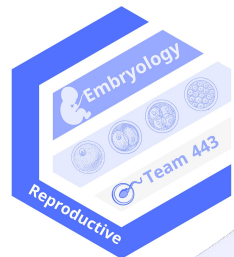
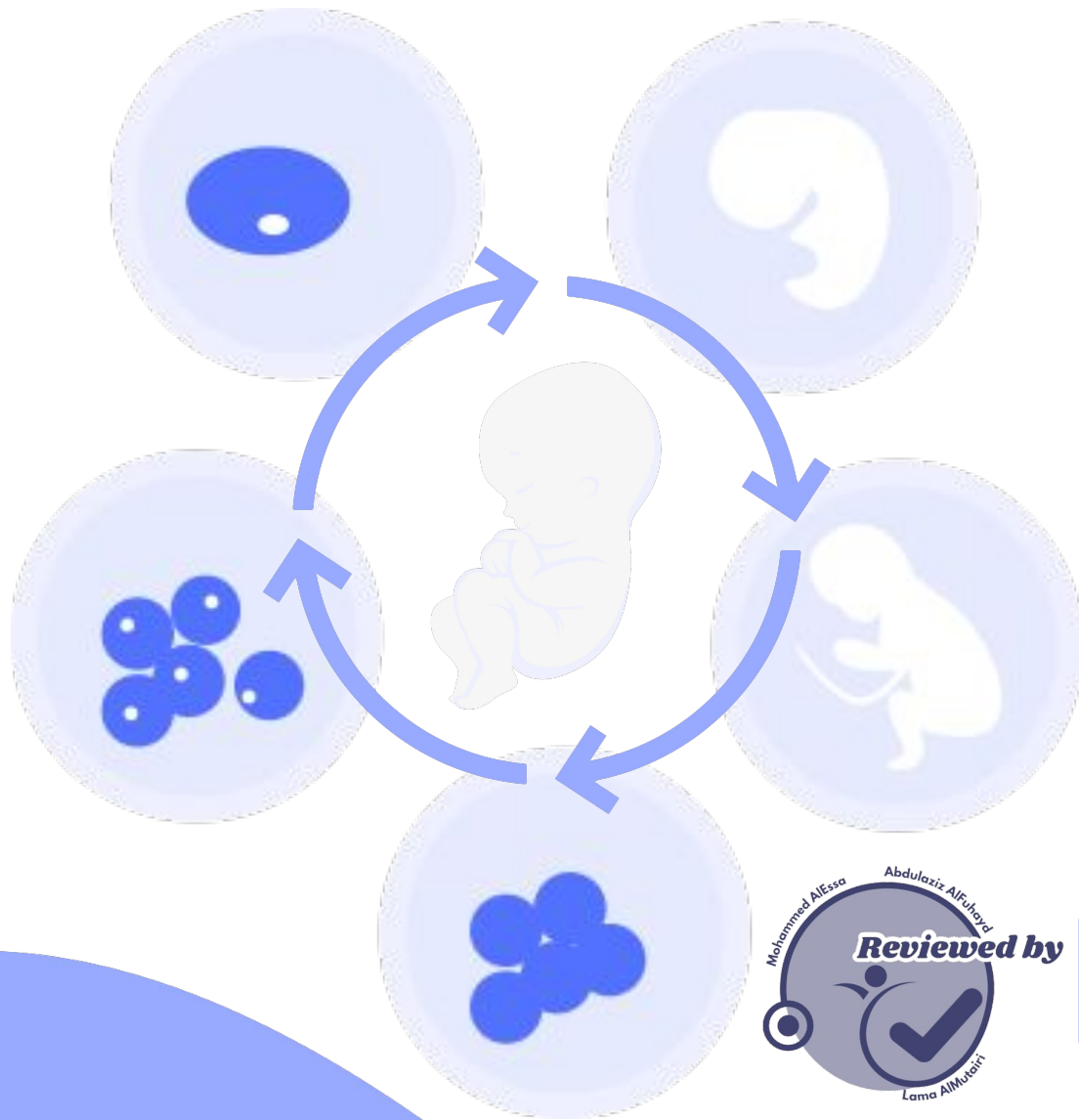


# Fertilization & implantation



# Objectives



Define fertilization, **cleavage** & implantation.



Enumerate phases & results of fertilization, as well as steps of implantation **and its mechanism**



Locate the site/s of fertilization and implantation and **List the sites of ectopic pregnancy.**



Identify the time of each event



Describe the formation of blastocyst and Describe the formation of primary chorionic villi.

**This lecture was presented by : DR.Ahmed Fathallah & DR.Tahani Al Matrafi**



[Click here for part 1](#)



[Video Board](#) , [Notes](#)



[Click here for part 2](#)



[Video Board](#) , [Notes](#)

**Editing File**

**Color index :**

Main text ( black)

Female Slides (Pink)

Male Slides (Blue)

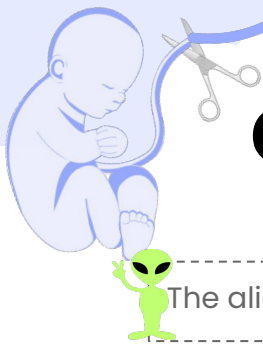
Important ( Red)

Dr's note (Green)

Extra Info ( Grey)



**embryologymed443@gmail.com**



# Overview by Lama Alotaibi

IMPORTANT

Extra

The alien from pathology took a trip to embryology to tell you a story

## Fertilization

A. After Ejaculation 200 million spermatozoa enter vaginal canal

B. seminal fluid is alkaline, which means it's capable of neutralizing acidic vaginal fluids.

C. Only 1% enter cervix & travel through uterus up to ampulla of uterine tube

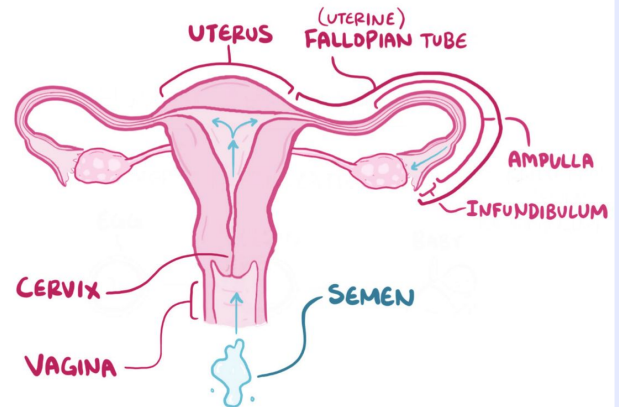
By this point, most of the 200 million sperm that entered the body during sex have died for numerous reasons: some got stuck in the vaginal mucus, others ended up lost in the cervix, and the rest were killed and absorbed by the white blood cells.

Two required processes :

1\ Capacitation: epithelial interactions between sperm, uterine wall

Glycoprotein coat, seminal plasma proteins covering acrosomal region removed → easier enzyme release acrosomal reaction

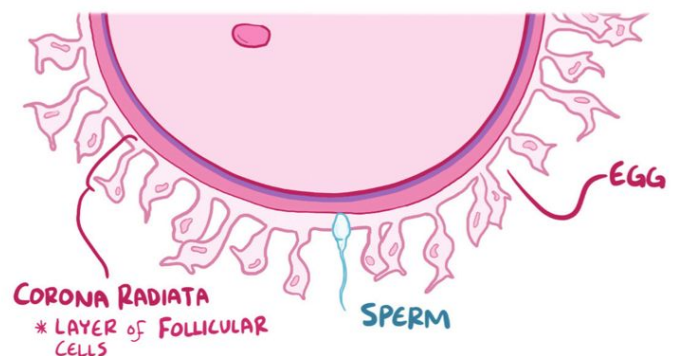
2\ Acrosomal reaction: after binding to zona pellucida Release of enzymes (e.g. acrosin, hyaluronidase) needed to penetrate zona pellucida



## Phase I " penetration of corona radiata "

A. Capacitated spermatozoa allowed to pass through corona radiata

### PHASE I



## Phase 2 “ penetration of zona pellucida ”

Zona pellucida: glycoprotein layer surrounding oocyte

A. **Facilitates binding of sperm cell, induces**

**acrosomal reaction mediated by**

**ligand zona pellucida sperm-binding protein 3 (ZP3):**

Sperm-binding initiates release of acrosin (hydrolytic enzyme) → sperm cell penetrates zona pellucida

→ sperm makes contact with oocyte cortical reaction

(release of lysosomal enzymes from cortical granules of oocyte) → cortical granules initiate zona reaction,

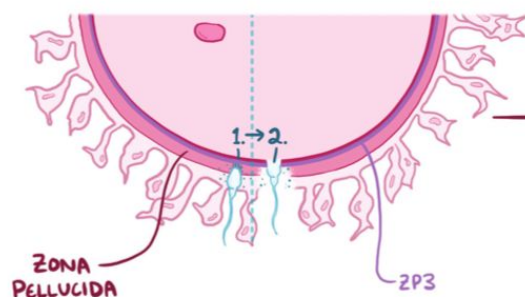
prevent further sperm penetration (polyspermy) by forming protective hyaline layer, inactivate receptor sites on zona pellucida

B. Cortical reaction also activates oocyte to prepare for second meiotic division

### PHASE II

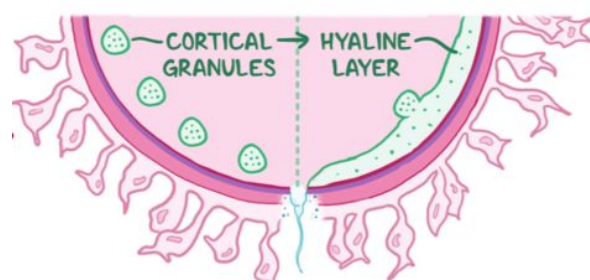
#### ACROSOMAL REACTION

1. RELEASES ACROSIN
2. SPERM & EGG FUSE



#### CORTICAL REACTION

- \* GRANULES FUSE WITH CELL MEMBRANE



## Phase 3 “ fusion of oocytes & sperm ”

A. Secondary oocyte completes meiosis II

→ forms female pronucleus, second polar body

B. Head, tail of spermatozoa enters oocyte → travels to female pronucleus (containing 23 chromosomes) using tail, energy generated by mitochondria

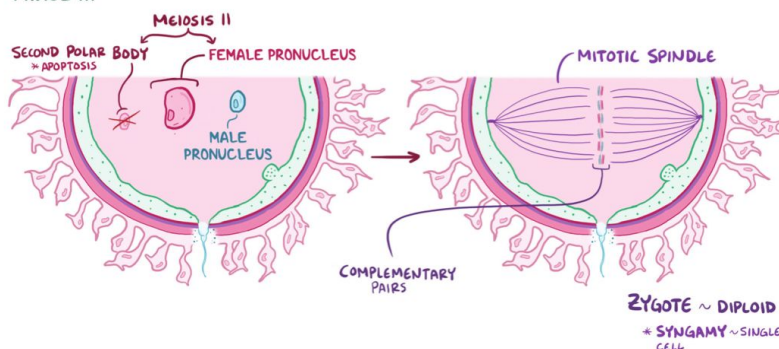
C. Tail, mitochondria detach

→ sperm nucleus becomes male pronucleus

D. Male, female pronuclei move toward each other merge into single nucleus → cell becomes diploid (zygote contains maternal, paternal genetic information)

C. Preparation for mitotic division

### PHASE III



## Blastocyst formation & Cleavage

**Cleavage** : Series of fast mitotic divisions of zygote → increase number of cells, decrease size

A. 36 hours after fertilization

→ first cleavage division → two cells (blastomeres)

B. Second division → four blastomeres;

third division → eight blastomeres; etc.

C. After third cleavage, blastomeres form compact ball of cells connected by tight junctions (compaction)

D. Three days after fertilization, cells of compacted embryo divide again

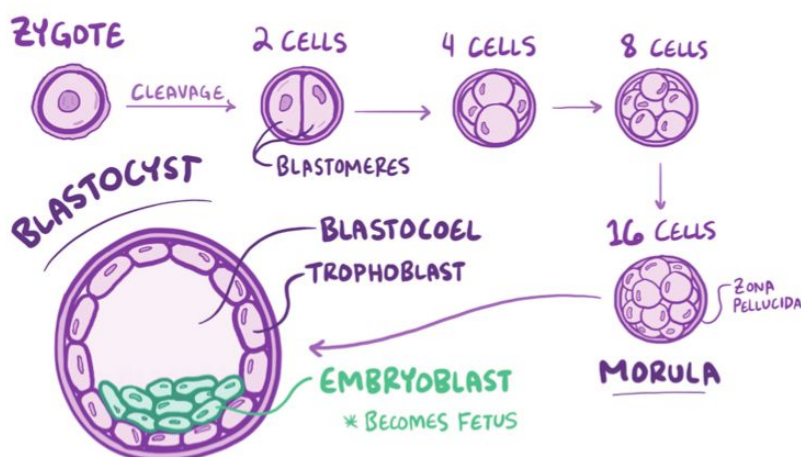
→ mulberry-shaped 16-cell morula

E. Fluid accumulates within internal cavity (blastocoel) → blastocyst

(Blastocyst: fluid-filled hollow cell, two zones)

■ **Trophoblast**: single layer of large flattened cells, stemming from morula's outer cell mass; gives rise to placenta

■ **Embryoblast**: 20-30 pluripotent cells located on one side, stemming from inner cell mass; gives rise to embryo



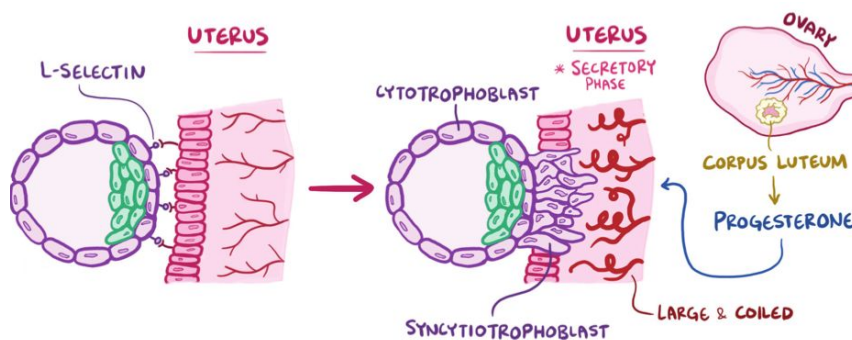
## Implantation

### Day 6 !

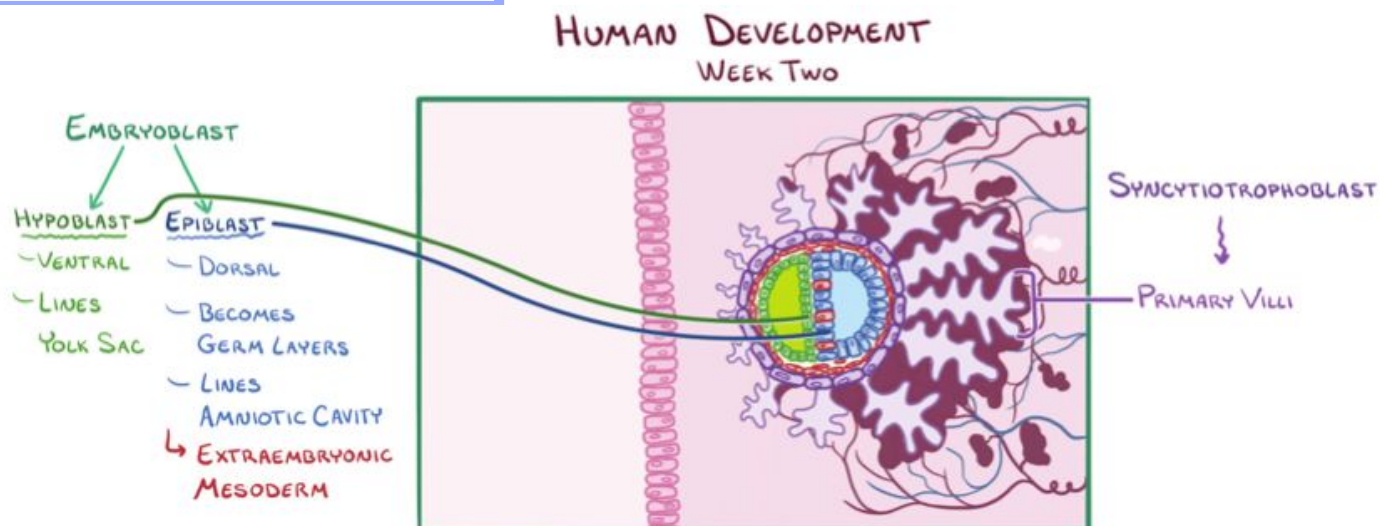
A. Trophoblast binds to uterine wall with L-selectin, integrin receptors & Penetrates between epithelial cells

B. High progesterone released from corpus luteum develops endometrium for implantation

C. Blastocyst implants into decidua basalis (layer of endometrium), along superior posterior wall of uterus



## Implantation



### Day 7 !:

A. Trophoblast Proliferates, forms two layers :

1. Cytotrophoblast (cellular trophoblast): inner layer of mononucleated cells (Produces primary chorionic villi, protrudes into syncytiotrophoblast later )
2. Syncytiotrophoblast: outer multinucleated mass of cells

### Day 8 !:

A. Syncytiotrophoblast Invades decidua basalis ( layer of endometrium ) with finger-like processes; makes enzymes that erode uterine cells; blastocyst burrows into decidua basalis surrounded by pool of blood leaked from degraded blood vessels

B. Human chorionic gonadotropin (hCG) maintains viability of corpus luteum → secretes estrogen, progesterone until week eight (hCG: basis for pregnancy tests)

### Day 9 !:

A. Lacunar stage of trophoblast development : Vacuoles appear in syncytium → vacuoles fuse → form large empty spaces (lacunae) ( it will form veins & arteries from placenta later in day 13 )

### Day 12 !:

A. Progesterone levels continue to rise decidua undergoes decidual reaction : where Decidual cells enlarge, become coated in sugar-rich fluid (helps sustain embryo)

B. Blastocyst embeds in endometrial stroma ( some sources say 10 as in the lecture some say 12 )

C. Lacunae form within syncytiotrophoblast (erodes endometrial sinusoids)

D. Lacunae fuse with sinusoids → fill with maternal blood → uteroplacental circulation established ( Remember That for Lecture 5 )

### Day 13 !:

A. Syncytiotrophoblast cells form little protrusions called primary villi (spaces)

B. Villi form around fetus; lacunae form between villi

c. Arteries, veins merge within lacunae form large pool of blood (junctional zone)



# Fertilization

## Definition

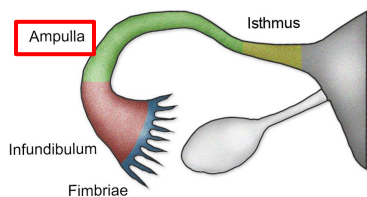
- it is the process of fusion of / during which a male gamete (**sperm**) unites with a female gamete (**oocyte**) (with haploid numbers of chromosomes = 23 each) to form/produce a single cell (**zygote**) (with diploid number of chromosomes = 46). (Zygote = 1 cell , Embryo > 1 cell)
- it is a **complex** process, it begins with contact between sperm and ovum and ends up with intermingling (تداخل) of the maternal and paternal chromosomes.

## Fertilization

male slides

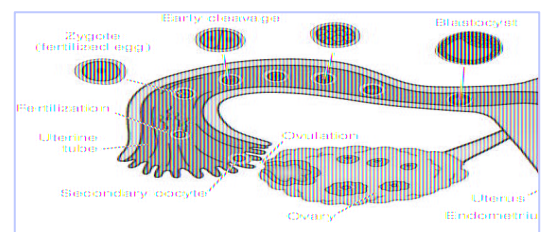
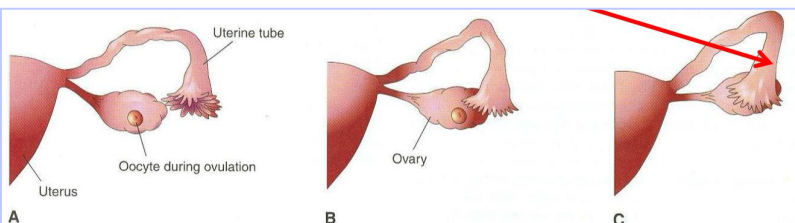
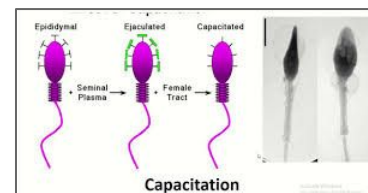
### Site of fertilization

- Usually in the **ampulla (WIDEST PART) of Uterine Tube.**
- Fertilization may occur in any other part of tube,
- **But Never occurs in the uterine cavity.**
- Chemical signal from oocyte attract the sperms.



### Sperm capacitation

- Before fertilization, the sperm undergoes "**capacitation**" which is a period of conditioning (**around 7 hours**) that occurs in the female reproductive tract during which the acrosome **prepare the enzymes used for perforation of walls of the oocyte.**
- Happens by clearing the head of the sperm and increasing the motility





# Phases of fertilization

**IMPORTANT**

Passage of the sperm through the **corona radiata cells**

By the effect of:

- A. Hyaluronidase enzyme secreted from the sperms.
- B. By movement of its tail.

Penetration of the / Passage of the sperm through **Zona Pellucida:**

These occurs by the action of acrosomal enzymes by **acrosine** (a substance secreted from acrosomal cap).

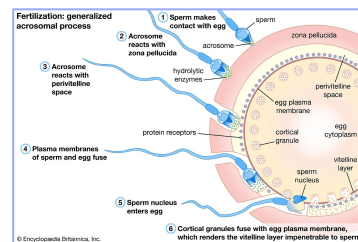
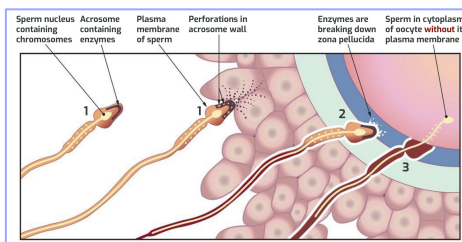
**Fusion** of plasma membranes of Oocyte & Sperm: **only head & tail** enter cytoplasm of oocyte.

Completion of 2nd meiotic division of oocyte to become a **mature ovum**.

Formation of female pronucleus: **the nucleus of the ovum becomes the female pronucleus.** (Female pronucleus is The egg nucleus, once it is haploid)

Formation of the male pronucleus: **the nucleus in the head of sperm enlarges to form the male pronucleus & the tail disappears.**

**Fusion of both male & female pronuclei to form the zygote.**



**male slides**

**Why** Only one sperm passes through the plasma membrane of the oocyte?

Due to the **ZONA REACTION**, which is a change in the properties of the zona pellucida occurs that makes it impermeable to other sperms.

**Female slides**

**Chromosomes of zygote**

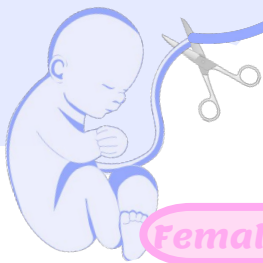
★ Zygote is genetically unique.

$\frac{1}{2}$  of its chromosomes comes from the **father**

$\frac{1}{2}$  of its chromosomes comes from the **mother**

New combination is formed which is different from either of the parents. This mechanism forms **biparental inheritance** and leads to variation of the human species.





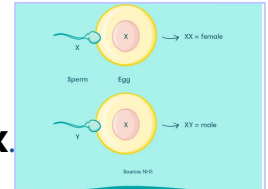
# Sex of embryo

Female slides

## Sex of embryo

Embryo's chromosomal sex is determined **at the time of fertilization**.

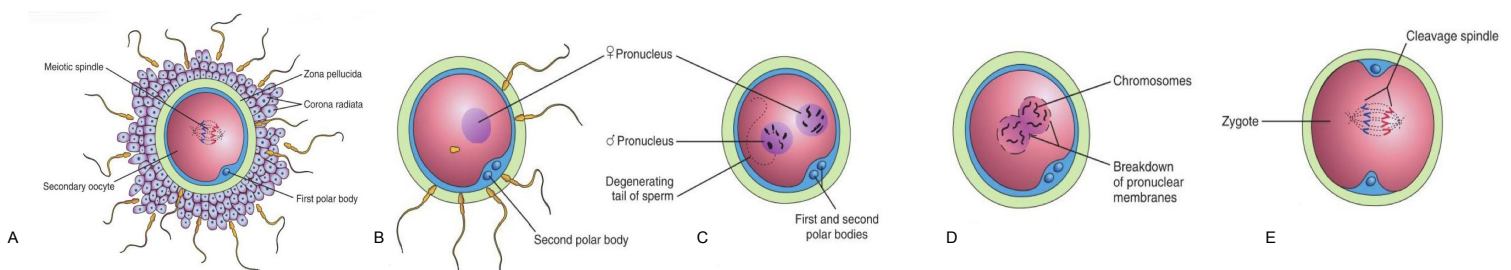
Sex is determined by the type of **sperm** (X or Y) that fertilizes the oocyte. So, it is the **father whose gamete decides the sex**.



## Results of fertilization

**IMPORTANT**

- 1 Restoration of the normal diploid number of chromosomes (46) in the zygote.**
- 2 Determination of the sex of the embryo.**
- 3 Variation in the features of human species** because of the mixing of maternal & paternal chromosomes.
- 4 Stimulates the penetrated oocyte to complete its 2nd meiotic division.**
- 5 Initiation of cleavage (cell division) of zygote.**





# Cleavage of zygote

## Cleavage of the zygote

- Cleavage consists of repeated **mitotic divisions** of the zygote resulting in a **rapid increase** in the number of the cells.
- **Normally occurs in the uterine tube.**
- **These smaller embryonic cells** are called "**blastomeres**".
- During cleavage, the dividing zygote passes along the uterine tube toward the uterus (**from lateral to medial**).

### 1 Cleavage of zygote

- It begins about **30 hours** after fertilization.
- Zygote divides into 2, then 4, then 8, then 16 cells.
- Zygote lies within the **thick zona pellucida during cleavage.**
- Under the microscope, the zona pellucida is a translucent membrane.

### 2 Morula

- When there are **16-32 blastomeres** the developing human is called **MORULA**.
- The Morula reaches the **uterine cavity** at this stage.
- Spherical Morula is formed about **3 days** after fertilization.
- It resembles mulberry or blackberry.

### 3 Blastocyst

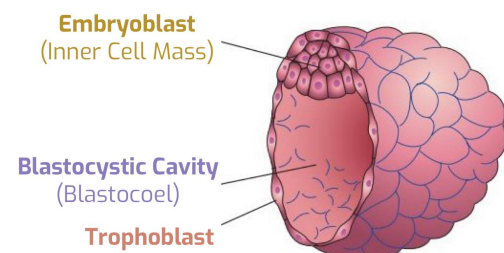
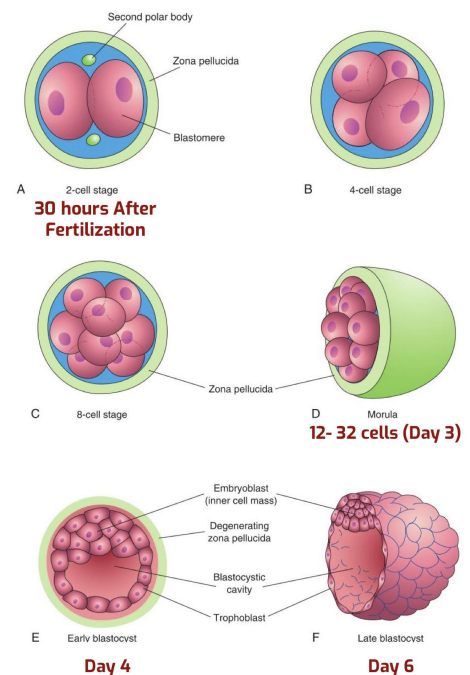
- A cavity appears within the morula dividing its cells into **2 Groups**:
  1. **Outer cell layer** called **Trophoblast**. (راح تشترك مع الرحم في تكوين المشيمة)
  2. **Inner cell layer (mass)** called **Embryoblast** attached to one of the poles of the blastocyst. (حتكون المسؤولة عن تكوين الجنين)
- The cavity is called **Blastocystic Cavity** or **Blastocoel**.

#### Males' slides

- A. **Trophoblast** → **Fetal Membranes**
- B. **Embryoblast** → **Embryo**

### Female slides

Note: Male Doctor explained them in the pictures





# Implantation

## Definition

1

It is the process by which the blastocyst penetrates the superficial (compact) layer of the endometrium of the uterus and becomes embedded in the endometrium (mucous membrane) of the uterus.

## Normal Site

2

In the upper part of the posterior wall of the uterus near the fundus.

3

It begins about the 6th day after fertilization.  
It is completed by the 11th or 12th day.  
**From day 6 to day 10**

دكتور الأولاد 442 يقول اعتمدوا اللي بسلايداتي = اليوم العاشر

Time/Duration

4

Zona pellucida disappears at Day 5

Important event preceding implantation

male slides

## WHAT is the role of the ZONA PELLUCIDA?

### 1. DURING FERTILIZATION:

Zona Reaction makes the Zona Pellucida impermeable to other sperms.

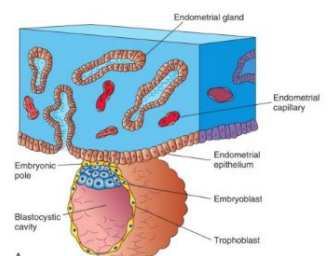
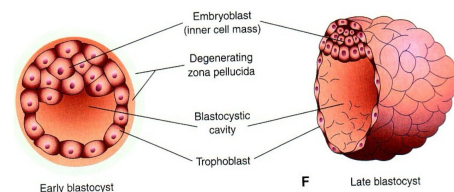
### 2. DURING CLEAVAGE:

A- Keeps the blastomeres together.  
B- Prevents the sticky blastomeres from adhering to the wall of the uterine tube.

## Mechanism of Implantation

Female slides

- ★ The Morula reaches the uterine cavity by the **4th day** after fertilization, & remains free for one or two days.
- ★ Fluid passes from uterine cavity to the Morula.
- ★ Now the Morula is called Blastocyst, its cavity is called blastocystis cavity, its cells divided into Embryoblast & Trophoblast.
- ★ By the **5th day** the Zona pellucida degenerates.





# Steps of Implantation

## 6th Day

The blastocyst **adheres** to endometrium & **begins implantation**, Trophoblast cells penetrate the epithelium of the endometrium. Penetration results from proteolytic enzymes (eg. **COX-2**) produced by the trophoblast.

## 7th Day

The trophoblast **differentiates** into 2 layers:

- 1. Cytotrophoblast:** inner layer, mitotically **active**.
- 2. Syncytiotrophoblast:** outer multinucleated mass, with indistinct cell boundary; it invades the endometrial epithelium and underlying CT.

(كثفتها أصابع تساعد على اختراق الشعيرات الدموية عشان تغذي الجنين إلى ما تنمو المشيمة)

## 8th Day

The syncytiotrophoblast **erodes** endometrial tissues & the blastocyst **starts to embed in the endometrium** / is superficially embedded in the compact layer of the endometrium.

## 9th Day (10th or 11th)

**Blood-filled lacunae** appear in **syncytiotrophoblast** which communicate forming a network by the 10th or 11th day. Syncytiotrophoblast erodes the endothelial lining of the maternal capillaries which known as sinusoids. Now blood of maternal capillaries reaches the lacunae so, **Uteroplacental circulation is established by 11th or 12th day**.

## 10th Day

*male slides*

The blastocyst is **completely embedded** in the endometrium. The defect (Lacunae) **is filled by a closing plug**.

## 13th Day

Proliferation of **Cytotrophoblast cells** produce extension inside the Syncytiotrophoblast to form the **primary chorionic villi**.

# Implantation site

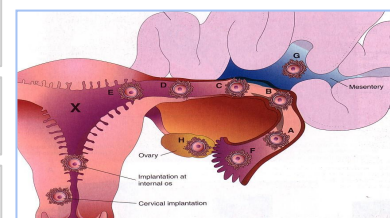
X = Usual Site of implantation is the posterior wall of the body of uterus.

A-H = Ectopic Pregnancy (Pregnancy Outside Uterus).

A-F = Tubal Pregnancy (**MOST COMMON ECTOPIC PREGNANCY**): May lead to rupture of uterine tubes.

G = Abdominal Pregnancy

H = Ovarian Pregnancy (**LEAST COMMON ECTOPIC PREGNANCY**)





# Implantation Cont.

Female slides

Implantation can be detected by

1. Ultrasonography. (can be detected in 5th week)
2. **hCG** (human chorionic gonadotropin which is secreted by the Syncytiotrophoblast about the end of **2nd week** (excreted in the mother's urine).

## Early Pregnancy Factor

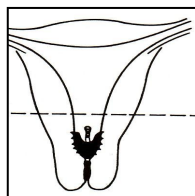
- Is an immunosuppressant protein.
- Secreted by trophoblast cells.
- Appears in maternal serum within 24--48 hrs after implantation.
- It is the basis for EPT (Early pregnancy test) in the first 10 days of development. (fastest way to detect pregnancy)

# Ectopic Pregnancy

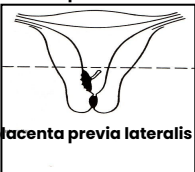
- It means implantation outside the uterine cavity.
- 95 to 97% of ectopic pregnancies occurs in the uterine tube.
- Most ectopic pregnancy are in the ampulla & isthmus of uterine tubes.
- Placenta previa: implantation occurs in the lower uterine segment.
- Pregnancy in cervix may occur : leads to antepartum hemorrhage & placenta previa (المشيمه تنزل وقت الولادة قبل الجنين) (Antepartum haemorrhage (APH) is defined as bleeding from or in to the genital tract, occurring from 24+0 weeks of pregnancy and prior to the birth of the baby)

## Ectopic pregnancy:

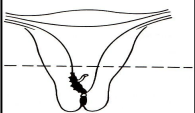
1. Placenta Previa.
2. Tubal.
3. Ovarian.
4. Abdominal.
5. Pelvic.
6. Cervical.



placenta previa centralis



placenta previa lateralis



placenta previa marginalis

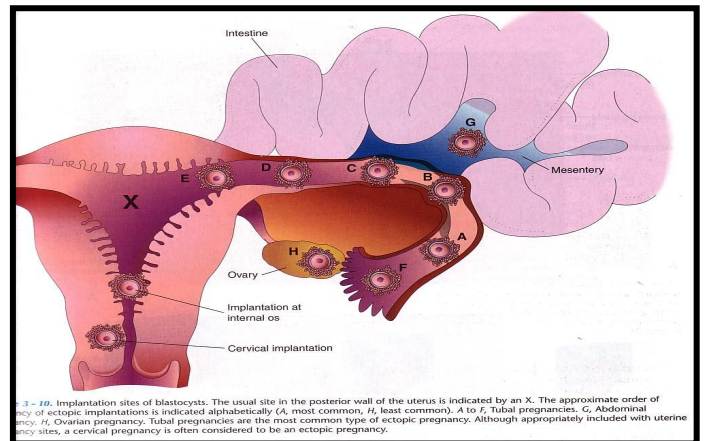


Fig. 3-10. Implantation sites of blastocysts. The usual site in the posterior wall of the uterus is indicated by an X. The approximate order of ectopic implantations is indicated alphabetically (A, most common, H, least common). A to F, Tubal pregnancies; G, Abdominal pregnancy; H, Ovarian pregnancy. Tubal pregnancies are the most common type of ectopic pregnancy. Although appropriately included with uterine pregnancy sites, a cervical pregnancy is often considered to be an ectopic pregnancy.

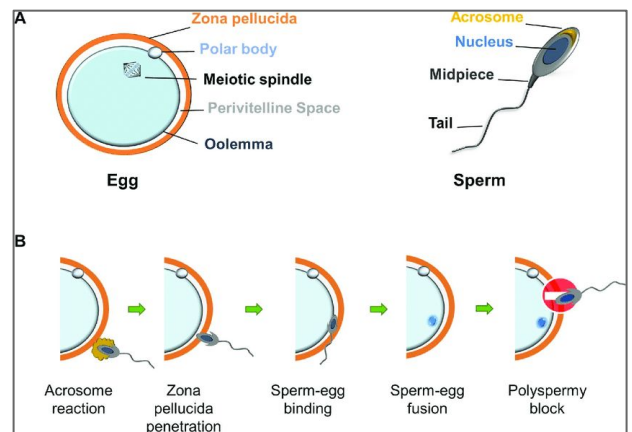
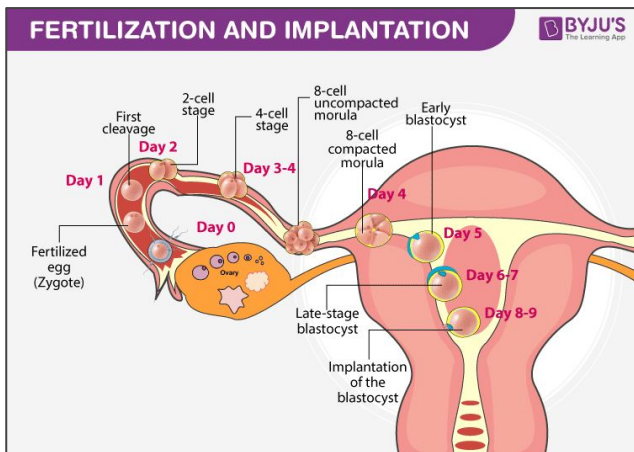
Check this case of ectopic pregnancy!



# Summary

male slides

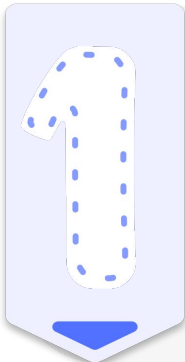
<p><b>Fertilization</b></p>	<ul style="list-style-type: none"> <li>is fusion of male &amp; female gametes (with 23 chromosomes each) to produce a zygote (with 46 chromosomes). It occurs in the ampulla of uterine tube.</li> <li>Fertilization begins by penetration of one sperm through corona radiata then zona pellucida &amp; ends by fusion of male &amp; female pronuclei to form the zygote.</li> </ul>
<p><b>Cleavage</b></p>	<ul style="list-style-type: none"> <li>is repeated mitotic divisions of the zygote into blastomeres. The dividing zygote passes along the uterine tube toward the uterus.</li> </ul>
<p><b>Implantation</b></p>	<ul style="list-style-type: none"> <li>is the process by which the blastocyst becomes embedded in the endometrium of the uterus. It usually occurs in the upper part of the posterior wall of the uterus from day 6 to day 10.</li> <li>Tubal pregnancy is the most common ectopic pregnancy.</li> </ul>





# MCQ

male slides



WHICH ONE OF THE FOLLOWING IS THE FIRST PHASE IN FERTILIZATION?

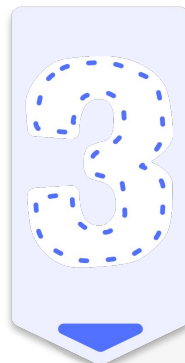
- A** Passage of sperm through zona pellucida.
- B** Fusion of male & female pronuclei.
- C** Passage of sperm through corona radiata.
- D** Fusion of plasma membranes of oocyte & sperm.

male slides



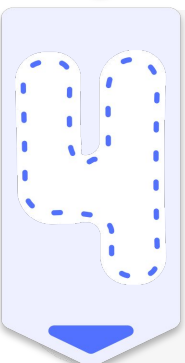
IMPLANTATION BEGINS AT:

- A** Day 5
- B** Day 7
- C** Day 6
- D** Day 8



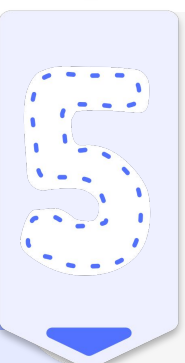
Which of the following is the most common ectopic pregnancy?

- A** Tubal Pregnancy
- B** Posterior wall of the uterus
- C** Ovarian pregnancy
- D** Abdominal pregnancy



Usually the zygote have?

- A** Haploid number of chromosome
- B** 46 chromosome
- C** 23 chromosome
- D** 24 chromosome



Which of the following is the most common site of implantation?

- A** Ampulla of fallopian tube
- B** Ovary
- C** Uterus
- D** Abdomen

# Embryology Team



Leader

سلطان البقمي

Leader

رهف الشويهي



أبو عويد



ريناد صالح الشهري



عبدالله الكودري



ريوف الأحمري



خالد العنزي



ريماس المحمود



فراس مازن



شادن الهزاني



زياد العتيبي



ريناد محمد الشهري



فيصل الشويعر



لمى العتيبي



ريم العمير

Special thanks and gratitude to the amazing Lama Alotaibi for this fabulous designing of the theme