Physiology of pregnancy

DR. HANA ALZAMIL

Objectives

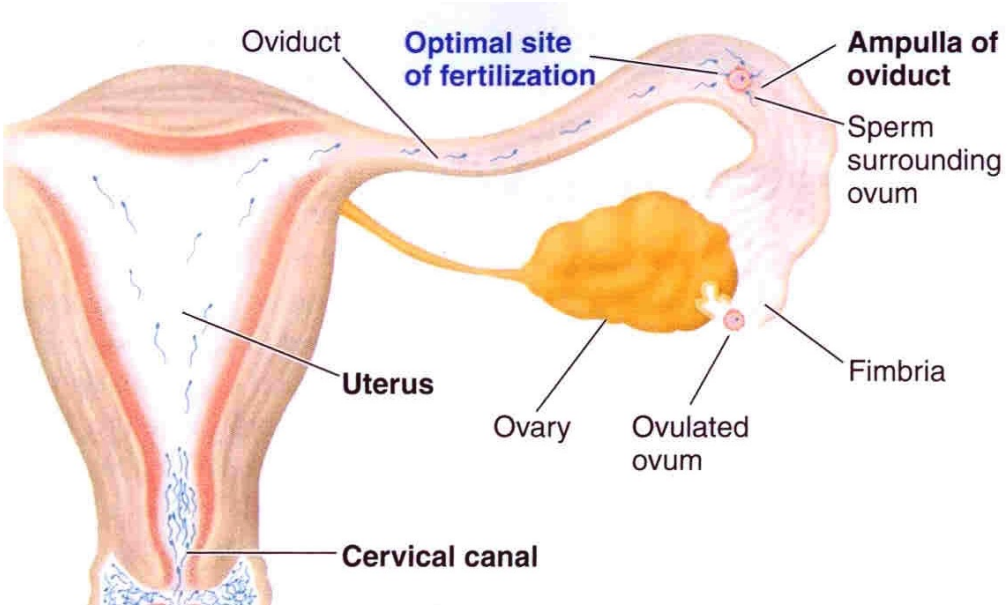
- Describe Fertilization & implantation of the blastocyst into the endometrium.
- Recognize the development and normal physiology of the placenta
- Describe the physiological functions of placental hormones during pregnancy
- Explain the physiological responses of mother's body to pregnancy

Revision (large group activity)

- How many sperms in the ejaculated semen?
- In which stage the ova is after ovulation?
- What is the % of ovulated ova that can reach fallopian tube?
- Can the ova that is released from the right ovary reaches the left fallopian tube?

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



Small group activity

- What are the factors that help the ovulated ova to reach the fallopian tube ?
- Is there any obstacles?
- What are the factors that help the sperm to travel in the female genital tract ?
- Is there any obstacles?

Fertilization

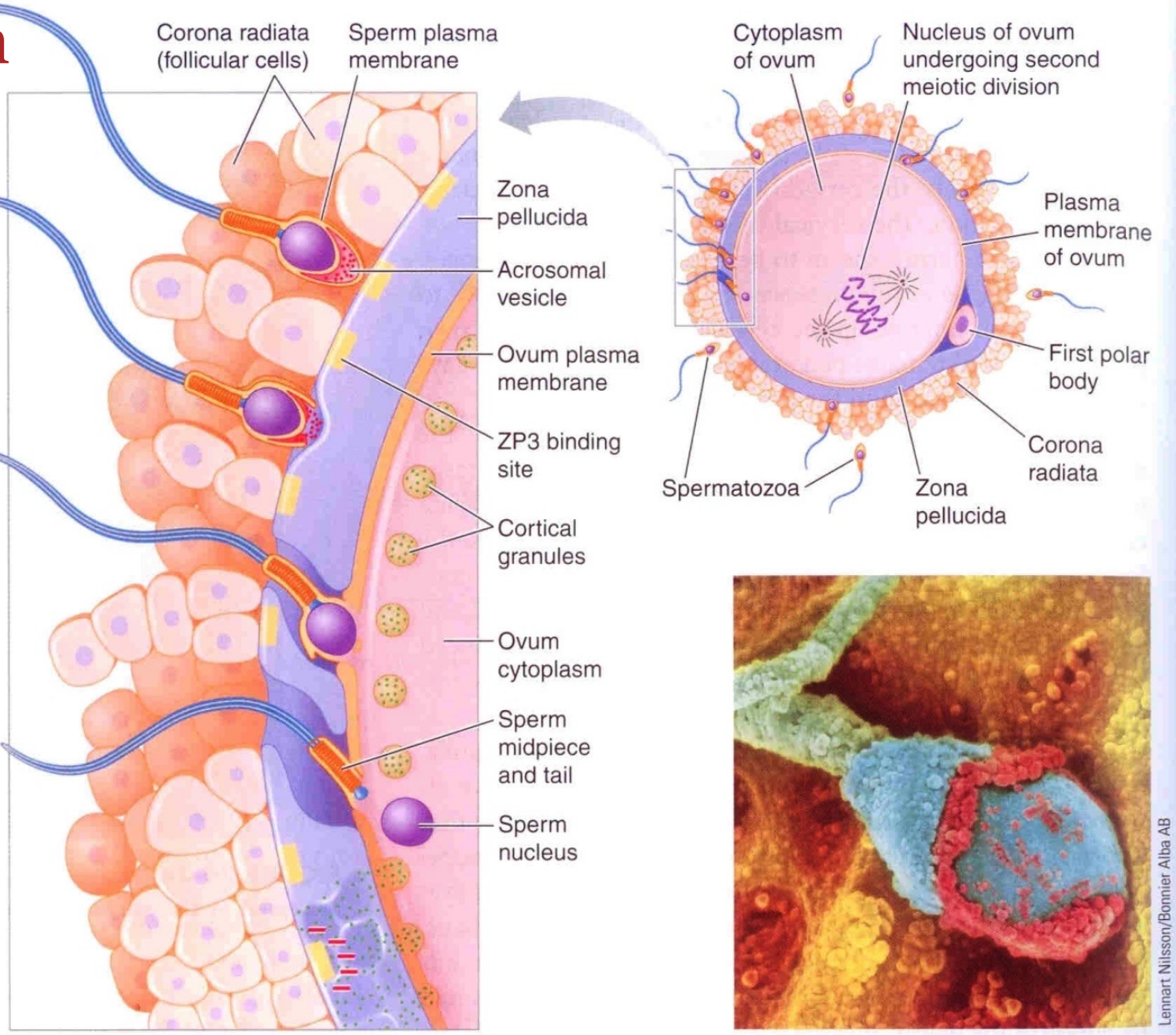
1 The fertilizing sperm penetrates the corona radiata via membrane-bound enzymes in the plasma membrane of its head and binds to ZP3 receptors on the zona pellucida.

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

Lennart Nilsson/Bonnier Alba AB

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

Fertilization

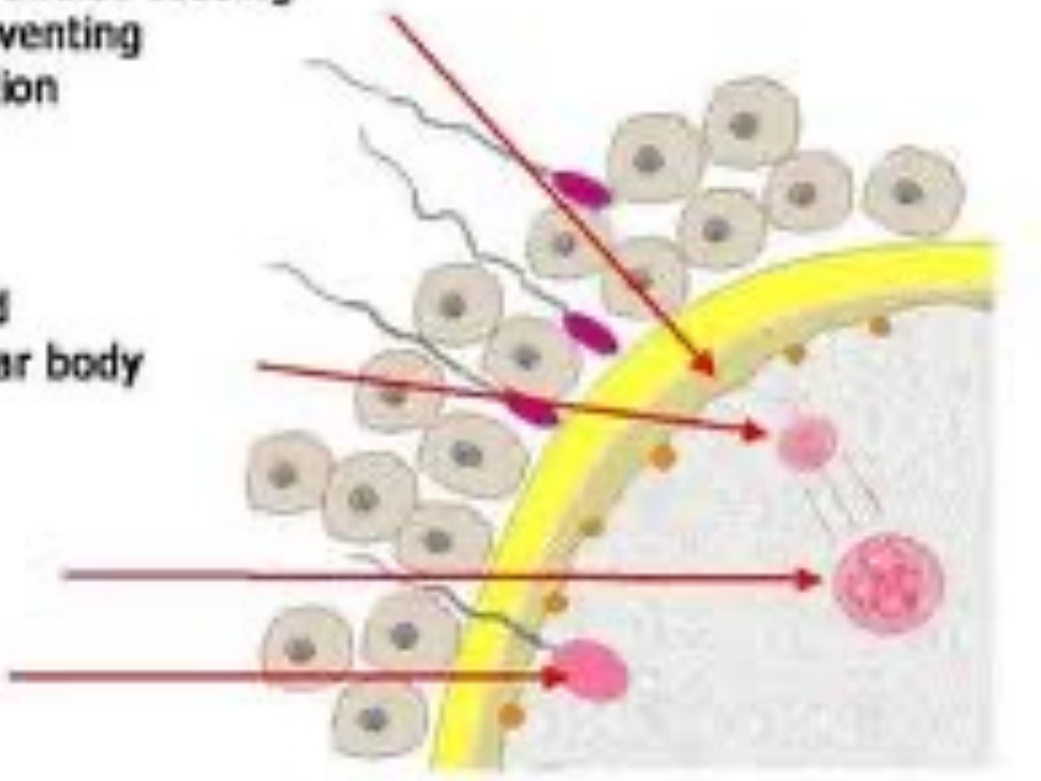
Fertilization

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

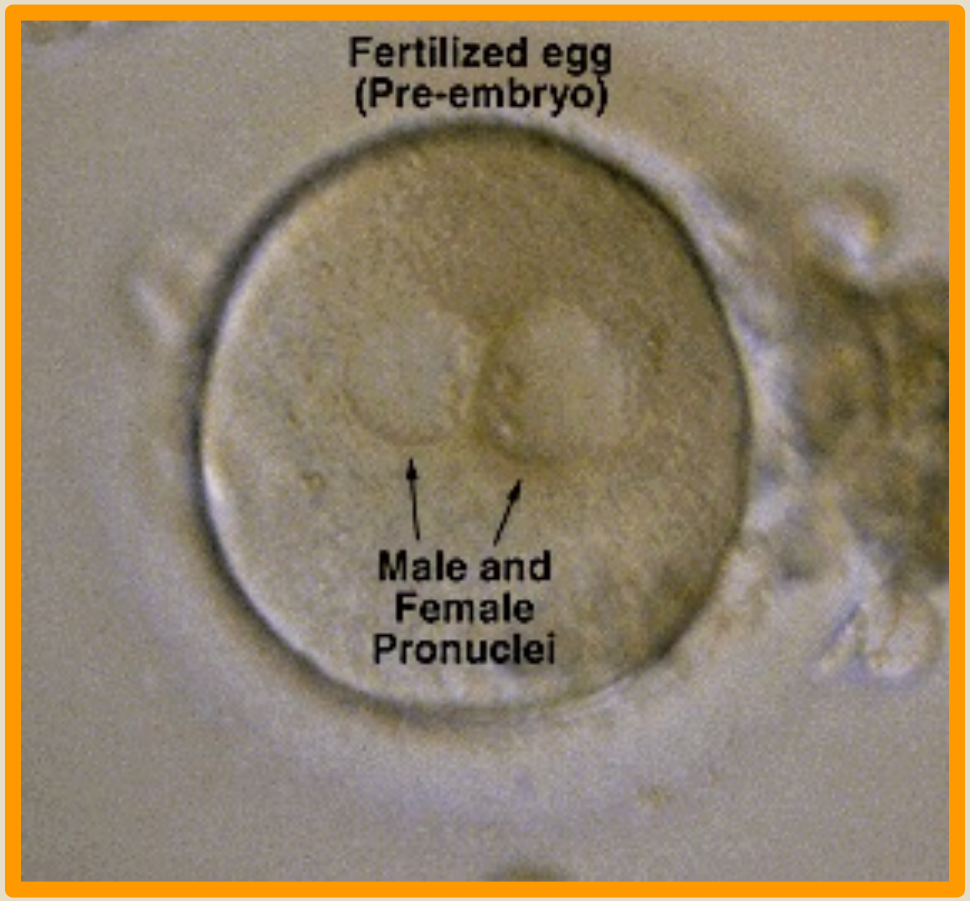
male pronucleus



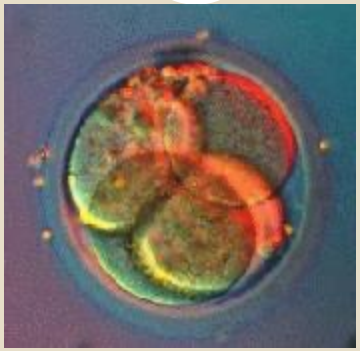
Fertilization

- After ejaculation sperms reach ampulla of fallopian tube within 30-60 min (ut cont)
- Sperm penetrate corona radiata and zona pellucida (hyaluronidase & proteolytic enzymes)
- 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

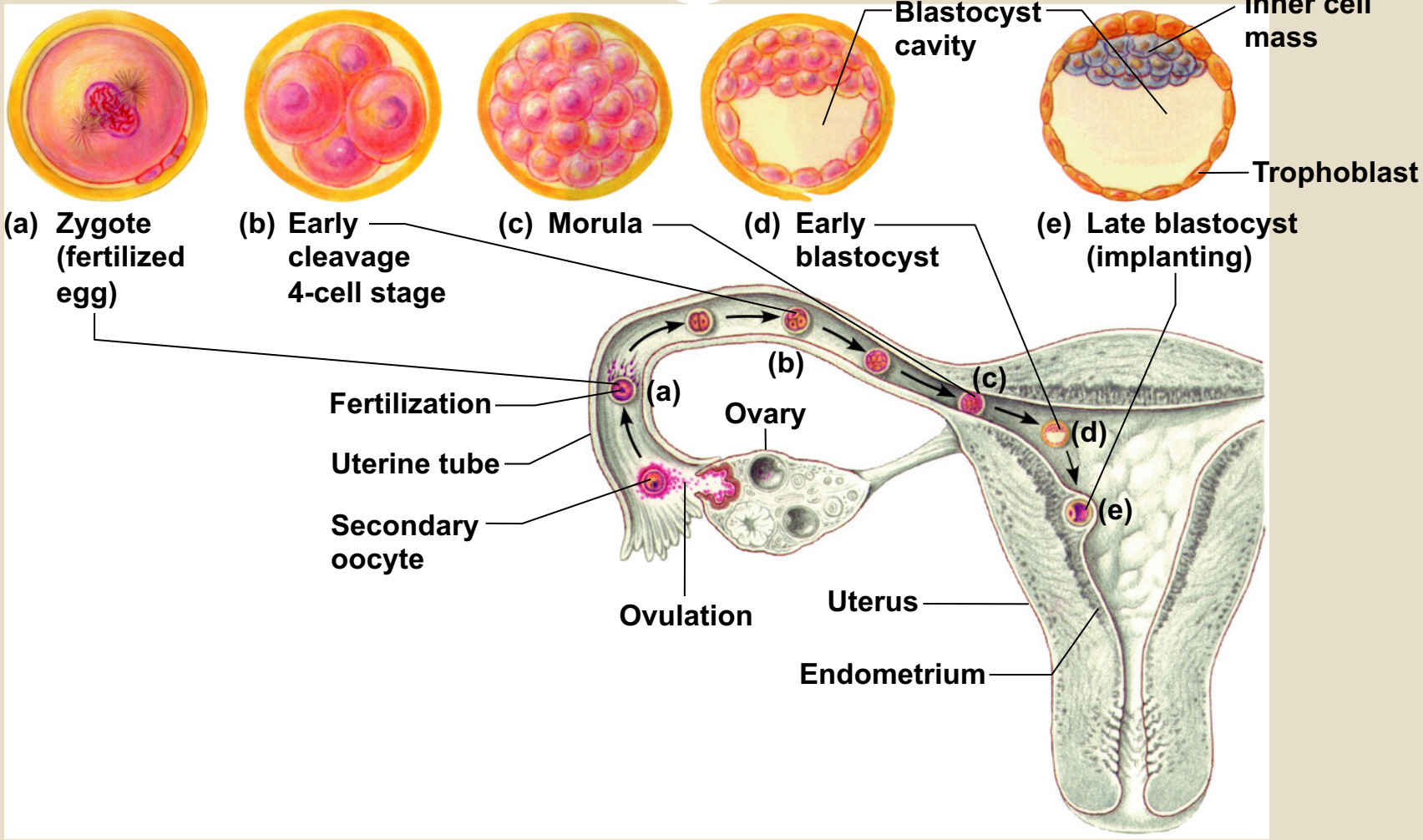


Cleavage


- 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

Cleavage


Blastocyst cavity
Inner cell mass
Trophoblast
(a) Zygote (fertilized egg)
(b) Early cleavage 4-cell stage
(c) Morula
(d) Early blastocyst
(e) Late blastocyst (implanting)
(a)
(b)
(c)
(d)
(e)
Fertilization
Uterine tube
Secondary oocyte
Ovulation
Ovary
Uterus
Endometrium

Cleavage

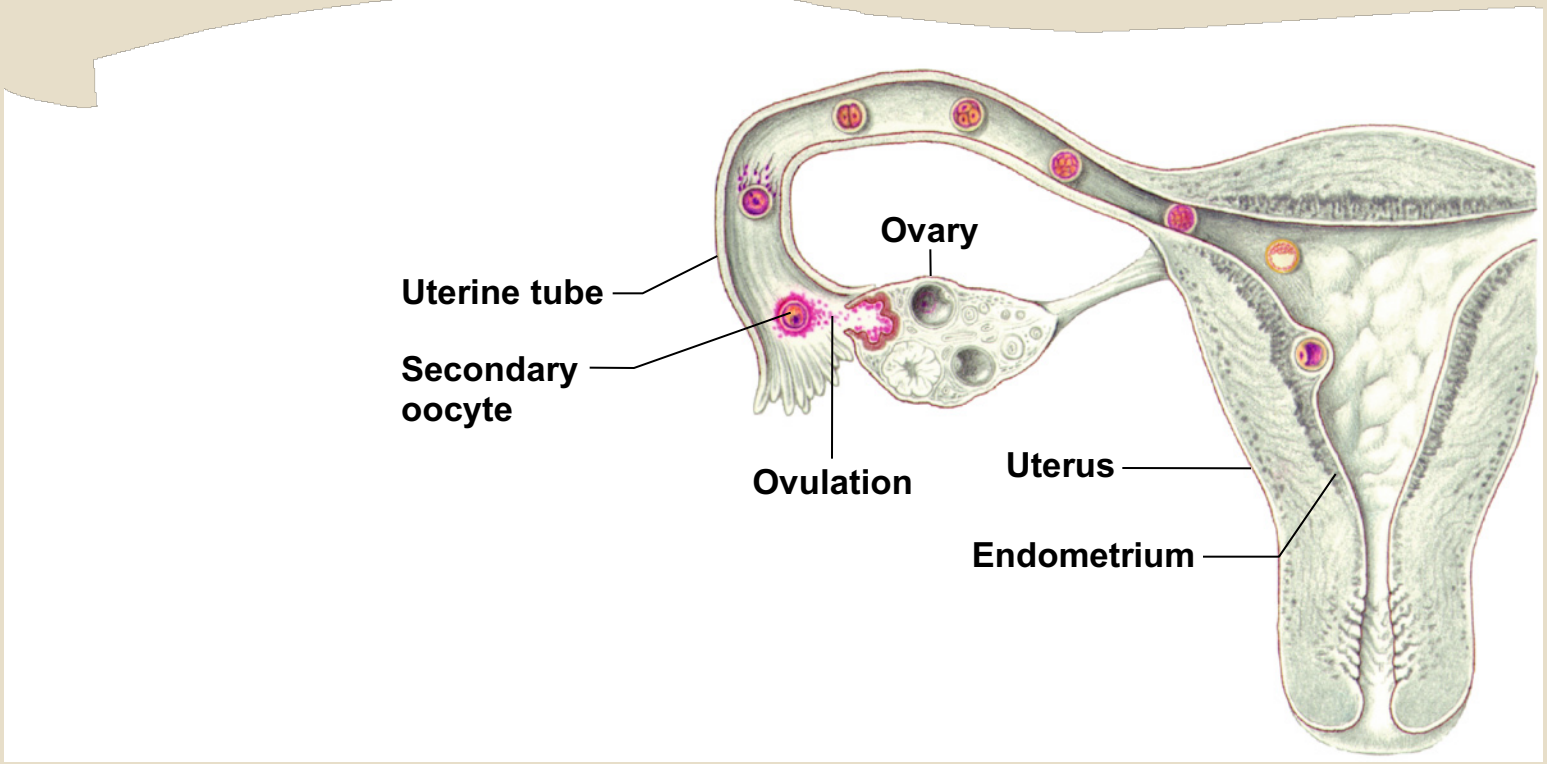


Figure 16.15, step 1

Cleavage

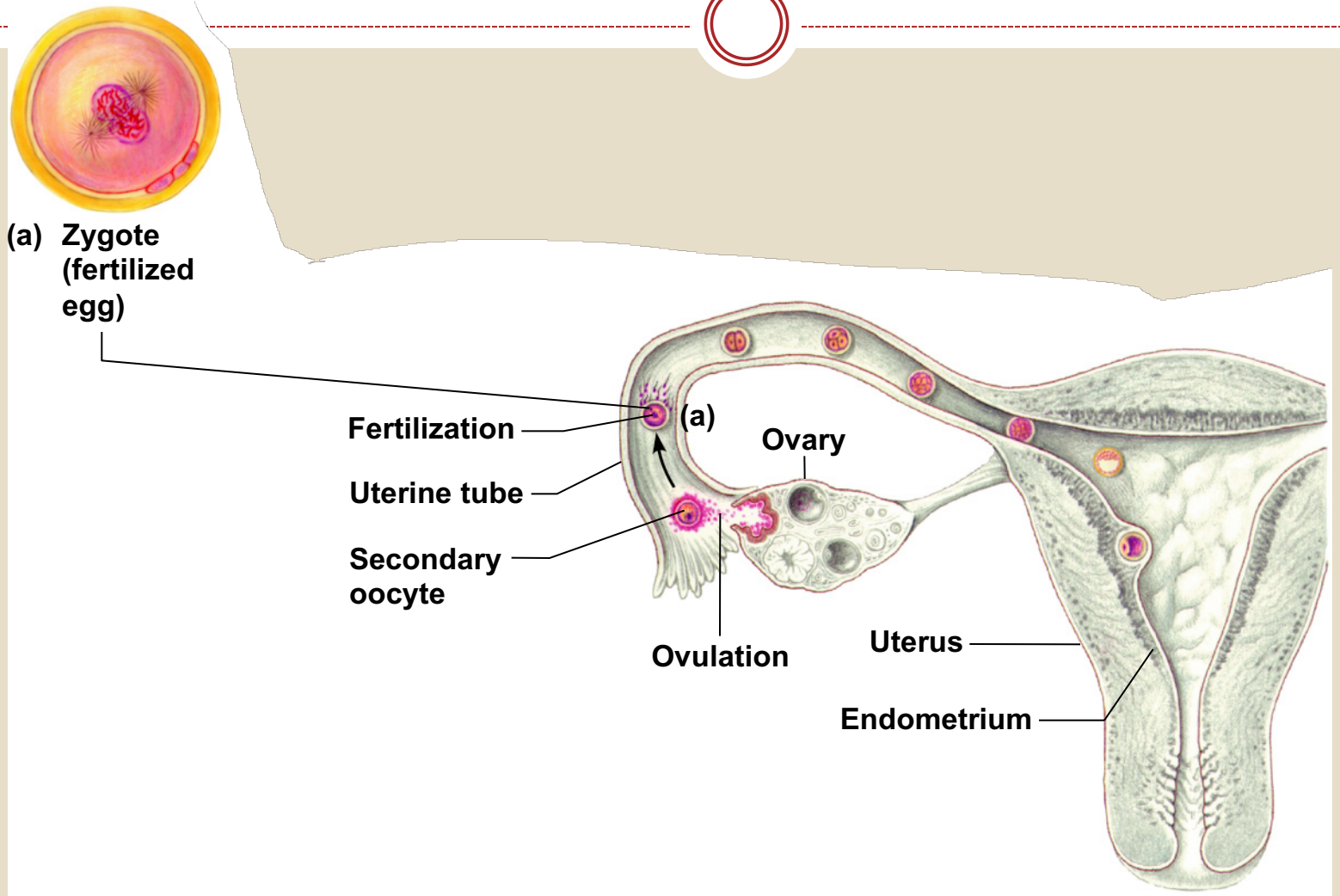


Figure 16.15, step 2

Cleavage

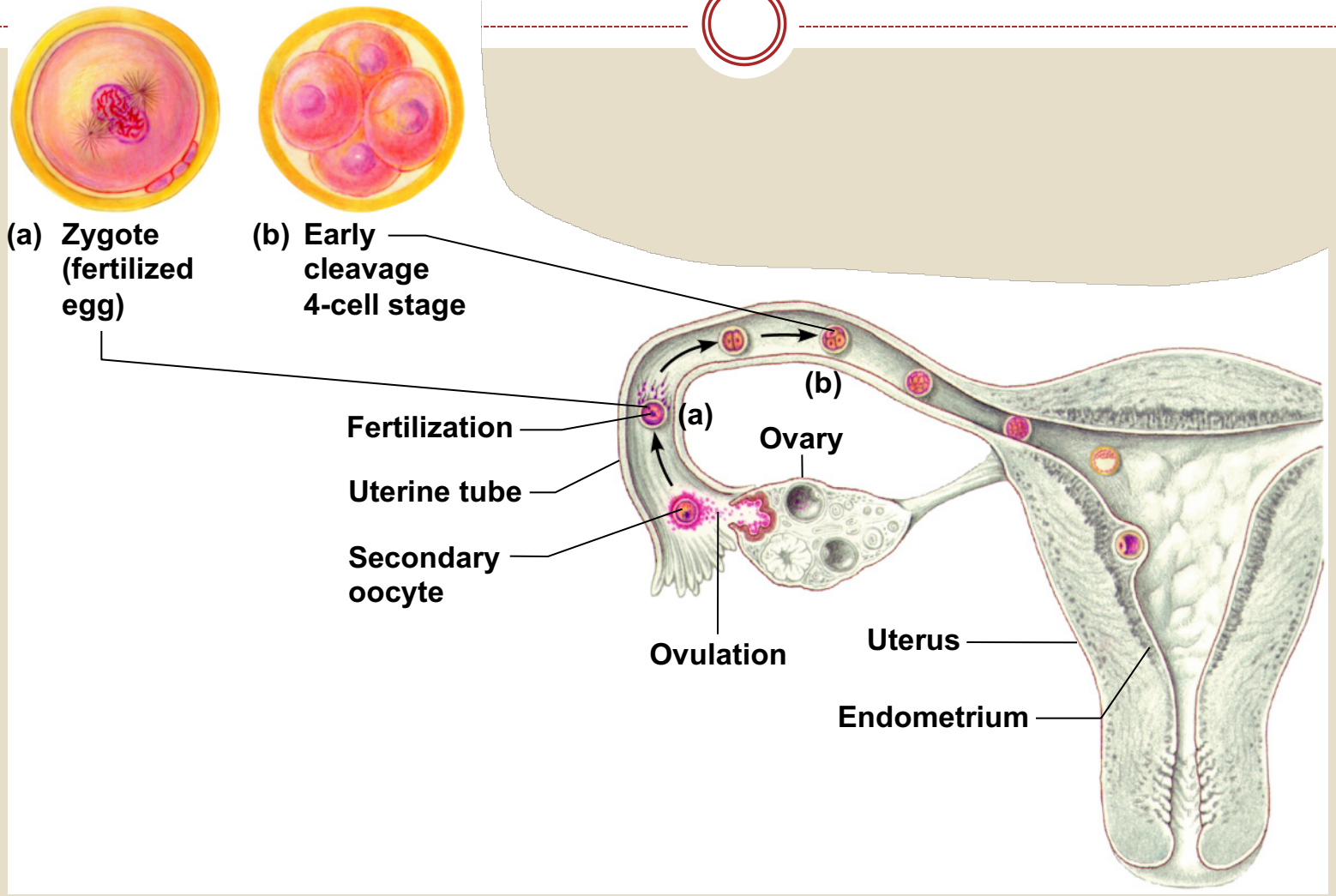


Figure 16.15, step 3

Cleavage

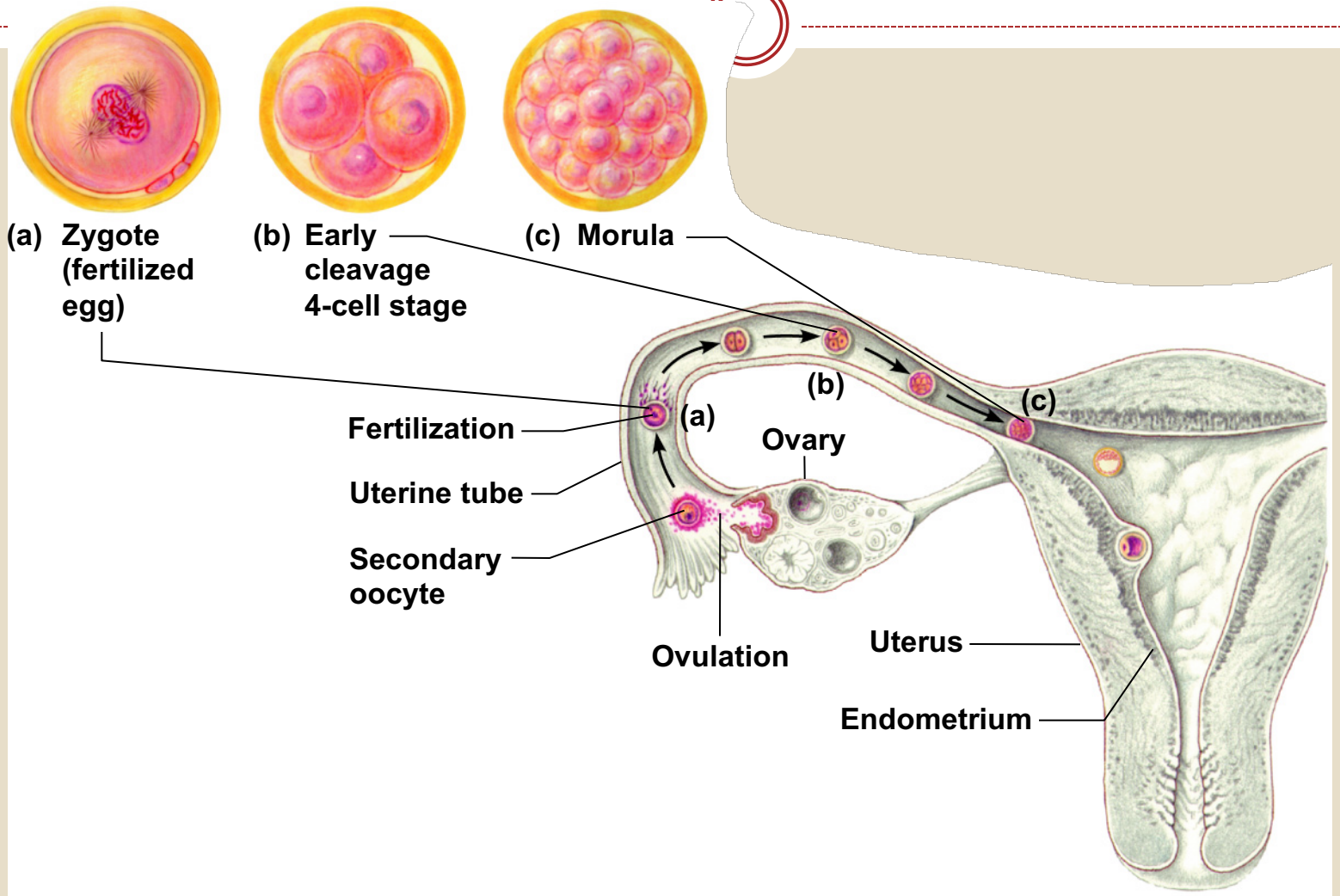


Figure 16.15, step 4

Cleavage

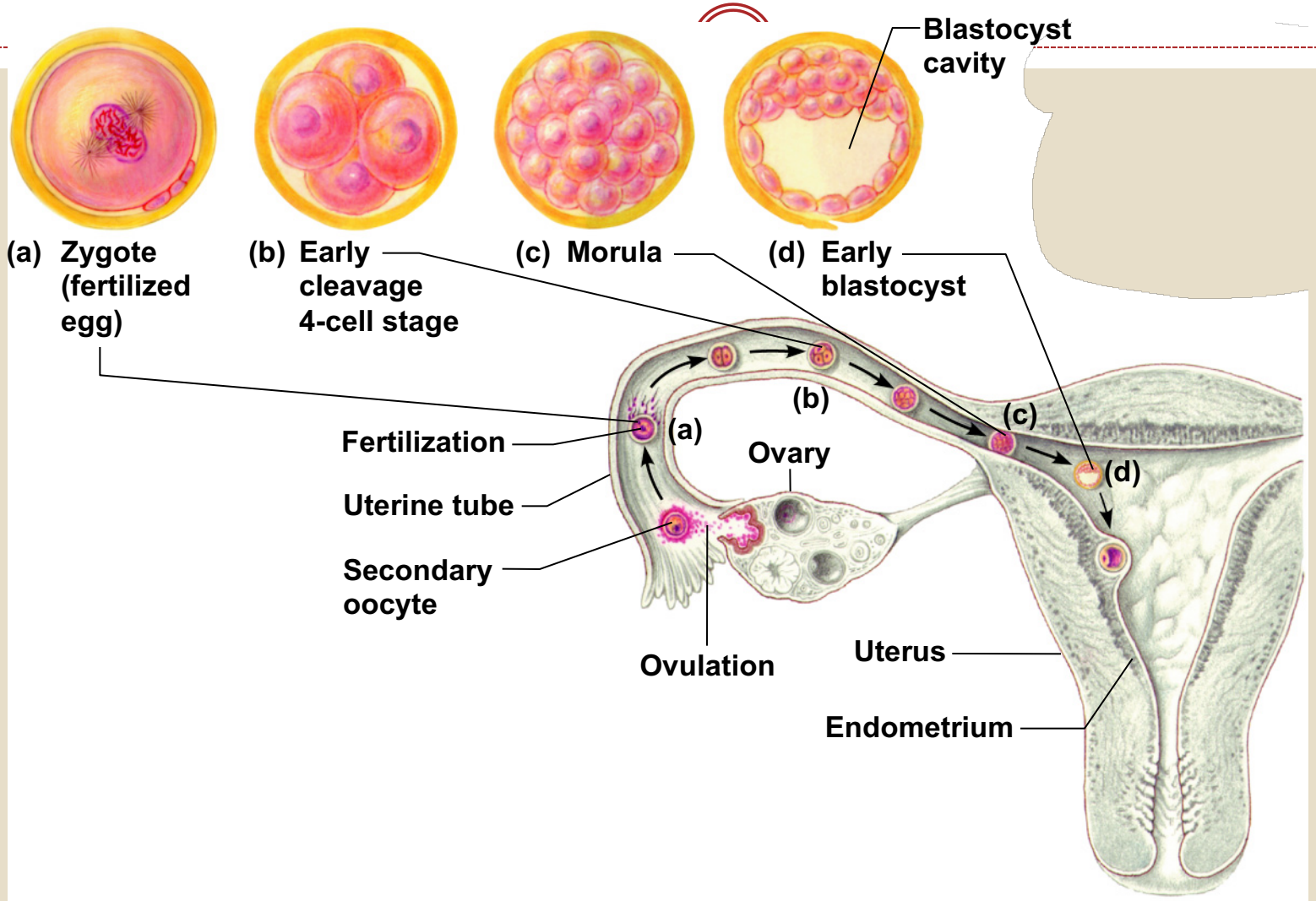
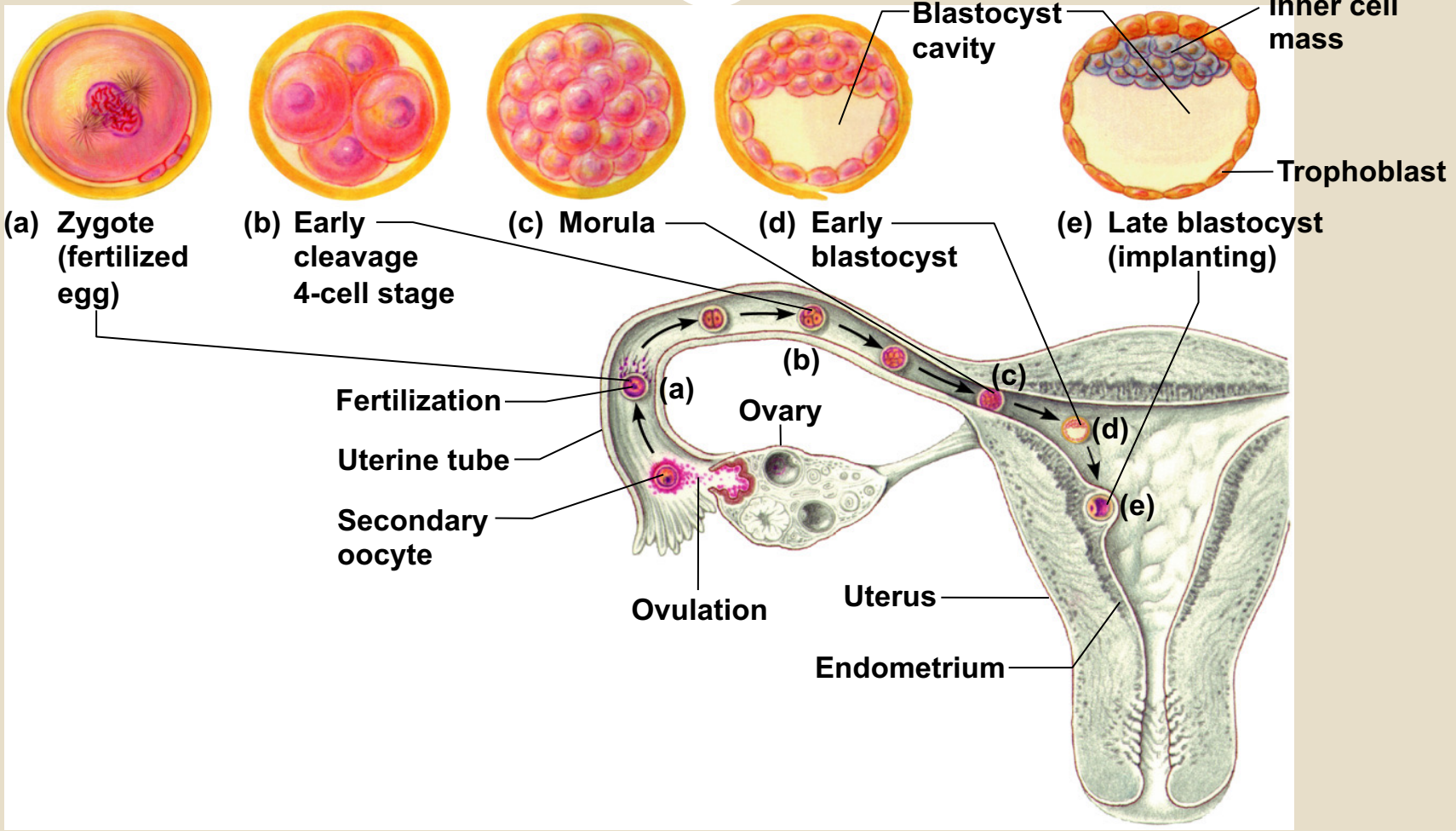


Figure 16.15, step 5

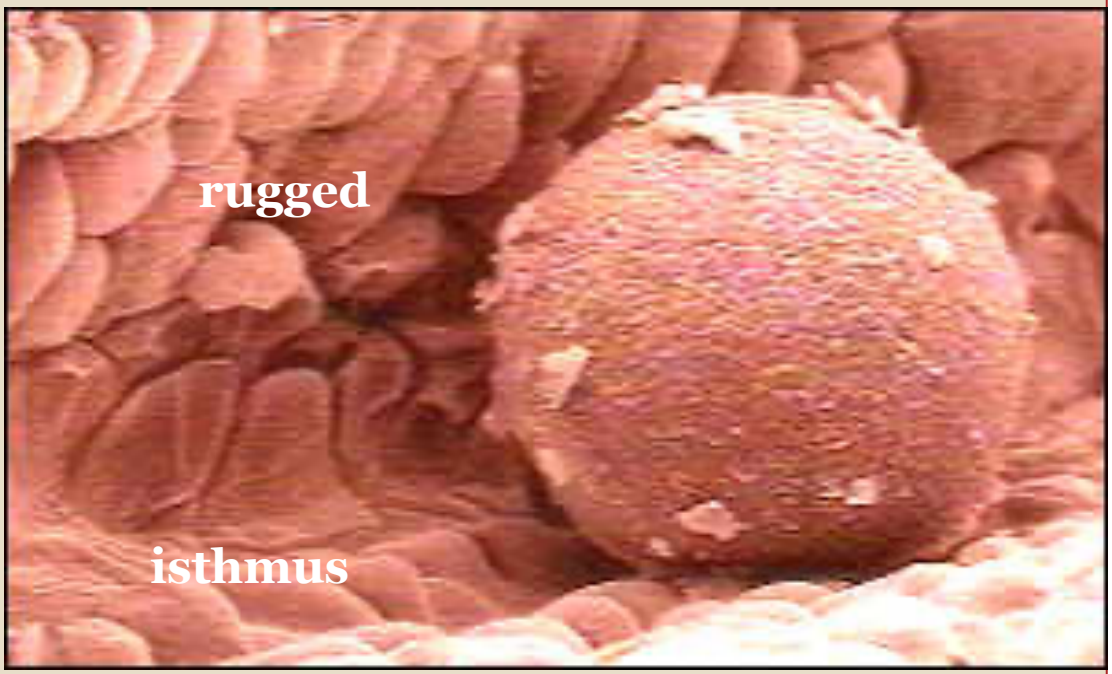
Cleavage


Blastocyst cavity
Inner cell mass
Trophoblast
(a) Zygote (fertilized egg)
(b) Early cleavage 4-cell stage
(c) Morula
(d) Early blastocyst
(e) Late blastocyst (implanting)
Fertilization
Uterine tube
Secondary oocyte
Ovulation
Ovary
Uterus
Endometrium
(a)
(b)
(c)
(d)
(e)

- How does the ova survive in the fallopian tube?

Traveling

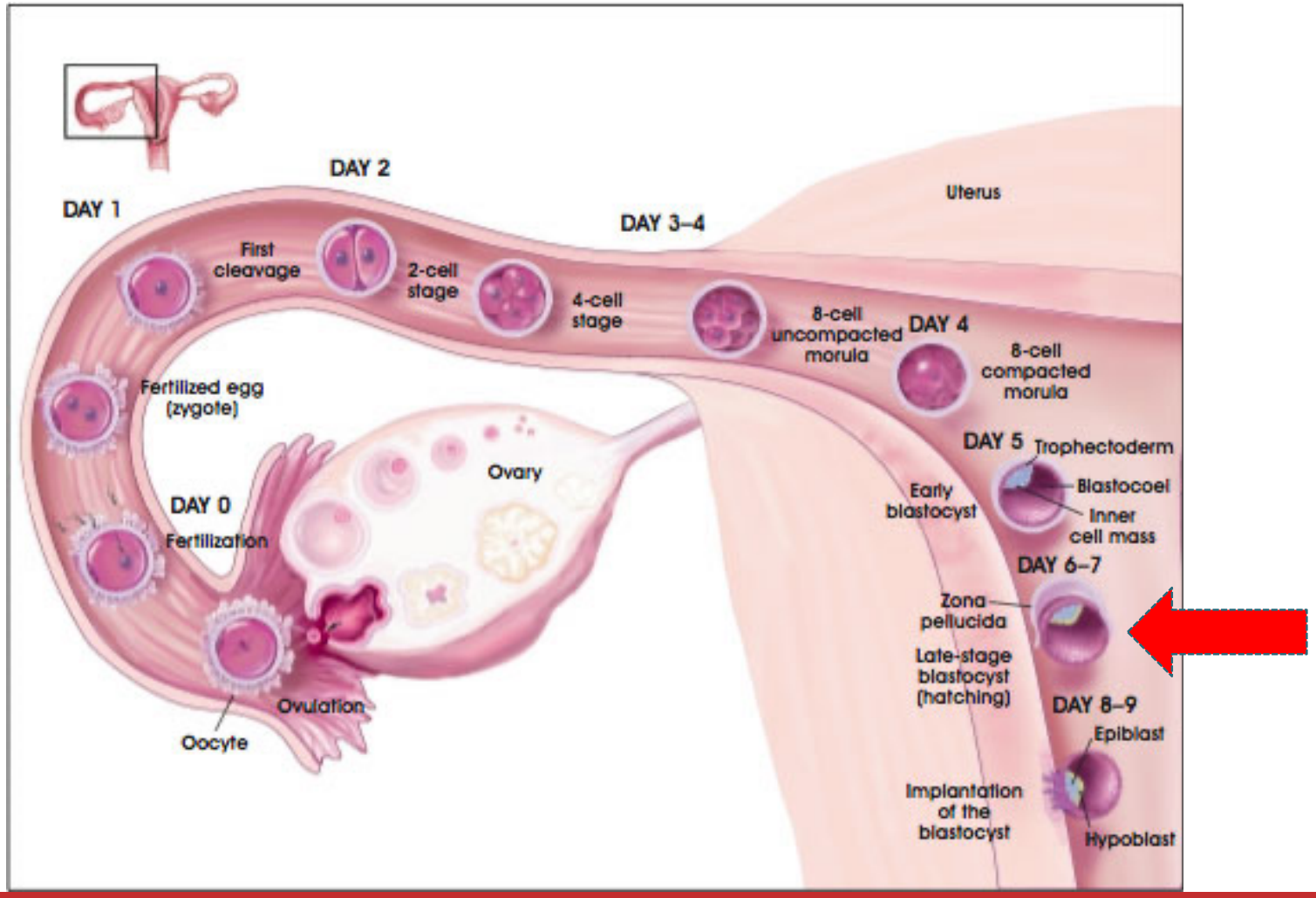
- Zygote begins to divide as it travels through oviduct
- Nutrition of blastocyst (secretory cells in fallopian tube)
- Effect of Progesterone on (SM) of isthmus



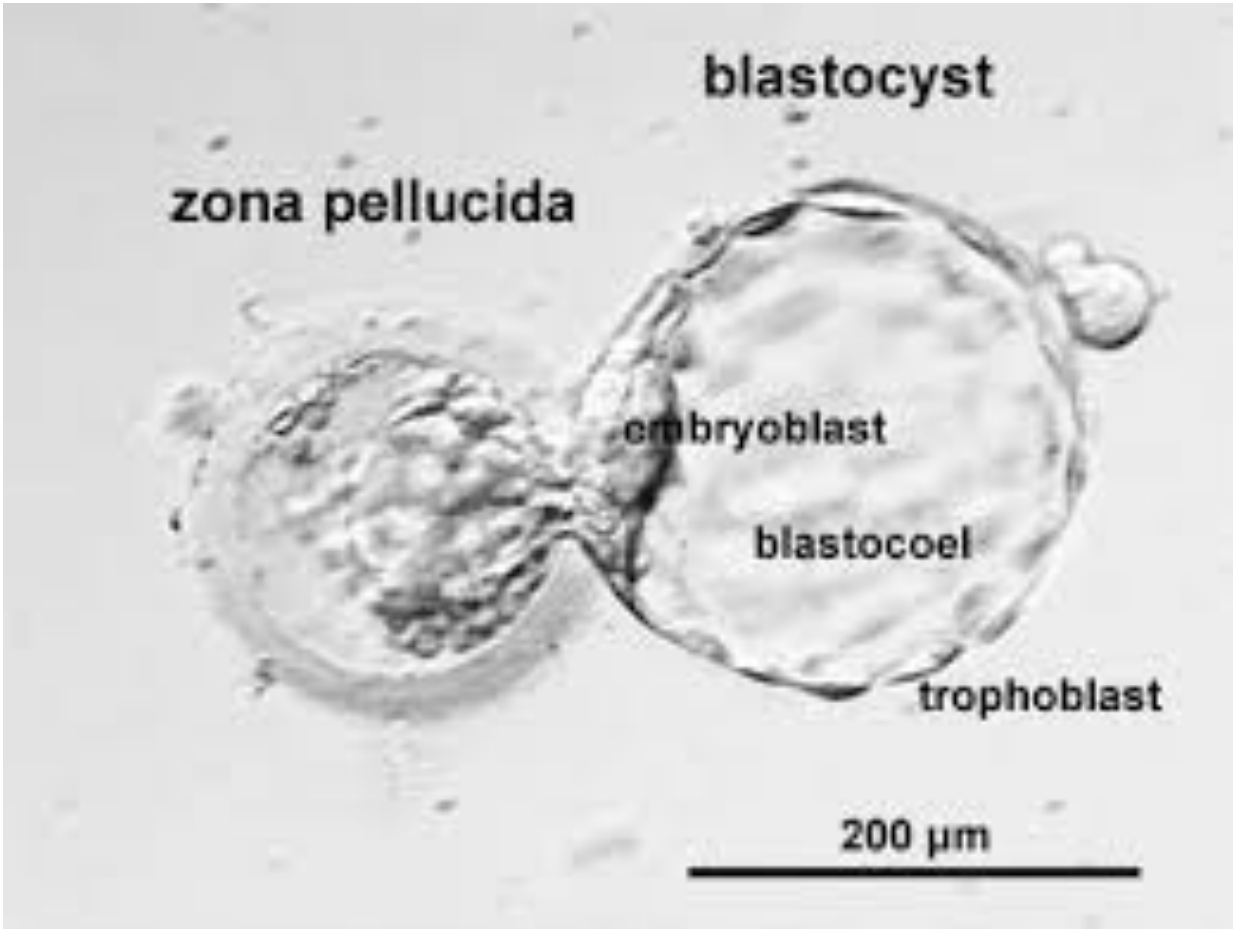
Transport of fertilized ovum

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

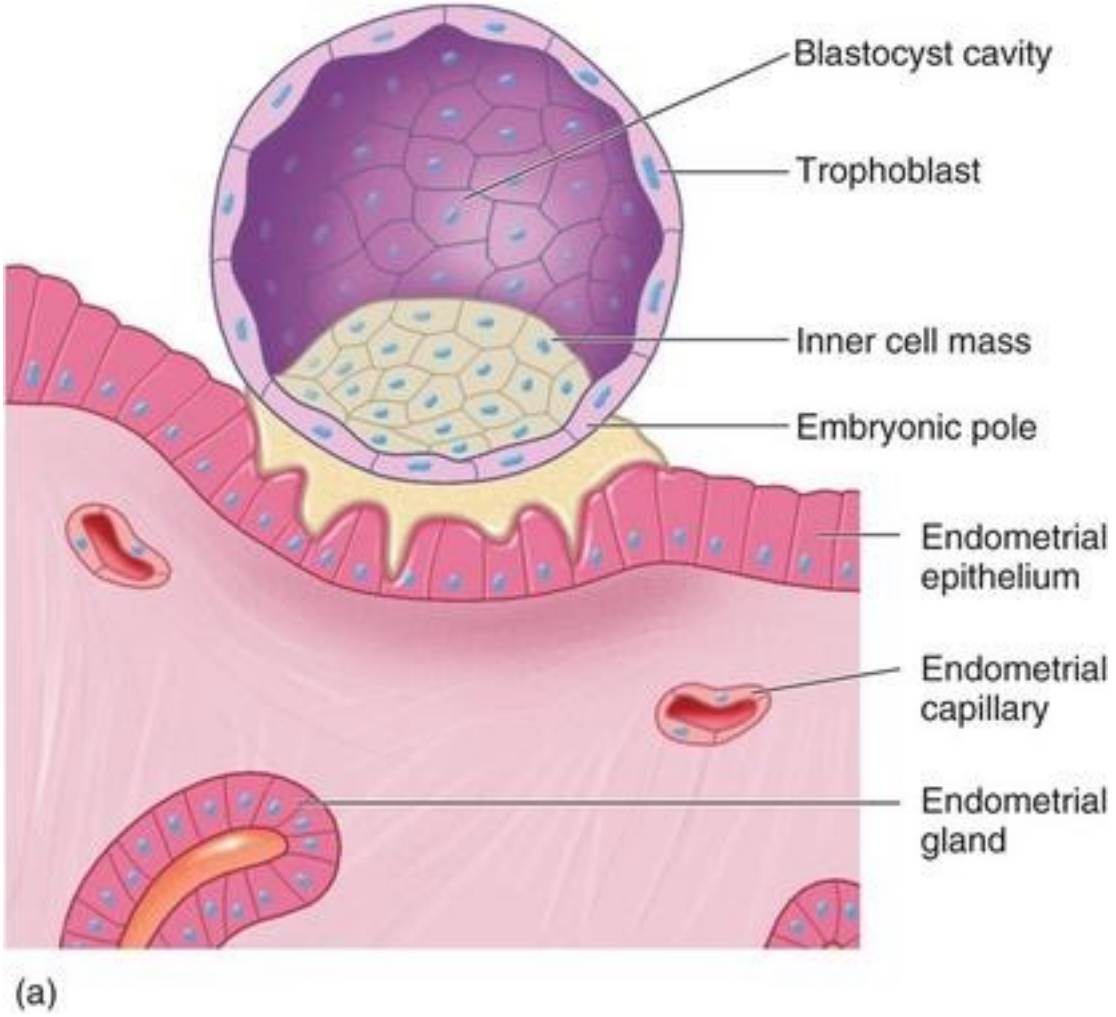
Transport of fertilized ovum



Hatching

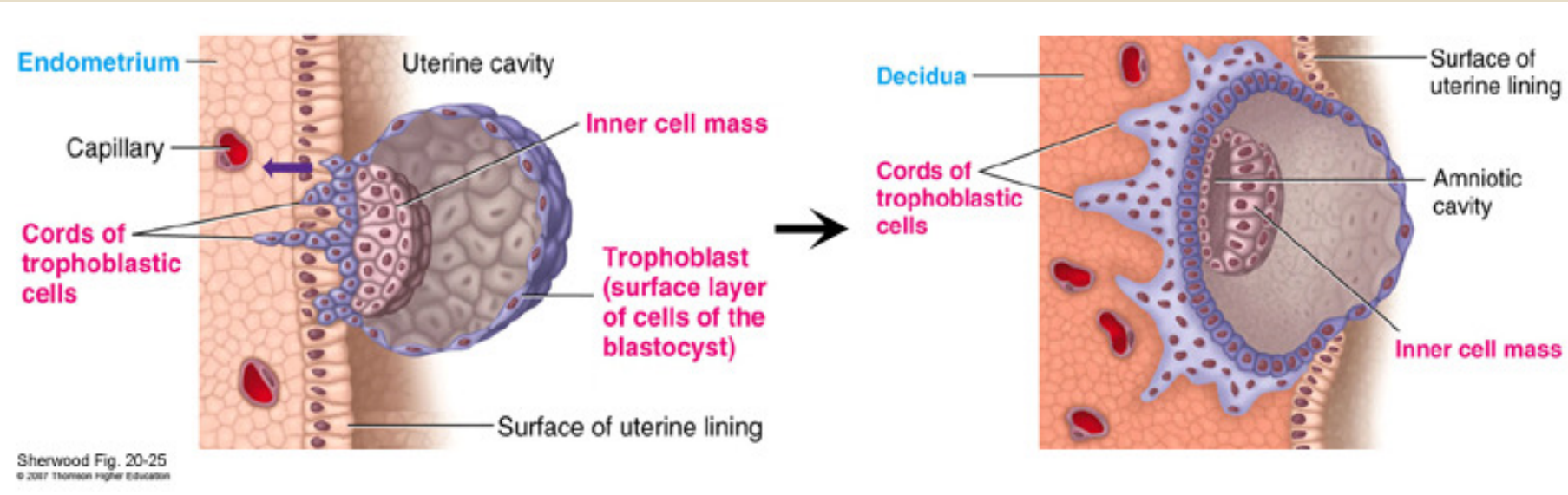

blastocyst
zona pellucida
embryoblast
blastocoel
trophoblast
200 µm

Blastocyst differentiation



Implantation

- Digestion of endometrium
- Decidual cells (glycogen, proteins, lipids & minerals)



(والله أنبتكم من الأرض نباتا)

يسمي علماء الأجنة عملية إنغراس النطفة الأمشاج المنقسمة والتي تعرف باسم الأرومة المتكيسة في جدار الرحم باسم عملية الاستنبات أو الاستزراع

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
- More and more trophoblast projections develop (placental villi)

Placenta

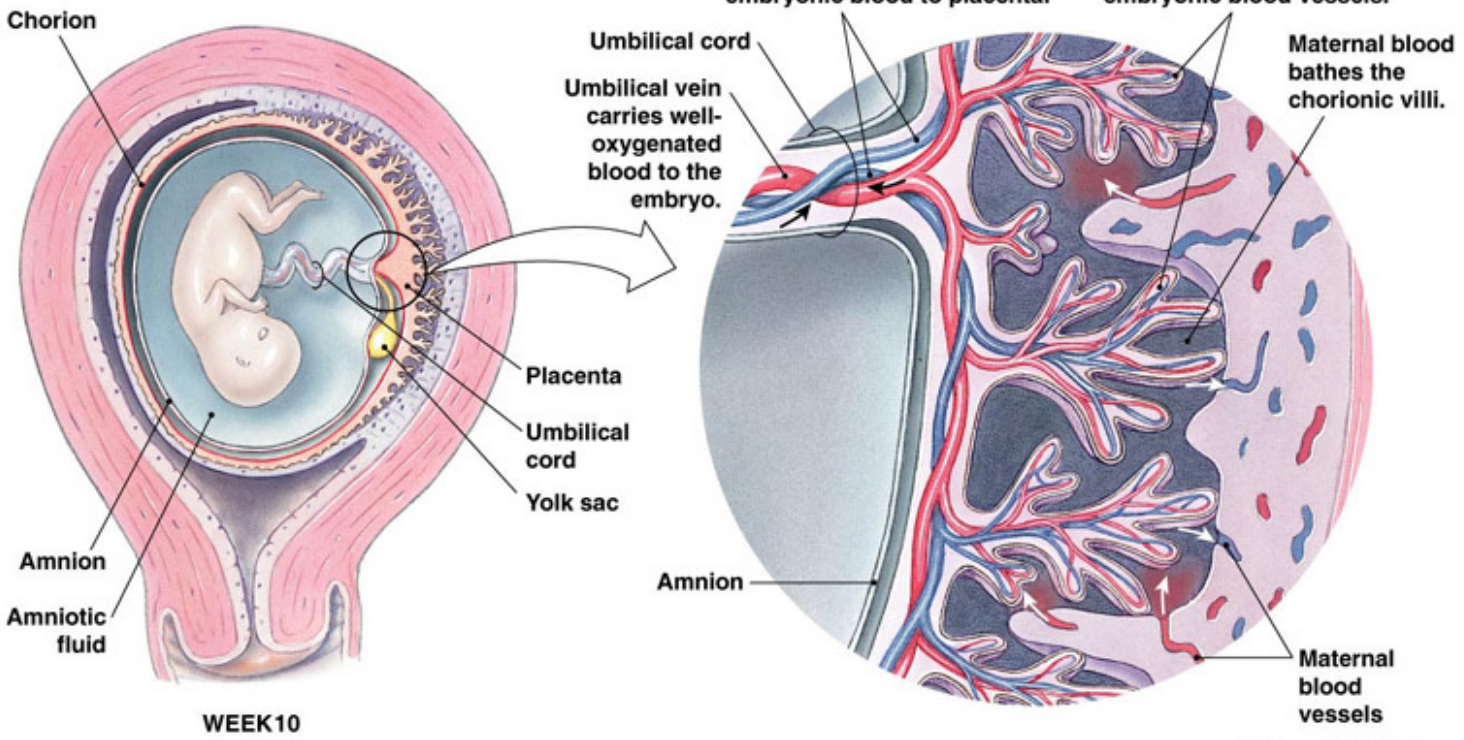
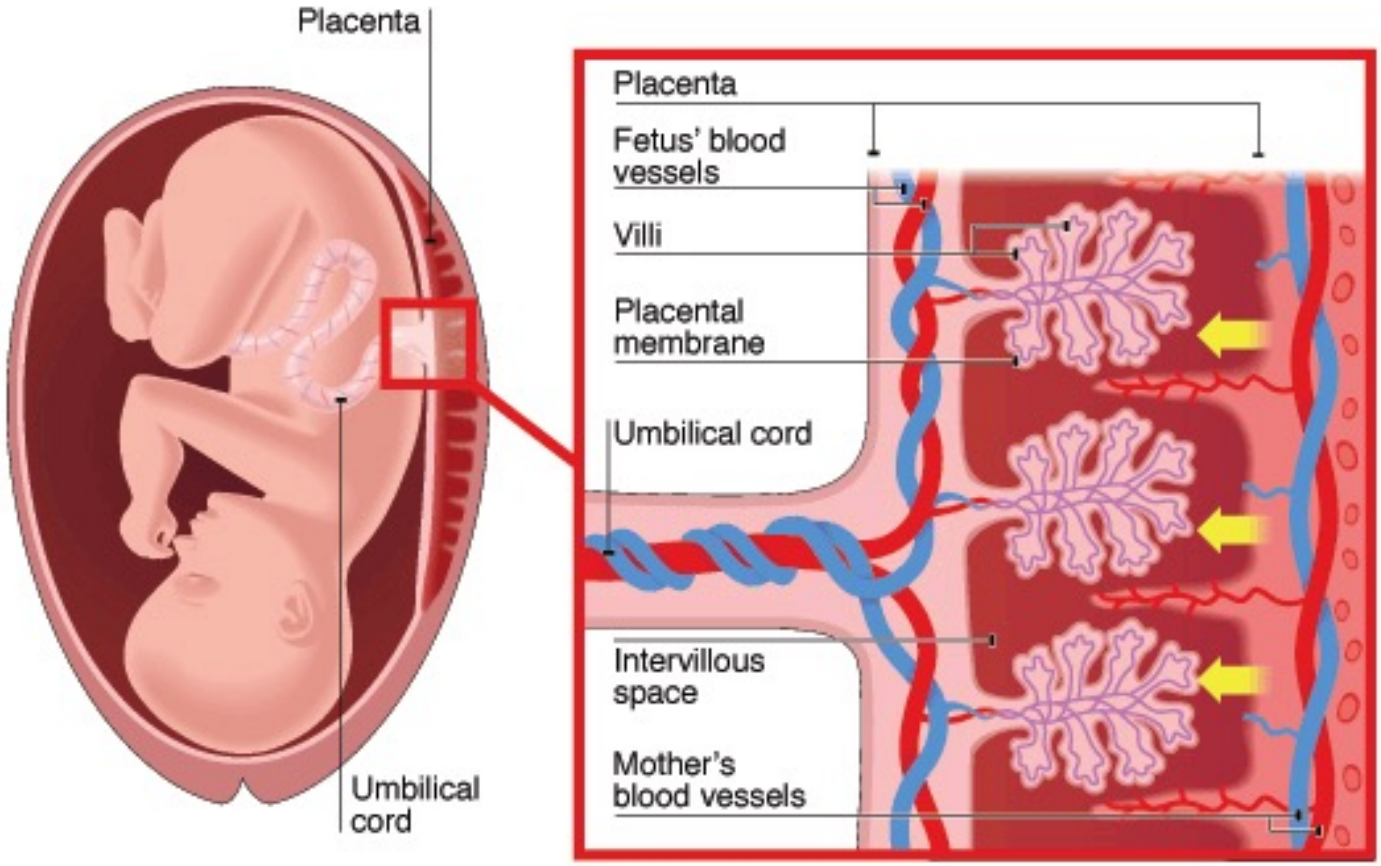


Fig. 26-19

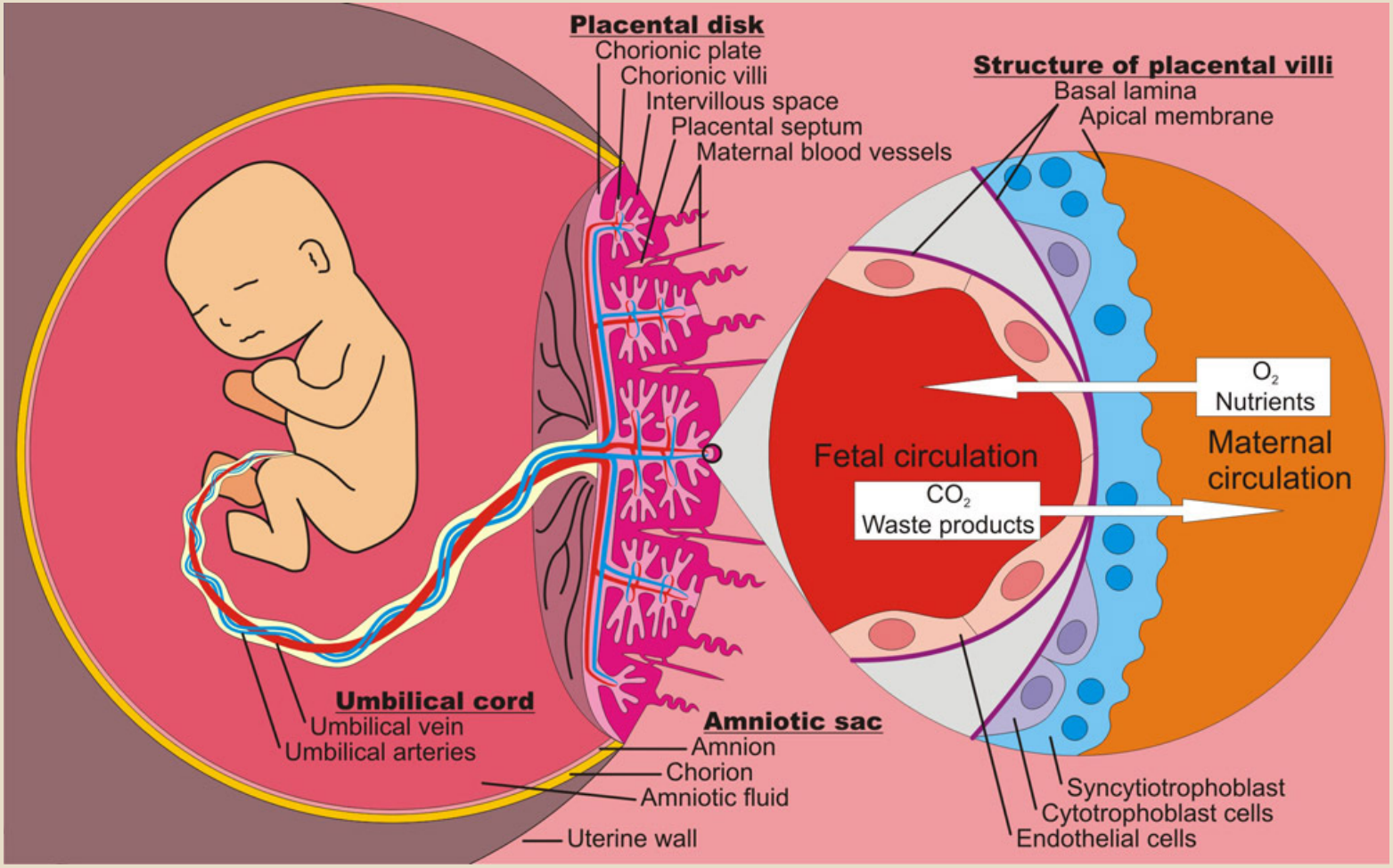

Placenta
Umbilical cord
Placenta
Fetus' blood vessels
Villi
Placental membrane
Umbilical cord
Intervillous space
Mother's blood vessels

Function of the placenta

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

- يَخْلُقُكُمْ فِي بُطُونِ أُمَّهَاتِكُمْ خَلْقًا مِنْ بَعْدِ خَلْقٍ فِي ظُلُمَاتٍ ثَلاثٍ

Respiration

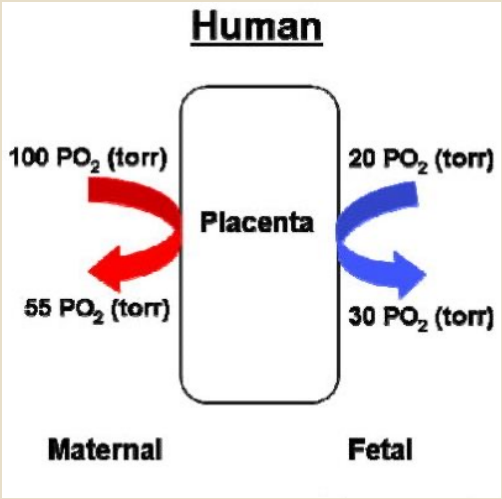


Respiration

- 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

  PO_2 50 mm Hg (M) - 30 mm Hg (F) =20 mmHg

  - At low PO_2HbF carry 20-50% more O_2 than HbA (HbF has a higher oxygen carrying capacity than HbA)
  - HbF conc 50% higher than HbA in mother



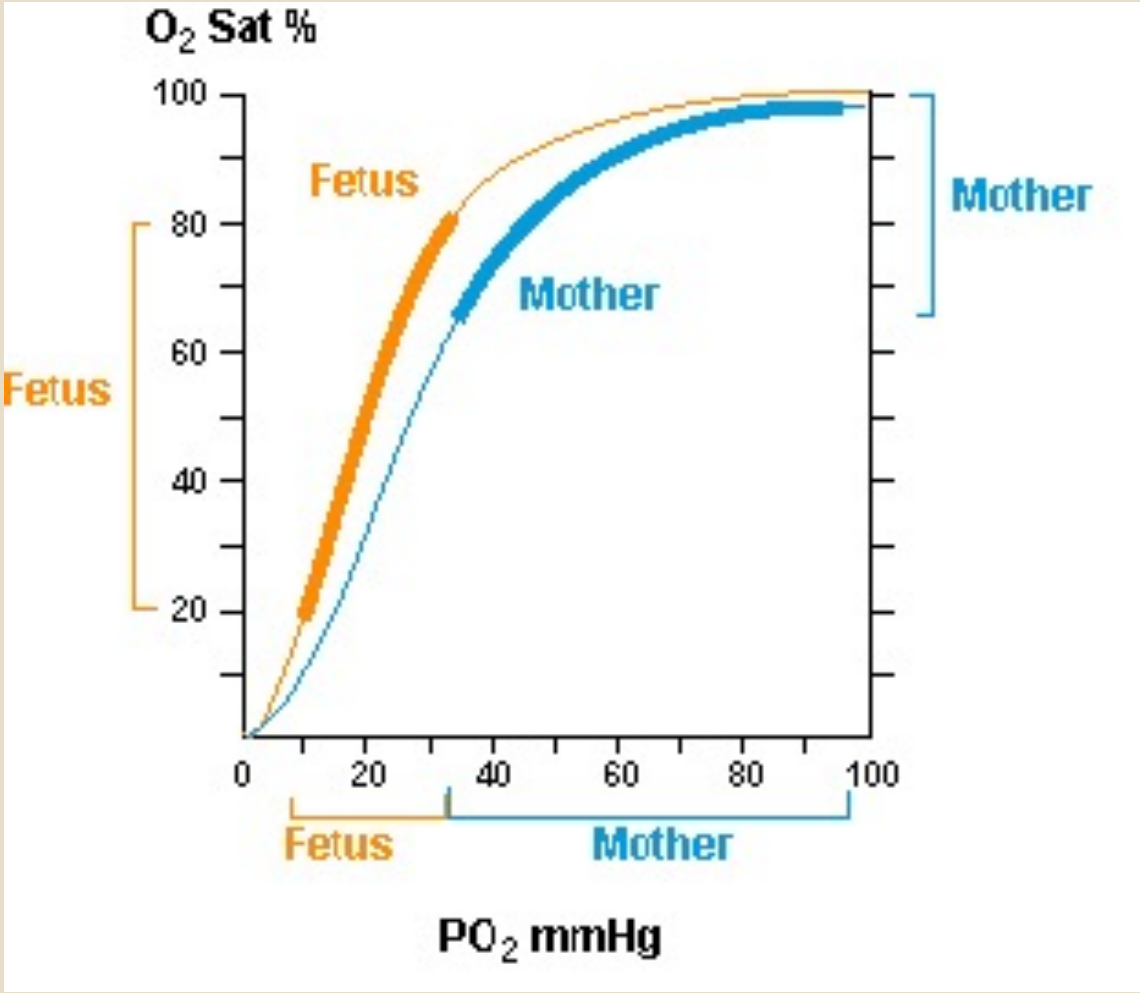
Respiration

- 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.

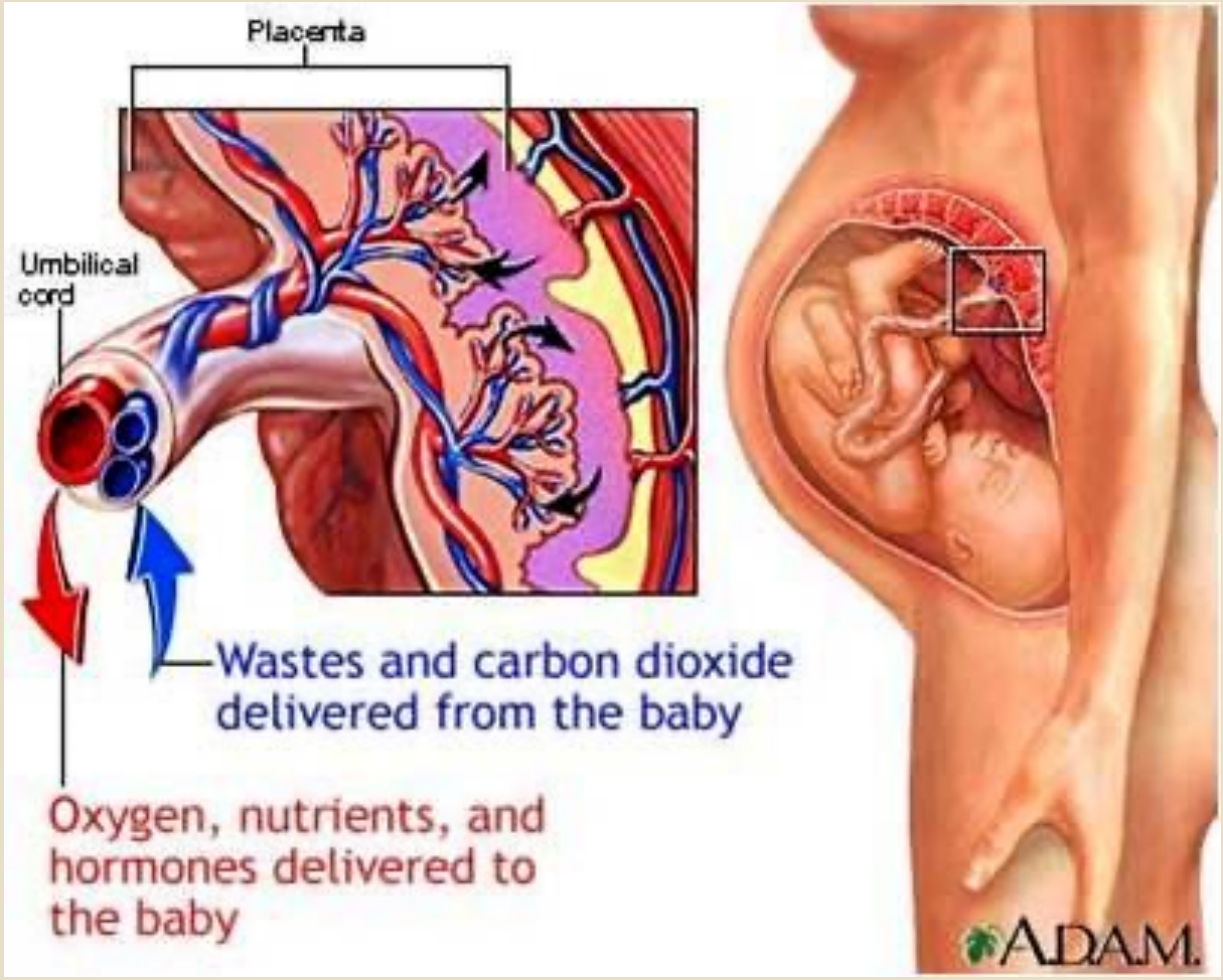
Oxygen dissociation curve



Important factors facilitate 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.

Respiration



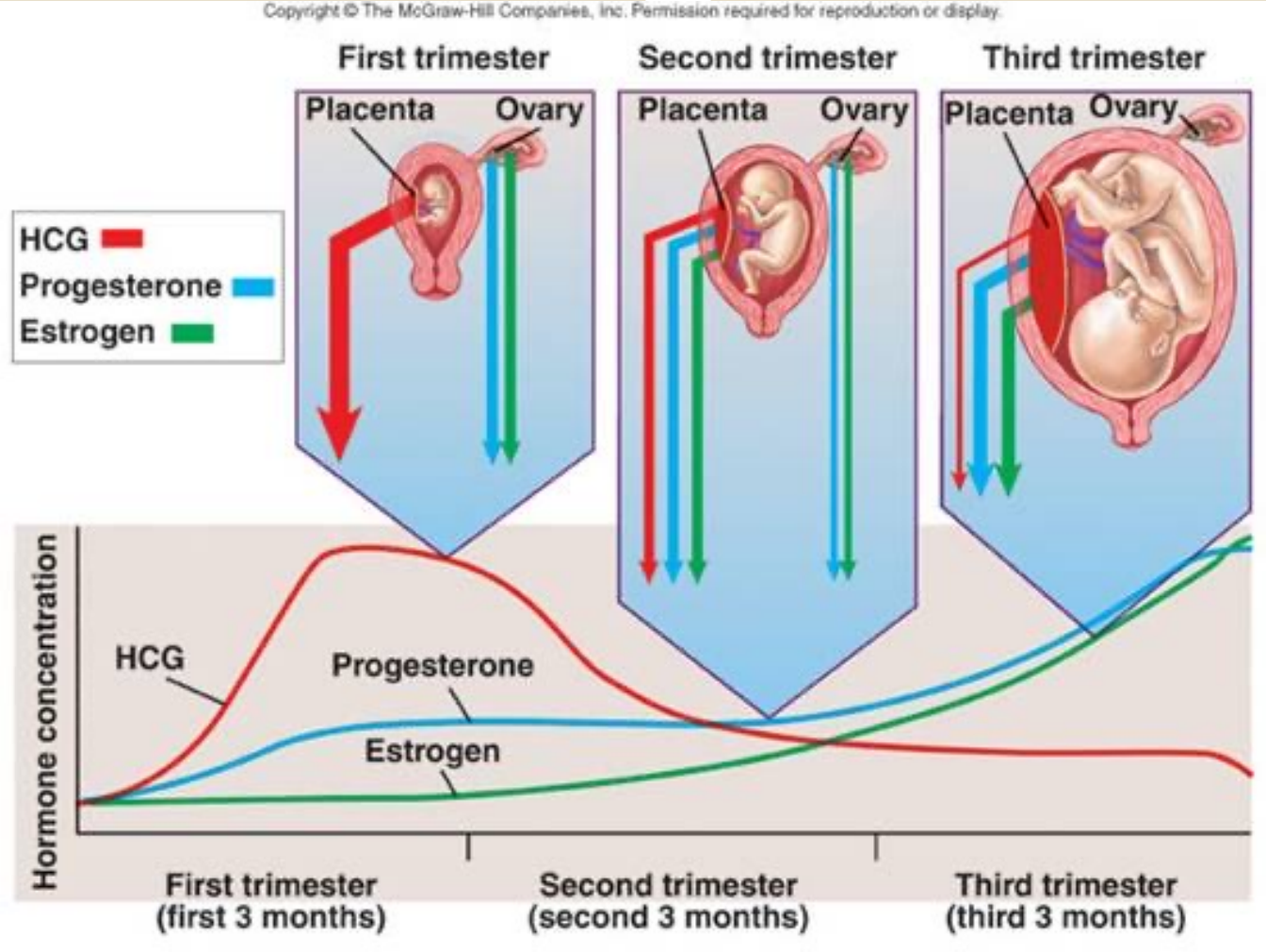
Nutrition

- 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 insures continuous diffusion of these substances to the maternal blood

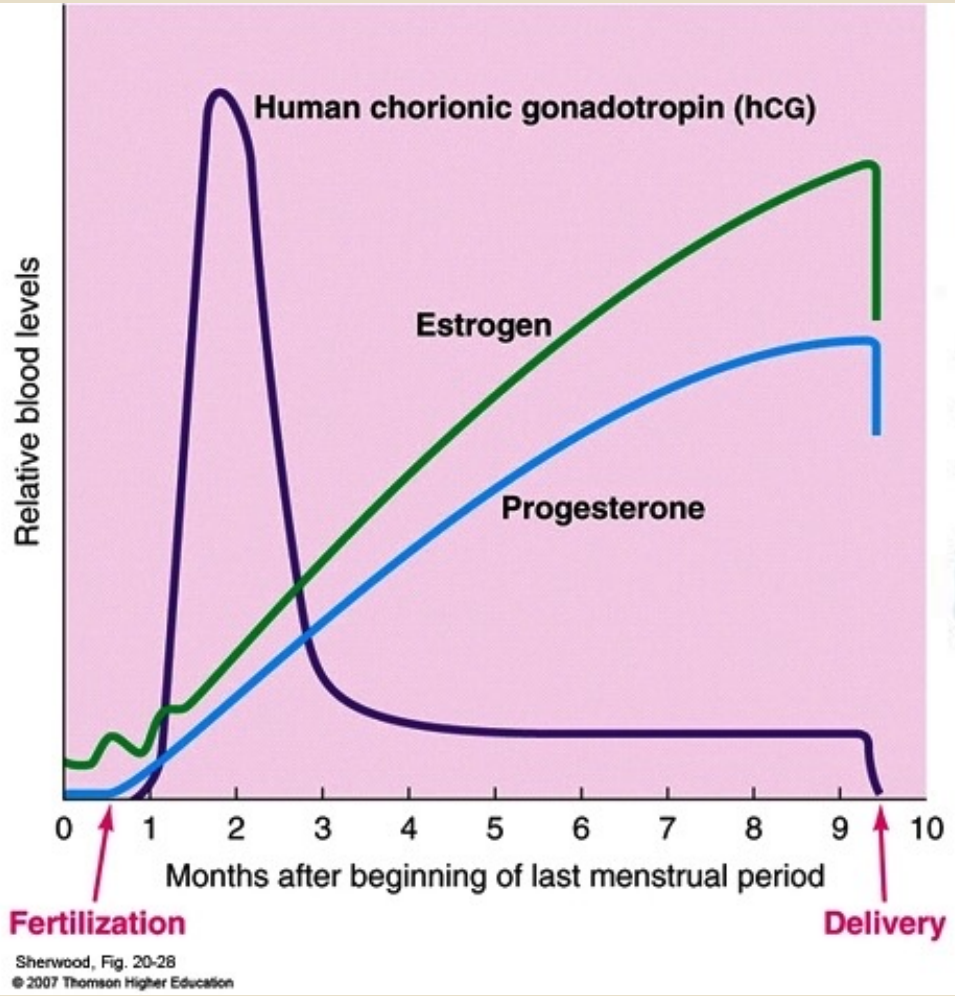
Endocrine


Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.
First trimester
Second trimester
Third trimester
Placenta
Ovary
HCG
Progesterone
Estrogen
Hormone concentration
First trimester (first 3 months)
Second trimester (second 3 months)
Third trimester (third 3 months)

Endocrine

- 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)

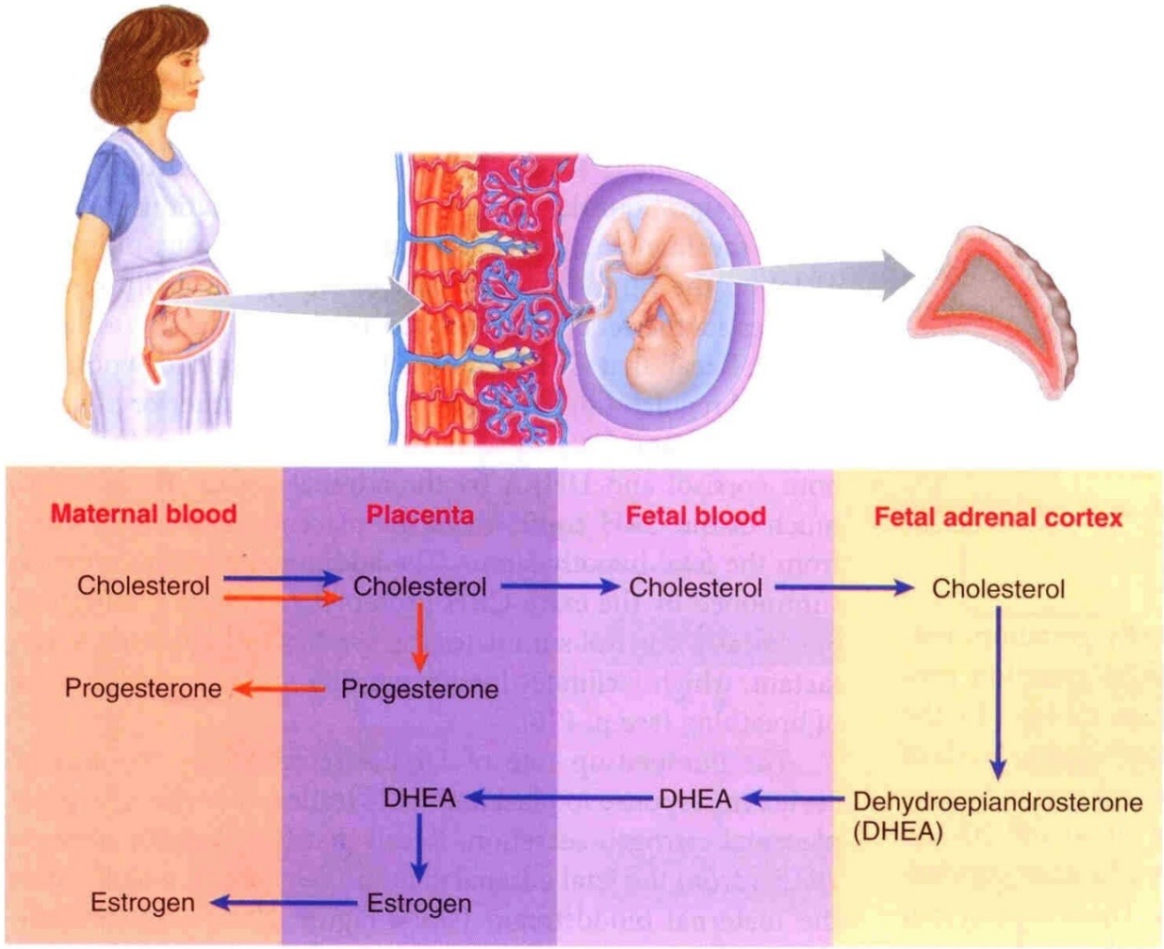


Endocrine

- 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 ducts & external genitalia
  - **Relaxation** of pelvic ligaments in preparation to labor
  - **Activation** of the uterus (gap junctions)

Endocrine

- Progsterone
  - Steroid hormone
  - Secreted by **syncytial trophoblast** cells
  - Towards end of pregnancy reaches **10×**
  - Derived from **cholesterol**
- Functions in the mother
  - **Development** of the breast lobules.
  - **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)*.

Endocrine

- Human Chorionic Somatomamotropin
  - Protein hormone
  - Secreted by **placenta around 5th gestational week**
- Functions in the mother
  - Breast development (hPL)
  - Weak growth hormone‘s action
  - Inhibit insulin sensitivity =↓ glucose utilization
  - Promote release of fatty acids

Endocrine

- 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 40%)

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× RR**) 50%
  - Progesterone ↑ sensitivity of respiratory center (RC) to CO_2 leading to ↑ RR


فاعلم أنه
لا إله إلا الله
محمد رسول الله