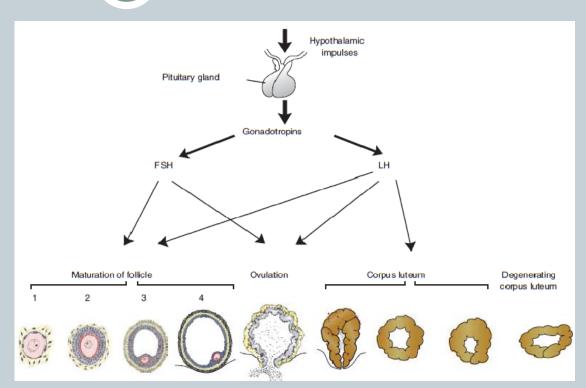
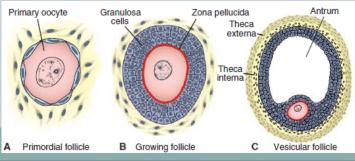
# First week of development

# Ovulation To Implantation

# Ovarian cycle

- At puberty
- Sexual cycles
- Hypothalamus (GnRH)
- Adenohypophysis (gonadotropins)
   LH & FSH
   Folicle growth & atresia
   Corpus atreticum
- Follicular cell growth
   GDF-9 (TGF-β)
- Follicular cell maturation FSH

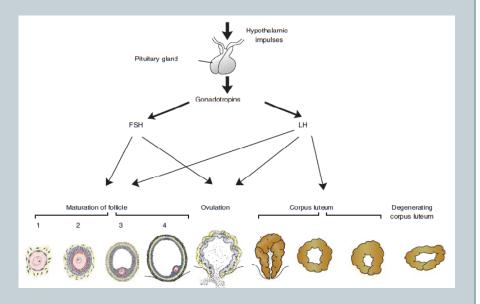




## First week of development

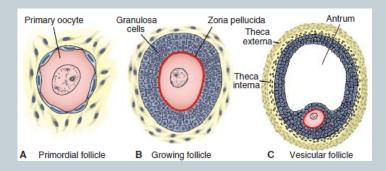
## Theca & granulosa cells secret estrogens:

- Uterus enters to follicular or proliferative phase
- Thinning the cervical mucosa
- Pituitary gland stimulation for LH secretion



### LH surge in mid cycle:

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

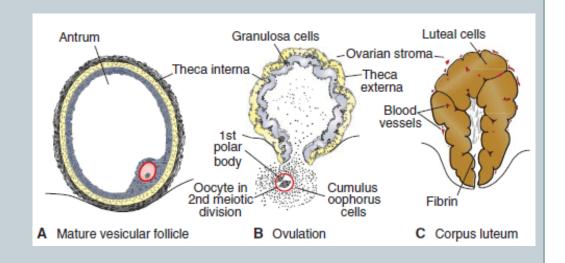


## **Ovulation**

- FSH & LH
- Follicle growth: 25 mm

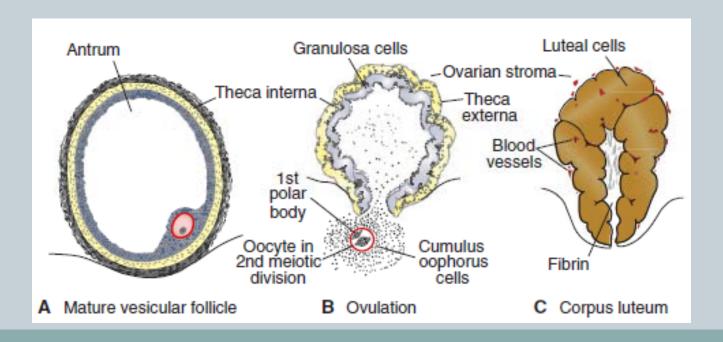
## LH surge

- Meiosis I completion
- Meiosis II initiation
- Stops 3 hours before ovulation
- Stigma
- Lhsurge & ovulation
- Collagenase
- Prostaglandins
- Oocyte-crona radiata complex



# Corpus luteum

- Vascularization & Progesterone production
- Progestational or secretory stage
- Preparation for embryo implantation

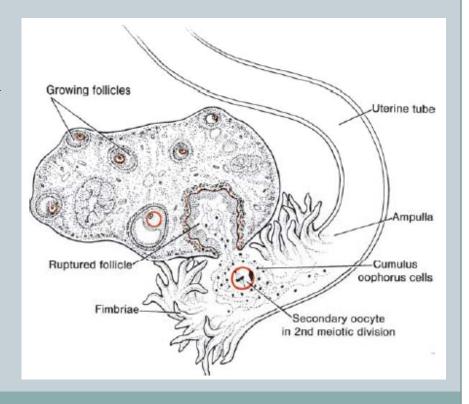


## Oocyte transfer

- Uterine fimbriae & Tube rhythmic contract
- cumulus cells withdraw cytoplasmic processes from the zona pellucida
- fertilized oocyte reaches the uterine lumen in 3 to 4 days

## regulated by:

endocrine status during and after ovulation



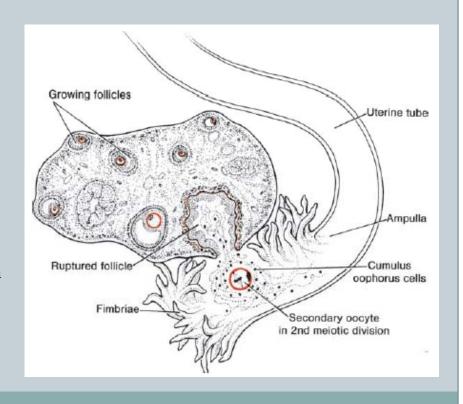
# Corpus albicans

#### No fertilization

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

#### **Fertilization**

- Prevention of corpus luteum degeneration by:
- hCG (syncytiotrophoblast)
- corpus luteum of pregnancy
- end of the third month  $\frac{1}{2}$  -1/3 of the size of the ovary
- Luteal cells secrete progesterone until end of the 4<sup>th</sup> month
- then regress (placental progesterone)
- corpus luteum Removal before 4th month leads to abortion



- Ovulation(Midcycle) & midpain
- Higher basal temperature

- Low level of gonadotropins (no ovulation)
- Synthetic gonadotropin (10 times more in multiple pregnancy)

## 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

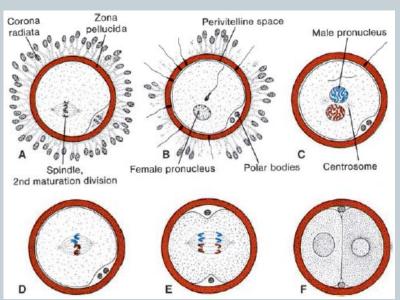
ovulate because of a low concentration of gonadotropins. In these cases, administration of an agent to stimulate gonadotropin release, and hence ovulation, can be employed. Although such drugs are effective, they often produce multiple ovulations, so that the likelihood of multiple pregnancies is 10 times higher in these women than in the general population.

## **Fertilization**

Ampullary region of the uterine tube

Sperm capability

- **Capacitation** (female reproductive tract, 7 hours) Removal of a glycoprotein coat and seminal plasma proteins from plasma membrane
- **Acrosome reaction** (induced by zona protein, release of enzymes, including acrosin- and trypsin-like substances)

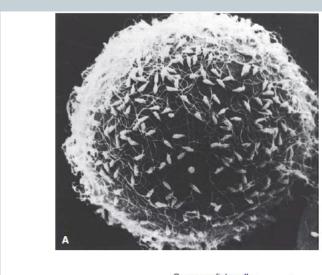


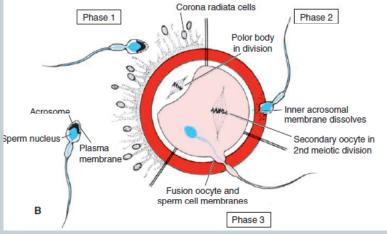
## **Phases of Fertilization**

- 1. Phase 1, penetration of the corona radiata
- 2. Phase 2, penetration of the zona pellucida
- 3. Phase 3, fusion of the oocyte and sperm cell membranes

## **Sperm interance to oocyte:**

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

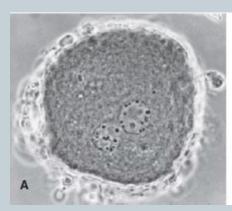




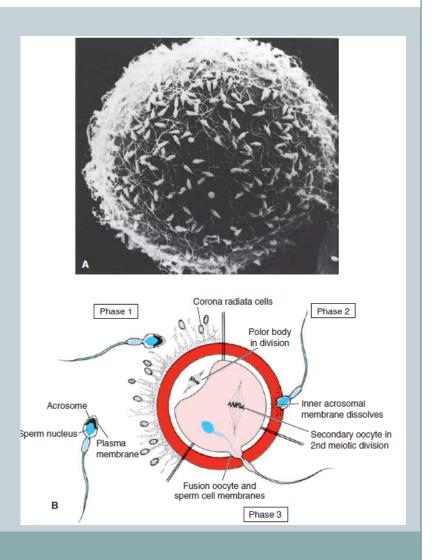
## **Phases of Fertilization**

#### **Fertilization results in:**

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





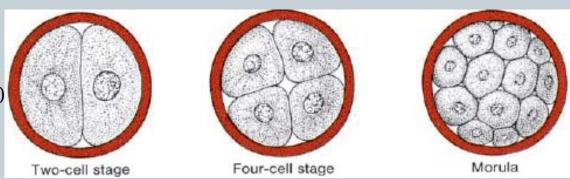


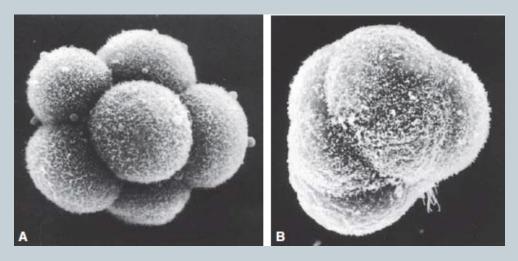
# Cleavage

- Zygote
- 2 cells embryo
- 4 cells embryo
- 8 cells embryo

Compaction (tight & gap junctions)

• 16 cells embryo (morula)





# Blastocyst formation

- Uterus enterance
- Fluid penetration to intercellular space
- Blastocele

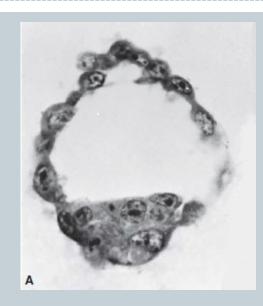
## Blastocyst

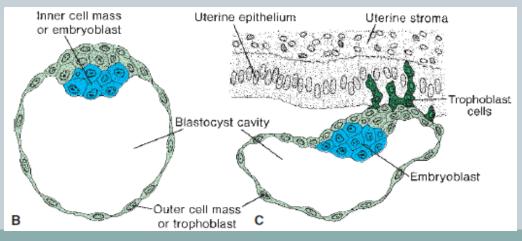
- Inner cell mass
- Outer cell mass

## 6<sup>th</sup> day:

Embryo (L-selectin, integrins)

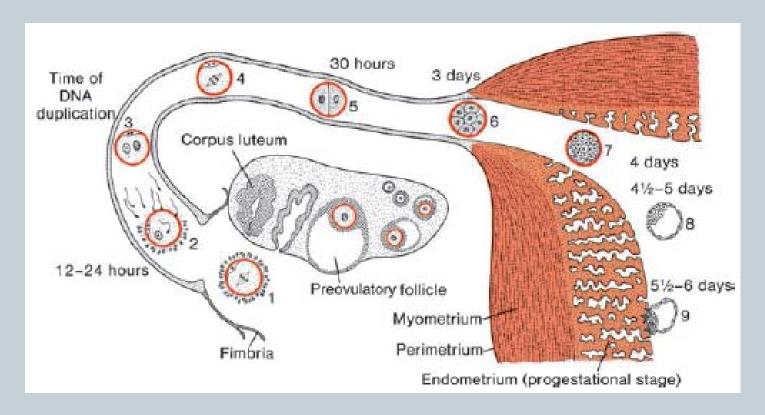
Uterus (carbohydrate receptor, laminin & fibronectin)





# **Uterus layers**

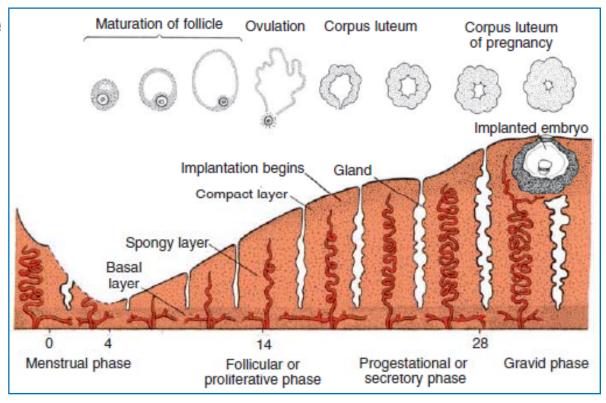
- 1. Endometrium
- 2. Myometrium
- 3. perimetrium

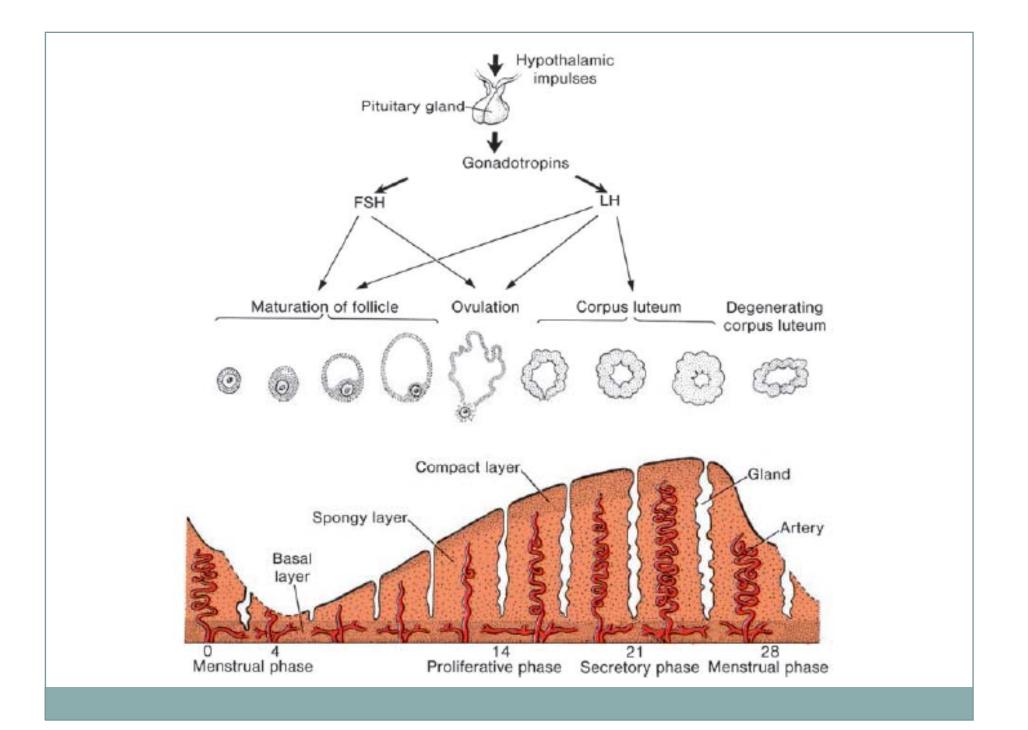


## Menstrual cycle

- 1 Follicular or proliferative phase
- 2 Secretory or progestational phase
- 3 Menstrual phase

- implantation Endometrium
- Compact layer
- Spongy layer
- Basal layer





## 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.

