المحاضرة سهلة و 22 سلايد فقط، الباقي اكسترا

All numbers in this lecture are Important

MEDICINE
KING SAUD UNIVERSITY

Physiology Team 436

تمت المراجعة
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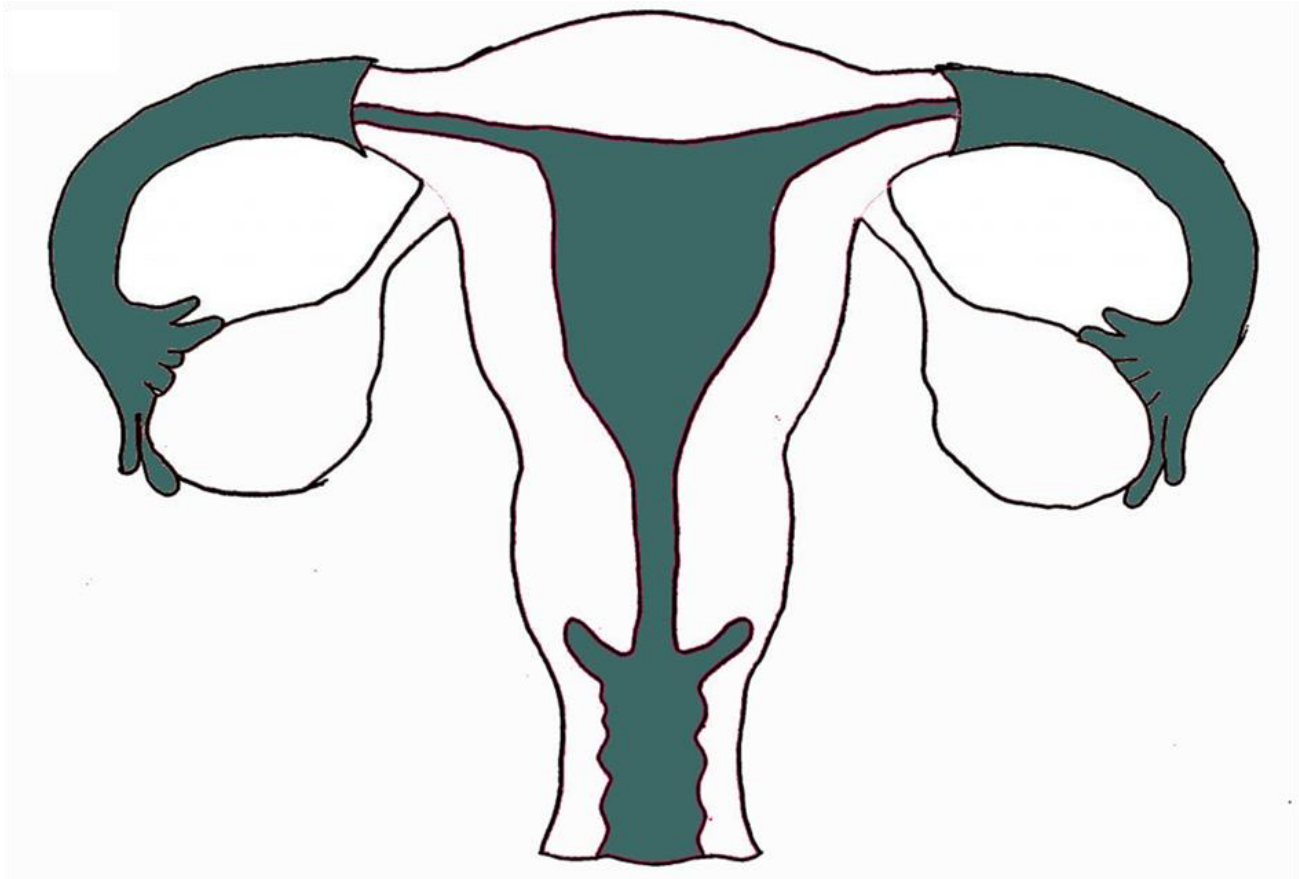

- Text
- Only in Females' slide
- Only in Males' slides
- Important
- Numbers
- Doctor notes
- Extra Notes

Reproductive Block

﴿قُل سِيروا في الأرضِ فانظُروا كيف بدأَ الخلقَ﴾
صدق الله العظيم

Physiology of Pregnancy

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

1. Describe Fertilization & implantation of the blastocyst into the endometrium.
2. Recognize the development and normal physiology of the placenta.
3. Describe the physiological functions of placental hormones during pregnancy.
4. Explain the physiological responses of mother's body to pregnancy.

All numbers in this lecture are Important

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Revision (Large Group Activity)

1. How many sperms in the ejaculated semen?

- ✓ Range of sperms 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 = half a billion of sperms.

2. In which stage the ova is after ovulation?

Metaphase of the 2nd meiotic division.

3. What is the parentage of ovulated ova that can reach fallopian tube?

95-98% of ova will reach the fallopian tube.

4. Can the ova released from the right ovary reaches the left fallopian tube?

The ova can enter the opposite fallopian tube

5. What are the factors that help the ovulated ova to reach the fallopian tube?

1. Fallopian tube contraction.
2. Fimbrial.
3. cilia with fluid

6. What are the factors that help the sperm to travel in the female genital tract?

Contractions of the uterus and fallopian tubes which stimulated by prostaglandins.

Maturation of The Ovum

- While still in the ovary, the ovum is in the primary oocyte stage. Shortly before it is released from the ovarian follicle, its nucleus divides by meiosis and a first polar body is expelled from the nucleus of the oocyte.

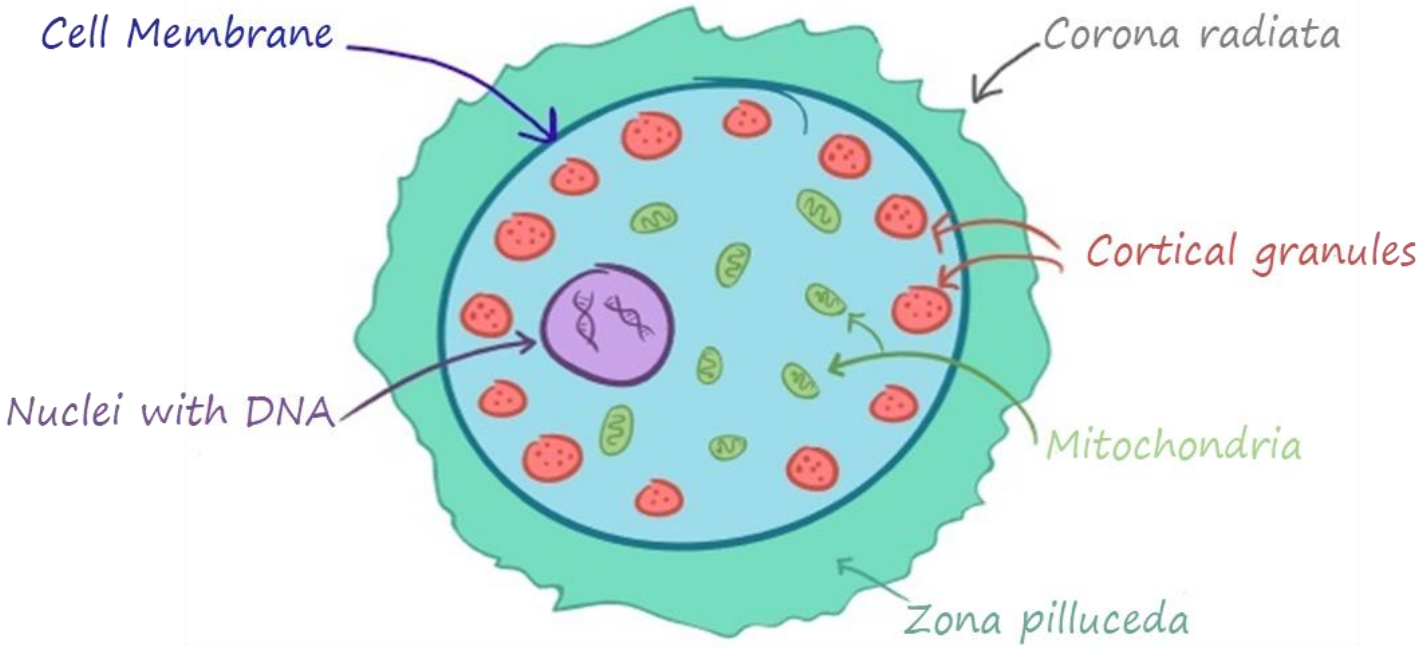
- The primary oocyte then becomes the secondary oocyte. In this process, each of the 23 pairs of chromosomes loses one of its partners, which becomes incorporated in a polar body that is expelled.

- This leaves 23 unpaired chromosomes in the secondary oocyte. It is at this time the ovum, which is still in the secondary oocyte stage, is ovulated into the abdominal cavity. Then, almost immediately it enters the fimbriated end of one of the fallopian tubes → fertilization.

Layers of The Ovum

- What are the layers that the sperms needs to reach the ovum? (from outer to inner)

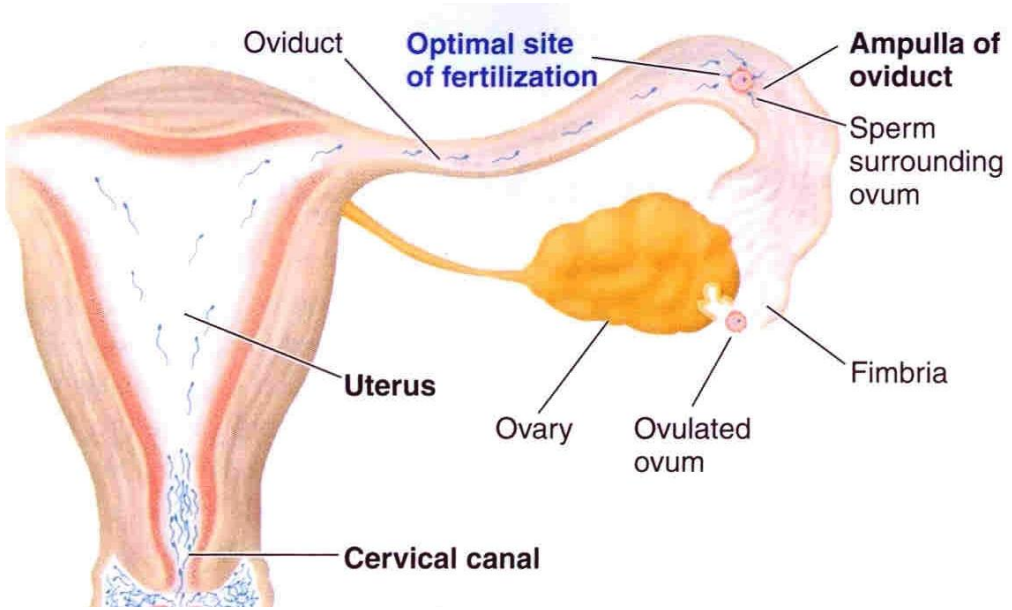
1. Corona radiata. (Before ovulation it is called granulosa cells After ovulation it names becomes (corona radiate) We have ZP3 receptor on zona pellucida and corona radiata only).
2. Zona pilluceda.
3. Cell membrane.
4. Cortical granules.



Fertilization

- If the ovum becomes fertilized, a new sequence of events called gestation or pregnancy takes place, and the fertilized ovum eventually develops into a full-term fetus.
- during intercourse, half billion sperms are made but only thousands will enter the female reproductive tract (that's why we need a lot of sperms)

Location	Time of appearance (min after ejaculation)	Percent of ejaculated sperm*
Fertilization site (upper third of oviduct)	30–60	0.001
Uterus	10–20	0.1
Cervical canal	1–3	3



Important

Process Fertilization

Q: what leads to the block of polyspermy? Inhibition of ZP3 receptor by stimulation of Ca release stored in cortical granules.

Step 1: After the male ejaculate the semen into the vagina during intercourse, the sperm reach the ampulla of fallopian tube within 30 - 60 minutes (PG & OT actions)

Step 2: The fertilizing sperm penetrates the corona radiata via membrane-bound enzymes in the plasma membrane of its head and binds to ZP3 receptors on the zona pellucida.

Step 3: binding of sperm to these receptors triggers the acrosome reaction, in which hydrolytic enzymes in the acrosome are released onto the zona pellucida.

Step 4: The acrosomal enzymes digest the zona pellucida, creating a pathway to the plasma membrane of the ovum.

When the sperm reaches the ovum, the plasma membrane of the two cells fuse.

Step 5: The sperm nucleus enters the ovum cytoplasm.

Step 6: The sperm stimulates release of Ca^{+2} stored in cortical granules in the ovum, which in turn, inactivate ZP3 receptors, leading to the block to polyspermy.

شرح الكلام بالسلايد الجاي ☺

Cont.

شرح الكلام: (افهموا الlayers لتسهيل تذكّر الخطوات)

المرحلة الأولى: الحيوان المنوي بعد ما يخرج من الذكر يدخل لقناة فالوب، وبالتحديد في الampulla في غضون ٣— ٦٠ دقيقة.

المرحلة الثانية: الحيوان المنوي يتغلغل داخل الـ zona pellucida (الطبقة الخارجية) بواسطة انزيمات داخل رأسه (تكلمنا عن إنزيمات الAcrosome في المحاضرة الرابعة) ثم يرتبط بـ ZP3 receptor الي يكون على الzona pellucida.

المرحلة الثالثة: بعد الارتباط تفرز الhydrolytic enzymes من رأس الحيوان المنوي (الAcrosome).

المرحلة الرابعة: الانزيمات تهضم الzona pellucida وتمهد الطريق عشان الحيوان المنوي يوصل للبويضة، اول مايوصل يلتحم الcell membrane للبويضة مع الـ cell membrane للحيوان المنوي ويصيرون مع بعض.

المرحلة الخامسة: نواة الحيوان المنوي تدخل لسايتوبلازم البويضة.

المرحلة السادسة: الحيوان المنوي يحفز اخراج الكالسيوم المخزن في الcortical granules حقت البويضة وبالتالي يثبط الZP3 receptor ويمنع دخول حيوان منوي آخر وبكذا نمنع الpolyspermy ويكون عندنا حيوان منوي واحد فقط.

Results of Fertilization

1. Oocyte divides to form mature ovum (female pronucleus 23 unpaired chromosomes) + 2nd polar body.
2. Head of sperm swells (male pronucleus 23 unpaired chromosomes).
3. Fertilized ovum (zygote) contain 23 paired chromosomes.

- The 23 chromosomes of the male and female pronuclei align themselves to re-form a complete complement of 46 chromosomes.
- Male sperm either x or y arrive to fertilize the ovum; thus it's the one determining the embryo's sex.
- .Theory: if a couple wants to have a boy they must do the intercourse in the day of the ovulation cause the y sperm is more faster and if they want a girl do the intercourse 2 days before the ovulation so the y sperm will die by then (sperm could stay in the female maximum 3 days) and the x sperm could penetrate the ovum.

شرح الكلام:
قبل التلقيح: البويضة والحيوان المنوي يكون كل واحد منهم يحتوي على 23 unpaired chromosomes (ركزوا أنهم unpaired)
(و 2nd polar body بالنسبة للبويضة).
بعد التلقيح: يتكون عندي الzygote وهو عبارة عن ٢٣ زوج من الكروموسومات = ٤٦ كروموسوم.

Important

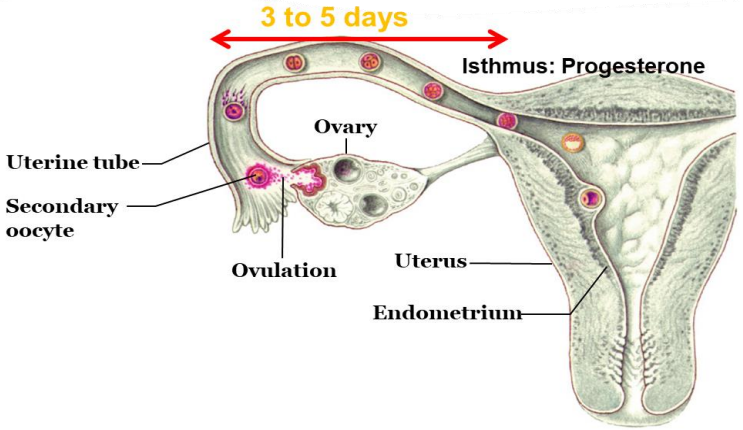
Transport of the Fertilized Ovum (Zygote)

- Definition: Zygote begins to divide as it travels through oviduct (fallopian tube).
- Duration: After fertilization 3-5 days till zygote reach uterine cavity, delayed transport allows cell division to occur before the dividing ovum
- Secretory cells in fallopian tube nourish the blastocyst.
- Transport is effected mainly by:
  1. Fluid current.
  2. Action of cilia.
  3. Weak contractions of the fallopian tube (estrogen & progesterone).
- Isthmus (last 2 cm of the oviduct) relaxes under effect of progesterone.
- Blastocyst (100 cells) enters the uterus.

شرح الكلام:
بعد التلقيح الzygote لازم ينتقل من قناة فالوب الى الرحم وتقريبا يأخذ من ٣-٥ أيام وفي هذه الاثناء الخلايا تنقسم.
العوامل المساعدة لنقل الzygote هي: قوة اندفاع وتيار السوائل (زي النهر الغزير يجرّ كل شيء معاه) ، والcilia الي تكون في قناة فالوب وانقباضاته الي تكون بسبب الاستروجين والبروجسترون.
طيب إيش هي العوائق؟

1. Isthmus of tube (narrow).
2. The Wall is not smooth (projections, rugae).

ليش ربي خلق هذي العوائق قدام الزيقوت قبل ما توصل الرحم؟ مافي شيء مخلوق عبث، فائدتها تعطي وقت للزيقوت عشان تنقسم قبل ما توصل هناك، ولو وصلت وهي ما انفسمت كفاية يحصل abortion.
طيب كيف نتغلب على هذي العوائق؟ بمعنى أنها تقدر توصل بس مو بسرعة عشان يمديها تنقسم.
الrugae ماراح نقدر نسوي لها شيء، أما نهاية قناة فالوب اللي هي الisthmus وهي بالحالة الطبيعية تعتبر اضيق مكان فالقناة، راح يحصل له ريلاكيشن وبالتالي يتوسّع عشان تمر البويضة الملقحة، وهذا يتم تحت تأثير البروجسترون.



If any of the transport mechanisms (very high progesterone, no fluid, no cilia and absent contractions) is absent, it will increase the risk of ectopic pregnancy.

Entry of The Ovum Into The Uterus

At day 19-20 of ovulatory cycle, transportation is done and the zygote entered the uterus.

- When ovulation occurs, the ovum, along with a hundred or more attached granulosa cells that constitute the corona radiata, is expelled directly into the peritoneal cavity and must then enter one of the fallopian tubes (also called uterine tubes) to reach the cavity of the uterus.

- The fimbriated ends of each fallopian tube fall naturally around the ovaries. The inner surfaces of the fimbriated tentacles are lined with ciliated epithelium, and the cilia are activated by estrogen from the ovaries, which causes the cilia to beat toward the opening or ostium of the involved fallopian tube. One can actually see a slow fluid current flowing toward the ostium. By this means, the ovum enters one of the fallopian tubes.

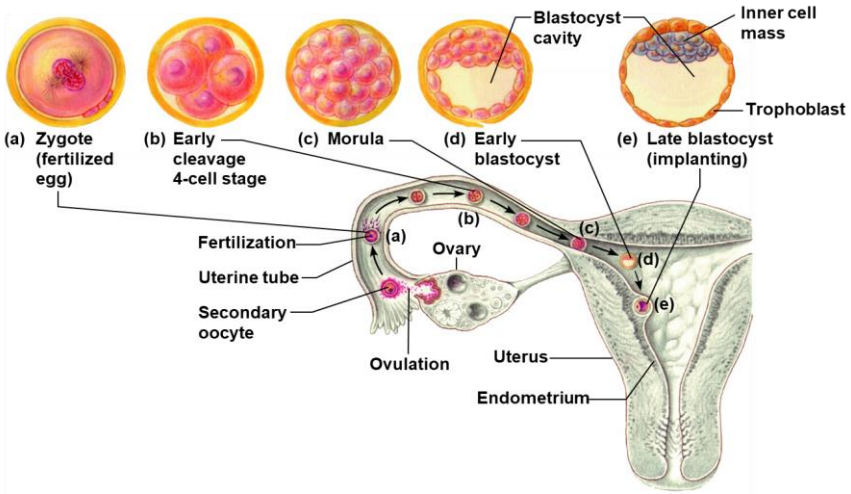
- Although one might suspect that many ova fail to enter the fallopian tubes, conception studies suggest that up to 98 percent of ova succeed in this task. Indeed, in some recorded cases, women with one ovary removed and the opposite fallopian tube removed have had several children with relative ease of conception, thus demonstrating that ova can even enter the opposite fallopian tube.

Doctor said: we wont ask about the name of the cells. Remember it just in case..

Cleavage

- Following fertilization (1st thing happening after 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[1].
- Divisions continue rapidly until the 32 cell stage AKA Morula.
- Blastocyst (100 cells) enters the uterus.

(the zygote will not enter the uterus unless it become Blastocyst which mean 100 cells)



شرح الكلام:
بعد التلقيح تبدا عملية الانقسام المايتوزي داخل الzona pellucida لكن الحجم ما يزيد في هذا الإنقسام.
اول انقسام يعطينا خليتين اسمهم blstomere وهذا النوع ممكن يعطينا أي نوع من الخلايا مستقبلا.
الانقسامات راح تكمل الين متى؟ الى ما يصير عندنا ٣٢ خلية.
الـ zygote مايدخل الرحم الا لو وصل الـ ١٠٠ خلية ويصير اسمه blastocyst (مهمه)

1:Totipotent embryo cells can differentiate into any cell type.

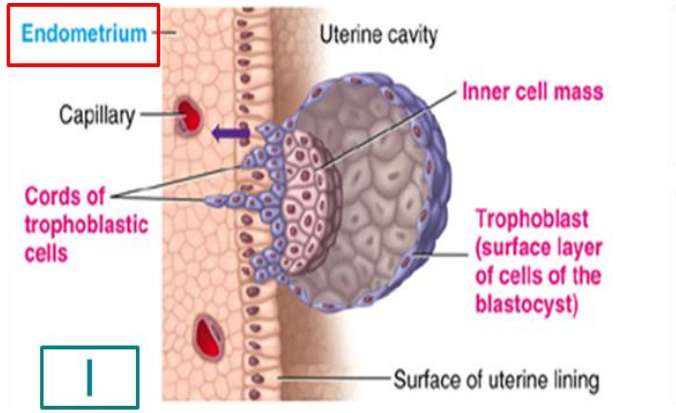
Important

Implantation

The blastocyst will plant itself by sending projections from chorionic cells into the endometrium (eating Decidua cells which are filled with glycogen & nutrient).

When the implantation occur?

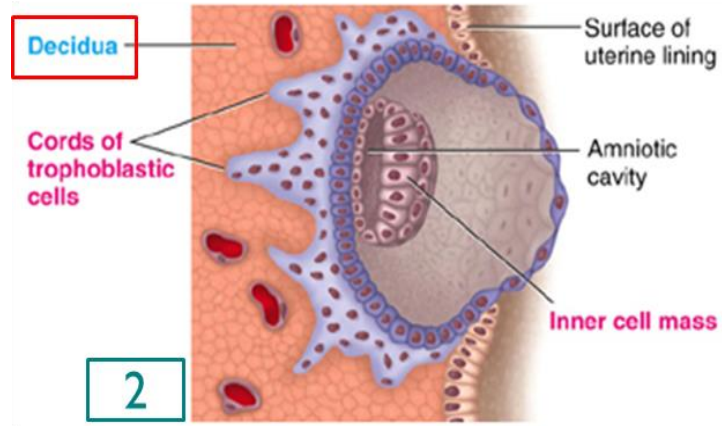
Implantation occurs on 5-7 day after ovulation (day 21).



Steps of implantation:

Implantation results from the action of trophoblastic cords from the surface of blastocyst.

1. Digestion of endometrium.
2. Decidua cells[1] : (glycogen, proteins, lipids & minerals)



Both estrogen and progesterone are important at this stage:

1. Estrogen for proliferation of the endometrium.
2. Progesterone for the secretory phase (uterine milk) With increasing of the size of the endometrium due to estrogen and progesterone (secretions) it is called (Decidua; endometrium during pregnancy only).

شرح الكلام:

الطبقة الخارجية من الblastocyst اللي دخلت الرحم اسمها trophoblast وهذي هي الي تساهم في عملية الimplantation.

كيف تساهم ؟ بأنها تبدأ في غرس نفسها وفي نفس الوقت هضم طبقة الendomerium و الdecidua cells الي هي المشيمة التابعة للأم.

1: The **decidua** is the uterine lining (endometrium) during a pregnancy, which forms the maternal part of the placenta.

Embryological Development of Placenta

1. Blastocyst → Trophoblastic cords attaching to the uterus (Maternal blood sinuses develop around the trophoblastic cords) → blood capillaries grow into the cords from the vascular system of the newly forming embryo.

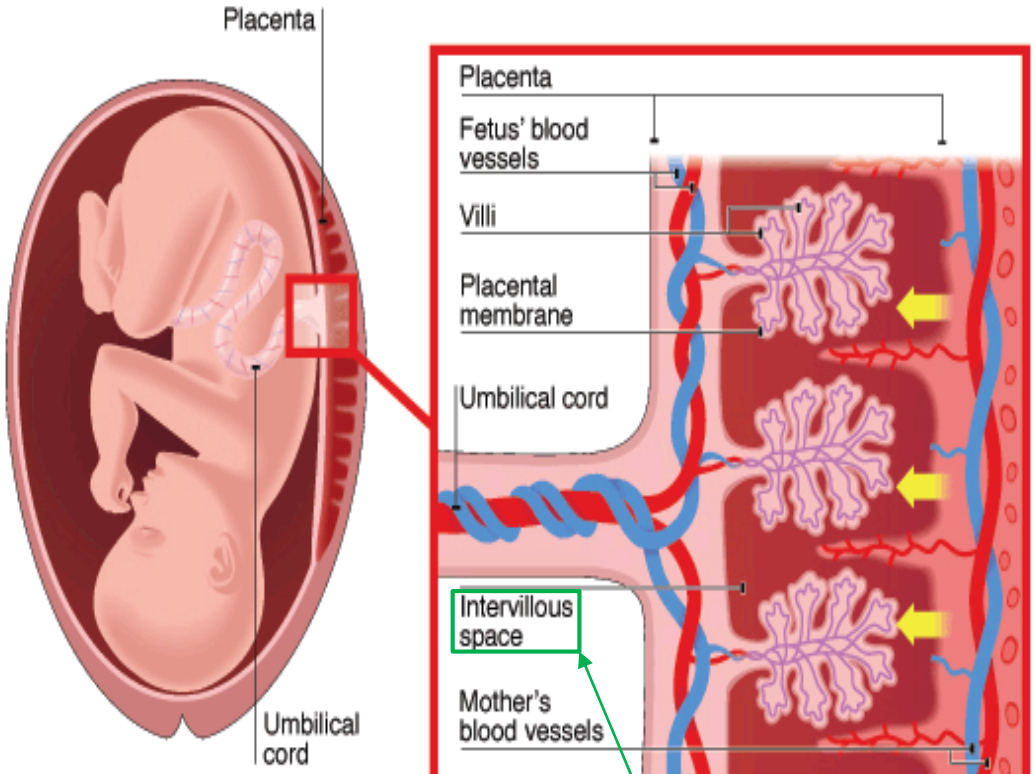
2. 21 days after fertilization, blood starts to be pumped by fetal heart into the capillaries.

3. When implantation occur Blood sinuses appear supplied with blood from the mother develop around the outsides of the trophoblastic cords.

4. More and more trophoblast projections develop (placental villi).

شرح الكلام:
بعد الimplantation، الاوعية الدموية تبدأ تتكون حولين الtrophoblastic cord وكمان الاوعية الدموية للجنين تنمو من الجهة الأخرى.
بعد ٢١ يوم يبدأ قلب الجنين بضخ الدم داخل الأوعية.
نتوءات الtrophoblasts (الي تمثل الplacental villi) تزيد وبالتالي تزيد الsurface area مما يساعد على تبادل الـ nutrients من الأم الى الجنين.

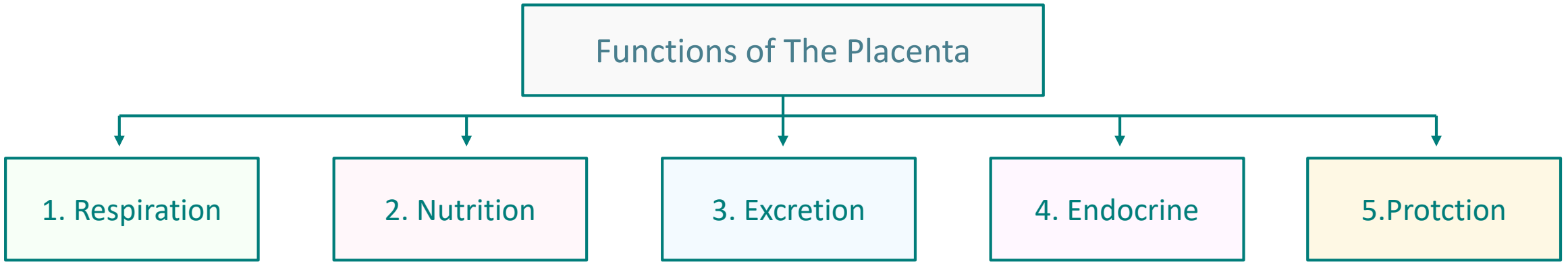
Physiologic Anatomy of The Placenta



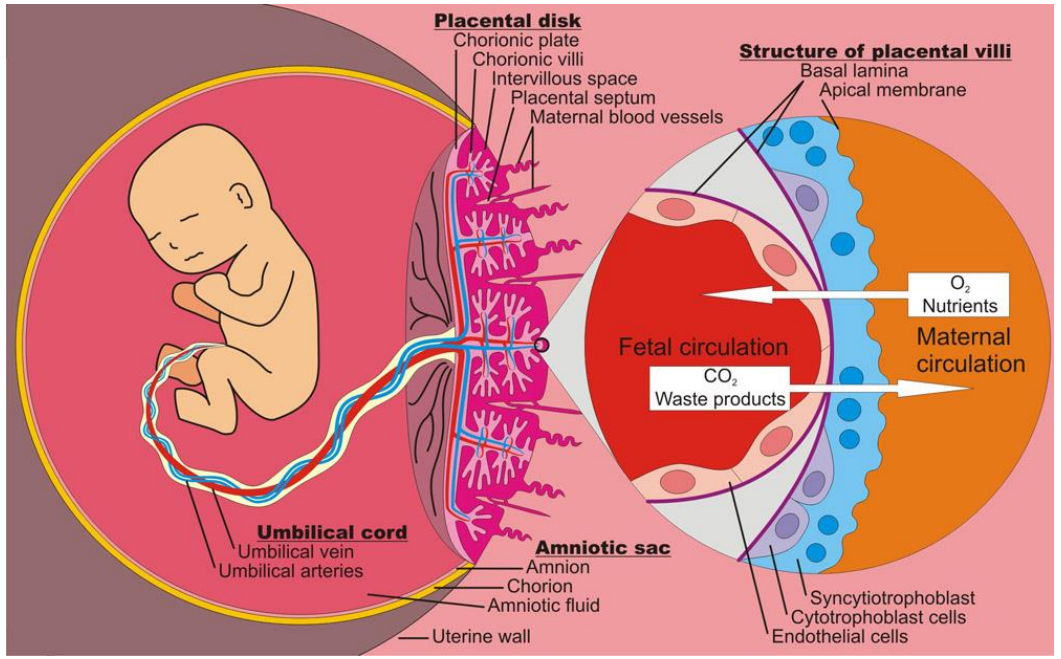
The area with concentrated blood that's why it is important to prevent this area for rupturing during labor

- The final structure of the placenta is shown in picture.
- Note that the fetus's blood flows through two umbilical arteries, then into the capillaries of the villi, and finally back through a single umbilical vein into the fetus. (the umbilical cord consists of two arteries and one vein).
- 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 the uterine veins of the mother.
- the picture also shows the relationship between the fetal blood of each fetal placental villus and the blood of the mother surrounding the outsides of the villus in the fully developed placenta.
- The total surface area of all the villi of the mature placenta is only a few square meters - many times less than the area of the pulmonary membrane in the lungs.
- Nevertheless, nutrients and other substances pass through this placental membrane mainly by diffusion in much the same manner that diffusion occurs through the alveolar membranes of the lungs and the capillary membranes elsewhere in the body.

Functions of The Placenta



- The first three functions are the major functions of the placenta.
- We will discuss each one of these functions in next slides.



Respiration

يقصد بها انتقال الأوكسجين من الأم للجنين

Placental permeability and membrane diffusion conductance	
In the early months of pregnancy	In later pregnancy
✓ In the early months of pregnancy, the placental membrane is still thick because it is not fully developed. ✓ The surface area is small because the placenta has not grown. ✓ So, how does the fetus get the nutrient ? Through the uterine milk (remember: in secretory phase progesterone secrete substances in the endometrium which is called UTERINE MILK)	In later pregnancy, The permeability increases because of thinning of the membrane diffusion layers and because the surface area expands many times over.

شرح الكلام:
في شهور الحمل الأولى placenta تكون لسا ما اكتملت النمو تماما، بالتالي الplacental membrane يكون سميك والsurface area تكون صغيرة (تخيلوا أن شيء يكون طبقة سميكة بالتالي صعب اختراقها بينما لو كانت رقيقة بسهولة نخترقها) وهذا راح يعيق تبادل الأوكسجين بشكل كبير بين الأم والجنين.
بعد شهور الحمل الأولى، الـ membrane يصير thin والsurface area توسع وتتمدد بالتالي عملية التبادل تكون أسهل وبكميات أكبر.

Important

Cont.

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.
- Dissolved O_2 in mother's blood passes to fetal blood by simple diffusion.
- PCO_2 2-3 mm Hg higher in fetal than maternal blood.
- Mean pressure gradient= 50 mm hg –30 mm hg =20 mm hg.
- There are 3 reasons why this low PO_2 is sufficient to deliver O_2 to the fetal tissues:

1. Hemoglobin of the fetus.
2. Fetal hemoglobin concentration.
3. The Bohr effect.

For each point we know that Hb F has more affinity to bind to oxygen than Hb A which is normal human Hb.

شرح الكلام للسلايد هذي والجاية:
الco$_2$ للجنين يكون عالي لأن ما عنده رئة تتخلص هذا الغاز، فما عند الجنين طريقة للتخلص من هذا الغاز إلا الأم.
كيف راح يتم التخلص منه عن طريق الأم؟
ارتفاع الCo$_2$ راح يسوي concentration gradient فينتقل الغاز من العالي اللي هو الجنين إلى المنخفض اللي هي الأم ويتم التخلص منه (simple diffusion).

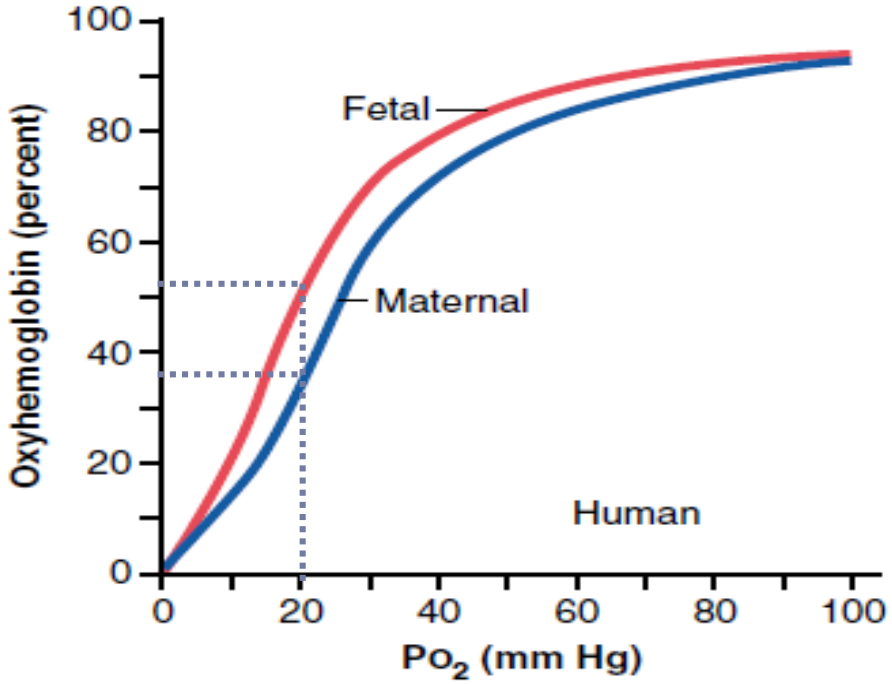
طيب الأوكسجين كيف؟
نفس الشيء فيه اختلاف في الPo$_2$ بين الأم والجنين، فيحصل diffusion من الأم للجنين بعكس الCo$_2$ كان يروح من الجنين للأم.
يعني باختصار: الأم تعطي للجنين كل ماهو مفيد وتاخذ منه الضار.

Note that 20 mm Hg seems to be low and not enough for exchange sufficient oxygen to the fetal blood. BUT due to these 3 special reasons it is sufficient more than enough to deliver O_2 and nutrients to the fetus.

Doctor said : There must be a question in the final exam each year about this topic

Cont.

- 1,2: Hemoglobin of the fetus & Fetal hemoglobin concentration



Oxygen-hemoglobin dissociation curves

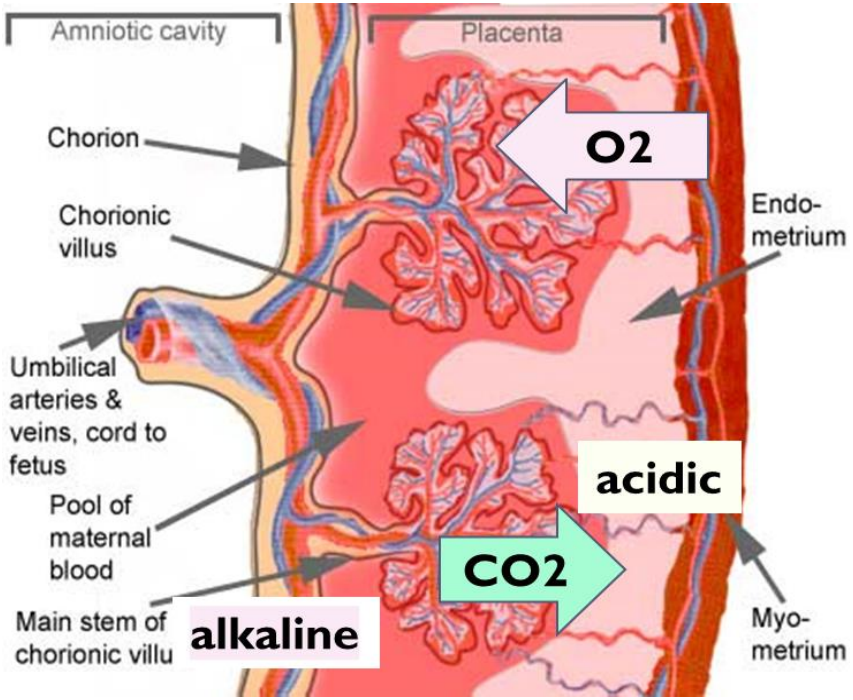
- What is the type of Hb of the fetus? Hemoglobin F (HbF).
- The fetal hemoglobin concentration is about 50% greater than that of the mother. So, At the low PO2 levels in fetal blood (While the PCO2 in the fetus will be high), the fetal hemoglobin (HbF) can carry 20% to 50% more oxygen than maternal hemoglobin (HbA) (HbF has a higher oxygen carrying capacity than HbA).
- Follow with the curves: In Maternal curve: when pressure of o_2 is 20 the Oxyhemoglobin become almost 38 and in the same time the oxyhemoglobin of the fetus if 46.
- Imp: Conclusion ; whenever the curve is shifted to the right more o_2 will be carried (fetal). While whenever the curve is shifted to the left less o_2 will be carried (mother).

Important

Cont.

- 3: Bohr effect

Recall The Bohr Effect refers to the observation that increases in the carbon dioxide partial pressure of blood or decreases in blood pH result in a lower affinity of hemoglobin for oxygen.



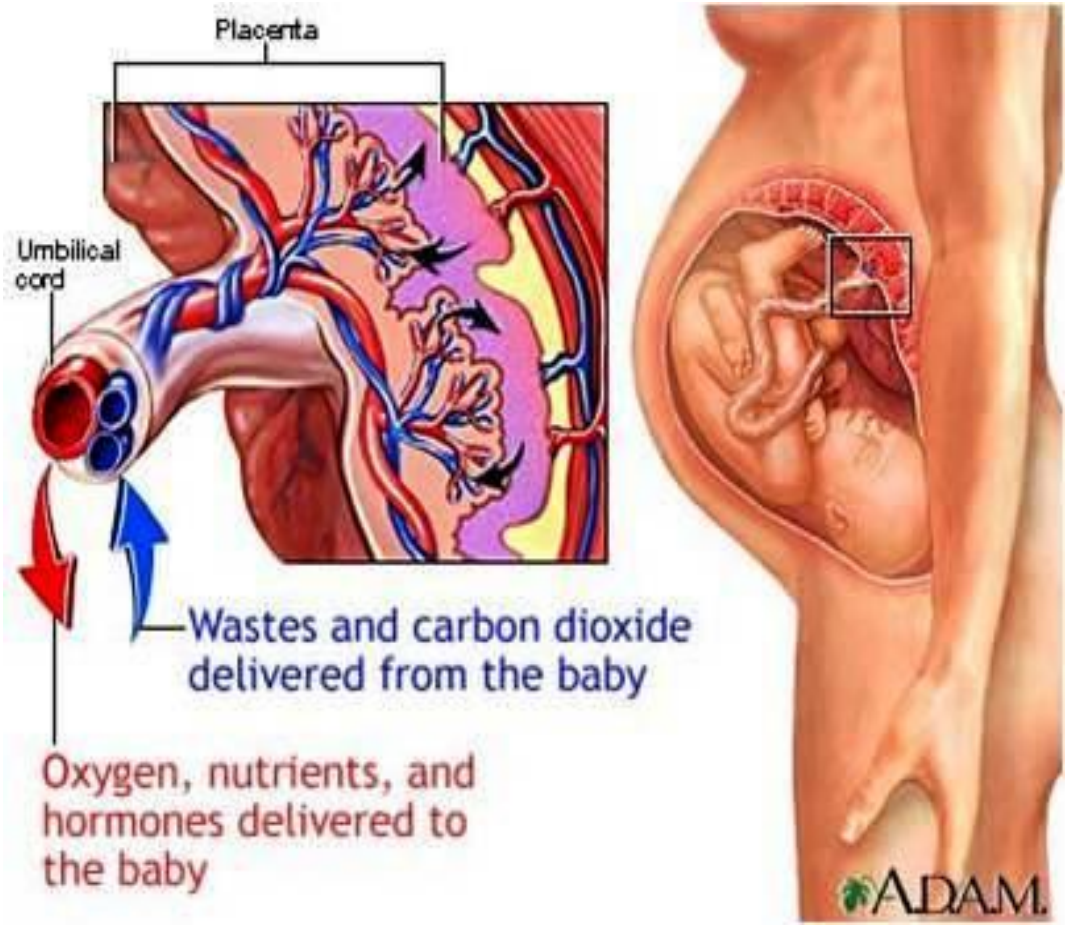
	Fetal blood	Maternal (mother) blood
PCO_2	Lost CO_2	Gains CO_2
PH	High pH (alkaline)	Low pH (acidic)
Shifts of the dissociation curves	Shifts to the left allowing additional oxygen uptake.	Shifts to the right releasing additional oxygen.
These changes cause the capacity of fetal blood to combine with O_2 to increase, and maternal blood to decrease, which forces more O_2 from the maternal blood while enhancing oxygen uptake by the fetal blood.		

- ✓ Normally before Exchange the fetal blood has high PCo_2 as a waste product due to his body activity, this will lead to make the PH in the fetal circulation to be more Acidic.
- ✓ Shown in the diagram: As a result of the above the CO_2 will diffuse from fetal circulation to the mother passively, this diffusion of Co_2 from the fetal to the mother will change the PH in both sides , when the Co_2 leave the fetal circulation it turns to be Alkaline because it lost (CO_2) which is an acid.

Cont.

- Important factors facilitate delivery of oxygen to the fetal tissues:

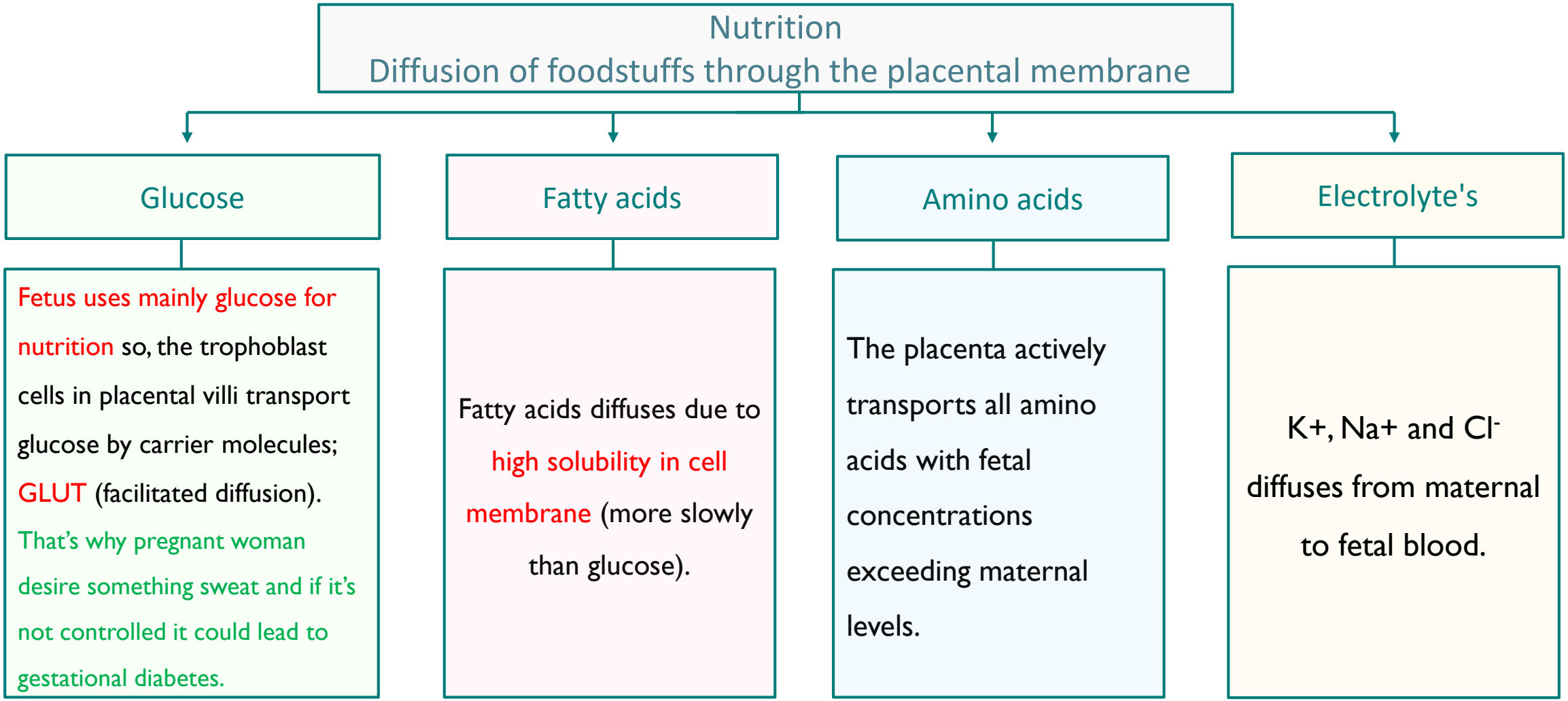
1. High maternal intervillous blood flow (almost double the fetal placental flow).
2. High fetal haemoglobin (16 - 17 g/dl).
3. High fetal cardiac output.
4. The fetal metabolic acidosis which shifts the curve to the right and thus aids delivery of oxygen to the tissues.



Important

Nutrition

يقصد بها انتقال الغذاء من الأم للجنين



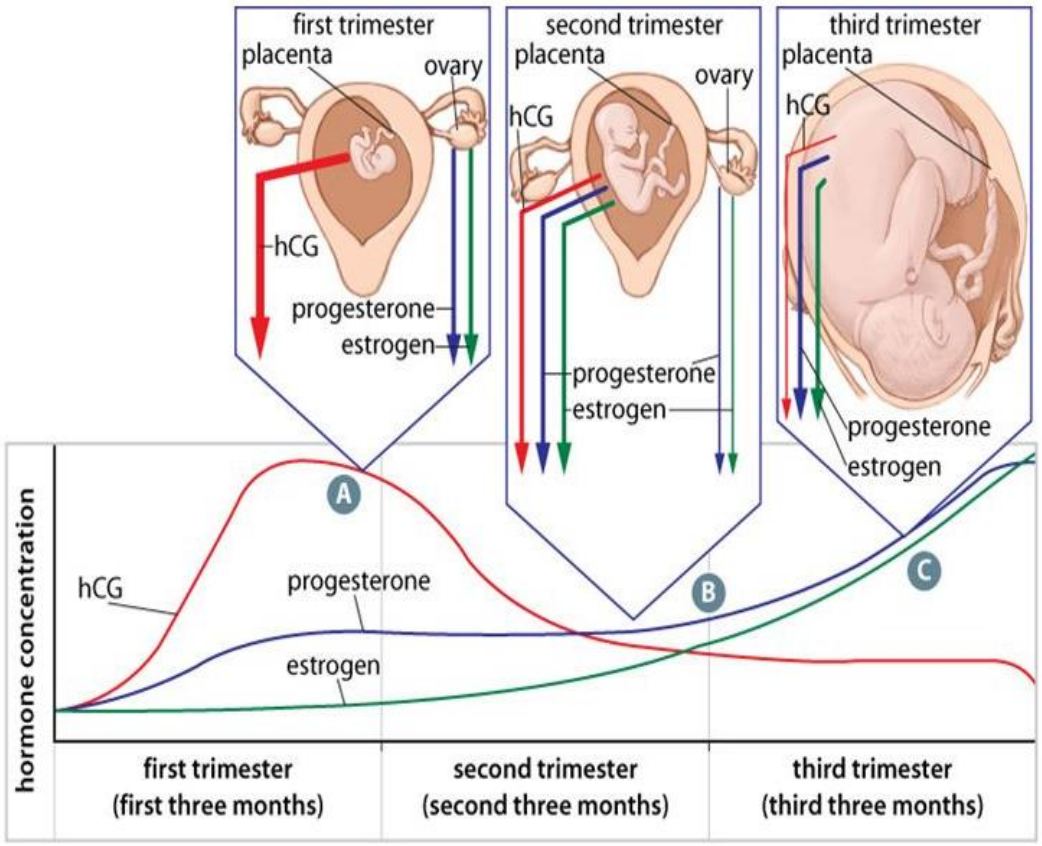
Excretion

يقصد بها الإخراج من الجنين للأم

- Excretory products of the fetus diffuse through placental membrane to maternal blood to be excreted with waste products of the mother (Urea, uric acid and creatinine).

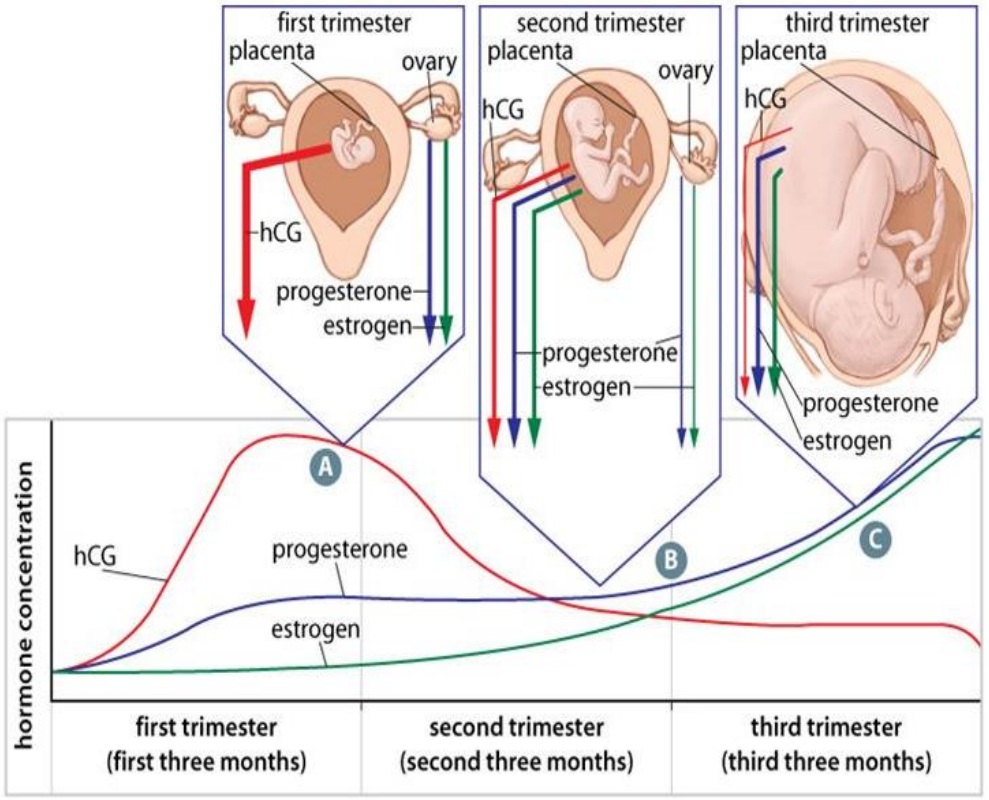
- Higher concentration of excretory products in fetal blood insures continuous diffusion of these substances to the maternal blood.

Endocrine



In the trimester (first 3 months)	A. The placenta is not yet formed. B. High level of hCG secreted by the trophoblast of the embryo. C. Progesterone & estrogen are secreted from corpus luteum.
Second trimester (second 3 months)	A. The placenta is formed & the corpus luteum start to degenerate. B. The placenta will secrete most of hGC, progesterone & estrogen with slight increase of estrogen and progesterone. C. Estrogen and progesterone are also secreted from the corpus leutum
Third trimester (Third 3 months)	A. The corpus luteum is completely degenerated. B. High estrogen and progesterone with low hCG, estrogen & Progesterone are only secreted by placenta.

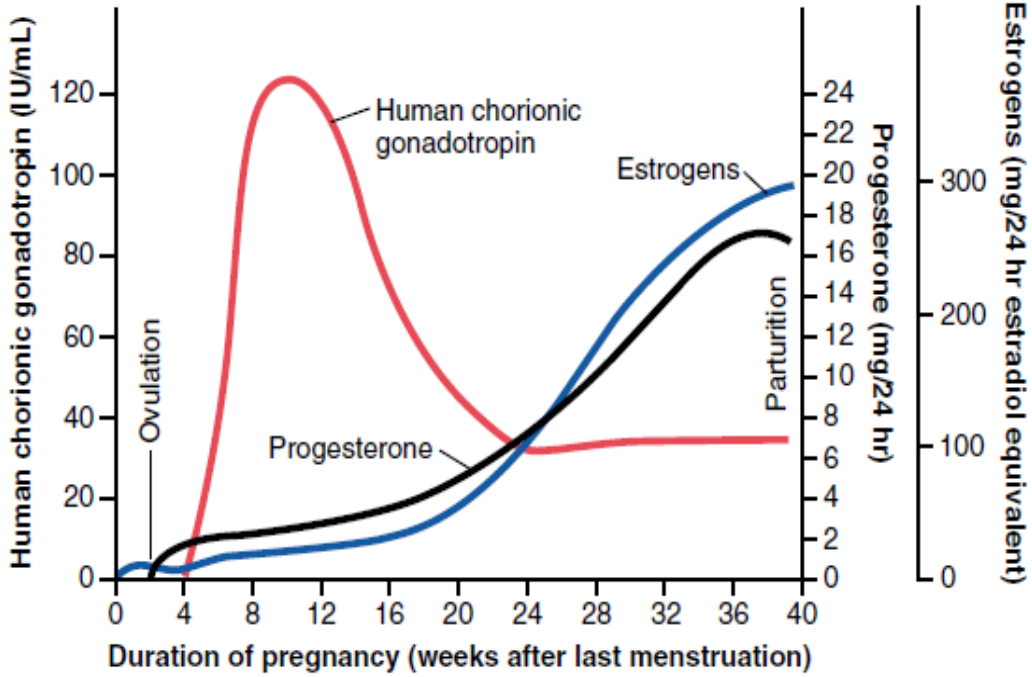
Cont. In Other Word (same of the previous slide)



A. Human chorionic gonadotropin (hCG)	Will increases until it reaches a maximum concentration near the end of the first trimester. Then it decrease to low level for the reminder of the pregnancy.
B. Progesterone	✓ Progesterone continue to increase until it level off near the end of the pregnancy. ✓ Early in the pregnancy, progesterone is produced by the corpus luteum in thee ovary. ✓ By the second trimester, its production shifts to the placenta.
C. Estrogen	✓ Estrogen levels increase slowly throughout the pregnancy, but they increase more quickly as the end of the pregnancy approaches. ✓ Early in the pregnancy estrogen is produced only in the ovary. ✓ by the second trimester, its production shifts to the placenta.

Cont.

- hCG level (pregnancy test)



- Increase the most in the 1st trimester then it will decrease, but still it is high comparing with normal women.
- Blood hCG under 5 mIU/ml: Negative (Not pregnant)
- Blood hCG between 5-25 mIU/ml: "Equivocal", Maybe pregnant maybe not → Repeat test in a couple of days.
- Blood hCG over 25 mIU/ml: You are pregnant!
- One single hCG reading is not enough to make a clear diagnosis. Several hCG tests days apart give a more accurate assessment of the situation.
- The blood hCG levels should not be used to date a pregnancy since these numbers can vary so widely

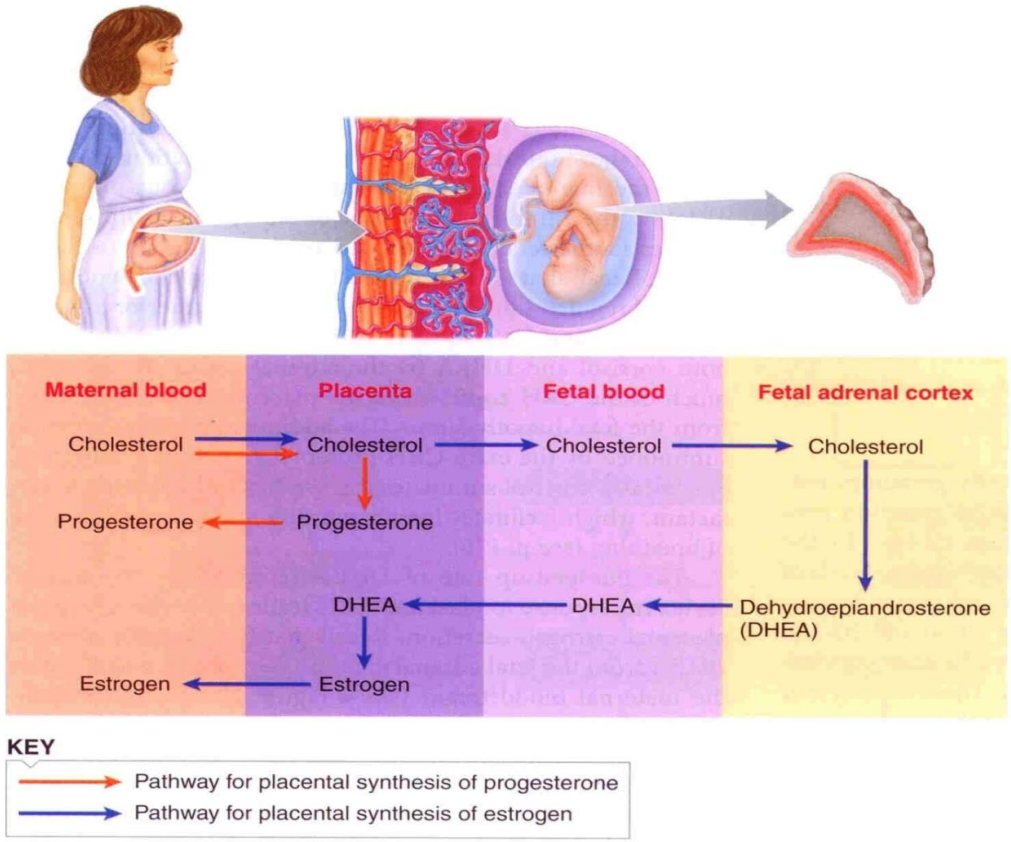
Cont.

Hormone	1. Human Chorionic Gonadotropin (hCG) (only in females' slides)	2. Estrogen
Nature of the hormone	Glycoprotein	Steroid hormone
Secreted by	Syncytial trophoblast cells, then after the formation of the placenta, hCG will be secreted from the placenta.	Syncytial trophoblast cells towards end of pregnancy reaches 30×
Derived from	-	Weak androgen (DHEA) released from maternal & fetal adrenals.
Functions in the mother	1. Most important function is to maintain corpus luteum (↑estrogen & progesterone) till 13-17 weeks of gestation. 2. Another function is that it act as LH hormone which in response, exerts interstitial (Leyding) cell-stimulating effect on testes of the male fetus (growth of male sex organs).	1. Enlargement of uterus, breast ducts & external genitalia. 2. Relaxation of pelvic ligaments in preparation to labor. 3. Activation of the uterus (gap junctions).

Cont.

Hormone	3. Progsterone	4. Human Chorionic Somatomamotropin or Human placental lactogen (hPL)	5. Relaxin
Nature of the hormone	Steroid hormone	Protein hormone	Polypeptide
Secreted by	Syncytial trophoblast cells towards end of pregnancy reaches 10×	Placenta around 5th gestational week	1. Corpus luteum 2. Placenta
Derived from	Cholesterol	-	-
Functions in the mother	1. Development of the breast lobules. 2. Provides nutrition to developing embryo (uterine secretory phase. 3. Development of decidual cells. 4. Inhibit the contractility of the uterus.	1. Breast development (hPL). 2. Weak growth hormone's action. 3. Inhibit insulin sensitivity =↓ glucose utilization. 4. Promote release of fatty acids.	1. Relaxation of symphysis pubic ligament (weak). 2. Softens the cervix at delivery.

Sources of Placental Estrogen & Progesterone



● **FIGURE 20-31 Secretion of estrogen and progesterone by the placenta.** The placenta secretes increasing quantities of progesterone and estrogen into the maternal blood after the first trimester. The placenta itself can convert cholesterol into progesterone *(orange pathway)* but lacks some of the enzymes necessary to convert cholesterol into estrogen. However, the placenta can convert DHEA derived from cholesterol in the fetal adrenal cortex into estrogen when DHEA reaches the placenta by means of the fetal blood *(blue pathway)*.

- Estrogen Production:

1. Cholesterol from maternal blood will diffuse through placenta to fetal blood then it will reach fetal adrenal cortex.
2. Fetal adrenal cortex will use the cholesterol to synthesis DHEA (Androgen).
3. DHEA will diffuse to the placenta and it will be converted to Estrogen.
4. Also maternal adrenal cortex will release DHEA which will be converted to Estrogen in placenta.
5. Finally, Estrogen will go back to maternal blood.

- Progesterone Production:

1. Cholesterol from maternal blood will diffuse to placenta.
2. Placenta will use cholesterol to synthesis Progesterone.
3. Finally, Progesterone will diffuse back to maternal blood.

Physiological Adaptation To Pregnancy

Changes in maternal endocrine system (Almost everything n the body increases during pregnancy)	
Anterior pituitary gland enlargement (50%)	1. Release of ACTH, TSH and PL increase. 2. FSH and LH almost totally suppressed due to increase of progesterone & estrogen.
Adrenal gland	1. Increase glucocorticoids secretion (mobilize aa). 2. Increase aldosterone (retain fluid).
Thyroid gland enlargement 50%	Increase thyroxine production (hCG) (Retain Na & water to increase maternal blood concentration even more blood cells will be produced from bone marrow. To prepare her for losing blood in labor)
Parathyroid gland enlargement	Increase PTH secretion (maintain normal Ca^{+2})

Cont.

Changes in Different Organs:

1. Increase in uterine size (50 gm to 1100 gm).
2. The breasts double in size.
3. The vagina enlarges to facilitate labor.
4. Development of edema and acne due to increase in androgen and water absorption.
5. Masculine or acromegalic features
6. Weight gain 10-12 kg (last 2 trimesters)
7. Increase appetite:
   - Removal of food by fetus.
   - Hormonal effect.

Changes in respiration:

1. Increase in O2 consumption 20%
   - Increase basal metabolic rate (BMR
   - Increase in body size
2. Growing uterus presses upwards (restriction)
3. Increase in RR (respiratory rate).
4. Increase in minute ventilation (TV* × RR) by 50%:
   - Progesterone ↑ sensitivity of RC to CO_2

*TV= Tidal volume

Cont.

Changes in circulatory system:

1. Increase in Cardiac output (30 - 40%) by 27 weeks.
2. Increase in blood flow through the placenta.
3. Increase in maternal blood volume 30% due to:
   - Increase aldosterone and estrogen (↑ ECF)
   - Increase activity of the bone marrow (↑ RBCs 40%)

Changes in metabolism:

دائماً الحامل تحس أنها حرّانة.

1. Increase basal metabolic rate (BMR) 15%
2. Increase in daily requirements for:
   - Iron
   - Phosphates
   - Calcium & Vitamin D (Ca^{+2} absorption)
   - Vitamins
3. The renal tubules' reabsorptive capacity for Na, Cl, and water is increased as much as 50%.
4. The renal blood flow and GFR* increase up to 50%.
5. Normal pregnant woman accumulates only about 5 pounds (2.27Kg) of extra water and salt.

* GFR= Glomerular filtration rate.

Summary

1- Fertilization

Step 1: After ejaculation during intercourse, the sperm reaches the ampulla of fallopian tube within 30 - 60 minutes.

Step 2: The fertilizing sperm penetrates the corona radiata via membrane-bound enzymes in the plasma membrane of its head.

Step 3: binding of sperm to **ZP3 receptors** on the zona pellucida triggers the release of acrosomal hydrolytic enzymes onto the zona pellucida **(acrosome reaction).**

Step 4: The acrosomal reaction creates a pathway to the plasma membrane of the ovum so that the plasma membrane of both ovum and sperm fuse.

Step 5: The sperm's nucleus enters the ovum's cytoplasm.

Step 6: The sperm stimulates release of **Ca^{+2}** stored in cortical granules in the ovum, which **inactivates ZP3** receptors, leading to the **block to polyspermy.**

Results of fertilization:-

1. Oocyte divides to form mature ovum (female pronucleus 23 unpaired chromosomes) + 2nd polar body.
2. Head of sperm swells (male pronucleus 23 unpaired chromosomes).
3. Fertilized ovum (zygote) contain 23 paired chromosomes.

2- Zygote cleavage

-Following fertilization (1st thing after fertilization) the zygote undergoes several mitotic divisions inside the zona pellucida (overall size does not change).

-Zygote begins to divide as it travels through oviduct.

-1st cleavage yields a 2 celled embryo, each cell is called a blastomere and is totipotent, Divisions continue rapidly until the 32 cell stage AKA Morula.

-Isthmus (last 2 cm of the oviduct) relaxes under effect of progesterone.

-After fertilization, 3-5 days till zygote reach uterine cavity as a Blastocyst (100 cells), delayed transport allows cell division to occur before the dividing ovum.

Transport is effected mainly by:

1. Fluid current.
2. Action of cilia.
3. Weak contractions of the fallopian tube (estrogen & progesterone).

-Implantation occurs on 5-7 day after ovulation.

-Implantation results from the action of trophoblastic cords from the surface of blastocyst.

-Steps of implantation:

1. Digestion of endometrium.
2. Decidua cells: (glycogen, proteins, lipids & minerals)

3- Placenta

1. Blastocyst → Trophoblastic cords attaching to the uterus (Maternal blood sinuses develop around the trophoblastic cords) → blood capillaries grow into the cords from the vascular system of the newly forming embryo.
2. 21 days after fertilization, blood starts to be pumped by fetal heart into the capillaries.
3. When implantation occur Blood sinuses appear, supplied with blood from the mother and develops around the outsides of the trophoblastic cords.

Functions of placenta:

1. Respiration | 2. Nutrition | 3.Excretion | 4. Endocrine | 5.Protection

1. Respiration

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..
(Mean pressure gradient= 50 mm hg –30 mm hg =20 mm hg)

There are 3 reasons why this low PO2 is sufficient to deliver O2 to the fetal tissues:

1. Hemoglobin of the fetus.
2. Fetal hemoglobin concentration.
3. The Bohr effect.

1,2: Hemoglobin of the fetus & Fetal hemoglobin conc.

-What is the type of Hb of the fetus? Hemoglobin F (HbF).

-The fetal hemoglobin concentration is about 50% greater than that of the mother. So, At the low PO2 levels in fetal blood (While the PCO2 in the fetus will be high), the fetal hemoglobin can carry 20% to 50% more oxygen than maternal hemoglobin.

-Conclusion ; whenever the curve is shifted to the right more o_2 will be carried (fetal). While whenever the curve is shifted to the left less o_2 will be carried (mother).

3: Bohr effect

	Fetal blood	Maternal (mother) blood
PCO_2	Lost CO_2	Gains CO_2
PH	High pH (alkaline)	Low pH (acidic)
Shifts of the dissociation curves	Shifts to the left allowing additional oxygen uptake.	Shifts to the right releasing additional oxygen.
These changes cause the capacity of fetal blood to combine with O_2 to increase, and maternal blood to decrease, which forces more O_2 from the maternal blood while enhancing oxygen uptake by the fetal blood.		

Here the summaries are clear

Summary

3- Placenta

1. Respiration

Important factors facilitate delivery of oxygen to the fetal tissues:

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

2. Nutrition

Glucose	Fatty acids	Amino acids	Electrolyte's
Fetus uses mainly glucose for nutrition so, the trophoblast cells in placental villi transport 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 with fetal concentrations exceeding maternal levels.	K+, Na+ and Cl- diffuses from maternal to fetal blood.

3.Excretion

Excretory products of the fetus diffuse through placental membrane to maternal blood to be excreted with waste products of the mother (Urea, uric acid and creatinine).

Higher concentration of excretory products in fetal blood insures continuous diffusion of these substances to the maternal blood.

Pregnancy Hormones

Human chorionic gonadotropin (hCG):

-Maintains corpus luteum till 13-17 weeks.
-Acts as LH (the baby needs it to grow male sex organs).

Estrogen:

-Enlargement of uterus, breast ducts & external genitalia.
-Relaxation of pelvic ligaments in preparation to labor.
-Activation of the uterus (gap junctions).

Progesterone:

-Development of the breast lobules.
-Provides nutrition to developing embryo (uterine secretory phase.
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Human chorionic somatomamotropin or (HPL) Human placental lactogen:

-Breast development (hPL).
-Weak growth hormone's action.
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Relaxin:

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MCQ's

1. Which of the following stages is the one that is implanted into the endometrium of the uterus?

A. Zygote
B. Morula
C. Early Blastocyst
D. Late Blastocyst

2. How many days does it take for the fertilized zygote to travel through the oviduct?

A. 2-4
B. 3-5
C. 4-5
D. 5-6

3. DHEA is converted to Estrogen in …?

A. Placenta.
B. Maternal blood.
C. Fetal blood .
D. Fetal adrenal cortex.

4. Which of the following will inhibit the contractility of uterus?

A. Estrogen.
B. Oxytocin.
C. Prolactin.
D. Progesterone

5. Which ONE of the following is a function of RELAXIN ?

A. Act upon uterine cervix
B. Developmental function
C. Promotes release of fatty acids
D. Decrease glucose sensitivity

6. Which ONE of the following is secreted by placenta around 5th gestational week ?

A. Human Chorionic Gonadotropin
B. Human Placental Lactogen
C. Relaxin
D. Gonadotropins

1=D 2=B 3=A 4=D 5=A 6=A

Thank you for checking our work!

اعمل لترسم بسمة، اعمل لتمسح دمعة، اعمل و أنت تعلم أن الله لا يضيع أجر من أحسن عملا.

قادة الفريق:

ليلى مذكور & محمد نصر

خالص الشكر لأعضاء الفريق الكِرام:

لمى التميمي

ريما الشايع

لينا الوكيل

ندى الدخيل

آمال الشيبي

حسان الشمري

عبدالرحمن الراشد

فؤاد بهجت

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محمد المطلق

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