

Physiological changes in pregnancy

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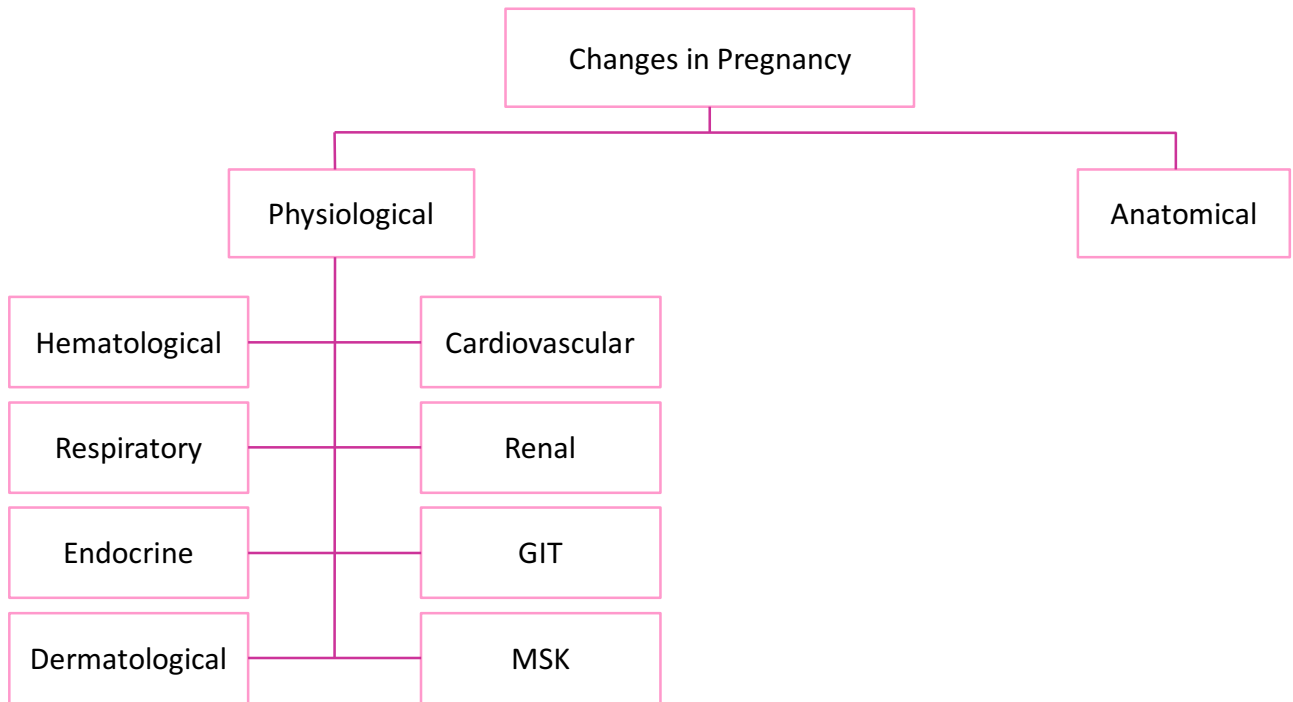
References: 436 doctor's slides and notes , Kaplan

Color code: Notes | Important | Extra | Kaplan

Editing file: <https://docs.google.com/presentation/d/1-BVEbLfTvdm-wTAEgyY9476Nr6VPVwpwSZWq6bfeMo/edit#slide=id.p>

Objectives:

1. Symptoms and physical findings of each organ system
2. Physiologic versus pathologic changes
3. Diagnostic tests and interpretations during physiological changes



This lecture talks about **physiological** findings, so whenever we say increase or decrease it means within the normal limits.

For example, the normal heart rate is between 60-100 Bt/min. And the average of young non-pregnant women is 70, so the pregnant women could have an average of 90-95 (higher than usual but within the normal range). But if the HR of a pregnant woman is 120 this is abnormal and **pathological**.

Hematological changes

Hypercoagulable pregnancy is hypercoagulable state! More risk for DVTs and PEs.

- High Estrogen & Vascular stasis.
- Increased risk for thromboembolic disease¹
 - Increase in fibrinogen, **all** coag factors except II, V, XII, VII, VIII, IX and von Willebrand Factor)
 - Fall in protein S and sensitivity to APC
- Fall in platelets. Normally (non-pregnant) 150000-300000, but in pregnancy it is about 160000 (lower normal) but if it's less than 150000 this is pathological and factor XI and XIII.
- Increase in WBC (same concept as the platelets).

¹ even if you want to investigate thrombophilic profile you have to wait postpartum 2-3 months until everything goes back to normal.

- Hemoglobin:
 - Stays the same (12-16 g/dL) initially.
 - May drop down to 10 g/dL and still be normal physiological anemia. **But Hb of 8 is not normal!**
 - Normal pregnancy Hgb is 10-14 g/dL. **9 is not normal**
- Decrease Hematocrit (Hct): 38-47%.
 - Normal pregnancy Hct (Hematocrit) is 32-42 later in pregnancy.

Physiologic anemia of pregnancy

- Plasma volume increases 50-70 % (Beginning by the 6th week).
- RBC mass increases 20-35 % (Beginning by the 12th week).
- Note the difference in the increase between the two components, the plasma increases way more than the RBC and that results in hemodilution and not polycythemia for example.
- Hemodilution. Plasma volume increases and that is what causes physiological anemia.

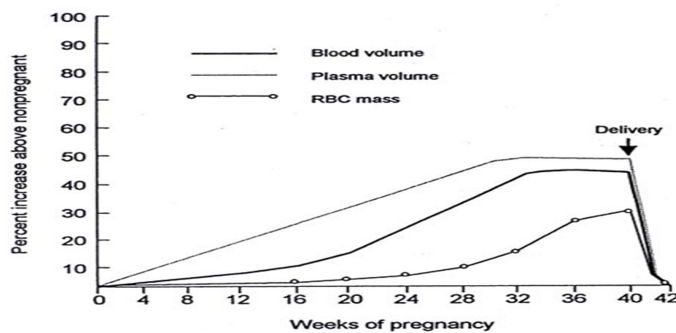


Figure 3-11. Blood volume changes during pregnancy. (From Scott D: Anemia during pregnancy. *Obstet Gynecol Ann* 1:219, 1972.)

The graph clearly shows when does physiological anemia happen. Plasma volume will start to increase earlier than RBCs mass. The blood volume will hugely increase in the 2nd trimester due to both plasma and RBCs increase. After delivery everything goes back to normal.

Hematological change in summary

- Decreases in:
 - Haemoglobin concentration & Haematocrit.
 - Plasma folate concentration.
- Increases in:

- White cell count.
- Erythrocyte sedimentation rate & Fibrinogen.

A useless test in pregnancy is D-dimer when you are suspecting DVT because it's also will be high physiologically.

Cardiovascular system

Normal changes in heart sounds during pregnancy

- Increased loudness of both s1 and s2.
- Increased splitting of mitral and tricuspid components of s1.
- No constant changes in s2.
- Loud s3 by 20 weeks' gestation.
- <5% with s4.
- >95% develop systolic murmur which disappears after delivery (Ejection systolic murmur especially in 3rd trimester at left sternal border due to increased CO passing through the aortic and pulmonary valves).
- 20% have a transient diastolic murmur. Diastolic murmurs are never normal in pregnancy and must be investigated.
- 10% develop continuous murmurs due to increased mammary blood flow, so it's not coming from the heart.

Cardiovascular changes

- Heart rate increases (10-20%).
- Stroke volume increases (10%).
- Cardiac output increases (30-50%).
- Mean arterial pressure decreases (10%).

Systolic and diastolic values both decline early in the first trimester, reaching a nadir by 24–28 weeks, then they gradually rise toward term but never return quite to prepregnancy baseline. Arterial blood pressure is never normally elevated in pregnancy. Central venous pressure (CVP) is unchanged with pregnancy.

- Peripheral resistance decreases (35%) تقدر وتنبؤ المعلومة هذي بأن ضغط المرأة الحامل ما يزيد في (35%) والأوضاع الطبيعية مع إن حجم الدم زاد مرة! معناها مقاومة الأوعية الدموية قلت لأن الضغط يتكون من كمية الدم ومقاومة الأوعية الدموية.

Blood pressure = Vascular resistance + Blood volume.

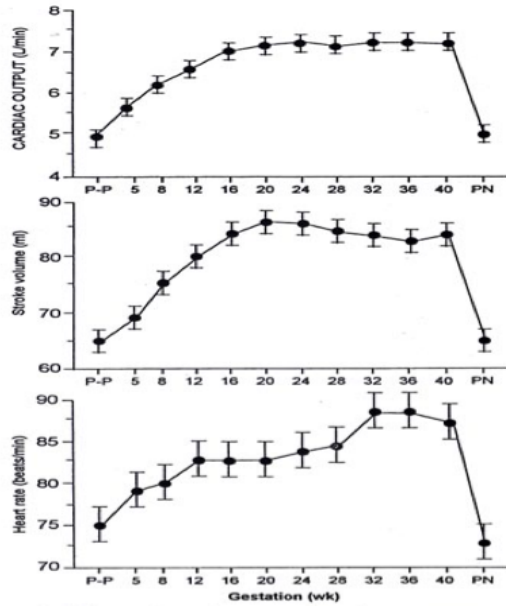
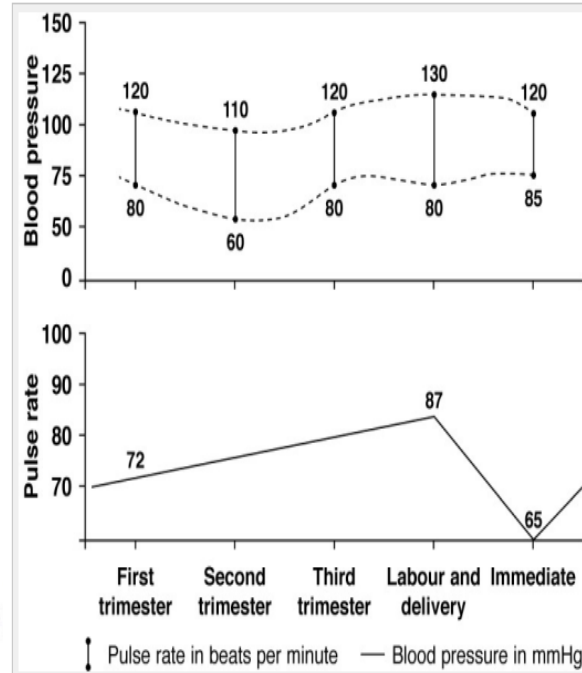


Figure 3-3. Increase in cardiac output from the nonpregnancy state throughout pregnancy. P-P, pre-pregnancy; PN, postnatal. (From Hunter S, Robson S: Adaptation of the maternal heart in pregnancy. Br Heart J 68:540, 1992, with permission.)



Left graph: The graph shows how high HR (**but still under 100!**) is in the pregnancy and how immediately after delivery it drops back to normal as soon as the placenta is out and the uterus contracts.

Right upper graph: Notice the slight BP drop in 2nd trimester which may lead to postural hypertension.

Right lower graph: Notice the slight increase within the normal range. As discussed before.

Signs & Symptoms of Normal Pregnancy that may Mimic Heart Disease:

Signs	<ul style="list-style-type: none"> Peripheral edema dig more in history because there is a fine line between physiological and pathological causes. JVD increases a little especially in 3rd trimester. Arrhythmia is a pathological not a physiological finding.
Symptoms	<ul style="list-style-type: none"> Reduced exercise tolerance. Dyspnea dig in history! There is a huge difference between someone who is short of breath at rest and someone who's short of breath after walking.
Auscultation	<ul style="list-style-type: none"> S3 gallop. Systolic ejection murmur.
Chest X-ray	<ul style="list-style-type: none"> Change in heart position & size Increased vascular markings.
EKG	<ul style="list-style-type: none"> Nonspecific ST-T wave changes.



- Axis deviation.
- LVH.

All the changes are slight and not that significant.

Renal change

Change in filter

Renin – stimulated by progesterone

- Also made by placenta.
- Angiotensinogen → Angiotensin I → Angiotensin II → Aldosterone Distal tubule (and that's what causes edema and water retention).
 - Net absorption of Na+.
 - Excretion of K+.
 - Water retention: 6-8 liters. most of the time water retention in pregnancy is due to renal reasons not cardio

So the total reabsorption and excretion is changed.

Increased renal blood flow due to increased cardiac output

- 50-75% increase.
- GFR – 50% increase.
- Decreased Albumin = lower colloid oncotic pressure.

Other urinary tract change

- Ureteral dilation / hydroureter.
 - Smooth muscle relaxation, due to the effect of prostaglandin.
 - Later exacerbation by uterine obstruction.
 - Urinary stasis causing mild hydronephrosis.
- Dilation of the pelvis and calyces.
- Increased kidney size, due to increase in renal blood flow. This doesn't reverse until 3 months postpartum.

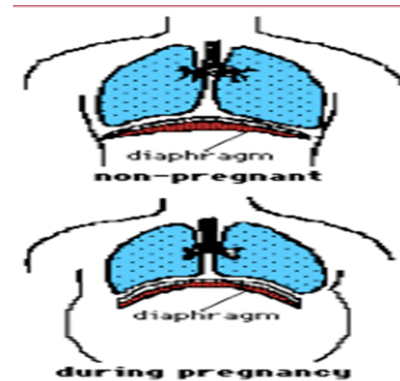
The urinary tract and renal function

Renal changes

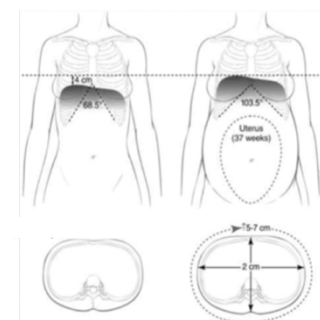
- Blood flow increases (60-75%).
- Glomerular filtration increases (50%).
- Clearance of most substances is enhanced including iodine.
- Plasma creatinine, urea and urate are reduced.
- Glycosuria is normal, due to enhanced clearance of substances. The tubular reabsorption threshold falls from 195 to 155 mg/dL.
- Proteinuria—Urine protein remains unchanged.

Respiratory system

- Mechanical:
 - Diaphragm pushed up and the lung capacity is changed. And different sternal angle and chest diameter.
- Consumption:
 - Increase in needed oxygen.
 - O₂ consumption Increases 15-20%.
 - 50% of this increase is required by the uterus.
 - Despite increase in oxygen requirements, with the increase in Cardiac Output and increase in alveolar ventilation oxygen consumption exceeds the requirements. Therefore, arteriovenous oxygen difference falls and arterial PCO₂ falls. The rise in V_t produces a respiratory alkalosis with a decrease in Pco₂ and an increase in pH. An increased renal loss of bicarbonate helps compensate, resulting in an alkalotic urine.
- Stimulation: Progesterone stimulation.



- **Other change**
 - Increase in Subcostal angle and chest circumference and diameter
 - Mucosal hyperemia
 - Mild respiratory alkalosis
 - Total lung capacity decrease by 15%
 - Tidal volume (V_t): increases with pregnancy to 40% (30 – 40%). It is the only lung volume that does not decrease with pregnancy.
 - Minute ventilation (V_e): increases up to 40% (30 – 40%) its the product of respiratory rate (RR) and V_t. RR remains unchanged with V_t increasing.
 - Residual volume (RV): decreases up to 20% due to upward displacement of intraabdominal contents.



Endocrine glands

1- Pituitary gland

- Pituitary size increases by 100% making it susceptible to ischemic injury (Sheehan syndrome) from postpartum hypotension following postpartum bleeding.
- FSH and LH ↓ أنا ما أحتاج أحفز بويضات جديدة تكبر الريدي عندي حمل.
- ACTH, Thyrotrophin, melanocyte hormone (causing skin pigmentation) and prolactin ↑.
- Prolactin level ↑ until the 30th week of pregnancy then more slowly to term. sometimes the pregnant lady may tell you her breast is secreting milk and that is completely normal

2- Adrenal gland

- Adrenal gland size is unchanged
- Total corticosteroids ↑ progressively to term. This will ↑ the tendency of pregnant women to develop abdominal strine, glycosuria and hypertension.

3- Thyroid gland

- Enlarges during pregnancy, occasionally to twice its normal size. This is mainly due to colloid deposition caused by a lower plasma level of iodine, consequent on the increased ability of the kidneys to excrete during pregnancy.
- Oestrogen stimulates or increased secretion of thyroxine in binding globulin.
- Both T3 and T4 levels rise. This rise will not indicate hyperthyroidism.


Other endocrine




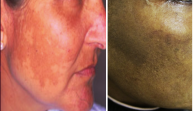
- Pancreas:
 - Carbohydrate metabolism.
 - Increased Insulin resistance.
 - Those changes are due to Human placental lactogen, cortisol.
- Thyroid Function:
 - Increased thyroid binding globulin TIBG (via liver) resulting in Increased total T4 and T3. However, free levels is unchanged. This is because HCG suppresses TSH
- Adrenal function:
 - Free plasma cortisol is elevated bc CRH from placenta stimulates ACTH.

Gastrointestinal tract

- Slowed GI motility:
 - Constipation very common mainly due to decreased GI motility
 - early satiety due to the compression of the uterus on the abdomen.
- Relaxation of LES causing GERD (Heartburn) due to high progesterone levels. Mostly in 3rd trimester.
- Nausea / vomiting: Often proportional to HCG level so a women with twins will have more vomiting.
- Liver / gallbladder:
 - Biliary stasis, cholesterol saturation leading to more stones.
 - Bile salt buildup which may lead to itching (this is pathological and dangerous to the baby and the mum so any pregnant complain of itching check the bile).
 - Coagulation factors.
 - Increased binding proteins (thyroid, steroid, vitamin D)
- Digestive system slow due to progesterone.
- Nausea and vomiting.
- Ptyalism: increase salivation.
- Hemorrhoids due to the mechanical pressure (constipation).
- Displacement of the stomach and intestines.
- Appendix can be displaced to reach the right flank.
- Gastric emptying and intestinal transit times are
 - Delayed secondary to hormonal and mechanical factors.
- Pyrosis is common due to the reflux of secretions.
- Vascular swelling of the gums due to hypervolemia.
- Gastric motility decreases and emptying time increases, this increase in stomach residual volumes, predisposes to aspiration pneumonia with general anesthesia at delivery

Dermatological changes a lot of it is not reversible

Skin change	Definition
Striae gravidarum Starts red and then white	"Stretch marks" that develop in genetically predisposed women on the abdomen and buttocks. 

Spider angiomata and palmer erythema	From increased skin vascularity	
Chadwick sign	Bluish or purplish discoloration of the vagina and cervix as a result of increased vascularity.	
Linea nigra	Increased pigmentation of the lower abdominal midline from the pubis to the umbilicus.	
Chloasma or melasma gravidarum	Blotchy pigmentation of the nose and face.	

MSK changes

- Musculoskeletal consequences that ensue as a result of hormonal changes and weight gain (28lbs ave) include:
 - Force across a joint is increased up to two-fold
 - Joint laxity (Relaxin) in the anterior and posterior longitudinal ligaments of the lumbar spine put strain on the lumbar spine.
 - There is widening and increased mobility of the sacroiliac joints and pubic symphysis to facilitate the baby's passage through the birth canal.
 - A significant increase in the anterior tilt of the pelvis occurs, with increased use of hip extensor, abductor, and ankle plantar flexor muscles

Weight change

- **there is an increase weight** of approximately 12.5kg at term. During the 1st trimester: 1 kg, during 2nd trimester: 5 kg and during 3rd trimester: 5 kg

- the main increase occurs in the 2nd half of the pregnancy (0.5 kg/week)

Weight.. Where do the pregnancy Kilos go?

Where do the pregnancy Kilos go?	
Maternal stores of nutrients and muscle development	3 Kg
Increased body fluid	2 Kg
Increased blood	1.5 - 2 Kg
Breast growth	600g
Enlarged uterus	1 Kg
Amniotic fluid	1 Kg
Placenta	600g
Baby	3.4 - 4 Kg
Total	11 - 16 Kg

Healthy weight gain during pregnancy

Pre-pregnancy BMI	Weight gain in kilograms	Weight gain in pounds
Underweight (under 18.5 BMI)	12.5-18	28-40
Normal weight (18.5-25 BMI)	11.5-16	25-35
Overweight (25-30 BMI)	7-11.5	15-25
Obese	5-9	11-20

TRISH McALASTER / THE GLOBE AND MAIL
SOURCE: U.S. INSTITUTE OF MEDICINE



Anatomical change

Genital tract change

A. Uterus: Uterine muscles grow to 15 times than pre-pregnancy length.

- Uterine weight increases from 50 g before pregnancy to 950 g at term.
- In the early weeks of pregnancy the growth is by hyperplasia and more partially by hypertrophy of the muscle fibers.
- By 20 weeks growth ceases and the uterus expands by distension.
- The uterine blood vessels also undergo hypertrophy and become increasingly coiled in the first half of pregnancy but no further growth after that.
- The lower uterine segment is that part of the lower uterus and upper cervix lying between the line of attachment of the peritoneum of the utero vesical pouch superiorly and the histological internal os inferiorly.

B. The Cervix

- Becomes softer and swollen in pregnancy, with the result that columnar epithelium lining the cervical canal becomes exposed to the vaginal secretions.
- Prostaglandins act on the collagen fibres, especially in the last week of pregnancy. At the same time collagenase is released from leukocytes, which also helps in breaking down collagen. The cervix becomes softer and more easily dilatable the so called ripening of the cervix.



C. Vagina

- The vaginal mucosa becomes thicker, the vaginal muscle hypertrophy.
- There is an alteration in the composition of the connective tissue, with the result that the vagina dilates more easily to accommodate the fetus during delivery.
- Oestrogen → desquamation of the superficial vaginal mucosal cells with ↑ in vaginal discharge when pathogenesis enter the vagina (candida, trichomonas) they will flourish rapidly.

Breast changes

Summary

Hematology	<ul style="list-style-type: none"> • RBC mass increase by ~25% and plasma volume by ~50% (not proportional)that will lead to dilutional physiological anemia hg>10 with no symptoms. • WBC,ESR increase. • coagulation profile changes(increase in factors 6,7,10 and fibrinogen,and decrease level of protein C,S) pregnancy is hypercoagulable state.
Cardiovascular	<ul style="list-style-type: none"> • Normal changes in heart sounds:loud S1,S2 with systolic murmurs that disappear after delivery. • increase in heart rate(20%),stroke volume(10%) and cardiac output(50%). • postural hypotension due to decrease peripheral vascular resistance.
Others	<ul style="list-style-type: none"> • Increase O₂ consumption. • Glucosuria. • Increase in total T3,T4 the free is unchanged. • Increase insulin resistant.

MCQs

1- which of the following is normal during pregnancy:

- A- hemoglobin of 8.
- B- glucosuria
- C- grade 6 diastolic murmurs.
- D- proteinuria.

2- In a normal cardiovascular adaptation during pregnancy. Which of the following tend to decrease:

- A- Blood volume
- B- Cardiac output.
- C- Heart rate.
- D- Peripheral resistance

3- How much does the Cardiac output increase during pregnancy?

- A- 25%.
- B- 50%.
- C- 100%.
- D- 78%.

4- in normal pregnancy are there any Ptt,pt or INR changes?

- A- Yes
- B- No

Answers: 1- B. 2- D. 3- B. 4 – B.