# FERTILISASI DAN IMPLANTASI

**Kuliah 8**

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# Fertilization

- Definition: the union of male and female gametes
- Can take place during fertile period in each cycle
- Normally occurs in ampulla (upper third of the oviduct
- Thus, both ovum and sperm must be transported from their site of production to the ampulla

# .....Fertilization

- **Ovum:**

  **If not fertilized, begins**

  - **to disintegrate within 12-24 hours**
  - **phagocytized by cells that line reproductive tract**
  - **fertilization must occur within 24 hours**

- **Sperm:**

  - **survive ± 48 hours, and up to 5 days in female reproductive tract**
  - **Sperm deposited from 5 days before ovulation may be able to fertilize ovum**

# Ovum Transported to Oviduct

- Releasing ovum at ovulation is quickly picked up by oviduct through fimbriae,
  - fingerlike projections
  - contract in a sweeping motion to guide the released ovum into oviduct
  - lined by cilia that beat in waves toward the interior of oviduct
- Within oviduct ovum is rapidly propelled by peristaltic contractions and ciliary action to ampulla

# …..Ovum Transported to Oviduct

- Occasionally, ovum fails to be transported into oviduct
- If fertilized resulting in ectopic abdominal pregnancy
- Egg implants in reach vascular supply to digestive organs $\Rightarrow$ dangerous
  - hemorrhage
  - if proceed to term, baby must be delivered surgically
  - maternal complications at birth

# Sperm Transported to Oviduct

**Arrive in oviduct within 30 min. after ejaculation by:**

- **Whip-like contractions of  by sperm tail**
- **Female reproductive tract condition / act:**
  - **Cervical canal penetrable : thin and watery mucus by estrogen: 2-3 days around time of ovulation**
  - **contraction of  myometrium and oviduct smooth muscle facilitated by high estrogen level and seminal prostaglandin**

# Process of Sperm Attracted Toward Ovum

**Recent researches:**

- **Ova are not passive partner in conception**
- **Mature eggs release allurin, chemical that attracts sperm and causes them to propel themselves toward the waiting female gamete**
- **Sperm receptor that detects and responds to the ovum-released chemo-attractant**
- **Receptor hOR 17-4 of sperm is an olfactory receptor (OR)**

# …..Process of Sperm Attracted Toward Ovum

- Activation of hOR 17-4 receptor on binding with allurin (or other signal) triggers a second messenger pathway in sperm that brings about intracellular $Ca^{2+}$ release which turn on microtubule sliding that brings about tail movement and sperm swimming in direction of chemical signal

# …..Process of Sperm Attracted Toward Ovum

- **Reasons why sperm concentration must be so high (20 million/ml of semen) for a man to be fertile:**
  - **Only a very small percentage of deposited sperm ever reach its destination**
  - **Acrosomal enzymes of many sperm are needed to break down barriers surrounding ovum**

# Sequencing of Fertilization

1. Sperm pass through corona radiata and zona pellucida surrounding ovum
2. Acrosomal membrane disrupts on contact with corona radiata which releasing acrosomal enzymes that enable sperm to tunnel a path through protective barriers.

   Sperm can penetrate zona pellucida only after binding with specific receptor sites on surface of this layer

# …..Sequencing of Fertilization

3. **Fertilin, a protein found on plasma membrane of sperm binds with egg receptor, integrin, a type of cell adhesion molecule that protrudes from outer surface of plasma membrane**

   **Only sperm of the same species can bind to integrin and pass through plasma membrane of ovum**

# …..Sequencing of Fertilization

4. **Sperm fuses with plasma membrane of ovum (secondary oocyte), triggering chemical change in ovum's surrounding membrane that makes this outer layer impenetrable to any other sperm, which is called Block to Polyspermy phenomenon**
5. **Head of fused sperm is gradually pulled into ovum's cytoplasm by a growing cone that engulfs it. Sperm's tail is frequently lost in this process.**

# .....Sequencing of Fertilization

6. Sperm release nitric oxide when it has completely penetrated ovum's cytoplasm.
7. Nitric oxide promotes release of stored $Ca^{2+}$ within egg
8. Intracellular $Ca^{2+}$ release triggers the final meiotic division of secondary oocyte
9. Within an hour, sperm and egg nuclei fuse $\Rightarrow$ zygote
10. Victorious sperm activates ovum enzymes essential for early embryonic development

# Process Following Fertilization

- During first 3-4 days following fertilization, zygote remains within ampulla, because of constriction between ampulla and remainder oviduct canal prevents further movement of zygote into uterus

# Beginning Steps In Ampulla

- A number mitotic cell divisions of zygote to form morula during in ampulla
- Glycogen released from endometrium into lumen stimulated by progesterone from CL for energy used by early embryo
  - Nutrients stored in ovum's cytoplasm can sustain product of conception for < 1 day
  - Concentration of secreted nutrients increases more rapidly in ampulla than in uterine lumen

# Descent of Morula to Uterus

- ± 3-4 days after ovulation, progesterone produce is sufficient to relax oviduct contraction ⇒ morula rapidly propelled into uterus by oviductal peristaltic and ciliary activity
- Temporary delay of descending embryo into uterus, lets enough nutrients accumulate in uterine lumen to support embryo until implantation can take place
- Morula will die, if it arrives prematurely

# ……Descent of Morula to Uterus

- **Morula floats freely within uterine cavity for 3-4 days, living on endometrial:**
  - **secretions and continuing to divide**
  - **being prepared for implantation under influence of luteal-phase progesterone**
  - **storing up glycogen**
  - **becoming richly vascularized**
- **Morula which fails to descend into uterus will lead to ectopic tubal pregnancy (95% of ectopic pregnancy)**

# Implantation

- ± 1 week after ovulation, morula has descended into uterus and continued to proliferate and differentiate into blastocyst which capable to implantation
- Blastocyst is consisted of 2 parts: inner cell mass (which become fetus) and trophoblast (outermost layer of blastocyst)
- Trophoblast accomplish implantation, after which develops into fetal portion of placenta

# …..Implantation

- When blastocyst is ready to implant, its surface becomes sticky
- By the time endometrium is ready to accept the early embryo
- Blastocyst adheres to uterine lining on the side of its inner cell mass which release protein-digesting enzyme, permitting finger-like cords of trophoblastic cells to penetrate into depths of endometrium, where they continue to digest uterine cells

# …..Implantation

**Through cannibalistic actions, trophoblast performs the dual functions:**

1. **Accomplishing implantation as it carves out a hole in endometrium for blastocyst**
2. **Making metabolic fuel and raw materials available for developing embryo as advancing trophoblastic projections break down the nutrient-rich endometrial tissues.**

   **Cell walls of advancing trophoblastic cells breakdown, forming multinucleated syncytium that will become fetal portion of placenta**

# …..Implantation

- Stimulated by invading trophoblast, endometrial tissue at the contact site undergoes dramatic changes that enhance its ability to support the implanting embryo
- In response to chemical messenger released by blastocyst, the underlying endometrial cells secrete prostaglandins which locally increase vascularization, produce edema, and enhance nutrient storage

# …..Implantation

- Endometrial tissue so modified at implantation site is called decidua
- Blastocyst becomes embedded into super-rich decidual tissue
- After blastocyst burrows into decidua by means of trophoblastic activity, a layer of endometrial cells covers over the surface, completely burying blastocyst within uterine lining
- Trophoblastic layer continue to digest surrounding decidual cells providing energy for embryo until placenta develops

# Preventing Rejection of Embryo

## Theory I:

- **Trophoblast produce Fas ligand which binds with Fas, a specialized receptor on surface of approaching activated maternal cytotoxic T cells (immune cells that carry out the job of destroying foreign cells)**
- **The binding triggers immune cells that are targeted to destroy the developing foreigner to undergo apoptosis, sparing embryo/fetus from immune rejection**

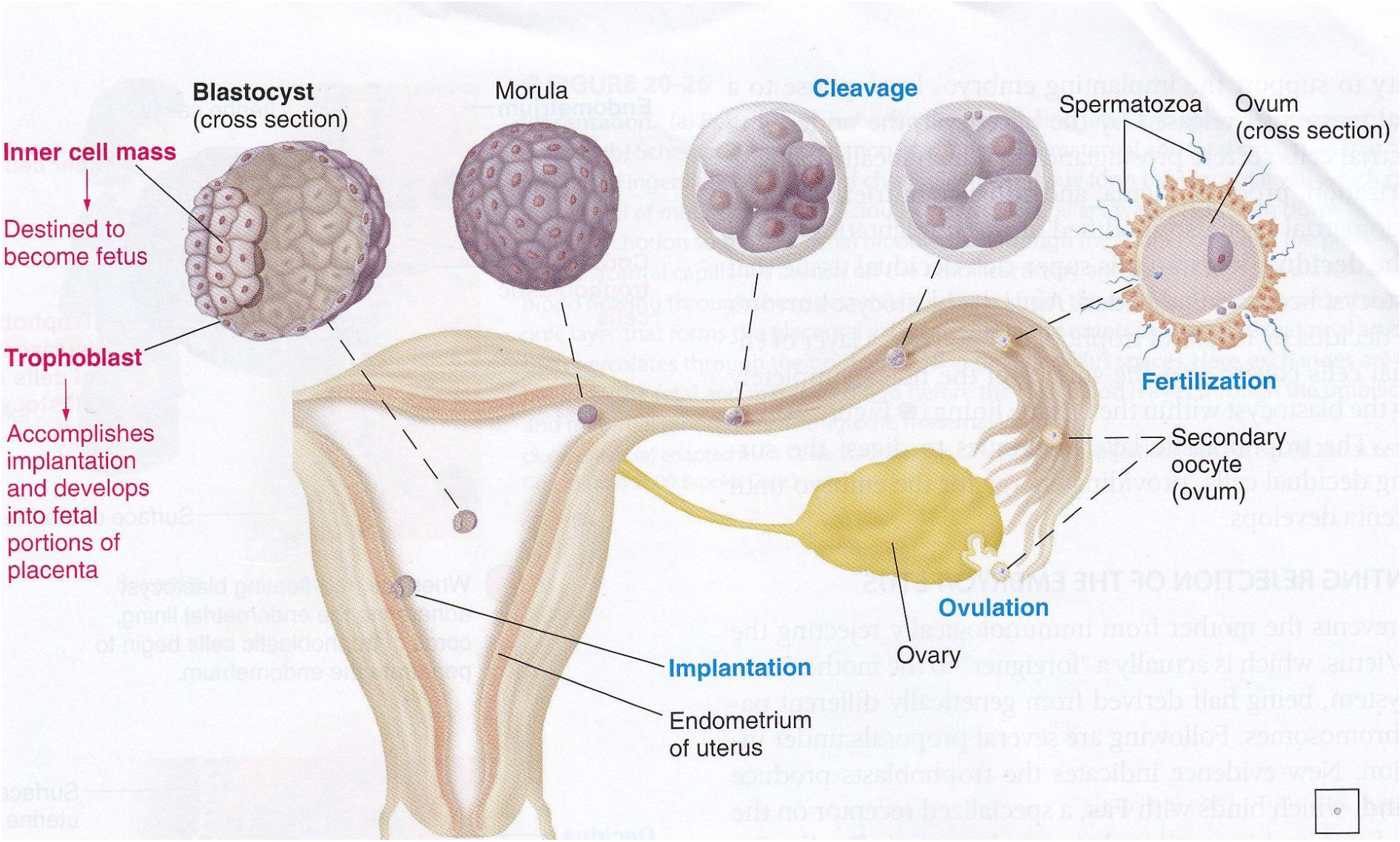
# …..Preventing Rejection of Embryo

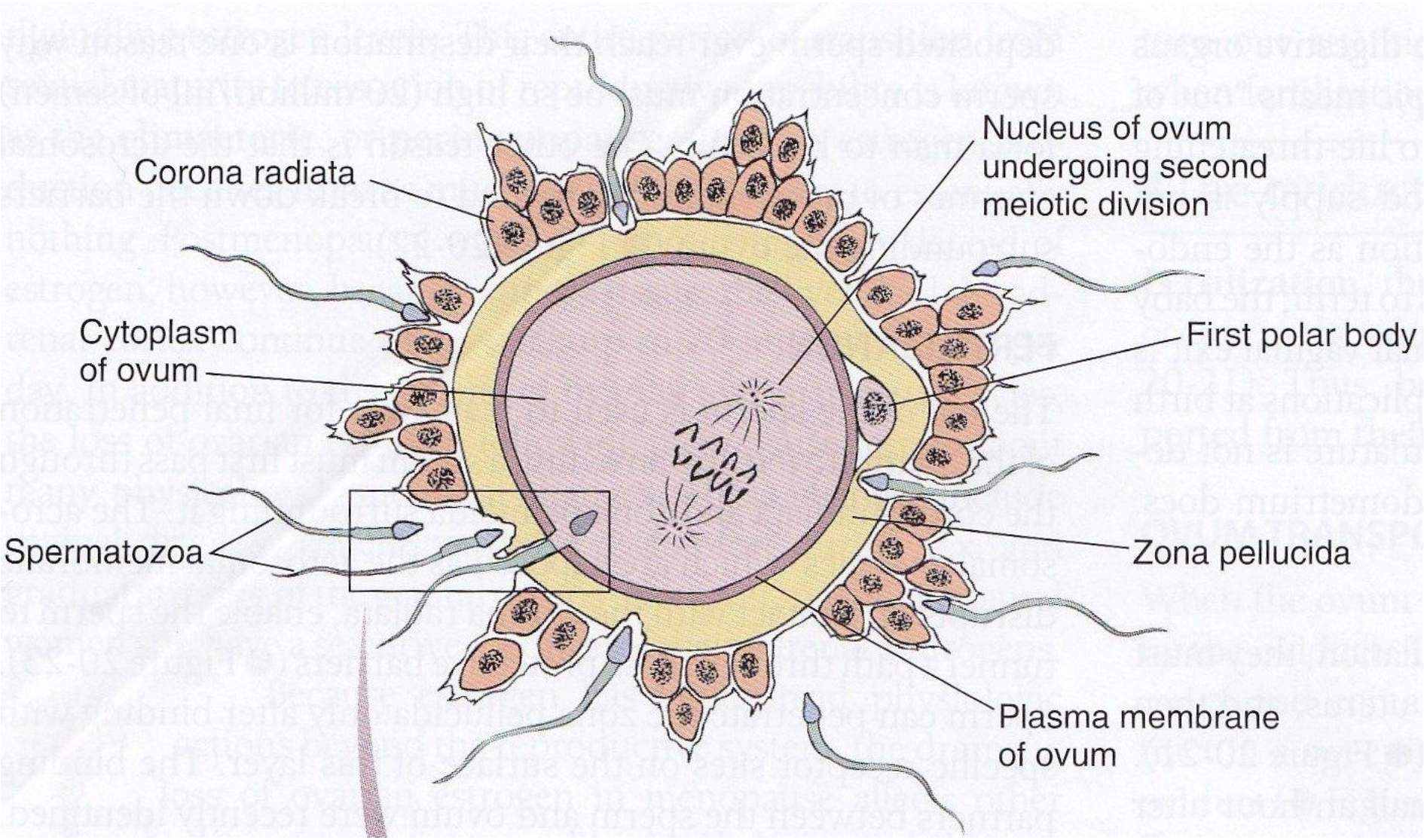
## Theory II:

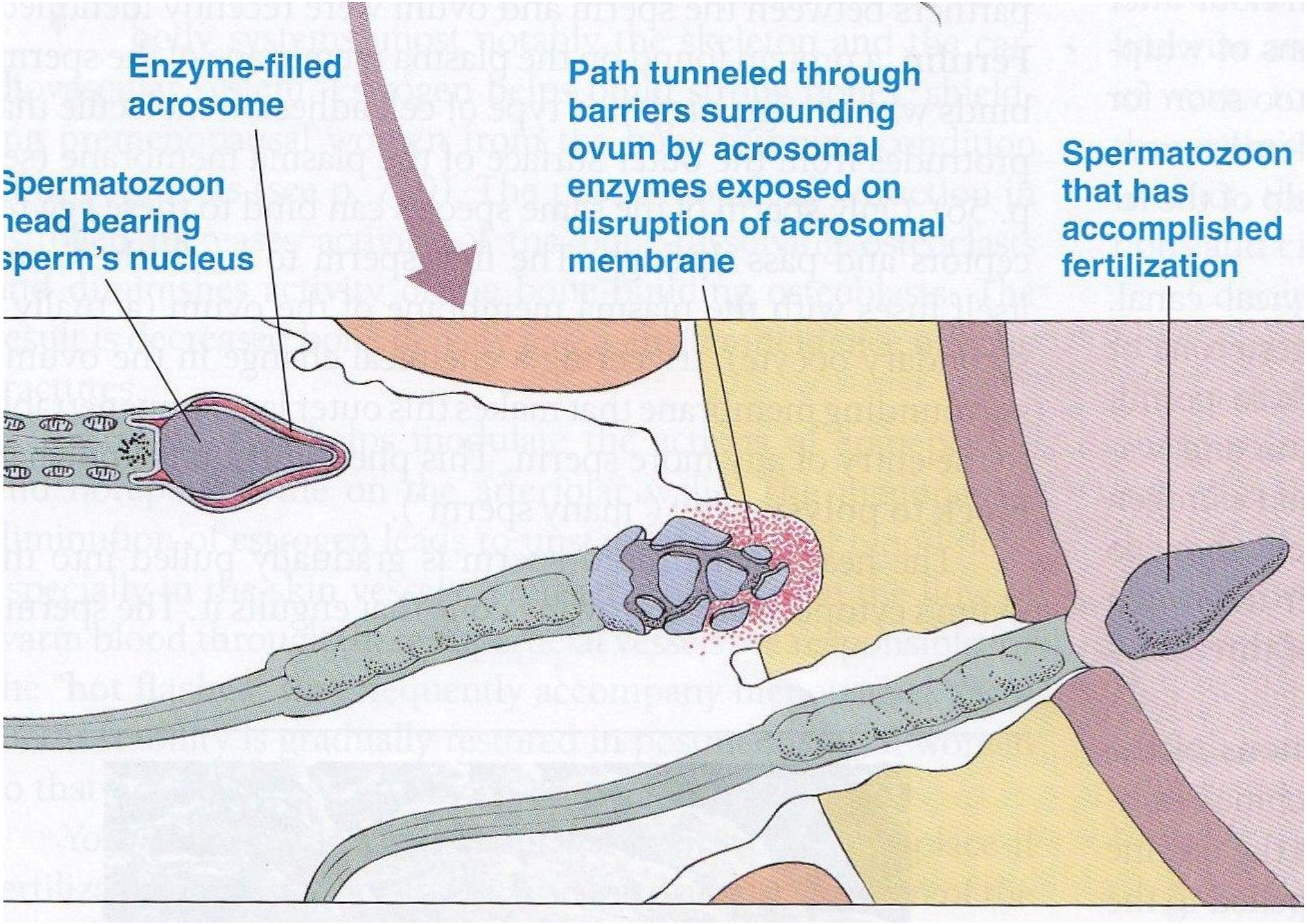
- Fetal portion of placenta which derived from trophoblast produce enzyme indoleamine 2,3-dioxygenase (IDO) which destroy tryptophan (critical factor in activation of maternal cytotoxic T cells)

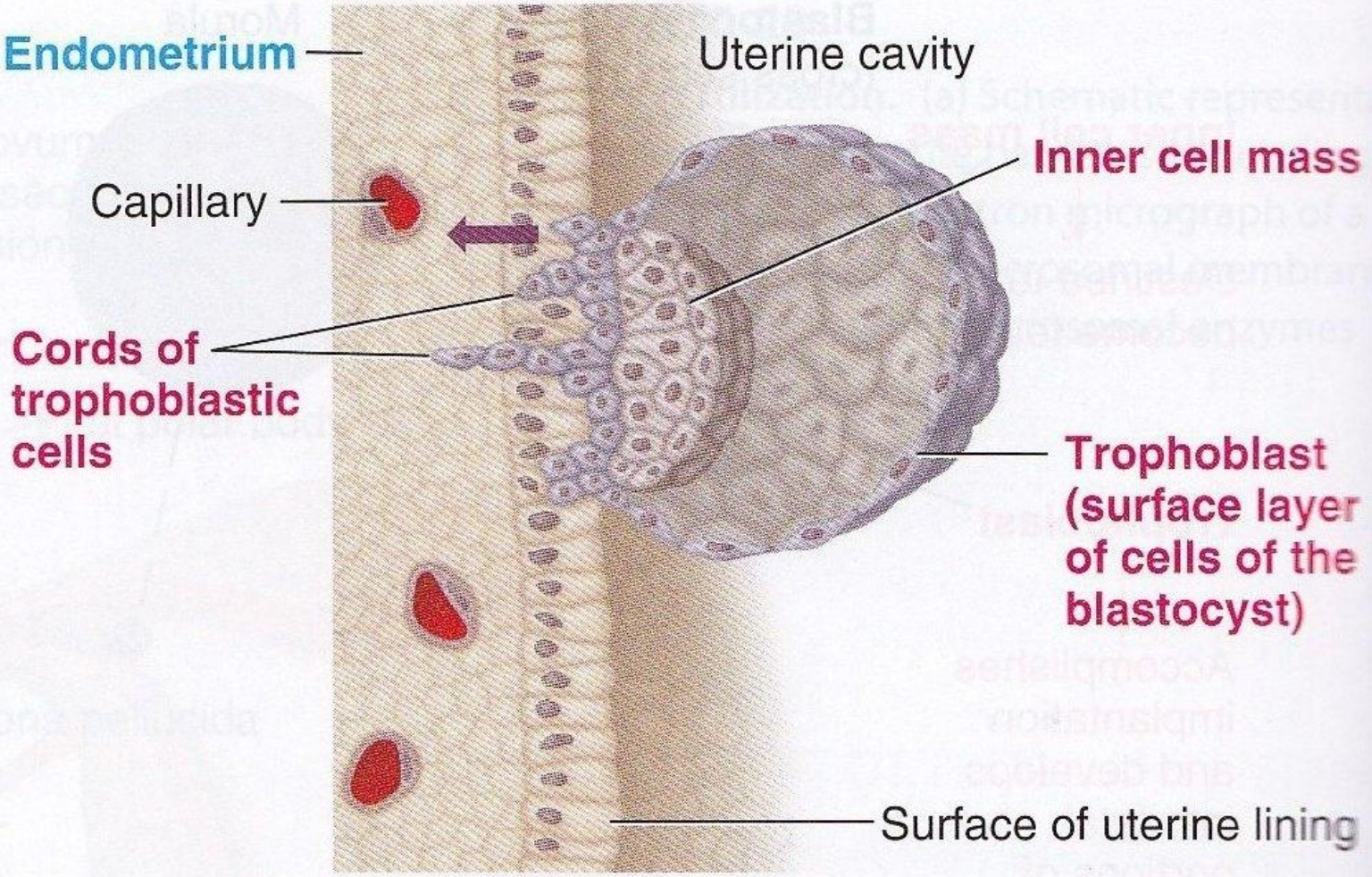
## Theory III:

- In pregnancy production of regulatory T cells is doubled or tripled which suppress maternal cytotoxic T cells

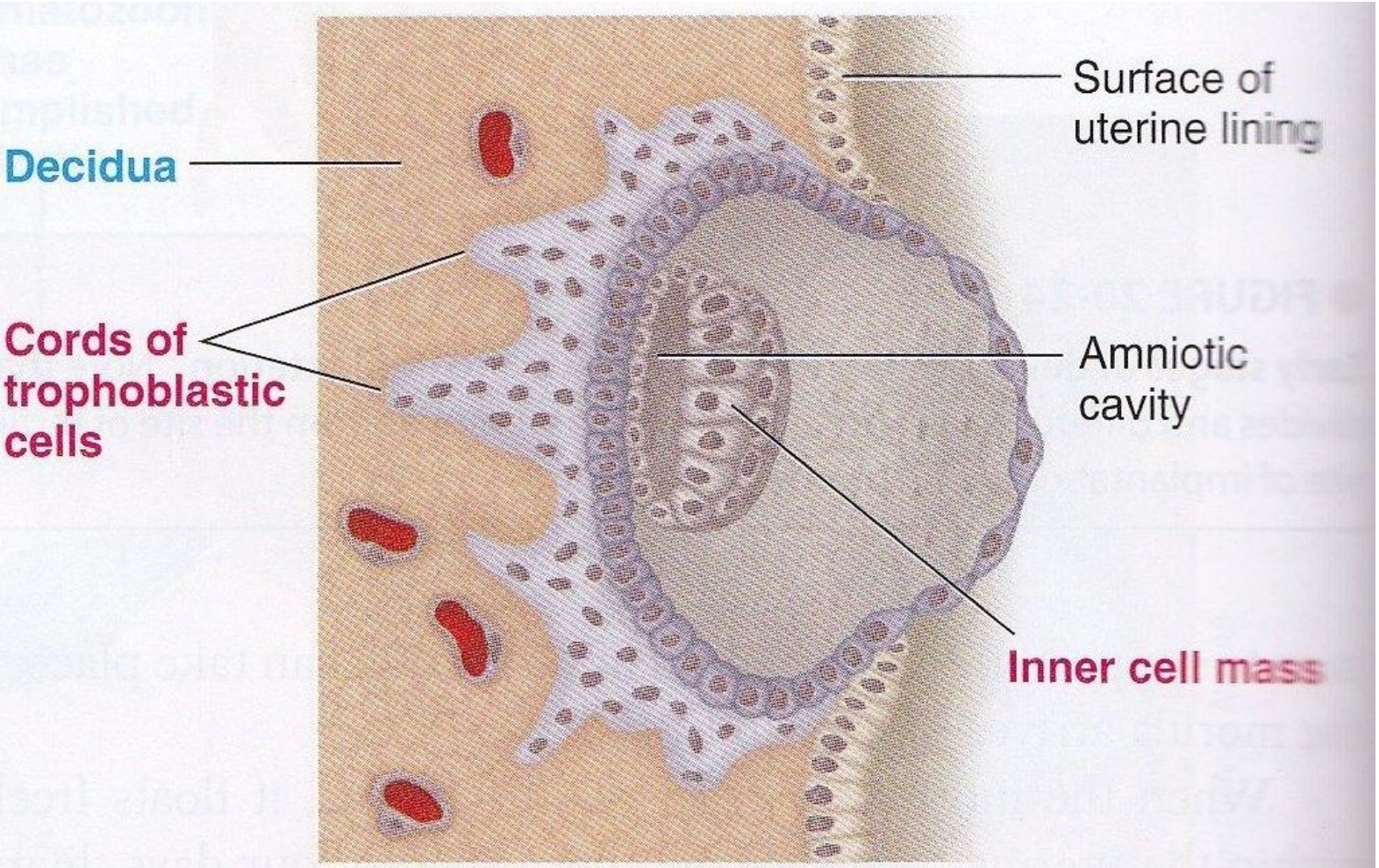

Blastocyst
(cross section)
Morula
Cleavage
Spermatozoa
Ovum
(cross section)
Inner cell mass
Destined to
become fetus
Trophoblast
Accomplishes
implantation
and develops
into fetal
portions of
placenta
Fertilization
Secondary
oocyte
(ovum)
Ovulation
Ovary
Implantation
Endometrium
of uterus


Corona radiata
Nucleus of ovum undergoing second meiotic division
Cytoplasm of ovum
First polar body
Spermatozoa
Zona pellucida
Plasma membrane of ovum

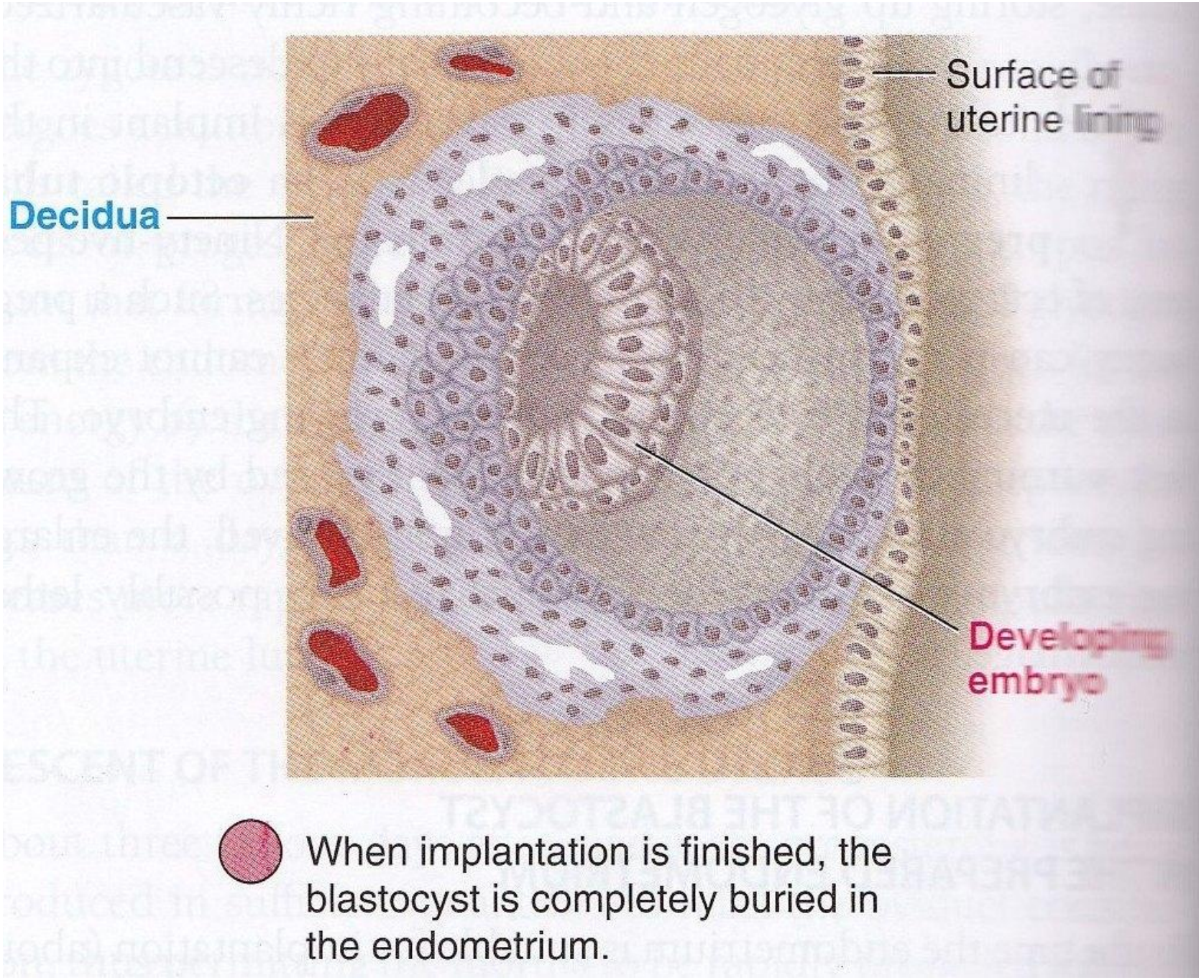

Enzyme-filled acrosome
Spermatozoon head bearing sperm's nucleus
Path tunneled through barriers surrounding ovum by acrosomal enzymes exposed on disruption of acrosomal membrane
Spermatozoon that has accomplished fertilization




When the free-floating blastocyst adheres to the endometrial lining, cords of trophoblastic cells begin to penetrate the endometrium.




Advancing cords of trophoblastic cells tunnel deeper into the endometrium, carving out a hole for the blastocyst. The boundaries between the cells in the advancing trophoblastic tissue disintegrate.




When implantation is finished, the blastocyst is completely buried in the endometrium.

# Contraception

- Blockage of sperm transport to ovum
- Prevention of ovulation
- Blockage of implantation
- Future possibilities:
  - immunocontraception
  - trigger premature release of acrosomal
  - male contraception:
    > block sperm production
    > chemical sterilization
  - Ca-blocking drugs

# Failure Rate of Contraceptive Techniques

| Methods | Average Failure Rate<br>Annual pregnancies/100 women |
|---|---|
| None | 90 |
| Natural (rhythm) methods | 20 – 30 |
| Coitus interruptus | 23 |
| Chemical contraceptives | 20 |
| Barrier methods | 10 – 15 |
| Oral contraceptives | 2 – 2.5 |
| Implanted contraceptives | 1 |
| Intrauterine device | 4 |


Thank You

# Tugas

**Placenta**

- **Pembentukan**
- **Fungsi**
- **Hormon placenta dan fungsinya**