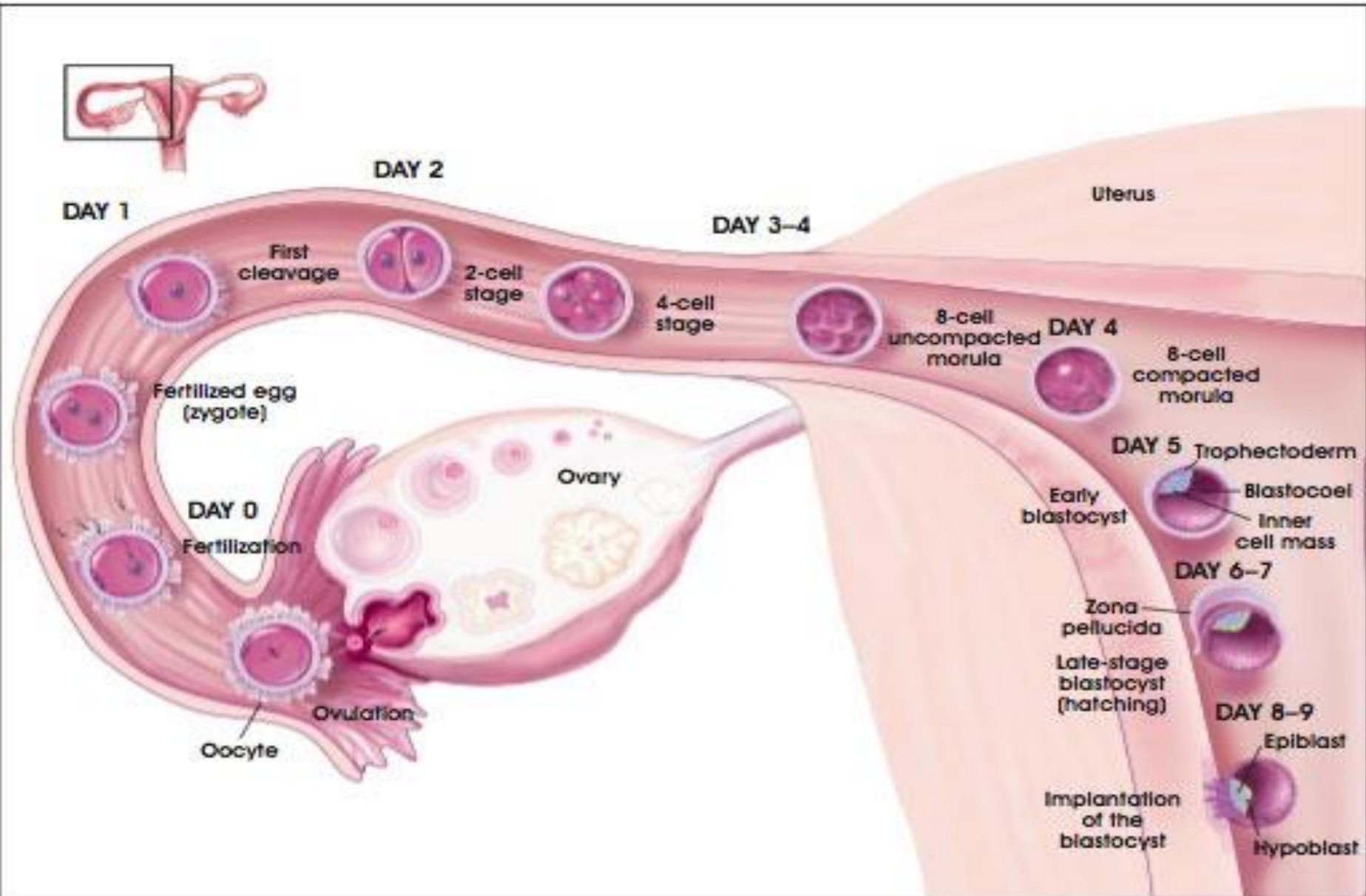
Traveling



- Zygote begins to divide as it travels through oviduct
- Implants into lining of uterus



Transport of fertilized ovum

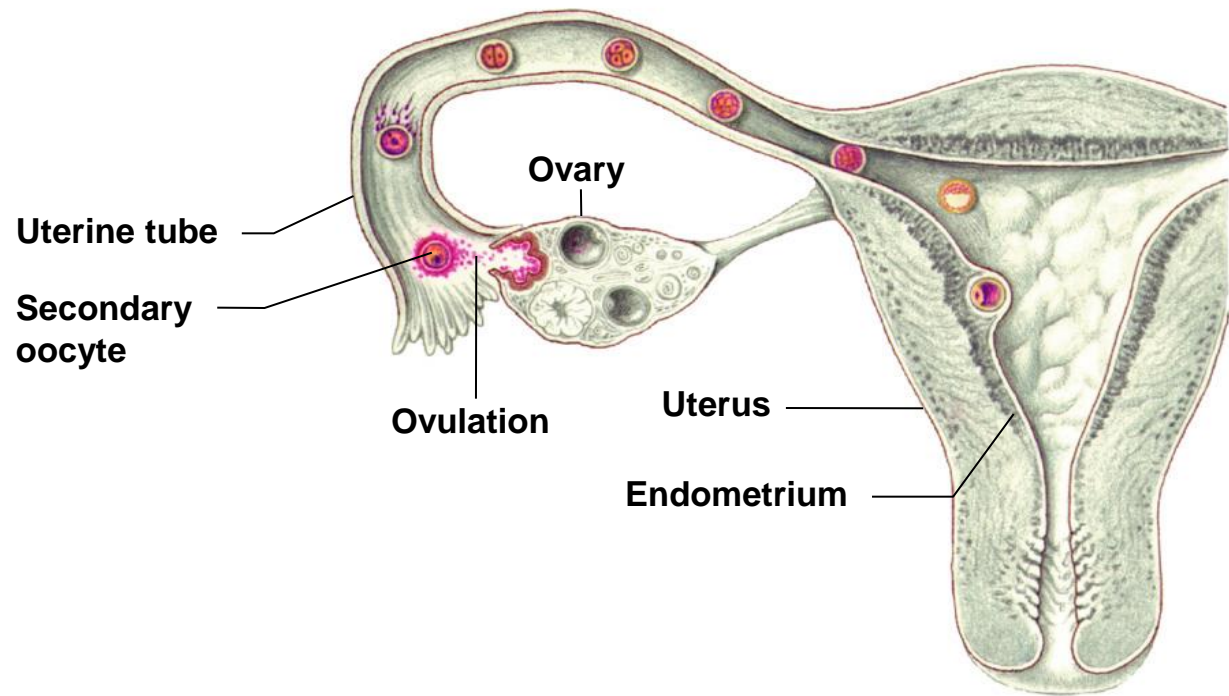


Transport of fertilized ovum



- 3-5 days after fertilization, the zygote reaches uterine cavity
- **Transport:** fluid current + action of cilia + weak contractions of the fallopian tube
- Isthmus (last 2cm) relaxes under effect of progesterone
- Delayed transport allows cell division
- Blastocyst (100 cells) enters the uterus

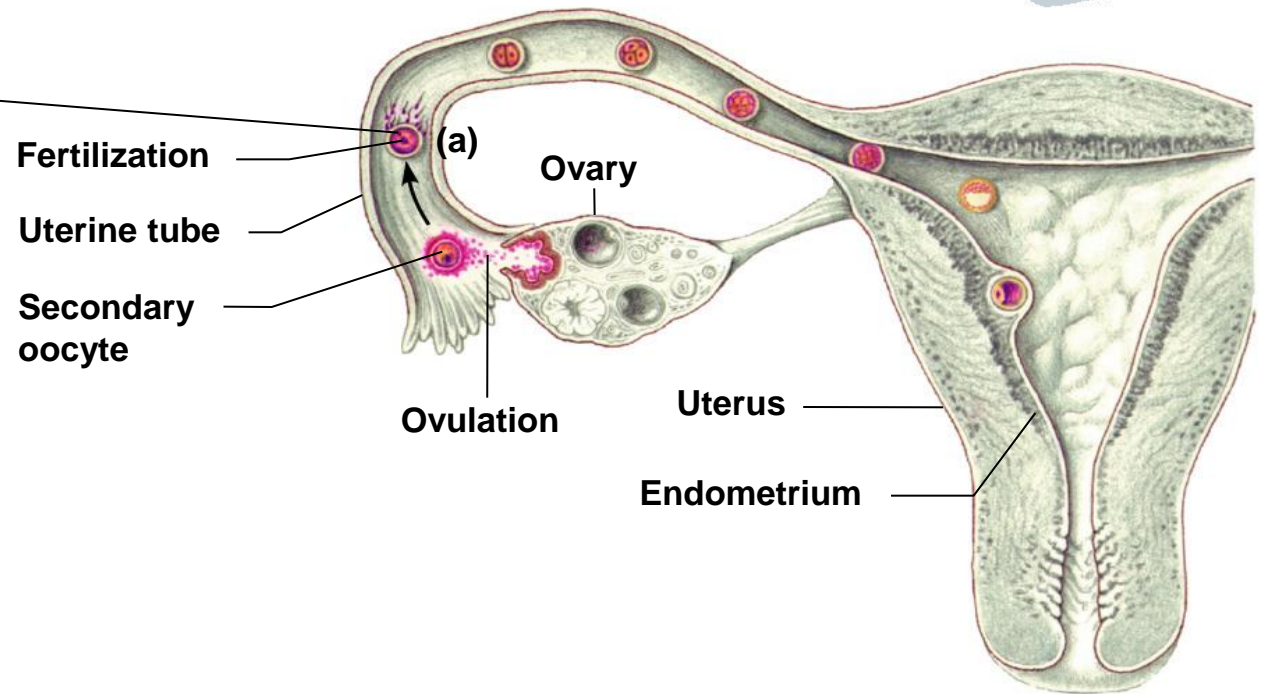
Cleavage



Cleavage



(a) Zygote
(fertilized
egg)



Cleavage



(a) Zygote
(fertilized
egg)



(b) Early
cleavage
4-cell stage

Fertilization

Uterine tube

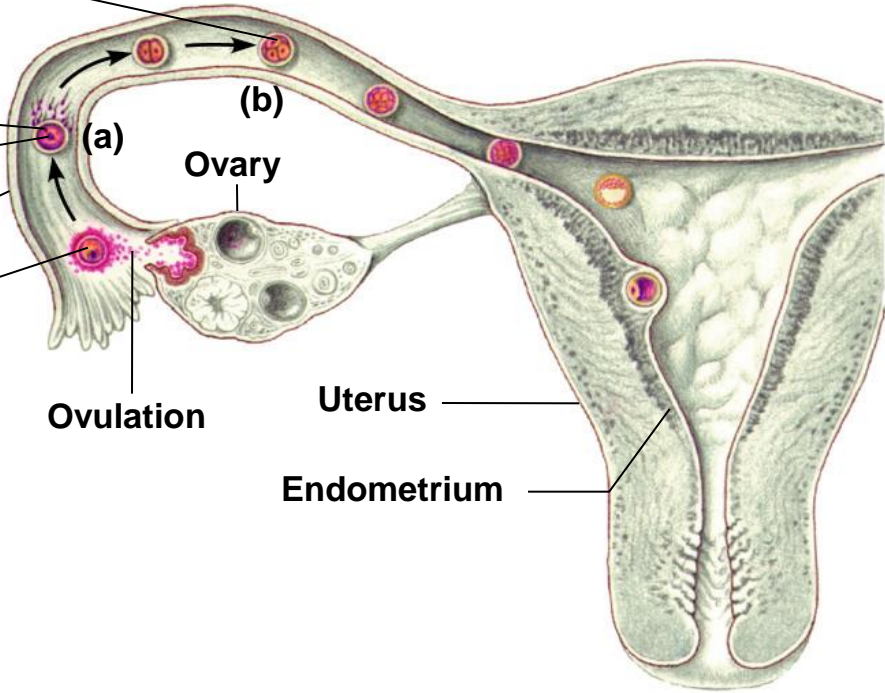
Secondary
oocyte

Ovulation

Ovary

Uterus

Endometrium



Cleavage



(a) Zygote
(fertilized
egg)



(b) Early
cleavage
4-cell stage



(c) Morula

Fertilization

Uterine tube

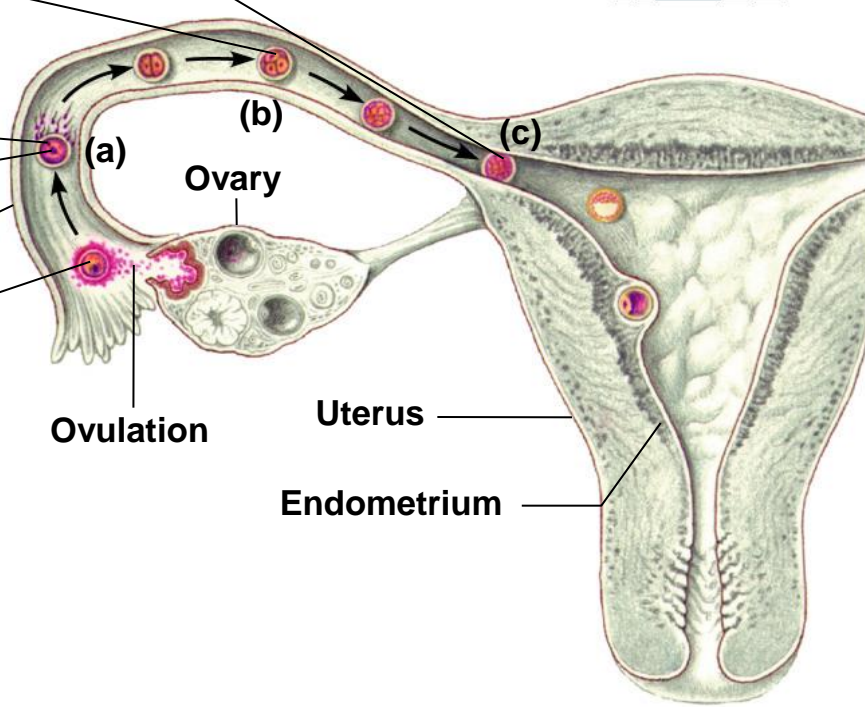
Secondary
oocyte

Ovulation

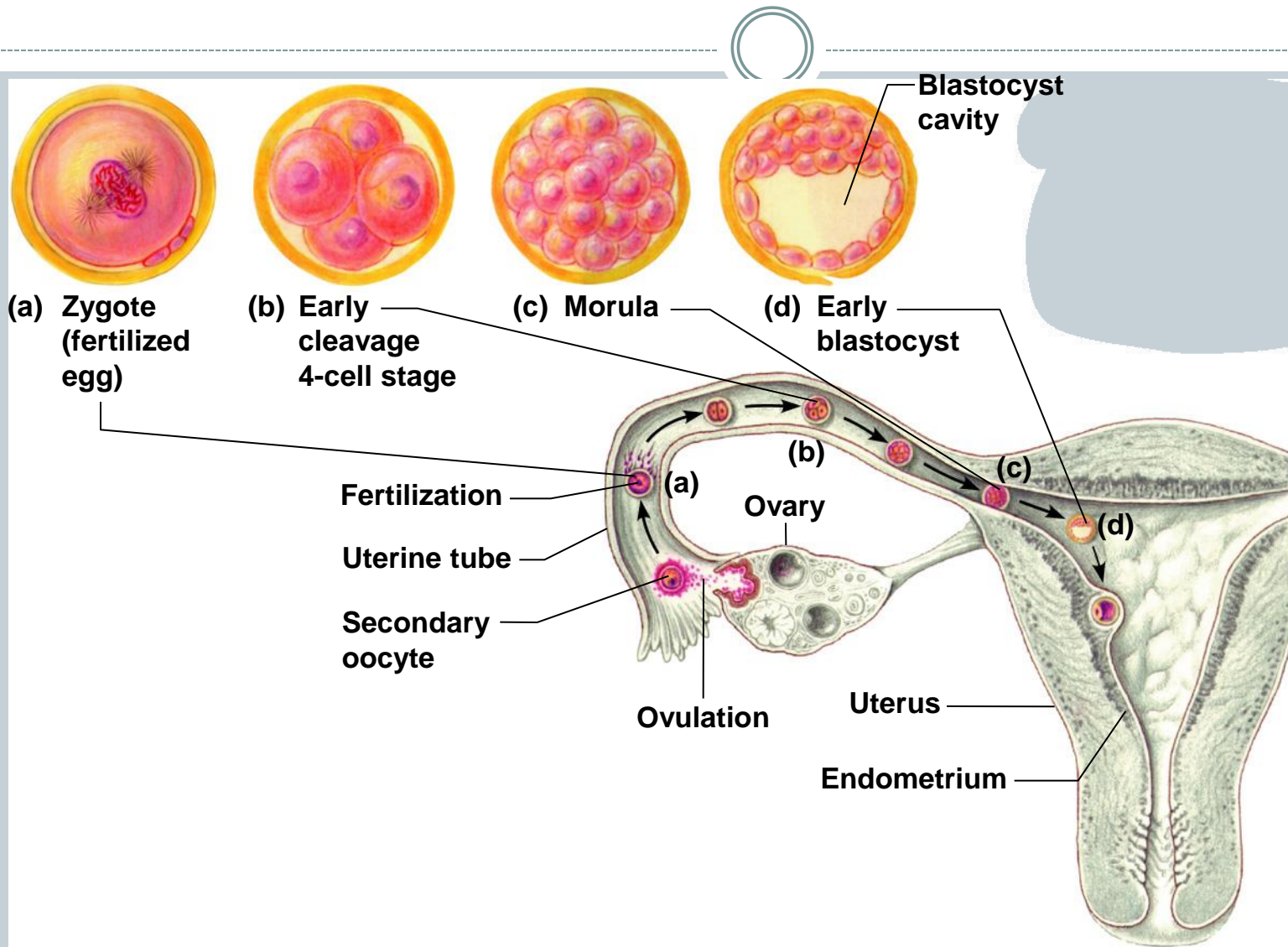
Ovary

Uterus

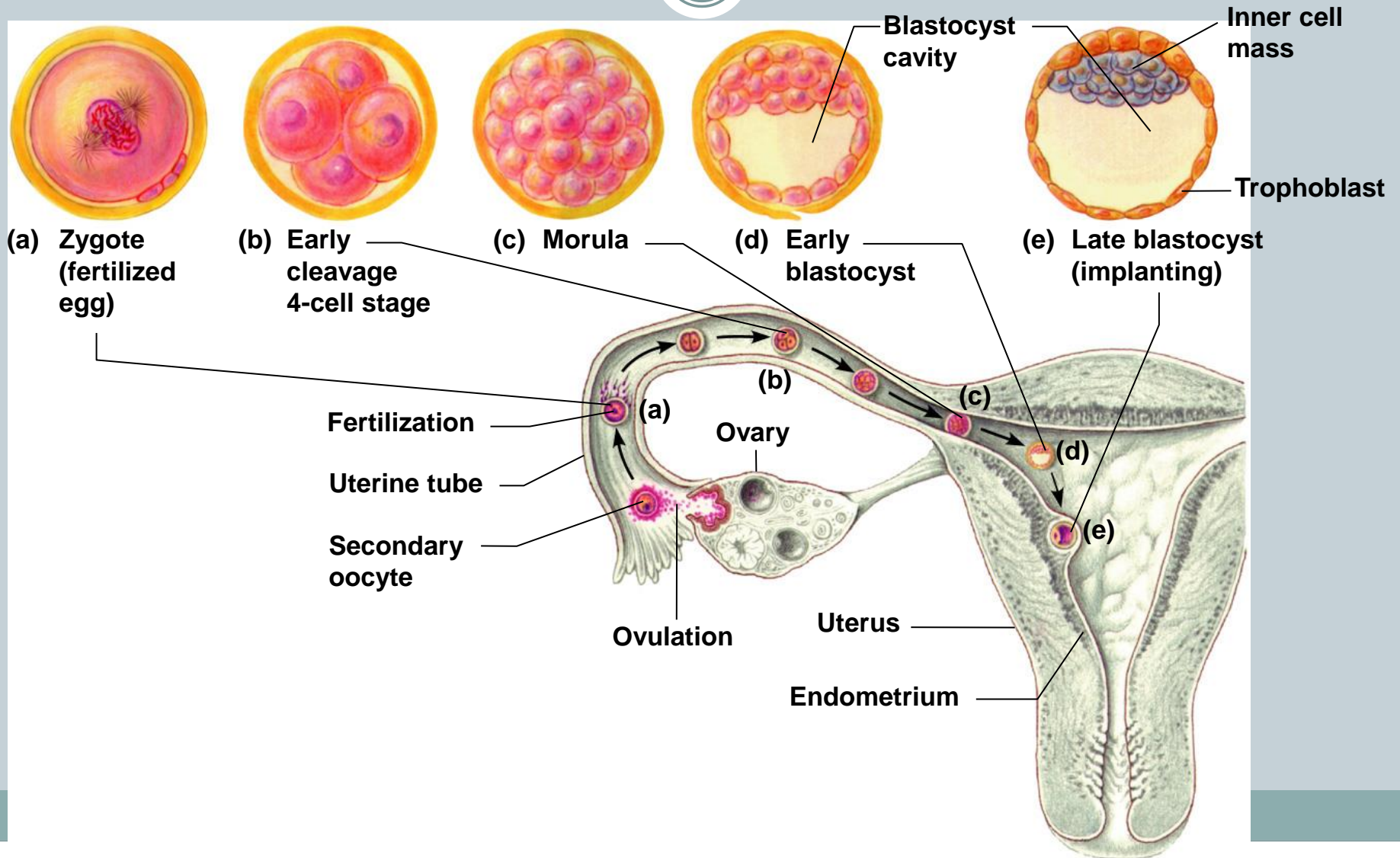
Endometrium



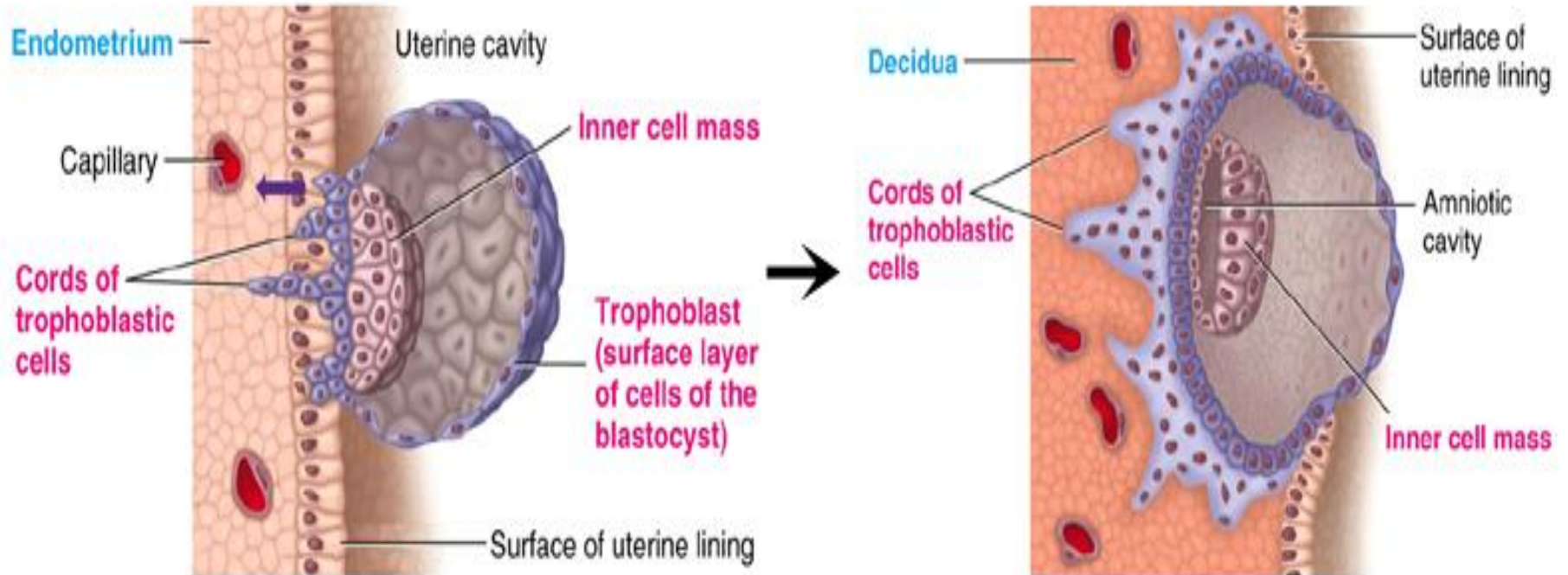
Cleavage



Cleavage



Implantation



Implantation

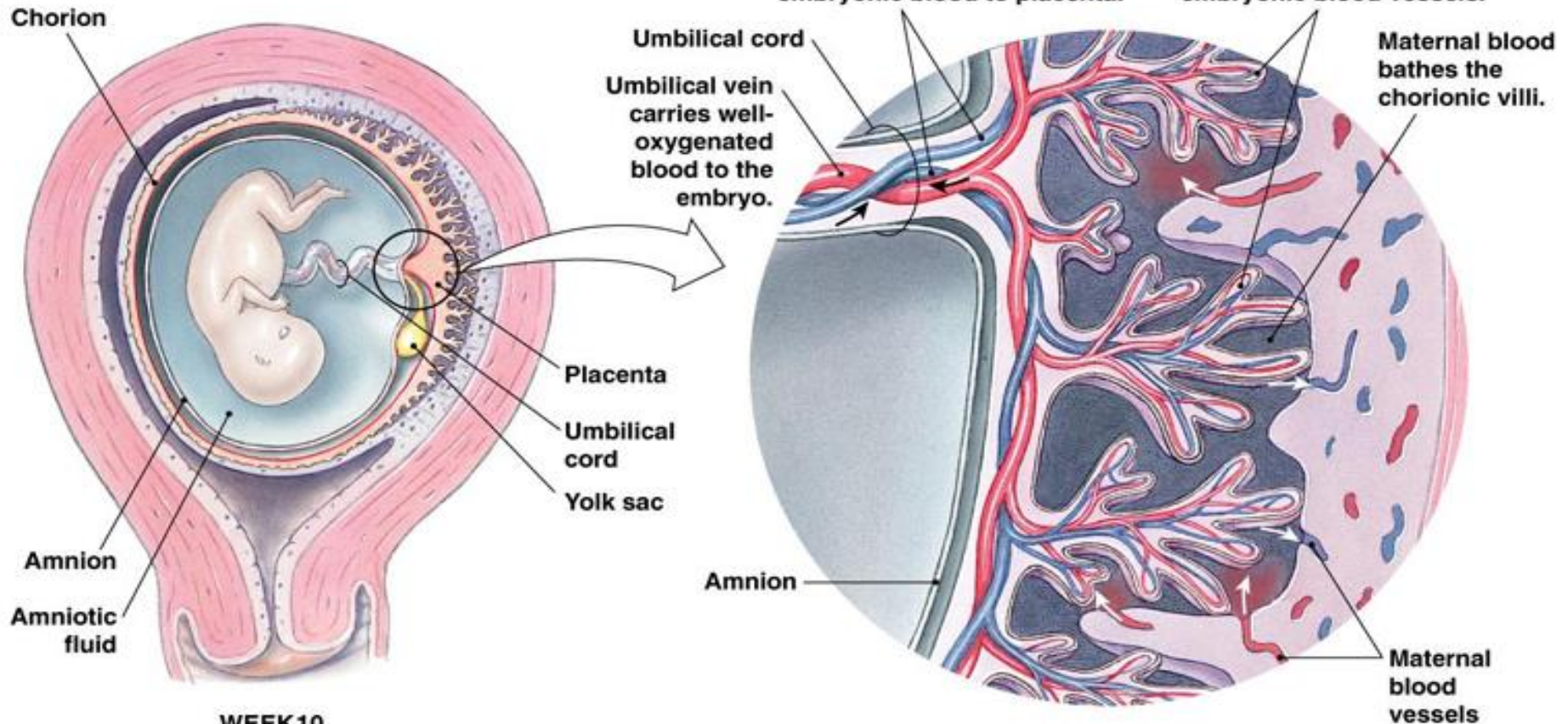


- Trophoblastic cords from **blastocyst**
- Blood capillaries grow in the cords
- 21 days after fertilization, blood starts to be pumped by fetal heart into the capillaries
- Maternal blood sinuses develop around the trophoblastic cords
- More and more trophoblast projections develop (placental villi)

Placenta

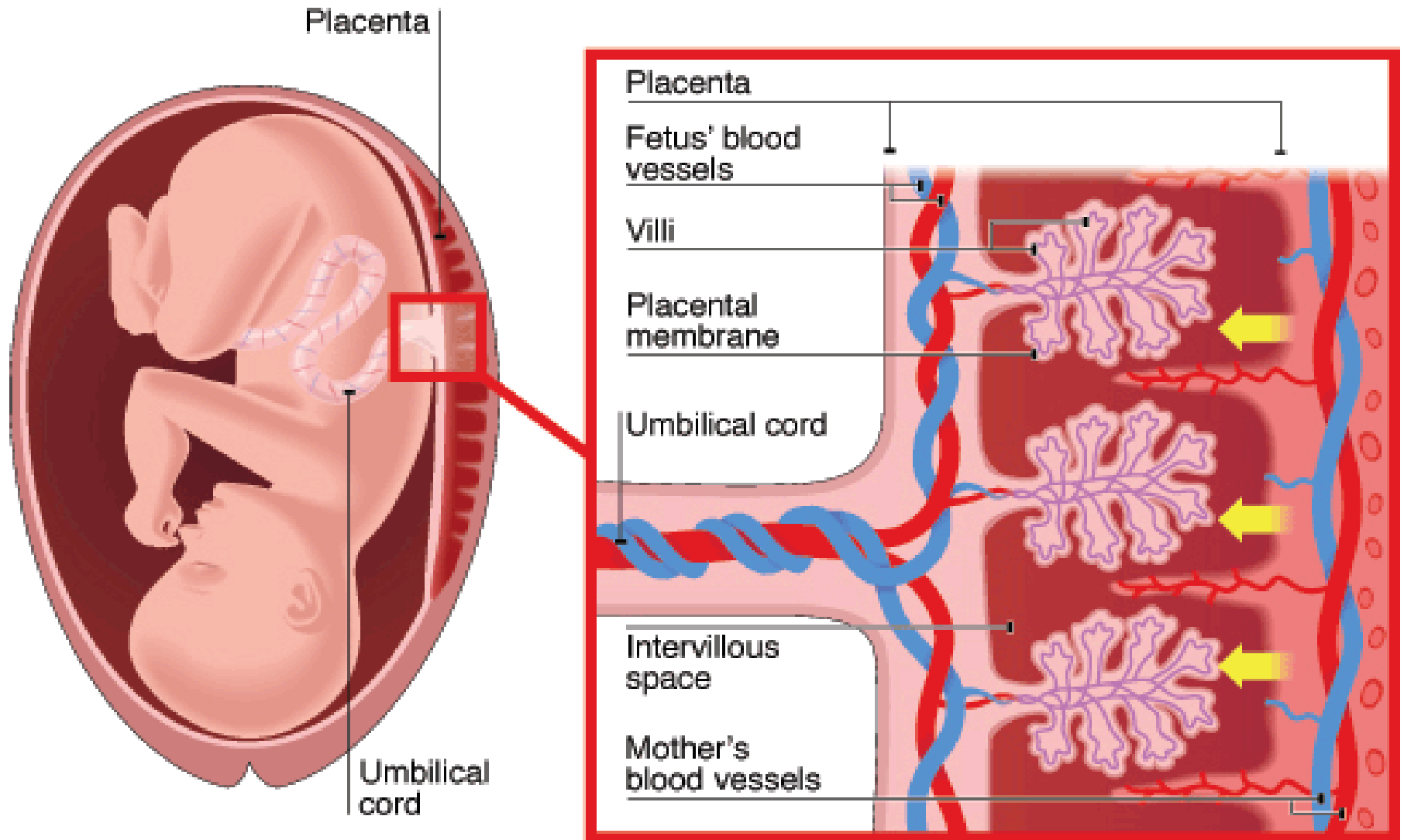


Some material is exchanged across placental membranes by diffusion, but other material must be transported.



WEEK 10

Placenta



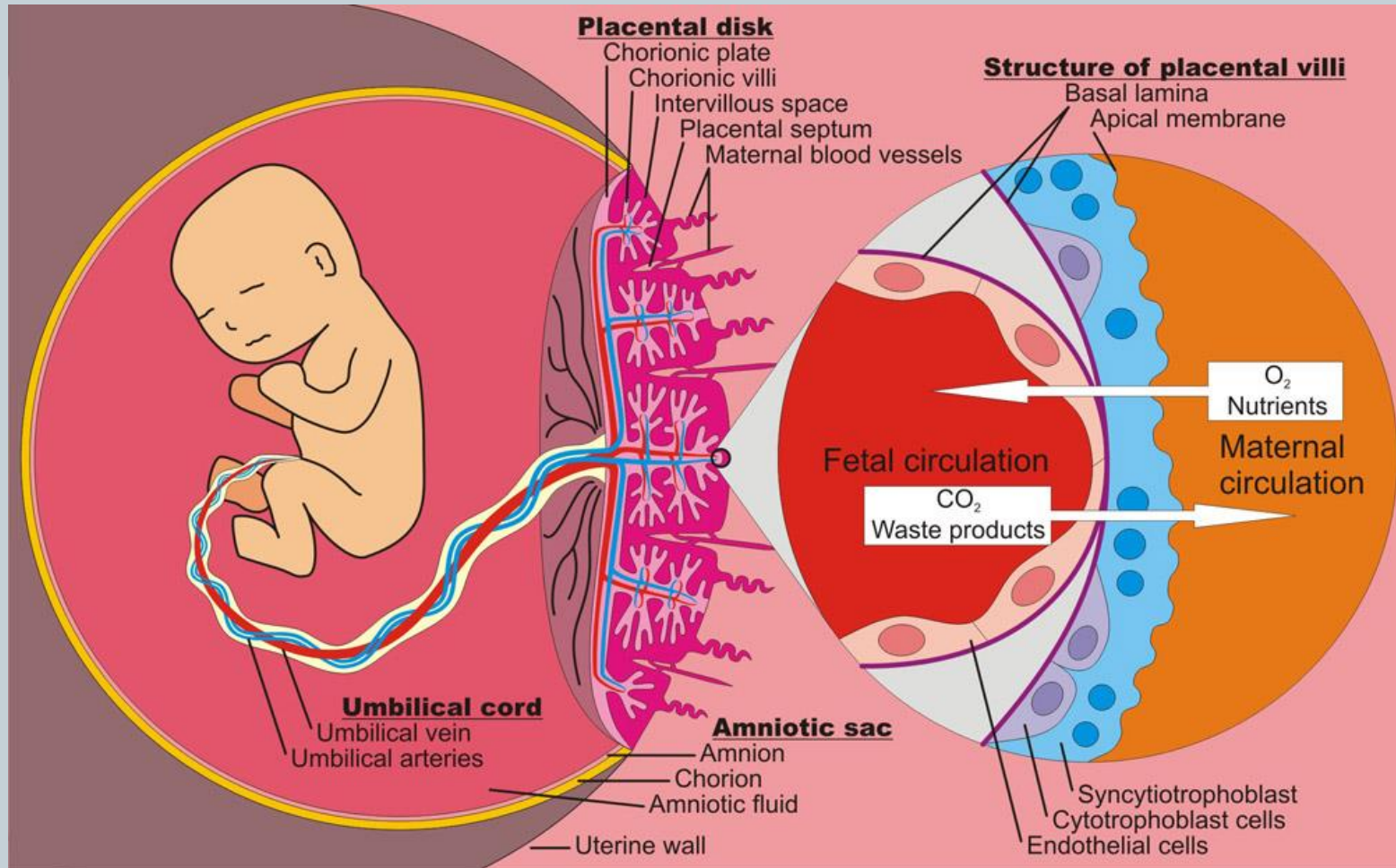
Function of the placenta



Major function:

- Respiration
- Nutrition
- Excretion
- Endocrine
- Protection

Respiration



Respiration

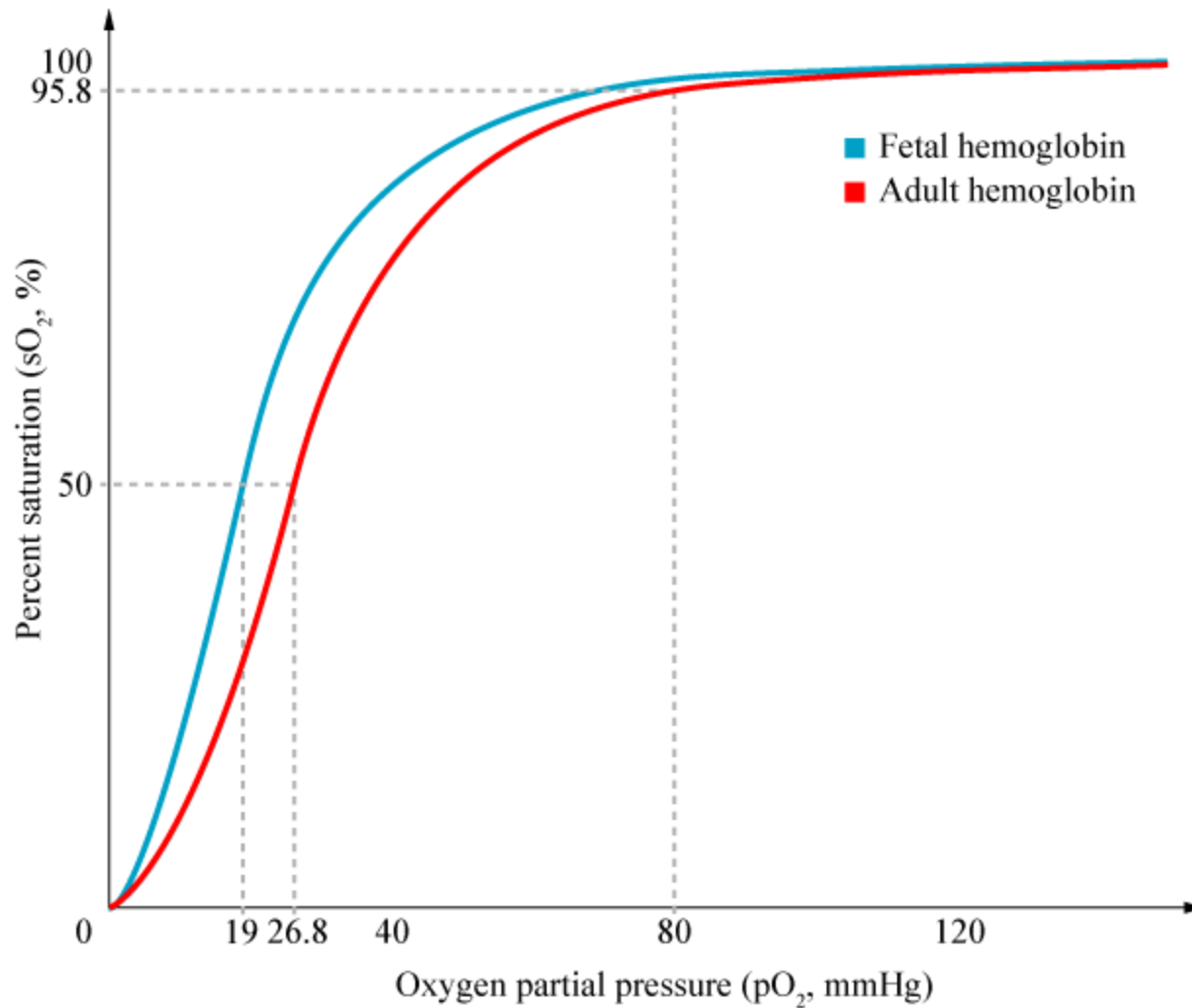


- PCO_2 2-3 mm Hg higher in fetal than maternal blood
- Dissolved O_2 in mother's blood passes to fetal blood by simple diffusion

$$\text{PO}_2 \text{ 50 mm Hg (M) - 30 mm Hg (F) = 20 mmHg}$$

- HbF conc. is 50% higher than HbA in mother
- At low PO_2 HbF carries 20-50% more O_2 than HbA (HbF has a higher oxygen carrying capacity than HbA)

HbA vs. HbF saturation curve



Respiration



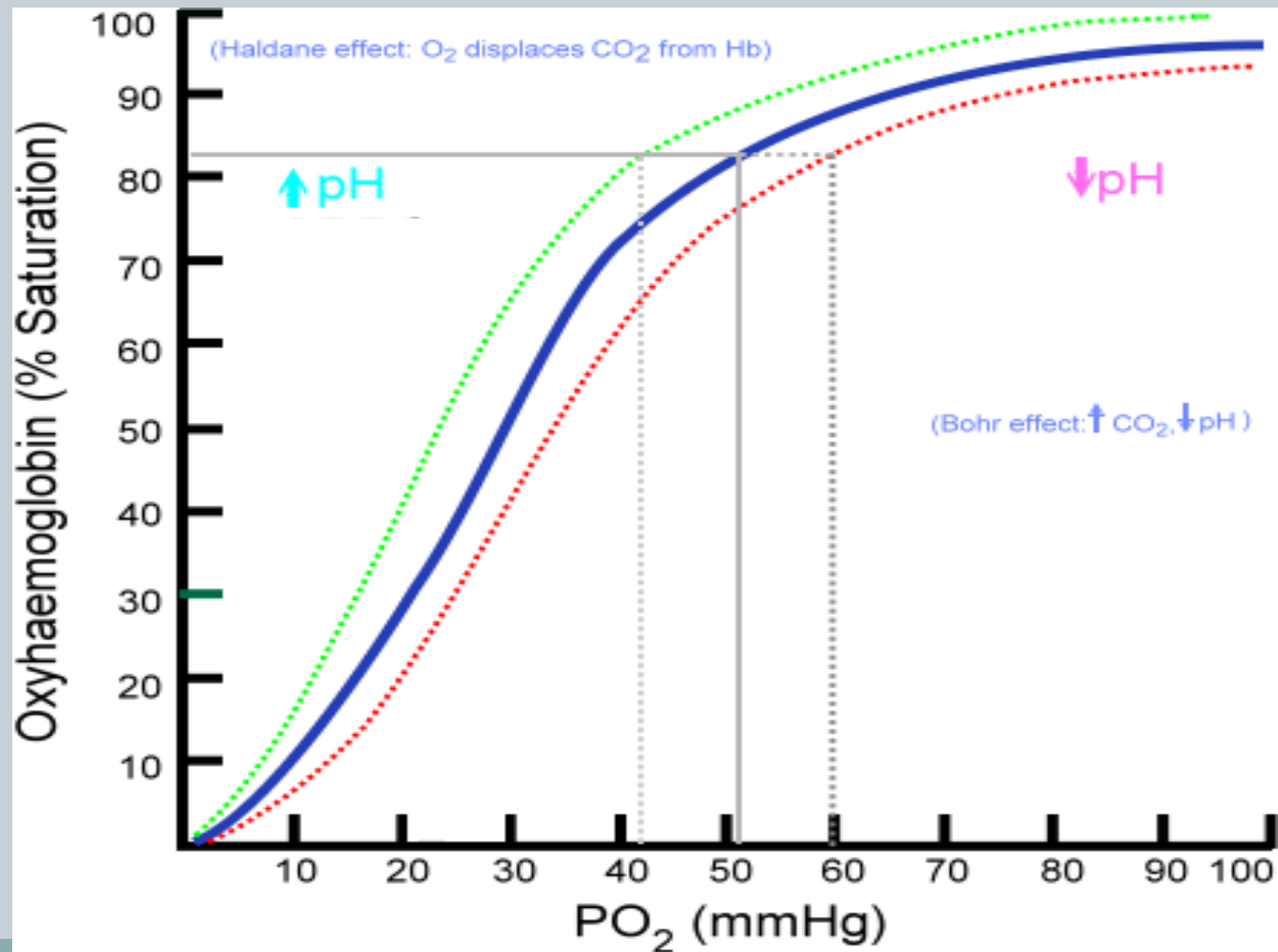
- Double Bohr effect

- ✦ Low pH in mother's blood (acidic)
- ✦ High pH in fetal blood (alkaline)

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

- The maternal blood gains CO_2 , the pH falls and the curve shifts to the right releasing additional oxygen.
- 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.

Bohr effect



Important factors facilitating delivery of oxygen to the fetal tissues



- High maternal intervillous blood flow (almost double the fetal placental flow)
- High fetal haemoglobin (16 - 17 g/dl)
- High fetal cardiac output
- The fetal metabolic acidosis which shifts the curve to the right and thus aids delivery of oxygen to the tissues.

Nutrition



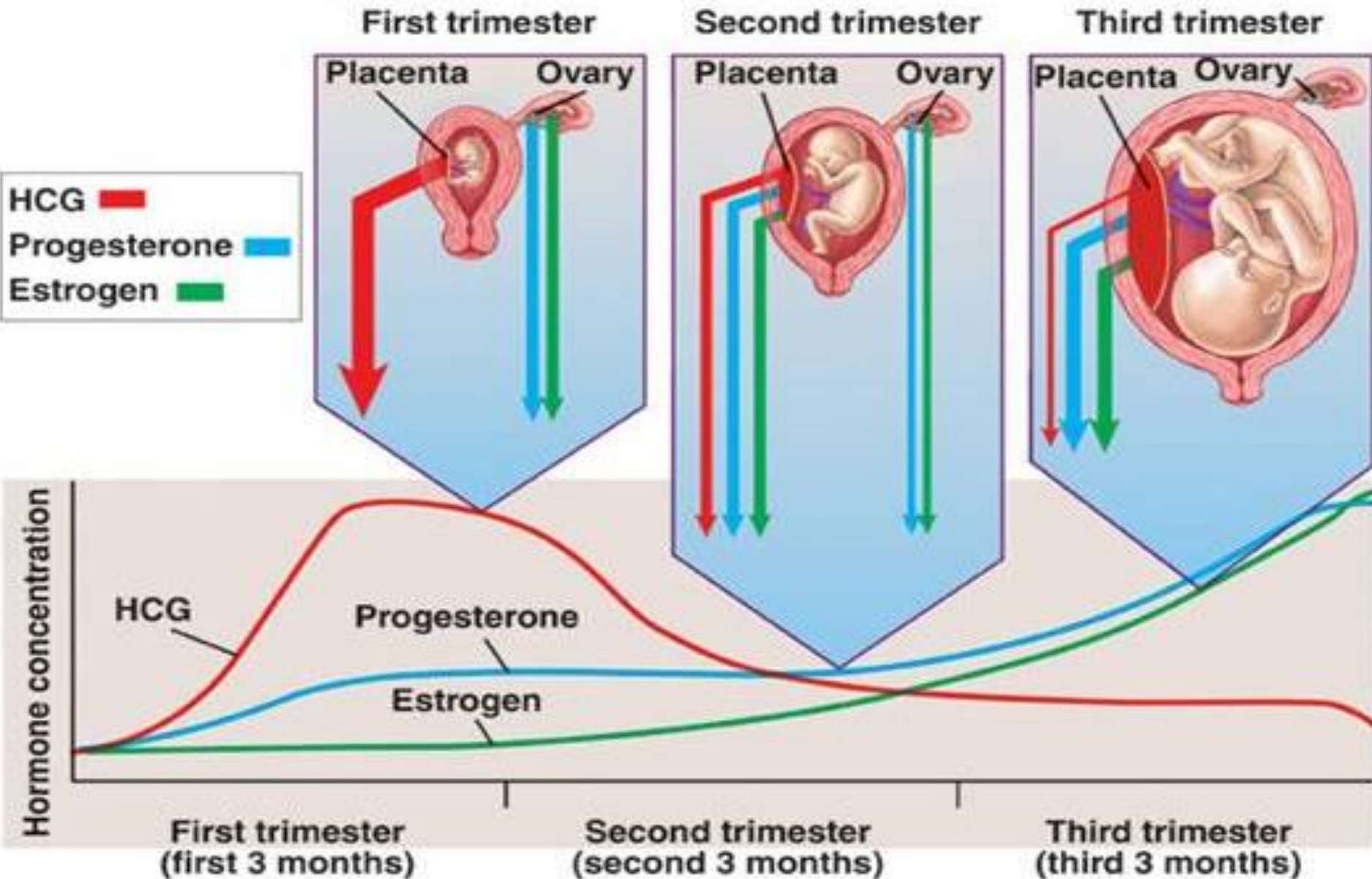
- Fetus uses mainly glucose for nutrition so the trophoblast cells in placental villi transport glucose by carrier molecules; GLUT (facilitated diffusion)
- Fatty acids diffuses due to high solubility in cell membrane (more slowly than glucose)
- The placenta actively transports all amino acids, with fetal concentrations exceeding maternal levels.
- K^+ , Na^+ and Cl^- diffuses from maternal to fetal blood

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 ensures continuous diffusion of these substances to the maternal blood

Endocrine

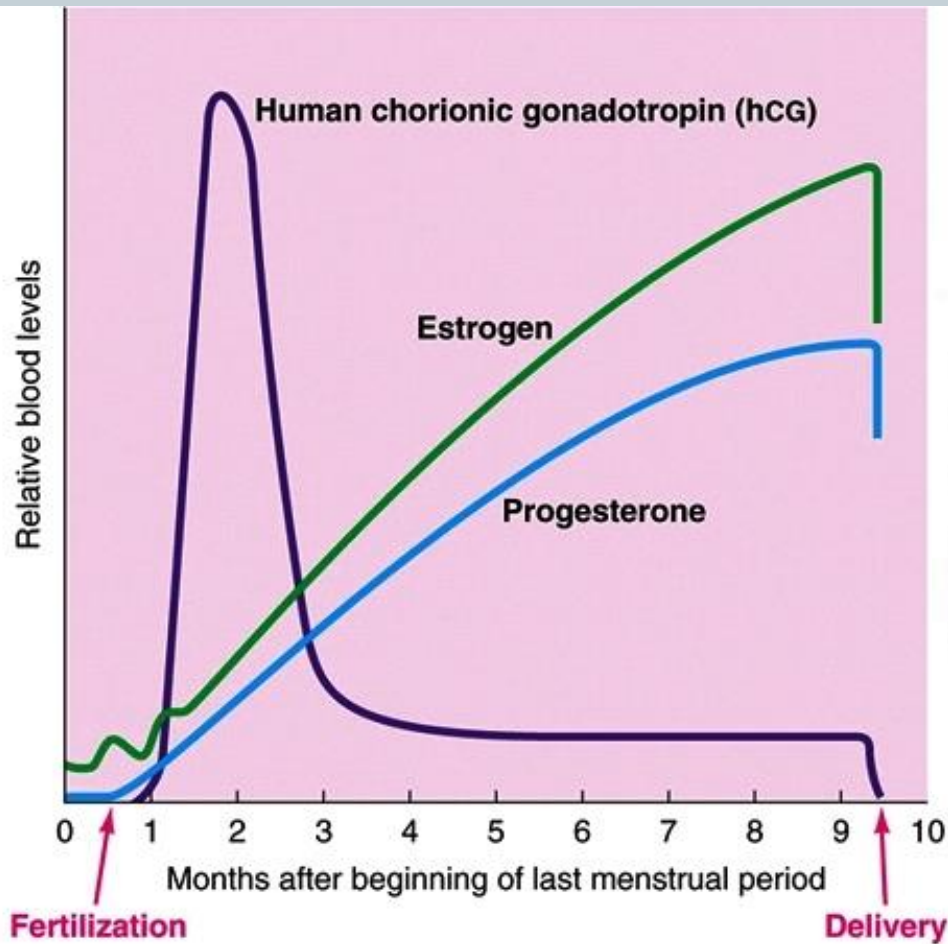


Placenta as Endocrine Organ



- Human Chorionic Gonadotropin (hCG)
 - Glycoprotein
 - 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 the male fetus (growth of male sex organs)

hCG level (pregnancy test)



Fertilization

Delivery

Sherwood, Fig. 20-28
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"Well... I think we should run a pregnancy test. Just to make sure!"

Placenta as Endocrine Organ

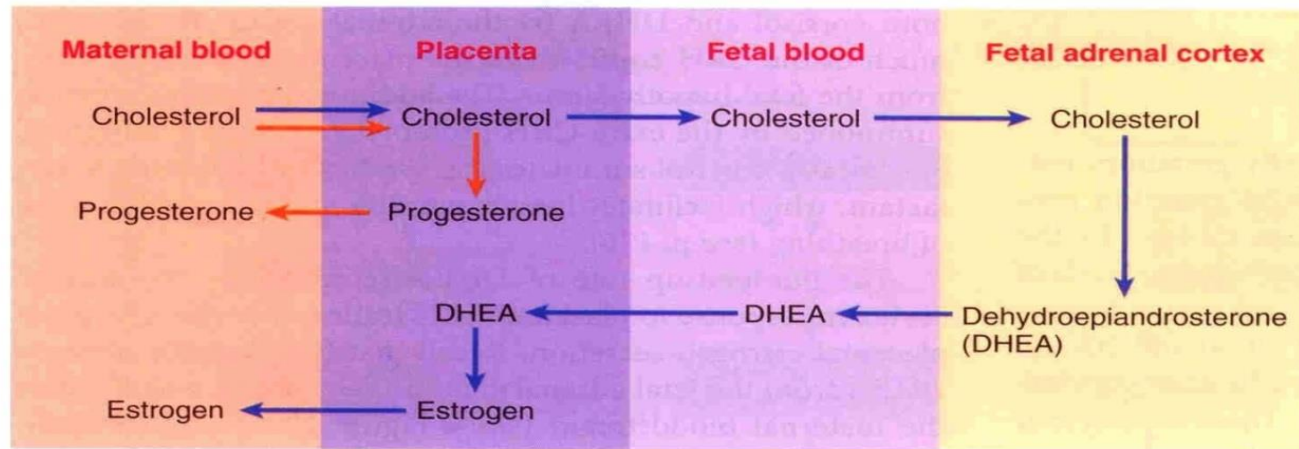
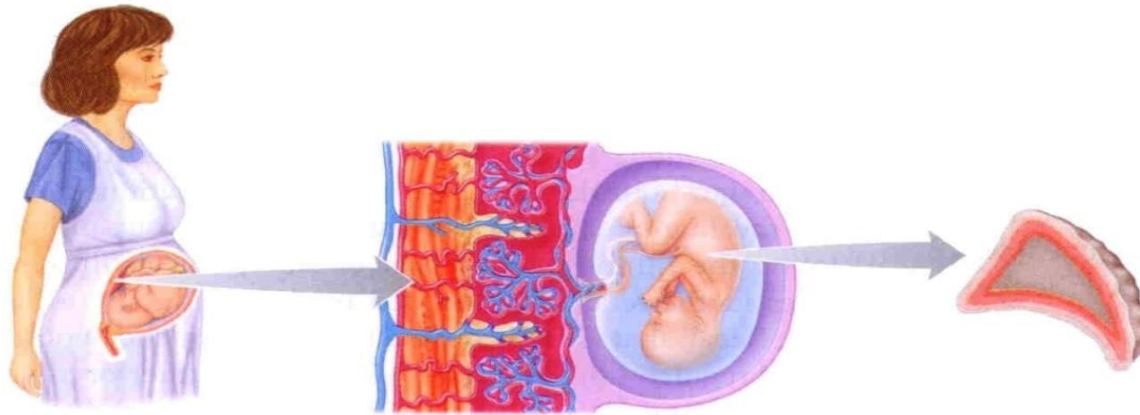


- **Estrogen**
 - Steroid hormone
 - Secreted by syncytial trophoblast cells
 - Towards end of pregnancy reaches 30×
 - Derived from weak androgen (DHEA) released from maternal & fetal adrenals cortex
- **Functions in the mother**
 - Enlargement of uterus, breast & external genitalia
 - Relaxation of pelvic ligaments in preparation to labor
 - Activation of the uterus (gap junctions)

Placenta as Endocrine Organ



- **Progesterone**
 - Steroid hormone
 - Secreted by syncytial trophoblast cells
 - Towards end of pregnancy reaches 10×
 - Derived from cholesterol
- **Functions in the mother**
 - Provides nutrition to developing embryo
 - Development of decidual cells
 - Inhibits the contractility of the uterus



KEY

- Pathway for placental synthesis of progesterone
- Pathway for placental synthesis of estrogen

- **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*).

Placenta as Endocrine Organ



- Human Chorionic Somatomamotropin or Human placental lactogen (hPL)
 - Protein hormone
 - Secreted by placenta around 5th gestational week
- Functions in the mother
 - Breast development
 - Weak growth hormone's action
 - Inhibits insulin sensitivity = ↓ glucose utilization
 - Promotes release of fatty acids

Placenta as Endocrine Organ



- **Relaxin**
 - Polypeptide
 - Secreted by corpus luteum and placenta
- **Functions in the mother**
 - Relaxation of symphysis pubic ligament (weak)
 - Softens the cervix at 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
- Adrenal gland
 - Increase glucocorticoids secretion (mobilize AA)
 - Increase 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
- Masculine or acromegalic features
- 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%)
- Increase in daily requirements for
 - Iron
 - Phosphates
 - Calcium
 - Vitamins
 - ✦ Vitamin D (Ca^{+2} absorption)

Changes in circulatory system



- Increase in COP (30-40%) by 27 weeks
- 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)

Changes in respiration



- Increase in O_2 consumption (20%)
 - Increase BMR
 - Increase in body size
- Growing uterus presses upwards (restriction)
- Increase in respiratory rate (RR)
- Increase in minute ventilation ($TV \times RR$) by 50%
 - Progesterone \uparrow sensitivity of RC to CO_2

The End

Thank You