Maternal physiology in pregnancy and fetal circulation

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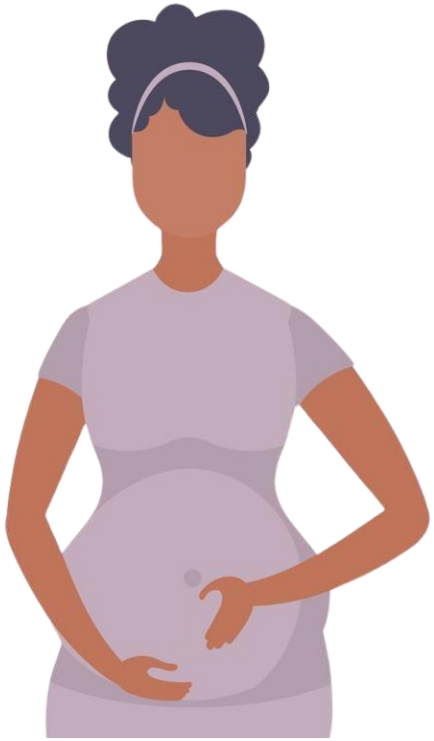


Cardiovascular & Hemodynamic changes

Fetal circulation

Hematologic changes

Renal & urinary tract changes

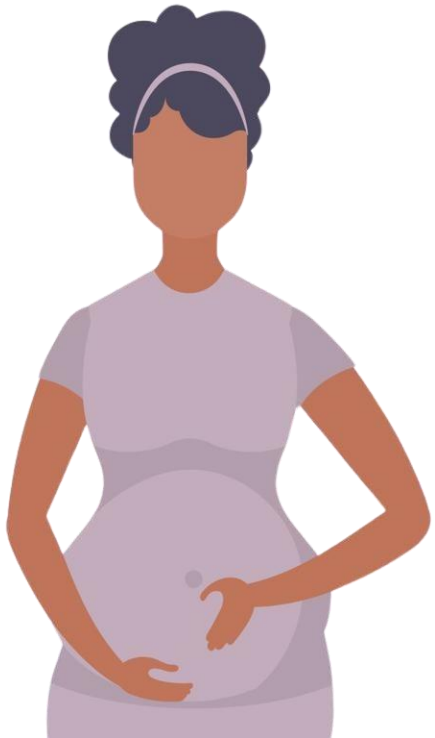
Gastrointestinal changes

Cardiovascular & Hemodynamic changes

Reference:williams-obstertics

General Concept

- The maternal physiologic changes that occur during pregnancy are directly linked to the specific metabolic demands of the fetus. The numerous physiologic adaptations of pregnancy are not the result of a single factor or event; rather, they are the culmination of the biochemical interactions that occur between three distinct interacting systems: maternal, fetal, and placental.



Antepartum adaptation

Which of these variables go up, go down or remain the same in pregnancy?

Heart rate

Stroke volume

Blood pressure

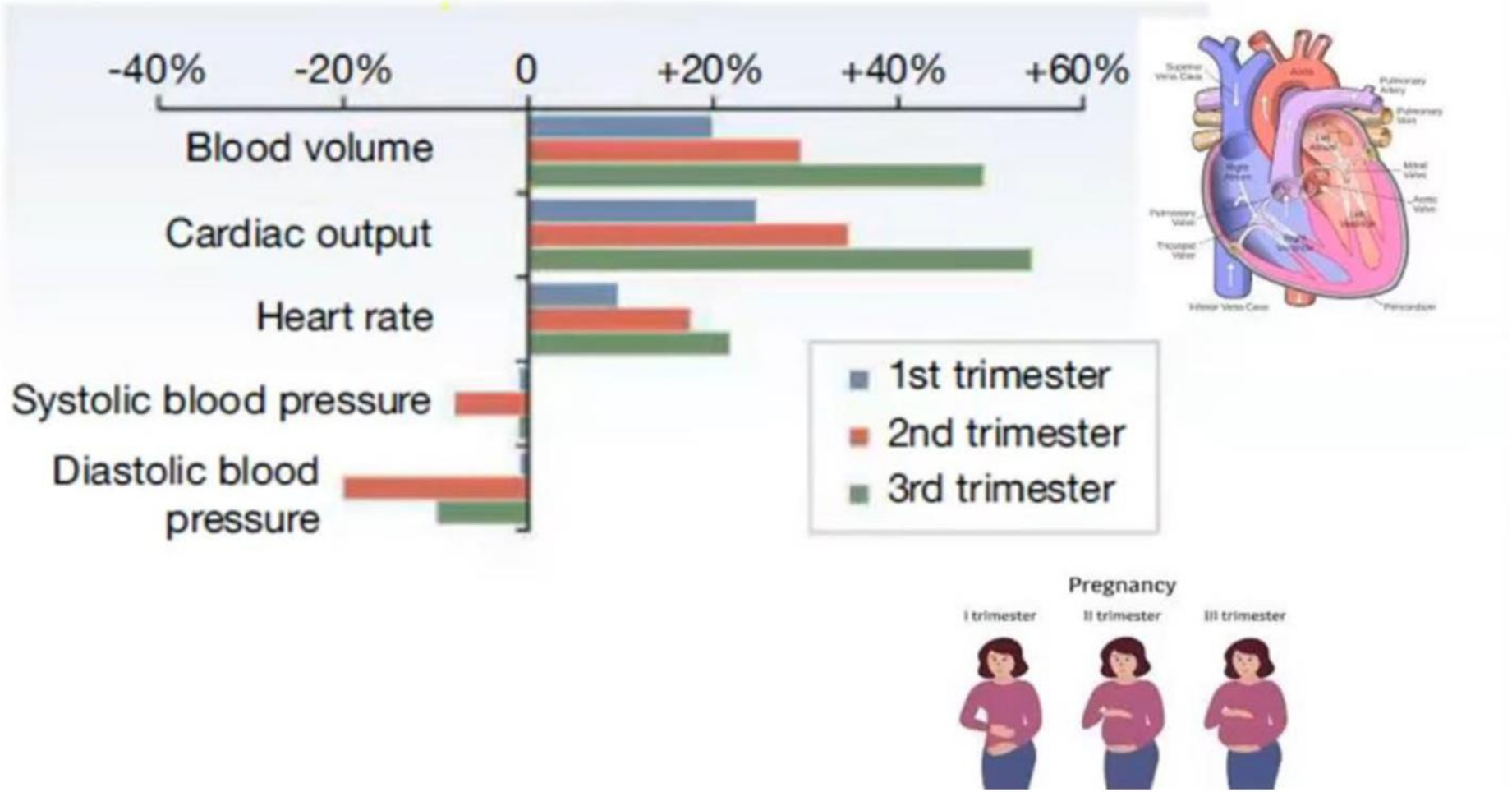
Cardiac output

CVP: Central venous pressure

SVR: Systemic vascular resistance

Blood volume

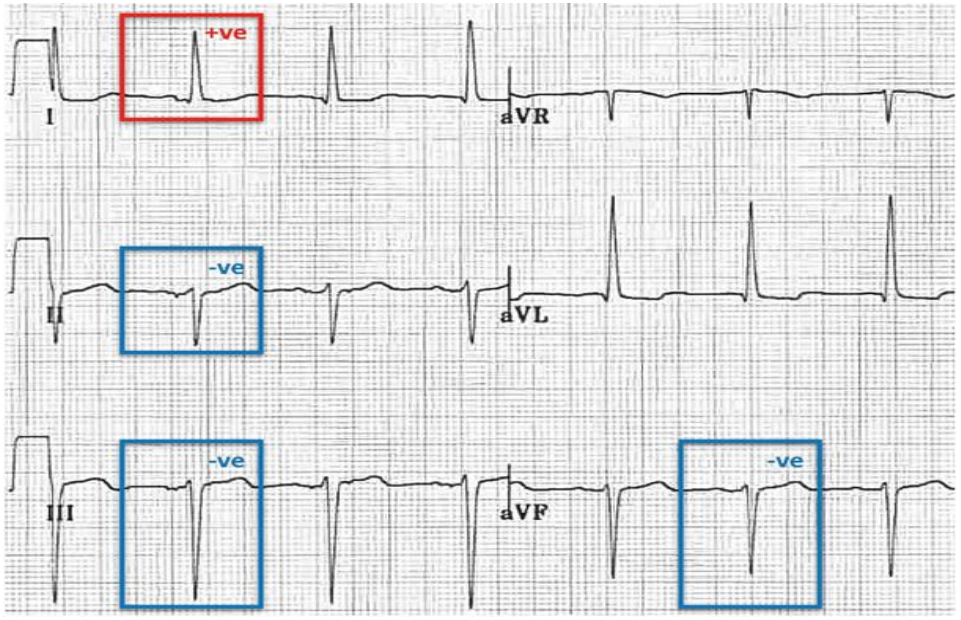
Consider cardiovascular adaptations during pregnancy

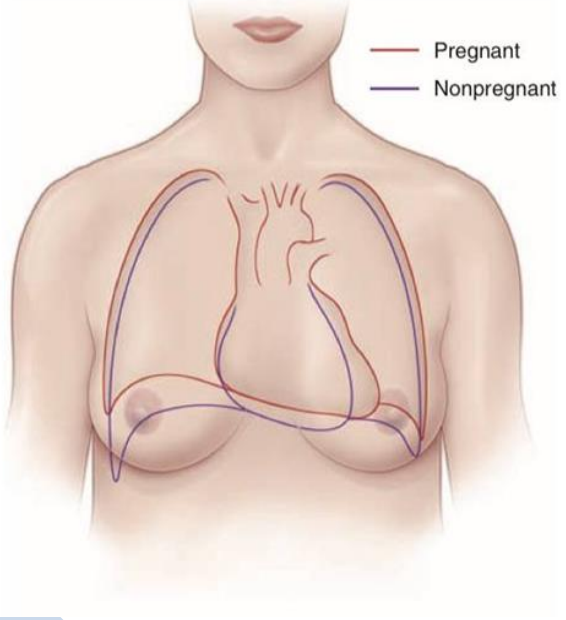


- The earliest and most dramatic changes in maternal physiology are cardiovascular.
- 'These changes improve fetal oxygenation and nutrition.
- *these changes devided into:

1.ANATOMIC CHANGES:

During pregnancy, the heart is displaced upward and to the left and assumes a more horizontal position as its apex is moved laterally. These position changes are the result of diaphragmatic elevation caused by displacement of abdominal viscera by the enlarging uterus. In addition, ventricular muscle mass increases and both the left ventricle and atrium increase in size parallel with an increase in circulating blood volume.





2.FUNCTIONAL CHANGES:

** The primary functional change in the cardiovascular system in pregnancy is **a marked increase in cardiac output.**

- **# Blood volume:**
- During pregnancy, the total blood volume increases by about 1.5 liters, mainly to supply the demands of the new vascular bed and to compensate for blood loss occurring at delivery, also to cope with the very large increases in blood flow to organs which require little extra oxygen, the skin ,uterus,breast and the kidneys. Of this, around one liter of blood is contained within the uterus and maternal blood spaces of the placenta. Increase in blood volume is, therefore, more marked in multiple pregnancies and in iron deficient states.
- Expansion of plasma volume occurs by 10–15 % at 6–12 weeks of gestation.
- Red cell mass (driven by an increase in maternal erythropoietin production) also increases, but relatively less, compared with the increase in plasma volume, the net result being a dip in hemoglobin concentration.Thus, there is dilutional anemia.

 # Heart rate: -Beginning to raise in the 1st trimester.The degree of HR increase is depending on the pt, however its likely that this increase will not exceed 100b/min.

Stroke volume:

These changes in stroke volume are due to alterations in circulating blood volume and systemic vascular resistance. Circulating blood volume begins increasing by 6 to 8 weeks' gestation and reaches a peak increase of 45% by 32 weeks' gestation. Systemic vascular resistance
decreases because of a combination of the smooth muscle- relaxing effect of progesterone, increased production of vasodilatory substances **(prostaglandins, nitric oxide, atrial natriuretic peptide),** and arteriovenous shunting to the uteroplacental circulation.

Cardiac output: CO=SV*HR

Overall, cardiac output increases 30% to 50%, with 50% of that increase occurring by 8 weeks' gestation. In the first half of pregnancy, cardiac output rises as a result of increased stroke volume, and in the latter half of pregnancy, as a result of increased maternal heart rate while the stroke volume returns to near-normal, nonpregnant levels..

Systemic vascular resistance :

- Systemic vasodilation begins at approximately five weeks of gestation and SVR drops progressively throughout pregnancy.
- The decline in SVR can be attributed to the high-flow, low-resistance circuit in the uteroplacental circulation and vasodilatation.
- The factors responsible for vasodilatation are incompletely understood, but one of the major findings is decreased vascular responsiveness to the pressor effects of angiotensin II and norepinephrine and also due to the effect of the dominant hormone in pregnancy which is **progesterone** .

Blood pressure: BP=CO*SVR

-Arterial pressure usually declines to a nadir at 24 to 26 weeks gestation and rises thereafter. Diastolic pressure decreases more than systolic >>> **decreased MAP**.

-Changes in posture affect arterial blood pressure.

Central venous pressure and EF:

- There is a lot of blood during pregnancy, the venous return as a consequency will be increased but the heart of pregnant women will be compensated .How?? There is a ventricular remodeling in the cardiac myocytes so the CVP and EF they both remain same during pregnancy. **(UNCHANGED)**

— central venous pressure remains in the normal range throughout pregnancy due to the reduction in cardiac afterload induced by the substantial decrease in both SVR and pulmonary vascular resistance.

 # Uteroplacental circulation:

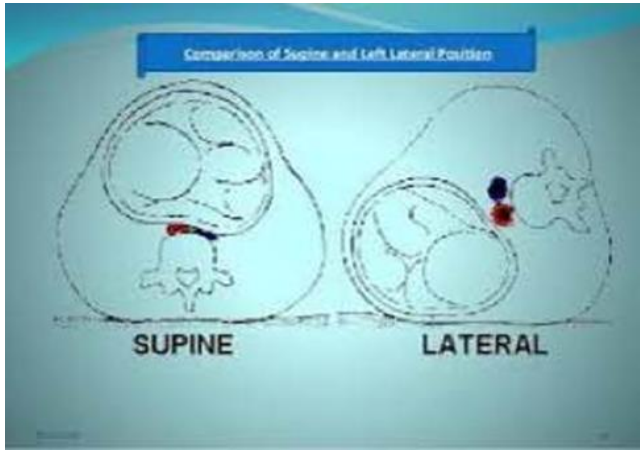
The uteroplacental circulation supports fetal growth and development. During pregnancy, uterine vascular tone is relaxed due to the varying effects of a variety of factors, including nitric oxide, renin- angiotensin, estrogen, progesterone, and prostacyclin, as well as uterine spiral artery dilation due to vascular remodeling in response to decidual natural killer (NK) cell activity and extravillous cytotrophoblast invasion

Supine Hypotension Syndrome

-occurs within 3 to 10 minutes of lying supine

-Late in pregnancy, when the mother assumes the supine position, the gravid uterus compresses the inferior vena cava and decreases venous return to the heart. This results in decreased cardiac output and symptoms of dizziness, light-headedness, and syncope. This significant arterial hypotension resulting from inferior vena cava compression is known as supine hypotensive syndrome or inferior vena cava syndrome. Therefore, it is not recommended that women remain in the supine position for any prolonged period of time in the latter part of pregnancy. When patients describe symptoms of the supine hypotensive syndrome, there is no need to proceed with additional cardiac or pulmonary workup

-The earliest sign of developing supine hypotension is an increase in maternal heart rate and a decrease in pulse pressure, indicating significantly reduced venous return, these alterations are the best indicators of an impending attack, many individuals remain asymptomatic



*A reduction in placental perfusion may result in non-reassuring changes in the fetal heart rate, even with no or minimal decrease in upper extremity maternal BP. Therefore, it is important to avoid the supine position even in symptom-free patients and to ensure that pregnant patients are positioned in the left lateral tilt position for procedures (e.g. labor and delivery, surgery, nonstress test, ultrasound), particularly after 20 weeks of gestation.

The venous system is a high-fow, low-resistance circulation during pregnancy . While antecubital venous pressure remains unchanged, in the supine position, femoral venous pressure rises steadily, from approximately 8 mm Hg early in pregnancy to 24 mm Hg at term. Venous blood flow in the legs is retarded except when the lateral recumbent position is assumed. This tendency toward blood stagnation in the lower extremities during later pregnancy is attributable to occlusion of the pelvic veins and inferior vena cava by the enlarged uterus. The elevated venous pressure returns to normal when the pregnant woman lies on her side and immediately after delivery. These alterations contribute to the dependent edema frequently experienced and to development of hemorrhoids and varicose veins in the legs and vulva. These changes also predispose to deep-vein thrombosis and pulmonary embolism.

ANTEPARTUM EVALUATION OF THE CVS:

1) History:

- *Palpitations occur frequently during pregnancy and are a common indication for cardiac evaluation. The differential diagnosis of palpitations is extensive and the diagnostic evaluation of pregnant individuals with palpitations does not differ from that in nonpregnant patients.
- *Dyspnea is common as pregnancy progresses because progesterone directly increases minute ventilation.
- *Increased fatigue and decreased exercise tolerance commonly occur during pregnancy.

2.Examination of CVS of a pregnant woman:

- JVP :Mean jugular venous pressure, as estimated from the superficial jugular vein, remains normal
- small water hammer: Beginning in the first trimester, the systemic arterial pulse is characterized by a rapid rise and a brisk collapse.
- Apex beat: normally in 5th intercostal space near to mid clavicular line but in pregnancy it will go to 4th intercostal space lateral to mid clavicular line.

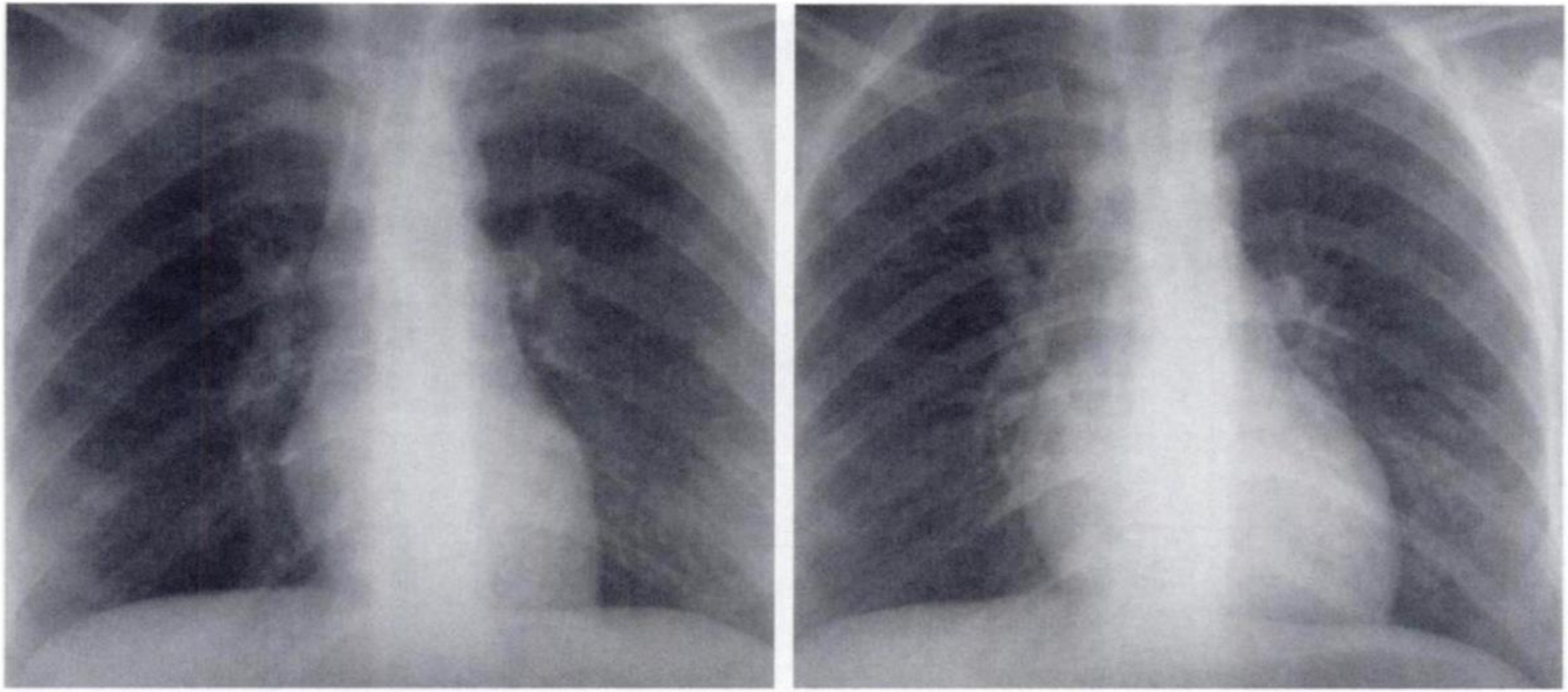
Heart sounds:> **Begin to change in the late first trimester**

load heart sound as a result of more blood pass through the walls of the heart and more turbulent of blood in the heart itself.
#S1 : exaggerated splitting of S1.
#S3 (ventricular gallop) : >>over the apical area. (resulted from excessive rapid early diastolic ventricular filling).
#Heart murmur: {ejection systolic murmur}>>over aortic and pulmonary area.
"It is common in pregnancy because of the increased volume of blood flowing through the heart, (up to grade 2/6). Changes in heart sounds often begin around 12-20 weeks of pregnancy and disappear within a week after delivery. Most heart murmurs that develop during pregnancy are harmless. A systolic ejection murmur has been reported in more than 90% of pregnant women resulted from increased flow through the right and left ventricular outflow tracts.

- peripheral edema.

3) Chest radiograph

- The left, anterior, superior rotation of the heart and hypervolemia give the illusion of ventricular hypertrophy and cardiomegaly on chest radiographs; increased pulmonary vascular markings are also common. Rotation of the heart may also cause an indentation of the esophagus by the left atrium and straightening of the left heart border. The majority of these changes are transient and return to normal in the early postpartum period.
- Elevation of the diaphragm 4 cm



A

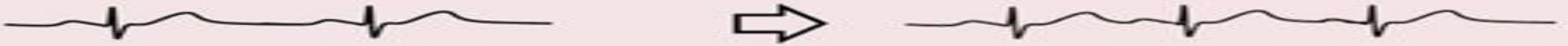
B

4) ECG

•*The heart is rotated toward the left, resulting in a 15- to 20-degree left axis deviation.
*Sinus tachycardia is common, as the heart rate increases approximately 10 percent above baseline values reaching the peak during third trimester
•*Premature ventricular or atrial ectopic beats may be seen in 50 to 60 percent of pregnant patients presenting with palpitations and generally resolve spontaneously after delivery
•Q wave in lead DIII

Pre-pregnancy | Pregnancy

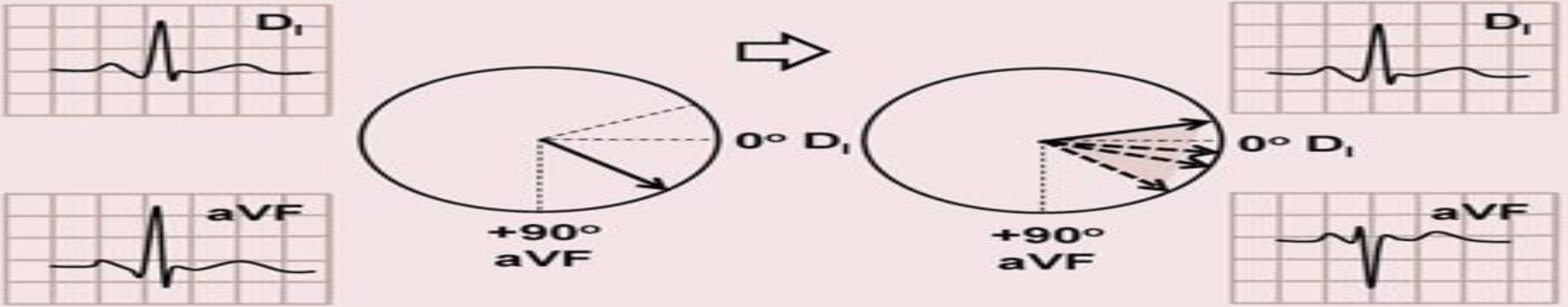
(A) Increase in heart rate



(B) Q wave in lead D_{III}

(C) Reduction in PR interval

(D) Leftward deviation of the mean QRS axis



5) Echocardiograph

- The volume of the cardiac chambers increases slightly, reflected in an increase of 0.4 to 0.5 cm in the left atrial size and 0.2 to 0.4 cm in the left ventricular diastolic dimension.
- The left ventricular mass increases by 5 to 10 percent, which results in eccentric hypertrophy .
- Each of the valves may develop trivial-to-mild regurgitation especially mitral and tricuspid valves in 28% and 94% respectively , particularly in the third trimester.

INTRAPARTUM CHANGES

- Significant hemodynamic changes can occur intrapartum due to multiple factors, such as pain, uterine contractions, exertion, uterine involution, hemorrhage, infection, and administration of medications, such as for anesthesia, analgesia, or tocolysis (eg, terbutaline, nifedipine).

1) Cardiac output

•In patients without epidural anesthesia, basal cardiac output between contractions increases by 12 percent above prelabor levels . During contractions, cardiac output increases progressively as labor advances, increasing by a mean value of 34 percent above prelabor levels at full dilation. The increase is due to blood forced into the systemic circulation from the uterine sinusoids with each uterine contraction as well as pain, thereby increasing preload . While epidural anesthesia reduces the increase due to pain, the increase associated with uterine contractions persists.

•In the second stage, exertion associated with pushing increases cardiac output up to 50 percent above the prelabour level.

2) Blood pressure

- During each uterine contraction, systolic and diastolic BP can increase 15-25% and 10-15%, respectively. The rise in systemic BP depends upon the duration and intensity of the contractions, the parturient's position (changes are minimized in the left lateral position), and the degree of pain and anxiety experienced
- The increases in arterial pressure associated with each uterine contraction are mirrored by a rise in pressure in the amniotic fluid, intrathoracic veins, cerebrospinal fluid, and extradural compartment.
- Pushing during the second stage alters the BP and heart rate in a similar way to the Valsalva maneuver

The hemodynamic changes resulting from a Valsalva maneuver vary with its different phases:

•During phase 1 (onset of the maneuver), left ventricular output transiently increases.
•During phase 2 (straining phase), venous return, right and left ventricular volumes, stroke volumes, mean arterial pressure, and pulse pressure decrease accompanied by a reflex increase in heart rate.
•During phase 3 (release of Valsalva), which only lasts for a few cardiac cycles, left ventricular volume is further reduced.
•During phase 4, stroke volume and arterial pressure increase accompanied by reflex slowing of the heart rate (the overshoot).

POSTPARTUM CHANGES

•**Immediately postpartum** — Within the first 10 minutes following a term vaginal birth, the cardiac output and stroke volume increase by 59 and 71 percent, respectively . At one hour postpartum, both cardiac output and stroke volume remain increased (by 49 and 67 percent, respectively) while the heart rate decreases by 15 percent; BP remains unchanged . These changes may be altered in the setting of uterine atony, postpartum hemorrhage, or sepsis.

•The increases in stroke volume and cardiac output most likely result from improved cardiac preload from autotransfusion of uteroplacental blood to the intravascular space. Preload also increases following expulsion of the fetus, amniotic fluid, and placenta due to a reduction in the mechanical compression of the vena cava.

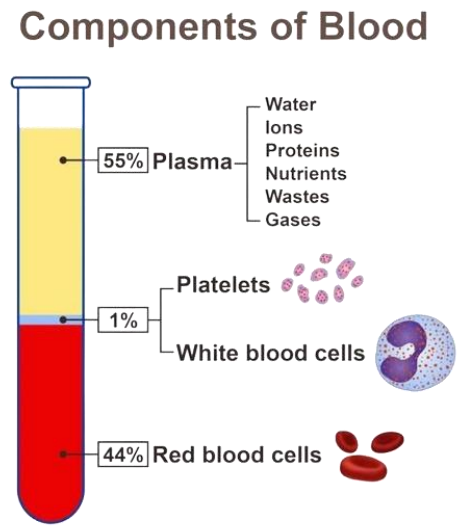
- **Resolution to prepregnancy parameters** — The cardiac output and systemic vascular resistance (SVR) gradually return to nonpregnant levels over a period of three months or more.

- BP peaks three to six days postpartum and then usually returns to baseline by 14 days postpartum . Heart rate also usually returns to baseline by 14 days postpartum.

Hematologic changes

Normal physiological changes

- **Expanded plasma volume** (in excess of the increase in red blood cell mass) and resultant **physiologic anemia**
- Mild **neutrophilia**
- Mild **thrombocytopenia**
- **Increased procoagulant factors**
- **Decreased natural anticoagulants**
- **Diminished fibrinolysis**



Hematologic changes of specific blood Components during pregnancy

Plasma volume

- Plasma volume increases by 10-15% at 6 to 12 weeks of gestation, expands rapidly until 30 to 34 weeks, and then plateaus or decreases slightly through term
- The total **gain at term averages 1100 to 1600 mL** and results in a total plasma volume of 4700 to 5200 mL, which is 30-50% above that in nonpregnant women
- Total plasma volume expansion is accompanied by retention of sodium and water, which is distributed among the fetus, amniotic fluid, and extracellular and intracellular spaces

Benefits of expanded plasma volume in pregnancy:

1. Meet the increased metabolic demands of the uterus and placenta
2. Facilitate delivery of nutrients to the developing fetus and removal of waste
3. Protect against the effects of impaired venous return when the mother is supine or standing
4. Protect the mother from excessive blood loss during delivery

- The rise in plasma volume during pregnancy is probably a response to an underfilled vascular system caused by systemic vasodilatation and the rise in vascular capacitance. During pregnancy, plasma renin activity tends to be increased and atrial natriuretic peptide levels are slightly reduced

- The hypothesis that vascular changes precede expansion of the plasma volume is also supported by the observation that increasing sodium intake does not lead to further volume expansion

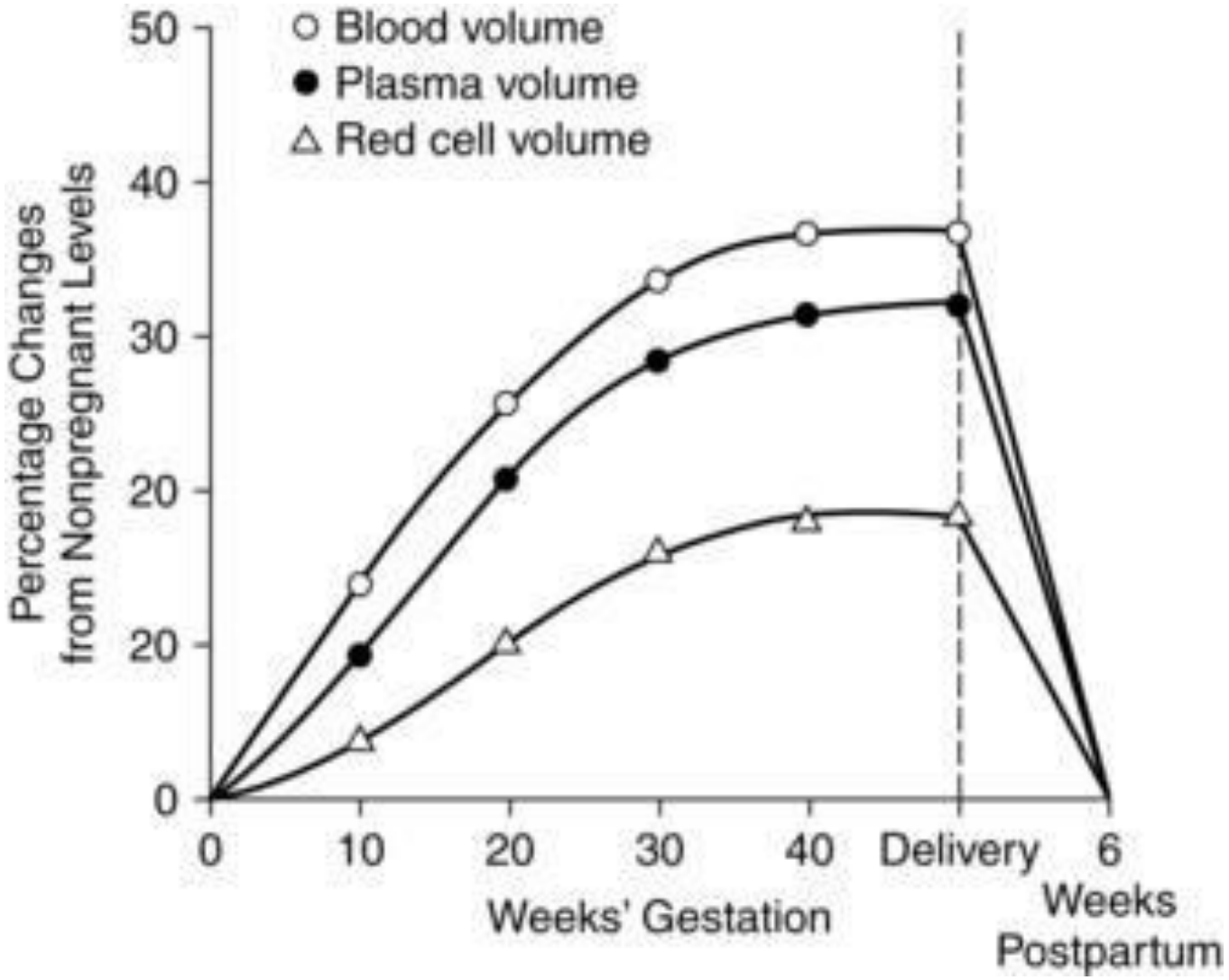
Red blood cells

Red blood cell **(RBC) mass begins to increase at 8 to 10 weeks of gestation**, steadily rises, and reaches levels 20-30% higher than in nonpregnant females by the end of pregnancy

The increased RBC mass is accompanied by a slight increase in the mean corpuscular volume in healthy pregnant people . However, the increase in RBC mass is smaller than the increase in plasma volume, which contributes to the physiologic anemia of pregnancy.

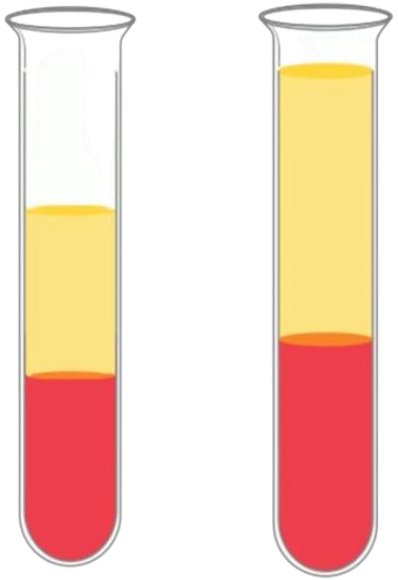
The major mediator of increased RBC mass is an increase in erythropoietin, which stimulates RBC production. **Erythropoietin levels increase by 50 percent**

The increase in RBC mass requires sufficient iron, folate, and vitamin B12; thus, individuals with deficiencies of iron or these vitamins will have blunted increases in RBC mass and are likely to develop more severe anemia


Blood volume
Plasma volume
Red cell volume
Percentage Changes from Nonpregnant Levels
50
40
30
20
20
0
0
10
20
30
40
Delivery
6
Weeks' Gestation
Weeks Postpartum

Dilutional/physiologic anemia

- In normal pregnancies, greater expansion of plasma volume relative to the increase in RBC mass is associated with a modest decrease in hemoglobin concentration, which is referred to as physiologic or dilutional anemia of pregnancy.
- The greatest disproportion between the rates at which plasma and RBCs are added to the maternal circulation occurs during the late second to early third trimester; thus, the lowest hemoglobin concentration is typically measured at 28 to 36 weeks. Nearer to term, hemoglobin concentration increases due to cessation of plasma expansion and continuing increase in RBC mass



Thresholds for diagnosing anemia in pregnancy are:

- CDC – **Anemia** in pregnancy is defined as a hemoglobin level <**11** g/dL (approximately equivalent to a hematocrit <33 percent) in the *first and third trimesters* and <10.5 g/dL (hematocrit <32 percent) *in the second trimester*
- The WHO – **Anemia** in pregnancy is defined as a hemoglobin level <110 g/L (<**11** g/dL) or a hematocrit <6.83 mmol/L (<33 percent). **Severe anemia** is defined as a hemoglobin level <70 g/L (<7 g/dL). **Very severe** anemia is defined as hemoglobin <40 g/L (<4 g/dL).

Iron and Folate requirement

Iron requirement – In a typical singleton gestation, maternal iron requirements average close to 1000 mg over the course of pregnancy: approximately 300 mg for the fetus and placenta and approximately 500 mg for the expansion of the maternal RBC mass. An additional 200 mg is shed through the gut, urine, and skin

Iron is commonly prescribed as part of a prenatal multivitamin or as a separate supplement. In general, pregnant patients taking iron supplements have a mean hemoglobin concentration that is 1 g/dL greater than that of those not taking supplements.

Folate requirement – The increased folate demand for RBC creation is more than met by the higher daily intake (400 to 800 mcg) already recommended for prevention of neural tube defects

White blood cells

An increase in WBC associated with fever, a large number of immature WBC forms, or any blasts in the peripheral blood are not normal and should be evaluated promptly.

The **neutrophil** count begins to increase in the second month of pregnancy and plateaus in the second or third trimester, at which time WBC counts range is 9000-15,000 cells/microL

Mean **WBC counts in laboring patients** were **10,000 to 16,000 cells/microL**

- The absolute lymphocyte count and the relative numbers of T and B lymphocytes **do not change**
- The monocyte count is generally stable.
- The basophil count may **decrease** slightly.
- The eosinophil count may **increase** slightly.

Platelets (normal range 150,000-450,000)

- **Platelet count declines** as pregnancy progresses but in the vast majority of uncomplicated pregnancies, the platelet count remains >=100,000/microL and returns to the prepregnancy baseline level by several weeks postpartum.

- The most common cause of a decline in platelet count is a normal physiologic response referred to as gestational thrombocytopenia (GT; also called incidental thrombocytopenia of pregnancy). GT is a diagnosis of exclusion and may recur in subsequent pregnancies. We generally do not evaluate patients with a mild decrease in platelet count during pregnancy if they are asymptomatic and their platelet count is >=100,000/microL

- Moderate to severe thrombocytopenia (platelet count <100,000/microL) is **rare** in pregnancy, but when it occurs, it may be a medical emergency.
- Possible causes include
- Immune thrombocytopenia,
  - Preeclampsia with severe features,
  - Sepsis with disseminated intravascular coagulation
  - HELLP syndrome (syndrome of hemolysis, elevated liver enzymes, and low platelets)

Coagulation and fibrinolysis

Normal pregnancy is a **prothrombotic state**
The shift in the balance between the hemostatic and fibrinolytic systems serves to prevent excessive hemorrhage during placental separation. Compared with nonpregnant females, pregnant people have a marked increase in some coagulation factors, reduced fibrinolysis, and increased platelet reactivity. Consequently, there is increased risk for thromboembolic complications. While these changes increase the risk of thrombosis, they are not an indication for intervention.

1. Increased procoagulant factors:

Procoagulant factors **fibrinogen (factor I), factors II, VII, VIII, and X**.

- The prohemostatic von Willebrand factor (VWF) can increase substantially during pregnancy. Studies have reported that VWF increases by two- to fourfold during pregnancy, peaks within 24 hours postpartum, and returns to baseline by one month postpartum

2. Reduced anticoagulant factors

- Anticoagulant protein S decreases physiologically in nearly all pregnant people (if patient develops venous thromboembolism and inherited thrombophilia is suspected, testing for protein S level should be delayed till after delivery)
- antithrombin (AT) levels, protein C, factor V, factor XI remain unchanged

3. Reduced fibrinolysis

- Activity of fibrinolytic inhibitors increases, including **thrombin activatable fibrinolytic inhibitor**, **plasminogen activator inhibitor-1 (PAI-1), and PAI-2** . PAI-1 levels increase markedly since it is partly derived from the placenta and decidua.

Postpartum resolution

Pregnancy-related hematologic changes return to baseline by six to eight weeks after delivery.

- **Plasma volume** – Plasma volume decreases immediately after delivery, then increases again two to five days later, possibly due to a rise in aldosterone. Plasma volume then decreases; remains elevated by 10-15% at 3 weeks postpartum but is usually at **normal nonpregnant levels at six weeks postpartum.**
- **White blood cells** – The white blood cell count falls to the normal nonpregnant range by the **sixth day postpartum.**
- **Physiologic anemia** – Physiologic anemia resolves by **six weeks** postpartum as plasma volume returns to normal.
- **Platelets** – For those with gestational thrombocytopenia, mild thrombocytopenia begins to resolve soon after delivery and is no longer present at **three to four weeks postpartum**.
- **Coagulation and fibrinolysis** – Postpartum normalization of coagulation parameters and return to baseline thromboembolic risk generally occur by **six to eight weeks** after delivery.

Hematologic changes of concern

The following findings should prompt additional evaluation :

- **Non-physiologic anemia or polycythemia,** especially when associated with symptoms out of proportion to the stage of pregnancy. Hemoglobin levels **<10 g/dL or >16 g/dL** should prompt hematologic evaluation

- **Evidence of iron deficiency** (e.g. Reduced iron stores or new microcytosis, which is a late finding of iron deficiency)

Iron deficiency is common because the demand for iron is increased in pregnancy.

However, pregnant patients can have iron deficiency anemia with ferritin levels in the low-normal reference range and approximately one-third of those with iron deficiency do not manifest microcytosis.

- **Thalassemia** is another major cause of microcytic anemia. In some cases, it is not diagnosed until pregnancy.

- **Leukocytosis** due to an excess of neutrophils can occur in some individuals during pregnancy in the absence of infection or inflammatory conditions.

Findings requiring hematological consultation includes:
WBC count >20,000/microL
WBC differential of marked excess of lymphocytes

- **Leukopenia** in association with an absolute neutrophil count <1000/microL

- **Gestational thrombocytopenia** with a reduced platelet count (80,000-149,000/microL) is common during pregnancy. Levels below this level should prompt hematologic consultation

- **Thrombocytosis** The new onset of thrombocytosis is unusual during pregnancy, and platelet counts >500,000/microL should prompt hematologic evaluation. Platelet counts >1,000,000/microL require urgent evaluation.

Gastrointestinal changes

Oropharynx and taste

Oropharynx

- The mucous membrane lining the oropharynx is responsive to the hormonal changes related to pregnancy. **The gingiva is primarily affected,** while the teeth, tongue, and salivary glands are spared, although excessive salivation during pregnancy (ptyalism) has been described.

Taste

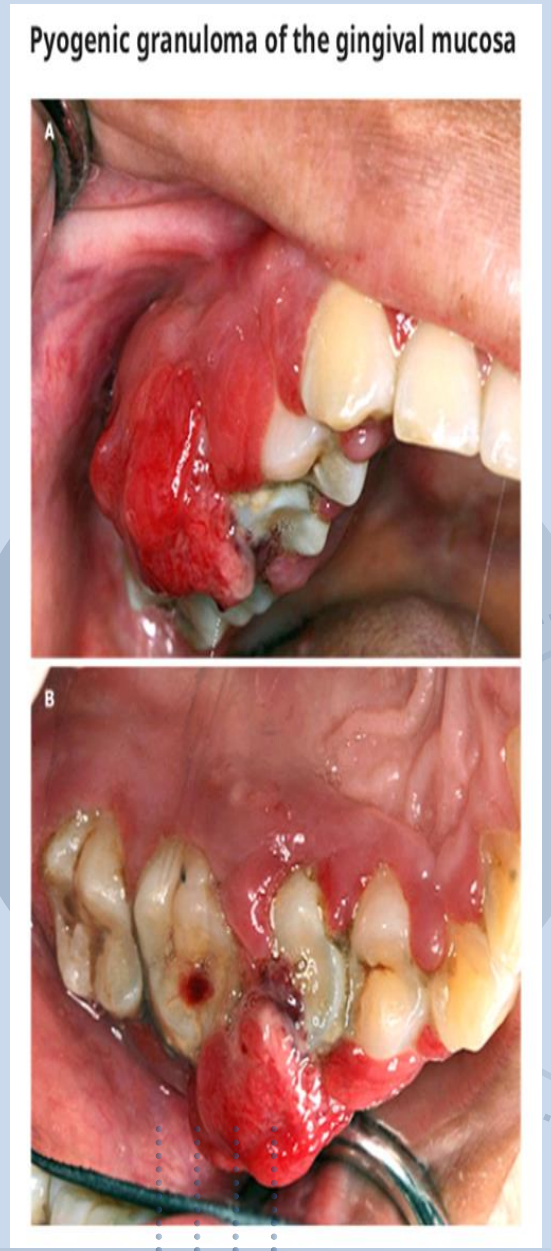
- Most studies suggest that taste perception changes during pregnancy. The etiology is unknown, and the direction of taste change varies among studies.

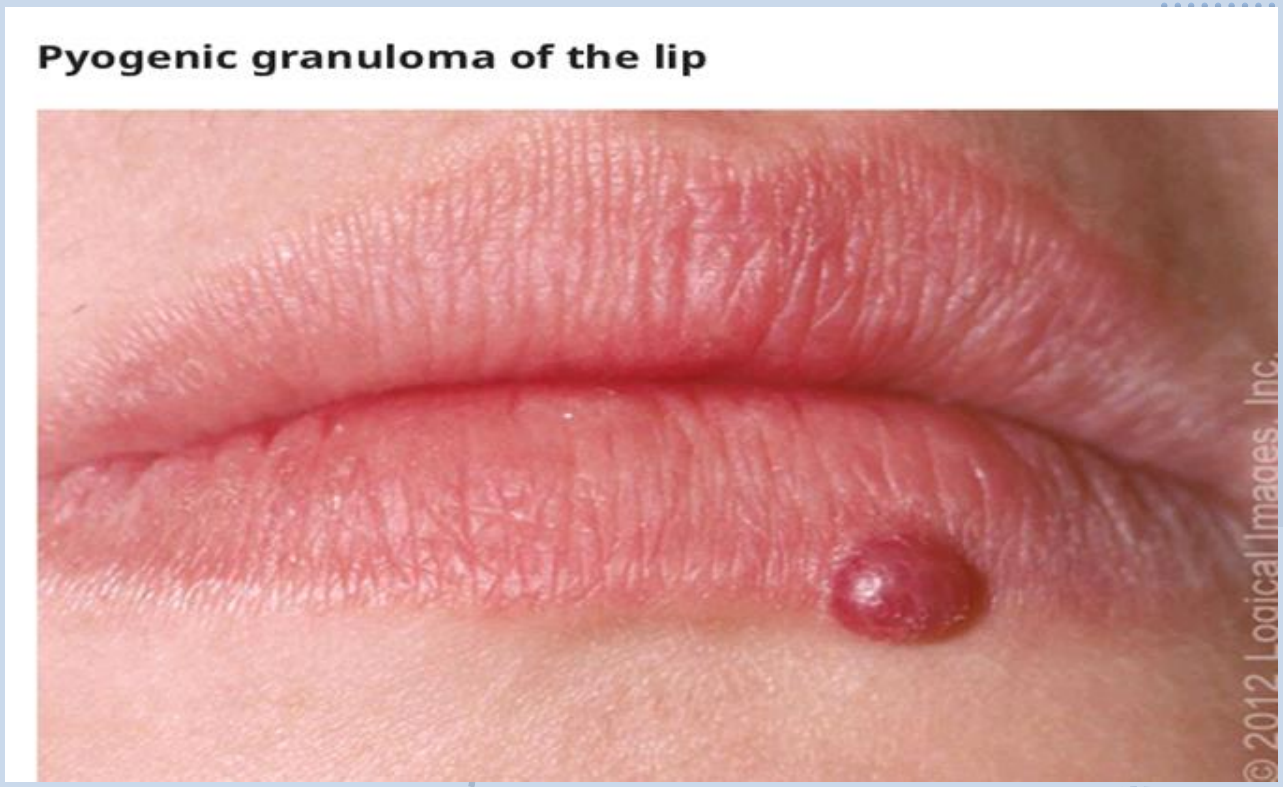
Gingiva

- **Enlargement and blunting** of the interdental papillae of the gingiva may result in gingivitis.
- Elevated circulating ostrogen and progesterone levels are implicated in increasing
- vascular permeability and decreasing immune resistance, thereby increasing susceptibility to gingivitis.

Pyogenic granuloma of pregnancy

Pyogenic granulomas (also known as lobular capillary hemangioma, pregnancy tumor or epulis, and granuloma gravidarum) are benign, vascular tumors with friable surfaces that develop over a few days to weeks in early pregnancy. The oral mucosa, lip, and tongue are common sites of occurrence





Pyogenic granuloma of pregnancy

Ptyalism or sialorrhea gravidarum

- Ptyalism or sialorrhea of pregnancy is an oral pathological condition consisting of **excessive salivation** that typically begins in the first trimester. Symptoms generally abate in the second trimester but can continue to term. Salivary volumes range from
  1.5 L to 2 L per day . Reported incidences range widely from 0.08 to 35 percent and depend upon the definition used (eg, inclusion of patients with pseudo-sialorrhea). Ptyalism can be bothersome, but it is not associated with increased maternal or perinatal morbidity.
- The mechanism in pregnancy is not known. It is commonly associated with nausea and vomiting as well as hyperemesis gravidarum. Causes of ptyalism unrelated to pregnancy include gastroesophageal reflux, medications (eg, clozapine), or irritants (eg, smoking)

Ptyalism cont.

For patients with a potential identified cause, treatment or removal of the underlying cause reduces excessive salivation. For those with symptoms resulting only from pregnancy, treatment is mainly aimed at lessening symptoms. Patients have reported relief with frequent expectoration ,chewing gum or using lozenges, frequent sips of water, and/or antiemetics.

Teeth

The effect of pregnancy on the initiation or progression of caries is not clear; pregnancy-related changes in the oral environment (salivary pH, oral flora) or in maternal diet and oral hygiene may increase the risk of caries

•Reduced gastrointestinal motility and tone during pregnancy due to increased levels of progesterone, which decrease the production of Motilin, a hormonal peptide that is known to stimulate smooth muscle in the gut. •Slower the transit time of food throughout the gut, more water is reabsorbed, leading to constipation.

Esophagus

- Esophagus dysmotility; esophageal peristalses is decreased, accompanied by gastric reflux because of the slower emptying time and dilatation or relaxation of the cardiac sphincter.

Stomach

- Reduced tone of the gastroesophageal junction sphincte
- Increases production of Gastrin hormone significantly, resulting in increased stomach volume and decreased stomach pH.

GERD CONT...

- Gastroesophageal reflux (GERD, or heartburn) is reported by 40 to 85 percent of pregnant people. Most studies describe an increasing prevalence of symptoms from the first to the third trimester, with relief postpartum. While GERD symptoms can be severe, erosive gastropathy and other complications are rare. GERD tends to recur in subsequent pregnancies, and similarly affects multiparous and nulliparous individuals

Aspiration of gastric contents

Pregnant people are at increased risk of aspiration during labor, birth, and immediately postpartum due to supine positioning, analgesia/anesthesia, and a combination of factors related to pregnancy (lower esophageal sphincter incompetence, gastroesophageal reflux, low gastric pH, distortion of the gastric anatomy due to the enlarging uterus, increased intra-abdominal pressure). Aspiration may also occur as a complication of intubation for general anesthesia for cesarean birth. Aspiration pneumonia, acute bronchospasm, or the acute respiratory distress syndrome may ensue.

Liver

- **Position:** In late pregnancy, the liver becomes difficult to palpate because of the expanding uterus. As the enlarging uterus pushes the diaphragm upwards to a maximum of 4 cm, the liver is forced further up into the chest as well. **A palpable liver is an abnormal finding.** The biliary tract however is usually normal.
- The **PT** and **aPTT** are **unchanged or slightly reduced**
- **Serum fibrinogen is markedly increased** (esp in late pregnancy)

Blood chemistries

- Serum **albumin** levels **decrease during the first trimester** because of hemodilution, and this decrease becomes more accentuated with advancing gestation.
- Serum **alkaline phosphatase** concentrations are **significantly higher** (up to two to four times normal) in the third trimester, primarily due to placental synthesis of alkaline phosphatase.
- Serum **gamma-glutamyl transpeptidase** is significantly reduced and **5'-nucleotidaseis** slightly increased

Blood chemical constituent changes during pregnancy

	Nonpregnant adult	First trimester	Second trimester	Third trimester
Alanine aminotransferase (unit/L)	7 to 41	3 to 30	2 to 33	2 to 25
Albumin (g/dL)	4.1 to 5.3	3.1 to 5.1	2.6 to 4.5	2.3 to 4.2
Alkaline phosphatase (unit/L)	33 to 96	17 to 88	25 to 126	38 to 229
Alpha-1 antitrypsin (mg/dL)	100 to 200	225 to 323	273 to 391	327 to 487
Alpha-fetoprotein (ng/mL)	-	-	Approximately 130 to 400	Approximately 130 to 590

Blood chemistries cont...

- **Serum total cholesterol and triglyceride concentrations increase** markedly. Values differ between studies, but the results of a large series are shown in the table below.
- Since the **increase in total cholesterol, LDL and triglycerides is physiologic, treatment is not indicated**
- Patients receiving statin therapy should stop it three months prior to conception .
- An increase in serum aminotransferase, bilirubin or fasting total bile acid concentrations during pregnancy may be pathologic and should be evaluated.

Biomarker	Second trimester	Third trimester
Total triglyceride	254 mg/dL	415 mg/dL
Total cholesterol	319 mg/dL	380 mg/dL
LDL	217 mg/dL	251 mg/dL
HDL	98 mg/dL	95 mg/dL

Gallbladder

- Pregnancy reduces gallbladder motility and increases the lithogenicity of bile (possibility of forming stones).
- On U/S, fasting gallbladder and residual volume after contraction may be increased but the size of the common hepatic duct remains unchanged.

Overall, studies have shown that **pregnancy increases risk for gallstone.**

Pancreas

amylase levels have been reported to be normal or slightly increased.

Acute pancreatitis in pregnant women is a **rare.**Most cases of acute pancreatitis in pregnancy are associated with gallstones and the incidence increases with advancing gestational age.

Bowel, rectum, anus

- **Bloating and constipation**: it is a frequent complaint among pregnant women, as some studies suggest a prevalence of 16% to 39% during pregnancy and postpartum (higher than baseline of 7%).
- Suggested causes of bloating and constipation include increased progesterone concentration which decreases the activity of colonic smooth muscle and increases intestinal transit time.

•Progesterone is also thought to inhibit motilin release which is a stimulatory gastrointestinal hormone.

- Moreover, the gravid uterus mechanically impedes small bowel transit.

Bowel, rectum, anus cont..

- **Hemorrhoidal disease** is particularly frequent in the last trimester and postpartum.
- Symptoms include pruritis, discomfort, and/or bleeding and constipation which is prevalent in pregnancy exacerbates these symptoms.
- Treatment includes conservative management like application of anti-inflammatory, antipruritic and local anesthetic agents. Sever cases require surgery which can be safely performed during pregnancy.
- **Incontinence of feces and flatus**: pregnancy appears to be a risk factor for this condition.
- **Maternal gut microbiome**: the gut microbiome of a woman changes across gestation. Massive bacterial colonization of newborn gut with mother's vaginal, fecal and skin microbiome occurs during labor and vaginal birth which plays a role in mucosal gut homeostasis and predisposition to chronic inflammation.

Renal & urinary tract changes

Renal changes

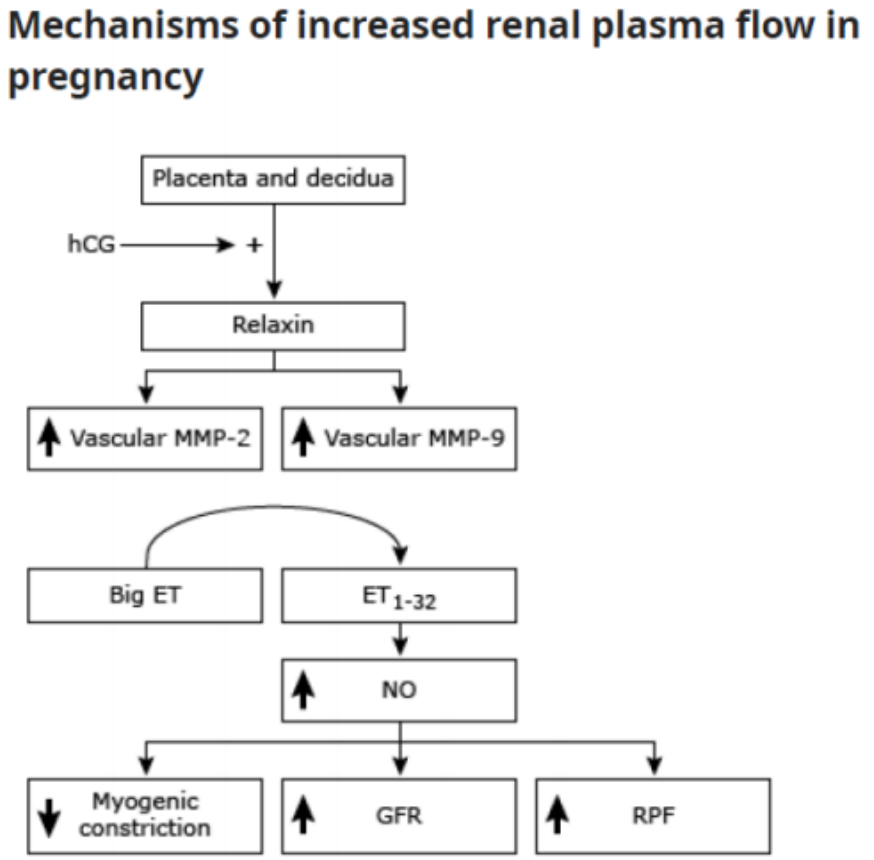
Pregnancy is associated with an increase in renal size ,renal plasma flow and GFR

Both kidney will increase in:
1. Length (1-1.5)
2. The volume increase by 30% due to:
 *increase in renal blood flow (so hpertrophy occurs)
*dilation in pelvic calyceal portion (hydronephrosis)
3. The size of collecting system (renal pelvises, caliceal system and uterus), due to progesteron and compression of uterus.

**No changes in number of nephrones.
** The hypertrophy doesn't resolve until 3 months postpartum.

Mechanism of increased renal plasma flow in pregnancy

Normal pregnancy is characterized by widespread vasodilation, with increased arterial compliance, leading to decreased systemic vascular resistance, increased cardiac output, and a small decrease in blood pressure. These global hemodynamic changes include increased renal perfusion and GFR.



Mechanism of increased GFR

1. Reduced vascular responsiveness to vaso pressor (eg:angiotension 2 , norepinephrine, ADH)

2. Increased nitric oxide synthesis

3. Relaxin which is secreted in large amounts from placenta,
Increases endothelin and nitric oxide.

All of them will cause vaso dailation

GFR, renal plasma flow, and creatinine

- Renal plasma flow increases by up to 80% by 12 w of gestation and then decreases in the third trimester.
- GFR increases within 1 month of conception, peaking at 40-50% above baseline levels by the early second trimester, it then declines slightly toward term.
- The increase in GFR results in decrease in serum creatinine concentration in the first trimester, it levels off in second trimester and rises again in third trimester.
- Therefore, a serum creatinine of >0.75 usually reflects renal impairment in pregnant women as a small rise in creatinine reflects a marked reduction in renal function.

Laboratory tests changes

- Plasma osmolality falls from 275-290 to 270 mOsm/kg

- Plasma sodium concentration falls 4-5 mEq/L below prepregnancy levels.

- This hyponatremia is mediated by increased HCG which in turn produces the hyponatremia by the release of relaxin.

- A serum concentration of sodium lower than 130 mEq/L should prompt evaluation for pathological causes of hyponatremia (such as SIADH) and high levels should prompt evaluation for possible diabetes insipidus

Proteinuria and glucosuria

• Urinary protein excretion increases in pregnancy it rises to 150-200 mg/day (so if urinary protein is >300 mg/day, it is considered abnormal but may be normal in twin pregnancies)

• Mechanisms include increased GFR, and glomerular basement membrane pore size, and reduced tubular reabsorption of filtered protein.

• Glucosuria: seen in ~50% of pregnant patients, it is primarily due to decreased proximal tubular glucose reabsorption.

• Other changes: chronic respiratory alkalosis, hypouricemia, and impaired tubular function.

Urinary tract

• Ureters: dilation of ureters and renal pelvis is seen in up to 80% of pregnancies and is more prominent on the right.

- The dilated collecting system causes stasis and may increase risk of pyelonephritis in pregnancy.
- Factors that contribute to hydroureter and hydronephrosis:
- Progesterone reduces ureteral tone, and peristalsis
- The Dextro rotated uterus kinks the right ureter
- Enlarged vessels may compress ureter
- Uterine enlargement

Bladder and VUR

- Bladder: mucosa is edematous and hyperemic. Progesterone induces bladder wall relaxation, but the enlarging uterus flattens the bladder and may decrease capacity.

- Vesicoureteral reflux: may occur in pregnancy due to bladder flaccidity and decreased intraureteral pressure. Symptoms include Frequency and nocturia, dysuria, urgency and stress incontinence.

Other urinary symptoms

• Urgency and incontinence: These symptoms may be due to uterine pressure on the bladder, hormonal effects on the suspensory ligaments of the urethra, and/or altered neuromuscular function of the urethral striated sphincter.

• Urinary retention: The bladder and urethra inevitably experience some trauma during labor and delivery. The traumatic changes include mucosal congestion and submucosal hemorrhage, Bladder sensitivity/sensation is also decreased from trauma. As a result, detrusor atony, increased postvoid residual urine, bladder overdistention, and urinary retention are common in the first few days after delivery.

• Postpartum: The pregnancy-induced physiologic changes described above return to the
nonpregnant state by four to six weeks following delivery. However, urinary incontinence may persist.

Summary of renal changes in normal pregnancy

Parameter	Alteration	Clinical relevance
Kidney size	Approximately 1 cm longer on radiograph.[1]	Size returns to normal postpartum.[2]
Ureteral dilation	Resembles hydronephrosis on sonogram (more marked on right).[3]	Can be confused with obstructive uropathy; retained urine leads to collection errors; renal infections are more virulent.
Renal function	Glomerular filtration rate and renal plasma flow increase approximately 50%.[4]	Serum creatinine decreases during normal gestation; creatinine >0.8 mg/dL (>72 micromol/L) should be considered abnormal; protein, amino acid, and glucose excretion all increase.[5-7]
Acid-base balance	Hyperventilation and respiratory alkalosis due to progesterone stimulation of respiratory center. Renal bicarbonate excretion increases appropriately.[7]	PCO_2 decreases to 27 to 32 mmHg; serum bicarbonate decreases to 22 mmol/L; pH remains in high-normal range.[7]
Plasma osmolality	Osmotic thresholds for AVP release and thirst decrease; metabolic clearance of AVP increases.	Serum osmolality decreases 10 mOsm/L (serum Na approximately 5 mEq/L) during normal gestation; increased placental metabolism of AVP may cause transient diabetes insipidus during pregnancy.

AVP: vasopressin; IVP: intravenous pyelography; PCO_2; partial pressure carbon dioxide.

Fetal circulation

Introduction

- The **fetal circulation** is the circulatory system of a fetus
- The term usually include the entire fetoplacental **circulation**, which includes the umbilical cord and the blood vessels within the placenta that carry **fetal** blood.
- Fetal circulation — In the fetus, the placenta has the lowest vascular resistance and receives 40 % of the fetal cardiac output, which results in a low systemic pressure
- In contrast, the lungs are filled with fluid, resulting in a high vascular resistance and as a result a significantly lower amount of cardiac output goes to the lungs

- Before birth, the fetus obtains oxygen and nutrients from the mother through the placenta and the umbilical cord
- Blood from the fetal heart that is destined for the lungs is shunted away from the lungs through a short vessel called the ductus arteriosus and returned to the aorta.
- When this shunt is open, it is said to be a patent ductus arteriosus (PDA).

The placenta

The placenta is an organ that connects the developing fetus to the uterine wall to allow nutrient uptake, provide thermo-regulation to the fetus, waste elimination, and gas exchange via the mother's blood supply, fight against internal infection and produce hormones to support pregnancy.

Placental Role

- The core concept behind fetal circulation is that **fetal hemoglobin has a higher affinity for oxygen** than adult hemoglobin, which allows diffusion of oxygen from the mother's circulatory system to the fetus.
- The mother's circulatory system is not directly connected to the fetus's, so the placenta functions as the fetus's respiratory center and **a site of filtration for plasma nutrients and wastes.**
- Water, glucose, amino acids, vitamins, and inorganic salts freely diffuse across the placenta along with oxygen.
- The **umbilical arteries carry blood to the placenta**, and the blood permeates the sponge-like material there. Oxygen then diffuses from the placenta to the chorionic villus, an alveolus-like structure, where it is then carried to the umbilical vein.

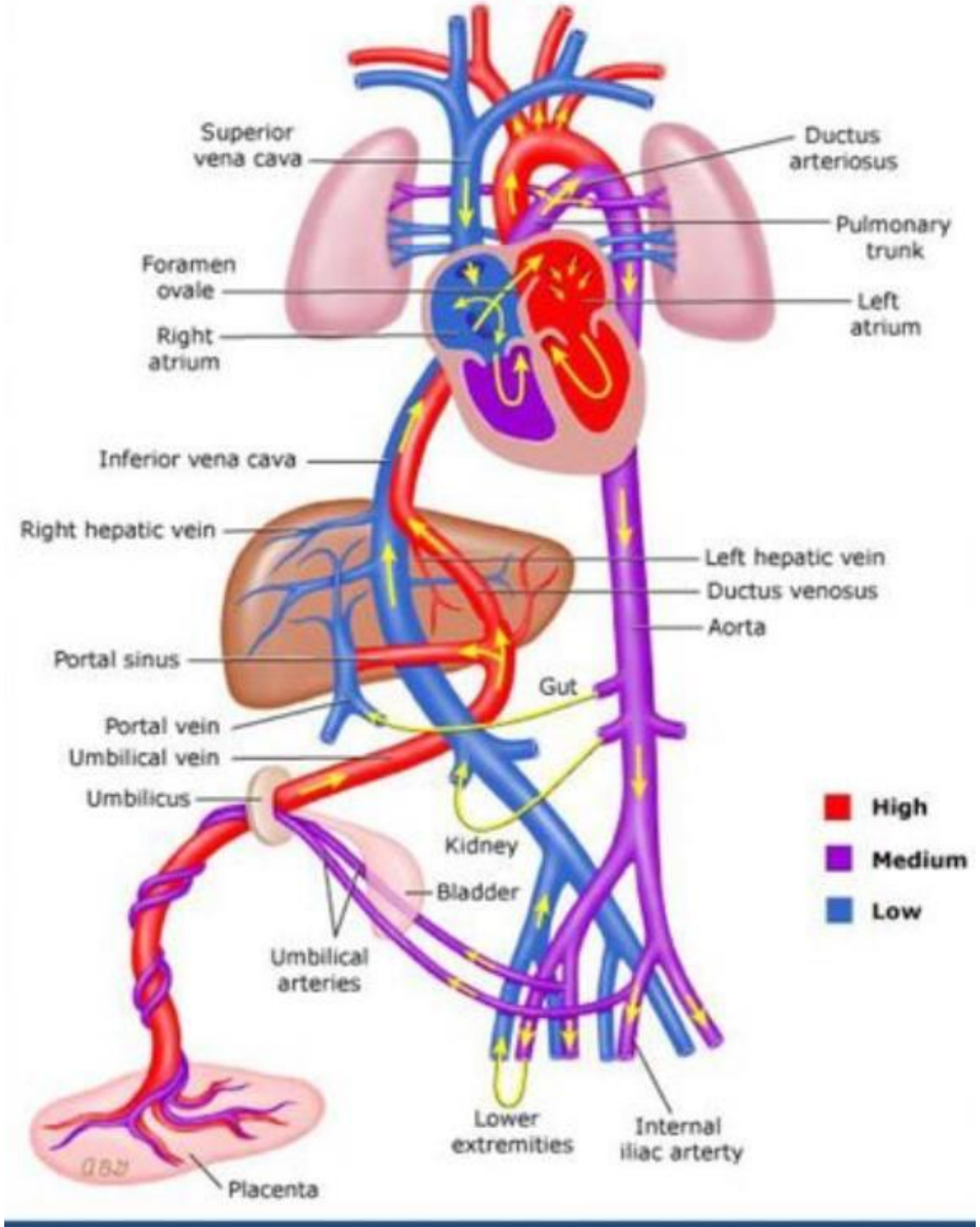
Special Structures

- Connection between the **right and left atria** via the **foramen ovale**
- Connection between the **truncus pulmonalis and the aorta** via the **ductus arteriosus**
- The **ductus venosus** shunts most of the left umbilical vein blood flow directly to the inferior vena cava. Thus, it allows oxygenated blood from the placenta to bypass the liver.
- The **hypogastric arteries** enter the umbilical cord and are then known as the **umbilical arteries**.

Circuit

- From the placenta, oxygenated blood flows through the umbilical vein and splits upon entering the abdomen of the fetus.
- The majority flows through the ductus venosus into the inferior vena cava, and then the right atrium; the remaining blood perfuses the liver.
- Blood originating from the ductus venosus enters the right atrium and, because of a streaming effect, is largely shunted through the foramen ovale into the left side of the heart and aorta.

- In contrast, less oxygenated blood from the superior vena cava and the inferior vena cava distal to the ductus venous flows from the right atrium into the right ventricle with minimal mixing with the oxygenated blood originating from the ductus venosus .
- Almost all the right ventricular output (90 percent) bypasses the lung and is shunted through the patent ductus arteriosus to the descending aorta distal to the origin of the carotid arteries.
- This deoxygenated blood is transported through the aorta and the umbilical arteries to the placenta, where it releases carbon dioxide and waste products and collects oxygen and nutrients.


Superior vena cava
Ductus arteriosus
Pulmonary trunk
Foramen ovale
Left atrium
Right atrium
Inferior vena cava
Right hepatic vein
Left hepatic vein
Ductus venosus
Aorta
Portal sinus
Gut
Portal vein
Umbilical vein
Umbilicus
Kidney
Bladder
Umbilical arteries
Lower extremities
Internal iliac arterty
Placenta
High
Medium
Low

Differential blood flow

- In the fetus, the blood flow is structured so that vital organs (eg, liver, heart, and brain) receive blood with a relatively high degree of oxygen saturation.

1<u>LIVER:</u> receives blood directly from the umbilical vein without mixing with deoxygenated fetal blood.

2<u>HEART AND BRAIN:–</u> Blood flowing through the coronary and carotid arteries has a high degree of oxygen saturation because oxygenated blood from the umbilical vein flows to the right atrium (via the ductus venosus and inferior vena cava) and is shunted through the foramen ovale to the left side of the heart and aorta

The deoxygenated blood is directed toward the right ventricle and shunted through the ductus arteriosus to the aorta, but distal to the origin of the carotid and coronary arteries

TRANSITION AT DELIVERY

To successfully make the transition from intrauterine to extrauterine life when the umbilical cord is clamped at birth, the neonate must rapidly make physiologic changes in cardiopulmonary function. **A successful transition is characterized by the following feature:**

1**Alveolar fluid clearance** — Several mechanisms contribute to the clearance of alveolar fluid and lung aeration, including labor, initial breaths, and thoracic squeeze

2**Circulatory changes** — With the clamping of the umbilical cord, the placenta with its low vascular resistance is removed from the neonatal circulation, resulting in a rise in neonatal systemic blood pressure.

3**Lung expansion** — With the first effective breath, air movement begins as intrathoracic pressure falls, starting at pressures of less than -5 cm H O. Increasing inspiratory pressure expands the alveolar air spaces and establishes functional residual capacity (FRC).

Lung expansion also stimulates surfactant release, which reduces alveolar surface tension, increases compliance, and stabilizes the FRC

DIFFICULTIES IN TRANSITION

Although most neonates successfully transition between intrauterine and extrauterine life, about 10 percent will have some difficulty and require resuscitative efforts at birth.

Neonatal difficulties at birth include the following:

1- Lack of respiratory effort 2- Blockage of the airways 3- Impaired lung function

4- Persistent increased pulmonary vascular resistance (also referred to as persistent pulmonary hypertension or persistent fetal circulation)

Risk factors

The following risk factors are associated with a greater likelihood of having difficulty making a successful transition and of requiring resuscitation:

1**Maternal conditions** – Advanced maternal age, maternal diabetes mellitus or hypertension, maternal substance use disorder, or previous history of stillbirth, fetal loss, or early neonatal death

2 **Neonatal conditions** – Prematurity, postmaturity, congenital anomalies, or multiple gestation

3**Antepartum complications** – Placental anomalies (eg, placenta previa), or either oligohydramnios or polyhydramnios

4 **Delivery complications** – Transverse lie or breech presentation, chorioamnionitis, foul smelling or meconium-stained amniotic fluid.

Changes in the Fetal Circulation after birth

Foramen ovale → Fossa ovalis
Ductus arteriosus→ Ligamentum arteriosum Ductus venosus → Ligamentum venosum Umbilical arteries → Umbilical ligament Umbilical vein → Ligamentum teres

Fetal Vs Infant Circulation

Fetal	Infants
• Low pressure system • Right to left shunting • Lungs non-functional • Increased pulmonary resistance • Decreased systemic resistance	• High pressure system • Left to right blood flow • Lungs functional • Decreased pulmonary resistance • Increased systemic resistance