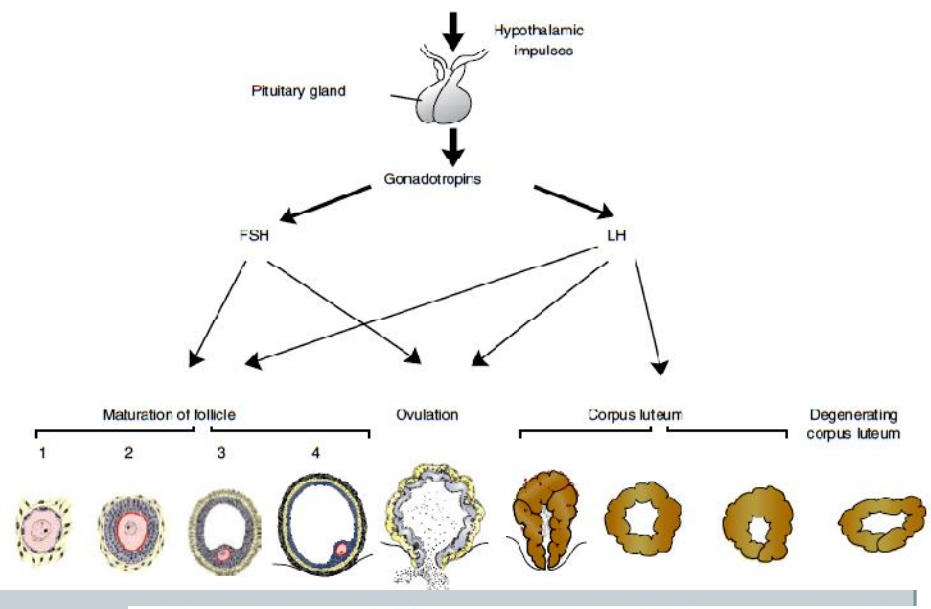
First week of development: ovulation to implantation

Dr. Saeednia

First week of development: ovulation to implantation

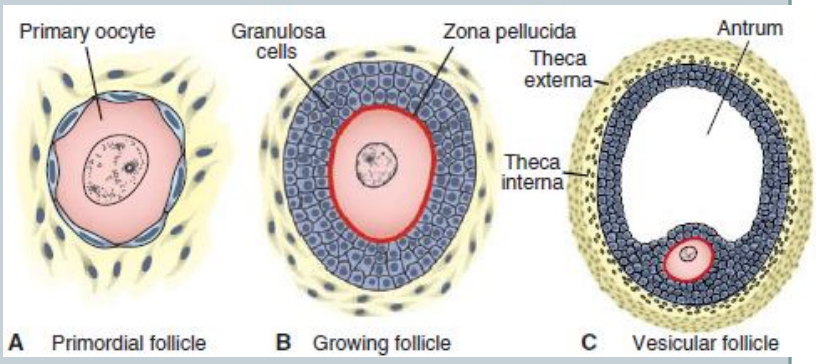
- At puberty
- Sexual cycles
- Hypothalamus (GnRH)
- Adenohypophysis (gonadotropins)

LH & FSH



FSH induce :

- ❖ Folicle growth & corpus atreticum
- ❖ Growth mediated by GDF-9 (TGF-β)



First week of development: ovulation to implantation

Theca & granulosa cells secret estrogens:

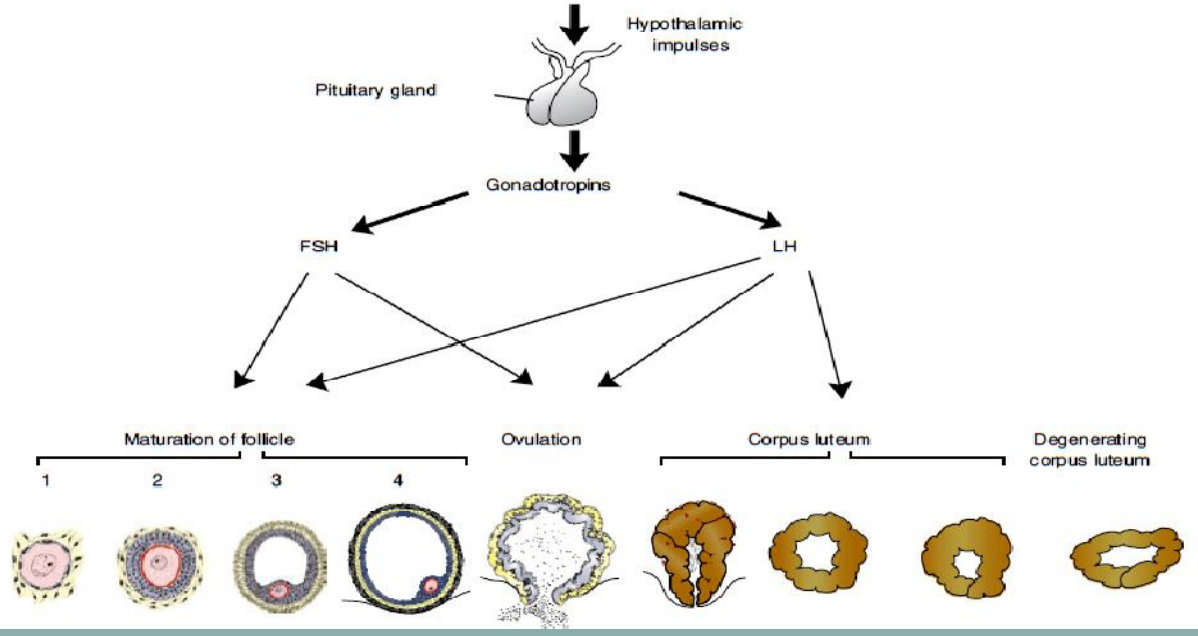
Uterus enters to follicular or proliferative phase

Thinning the cervical mucosa

Pituitary gland stimulation for LH secretion

LH surge in mid cycle (day = 12):

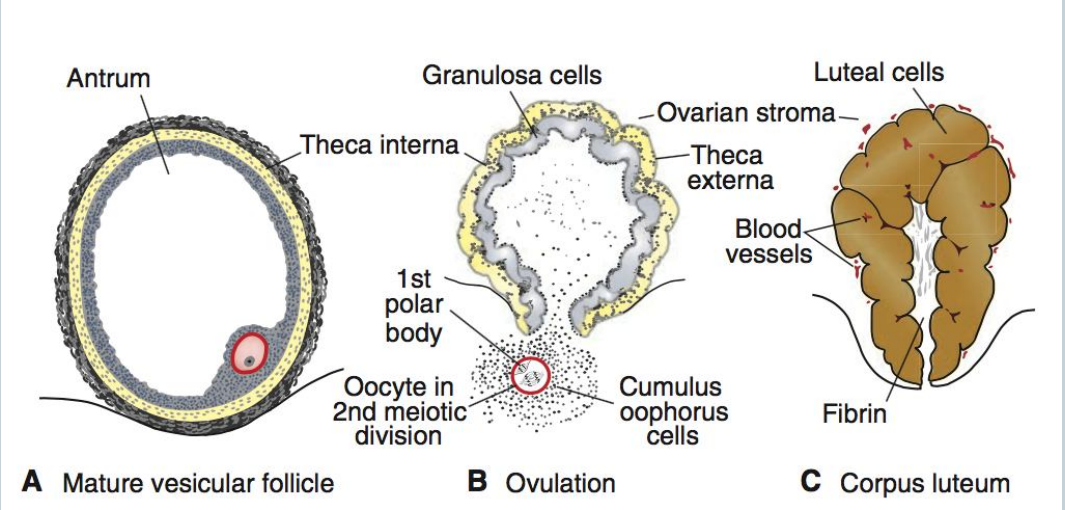
1. MPF increase, meiosis I completion & meiosis II initiation
2. Follicle rupture & ovulation
3. Progestron production by follicular cells (luteinization)



ovulation

Before ovulation FSH & LH induce:

- Follicle growth: 25 mm (vesicular follicle)



- **LH surge :**

- Restart Meiosis I & complete
- start Meiosis II
- Arrest 3 hours before ovulation in metaphase meiosis II
- Stigma formation

- **LH surge :**

- Collagenase activity
- Prostaglandins increase / muscular contraction / ovulation
- Oocyte-**crona radiata** complex formation

❖ ***After ovulation:***

- ❖ Granulosa cell & internal theca cell / vessels formation / LH induction / yellowish cell formation / luteum cell / Corpus luteum
- ❖ Progestrone production
- ❖ Progestrone & estrogen = Progestational or secretory stage of uterus
- ❖ Preparation of uterus for implantation of the embryo

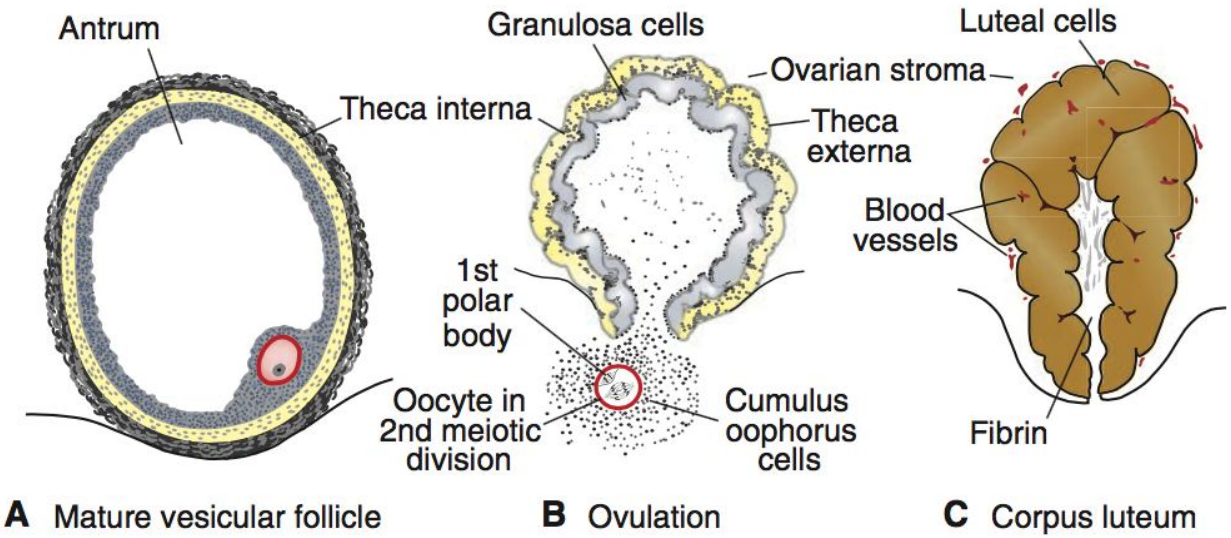


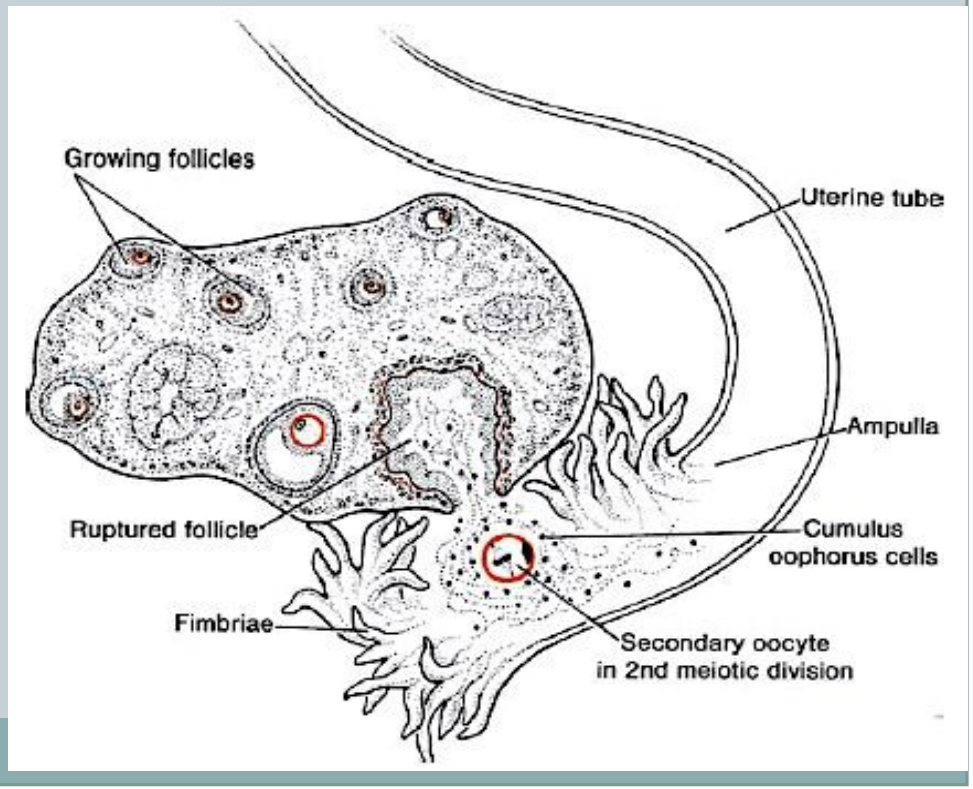
Figure 3.3 **A.** Mature vesicular follicle bulging at the ovarian surface. **B.** Ovulation. The oocyte, in metaphase of meiosis II, is discharged from the ovary together with a large number of cumulus oophorus cells. Follicular cells remaining inside the collapsed follicle differentiate into lutean cells. **C.** Corpus luteum. Note the large size of the corpus luteum, caused by hypertrophy and accumulation of lipid in granulosa and theca interna cells. The remaining cavity of the follicle is filled with fibrin.

Oocyte transfer

- Uterine fimbriae & Tube rhythmic contract
- Transfer oocyte & corona radiata by sweeping movements of the fimbriae and by motion of cilia on the epithelial lining
- **cumulus cells withdraw cytoplasmic processes from the zona pellucida**
- fertilized oocyte reaches the uterine lumen in 3 to 4 days.

Oocyte transfer speed regulated by:

- endocrine status during and after ovulation



If Fertilization done:

- Prevention of corpus luteum degeneration by:

- hCG (syncytiotrophoblast) secretion
- corpus luteum development / corpus luteum of pregnancy formation
-
- **end of the third month:**

- corpus luteum of pregnancy size = 1/2 -1/3 of the size of the ovary
- Luteal cells secrete progesterone until end of the 4th month
- then regress (placental progesterone)
- corpus luteum Removal before 4th month leads to abortion

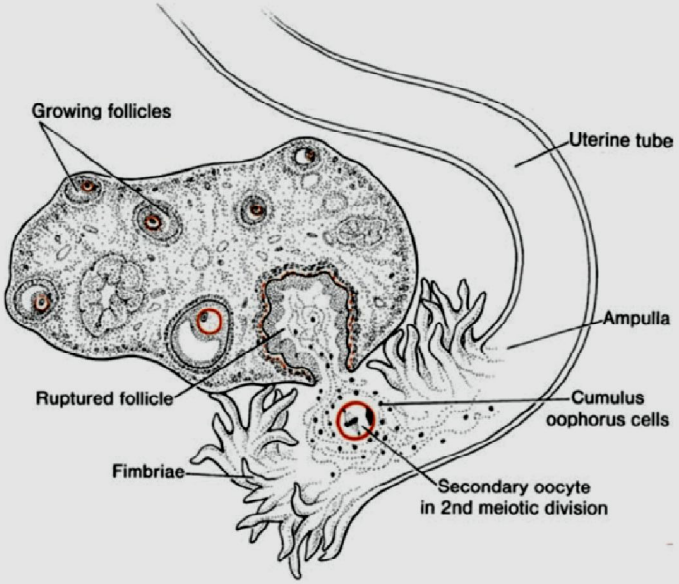


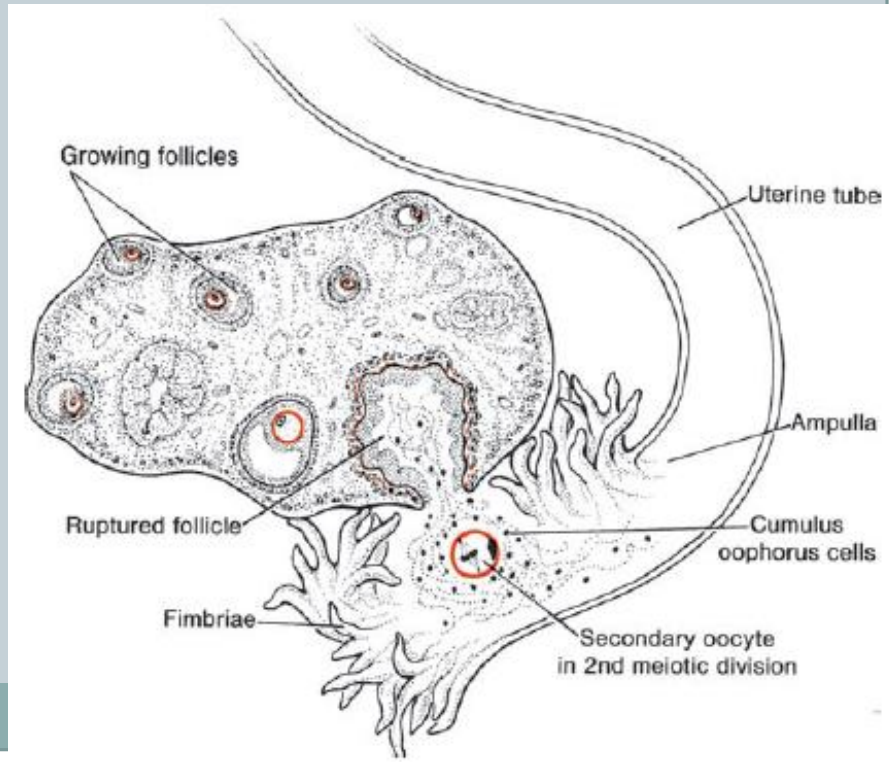
Figure 3.4 Relation of fimbriae and ovary. Fimbriae collect the oocyte and sweep it into the uterine tube.

Corpus albicans

without fertilization:

corpus luteum degeneration

- maximum size of corpus luteum 9 days after ovulation
- the corpus luteum shrinks because of lutean cells degeneration
- the corpus albicans formation
- progesterone production decreases
- menstrual bleeding start



Clinical Correlates

Ovulation

During ovulation, some women feel a slight pain, called **mittelschmerz** (German for "middle pain") because it normally occurs near the middle of the menstrual cycle. Ovulation is also generally accompanied by a rise in **basal temperature**, which can be monitored to aid couples in becoming pregnant or preventing pregnancy. Some women fail to ovulate because of a low concentration of gonadotropins. In these cases, administration of an agent to stimulate gonadotropin release, and hence ovulation, can be employed. Although such drugs are effective, they often produce multiple ovulations, so that the likelihood of multiple pregnancies is 10 times higher in these women than in the general population.

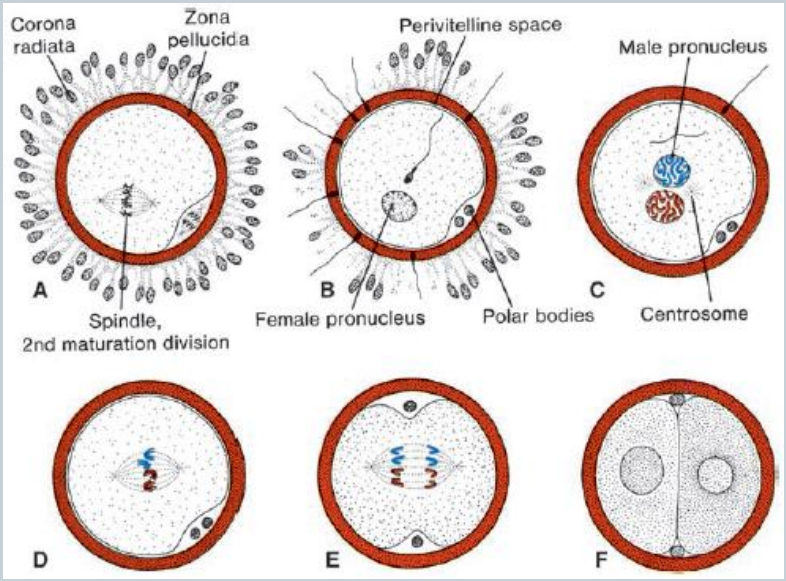
Fertilization

- **Ampullary region of the uterine tube**

Sperm capability

(1) **Capacitation** (in female reproductive tract, 7 hours duration) Removal of a glycoprotein coat and seminal plasma proteins from plasma membrane

(2) **Acrosome reaction** (induced by zona protein, release of enzymes including acrosin- and trypsin-like substances)



Phases of Fertilization

Phase 1: penetration of the corona radiata (**capacitation)**

Phase 2 : penetration of the zona pellucida (**Acrosome reaction)**

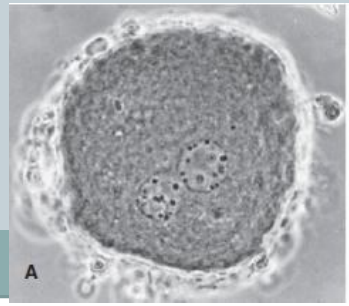
Phase 3 : fusion of the oocyte and sperm cell membranes (**integrin / oocyte + disintegrin / sperm)**

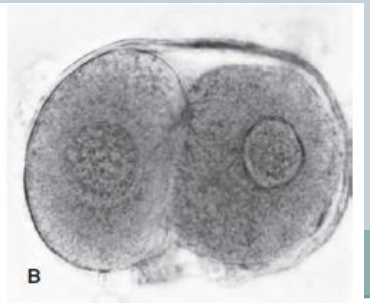
Sperm interance to oocyte:

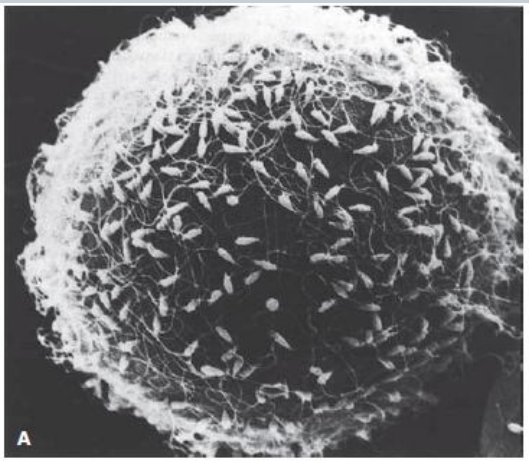
1. Cortical & zona reaction
2. Resumption of second meiosis division
3. Metabolic activation of the egg

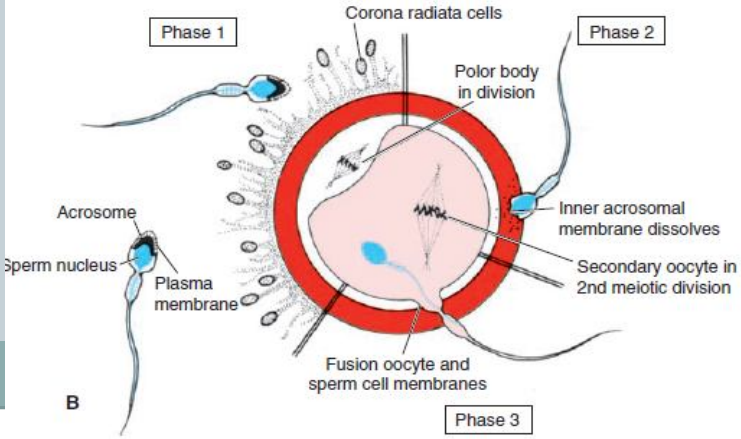
Fertilization results in:

1. Diploid number of chromosomes Restoration
2. Sex determination
3. Cleavage initiation









Phase 2: Penetration of the Zona Pellucida

The zona is a glycoprotein shell surrounding the egg that :

- ❖ Facilitates sperm binding
- ❖ maintains sperm binding
- ❖ induces the acrosome reaction

Penetration of the Zona Pellucida include:

1. binding & the acrosome reaction are mediated by the ligand ZP3, a zona protein
2. Release of acrosomal enzymes (acrosin) allows sperm to penetrate the zona
3. Sperm head in contact with the plasma membrane of the oocyte
4. Permeability of the zona pellucida changes when the head of the sperm comes in contact with the oocyte surface

❖This contact results in release of **lysosomal enzymes** from **cortical granules** lining the **plasma membrane of the oocyte**

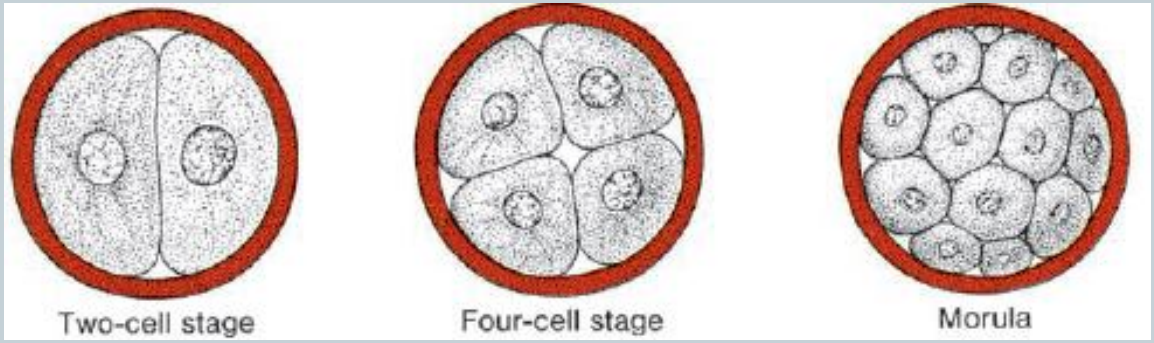
❖these enzymes alter properties of the zona pellucida **(zona reaction)** to prevent sperm penetration and inactivate receptor sites for spermatozoa on the zona surface

Other spermatozoa have been found embedded in the zona pellucida, but only **one seems to be able to penetrate the oocyte**

Cleavage

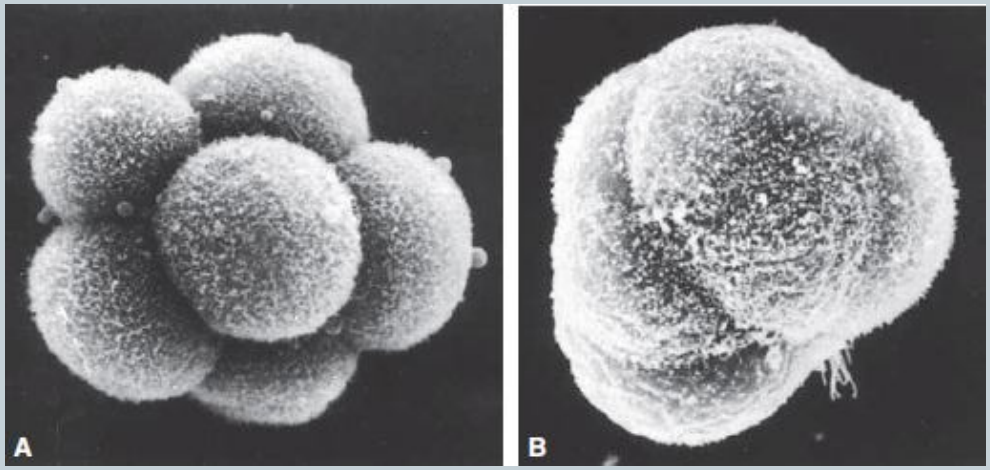
Zygote :

- 2 cells embryo (blastomer formation)
- 4 cells embryo
- 8 cells embryo
- 16 cells embryo (morula)



❖ Compaction :

- Inner cell mass (gap junction)
- Outer cell mass (thigh junction)



Blastocyst formation

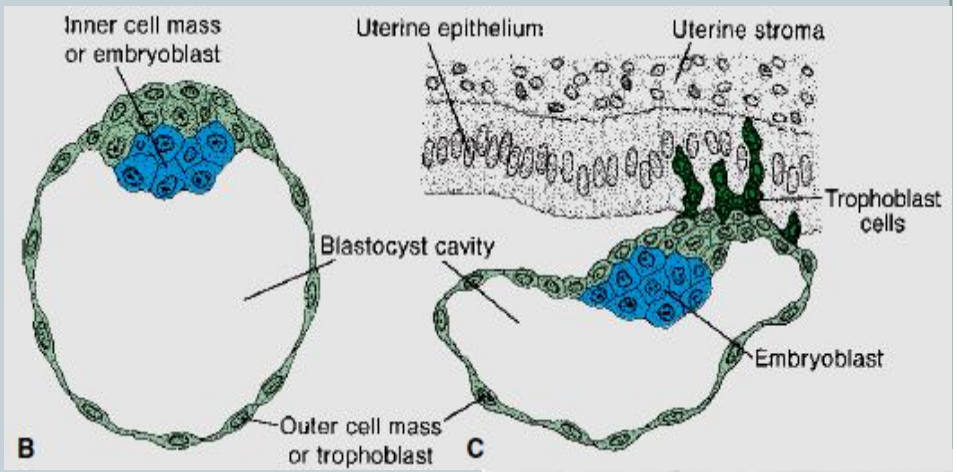
- Morulla enterance Uterus
- Start Fluid penetration to intercellular space of inner cell mass / from **Zona Pellucida**
- Blastocele formation
- Formation of blastocyte

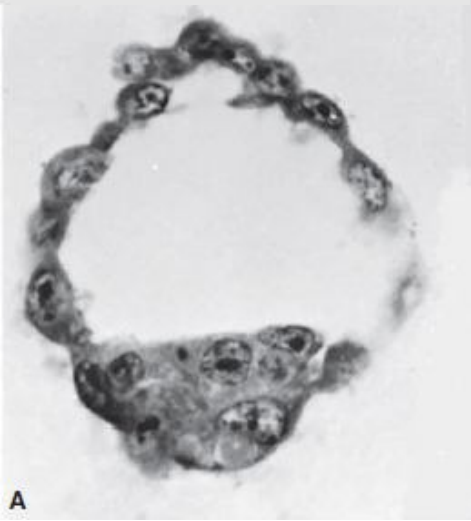
Blastocyst include :

- Inner cell mass (embryo blast)
- Outer cell mass (trophoblast)

Point :

Zona Pellucida disappear





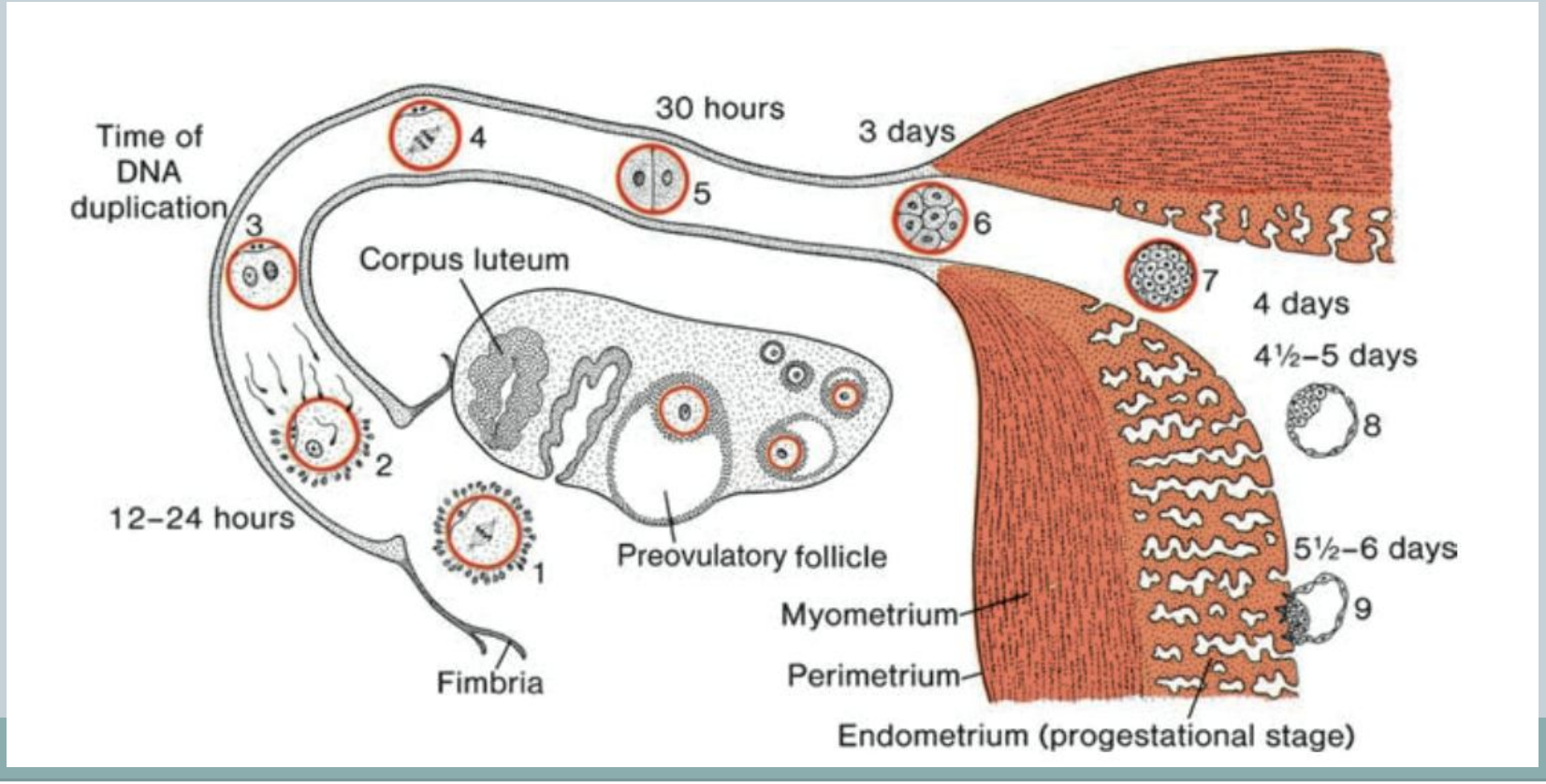
❖In 6th day trophoblast on embryoblastic pole penetrate to uterus epithelial cell

Embryo (L-selectin, integrins)

Uterus (carbohydrate receptor, laminin & fibronectin)

Uterus layers

1. Endometrium
2. Myometrium
3. perimetrium

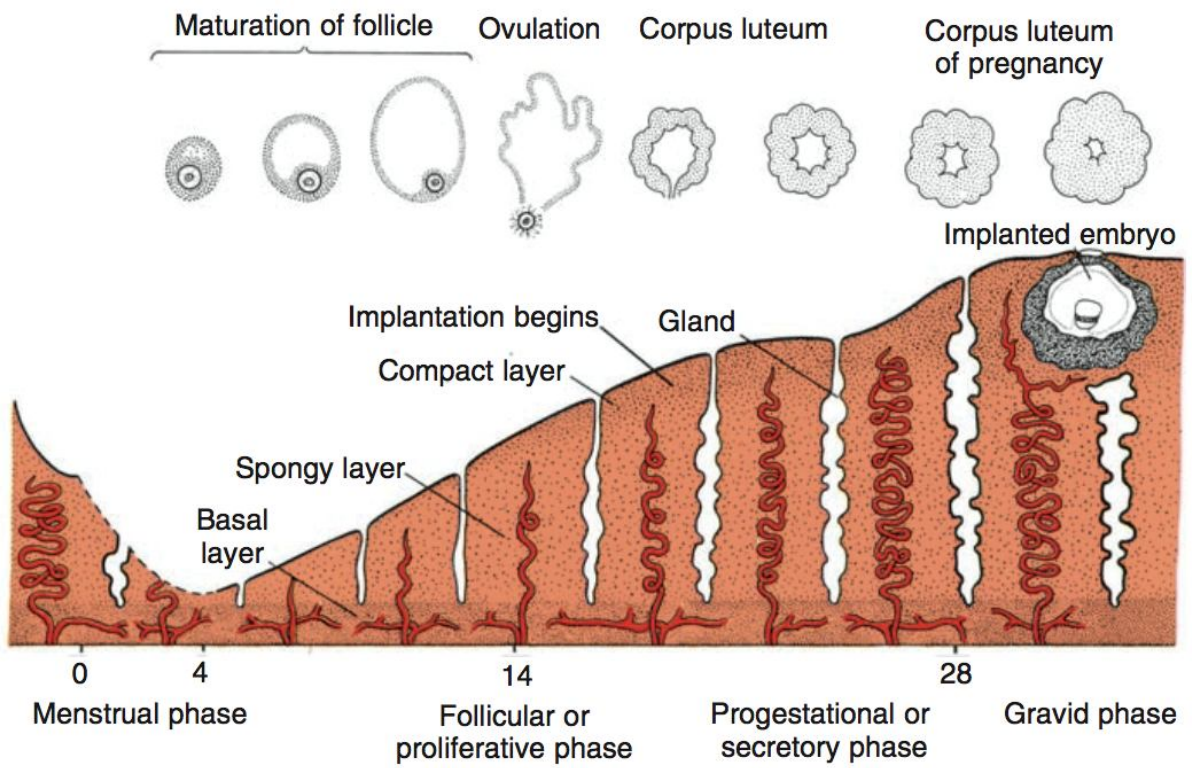


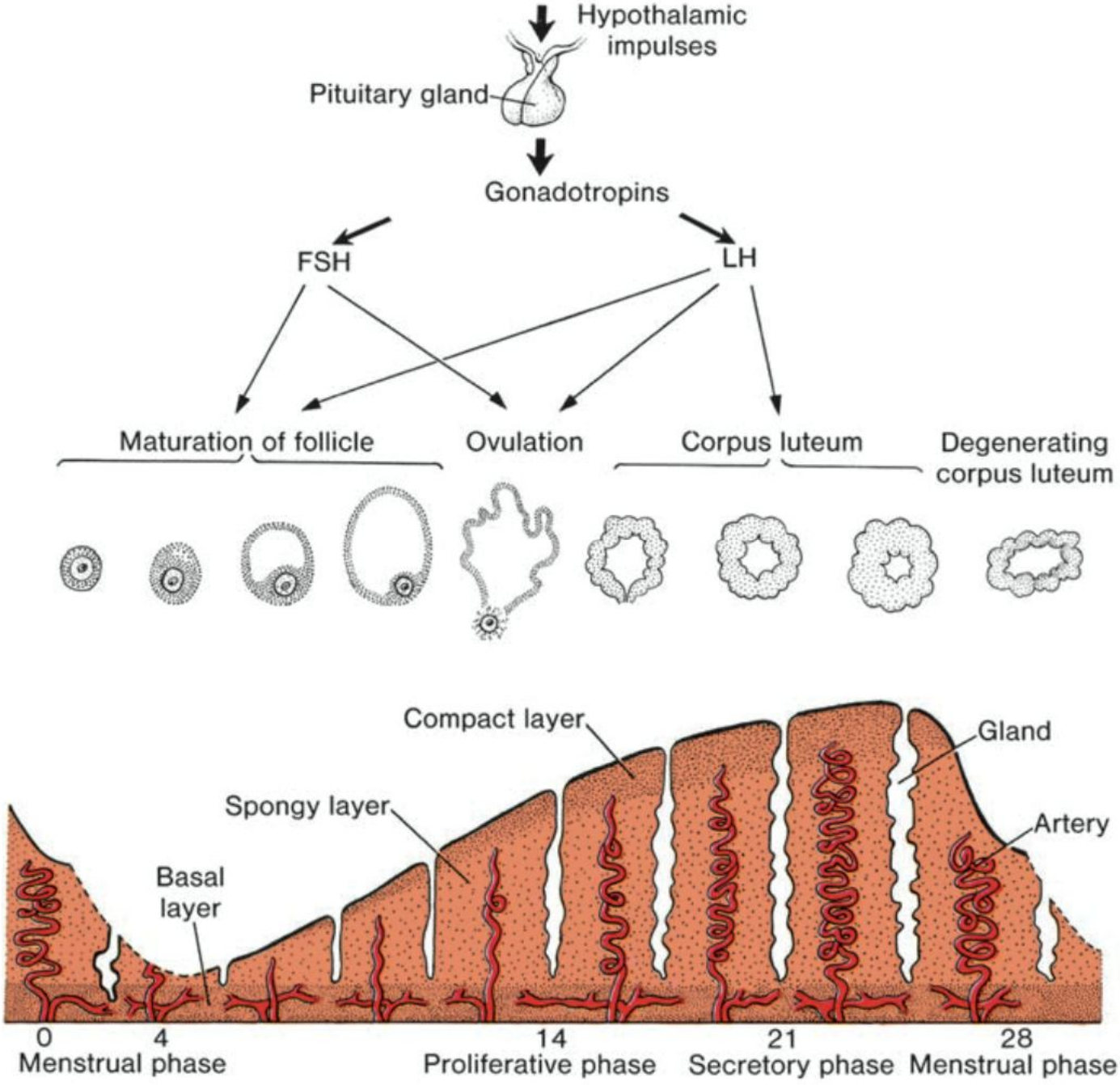
Menstrual cycle

1. **Follicular or proliferative phase**
2. **Secretory or progestational phase**
3. **Menstrual phase**

In implantation period
Endometrium consist of :

- Compact layer
- Spongy layer
- Basal layer




Hypothalamic impulses
Pituitary gland
Gonadotropins
FSH
LH
Maturation of follicle
Ovulation
Corpus luteum
Degenerating corpus luteum
Compact layer
Gland
Spongy layer
Artery
Basal layer
0
4
14
21
28
Menstrual phase
Proliferative phase
Secretory phase
Menstrual phase

Contraceptive Methods

- Barrier methods
- Hormonal methods
- intrauterine device (IUD)
- Emergency contraceptive pills (ECPs)
- Sterilization

Infertility

- 15-30%
- Male factor
- Female factor

- ART
- In vitro fertilization (IVF)
- Intracytoplasmic sperm injection (ICSI)

Clinical Correlates

Embryonic Stem Cells

Embryonic stem cells (ES cells) are derived from the inner cell mass of the embryo. Because these cells are **pluripotent** and can form virtually any cell or tissue type, they have the potential for curing a variety of diseases, including diabetes, Alzheimer's and Parkinson's diseases, anemias, spinal cord injuries, and many others. Using animal model research with stem cells has been encouraging. For example, mouse ES cells in culture have been induced to form insulin-secreting cells, muscle and nerve stem cells, and glial cells. In whole animals, ES cells have been used to alleviate the symptoms of Parkinson's disease and to improve motor ability in rats with spinal cord injuries.

ES cells may be obtained from embryos after **IVF**, a process called **reproductive cloning**. This approach has the disadvantage that the cells may cause immune rejection, because they would not be genetically identical to their hosts. The cells could be modified to circumvent this problem, however. Another issue with this approach is based on ethical considerations, as the cells are derived from viable embryos.

As the field of stem cell research progresses, scientific advances will provide more genetically compatible cells, and the approaches will be less controversial. Most recently, techniques have been devised to take nuclei from adult cells (e.g., skin) and introduce them into enucleated oocytes. This approach is called **therapeutic cloning** or **somatic nuclear transfer**. Oocytes are stimulated to differentiate into blastocysts, and ES cells are harvested. Because the cells are derived from the host, they are compatible genetically, and because fertilization is not involved, the technique is less controversial.

Adult Stem Cells

Adult tissues contain stem cells that may also prove valuable in treating diseases. These cells are restricted in their ability to form different cell types and, therefore, are **multipotent**, not pluripotent, although scientists are finding methods to circumvent this disadvantage. Adult stem cells isolated from rat brains have been used to cure Parkinson's disease in rats, suggesting that the approach has promise. Disadvantages of the approach include the slow rates of cell division characteristic of these cells and their scarcity, which makes them difficult to isolate in sufficient numbers for experiments.

Abnormal Zygotes

The exact number of **abnormal zygotes** formed is unknown because they are usually lost within 2 to 3 weeks of fertilization, before the woman realizes she is pregnant, and therefore are not detected. Estimates are that as many as **50% of pregnancies end in spontaneous abortion** and that half of these losses are a result of chromosomal abnormalities. These abortions are a natural means of screening embryos for defects, reducing the incidence of congenital malformations. Without this phenomenon, approximately 12% instead of 2% to 3% of infants would have birth defects.

With the use of a combination of IVF and **polymerase chain reaction**, molecular screening of embryos for genetic defects is being conducted. Single blastomeres from early-stage embryos can be removed, and their DNA can be amplified for analysis. As the Human Genome Project provides more sequencing information, and as specific genes are linked to various syndromes, such procedures will become more commonplace.