Reproductive Physiology

Lecture 6

Physiology of Pregnancy

GUYTON & HALL, Chapter 82

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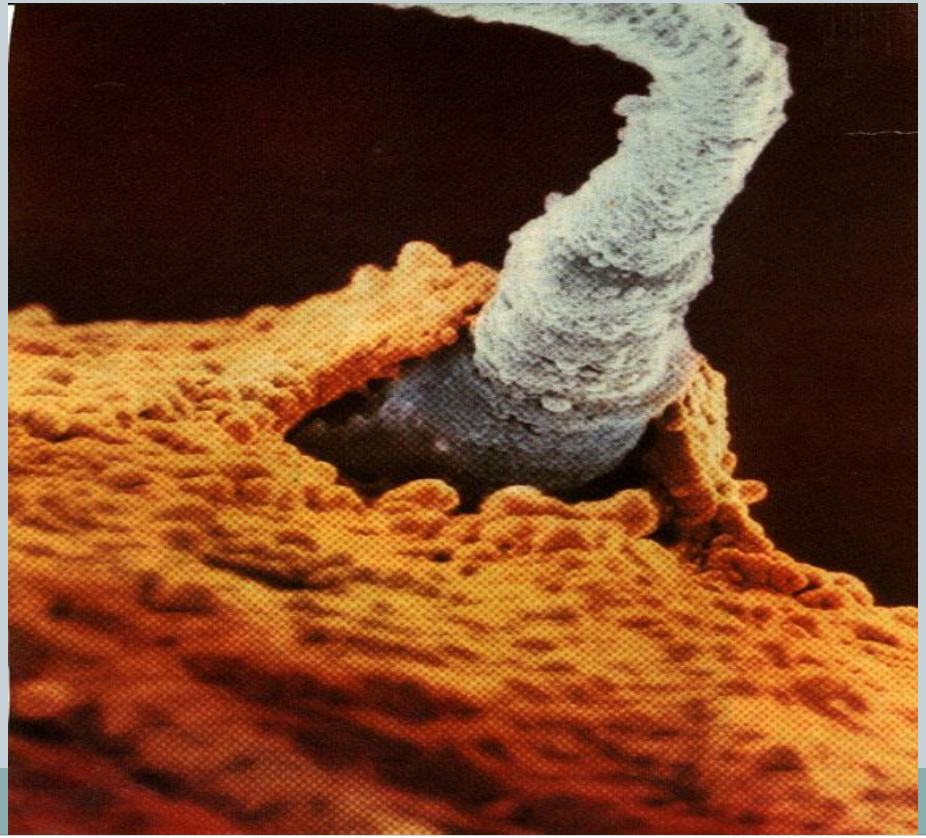
Objectives

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

- 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

Fertilization

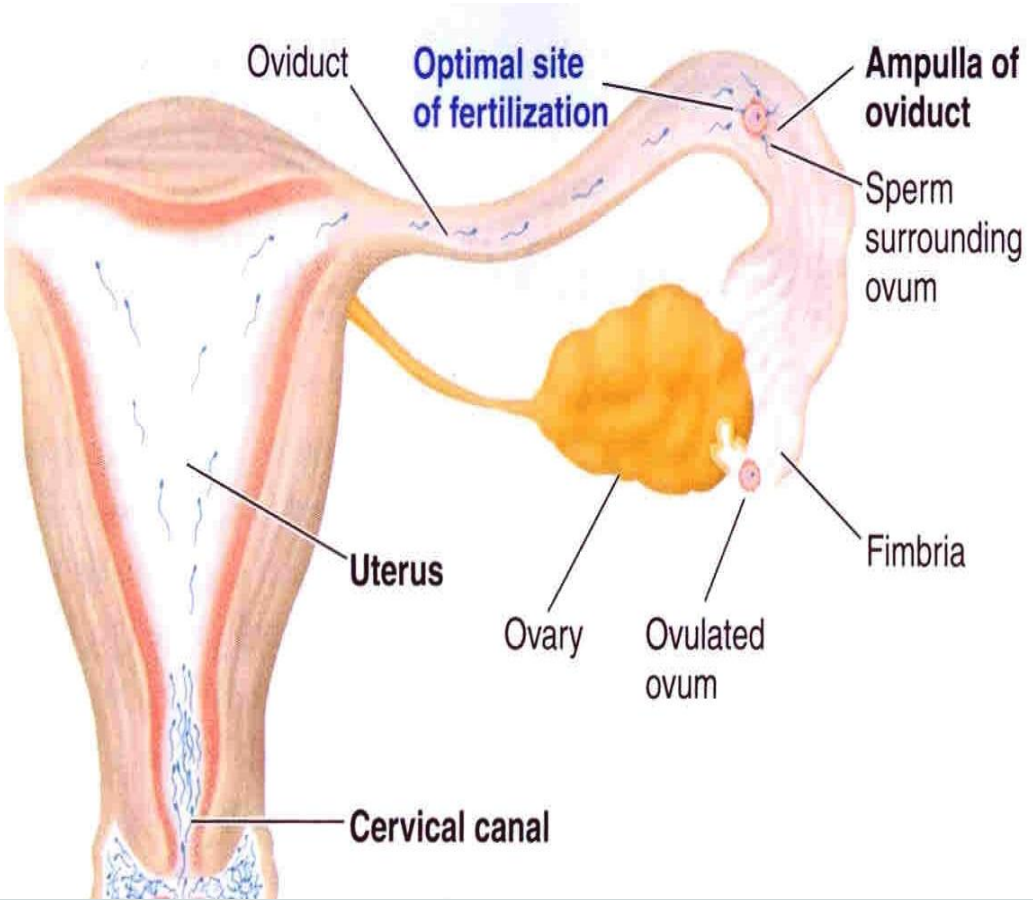
If the ovum becomes fertilized by a sperm, a new sequence of events called ***gestation*** or ***pregnancy*** takes place, and the fertilized ovum eventually develops into a full-term fetus.



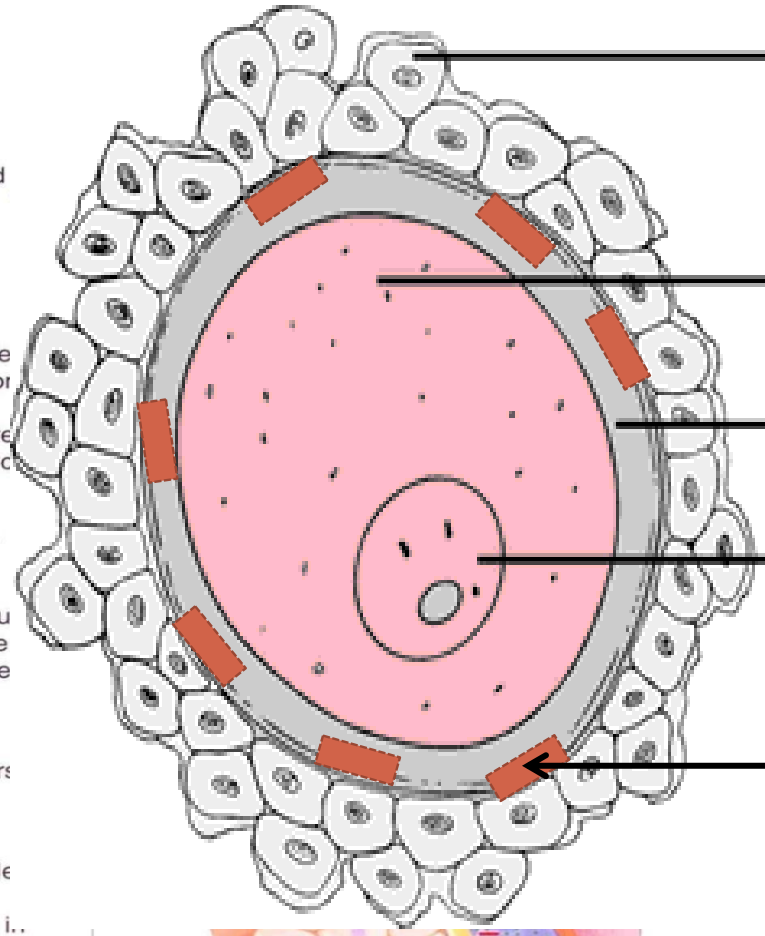
Fertilization

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

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.

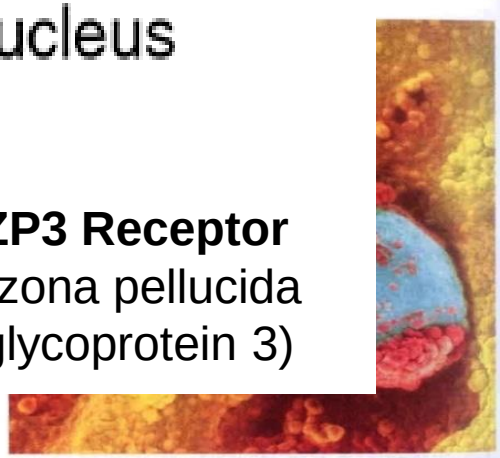
2 Binding of sperm to these receptors triggers the acroso reaction, in which hydrolytic enzymes in the acrosome are released onto the zona pellu

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

4 The sperm nucleus enters the ovum cytoplasm.

5 The sperm stimulates rele of Ca^{2+} stored in cortical granules in the ovum, which i.. 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

Fertilization

- Oocyte divides to form **mature ovum** (female pronucleus 23 unpaired chr.)
- Head of sperm swells (male pronucleus 23 unpaired chr)
- Fertilized ovum (zygote) contains 23 paired chr.

The 23 chr. of the male and female pronuclei align themselves to re-form a complete complement of 46 chromosomes

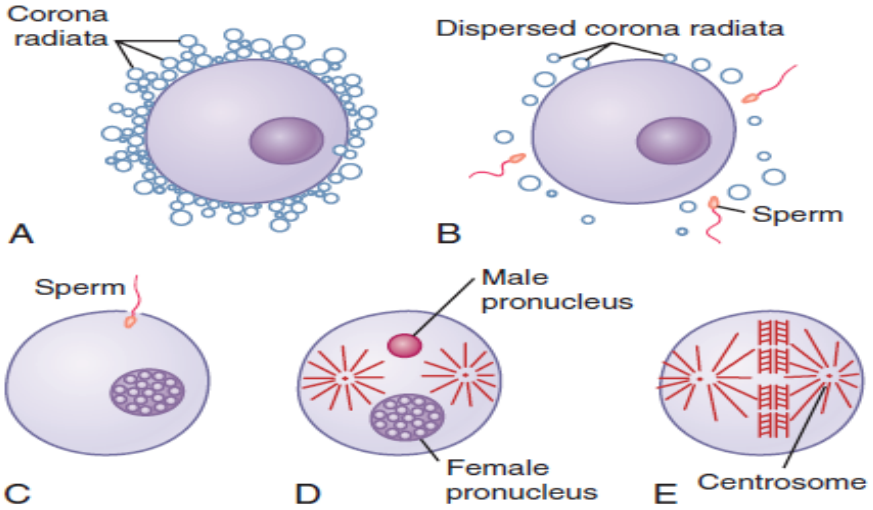
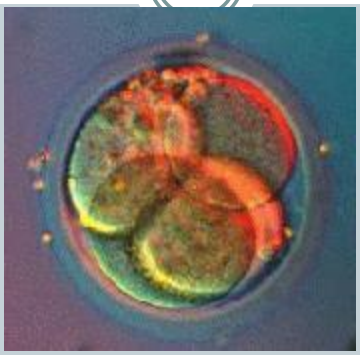


Figure 83-1. Fertilization of the ovum. **A,** The mature ovum surrounded by the corona radiata. **B,** Dispersal of the corona radiata. **C,** Entry of the sperm. **D,** Formation of the male and female pronuclei. **E,** Reorganization of a full complement of chromosomes and beginning division of the ovum. *(Modified from Arey LB: Developmental Anatomy: A Textbook and Laboratory Manual of Embryology, 7th ed. Philadelphia: WB Saunders, 1974.)*

Zygote

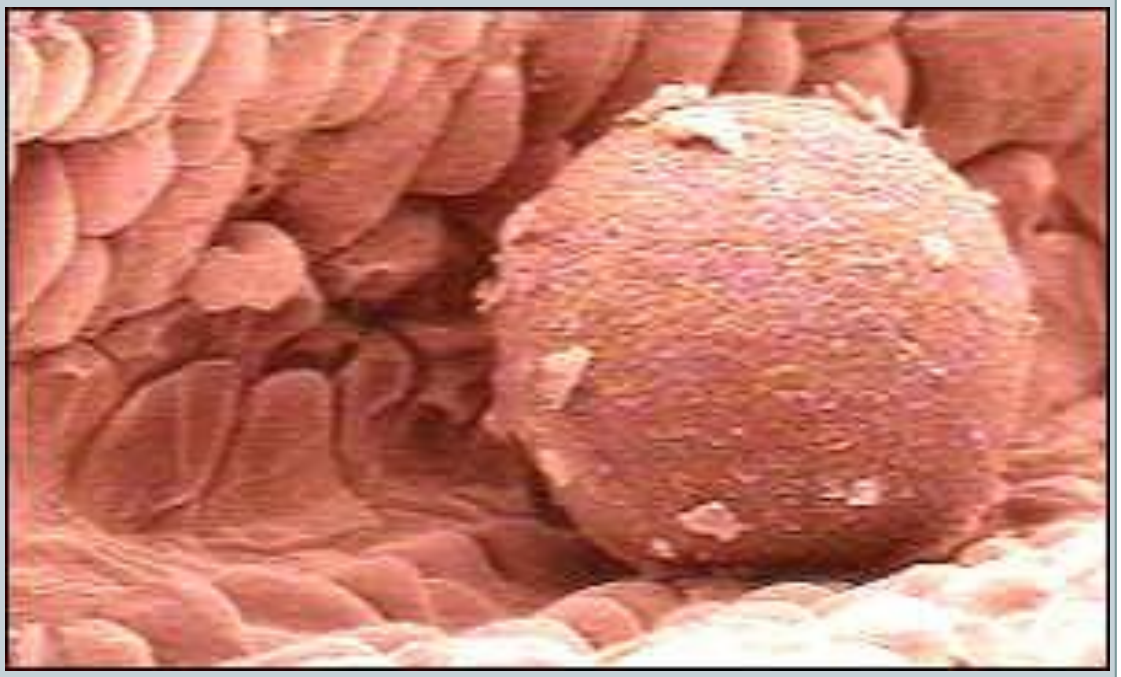
Cleavage


- 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 (morula)

Traveling

- Zygote begins to divide as it travels through oviduct.
- Implants into lining of uterus (endometrium).

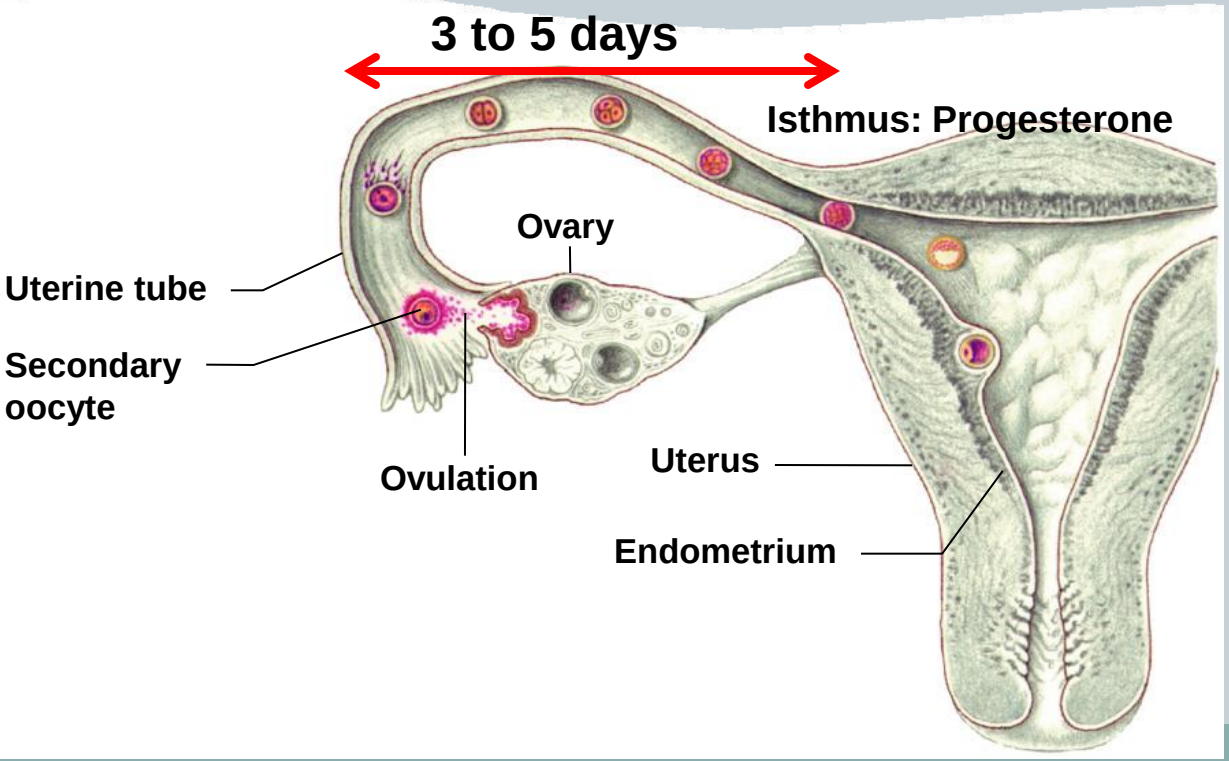


Transport of fertilized ovum

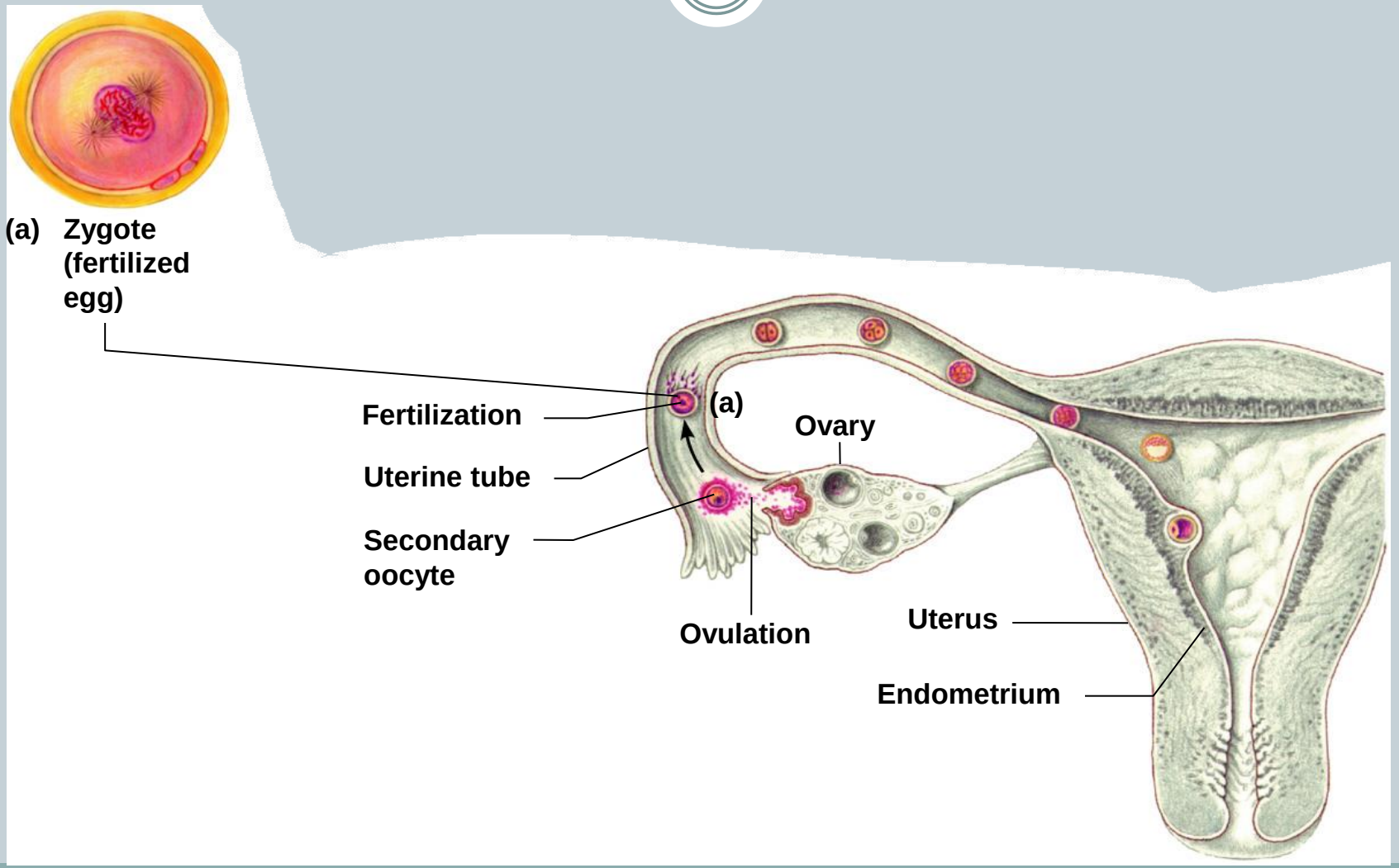
Transport: fluid current + action of cilia + weak contractions of the fallopian tube

Delayed transport allows cell division to occur before the dividing ovum

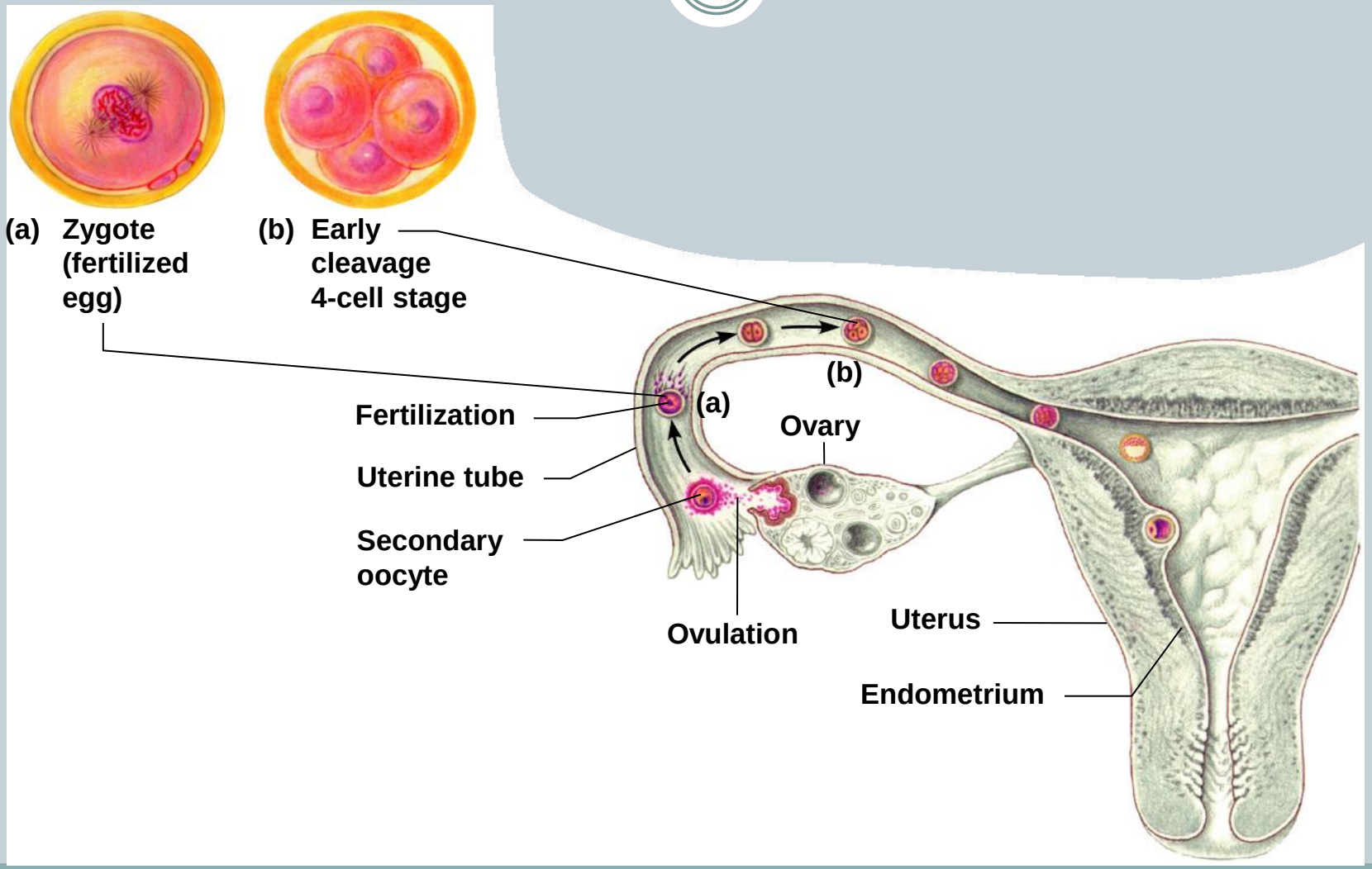
(Blastocyst ~100 cells) enters the uterus



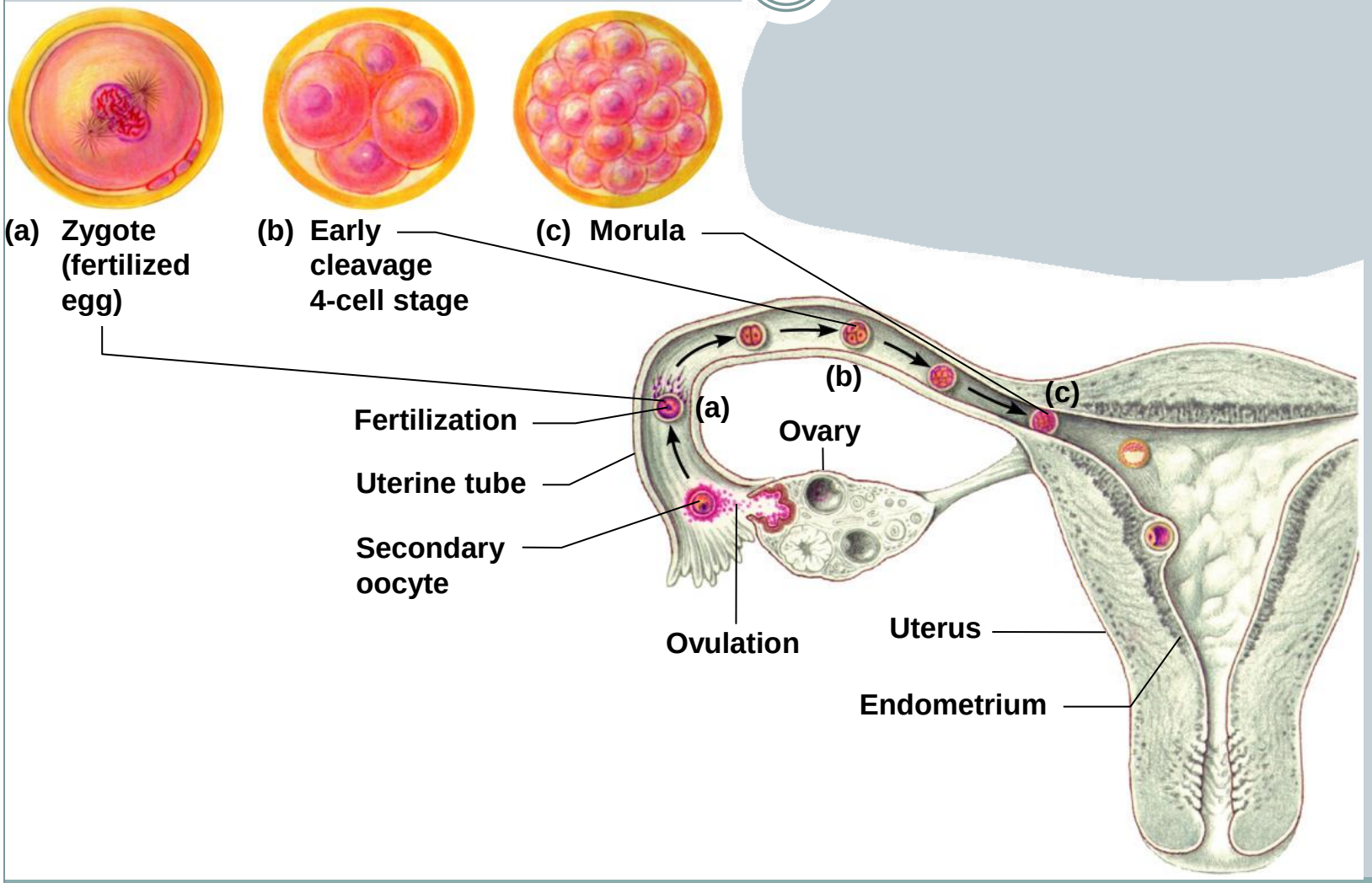
Cleavage


(a) Zygote (fertilized egg)
Fertilization
Uterine tube
Secondary oocyte
Ovulation
(a)
Ovary
Uterus
Endometrium

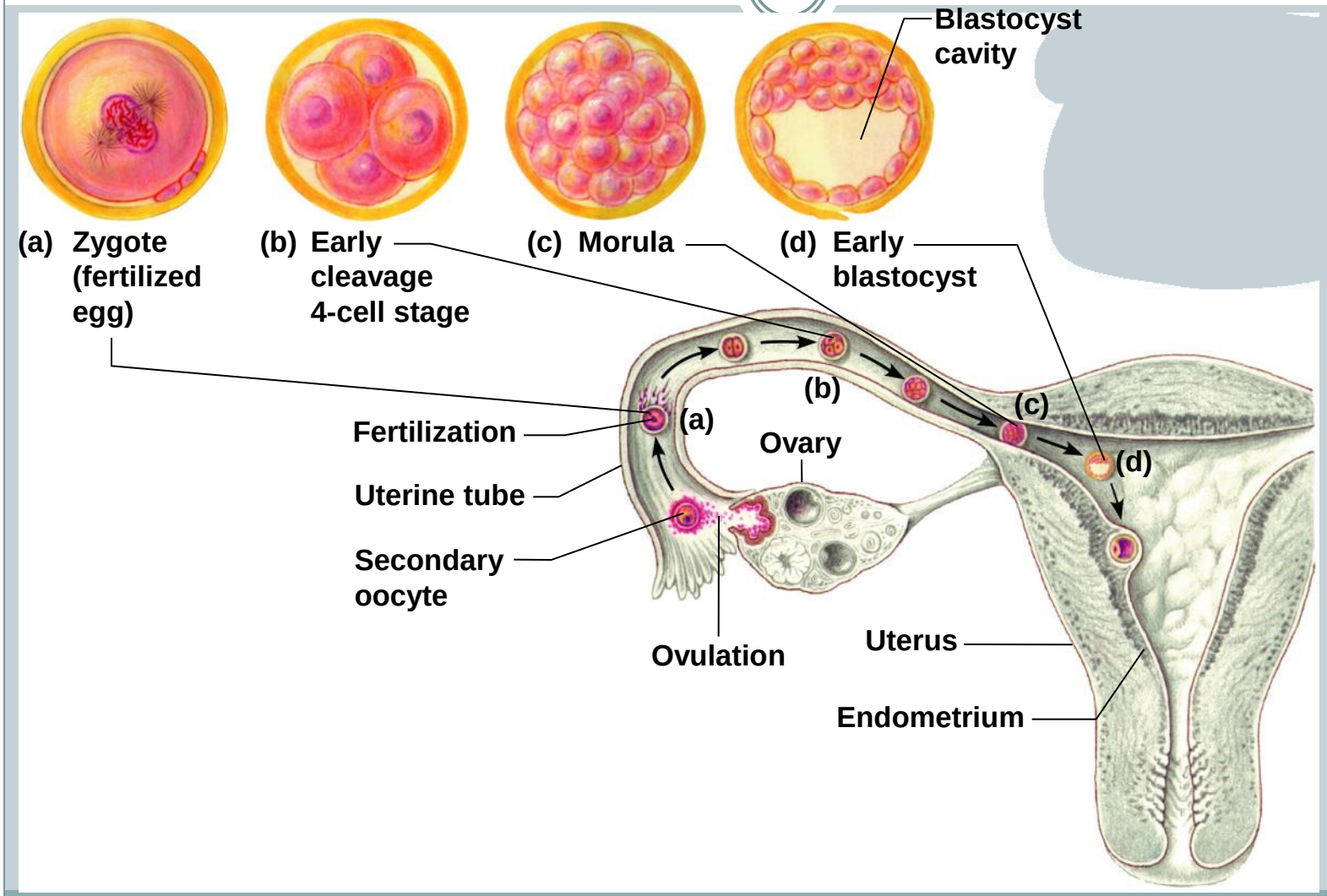
Cleavage


(a) Zygote (fertilized egg)
(b) Early cleavage 4-cell stage
Fertilization
Uterine tube
Secondary oocyte
Ovulation
(a)
(b)
Ovary
Uterus
Endometrium

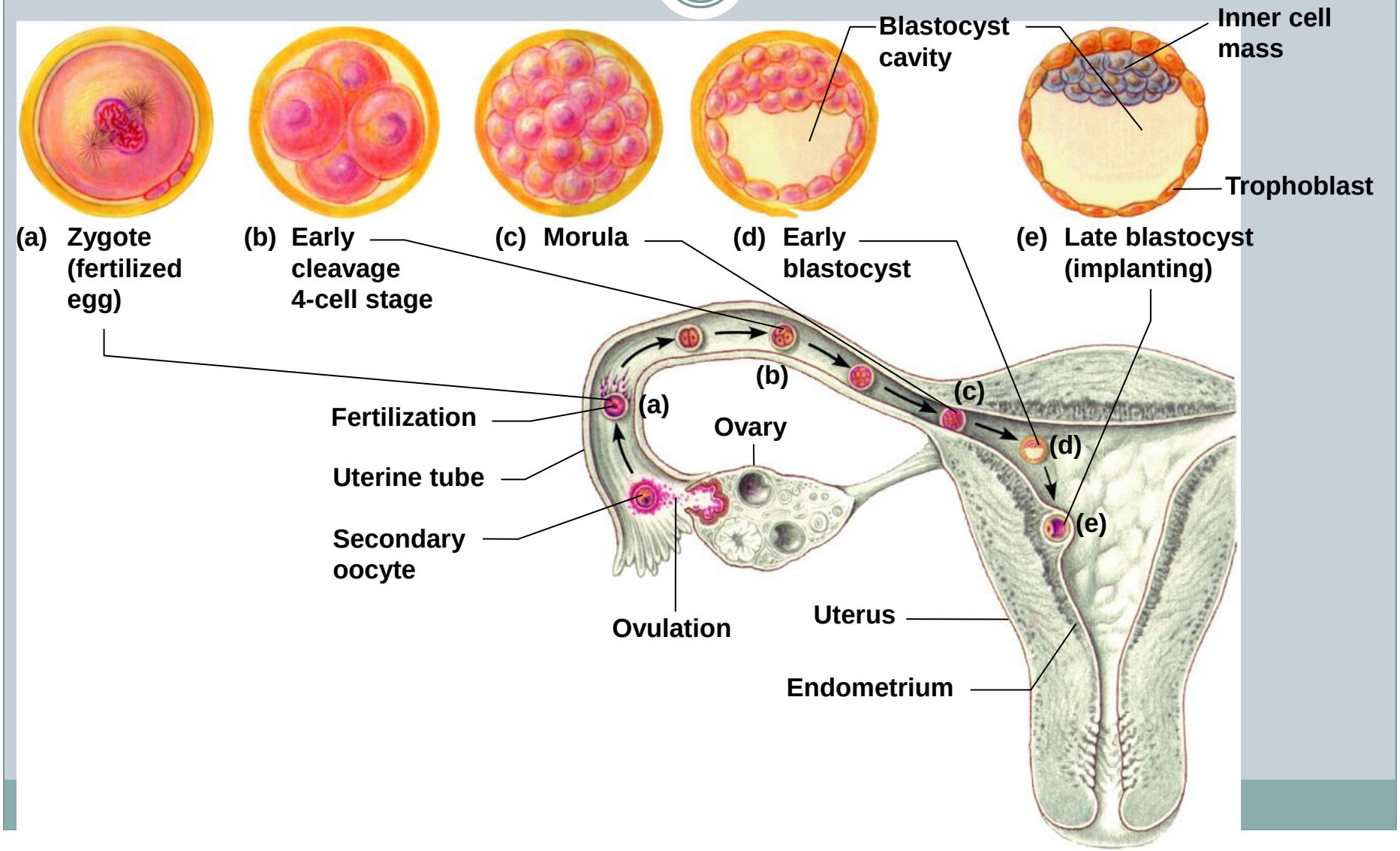
Cleavage


(a) Zygote (fertilized egg)
(b) Early cleavage 4-cell stage
(c) Morula
Fertilization
Uterine tube
Secondary oocyte
Ovulation
(a)
(b)
(c)
Ovary
Uterus
Endometrium

Cleavage


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

Cleavage

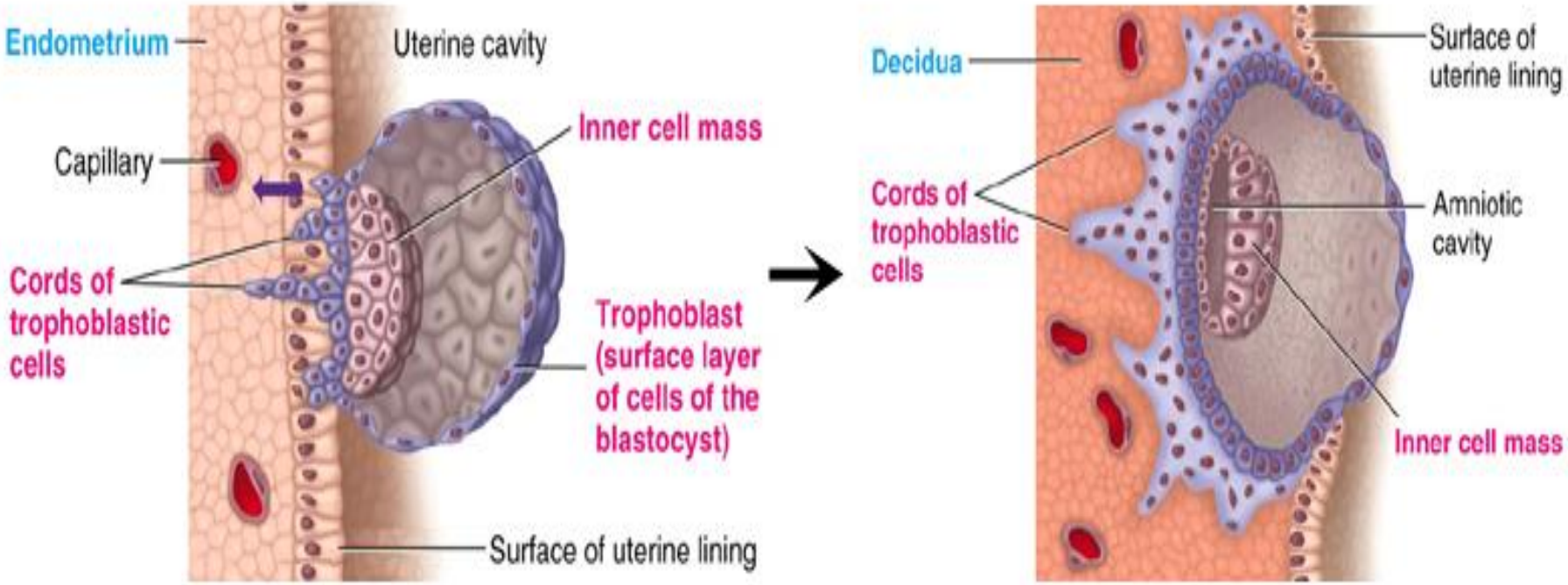

Blastocyst cavity
Inner cell mass
Trophoblast
(a) Zygote (fertilized egg)
(b) Early cleavage 4-cell stage
(c) Morula
(d) Early blastocyst
(e) Late blastocyst (implanting)
Fertilization
Uterine tube
Secondary oocyte
Ovulation
Ovary
Uterus
Endometrium

Implantation

- Implantation occurs on 5-7 day after ovulation.
- 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.

Implantation

Blood sinuses supplied with blood from the mother develop around the outsides of the trophoblastic cords.



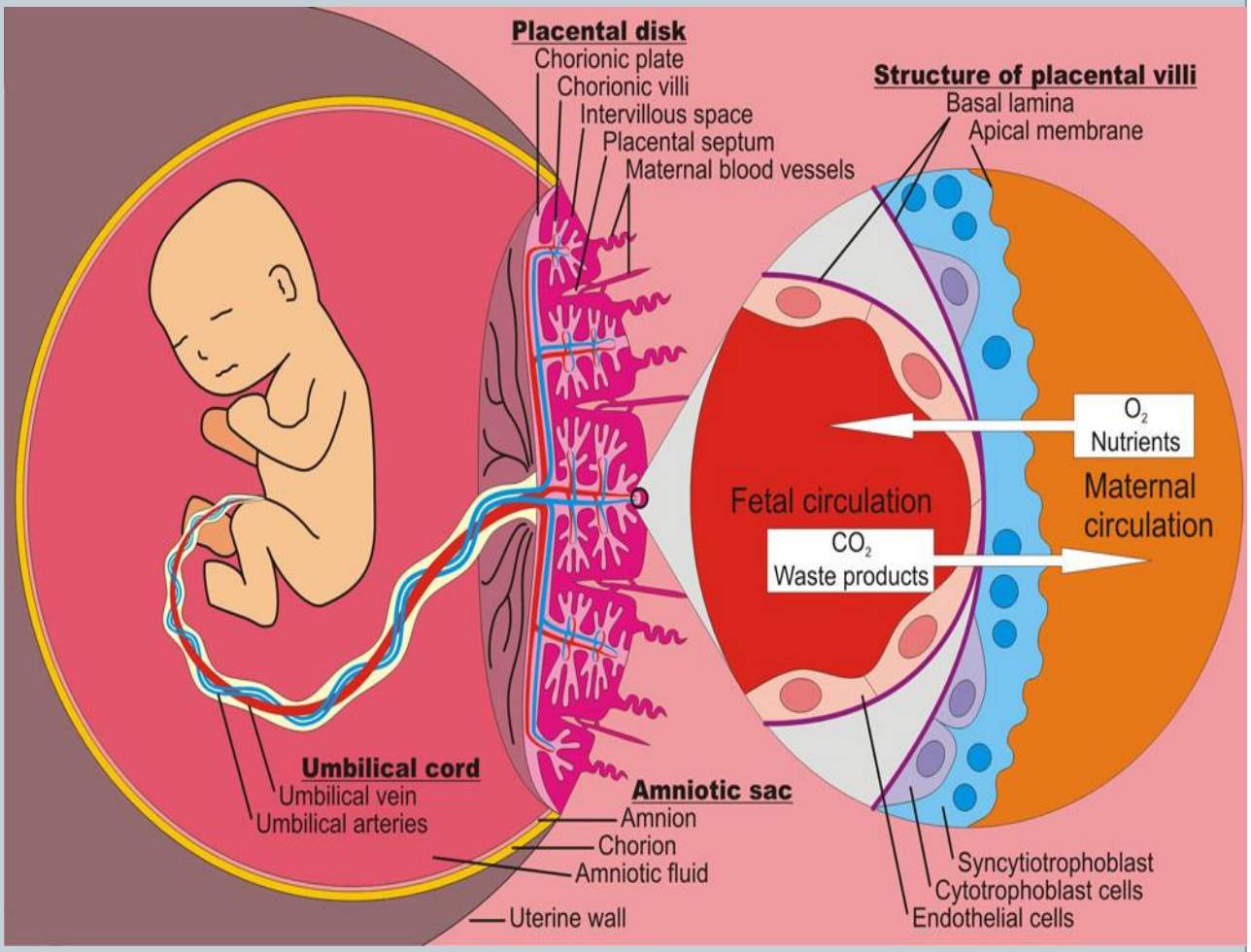
While the trophoblastic cords from the blastocyst are attaching to the uterus, blood capillaries grow into the cords from the vascular system of the newly forming embryo.

More and more trophoblast projections develop (placental villi)

Function of the Placenta

Major functions

- Respiration
- Nutrition
- Excretion
- Endocrine
- Protection

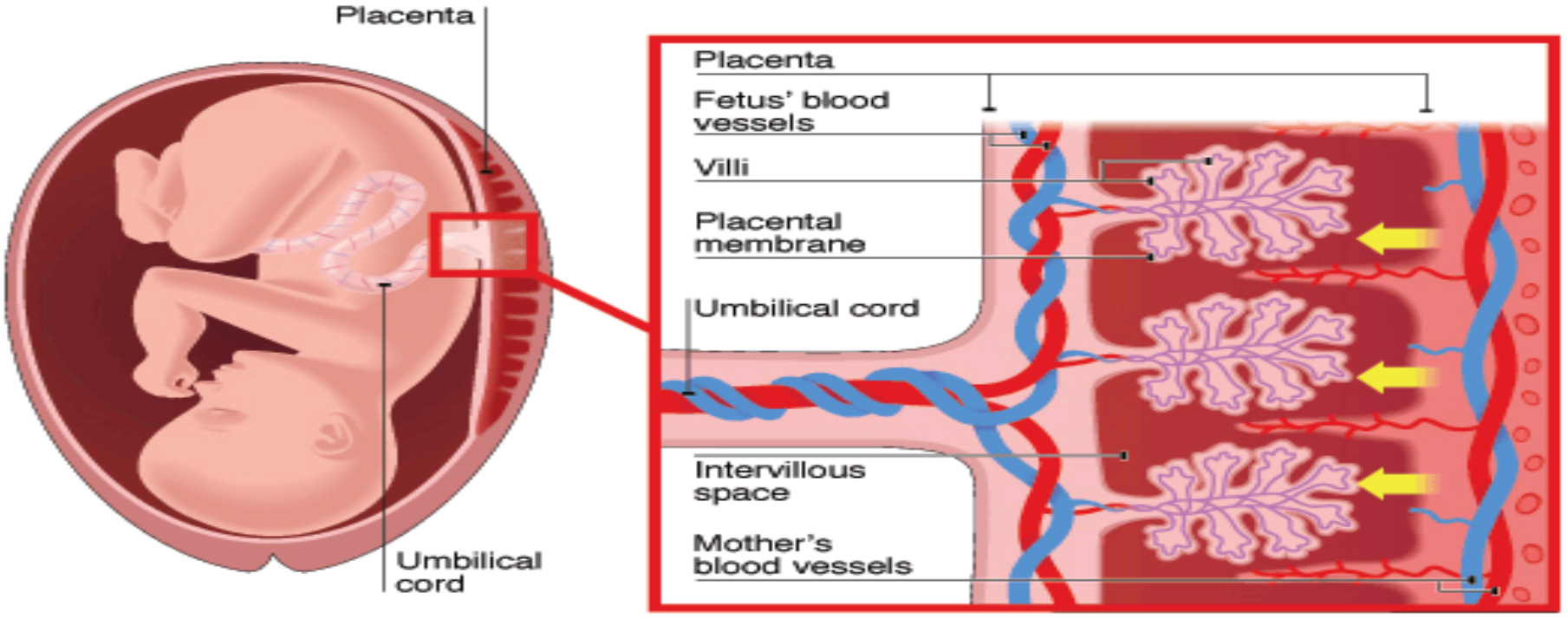


Placental permeability and membrane diffusion conductance

In the early months of pregnancy, the placental membrane is still thick because it is not fully developed.

The surface area is small because the placenta has not grown.

In later pregnancy, the permeability increases because of thinning of the membrane diffusion layers and because the surface area expands many times over.



Important factors facilitating delivery of oxygen to the fetal tissues

Diffusion of oxygen through the placental membrane

- The mean partial pressure of oxygen (PO2) of the mother's blood in the placental sinuses is about 50 mm Hg, and the mean PO2 in the fetal blood after it becomes oxygenated in the placenta is about 30 mm Hg.

50 mm Hg – 30 mm Hg = **20** mm Hg (mean pressure gradient)

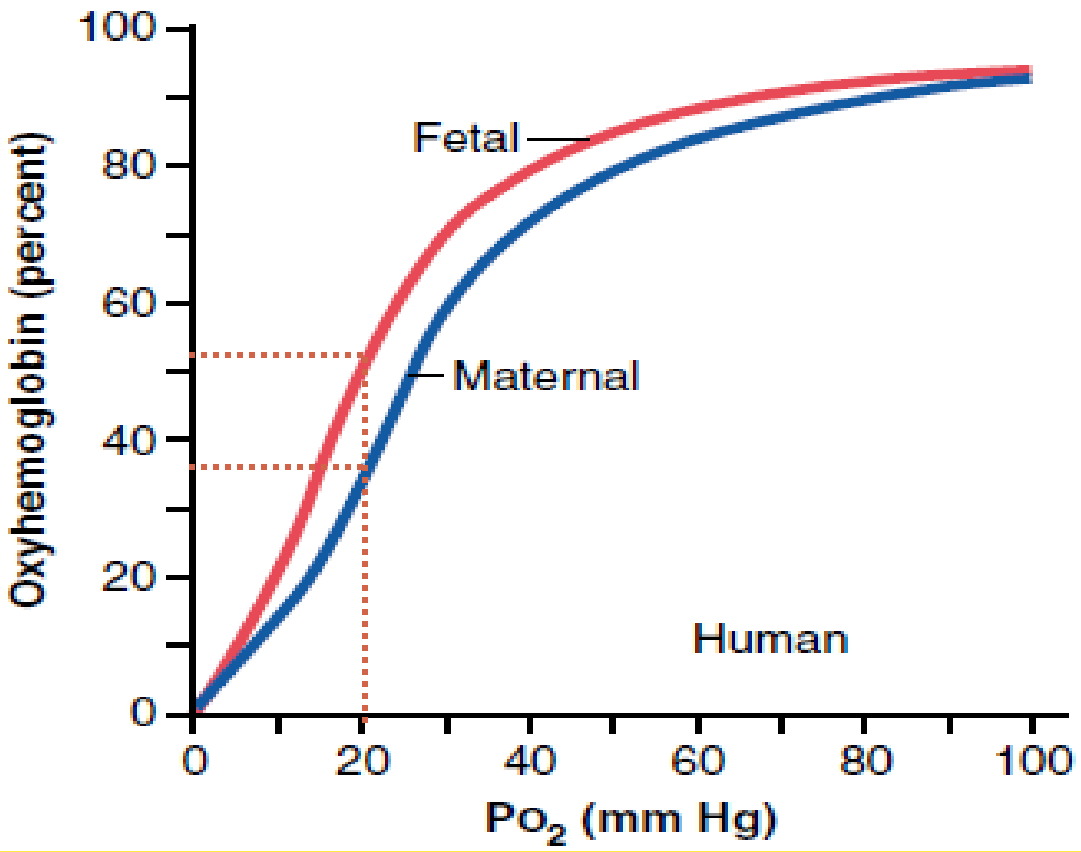
- There are <u>three reasons</u> why this low PO2 is sufficient to deliver O2 to the fetal tissues:

1. **Hemoglobin of the fetus**
2. **Fetal hemoglobin concentration**
3. **The Bohr effect**

Important factors facilitating delivery of oxygen to the fetal tissues

Hemoglobin of the fetus

Fetal hemoglobin (HbF)



Oxygen-hemoglobin dissociation curves

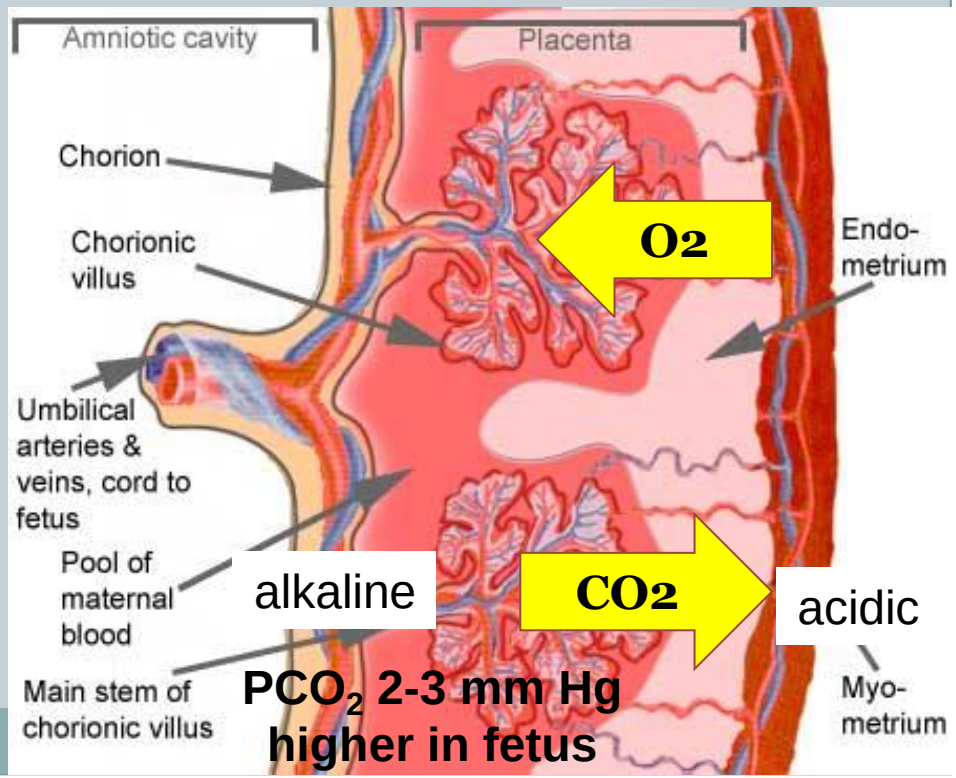
The fetal *hemoglobin concentration*
*is about 50% **greater** than that of the mother*

At the low PO2 levels in fetal blood, the fetal hemoglobin can carry 20 to 50% more oxygen than maternal hemoglobin can..

Important factors facilitating delivery of oxygen to the fetal tissues

- **Double Bohr Effect**
  - High pH in fetal blood (alkaline). Low pH in mother's blood (acidic)

These changes cause the **capacity** of fetal blood to combine with O2 to increase, and maternal blood to decrease, which forces more O2 from the maternal blood while enhancing oxygen uptake by the fetal blood.



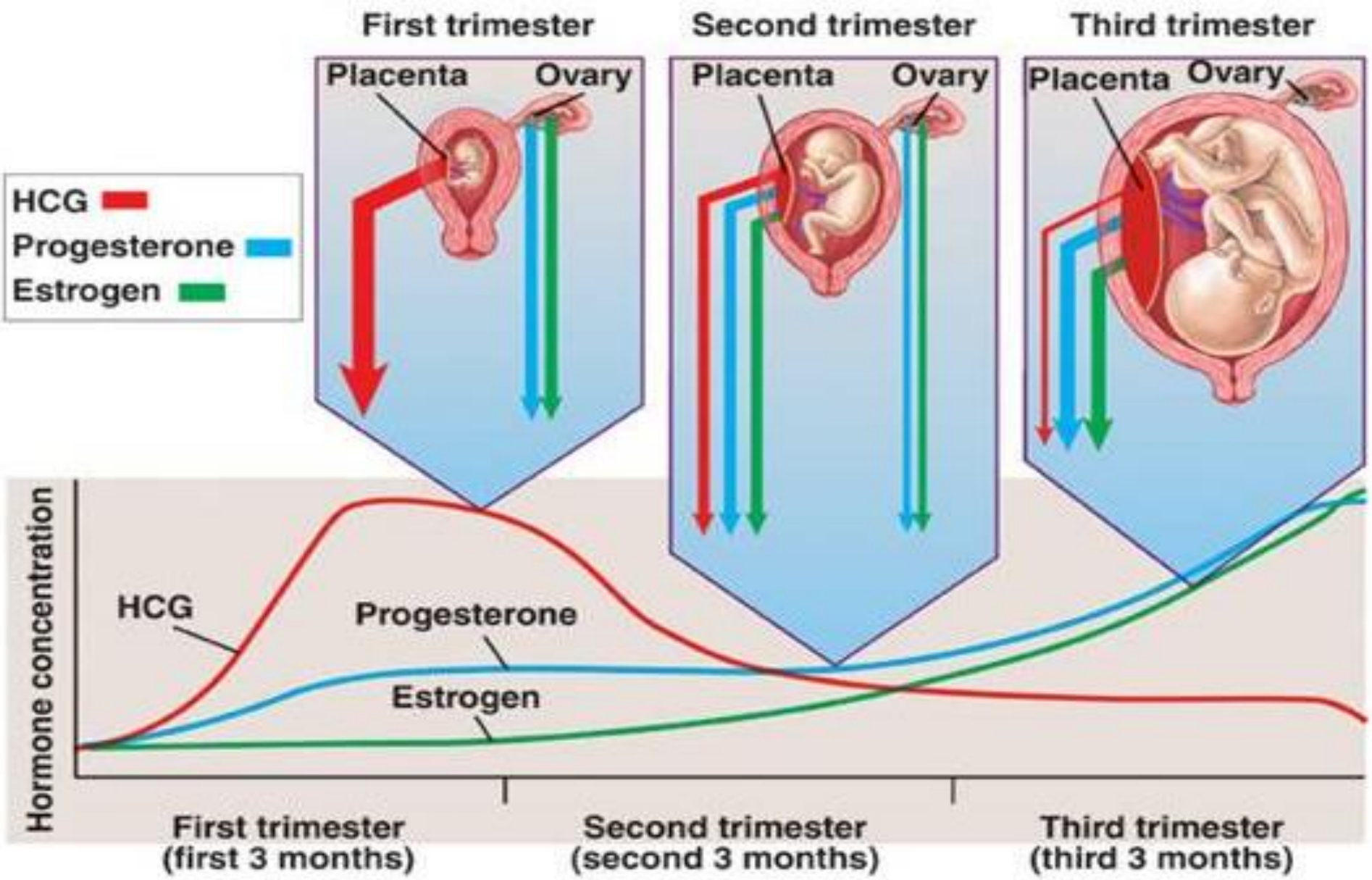
Diffusion of foodstuffs through the placental membrane

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

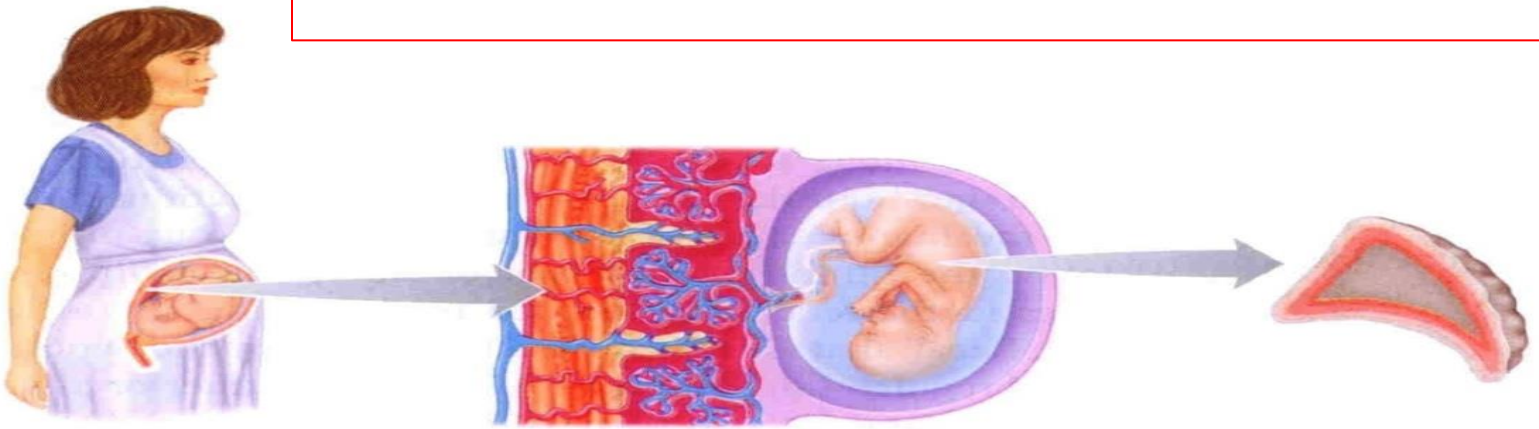
Excretion

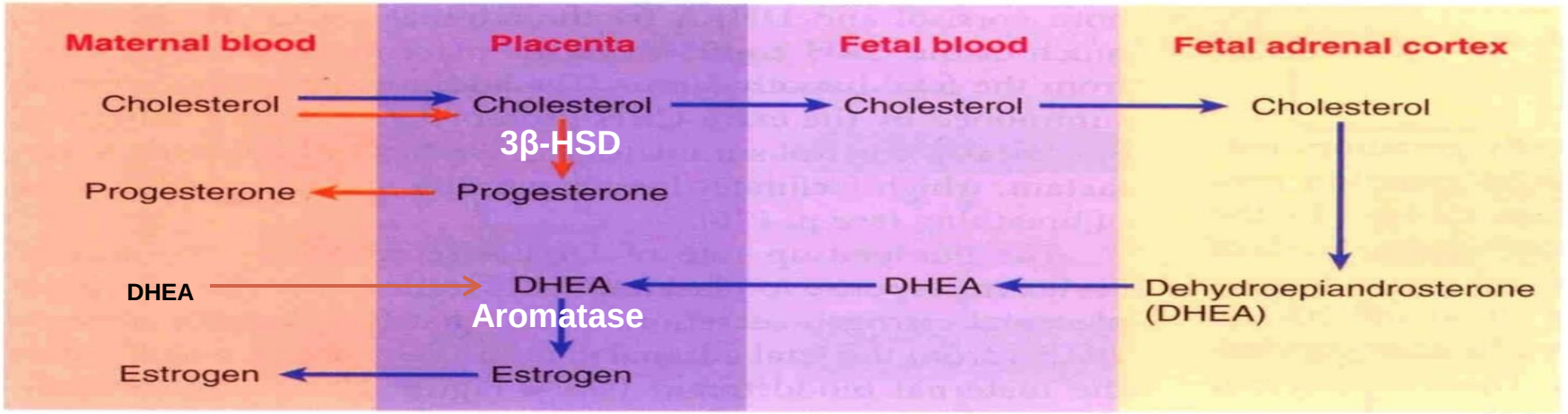
- Excretory products of the fetus *diffuse* through the placental membrane to maternal blood to be excreted with the waste products of the mother
  - Urea, uric acid and creatinine
- Higher conc. of excretory products in fetal blood ensures continuous diffusion of these substances to the maternal blood

Placenta as an Endocrine Organ



Sources of placental estrogen and progesterone





KEY

Pathway for placental synthesis of progesterone

Pathway for placental synthesis of estrogen

3β-*Hydroxysteroid dehydrogenase* (3β-HSD)

● **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

- 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 adrenals cortex
- Functions in the mother
  - Enlargement of uterus, breast & external genitalia
  - Relaxation of pelvic ligaments in preparation for labor
  - Activation of the uterus (gap junctions)

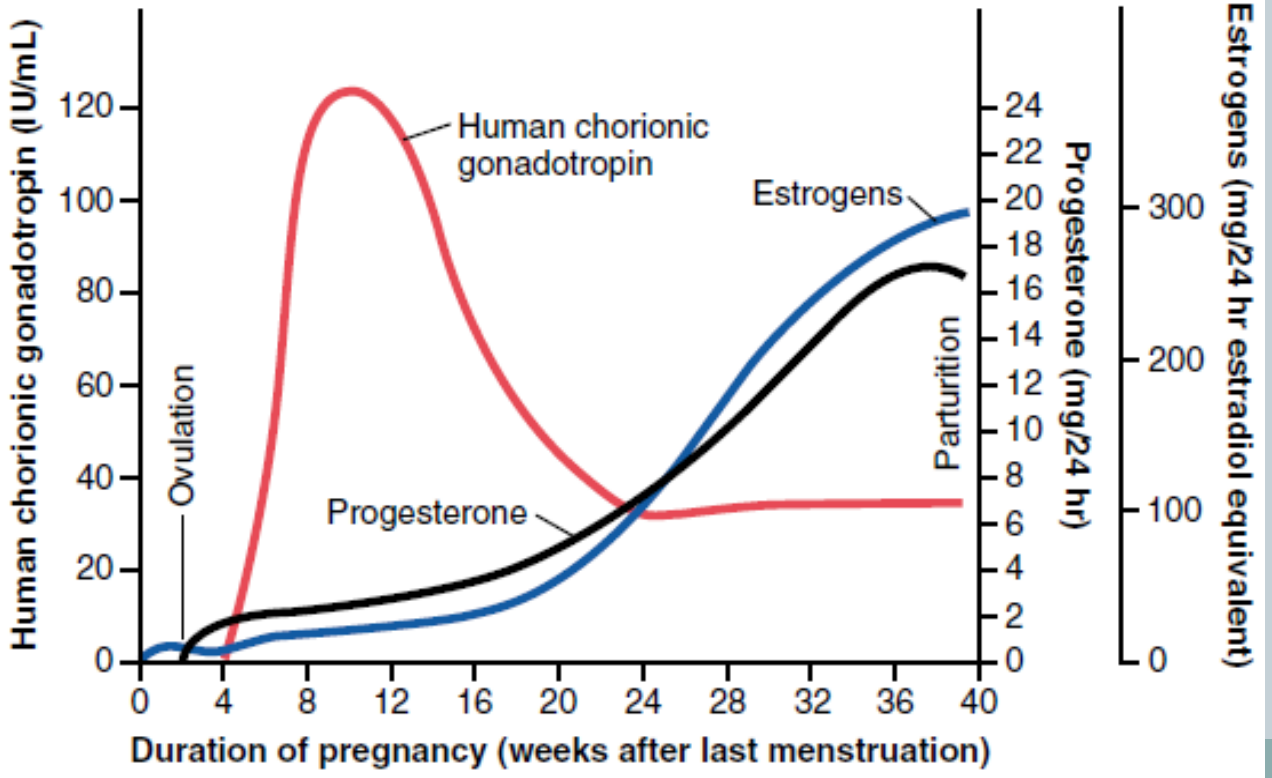
Placenta as Endocrine Organ

- Progsterone
  - Steroid hormone
  - Secreted by syncytial trophoblast cells
  - Towards the end of pregnancy it reaches 10×
  - Derived from cholesterol

- Functions in the mother
  - Provides nutrition to developing embryo (uterine secretory phase)
  - Development of decidual cells
  - Inhibits the contractility of the uterus

hCG level (pregnancy test)

"Well... I think we should run a pregnancy test. Just to make sure!"



Placenta as an Endocrine Organ

- Human Chorionic Gonadotropin (hCG)
  - Glycoprotein
  - Secreted by syncytial trophoblast cells
  - 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)

Placenta as an 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 an 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 systems

- Anterior pituitary gland enlargement (50%)
  - Release of ACTH, TSH and PL
  - 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 (maintains 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

Metabolism and kidney function during pregnancy

- 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.

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 (↑ ECF)
  - Increase activity of the bone marrow (↑ RBCs)

Changes in respiration

- Increase in O_2 consumption (20%):
  - Increase BMR
  - Increase in body size

- Increase in respiratory rate (RR).
- Progesterone ↑ sensitivity of respiratory centre to CO_2.
- Increase in minute ventilation by 50% and a decrease in arterial PCo2 to several millimeters.

The End

Thank You