Objectives

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

Primary oocyte (in the ovary) — before release from ovarian follicle — meiotic division — secondary oocyte (23 unpaired chromosomes) — ovulated in the peritoneal cavity (Ovum with granulosa cells (corona radiata)) — fimbria of fallopian tube.
## Fertilization

<table>
<thead>
<tr>
<th>Location</th>
<th>Time of appearance (min after ejaculation)</th>
<th>Percent of ejaculated sperm*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fertilization site</td>
<td>30–60</td>
<td>0.001</td>
</tr>
<tr>
<td>(upper third of oviduct)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uterus</td>
<td>10–20</td>
<td>0.1</td>
</tr>
<tr>
<td>Cervical canal</td>
<td>1–3</td>
<td>3</td>
</tr>
</tbody>
</table>

- **Ampulla of oviduct**
- **Sperm surrounding ovum**
- **Fimbria**
- **Ovary**
- **Ovulated ovum**
- **Uterus**
- **Cervical canal**
- **Optimal site of 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 spermatozoa with acrosomal enzymes (in red) exposed after acrosomal reaction

*FIGURE 20-25 Process of 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.


4. Male pronucleus.
Fertilization

- After ejaculation sperms reach ampulla of fallopian tube within 30-60 min (uterine contraction)
- Sperm penetrate corona radiata and zona pellucida (surrounding the ova) (hyaluronidase)
- Oocyte divides to form mature ovum (female pronucleus 23 unpaired chromosome) + 2nd polar body
- Head of sperm swells (male pronucleus 23 unpaired chromosome)
- Fertilized ovum (zygote) contain 23 paired chromosomes

Figure 83-2. A, Ovulation, fertilization of the ovum in the fallopian tube, and implantation of the blastocyst in the uterus. B, The action of trophoblast cells in implantation of the blastocyst in the uterine endometrium.

chromosome) and half carry a Y chromosome (the male chromosome). Therefore, if an X chromosome from a
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
If fertilized...

- Zygote begins to divide as it travels through oviduct
- Implants into lining of uterus
Transport of fertilized ovum
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
- Isthmus (last 2cm) relaxes under effect of progesterone
- Delayed transport allows cell division
- Blastocyst (100 cells) enters the uterus
Figure 16.15

Cleavage

(a) Zygote (fertilized egg)
(b) Early cleavage 4-cell stage
(c) Morula
(d) Early blastocyst
(e) Late blastocyst (implanting)

Fertilization
Uterine tube
Secondary oocyte
Ovary
Ovulation
Uterus
Endometrium

Blastocyst cavity
Inner cell mass
Trophoblast
Cleavage

Figure 16.15, step 1
Cleavage

Figure 16.15, step 2

(a) Zygote (fertilized egg)

Fertilization

Uterine tube

Secondary oocyte

Ovary

Ovulation

Uterus

Endometrium
Figure 16.15, step 3

Cleavage

(a) Zygote (fertilized egg)

(b) Early cleavage 4-cell stage

Fertilization

Uterine tube

Secondary oocyte

Ovulation

Uterus

Endometrium

(a) Ovary

(b)
Figure 16.15, step 5

Cleavage

(a) Zygote (fertilized egg)
(b) Early cleavage 4-cell stage
(c) Morula
(d) Early blastocyst

Blastocyst cavity

Fertilization
Uterine tube
Secondary oocyte

Ovary
Ovulation
Uterus
Endometrium

(a)
(b)
(c)
(d)
Cleavage

(a) Zygote (fertilized egg)
(b) Early cleavage 4-cell stage
(c) Morula
(d) Early blastocyst
(e) Late blastocyst (implanting)

Ovary
Uterine tube
Secondary oocyte
Fertilization
Ovulation
Uterus
Endometrium
Trophoblast
Inner cell mass
Blastocyst cavity
Inner cell mass

Figure 16.15, step 6
Implantation

Endometrium
Capillary
Cords of trophoblastic cells
Trophoblast (surface layer of cells of the blastocyst)
Inner cell mass
Uterine cavity
Decidua
Cords of trophoblastic cells
Surface of uterine lining
Amniotic cavity
Inner cell mass
Early nutrition of embryo

1- Progesterone convert the endometrial stromal cells into large swollen cells contain large amount of glycogen, protein and lipid necessary for development of embryo.

2- Embryo implanted the progesterone cause the endometrial cells to swell more and these cells now called decidual cells and the total cells called decidua
Early nutrition of embryo

3- THE TROPHOPLAST CELLS INVADE THE DECIDUA AND THE STORE NUTRIENT IN THE DECIDUA USED FOR THE GROWTH EMBRYO

4- THIS IS THE MAIN FEEDING PROCESS DURING THE FIRST WEEK AND CONTINUE AS PARTIAL FOR THE NEXT 8 WEEKS IN ADDITION TO THE PLACENTA

5- THE PLACENTA START TO PROVIDE NUTRITION AFTER 16 DAYS FROM FERTILIZATION AND LITTLE MORE THAN ONE WEEK AFTER IMPLANTATION
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)
- There are two umbilical arteries and one umbilical vein
- Mother’s blood flow from uterine arteries into maternal sinuses that surround the villi and return by uterine veins of the mother.
Figure 83-5. Top: Organization of the mature placenta. Bottom: Relation of the fetal blood in the villous capillaries to the mother's blood in the intervillous spaces.

Figure 83-6. 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 $P_{O_2}$. (Data from Metcalfe J, Moll W, Bartels H: Gas exchange across the placenta. Am J Obstet Gynecol Proc 23:775, 1984.)

30 mm Hg. Therefore, the mean pressure gradient for diffusion of oxygen through the placental membrane is about 20 mm Hg.

One might wonder how it is possible for a fetus to obtain sufficient oxygen when the fetal blood leaving the placenta has a $P_{O_2}$ of only 30 mm Hg. There are three reasons why even this low $P_{O_2}$ is capable of allowing the fetal blood to transport almost as much oxygen to the fetal tissues as is transported by the mother's blood to her tissues.

First, the hemoglobin of the...
Placenta

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

**Umbilical arteries return embryonic blood to placenta.**

**Chorionic villi contain embryonic blood vessels.**

**Umbilical cord**

**Umbilical vein carries well-oxygenated blood to the embryo.**

**Maternal blood bathes the chorionic villi.**

**Fig. 26-19**
Function of the placenta

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

- Dissolved O\(_2\) in mother’s blood passes to fetal blood by simple diffusion

\[ \text{PO}_2 \ 50 \text{ mm Hg (Maternal)} - 30 \text{ mm Hg (Fetal)} = 20 \text{ mmHg} \]

- At low PO\(_2\), HbF carry 20-50% more O\(_2\) than HbA
- Fetal Hb conc 50% higher than in mother
- Double Bohr effect
  - low pH in mother’s blood (acidic)
  - High pH in fetal blood (alkaline)

- PCO\(_2\) 2-3 mm Hg higher in fetal than maternal blood
Respiration

Wastes and carbon dioxide delivered from the baby

Oxygen, nutrients, and hormones delivered to the baby
Nutrition

- Fetus uses **mainly glucose** for nutrition so the trophoblast cells in placental villi transport glucose by carrier molecules (facilitated diffusion)

- Fatty acids diffuse due to high solubility in cell membrane (more slowly than glucose)

- Ketone bodies, K+, Na+ and Cl- diffuse from maternal to fetal blood
Excretion

- Excretory products of the fetus diffuse through placental membrane to maternal blood to be excreted with excretory products of the mother
  - Urea, uric acid and creatinine
- Higher concentration of excretory products in fetal blood insures continuous diffusion of these substances to the maternal blood
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)
Functions of hCG --

1. Produced by syncytiotrophoblasts (8-9 d after fertilization)
2. Maintains corpus luteum beyond normal lifespan
3. Stimulates secretion progesterone and estrogen from CL
4. Stimulates essential DHEA-S in fetal zone of adrenal gland
5. Stimulates testosterone production in male fetus
6. hCG receptors in endometrium and myometrium and can inhibit contractions produced by oxytocin
7. Immunosuppressant
Endocrine

- **Estrogen**
  - Steroid hormone
  - Secreted by syncytial trophoblast cells
  - Towards end of pregnancy reaches 30 times
  - 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
**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).
Estradiol

- initially produced by corpus luteum (first 5-6 wks)
- stimulated by hCG
- then placenta (from DHEA-S from fetus)
- inc. uterine blood flow
- Estriol -- excreted in urine -- index of fetal well-being
Endocrine

- **Progesterone**
  - Steroid hormone
  - Secreted by syncytial trophoblast cells
  - Towards end of pregnancy reaches $10 \times$
  - Derived from cholesterol

- **Functions in the mother**
  - Provides nutrition to developing embryo
  - Development of decidual cells in the uterine endometrium
  - Inhibits the contractility of the uterus
  - Contribute to the development and cleavage of the embryo
Human Chorionic Somatomammotropin
- Protein hormone
- Secreted by placenta around 5th gestational week.
- Secretion \( ^{\wedge} \) in direct proportion to the weight of placenta
- It is secreted greater than all other pregnancy hormones together

Functions in the mother
- Breast development (hPL)
- Weak like growth hormone ‘s action
- Inhibit insulin sensitivity = \( \downarrow \) glucose utilization in the mother to make it available to the growth fetus.
- Promote release of free fatty acids from the fat store in the mother to be use by the mother during pregnancy
Endocrine

- **Relaxin**
  - Polypeptide
  - Secreted by corpus luteum and placenta
- **Functions in the mother**
  - Relaxation of symphysis pubis ligament (weak)
  - Softens the cervix at delivery
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 amino acids)
  - Increase aldosterone (retain fluid)

- **Thyroid gland enlargement (50%)**
  - Increase thyroxine production (hCG, hCT)

- **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 acromegaly features
- Weight gain 10-12 kg (last 2 trimesters)
  - Increase appetite
  - Increased demand for nutrients by fetus & hormonal factor.
Changes in metabolism

- Increase basal metabolic rate (15%)
- Increase in daily requirements for
  - Iron
  - Phosphates
  - Calcium
  - Vitamins
    - Vitamin D ($\text{Ca}^{+2}$ absorption)
    - Vitamin K added to sufficient prothrombin to prevent hemorrhage during birth process
Changes in circulatory system

- Increase in cardiac output (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
- Increase in respiratory rate (RR)
- Increase in minute ventilation ($TV \times RR$) by 50%
  - Progesterone ↑sensitivity of respiratory center (RC) to $CO_2$
Maternal kidney function

1- INCREASE RENAL ABSORPTION FOR NA, CL AND WATER 50% BECAUSE INCREASE PRODUCTION OF SALT AND WATER RETAINING HORMONES, ESPECIALLY STEROID FROM PLACENTA AND ADRENAL CORTEX.

2- INCREASE GLOMERULAR FILTRATION 50%? INCREASE NO AND RELAXIN
Amniotic and its formation

1- Normal volume 0.5-1 liter can increase or decrease.
2- Water replace once every 3 hours.
3- Electrolytes, Na and K replace every 15 hours.
4- Large portion derived from renal excretion by the fetus, small amount by GIT and lungs.
Preeclampsia and eclampsia

PREECLAMPSIA IS RAPID RISE OF BLOOD PRESSURE ASSOCIATED WITH PROTEINUREA DURING LAST FEW MONTHS OF PREGNANCY
1- HYPERTENSION
2- EDEMA
3- WEIGHT GAIN
4- DECREASE RENAL BLOOD FLOW AND GLOMERULAR FILTRATION RATE
4- INSUFFICIENT BLOOD FLOW
5- IMPAIR VASCULAR ENDOTHELIAL FUNCTION
6- EXCESS WATER AND SALT RETENTION
7- ? AUTOIMMUNE
Eclampsia

EXTREME DEGREE OF PREECLAMPSIA
1- HYPERTENSION
2- SEIZURE AND COMA
3- GREATLY DECREASE KIDNEY OUTPUT
4- MALFUNCTION OF THE LIVER
5- GENERALIZE TOXIC CONDITION
6- OCCURS SHORTLY BEFORE BIRTH