435 team

#6 Physiology of pregnancy

Objectives: .

- **Describe** fertilization and the implantation of the blastocyst in the uterus
- **Recognize** the development and the normal physiology of the placenta
- **Describe** the physiological functions of placental hormones during pregnancy
- **Explain** the physiological response of mother's body to pregnancy

Important
Males notes
Females notes
Extra

Revised by
خولة العماري & هشام الغفيلي

Resources:

1. 435's Girls' & boys' slides.
2. Guyton & Hall textbook of medical physiology – 12th edition.
3. Pocket companion to Guyton & hall textbook of medical physiology – 13th edition.
4. Oocyte Development – USNW embryology website.

Editing file: Here

Revision (large group activity)

***How many sperms in the ejaculated semen?**	Range of sperms ejaculated depends on semen, average semen volume is 3-5 ml and the average of sperms is 100 million. So if the semen was 5 ml X 100 million so we will have **half a billion**.
In which stage the ova is after ovulation?	Metaphase of the second meiotic division.
***What is the % of ovulated ova that can reach fallopian tube?**	98-95% of ova will reach fallopian tube. معنى الكلام؟ خلال 100 سايكل.. 98 بويضة ناتجة عن الافيوليشن بتقدر انها توصل للتيوب.
***Can the ova released from the right ovary reaches the left fallopian tube?**	Patient had cancer in one ovary they removed the ovary in one side , and then she had an ectopic pregnancy and they removed the fallopian tube of the other side what will happen ? Can this lady get pregnant ? Yes, the ova can enter the opposite fallopian tube(الفالوبيان تيوب بيمد يده ويأخذ الاوفا من الجهه الثانية)
***What are the factors that help the ovulated ova to reach the fallopian tube ?**	1\ Slow fluid current flowing toward the opening of the fallopian tube (osteum). 2\ Cilia, lining the fimbriated ends of the fallopian tubes.
***What are the factors that help the sperm to travel in the female genital tract?**	By contractions of the uterus and fallopian tubes stimulated by prostaglandins in the male seminal fluid.

بيساعدكم بفهم سالفة الميوزز 2 المذكورة فوق + معنى بولار بودي اللي بنتكلم عنه بعد شوي

Meiosis in female (EXTRA)

- **From fetal life until puberty:** All eggs are arrested at an early stage (prophase I) of the first meiotic division as a primary oocyte (primordial follicle).
- **Following puberty "during each cycle":** pituitary gonadotrophin stimulates completion of **meiosis 1** the day before ovulation.
    - In **meiosis 1**, a diploid cell becomes 2 haploid (23 chromosomes) daughter cells, One cell becomes the secondary oocyte the other cell forms the first polar body.
- The 2ry oocyte then commences **meiosis 2** which arrests at metaphase and will not continue without fertilization.
    - At fertilization **meiosis 2** completes, forming a second polar body. Note that the first polar body may also undergo this process forming a third polar body.

***mentioned in Guyton.**

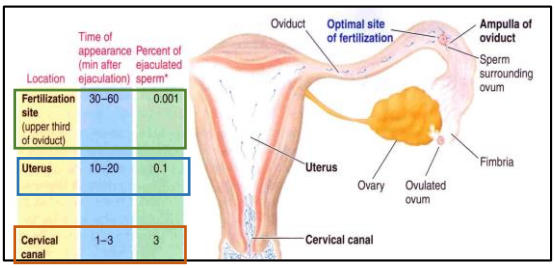
Introduction:

- After ejaculation, sperms reach ***ampulla*** of fallopian tube within **30-60 min** (PG and OT actions)

1- 500 million of sperms will be ejaculated and will reach to the cervix within 1-3 minute and only 3% from the 500 million = 15 million.
Average number of sperms in the semen = 120 million sperms

2- Only 0.1% (150 thousands) can pass to the uterine cavity "some of the sperms are weak and they wont make it through the immune system of the uterus

3- Only 0.001% (5 thousands) can pass to the upper 1\3 of the oviducts.
علشان بعض السبرمز اغبياء يروحون للتيوب الفاضي اللي مافيه الاوفيم



*mucus become thinner at time of ovulation – external orifice its tightly closed usually but at time of ovulation it slightly open
*pH of the uterus is alkaline.

1-Fertilization:

If the ovum becomes fertilized by a sperm, a new sequence of events called ***gestation*** or ***pregnancy*** takes place, and the fertilized ovum eventually develops into a full-term fetus.

Structure:

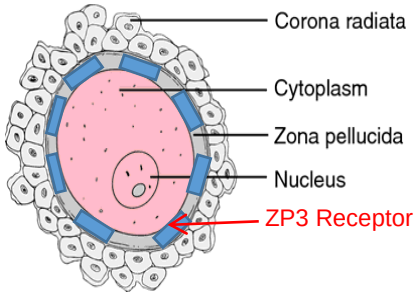
❖ **What are the layers that the sperms needs to go through to reach the ova ?**

1- corona radiata (granulosa cells before).

2-zona pilluceda (#####with ZP3 Receptors on them)

3- cell membrane (from out side to inside) ,

+ we have cortical granules filed with calcium inside the ovum "مهم"



Steps:

1. After ejaculation sperms reach **ampulla** of fallopian tube within 30-60 min (ut cont)
2. Sperm penetrate corona radiata using the enzymes (protease) on the plasma membrane of its head.
3. Then binds to **ZP3 recptors** located on the zona pellucida
4. This triggers **acrosome reaction**, in which **hyaluronidase** & **proteolytic** enzymes in the acrosome are released onto the zona pellucida
5. Penetration & digestion of the zona pellucida
6. The sperm nucleus enters the ovum cytoplasm

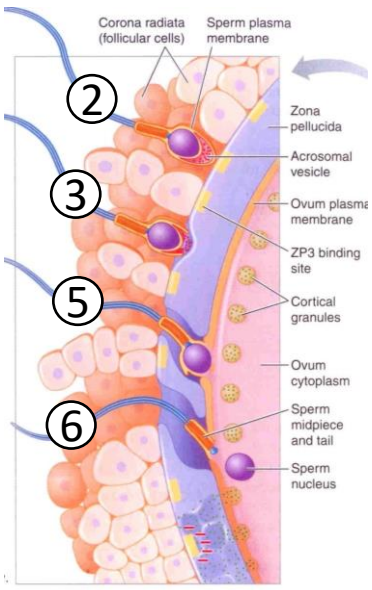
A. The sperm stimulates release of Ca2+ stored in cortical granules in the ovum, which in turn, **INACTIVATES ZP3 RECPTORS**, leading to the **block to polyspermy**. "(that's why only one sperm can fertilize the ovum)."

B. Oocyte complete the 2nd meiotic division and divides to form **mature ovum** (female pronucleus 23 unpaired chr)

C. Head of sperm swells (male pronucleus 23 unpaired chr)

D. Fertilized ovum (zygote) contain 23 **paired** chr. صحصحوا بالاختبار بايرد!!!! زوج من الكروموسومات!!

✓ The 23 chr. of the male and female pronuclei align themselves to re-form a complete complement of 46 chromosomes



Notes:

- The ovum is always X, the sperm could be X or Y. ونوع السبيرم الي يلتقي مع الأوفم هو الي يحدد جنس الجنين

- A theory: Y sperms are faster than X sperms. That's why when intercourse happens at the day of ovulation, the chance for the baby to be a boy is higher but when the intercourse happens 2 day before ovulation the chance for the baby to be a girl in higher.

2- Transport of the fertilized ovum in the fallopian tube:

Transport:

- After fertilization, additional **3-5 days** (رجاء لحد يلخبط فيها) are required for **transport** of the zygote through the reminder of the fallopian tube till the uterine cavity.

Nutrition of blastocyst:	secretory cells in fallopian tube.
This transport is affected mainly by:	**1- fluid current** in the tube resulting from epithelial secretion.
	2- Action of cilia lining the tube.
	3- weak contractions of the fallopian tube (estrogen, PGs).

Entry of the ovum into the uterus:

1. The fallopian tube are lined with a rugged, cryptoid surface that impedes passage of the ovum despite the fluid current.
2. Isthmus (last 2cm before the tube enter the uterus) relaxes under effect of **progesterone**.
   - ✓ **Delayed transport allows cell division** to occur before the dividing ovum (Blastocyst ~100 cells) enters the uterus.

❖ **اختصار السالفة** انه بأول 3 ايام بعد التبويض بيكون اليوترن تيوب زي شوارع الرياض مليان مطبات! فالواحد مايوصل إلا متأخر وطالعة روحه.. وزيادة على وجود المطبات فيه حفريات مضيقه الطريق "من ضيقه ماتمر إلا سيارة ☹"! الحفريات هذي تتمثل بالاسمس (ممر ضيق) والمطبات تتمثل باليوترن لاينتق..

➢ **تتوقعون ان هالشيء ممكن يستفاد منه؟** نعم! الزايقوت بتطول وهي تمشي فهالشيء بيضمن لنا انها بتنقسم وبتاخذ وقتها بالانقسام لأن لو الزايقوت ما انقسمت ووصلت للايت ستايج ومثلا بس وصلت لمرحلة الموريولا (بتتكلم عن المراحل بشكل مختصر بعد شوي) ماراح يصير امبلانتيشن! لأن فيه ادوات معينة مابتكون معها..

➢ **طيب هل هالشيء بيستمر؟** طبعا لا! بعد 3 ايام تقريبا بيزداد افراز البروجسترون من الكوربس لوتيم واللي نعرف ان تأثيرها ريلاكسيشن وبتفك الزحمة وبتقول للاوفيوم تفضلي روحي لبيتك (اليوترس).. نبي بروجسترون يفكنا من الزحمة ☹

Cleavage:

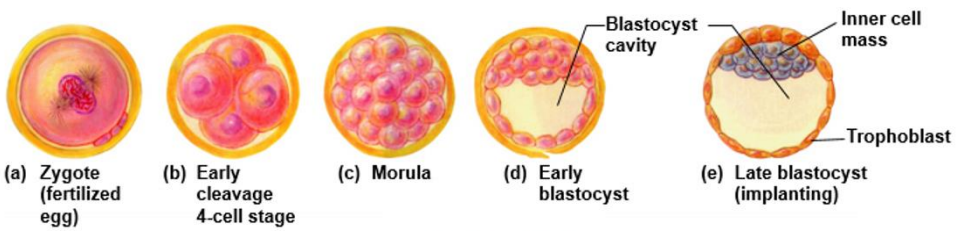
- Following fertilization, the zygote undergoes several mitotic divisions inside the zona pellucida (overall size **DOES NOT** change) as it travels through oviducts.
- 1st cleavage yields a 2 celled embryo,
  - each cell is called a **blastomere** and is **totipotent** → (can give placenta and embryo). Pluripotent can only form embryo.
- Divisions continue rapidly **until the** 32 cell stage.
- **Blastocyst** (100 cells) enters the uterus.

Notes:

- Blastocyst is 100 cells and more.
- And blastocyst cavity مالها أي أهمية حاليا بس عشان لمن يكبر الجنين يكون في مكان فقط
- **Trophoblast (هرمون HCG) مهمة جدا جدا جدا، اذا ما عندي تروفوبلاست ما بيكون عندي** before early blastocyst we don't have trophoblast → which means that the corpus luteum is still under LH stimulation.
- If there's any pathology in trophoblast cells at **day 21** of fertilization >> abortion. يعني التروفوبلاست لازم تشتغل يوم ٢١ اذا ما اشتغلت بعد ٥ أيام بتروح الكوربس ليوتم ويصير اجهاض

- **What helps the zygote to reach the uterine cavity?**

The corpus luteum goes after ovulation by 12 days (if no pregnancy occur) 14 + 12 = 26. >> هنا الكوربس ليوتم عايشة على ال اتش هورمون



3- Implantation:

When?

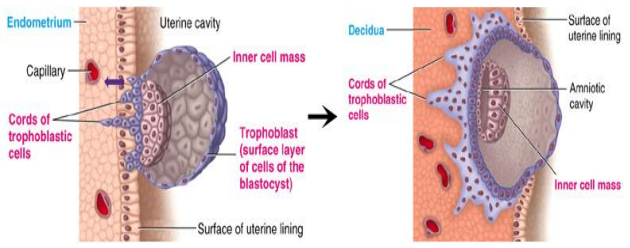
- After reaching the uterus, the developing blastocysts usually remains in the uterine cavity معلقة بالهواء an additional 1-3 days before it implants in the endometrium and it obtains its nutrition from the uterine endometrial secretions "**UTERINE MILK**".
- Thus, Implantation occurs on 5-7 day after ovulation.

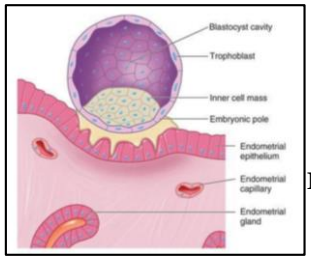
المشيمة ما تتكون الا في الشهر الثالث او الرابع وقبل الشهر الثالث يكون عندي بس تروفوبلاست بروجيكشنز الي تعمل عمل المشيمة.
طيب كيف يعيش الامبريو هنا وانا ما عندي مشيمة؟ هنا يكون عايش على افرازات الرحم الي اسمها uterine milk

How?

- Implantation results from the action of **trophoblastic** cords from the surface of **blastocyst**.
- **Digestion of endometrium:** Trophoblast of the blastocyst begin to secrete proteolytic enzymes that digest and liquefy the adjacent endometrium. Within a few days, blastocyst has invaded the endometrium and is firmly attached to it.
- **Decidual cells:** (glycogen, proteins, lipids & minerals).

لو تتذكرون بالمحاضرات الأولى ذكرنا ان البروجسترون الناتج عن الكوربس لوتيم يجهز اليوترس انه يستقبل الكنسبتس "الامبريو والأشياء اللي معه" بحيث ان السترومال اندومتريم تكون مليانه فاتس وبروتين.. الخ
بعد مايجي الكنسبتس ويصير له امبلانتيشين ذيك الخلايا بتنتفخ اكثر واكثر وبتخزن نيوترينتس اكثر.. هذي الخلايا نسميها دسجوا.
في مكان الامبلانتيشن الاندوميتيرم يصير اسمه decidua
Decidua is endometrium but thicker with more nutrients and blood vessels (endometrium in pregnancy) > when I say decidua that means that the lady is pregnant!





Blastocyst Differentiation

Placenta:

Development of the placenta:

- While the **trophoblastic cords** from the blastocyst are attaching to the uterus, blood capillaries grow into the cords from the vascular system of the newly forming embryo.

Blastocyst → Trophoblastic cords → Blood capillaries

- Abour **21 days** after fertilization blood start to be pumped by fetal heart into the capillaries.

اول عضو يتكون من الجنين هو القلب، بدون القلب ما بيضخ الدم!

- Simultaneously, ***Blood sinuses*** supplied with blood from the mother develop around the outsides of the trophoblastic cords.
- The trophoblastic cells send out More and more trophoblast projections develop (**placental villi**)

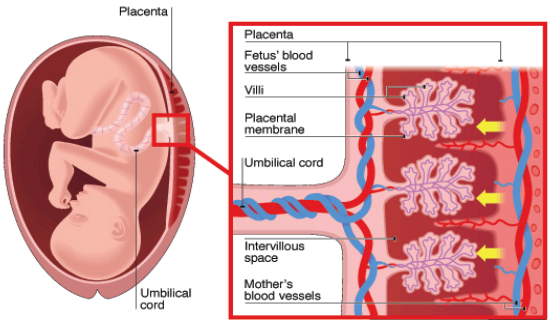
- The fertilized ovum stays 1-2 days in the uterine cavity before getting implanted to increase the cleavage.
- يعني احسب الاوفم تمشي بالفلوبيان تيوب ٣-٥ بعدين تقعد معلقة بالهواء يوم لثلاث أيام تقريبا يعني الامبلانتيشن يصير بعد 21 يوم من البليدنق او 5-7 day after ovulation (مره قاعد يركز على الأرقام ☺!!)

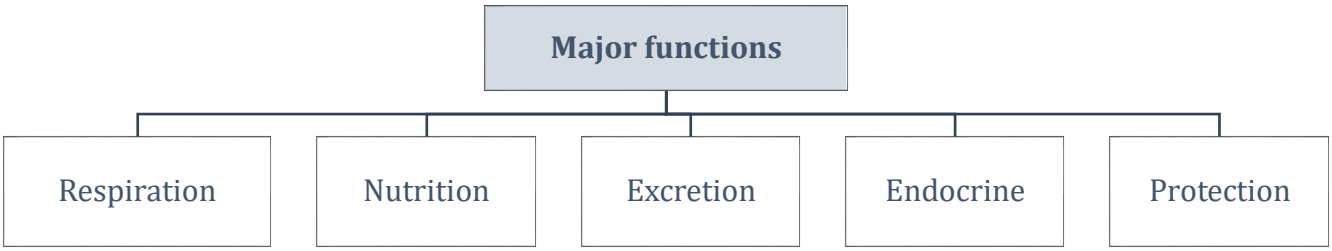
❖ **اختصار الكلام:** 21 يوم بعد الإخصاب (الحسبة موضحه بنوتس الدكتور^) ، يبدأ قلب الجنين بنبض الدم للأوعية الدموية (اللي يتكون داخل الـ تروفوبلاستيك كوردس)، بعدها أوعية الدم حقت الأم تتكون حول أوعية الجنين، ويصير فيه تبادل من خلال الـ trophoblast projections
+معلومة : *arteries contain the fetus' waste & veins carry the mother's good blood*

Placenta: Cont'd

Physiologic anatomy

- There's no direct connection between the mother blood vessels and the fetal blood vessels so we have a space called intervillous space
  - مكان زي الحوض هو الي يصير فيه تبادل الدم والغذاء والاكسجين
- if connection happens between them → nonstop hemorrhage during delivery.
- 40 days bleeding after delivery happens because the decidual layer gets removed





Nutrition:

Glucose (mainly):	Fetus uses **MAINLY GLUCOSE** for nutrition so the **trophoblast cells** in placental villi transport glucose by carrier molecules ; **GLUT** (**facilitated diffusion**). Trophoblast cell will transport the nutrients from maternal blood to fetal blood
Fatty acids:	• Fatty acids **diffuses** due to high solubility in cell membrane (more slowly than glucose so that glucose is used more easily for fetus).
Amino acids:	The placenta **actively transports** all amino acids, with fetal concentrations exceeding maternal levels.
Electrolytes:	K+, Na+ and Cl- diffuses from maternal to fetal blood.

Excretion:

- **Excretory products** of the fetus diffuse through placental membrane to maternal blood to be excreted with waste products of the mother.
- **Examples:** Urea, uric acid and creatinine.
- Higher concentration of excretory products in fetal blood insures **continuous diffusion** of these substances to the maternal blood

When I say excretion it means from the fetus to the mother.

Placenta: Cont'd

Respiration:

Placental permeability and membrane diffusion conductance:

In the early months of pregnancy,	In later pregnancy
○ **The placental membrane** is still **thick** because it is <u>not fully</u> developed. ○ **The surface area** is **small** because the placenta has not grown.	○ **The permeability** **increases** because of <u>thinning</u> of the membrane diffusion layers and because the surface area <u>expands</u> many times over.

Before the 3rd month of pregnancy the layers are very thick so it's difficult to the nutrition to pass, but after 3rd month the permeability increases because of the thinning of the surface area

Diffusion of oxygen through the placental membrane:

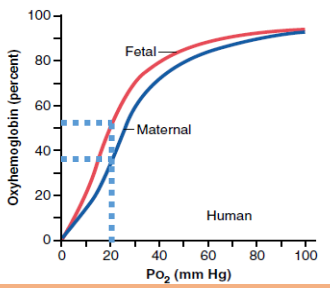
- The mean partial pressure of oxygen (PO2) of the mother's blood in the placental sinuses is about 50 mm Hg, and the mean PO2 in the fetal blood after it becomes oxygenated in the placenta is about 30 mm Hg.
- 50 mm Hg – 30 mm Hg = **20** mm Hg (mean pressure gradient The pressure that will let O2 go from the placenta to the fetus)
- There are <u>three reasons</u> why (Not 13 :P) this low PO2 is sufficient to deliver O2 to the fetal tissues:

1- Hemoglobin of the fetus

Remember:
Right shunt =
Reduced
"Low" affinity

- **Type: Fetal hemoglobin (HbF)**
- HbF has **greater** affinity to O2 than the Adult Hb.
  - ✓ So at the low Po2 levels in fetal blood, the fetal hemoglobin can carry 20 to 50% more oxygen than maternal hemoglobin can..

Example: when partial pressure = 20mmHg, the mothers (blue line) affinity of Hb to O2 = 38%
And at the same PO2 =20mmHg in the fetus (red line) the affinity in higher.
The fetal curve is shifted to **the left**. 20mmHg is the placental pressure.



Oxygen-hemoglobin dissociation curves

2- Fetal hemoglobin concentration

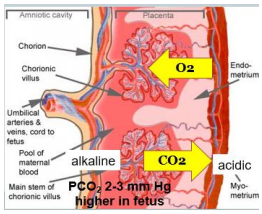
- **The fetal hemoglobin concentration** is about 50% **greater** than that of the mother

3- The Bohr effect

Very important – ركزوا فيها دايما نجيب عنها سؤال

The Bohr effect is a physiological phenomenon stating that Hemoglobin's **oxygen binding affinity is inversely related** both to <u>**acidity**</u> and to the <u>**concentration of carbon dioxide**</u>.

Maternal blood:	Fetal blood:
CO_2 is gained	CO_2 is lost
The <u>pH falls (**Acidic**)</u>	The <u>pH rises (**alkaline**)</u>
the curve shifts to the **right** <u>releasing</u> additional oxygen.	the curve shifts to the **left** allowing additional oxygen uptake
These changes cause the **capacity** of fetal blood to combine with O2 to increase, and maternal blood to <u>decrease</u>, which forces more O2 from the maternal blood while <u>enhancing</u> oxygen uptake by the fetal blood.	



If Co2 pressure in higher in the fetus, it will go from the fetus side to the mothers side.
When co2 goes out from a cell, this cell will be alkaline.
When you put Hb over O2 and you put them in an acidic medium what will happen?
بيتفككوا
بس اذا حطيتها بألكالاين بيزيد البايندنق

Placenta: Cont'd

Respiration:

Important factors facilitate delivery of oxygen to the fetal tissues:

High maternal intervillous blood flow (almost double the fetal placental flow)	**High** fetal cardiac output	The fetal **metabolic acidosis** which shifts the curve to the right and thus aids delivery of oxygen to the tissues	**High** fetal haemoglobin (16 - 17 g/dl)

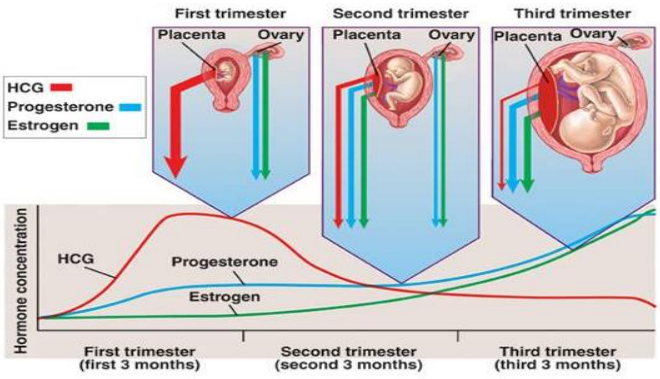
The mother suffers from hypotension due to increase amount of blood going to the placenta specially after the second trimester

Endocrine:

In the first 3 months:

Estrogen and progesterone come from corpus luteum and **HCG from trophoblasts**, this HCG maintain the life span of corpus luteum until placenta is fully developed

مهم جدا انك تعرف ان الانتش سي جي يكون عالي اول ٣ شهور



Second trimester:

- Corpus luteum begin to die **gradually**. Why?
Because the placenta will take over.
- HCG here is not that important but it should be present, if it goes away completely → a problem will happen

Third trimester:

All these hormones are mainly from placenta (no corpus luteum).
& HCG decrease

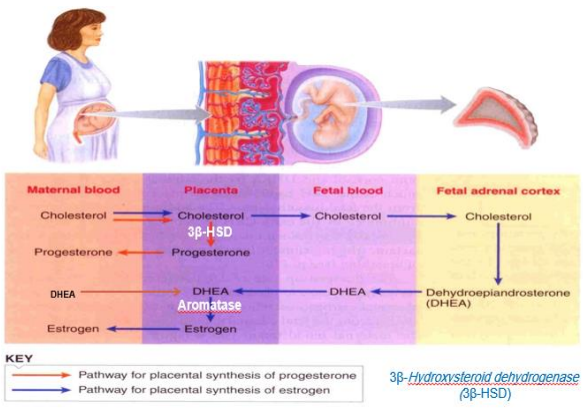
Sources of placental estrogen and progesterone:

❖ **Progesterone:**
the placenta has an enzyme called "3 beta hydroxysteroid dehydrogenase" it converts cholesterol to pregnenolone and pregnenolone to progesterone.

❖ **Estrogen:**
Cholesterol comes from the mother → cross the placenta → goes to adrenal cortex of the fetus → weak androgen → goes back to placenta → granulosa cells which convert the weak androgen to estrogen.

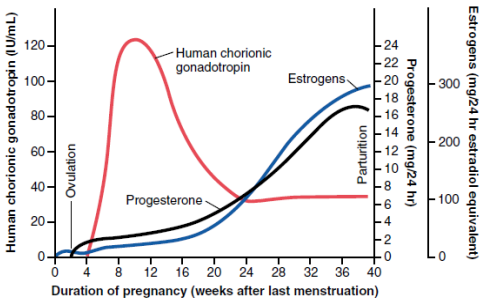
- ✓ If the fetus doesn't have a working adrenal cortex → no estrogen.

مهم تعرف ان الاندروجين جا من الفيتال كورتيكس.



hCG level (pregnancy test):

At the second HCG is low at the third trimester HCG is undetectable



Placenta: Cont'd

Endocrine:

Hormone	Nature:	Secreted by:	Derived from:	Functions in the mother
Human Chorionic Gonadotropin (hCG)	Glyco-protein	syncytial trophoblast cells	-	• Most important function is to **maintain corpus luteum** (↑estrogen & progesterone) till 13-17 weeks of gestation. • Exerts interstitial (Leyding) cell-stimulating effect on testes of the male fetus (growth of male sex organs). If the fetus was boy it works as LH on leyding cells.
Estrogen	Steroid hormone	syncytial trophoblast cells Towards end of pregnancy reaches 30x	weak androgen (DHEA) released from maternal & **fetal adrenals cortesx**	• Enlargement of uterus, breast ducts & external genitalia • **Relaxation** of pelvic ligaments in preparation to labor • Activation of the uterus (gap junctions) "Maternal cortex here is not that important, the large amount comes from fetal cortex"
Progsterone	Steroid hormone	syncytial trophoblast cells Towards the end of pregnancy it reaches 10×	**cholesterol**	• Development of the breast lobules. • Provides nutrition to developing embryo • Development of decidual cells • **Inhibit the contractility of the uterus** (It is very important to know that progesterone has nothing to do with contraction, it ALWAYS causes relaxation of the uterus!!) Progesterone = always relaxation. Please! Estrogen = more likely contraction.
Human Chorionic Somato-mammotropin or Human placental lactogen	Protein hormone	placenta around 5th gestational week	-	• Breast development (hPL) "human placental lactrogene" • Weak growth hormone's action • Inhibit insulin sensitivity =↓ glucose utilization "Spares glucose for the fetus" • Promote release of fatty acids. Only secreted during pregnancy, works like growth hormone.
Relaxin	Poly-peptide	by corpus luteum and placenta	-	• **Relaxation** of symphysis pubic ligament (weak) for preparation to open the pelvis • **Softens the cervix at delivery** "اسم على مسمى :)"

Physiological adaptation to pregnancy

Changes in maternal endocrine system	**Anterior pituitary gland enlargement (50%)**	•Release of ACTH, TSH and PL increase •FSH and LH almost totally suppressed : • because of increased levels of steroid hormones
	Adrenal gland	•Increase glucocorticoids secretion (mobilize AA) •Increase aldosterone (retain fluid). Why the pregnant lady is obese usually? Because of the action of aldosterone (water retention)
	Thyroid gland enlargement (50%)	Increase thyroxine production (hCG)
	Parathyroid gland enlargement	Increase PTH secretion (maintain normal Ca^{+2})
Changes in different organs	○ Increase in uterine size (50 gm to 1100 gm) ○ The breasts double in size ○ The vagina enlarges ○ Development of edema and acne ○ Masculine or acromegalic features ○ Weight gain 10-12 kg (last 2 trimesters) • Increase appetite ▪ Removal of food by fetus ▪ Hormonal effect	
Changes in metabolism	○ Increase basal metabolic rate (15%) ○ Increase in daily requirements for • Iron • Phosphates • Calcium • Vitamins - Vitamin D (Ca^{+2} absorption) ✓ The renal tubules' reabsorptive capacity for Na, Cl, and water is increased as much as 50%. ✓ The renal blood flow and GFR increase up to 50%. ✓ Normal pregnant woman accumulates only about 5 pounds (2.27Kg) of extra water and salt.	
Changes in circulatory system	○ Increase in COP (30-40%) by 27 weeks ○ Increase in blood flow through the placenta. ○ Increase in maternal blood volume (30%) due to 1. Increase aldosterone and estrogen (↑ ECF) 2. Increase activity of the bone marrow (↑ RBCs 40%) Water retention goes out with labor that's why pregnant women say احس اني خفيتafter delivery.	
Changes in respiration	○ Increase in O_2 consumption (20%) • Increase BMR • Increase in body size ○ Growing uterus presses upwards (restriction) ○ Increase in respiratory rate. الحامل دايم تنفسها سريع ○ Increase in minute ventilation(TV× RR) by 50% a <u>decrease</u> in arterial PCO2 to several millimeters. ✓ **Progesterone** ↑sensitivity of Respiratory center (RC) to CO_2	

SUMMARY

1-Fertilization:

1. After ejaculation sperms reach **ampulla** of fallopian tube within 30-60 min.
2. Sperm penetrate **corona radiata.**
3. Then binds to **ZP3 recptors** located on the zona pellucida**.**
4. Triggers **acrosome reaction**: **hyaluronidase** & **proteolytic** enzymes released onto zona pellucida.
5. Penetration & digestion of the **zona pellucida.**
6. The sperm nucleus enters the ovum cytoplasm:

- Ca2+ in cortical granules in ovum released, →**INACTIVATES ZP3 RECPTORS**, →**block to polyspermy.**
- Fertilized ovum (zygote) contain 23 **paired** chr.
- The 23 chr. of male &female pronuclei align themselves to re-form a complete complement of 46 chr

2- Transport of the fertilized ovum in the fallopian tube:

- After fertilization, **3-5 days** are required for **transport** of the zygote till the **uterine cavity**.
- This transport is affected by: **fluid current, Action of cilia & weak contractions of fallopian tube.**
- Isthmus relaxes under effect of **progesterone**. [**Delayed transport allows cell division** to occur before the dividing ovum (Blastocyst ~100 cells) enters the uterus].
- Following fertilization, the zygote undergoes several mitotic divisions inside the zona pellucida (overall size **DOES NOT** change).
- 1st cleavage yields a 2 celled embryo, each cell is called a **blastomere** and is **totipotent** → (can give placenta and embryo). Divisions continue rapidly **until the** 32 cell stage.

3- Implantation:

- blastocysts remains in the uterine cavity an additional 1-3 days before it implants in the endometrium and it obtains its nutrition from the uterine endometrial secretions "**UTERINE MILK**".
- **Thus, Implantation occurs on 5-7 day after ovulation.**

How? Trophoblastic cords action from **blastocyst, Digestion of endometrium &Decidual cells.**

Placenta:

Development :

1. Blastocyst → Trophoblastic cords → Blood capillaries.
2. About 21 days after fertilization blood start to be pumped by fetal heart into the capillaries.
3. ***Blood sinuses*** supplied with blood from the mother develop around the outsides of the trophoblastic cords.
4. The trophoblastic cells send out More and more trophoblast projections develop **(placental villi)**

Major functions:

1. **Nutrition:**

- Fetus uses **MAINLY GLUCOSE** by carrier molecules ; **GLUT** (**facilitated diffusion**).
- Fatty acids **diffuses** due to high solubility in cell membrane (more slowly than glucose).
- The placenta **actively transports** all amino acids.
- **Electrolytes:** diffusion of K+, Na+ and Cl-

2. **Excretion:**

- **Excretory products** of the fetus diffuse through placental membrane to maternal blood like Urea, uric acid and creatinine.
- Higher concentration of excretory products in fetal blood insures **continuous diffusion** of these

Major functions:

3. **Respiration:**

- **In the early months of pregnancy**, **the placental membrane** is still **thick** because it is not fully developed and **the surface area** is **small** because the placenta has not grown.
- **In later pregnancy**, **the permeability** **increases** because of thinning of the membrane diffusion layers and the surface area expands many times over.

- Mean pressure gradient: 50 mm Hg maternal – 30 mm Hg fetal = **20** mm Hg This low PO2 is sufficient to deliver O2 to the fetal tissues, why? There are three reasons:

1- Hemoglobin of the fetus: HbF has **greater** affinity (20-50%) to O2 than the Adult (maternal) Hb

2. Fetal hemoglobin concentration: about 50% **greater** than that of the mother.

3. The Bohr effect: Maternal blood[Gain CO_2 , acidic & shifts to the **right** releasing additional oxygen] While Fetal blood[Lose CO_2 , Alkaline & shifts to the **left** allowing additional oxygen uptake].

- **Delivery of oxygen to the fetal tissues facilitated by: High maternal intervillous blood flow, High** fetal COP, **High** fetal Hb (16 - 17 g/dl) & The fetal **metabolic acidosis.**

4. **Protection.**
5. **Endocrine:**

First trimester: Estrogen and progesterone come from corpus luteum and **HCG from trophoblasts.**
Second trimester: Corpus luteum begin to die **gradually.**
Third trimester: All these hormones are mainly from placenta (no corpus luteum) & HCG decrease.

hCG	Estrogen	Progesterone	hCS	Relaxin
- Glyco-protein. - Most important function is to **maintain corpus luteum** (↑estrogen & progesterone) till 13-17 weeks of gestation. - (Leyding) cell-stimulating effect on testes of fetus (male sex organs growth)	- Steroid hormone - Secreted by syncytial trophoblast cells .Derived from weak androgen (DHEA) released from maternal & **fetal adrenals cortesx**, - Enlargement of breast ducts. - - **Relaxation** of pelvic ligaments. - Activation of the uterus (gap junctions)	-Derived from **cholesterol**. - Development of the breast lobules & decidual cells. - **Inhibit the contractility of the uterus** (progesterone has nothing to do with contraction, it ALWAYS causes relaxation of the uterus!!)	Protein hormone Secreted by placenta around 5th gestational wk. - **(hPL)** Breast development. - Weak GH action - Inhibit insulin sensitivity =↓ glucose utilization - Promote release of fatty acids.	Poly-peptide Secreted by by corpus luteum and placenta. - **Relaxation** of symphysis pubic ligament (weak). - Softens the cervix at delivery.

Physiological adaptation to pregnancy

maternal endocrine sym.	•**AP gland enlargement: [**ACTH, TSH &PL increase] [FSH & LH suppressed]. •**Adrenal gland**:↑glucocorticoids (mobilize AA), ↑aldosterone (retain fluid).
different organs	**Increase size of uterine, breasts(double), vagina, Weight gain & ↑ appetite**
metabolism	**↑BMR, renal blood flow & reabsorption, GFR, daily req. of iron. Phosphate, ca & vit. D.**
circulation	**↑ COP, blood flow through the placenta & maternal blood volume.**
respiration	↑ O_2 consumption, respiratory rate, minute ventilation(TV× RR) &↓in arterial PCO2 and **Progesterone** ↑sensitivity of Respiratory center (RC) to CO_2

MCQs

1. which of the following is NOT major function of the placenta :

a) Respiration
b) Exocrine
c) Protection
d) Nutrition

2. After .... days of fertilization blood start to pump by fetal heart into capillaries :

a) 12
b) 23
c) 21
d) 11

3. Implantation occurs on … :

a) 5-7 days after ovulation
b) 5-7 hours after ovulation
c) 5-7 hours after fertilization

4. which of the following is diffuse through placenta membrane by facilitated diffusion :

a) Potassium
b) Amino acids
c) Fatty acids
d) Glucose

5. which of the following is consider as Glycoprotein :

a) hCG
b) Estrogen
c) Progesterone
d) Relaxin

6. development of decidual cells is function of:

a) Estrogen
b) Progesterone
c) hCG
d) Relaxin

7. regarding to changes in maternal endocrine systems, all the following increase EXCEPT :

a) FSH
b) PTH
c) Thyroxine
d) Aldosterone

Answer key:

1 (b) | 2 (c) | 3 (a) | 4 (d) | 5 (a) | 6 (b) | 7 (a)

Physiology 435 team

Thanks to this amazing team!

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