# First Week of Development

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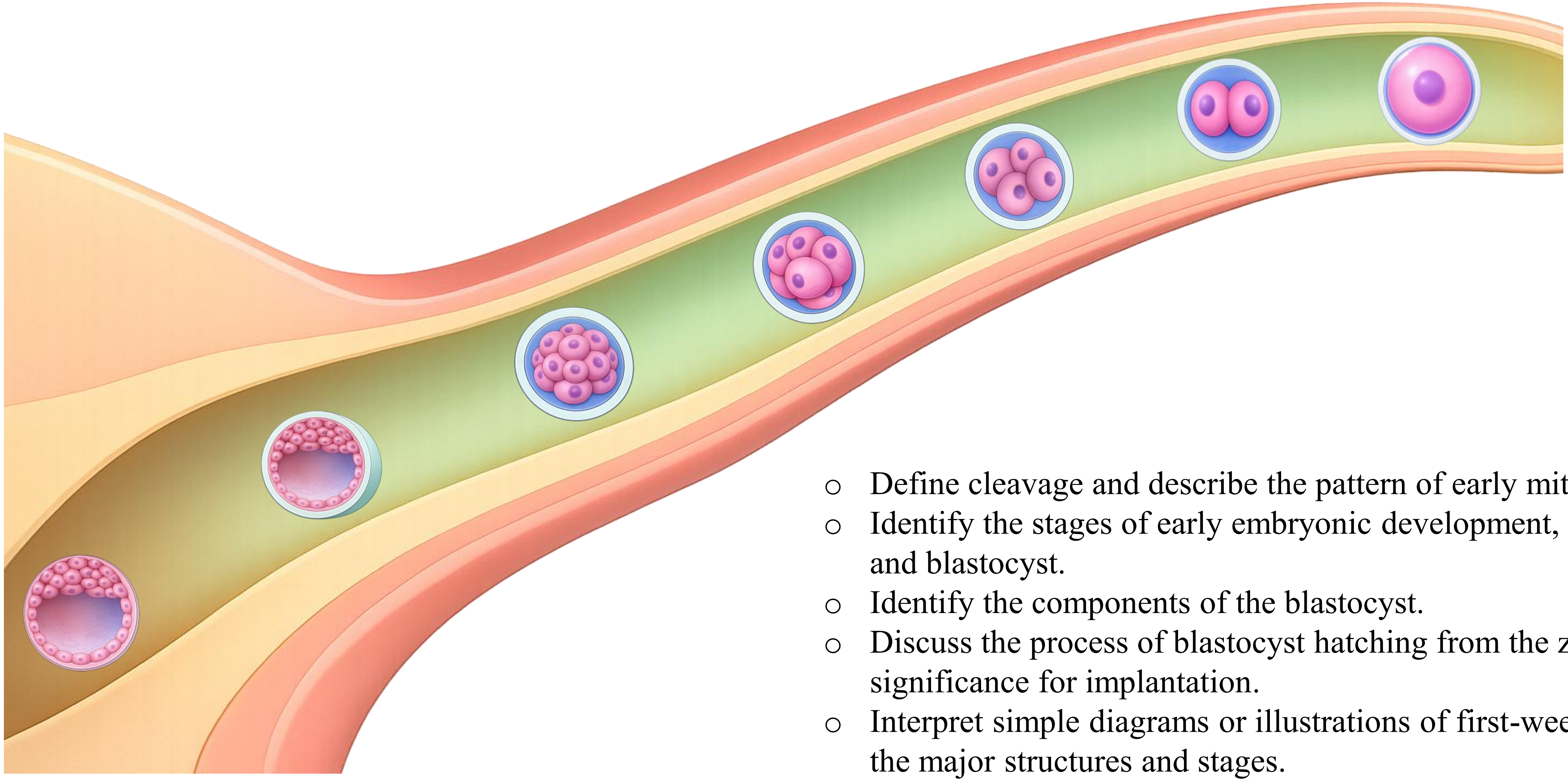
By the end of this lecture, students should be able to:

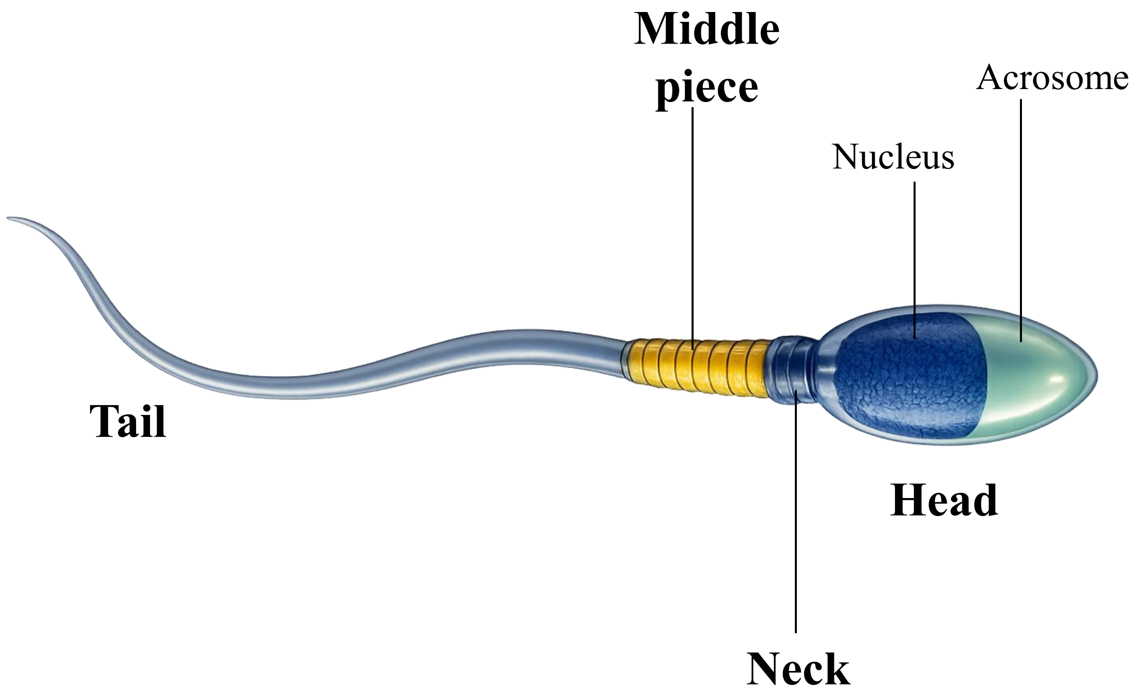
- Define fertilization and state its normal site.
- Describe the steps of fertilization including capacitation and acrosome reaction.
- Explain the biological significance of fertilization.
- Explain the mechanisms that prevent polyspermy.

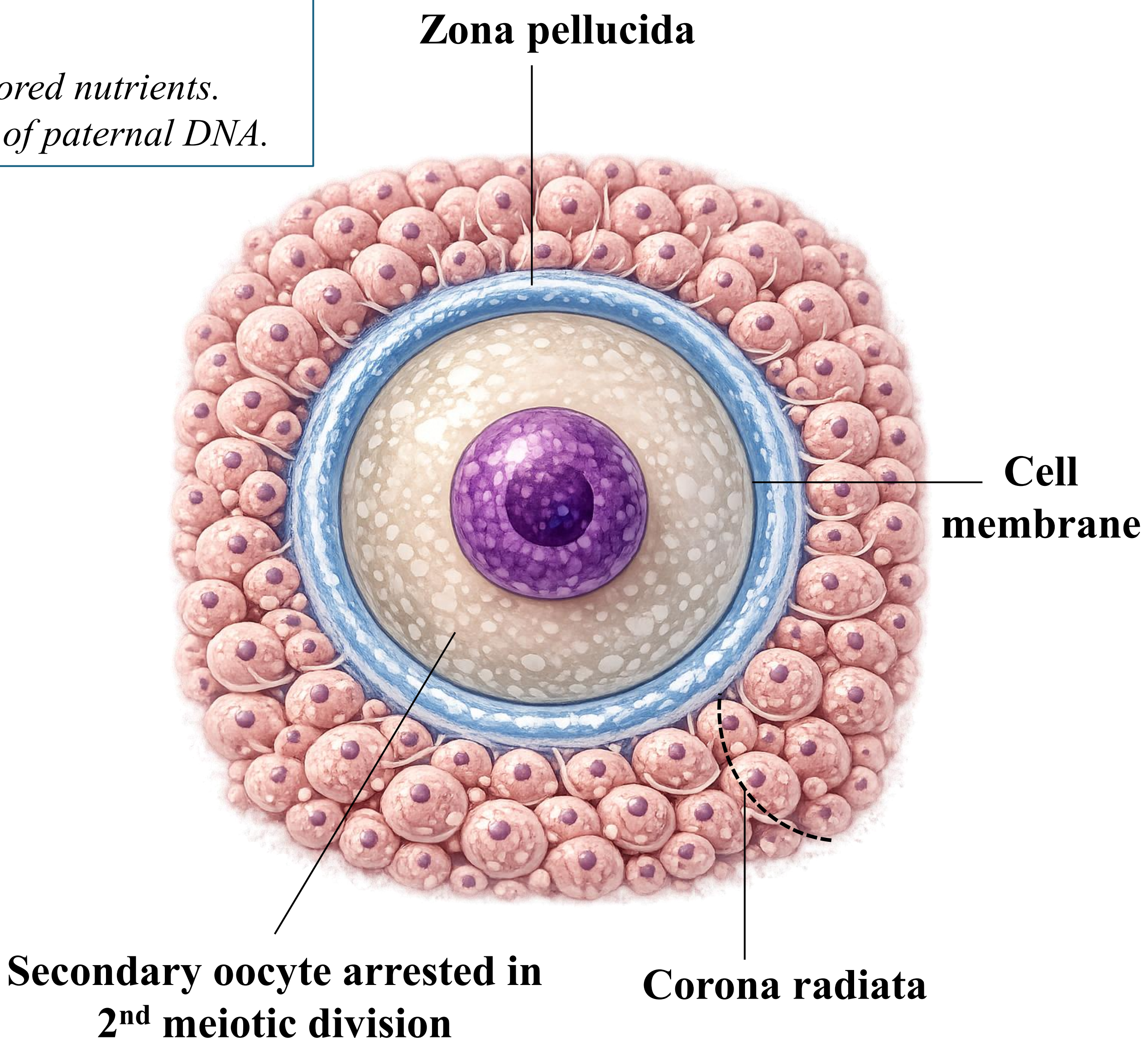


- Define cleavage and describe the pattern of early mitotic divisions of the zygote.
- Identify the stages of early embryonic development, including the zygote, morula, and blastocyst.
- Identify the components of the blastocyst.
- Discuss the process of blastocyst hatching from the zona pellucida and its significance for implantation.
- Interpret simple diagrams or illustrations of first-week development and identify the major structures and stages.

*The ovum (egg cell) is the largest cell in the human body, while the sperm cell is the smallest human cell.*

*The ovum is large because it contains abundant cytoplasm and stored nutrients.*
*The sperm is small because it is streamlined for motility and delivery of paternal DNA.*



**Fertilization:** It is the process by which a sperm units with the ovum.

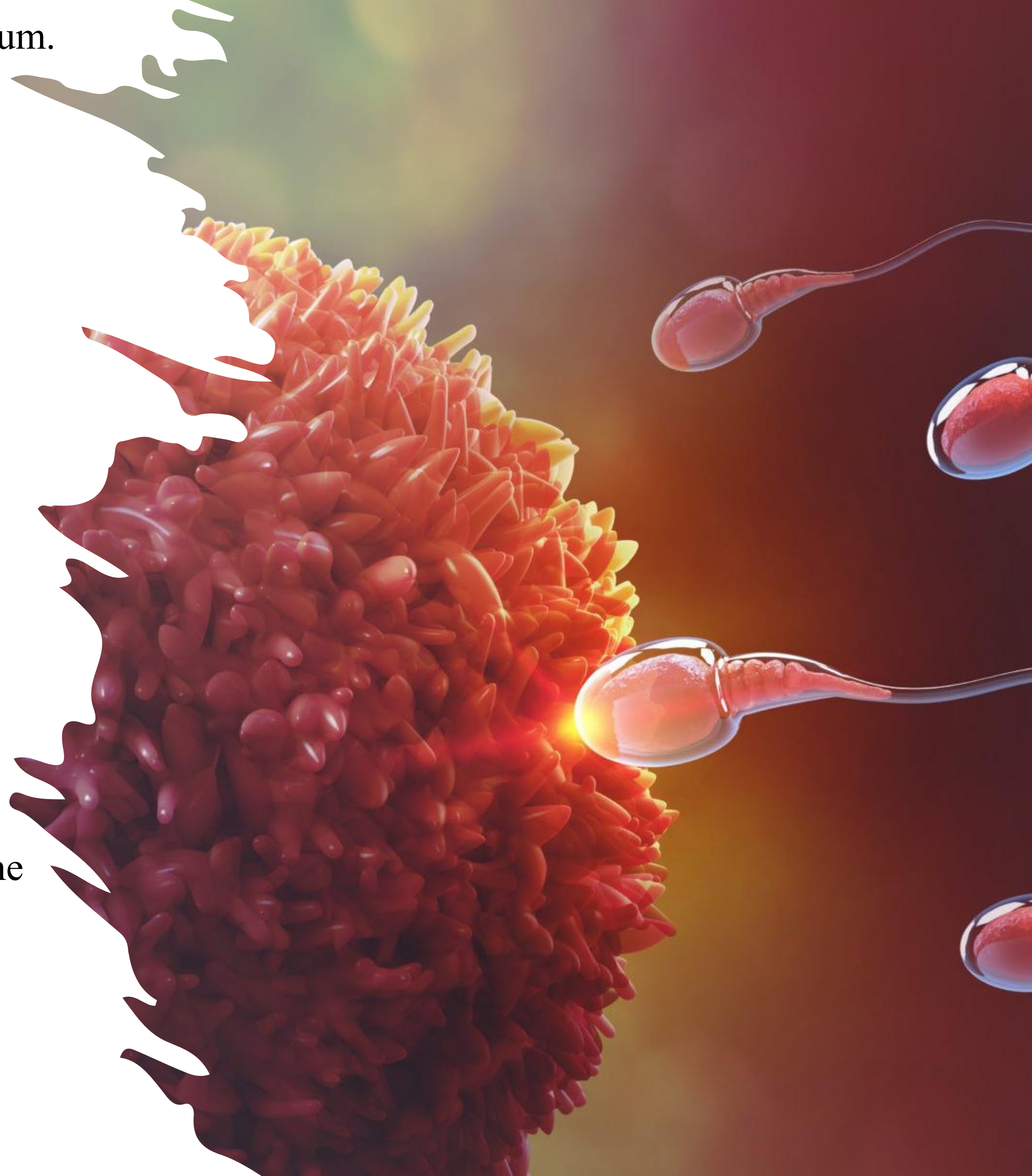
**Site:** Ampulla of uterine tube (outer 1/3 of uterine tube)

**Mechanisms of fertilization:**

- Capacitation of the sperms.
- Acrosomal reaction.
- Cortical & zona reaction.
- Secondary oocyte completes 2nd meiotic division.
- Nucleus of sperm enters the cytoplasm of ovum.
- Union between male and female pronuclei to form zygote.

**Results:**

- Formation of zygote.
- Restoration of diploid number (46 chromosomes).
- Determination of sex.
- Cleavage starts, during which the zygote travels through uterine tube by help of cilia and contraction of uterine tube.



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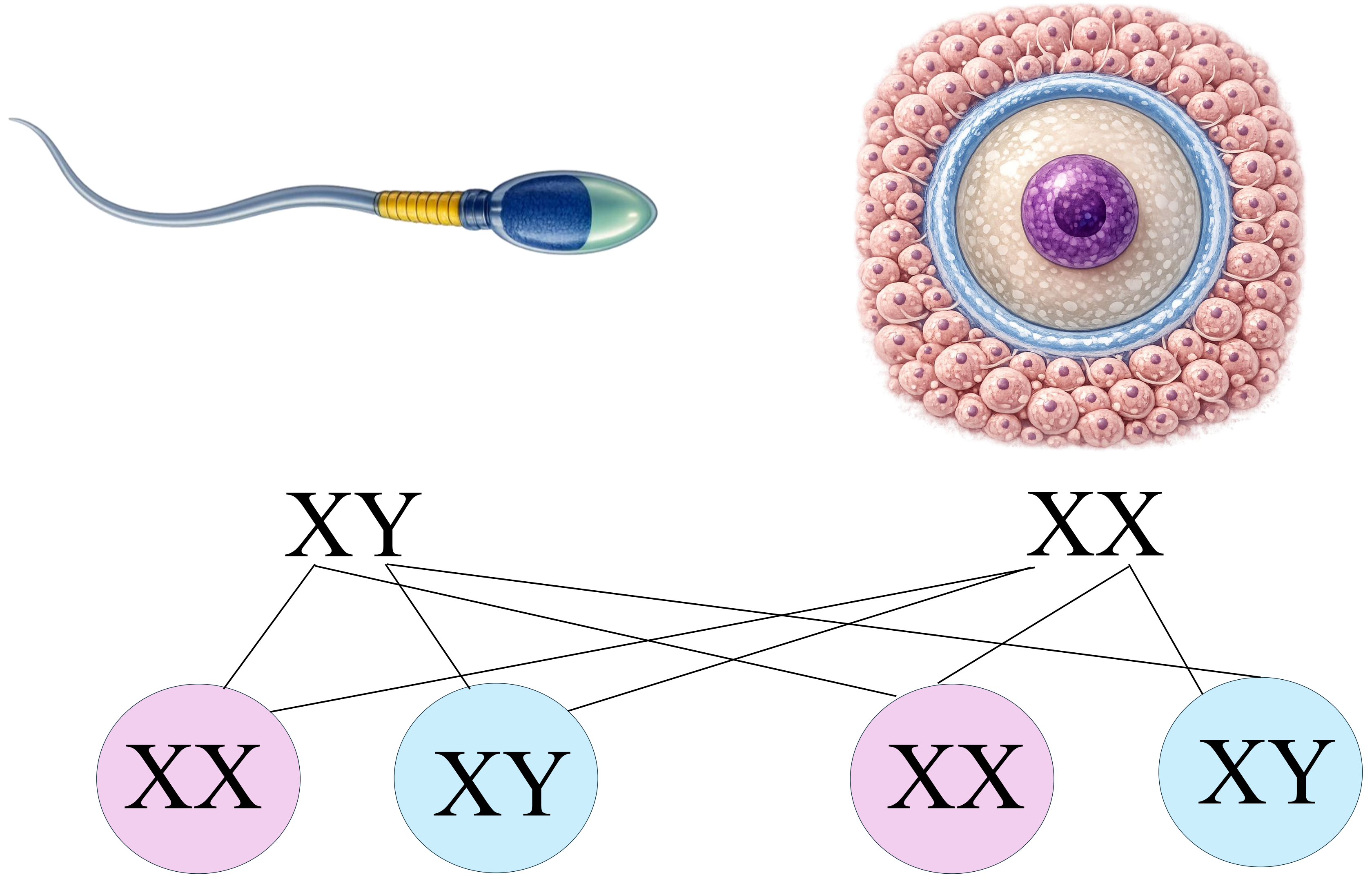
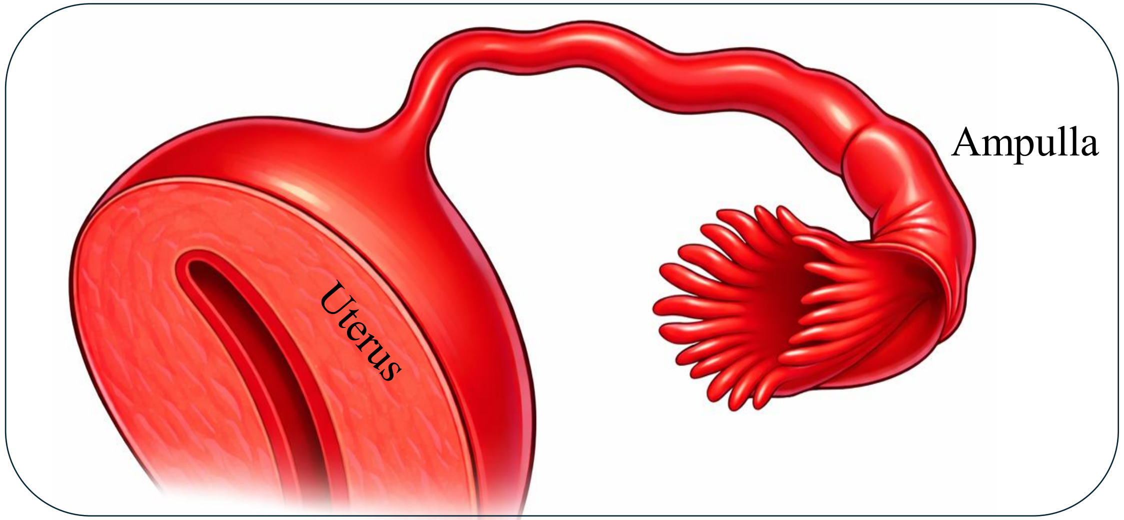
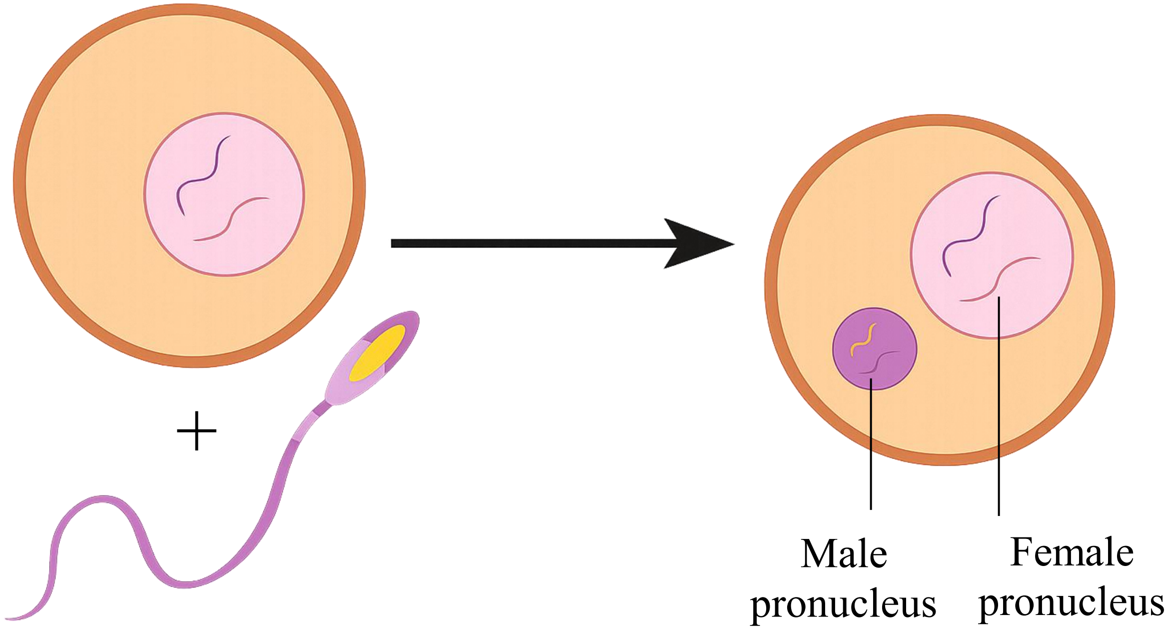
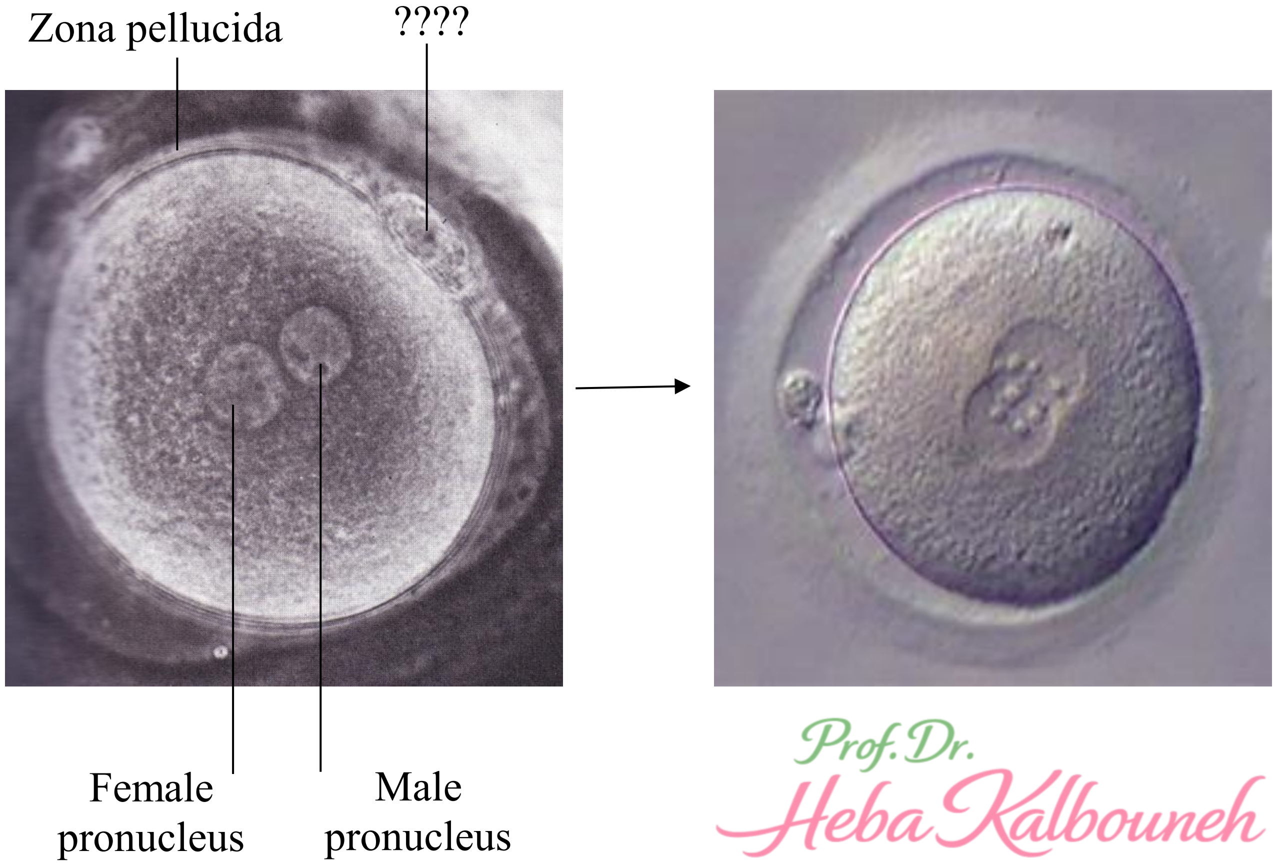



**Determination of sex**

- ✓ Fertilization begins when capacitated sperm reach the secondary oocyte in the ampulla of the uterine tube.
- ✓ The sperm first pass through the corona radiata using enzymes from the acrosome and strong tail movements.
- ✓ Binding of the sperm to the zona pellucida triggers the acrosome reaction, allowing the sperm to penetrate the zona.
- ✓ Fusion of the sperm and oocyte membranes then occurs, followed by the cortical and zona reactions, which prevent entry of additional sperm.
- ✓ The sperm penetrates the secondary oocyte, and the secondary oocyte completes its second meiotic division.
- ✓ Finally, the male and female pronuclei fuse to form a zygote, restoring the diploid chromosome number and marking the beginning of a new individual.

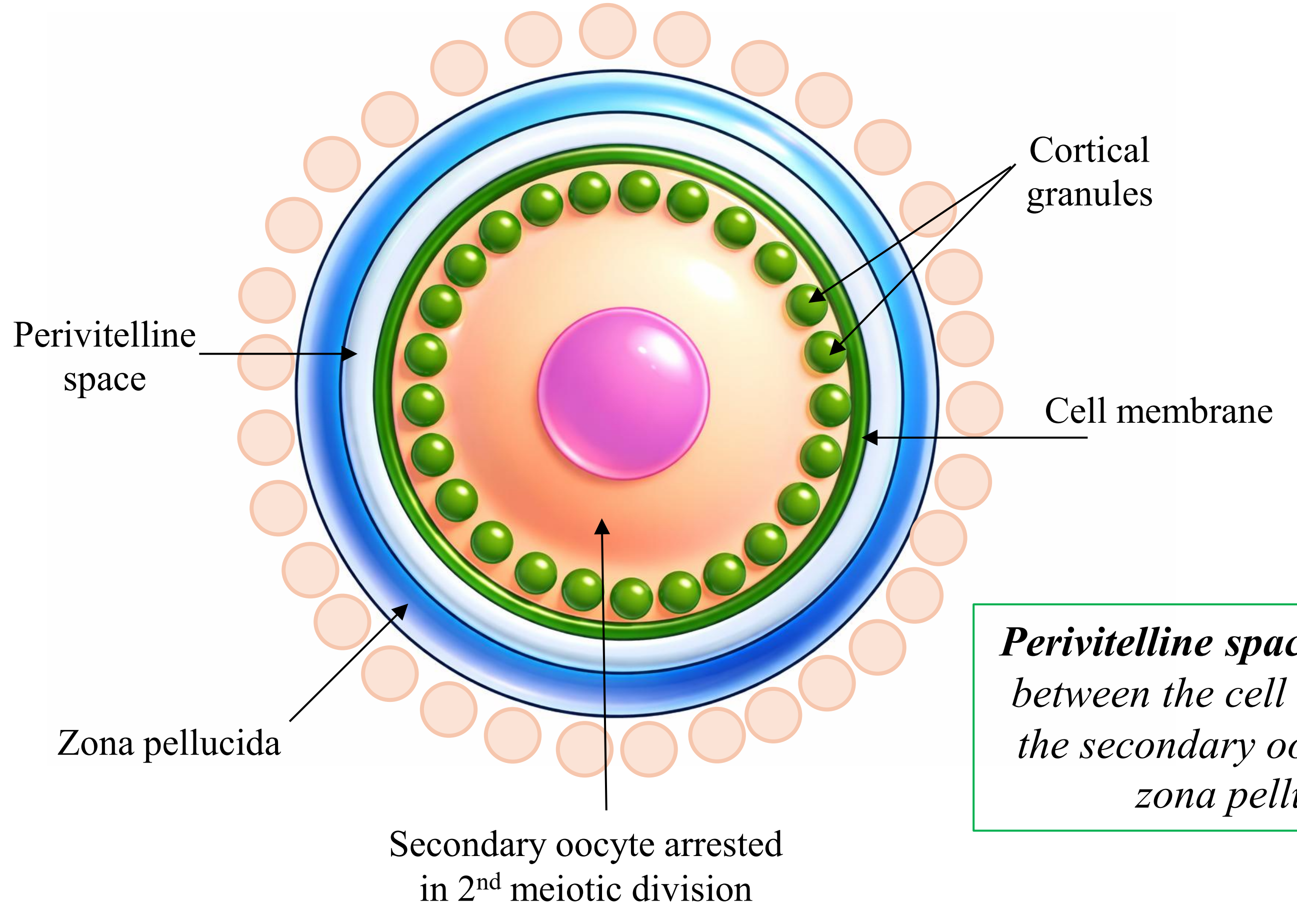


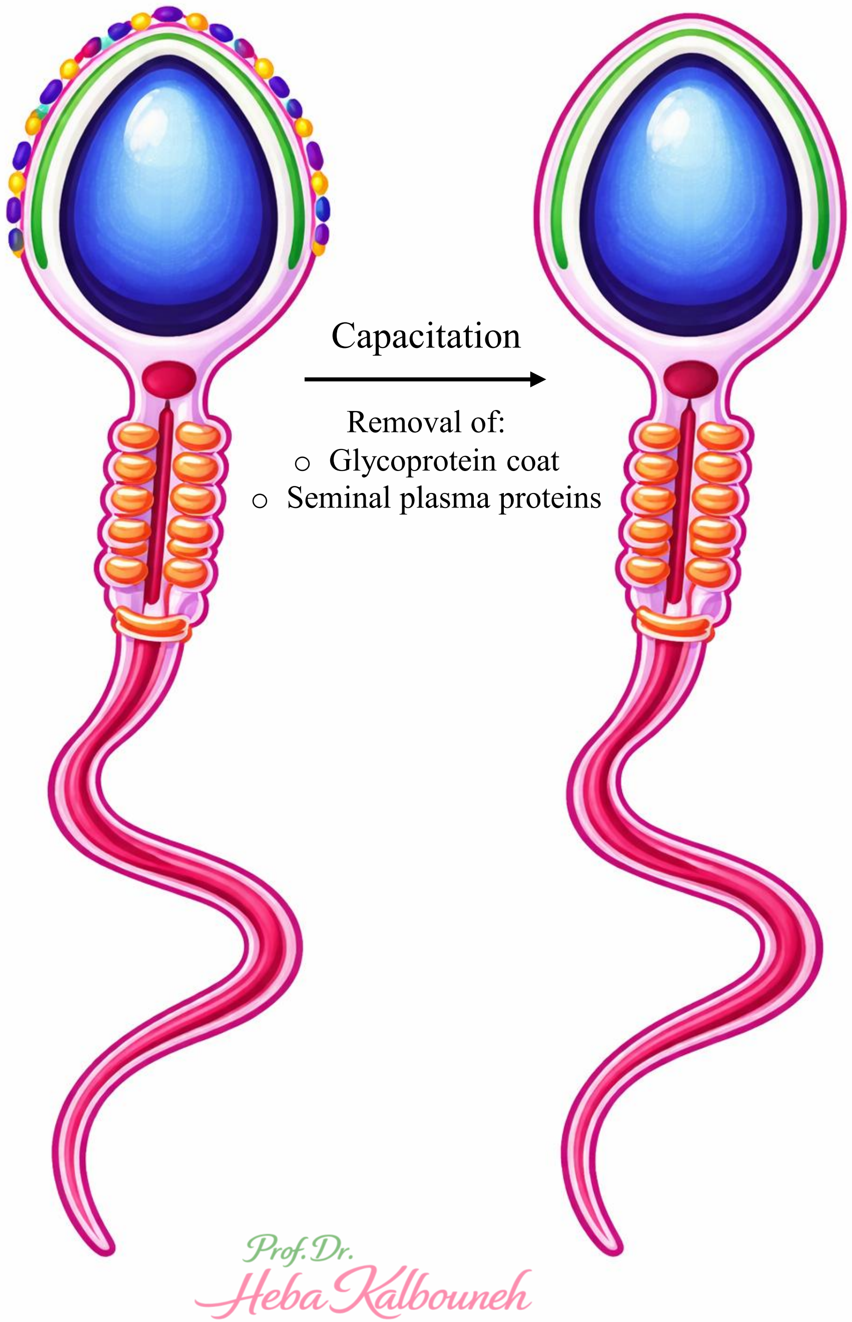



**Capacitation**

Capacitation is a functional maturation process that sperm undergo in the female reproductive tract. During this process, proteins and cholesterol are removed from the sperm cell membrane, increasing sperm motility and making the sperm capable of undergoing the acrosome reaction and fertilizing the oocyte.




***Perivitelline space*** *is the space between the cell membrane of the secondary oocyte and the zona pellucida.*

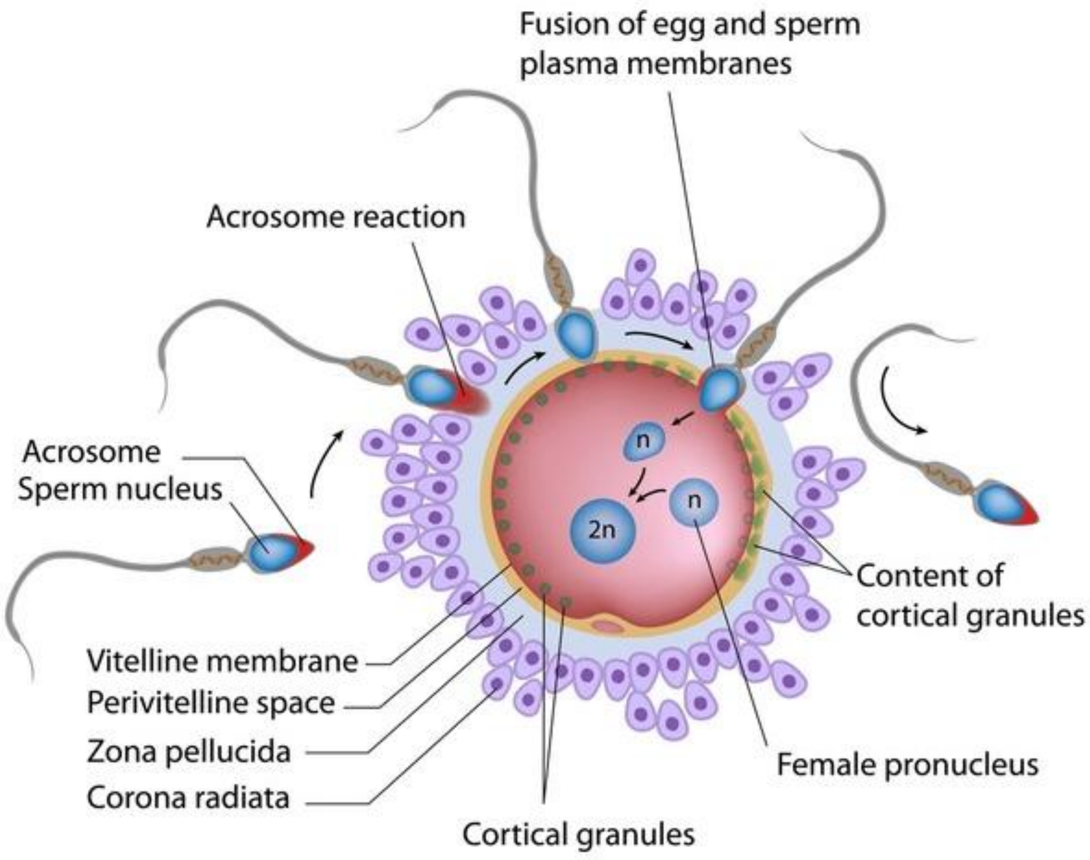


## Acrosome reaction

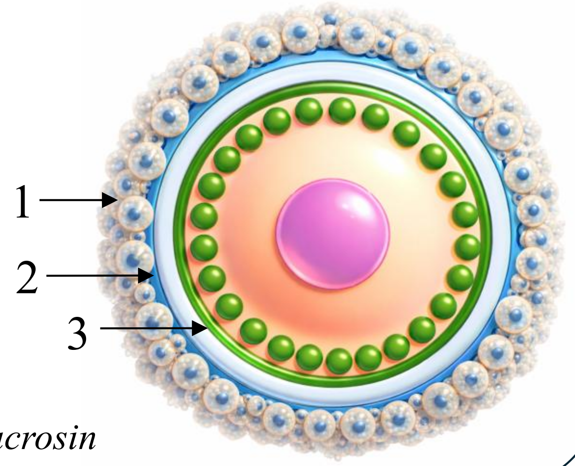
The acrosome reaction occurs when a capacitated sperm binds to the zona pellucida of the secondary oocyte. The sperm plasma membrane fuses with the outer acrosomal membrane, releasing enzymes, which allow the sperm to penetrate the zona pellucida.

## Cortical and Zona Reactions

After sperm–oocyte membrane fusion, the oocyte releases cortical granules from its cytoplasm (cortical reaction). These granules are discharged into the perivitelline space and cause biochemical changes in the zona pellucida (zona reaction), making it impermeable to other sperm. Together, these reactions prevent polyspermy.




1- Passage of sperm through corona radiata
2- Penetration of the zona pellucida
3- Penetration of oocyte plasma membrane




*Acrosomal enzymes: Hyaluronidase and acrosin*

The corona radiata is a layer of granulosa (cumulus) cells embedded in hyaluronic acid–rich matrix surrounding the oocyte. It is the first barrier sperm must traverse.

⇩

Sperm release hyaluronidase

⇩

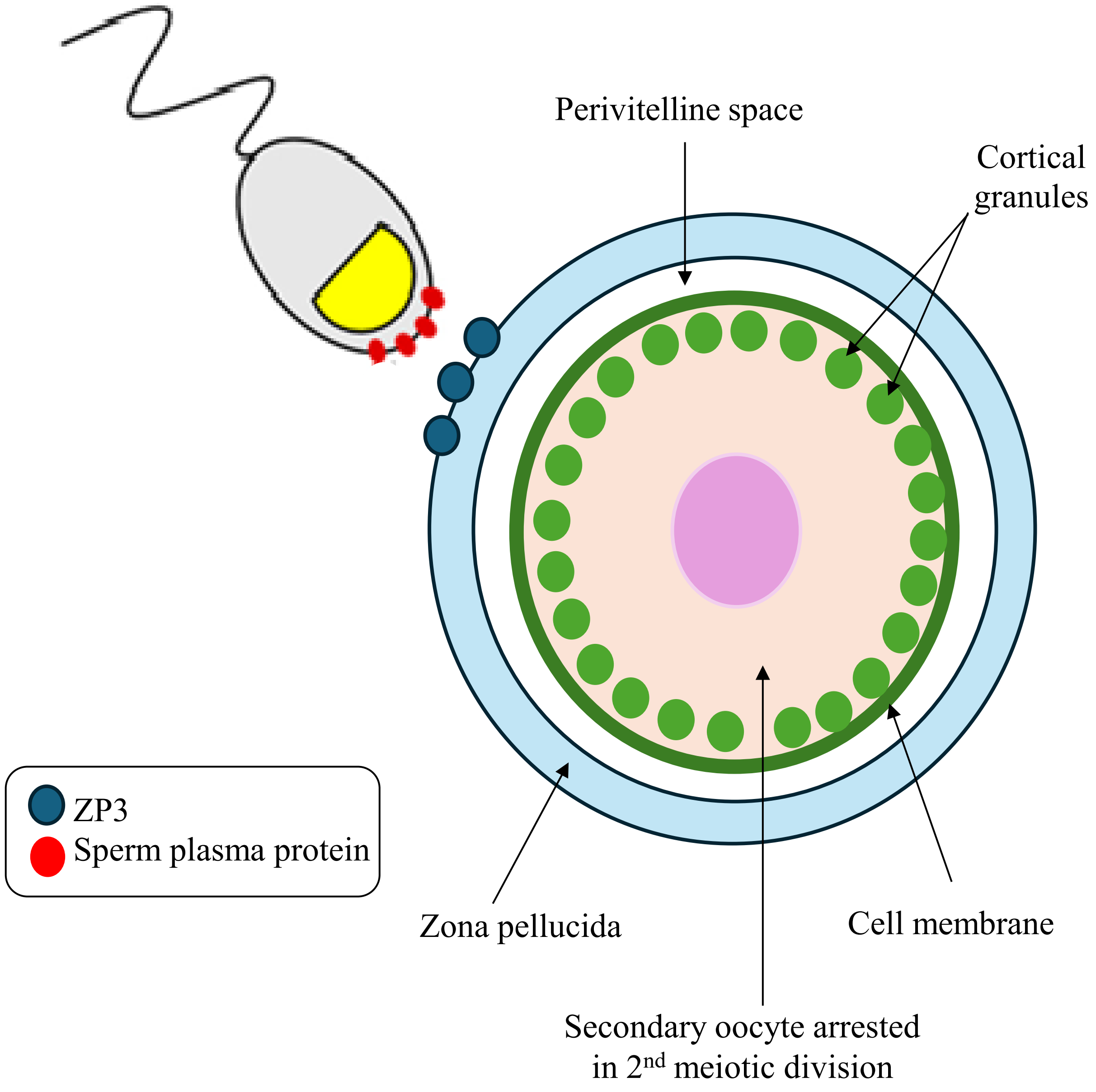
This enzyme breaks down hyaluronic acid → loosens cell cohesion

*Note: Many sperm help, but only one fertilizes*

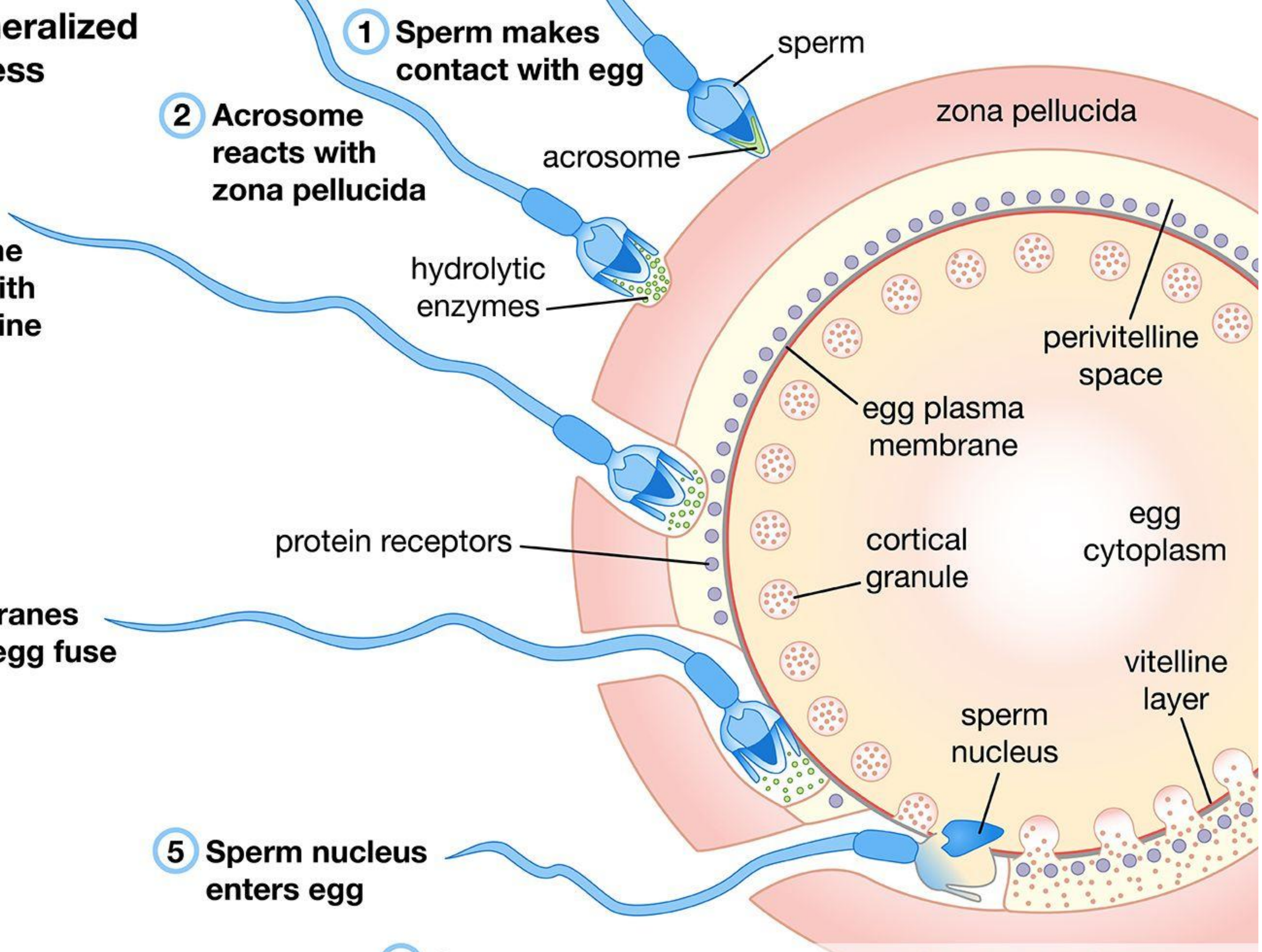
**How does sperm bind to the zona pellucida?**

After penetrating the corona radiata, a capacitated sperm binds to the zona pellucida through a specific receptor–ligand interaction:

1. The zona pellucida contains glycoproteins, especially ZP3.
2. ZP3 acts as a receptor that binds to complementary proteins on the sperm plasma membrane.
3. This binding is species-specific and ensures that only human sperm can fertilize a human oocyte.
4. Binding of the sperm to ZP3 triggers the acrosome reaction.
5. Enzymes released during the acrosome reaction allow the sperm to penetrate the zona pellucida.



# Fertilization: generalized acrosomal process




6 Cortical granules fuse with egg plasma membrane, which renders the vitelline layer impenetrable to sperm

# Cleavage & Migration

- ✓ Fertilization leads to formation of a zygote which is a fertilized ovum surrounded with zona pellucida.

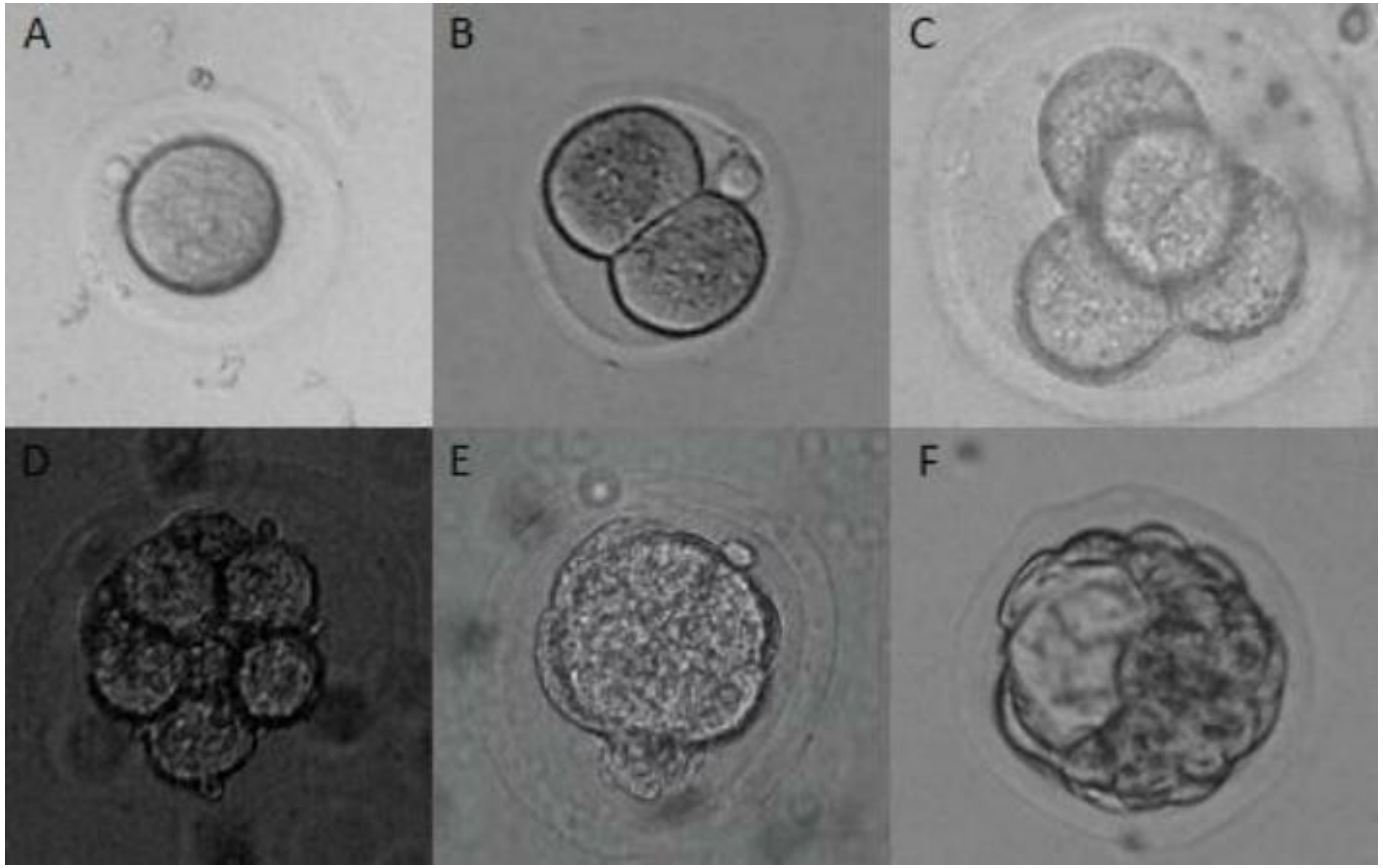
- ✓ Zygote divides by mitotic division to form:

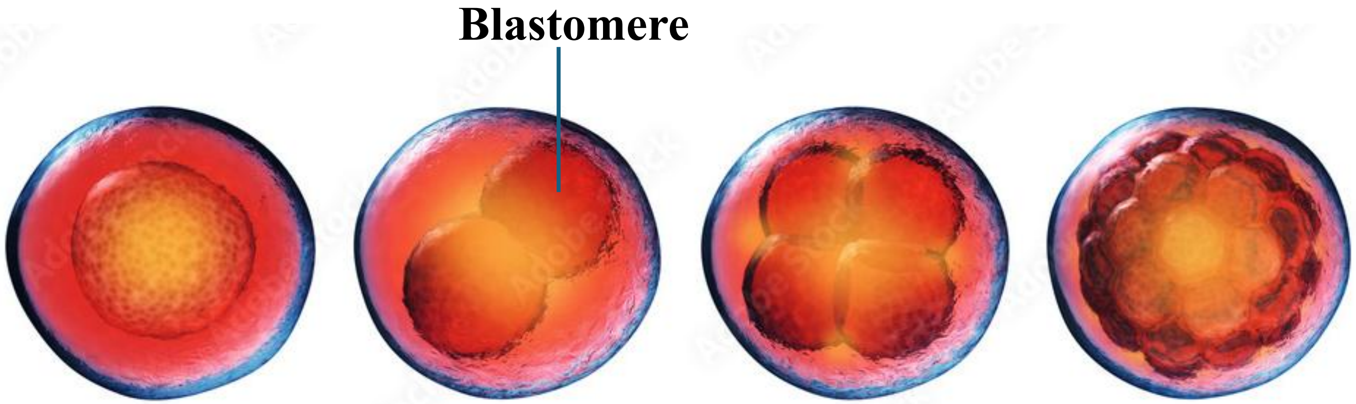
2-cell stage
4-cell stage
8-cell stage
16-cell stage (early morula)
32-cell stage (late morula)

- ✓ Formation of morula takes 3-4 days through which it is transmitted through the uterine tube.

- ✓ Zona pellucida prevents adhesion of zygote to uterine tube and prevents separation of cells.

*The cells produced by cleavage of the zygote during early embryonic development are called **blastomeres**.*

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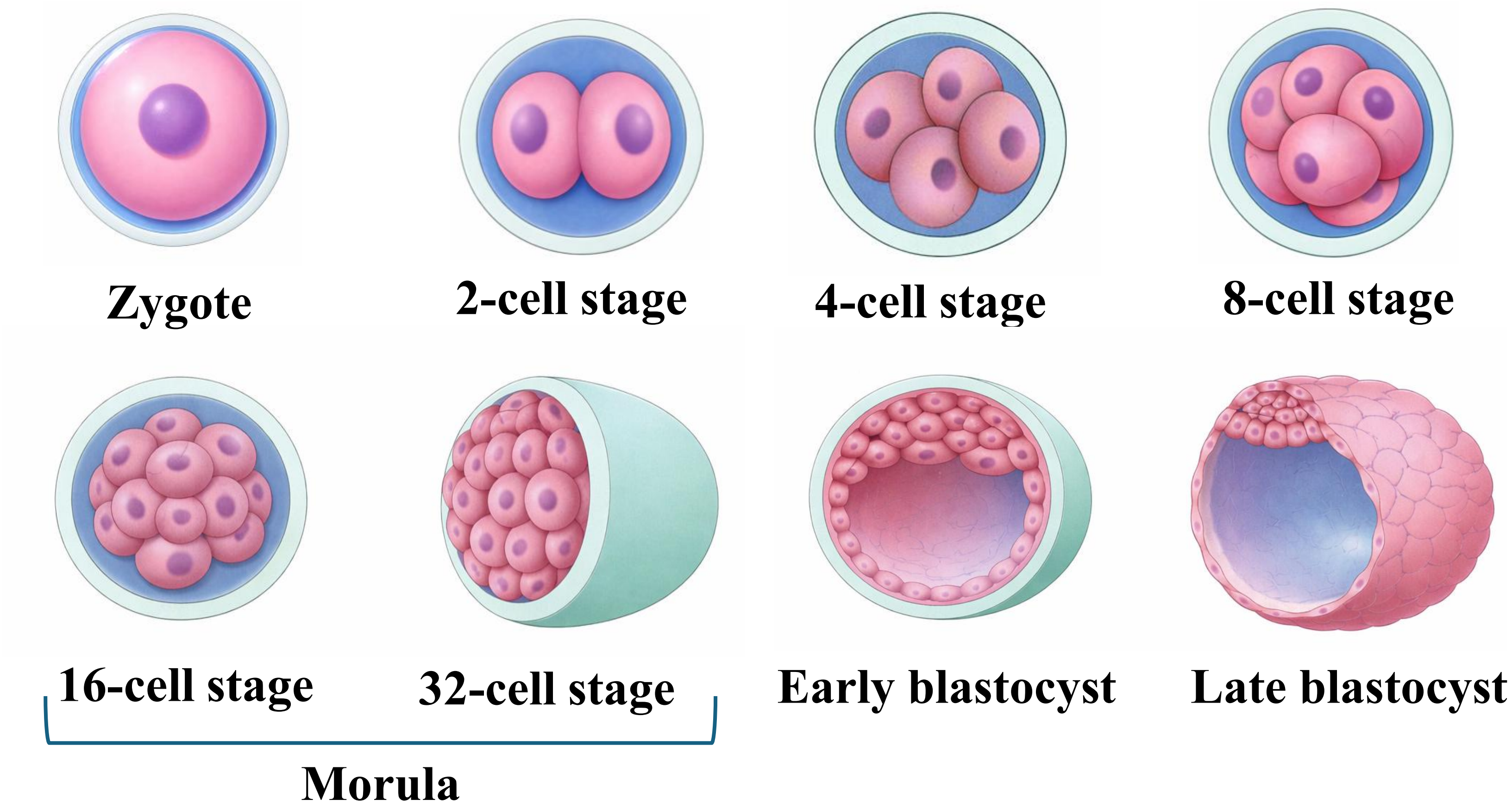
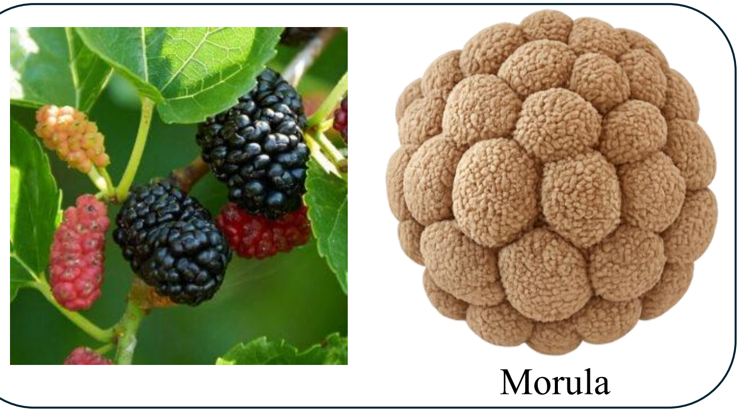
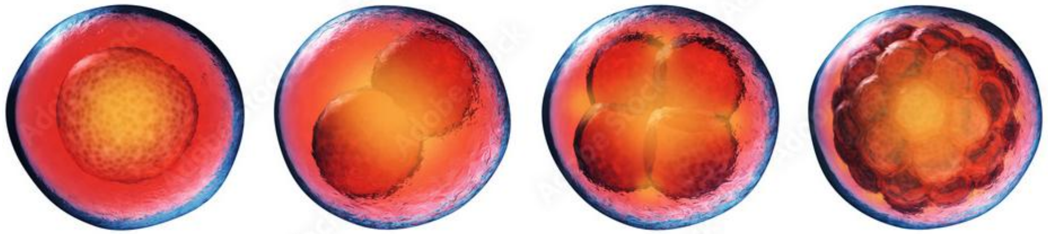



*The zona pellucida remains intact during the cleavage stages of embryonic development.*



The **morula** is a solid ball of blastomeres (about 16–32 cells) formed by repeated cleavage divisions of the zygote, before formation of the blastocyst.

- Occurs around day 3–4 after fertilization
- Cells are tightly packed (from *morus* = mulberry)
- Still enclosed by the zona pellucida
- Marks the transition from cleavage to blastocyst formation

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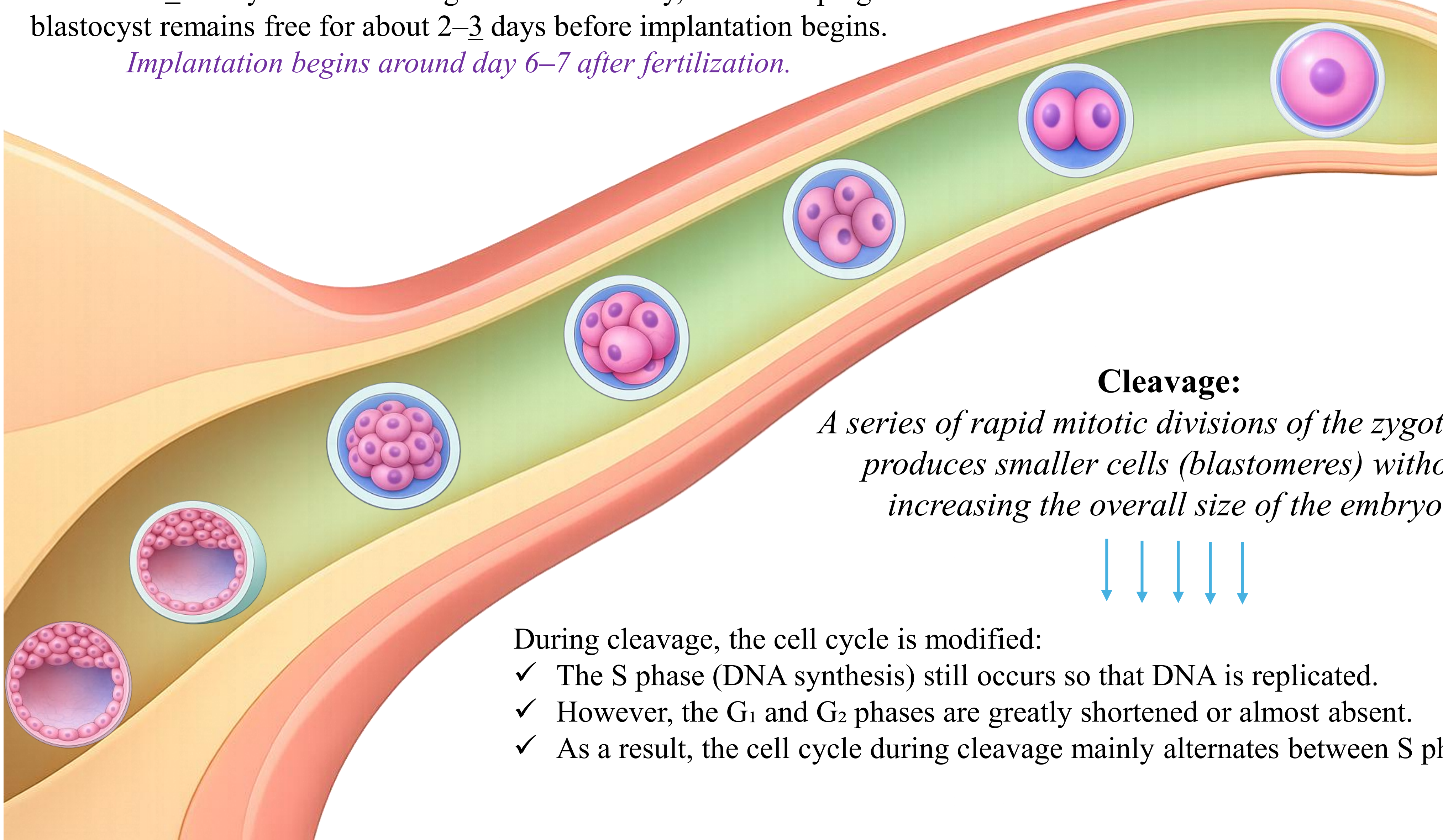
Sources of nourishment before implantation:

1. Nutrient reserves in the oocyte cytoplasm (ooplasm)
2. Tubal secretions during transport
3. Endometrial gland secretions (uterine milk) in the uterus

The zygote undergoes cleavage while traveling through the uterine tube for about 3–4 days. After entering the uterine cavity, the developing blastocyst remains free for about 2–3 days before implantation begins.

*Implantation begins around day 6–7 after fertilization.*



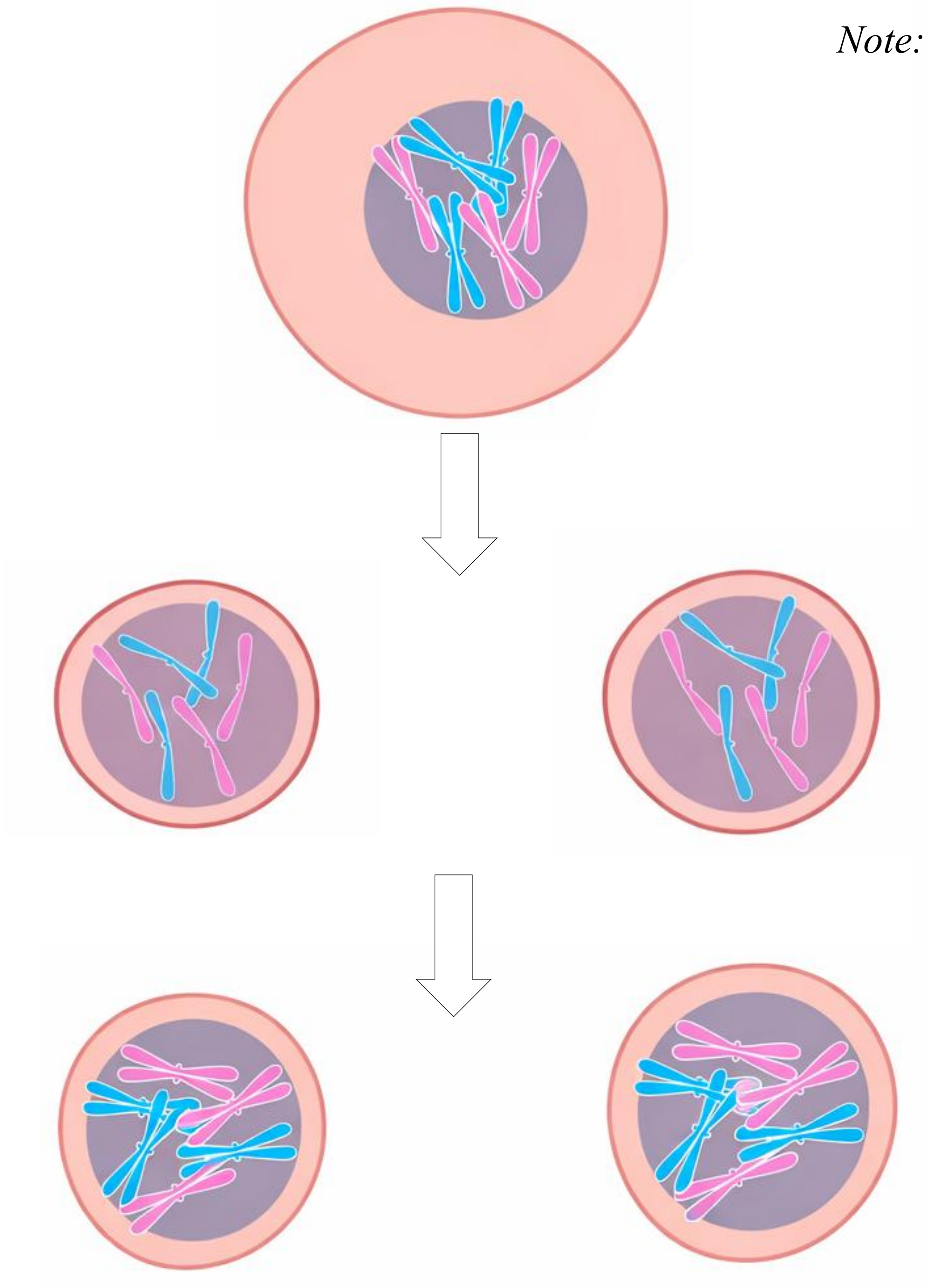
**Cleavage:**

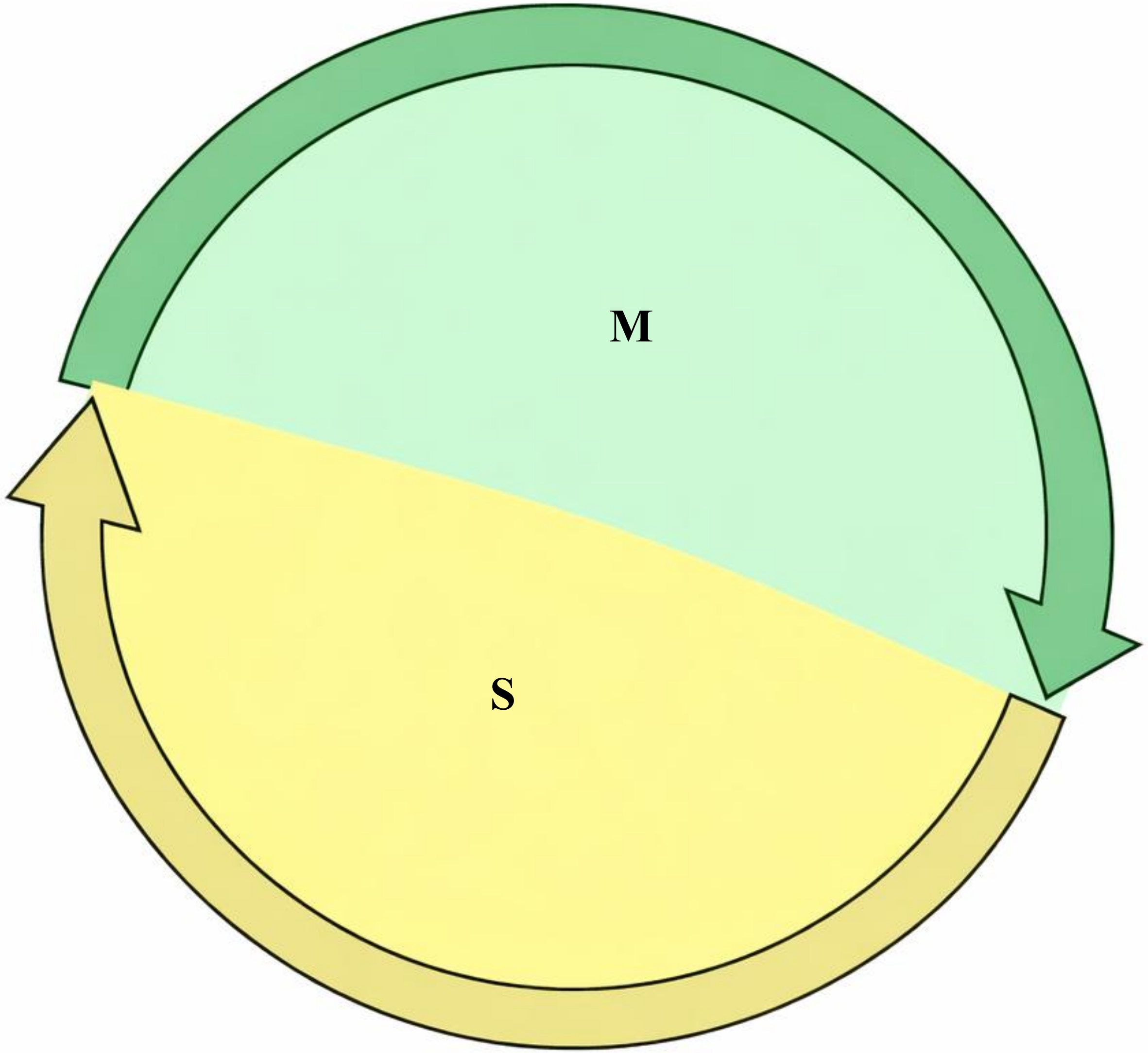
*A series of rapid mitotic divisions of the zygote that produces smaller cells (blastomeres) without increasing the overall size of the embryo.*

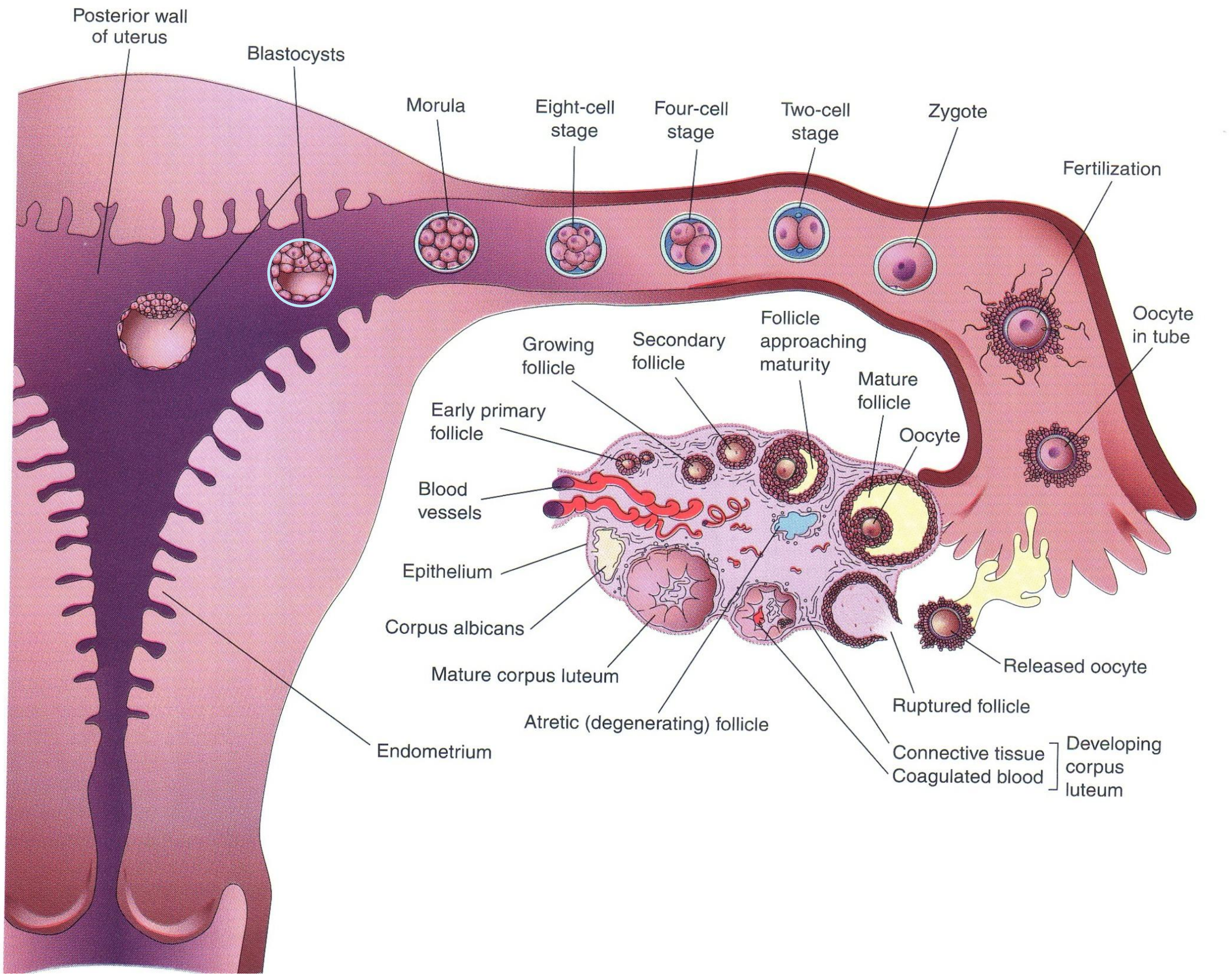
During cleavage, the cell cycle is modified:

- ✓ The S phase (DNA synthesis) still occurs so that DNA is replicated.
- ✓ However, the $G_1$ and $G_2$ phases are greatly shortened or almost absent.
- ✓ As a result, the cell cycle during cleavage mainly alternates between S phase and mitosis (M phase).

*Note: The cell cycle during cleavage mainly alternates between S phase and M phase*
*→ The $G_1$ and $G_2$ phases are greatly shortened or almost absent.*







Posterior wall of uterus
Blastocysts
Morula
Eight-cell stage
Four-cell stage
Two-cell stage
Zygote
Fertilization
Oocyte in tube
Growing follicle
Secondary follicle
Follicle approaching maturity
Mature follicle
Oocyte
Early primary follicle
Blood vessels
Epithelium
Corpus albicans
Mature corpus luteum
Atretic (degenerating) follicle
Endometrium
Released oocyte
Ruptured follicle
Connective tissue
Coagulated blood
Developing corpus luteum

# Formation of the Blastocyst



✓ After fertilization, the zygote undergoes a series of mitotic divisions to form a solid ball of cells called the **morula** by about day 3–4.

*During this stage, the embryo is still surrounded by the* ***zona pellucida****.*

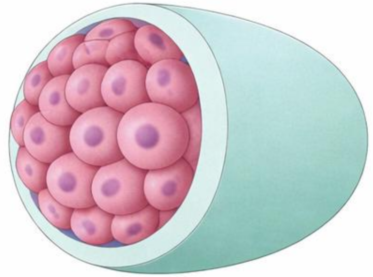
✓ Fluid enters between the cells of the morula and forms a fluid-filled cavity known as the **blastocoele**.

✓ The presence of this cavity separates the cells into two distinct populations:

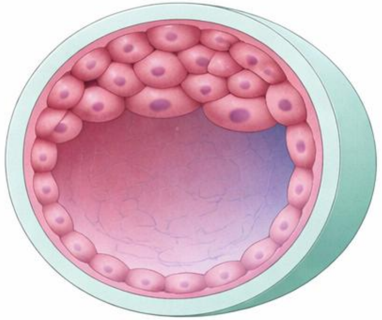
1. An **outer cell mass**, the **Trophoblast**
(which is responsible for implantation and for forming the chorion and the fetal part of the placenta.)
2. An **inner cell mass**, the **Embryoblast**
(will develop into the embryo and later the fetus)

Once these structures are established, the embryo is called a **blastocyst**, which is the stage that initiates implantation in the uterine endometrium.

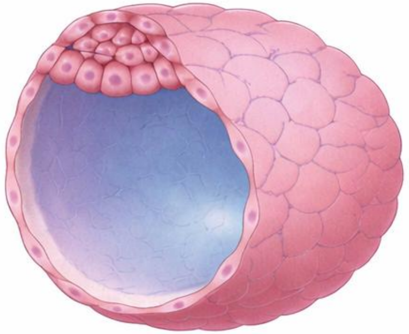
Note: Loss of the zona pellucida (hatching) is **essential for implantation** →
It allows trophoblast cells to directly contact the endometrial epithelium



**Morula**
*about day 3–4*

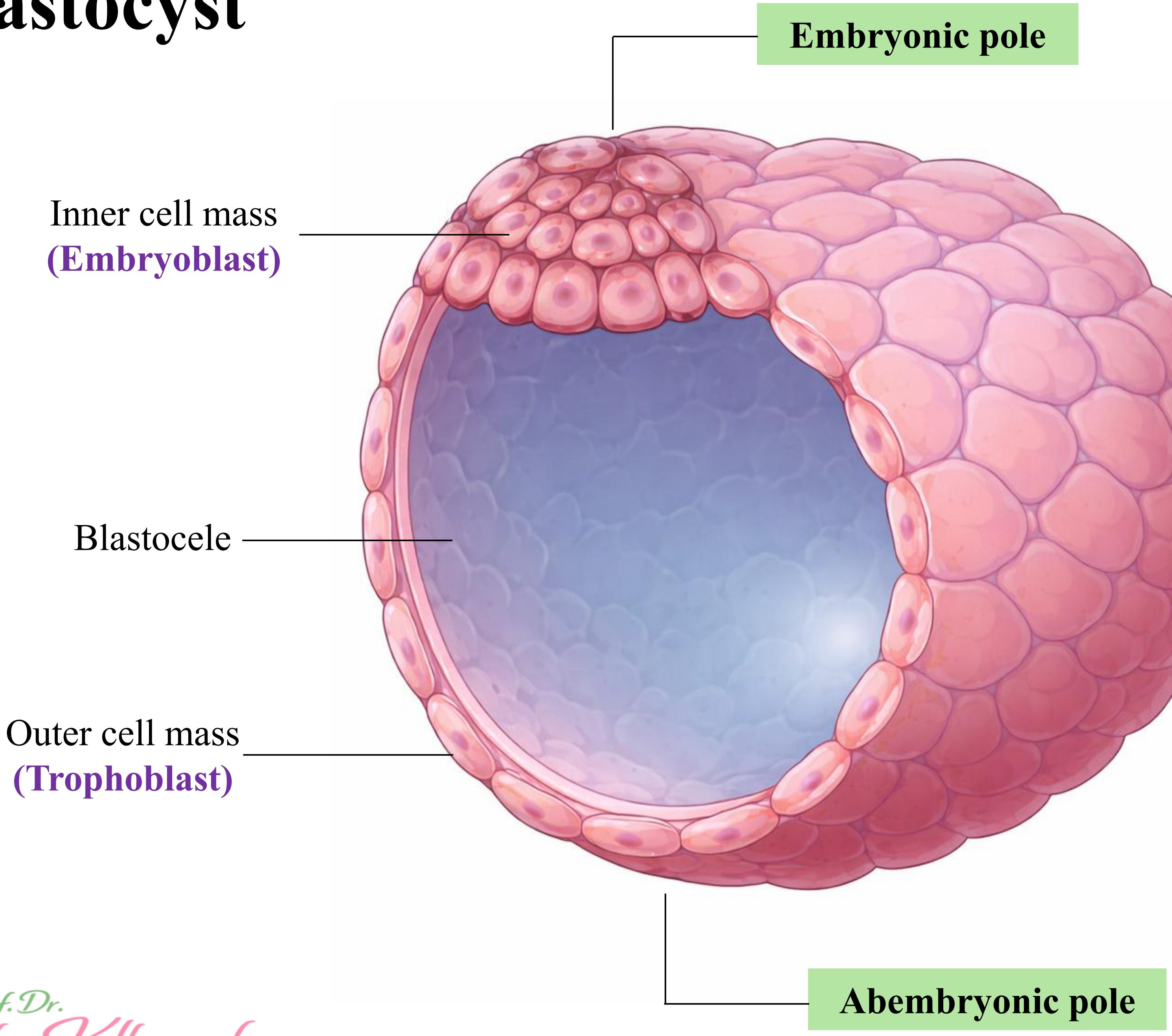


**Early blastocyst**
*about day 5*



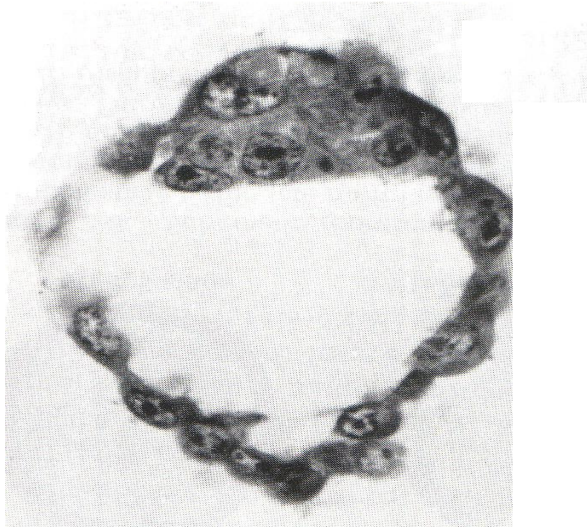
**Late blastocyst**
*about day 6-7*

# Blastocyst

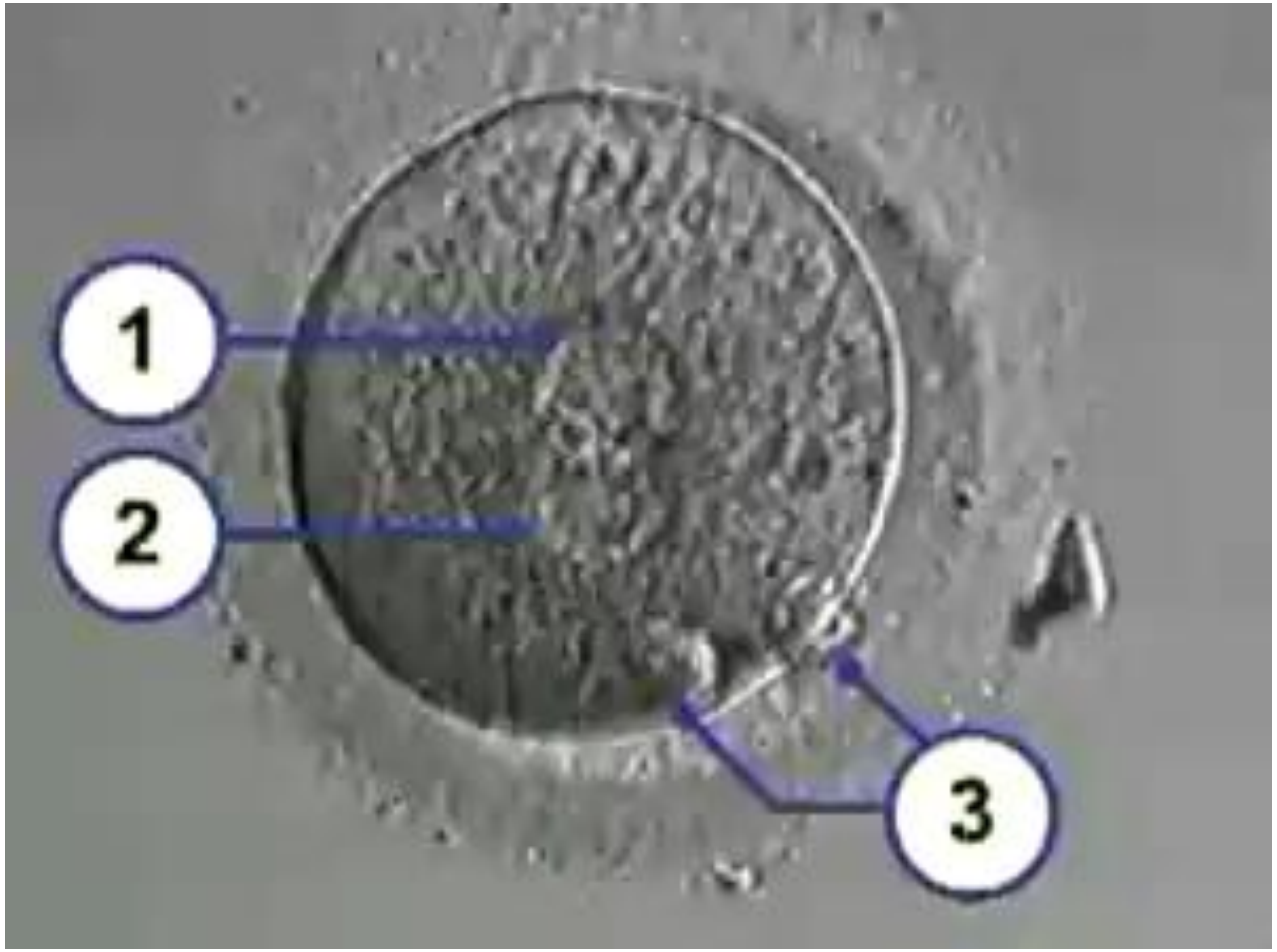


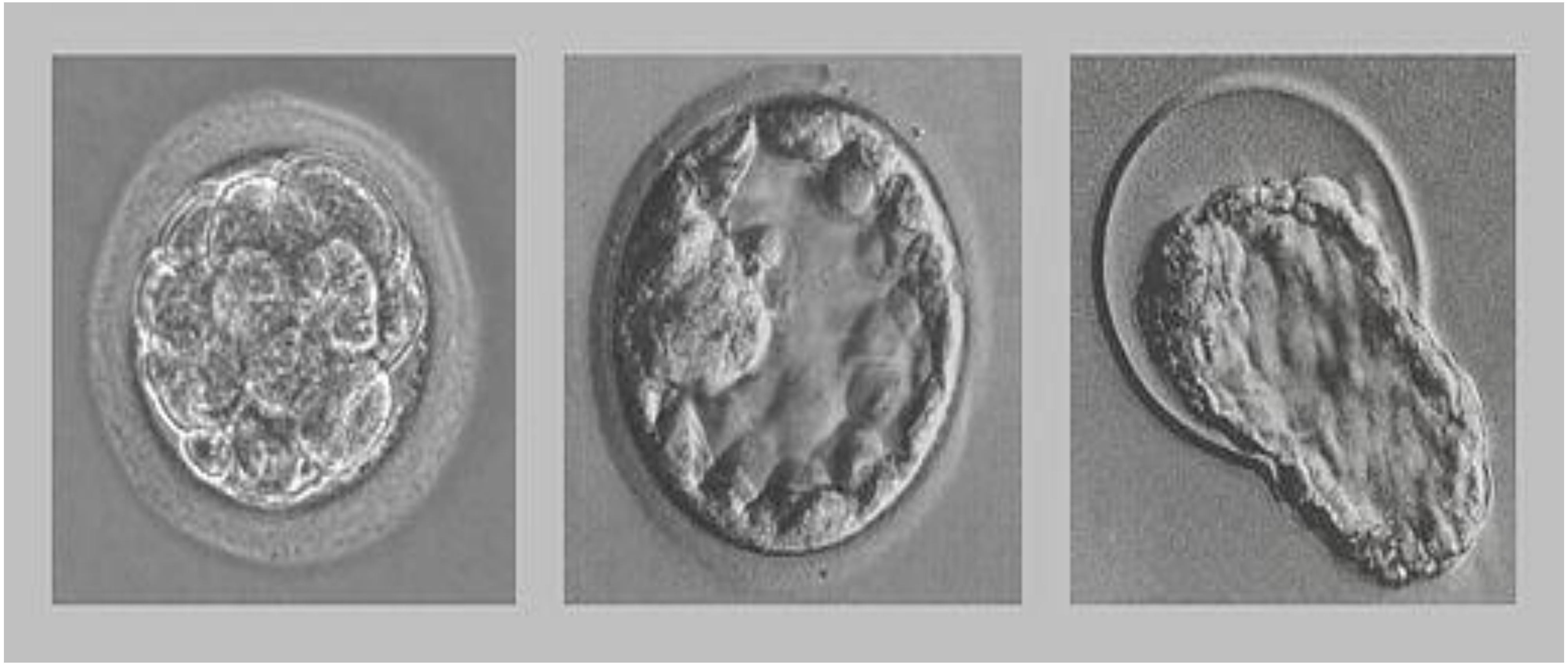

**Embryonic pole:** is the region of the blastocyst where the inner cell mass (embryoblast) is located.

**Abembryonic pole:** is the region of the blastocyst opposite to the embryonic pole.

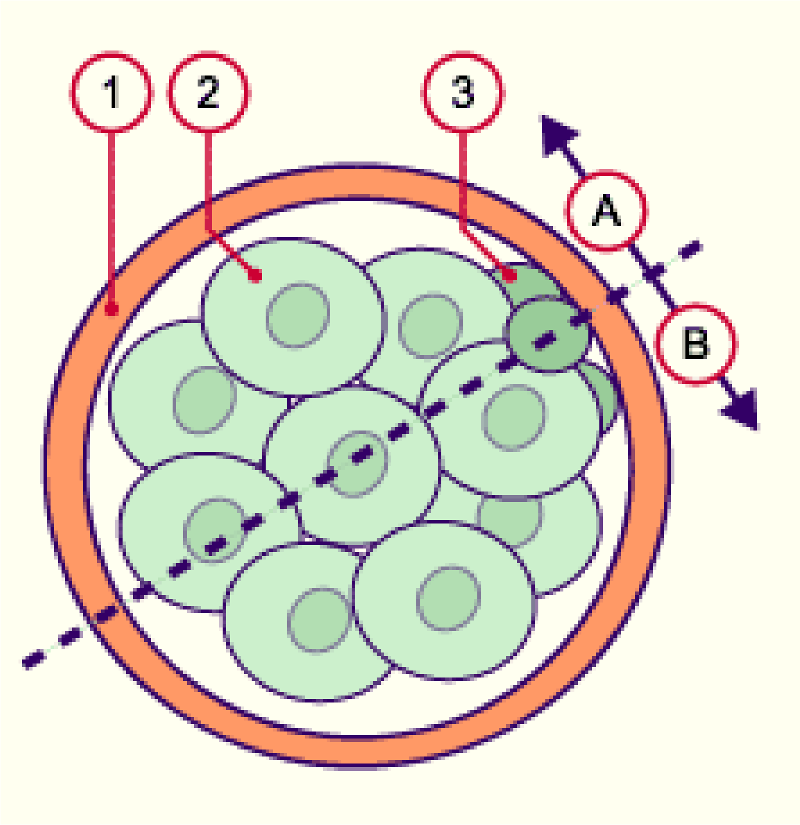


1.Paternal pronucleus
2.Maternal pronucleus
3.Polar bodies

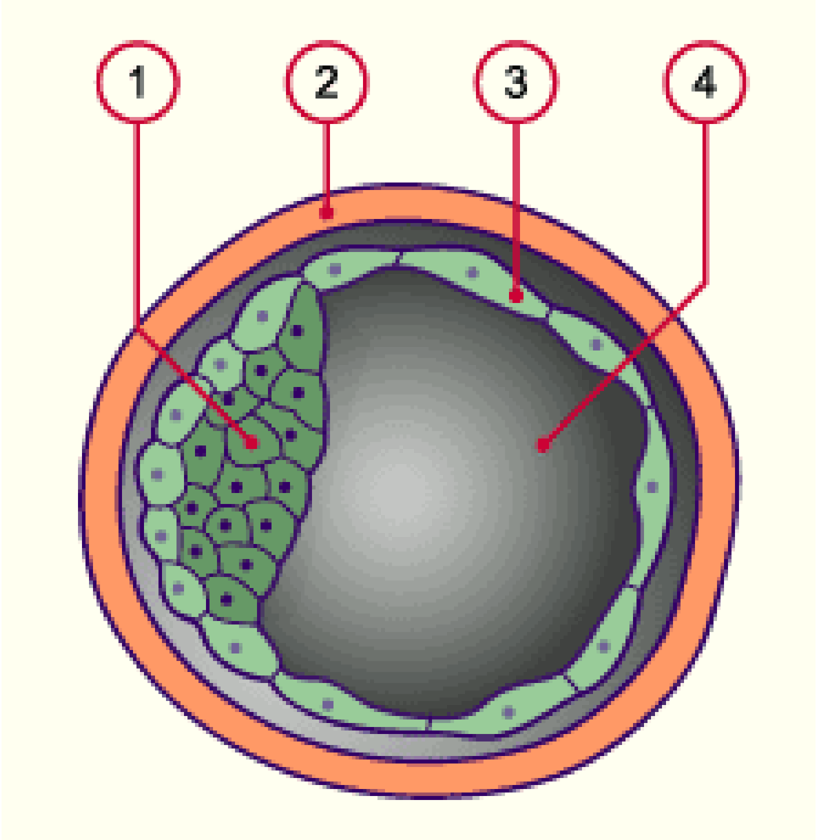


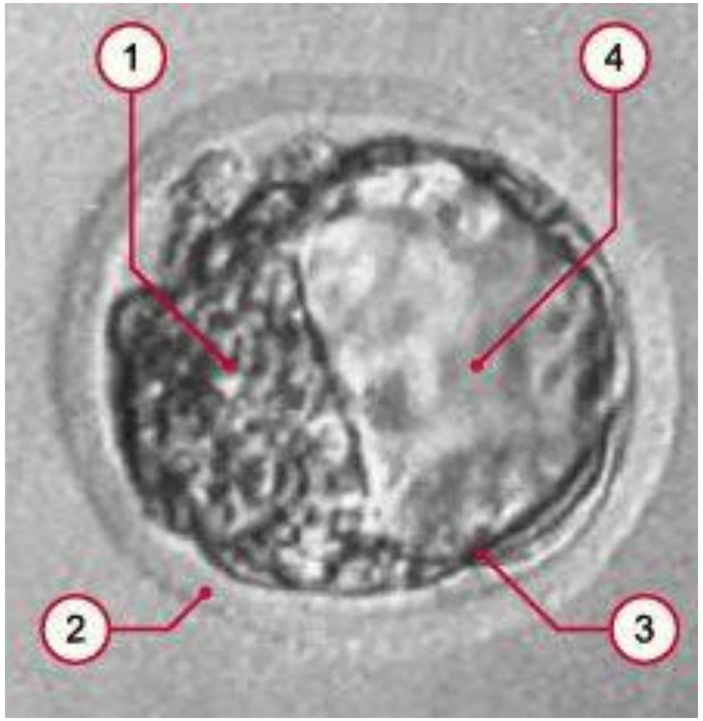


**Morula** **Early blastocyst** **A hatching blastocyst**




1. Zona pellucida
2. Blastomere
3. Polar bodies



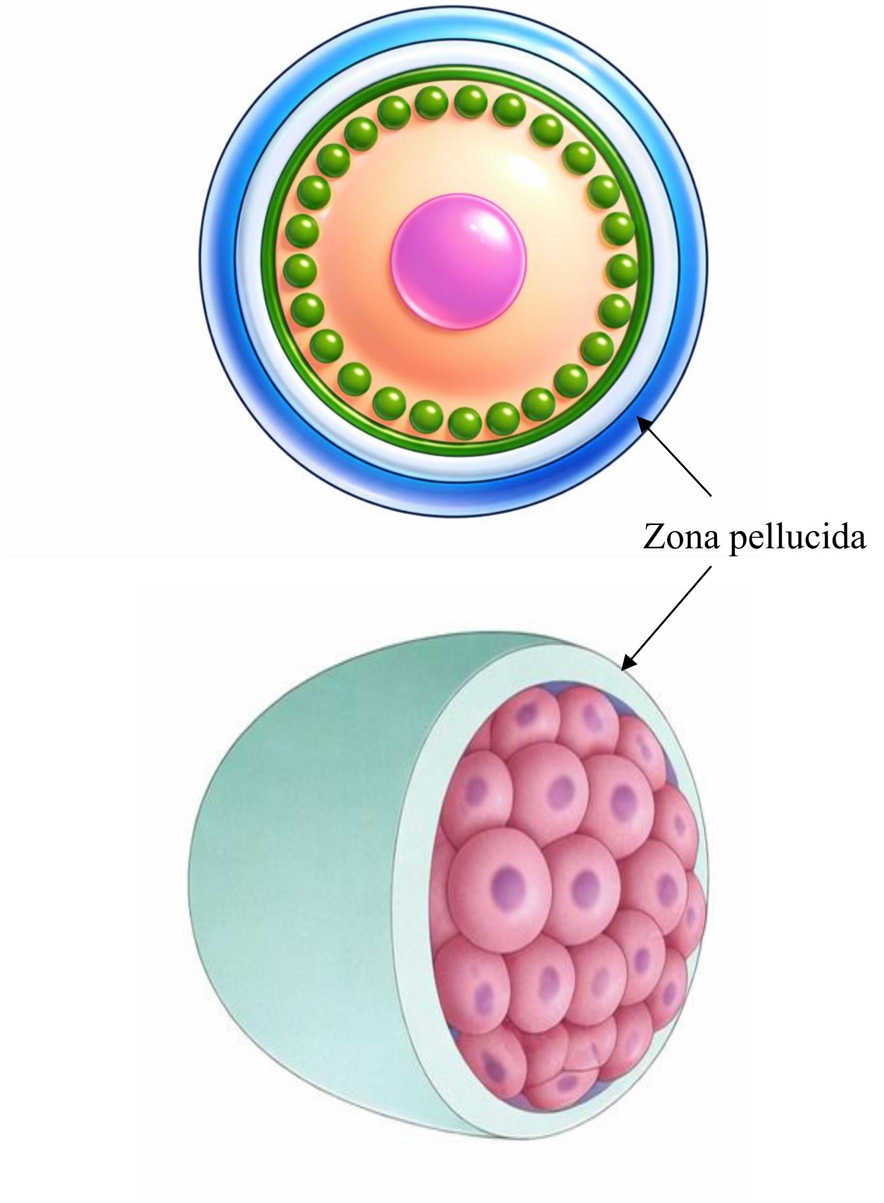




1. Embryoblast
2. Zona pellucida
3. Trophoblast
4. Blastocyst cavity

# Zona pellucida

The **zona pellucida** is a glycoprotein coat surrounding the oocyte and early embryo. Its main functions include:

**1. Species-specific sperm binding**
Glycoproteins of the zona pellucida (especially ZP3) act as receptors that allow sperm from the same species to bind to the oocyte.
**2. Induction of the acrosome reaction**
Binding of sperm to the zona pellucida triggers the acrosome reaction, allowing sperm enzymes to penetrate the zona.
**3. Prevention of polyspermy**
After fertilization, cortical granule release modifies the zona pellucida (zona reaction), preventing additional sperm from entering the oocyte.
**4. Protection of the early embryo**
The zona pellucida protects the cleaving embryo during its passage through the uterine tube.
**5. Maintains structural integrity of the embryo**
It keeps the blastomeres together during cleavage, maintaining the compact structure of the early embryo.
**6. Prevents premature implantation**
The zona pellucida prevents the embryo from implanting in the uterine tube; implantation occurs only after hatching of the blastocyst in the uterus.



**In vitro fertilization (IVF)** is an assisted reproductive technique in which fertilization takes place outside the human body, in a laboratory (“in vitro” means *in glass*). First, the ovaries are stimulated with hormones to produce multiple oocytes, which are then collected from the ovary. Prepared sperm are added to the oocytes in a culture dish, where fertilization occurs. The fertilized oocyte develops into an early embryo over several days. One or more healthy embryos are then transferred into the uterus, where implantation may occur. IVF is commonly used to treat infertility due to conditions such as blocked uterine tubes, male factor infertility, or unexplained infertility.

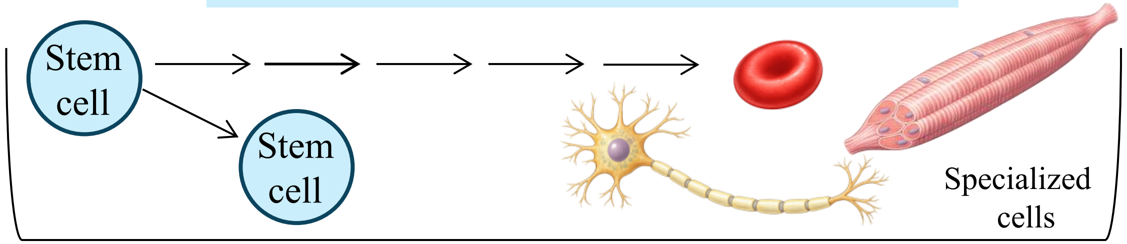
**Stem cells** are undifferentiated cells characterized by:

1. Self-renewal – ability to divide and maintain the stem cell pool.
2. Differentiation – ability to give rise to specialized cells.

*(Most to Least Potent)*
*Totipotent → Pluripotent → Multipotent → Unipotent*

*Toti = Total*
*Pluri = Plenty*
*Multi = Multiple*
*Uni = One*

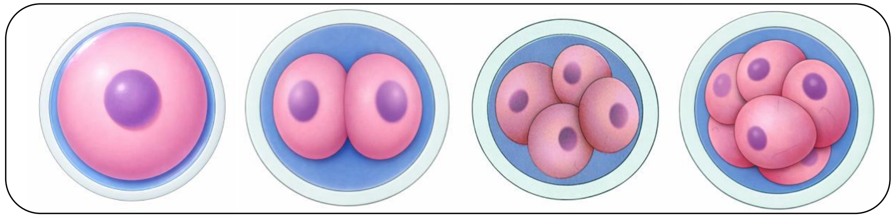
**Stem cells** can maintain the original population




## Totipotent

Cells that can give rise to all embryonic and extraembryonic tissues.

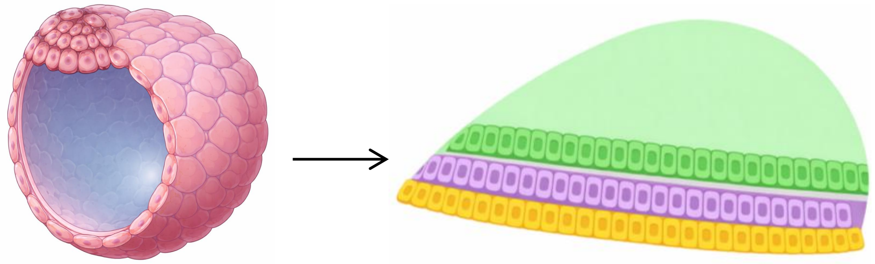
- Can form a complete organism.
- Example: zygote and early blastomeres (up to 8-cell stage).



## Pluripotent

Cells that can give rise to all three germ layers (ectoderm, mesoderm, endoderm).

- ❌ Cannot form extraembryonic tissues
- Cannot form a complete organism
- Example: inner cell mass of the blastocyst





## Multipotent

Cells that can differentiate into multiple related cell types within a specific tissue or lineage.

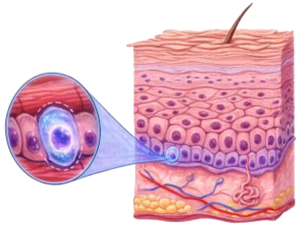
- More restricted than pluripotent
- Common in adult tissues
- Example: hematopoietic stem cells → all blood cell types

## Unipotent

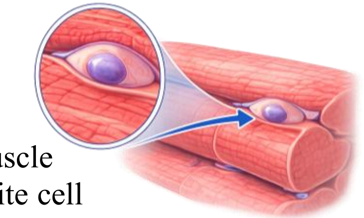
Cells that can produce only one specific cell type, but retain the ability to self-renew.

- Example: basal cells of epidermis, muscle satellite cells

Basal cell of epidermis



Muscle satellite cell



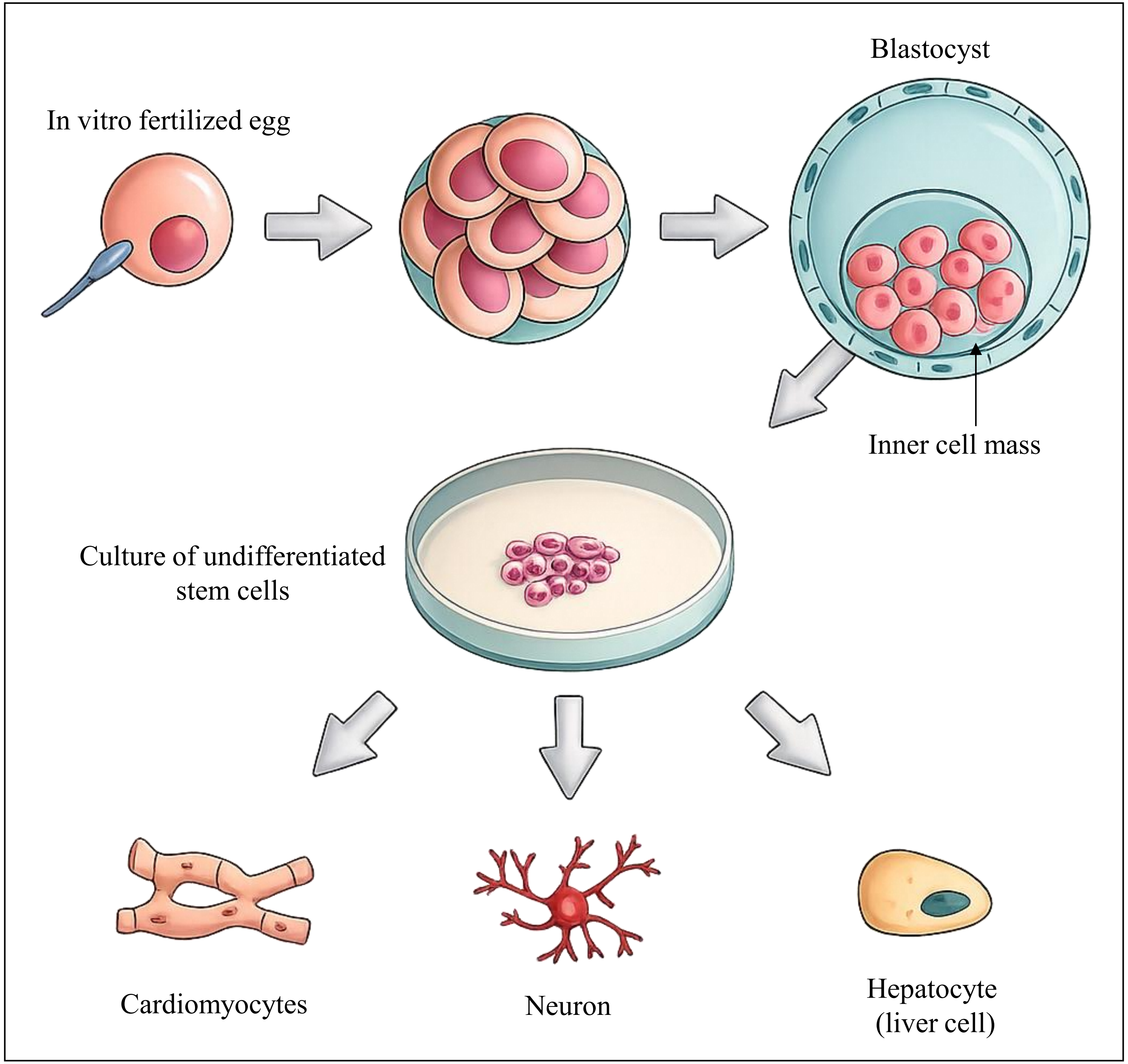
**Embryonic stem cells** = pluripotent cells from the inner cell mass of the blastocyst that can form all body cell types and can self-renew in culture.

*These cells can give rise to any type of tissues of the embryo EXCEPT the trophoblast.*

Embryonic stem cells are studied for regenerative medicine, including potential treatment of:

- Neurodegenerative diseases
- Heart damage after myocardial infarction
- Liver disease
- Diabetes

*However, their use raises ethical and regulatory considerations because they are derived from early embryos.*

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