# G.U.S.

# Physiology

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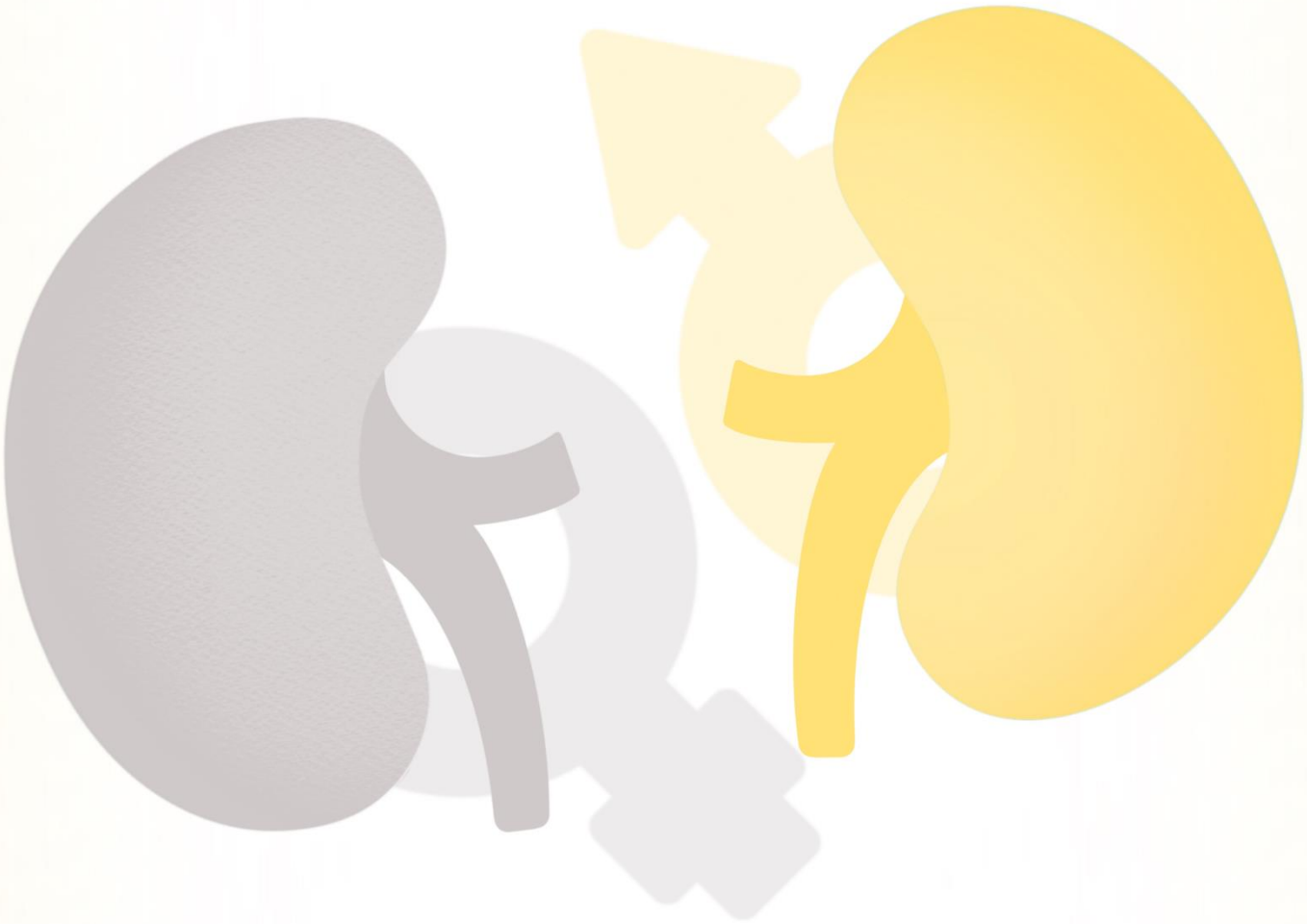

Sheet: fertilization

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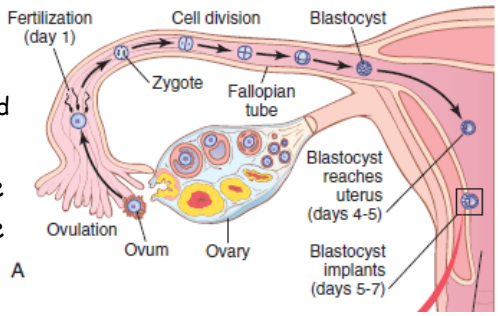
## Overview:




-Ovulation takes place in the ovaries when primary oocyte enters the first stage of meiosis, it will give a secondary oocyte (23 unpaired chromosomes). Then, secondary oocyte will be ready for meiosis 2 once it fertilizes with a sperm, if there is no sperm reaches to the oocyte, it won't go through meiosis 2. So, the ovaries will expel the oocyte while it is secondary oocyte with 23 unpaired chromosomes A into the abdominal cavity during ovulation process which is around 14th day of the ovarian cycle. The ovum at this stage will be surrounded by part of granulosa layers (corona radiata) and then it will enter the fallopian tube with the aid of its fimbriated end. Cilia of the fimbriated end (which move in the presence of estrogen) + the contraction of the fallopian tube smooth muscle cells, together, transport the ovum toward the ampulla of the fallopian tube.

-At this stage, fertilization by the sperm happens, the ovum completes the 2nd stage of meiosis to complete its maturation so it's ready to combine with the 23 chromosomes of the sperm.

**The normal site of fertilization is the fallopian tube, specifically in ampulla. After ejaculation, sperms reach the ampulla within 30-60 min with the aid of the seminal fluid prostaglandins and female oxytocin.

*In the cervix, 3% of the sperms survive after 1-3 min of ejaculation.

After 10-20 min of ejaculation, about 0.1% of the sperms are in uterus.

After 30-60 min of ejaculation, only 0.001% of the sperms are in the fertilization site (upper 1/3 of the duct).

## Fertilization

1- The fertilizing sperm penetrates the corona radiata via membrane-bound enzymes present on the plasma membrane of its head, and binds to ZP3 receptor on zona pellucida. This binding triggers an acrosomal reaction (a release of hydrolytic enzymes from the acrosome onto the zona pellucida takes place).

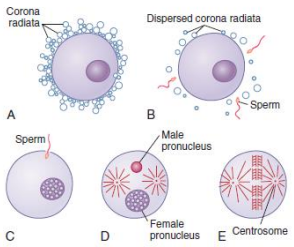
2- The acrosomal enzymes digest the zona pellucida, creating a pathway to ovum plasma membrane.

3- The plasma membranes of both cells fuse.

4- The nucleus of the sperm -only- enters the cytoplasm of the ovum (its midpiece and tail do NOT enter)

5- The sperm stimulates the release of $Ca^{+2}$ ions, which are stored in the cortical granules of the ovum. This, in turn, inactivates ZP3 receptors, leading to what is called "poly-sperm block" (prevention of any other sperm from penetrating).

**Complete union of sperm and ovum genetic materials:** Once a sperm has entered the ovum, the mature ovum is now termed the **female pronucleus**. Also, on entering the ovum, the sperm's head swells to form a **male pronucleus**. Then, the 23 unpaired **chromosomes** of the male pronucleus and the 23 unpaired chromosomes of the female pronucleus align themselves parallel to each other (with the aid of centrosomes on each pole) to form a complete complement of 46 chromosomes in the fertilized ovum.




from slides:

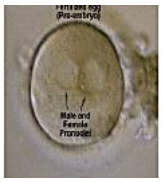
-Sperm penetrates corona radiata and zona pellucida (hyaluronidase)

-Oocyte divides to form mature ovum (female pronucleus; 23 unpaired chromosomes)

-Head of sperm swells (male pronucleus; 23 unpaired chromosomes)

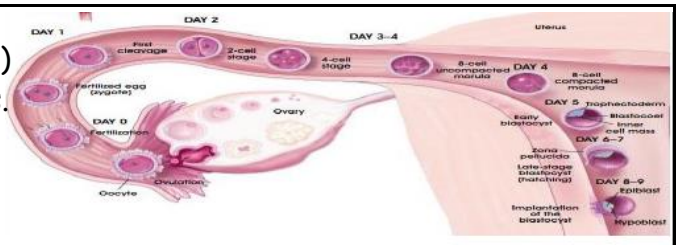
-Release of cortical granules preventing further sperm penetration

-Fertilized ovum (zygote) contains 23 paired chromosomes 46 chromosomes



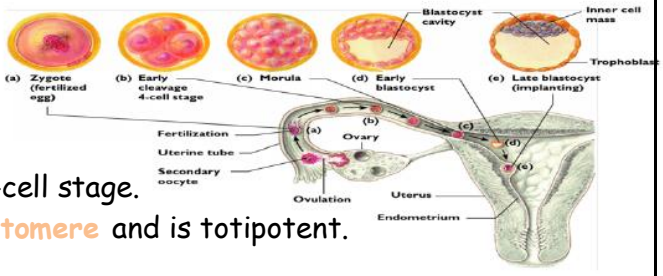
**A zygote before the union of both male and female genetic materials →

Timeline for after-fertilization stages (zygote process)




**Day one**: the 1st cleavage takes place resulting in 2cells.
**Day 3-4:** morula cell: 8 uncompacted cell.
**Day 4**: morula cell: 8 **compacted** cell.
**Day 4-5**: the compacted morula enters the uterus.
**Day 8-9:** implantation of the blastocyst (the fertilized ovum)

## Cleavage




-Following fertilization, the zygote undergoes several mitotic divisions inside the zona pellucida (overall size does not change). Divisions continue rapidly until the 32-cell stage.
-1st cleavage yields a 2 celled embryo; each cell is a blastomere and is totipotent.
- Early cleavage 4-cell stage
- Morula cell → the compacted enter the uterus
- Early blastocyte (implanted in the uterine lining (has a blastocyst cavity)).
- Late blastocyst the exact implanted cell that is composed of trophoblast, inner cell mass and a trophoblast layer.

**Traveling:** The zygote travels across the fallopian tube to finally reach the uterus where implantation takes place.

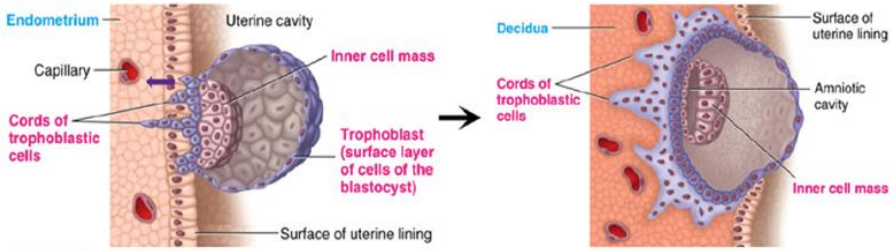
## Transport of fertilized ovum

-3-5 days after fertilization, the zygote reaches the uterine cavity, with the aid of the fluid current + the action of cilia of the fallopian tube + the weak contractions of the fallopian tube + the seminal prostaglandins + estrogens.
- Progesterone causes the isthmus of the fallopian tube (last 2cm) to relax which aids in the entrance of the zygote to the uterus.
-This delayed transport of the zygote allows cell divisions to occur before the blastocyst- which is now about 100 cells- enters the uterus.

## Implantation

-Trophoblastic cords from the blastocyst starts making the placenta.
-Blood capillaries grow in the cords from the fertilized ovum.
-21 days after fertilization, blood starts to be pumped by the fetal heart into the capillaries. The maternal blood sinuses develop around the trophoblastic cords of the implanted zygote.
-More and more trophoblastic projections develop forming the placental villi.

Notes on the figure beside:
* The trophoblast (surface layer of the blastocyst) invades the endometrium (uterine lining), forming cords of trophoblastic cells (which then grow and form part of the placenta)
*Decidua: the endometrial part after implantation (maternal part).
*Amniotic cavity is formed.
*Inner mass cell will form the embryo.



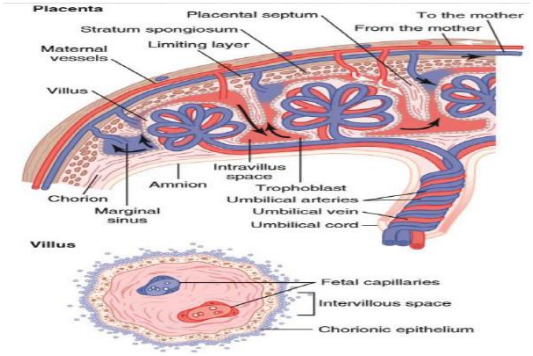
## Placenta

The primary source of nutrition and gases for the developing fetus from the 8th week of gestation.
Before that it gets nutrients from:

1- The fallopian tube secretion (under the effect of progesterone)
2- The uterine milk (under the effect of progesterone)
3- After implantation, the blastocyst gets nutrition from the endometrial lining of the uterus that has stored many nutrients such as: lipids, glycogen by the action of progesterone during the ovulation cycle.

** Placenta begins to provide nutrition at the 16th day after fertilization, but the embryo continues to obtain at least some of its nutrition from other sources for up to 8 weeks.

In the developed placenta, fetal blood flows through two umbilical arteries (unoxygenated blood), then into the villi capillaries to get oxygenated in the placenta, and finally back through a single umbilical vein (oxygenated blood) into the fetus. At the same time, the mother's blood flows from her uterine arteries into large maternal sinuses that surround the villi and then back into mother uterine veins.
** Exchange (diffusion) of gases between mother and fetus is very similar to the exchange that takes place in the pulmonary and other capillary beds in our bodies.

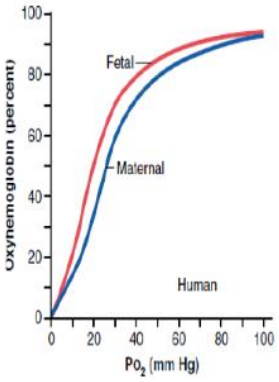



### Main functions of the placenta:

1-Respiration to provide the fetus with oxygen
2-Nutrition to provide the fetus with the needed nutrients (AA, sugars)
3-Excretion of waste product from metabolic reactions of hormones and metabolized products
4-Endocrine for the mother and the fetus
5-Protection for the fetus
* Maternal and fetal blood is related to provide the oxygen and nutrition to the fetus, and to eliminate waste products (CO2, waste products) from the fetal circulation.

### Important factors facilitating delivery of O2 from the maternal circulation to the fetus:

**1-Difference in pO2 (pressure/ concentration) between maternal and fetal blood**
The maternal pO2 (50mmgh) > fetal pO2(30mmgh → not a big difference between them (20mmgh), but it is sufficient to transport O2 to the fetus aided by the other factors.
**2-High fetus hemoglobin (HbF) (16 - 17 g/dl)**
HbF has a high affinity (tendency) for O2 than mother's hemoglobin (HbA) which means that HbF is shifted to the left, and the maternal hemoglobin is shifted to the right.
**NOTE:** At low PO2 levels in the fetal blood, HbF can carry 20- 50% more O2 than HbA .
3-**High fetal cardiac output**
Due to the combination of CO from both ventricles, and due to the shunting process in fetal circulation.
**4-Double Bohr Effect which takes place in both the maternal and fetal circulations**



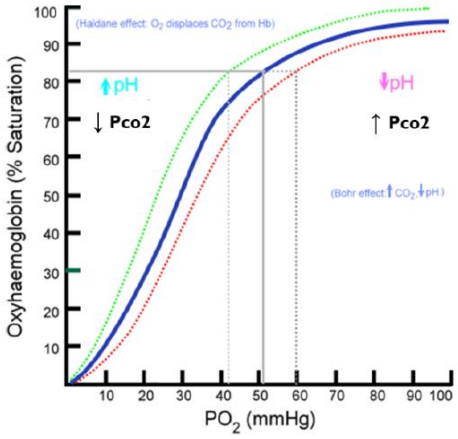
Hb has a high affinity to O2 in low concentrations of CO2, and O2 dissociates readily from the Hb molecules when there are high levels of CO2.

- Fetal blood has high PCO2 leading to O2 dissociation (leaving the circulation), get lost to maternal in placenta which makes the blood more alkaline (more tendency to combine with oxygen).

-Carbon dioxide diffuses from the fetal blood into the maternal blood, thus, the fetal blood pH rises and the curve shifts to the left allowing additional oxygen uptake.

- When the CO2 reaches the maternal blood through diffusion according to its gradient, the blood become acidic, and this decreases oxygen binding of the maternal blood.

-Maternal blood gains CO2 from the fetus, maternal pH falls, the curve shifts to the right→ releasing O2.




## Nutrition

-Fetus uses mainly glucose for nutrition so the trophoblastic cells in the placental villi transport glucose by carrier molecules; GLUT (facilitated diffusion).

-Fatty acids diffuse due to their high solubility in cell membranes (slower than glucose due to availability of the transporters for the glucose on the trophoblast).

-The placenta has active transporters for amino acids, because fetal concentrations of a.a. exceed their maternal levels → that's why we have amino acids active transporter not ONLY passive transporters.

-K+, Na+ and Cl- diffuse from the maternal to the fetal blood by bulk diffusion just like any capillary

## Excretion

-Excretory products of the fetus diffuse through the placental membrane to the maternal blood to be excreted with the waste products of the mother via the renal system such as; urea, uric acid, creatinine, and other muscle metabolites and proteins.

-Higher concentration of excretory products in the fetal blood ensures continuous diffusion of waste products from the fetus to the maternal blood.

**GOOD LUCK**