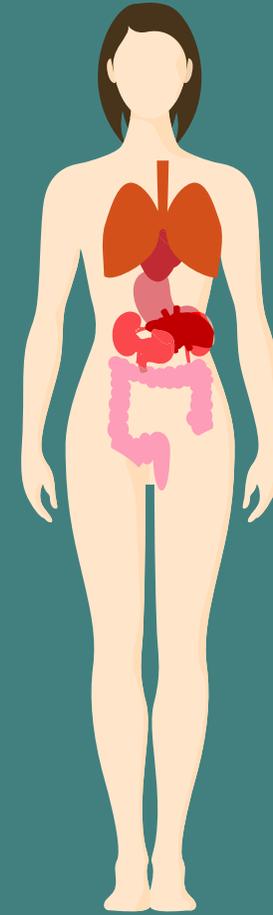


# Physiological Adaptations in Pregnancy

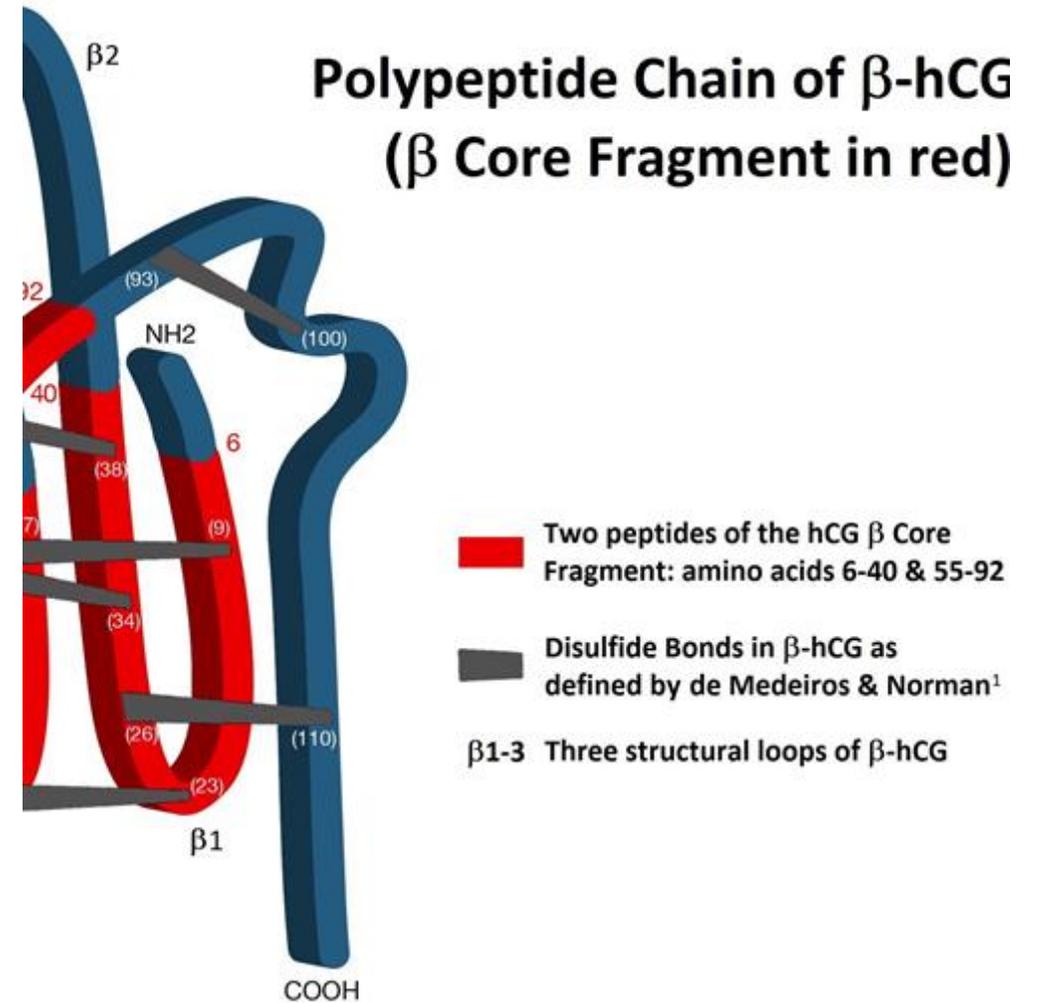


- “The pregnant woman experiences many physiologic changes to meet the demands of the developing fetus, maintain homeostasis and prepare for birth and lactation”

- Simpson and Creehan ( 2021) Chapter 3, pg. 48 (Blackburn)



- Elevated in multiple and molar pregnancies



# HUMAN PLACENTAL LACTOGEN

- Essential for fetal growth as it alters maternal protein, carbohydrate and fat metabolism and acts as an insulin antagonist
- ↑ free fatty acid availability for maternal metabolic and  
↓ maternal glucose uptake and use
  - Allows glucose to be reserved for fetal use
- ★ • Mother will be at a higher risk for ketosis with significant ↓ in maternal food intake

# A Word About Metabolic Demands

## ENERGY METABOLISM



Food



Digestion



Energy

# Metabolic Changes During the First Half of Pregnancy

In pregnant women **without** diabetes approximately at 8-15 weeks gestation an increase in Progesterone & Estrogen

- This causes an increase in the number of beta cells
- The increase in beta cells causes an increase in insulin production and secretion

There is an increased tissue sensitivity to insulin - ↑ in fat and glucose storage and ↓ in blood glucose by 10%

## Hyperinsulinemia State



Lipogenesis, which means mom can store energy in the form of fat

This is necessary to help prepare for the demands of growing this fetus in the second half of pregnancy

These changes may put mom at an increased risk of hypoglycemia

Insulin dependent diabetic moms may not need as much insulin during this time frame

# Metabolic Changes During the Second and Third Trimesters in Pregnancy

- Protein and fat breakdown characterized by:
  - ↑insulin resistance due to production of placental hormones :
    - Prolactin
    - Human placental lactogen (hPL)
    - Cortisol
    - Growth hormones

All of these hormones act as insulin antagonist and are aimed at giving the fetus more nutrients

## In Women Who Cannot Meet the Demands for Insulin Production

- Leads to an altered carbohydrate metabolism which progresses to hyperglycemia:
  - ↑ in hPL
  - ↑ in estrogen, progesterone, blood triglycerides, free fatty acids and corticosteroids

# ESTROGENS (estrone, estradiol & estriol)

- Prepares the breast for lactation
- Rapid<sup>↑</sup> last 6 weeks in pregnancy
  - Factor in onset of labor
- Hyperemia of the upper airway results from elevated estrogen levels and increased plasma volume can cause the tissues to become more friable and prone to increased bleeding.



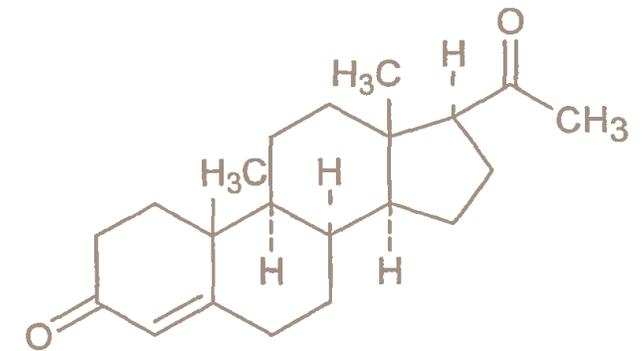
[https://encrypted-tbn1.gstatic.com/images?q=tbn:ANd9GcQdShy\\_kNLjgXwWoqZuZBmTHqqX8Cdqu7DUPQ3yQif-6h5o4Wn2](https://encrypted-tbn1.gstatic.com/images?q=tbn:ANd9GcQdShy_kNLjgXwWoqZuZBmTHqqX8Cdqu7DUPQ3yQif-6h5o4Wn2)

- Kikuchi, J and Deering, S. (2018) pg. 34

# PROGESTERONE

- Prevents rejection of the fetus
- Elevated levels of progesterone cause an increase in minute ventilation
  - Due to an increase in ventilation, pregnant patients typically experience mild respiratory alkalosis

- Kikuchi, J and Deering, S. (2018) pg. 34

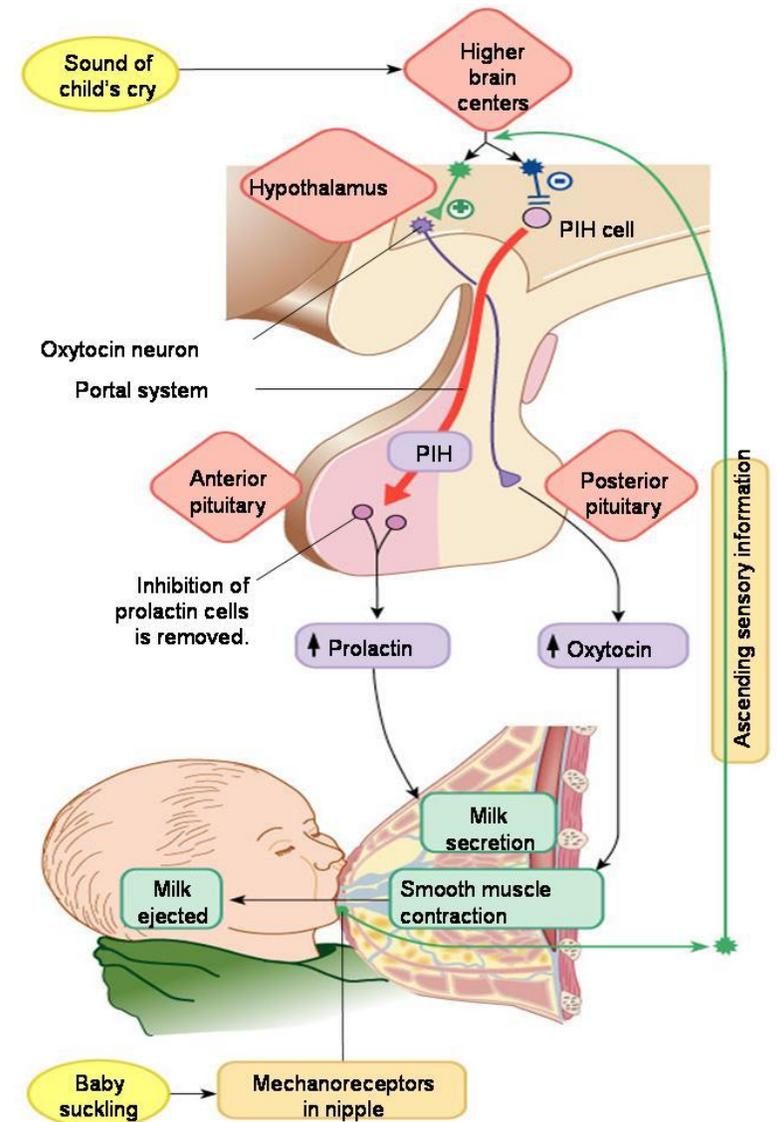


# PROSTAGLANDINS

- PGI<sub>2</sub> & Thromboxane thought to contribute to hypertensive disorders
- Effect smooth muscle contractility
  - Mediate the onset of labor, myometrial contractility and cervical ripening

# PROLACTIN

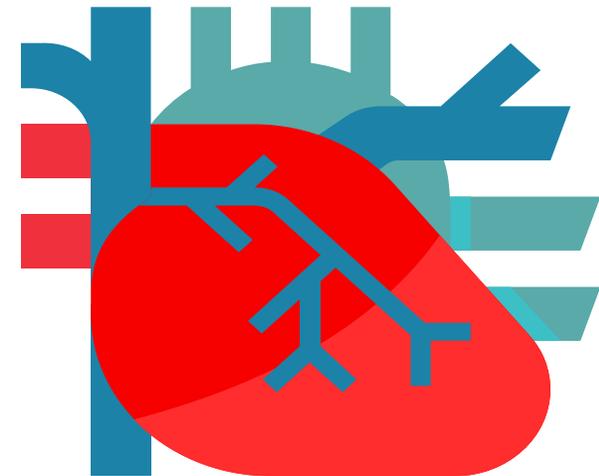
- Released from the anterior pituitary gland
- Increase in and maturation of ducts in the breast to aid in breastfeeding
  - After removal of the placenta, high levels of estrogen and progesterone disappear [prolactin inhibitors] signaling the anterior pituitary gland to produce prolactin
- Levels rise rapidly and are elevated by the infants suckling



# CARDIOVASCULAR

## ***Physiologic Changes in Pregnancy That Affect Cardiovascular Stress***

Pregnancy is a natural stress test because the cardiovascular system undergoes structural and hemodynamic adaptations to sustain a high-volume load. An understanding of these physiologic changes is essential for health care providers.



# CARDIOVASCULAR

- Size, position, & volume changes result in transient changes:
  - 96% develop transient systolic ejection murmur heard above the left sternal border. Usually disappear after birth
- Decreased vascular resistance and peripheral vasodilation
- Increased cardiac output
  - 30-50% by 25-30 weeks & on
- Heart rate may increase 10-15bpm above baseline



(Davidson et al., 2024 & Lowdermilk et al., 2024)

# CARDIOVASCULAR

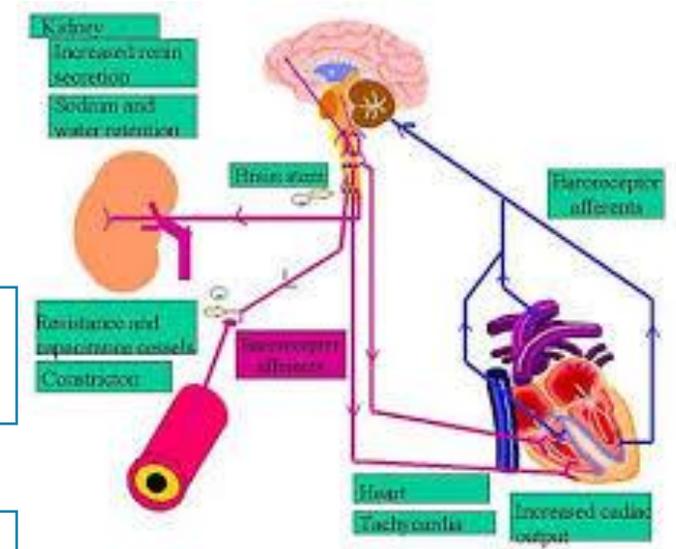


- BP slightly decreases & returns to near baseline by term
  - Lowest point during 2nd trimester
  - MAP more reliable
- Increased femoral venous pressure – uterus exerts increasing pressure on venous return
  - Dependent edema in lower extremities
  - Varicose veins in legs, vulva, rectum
  - Increase in postural hypotension
- Decreased plasma albumin
  - Further exacerbates edema through maintenance of fluid in extracellular spaces

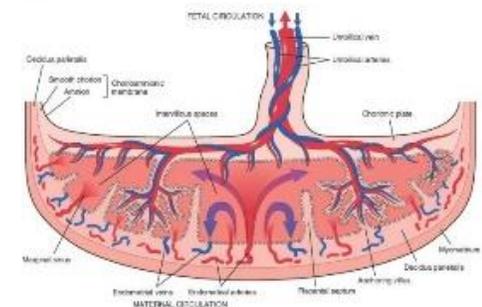
Increase in blood volume

Increase in cardiac output

Dilated low resistant blood vessels

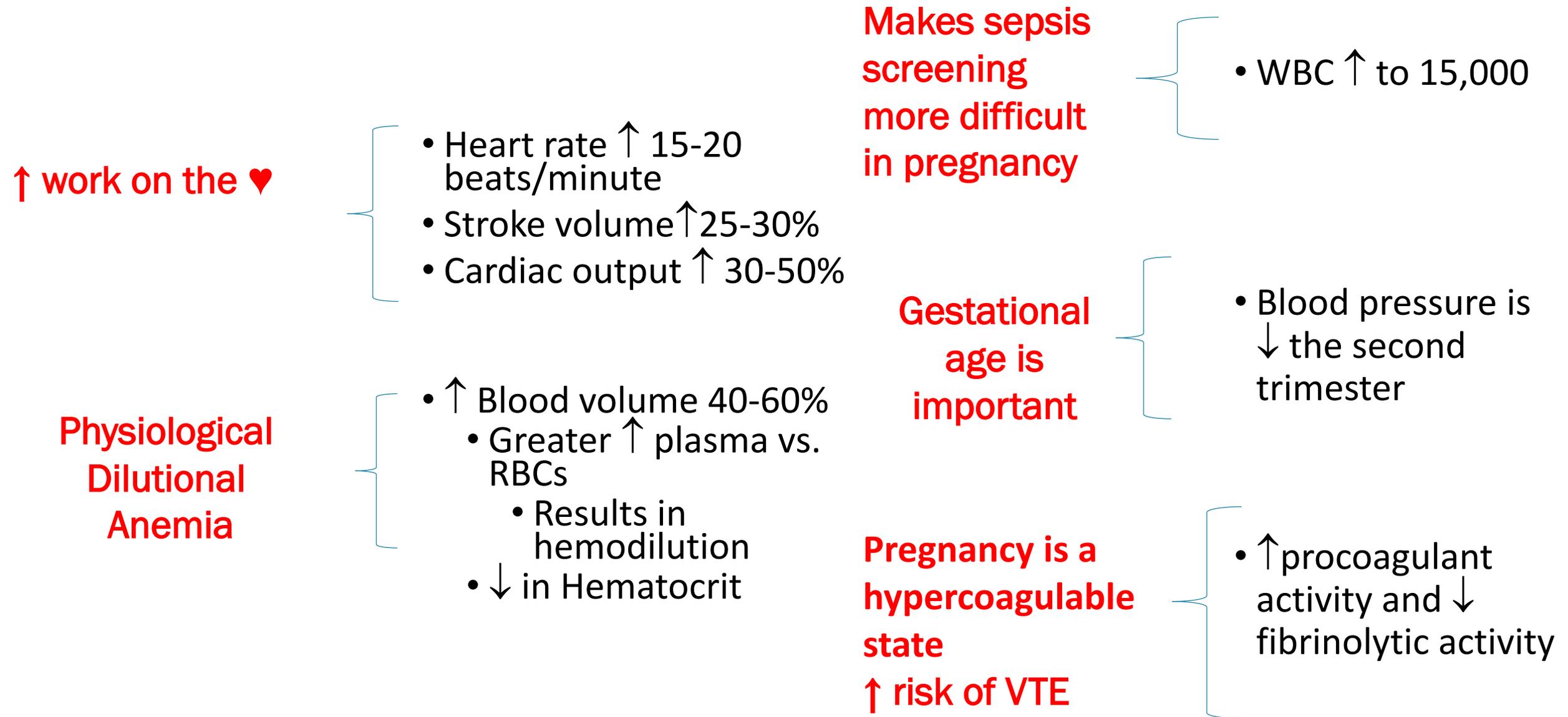


End Organ Perfusion



Think of the Placenta as an End Organ!

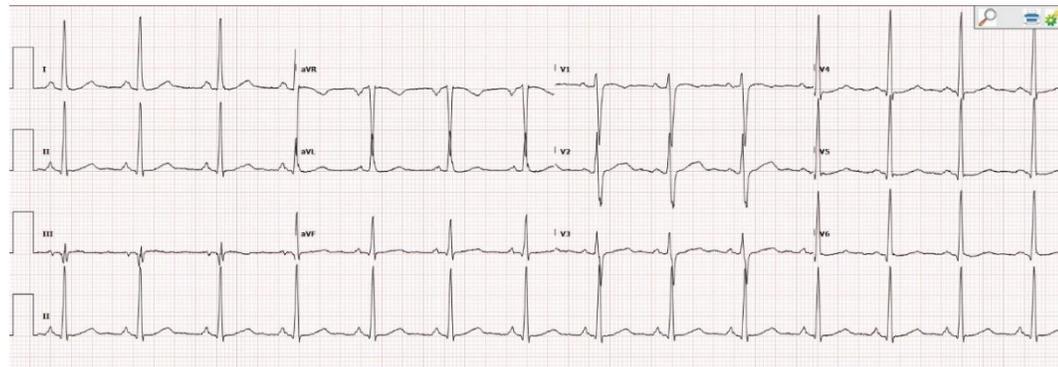
# NORMAL PHYSIOLOGIC CHANGES OF PREGNANCY

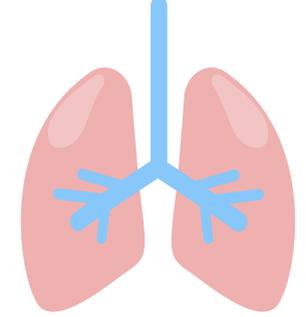


# EKG Changes

- Nonspecific T wave changes
- Left axis deviation
- Increased HR
- Increased QRS amplitude
- Intervals DO NOT CHANGE

Interpretation		History	
SINUS RHYTHM NONSPECIFIC T-WAVE ABNORMALITY			
Vent rate	83	BPM	
PR int	143	ms	
QRS dur	98	ms	
QT/QTc	390	430	ms
P-R-T axes	25	27	24
Avg RR	719	ms	





- Ph  $\uparrow$  7.40-7.45
  - Compensated respiratory alkalosis
    - This allows the transfer CO<sub>2</sub> from the fetus to the maternal circulation
    - Elevated levels of progesterone cause an increase in minute ventilation
    - ★ • Due to an increase in ventilation, pregnant patients typically experience mild respiratory alkalosis

• Kikuchi, J and Deering, S. (2018) pg. 34

- Expiratory Reserve Vol
  - $\downarrow$  15-20%
- $\uparrow$  in Oxygen consumption
  - Shortness of breath is a common complaint
    - $\uparrow$  in progesterone in pregnancy – Respiratory stimulant – may be the reason women complain of shortness of breath and hyperventilate during labor
- Hyperemia of the upper airway results from elevated estrogen levels and increased plasma volume can cause the tissues to become more friable and prone to increased bleeding.
- O<sub>2</sub> saturation should be at a minimum of **95%** to perfuse the fetus!

# KIDNEYS

↓ in serum  
uric acid &  
serum  
creatinine

- ↑ in renal blood flow increases by 80% and glomerular filtration rate ↑ by 40 – 60 %

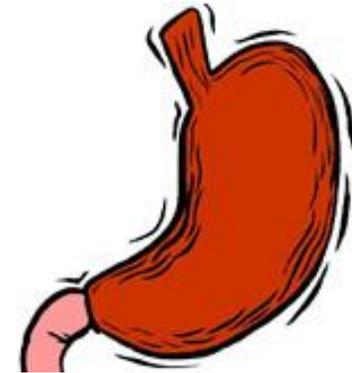
↑ in urine  
output

- Hypertrophy of the kidneys due to ↑ in blood volume
- ↑ Dilatation of the ureters on the right side is more pronounced than on the left side
  - Cushioning that occurs due to the displacement of the uterus by the sigmoid colon.
  - Increased risk of urinary tract infections



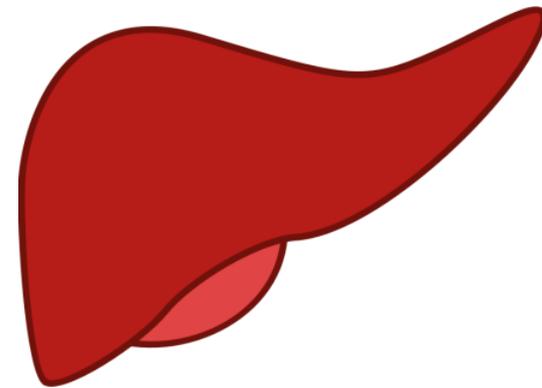
# STOMACH

- Progesterone
  - Decreases stomach gastric smooth muscle tone and motility
    - Longer for the stomach to empty
- Gravid uterus displaces the stomach



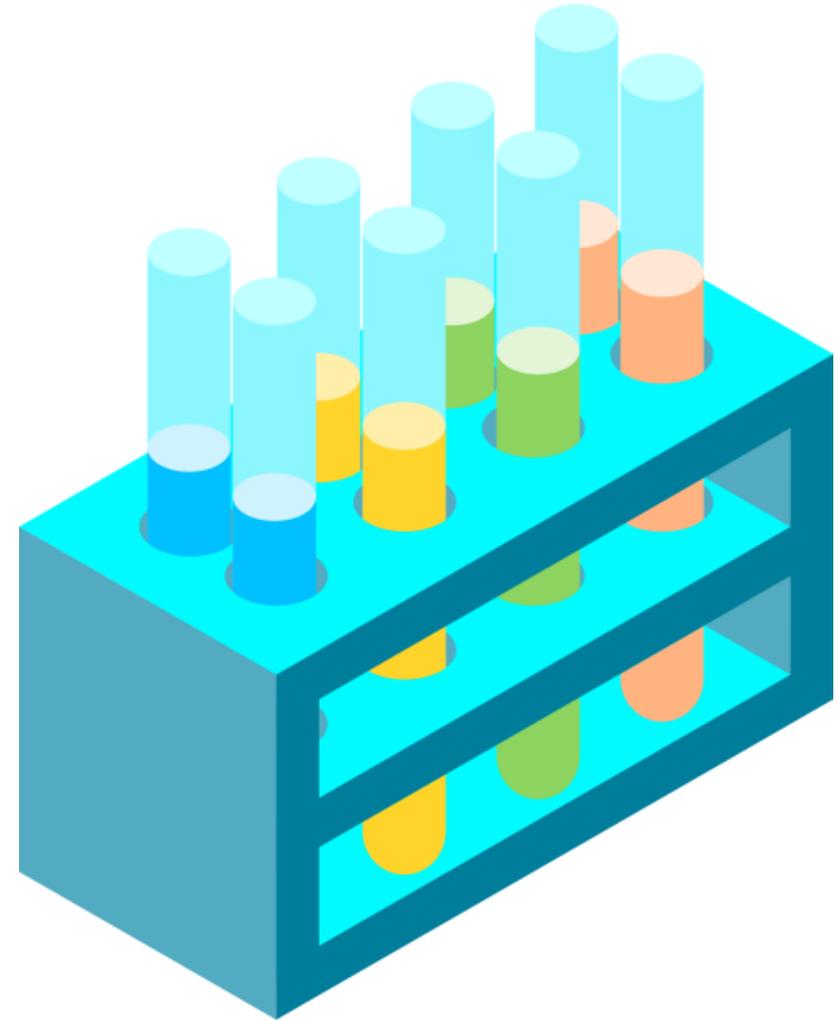
# LIVER

- Size and structure does not change during pregnancy
- Fibrinogen levels  $\uparrow$  by 50% by the end of 2<sup>nd</sup> trimester
- Plasma albumin concentrate  $\downarrow$



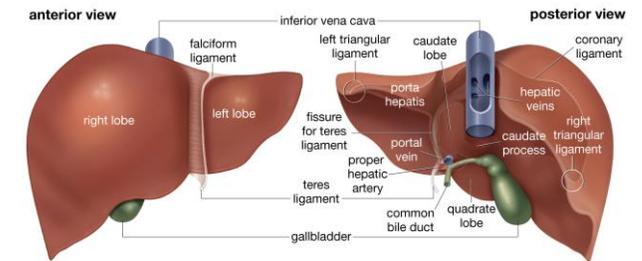
# LIVER Continued

- Serum alkaline phosphatase & serum cholesterol can be doubled and higher in multiple gestation
- Aspartate (AST), Serum bilirubin & Alanine aminotransferase (ALT) are normal or slightly lower in pregnancy – making these test good markers for liver disease in pregnancy



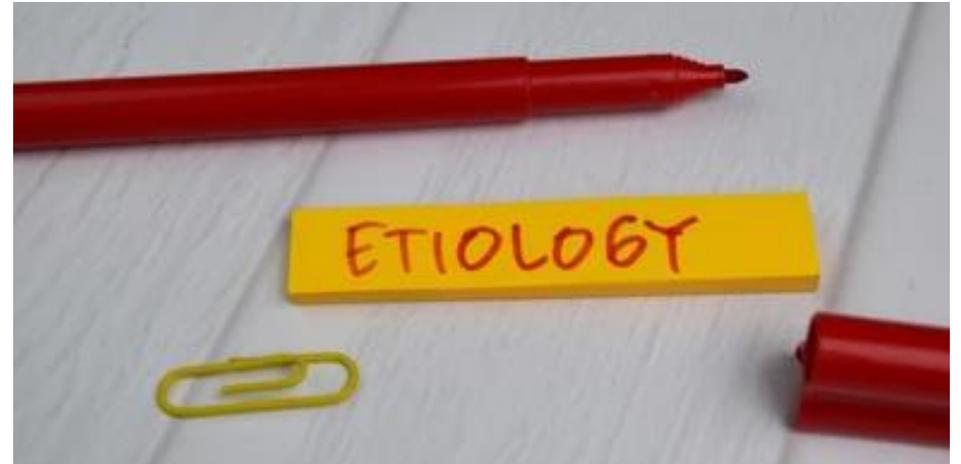
# Intrahepatic Cholestasis of Pregnancy (ICP)

- Characterized by pruritus and ↑serum bile acid concentrations
  - Typically developing in the late second and or third trimester and resolving after delivery
- Incidence
  - Varies widely worldwide ranging from <1 to 27.6 % (reasons unknown)
  - More common in the winter months and in some countries (Sweden, Finland and Chile)
  - Multiple gestations
  - Women with a history of ICP in previous pregnancies



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- Not completely understood
- Increased risk in first-degree relatives
  - ( mutation of ABCB4 gene)
- Estrogen and Progesterone
  - Occurs in 2<sup>nd</sup> half of pregnancy – when serum concentrations of estrogen reach peak levels
  - Women taking estrogen-progesterone contraceptives
  - Reported in women in early pregnancy who have had ovarian hyperstimulation
  - Resolves after delivery of placenta
    - Why???
    - Unknown if exogenous progesterone during pregnancy  $\uparrow$  ICP
- Seasonal and geographic variability
- Underlying liver disease



# Presentation

- Pruritus
  - Ranges from mild to intolerable
  - Usually starts on the palms and soles of the feet and worse at night
- Right upper quadrant pain
- Nausea
- Poor appetite
- Sleep deprivation
- Steatorrhea ( fatty stools due to ↓ fat absorption)



<https://www.todayparent.com/wp-content/uploads/2018/10/Obstetric-Cholestasis-1280x960-768x432-1540325242.jpg>

# Laboratory Findings

- ↑ in serum total bile acid concentration (levels up to 11.0  $\mu\text{mol/L}$ )
  - May be the first and only laboratory abnormality
- Serum aminotransferases – elevated 60% of cases
- Alkaline phosphatase
  - May be elevated fourfold but is not specific for ICP during pregnancy
- Total and direct bilirubin concentrations – may be elevated by 25%
  - Rarely exceed levels  $> 6\text{mg/dL}$

# Risks

- Are mainly for the fetus:
  - Intrauterine fetal demise
  - Meconium-stained amniotic fluid
  - Preterm delivery
  - Neonatal respiratory distress syndrome due to bile acids entering the lungs
- Maternal bile acid levels and risk of fetal demise:
  - <40 micromol/L (0.13%)
  - 40-99 micromol/L (0.28%)
  - $\geq$  100 micromol/L (3.44%)



<https://cdn.corporatefinanceinstitute.com/assets/accepting-risk-1024x599.jpeg>

# Pregnancy Management

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- May include biweekly modified biophysical profiles
  - The value of antepartum testing in ICP is unproven
    - Fetal demise may be due to a sudden event not the result of chronic placental dysfunction
  - Maternal bile acids cross the placenta and can accumulate in the fetus and amniotic fluid
    - Carries significant risks for the fetus
      - In normal pregnancies the bile salts are transported via the placenta
      - In ICP – transport is reversed which results in an increase in bile salts in the fetus and amniotic fluid



# Pharmacology

- Ursodeoxycholic acid (UDCA)
  - Optimal dose is not determined
  - 300mg TID or 15mg/kg per day until delivery
    - Side effects – nausea and dizziness in 25% of patients

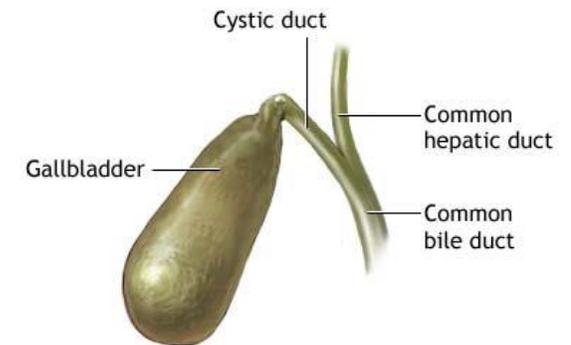
# Timing of delivery is based upon maternal bile acid concentrations



- $<40$  micromol/L
  - Delivery @ 37 0/7<sup>th</sup> to 38 6/7<sup>th</sup> weeks
- 40-99 micromol/L
  - 36 0/7<sup>th</sup> to 37 0/7<sup>th</sup>
- $\geq 100$  micromol/L
  - 36 0/7<sup>th</sup>
- Delivery may be sooner for women with:
  - A prior history of fetal demise before 36 weeks with ICP
  - Excruciating and unremitting maternal pruritis not relieved with pharmacotherapy.
  - Worsening hepatic function

# GALLBLADDER

- Unlike the liver, size and function are altered during pregnancy
- Elevated levels of progesterone cause the gallbladder to become hypotonic and distended



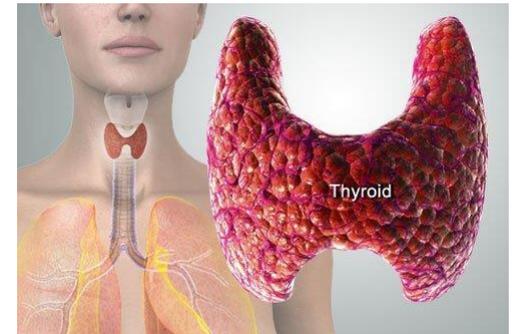
# WEIGHT GAIN IN PREGNANCY

- On average, 300 kcal are needed per day for the fetus
- Institute of Medicine Guidelines:
  - 1<sup>st</sup> Trimester - 1.1 to 4.0 lb. weight gain
  - 2<sup>nd</sup> and 3<sup>rd</sup> Trimesters varies with BMI
    - 0.8 to 1.0 lb./week for normal BMI
    - 1.0-1.3 lb./week for underweight women
    - 0.6 to 0.7 lb./week in overweight women
    - 0.4 to 0.6 lb./week in obese women



# THYROID

- Maternal thyroid hormone is critical for fetal CNS development
  - Especially during **early** pregnancy prior to the fetus ability to produce thyroid hormone
  - Poor control can lead to fetal loss, ↓ in brain development and later mental retardation



<https://images.medicinenet.com/images/slideshow/thyroid-symptoms-and-solutions-s2.jpg>



# IMMUNE SYSTEM

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- Immune Innate Responses in Pregnancy
  - ↑ in WBCs (especially neutrophils and monocytes)

# NEUROMUSCULAR AND SENSORY SYSTEMS

In general, no major CNS changes in pregnancy

- Decreased attention, concentration and memory reported
- Blood vessel changes increase risk of aneurysm rupture

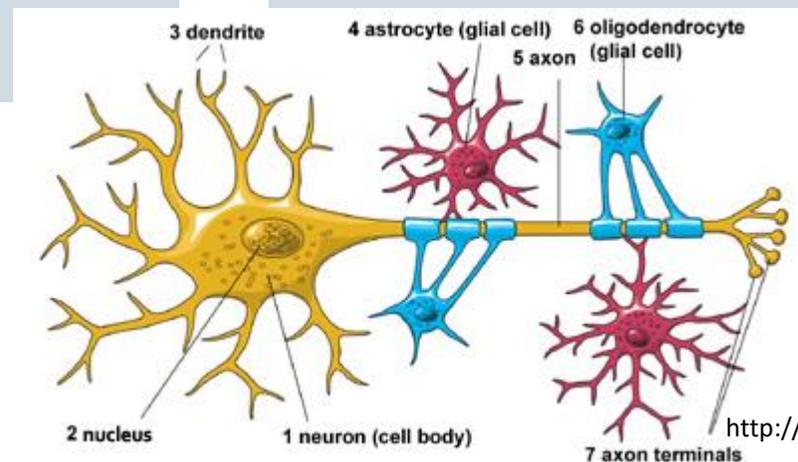
Mild frontal headaches 1<sup>st</sup> and 2<sup>nd</sup> trimester may be due to tension or hormones

- **Severe headache after 20 weeks gestation may be an indicator of preeclampsia**



Dizziness may be due to

- Vasomotor instability
- Postural hypotension
  - After long periods of sitting/standing
- Hypoglycemia



# VAGINA

- Mucosa thickens
- Connective tissue loosens
- Smooth muscle hypertrophies
- Increased vascularity
  - Blue/purple color
  - Chadwick sign



<https://encrypted-tbn0.gstatic.com/images?q=tbn:ANd9GcQwpC4zbSSfyK5u035z6TISgk8-21KxJ0qDig&usqp=CAU>

# UTERUS

- Growth initially simulated by increase in estrogen and progesterone, increased vascularity & dilation of blood vessels
- Later by mechanical distention
- Increase in blood and lymphatic vessels
- 1/6 total maternal blood volume contained within uterine vasculature

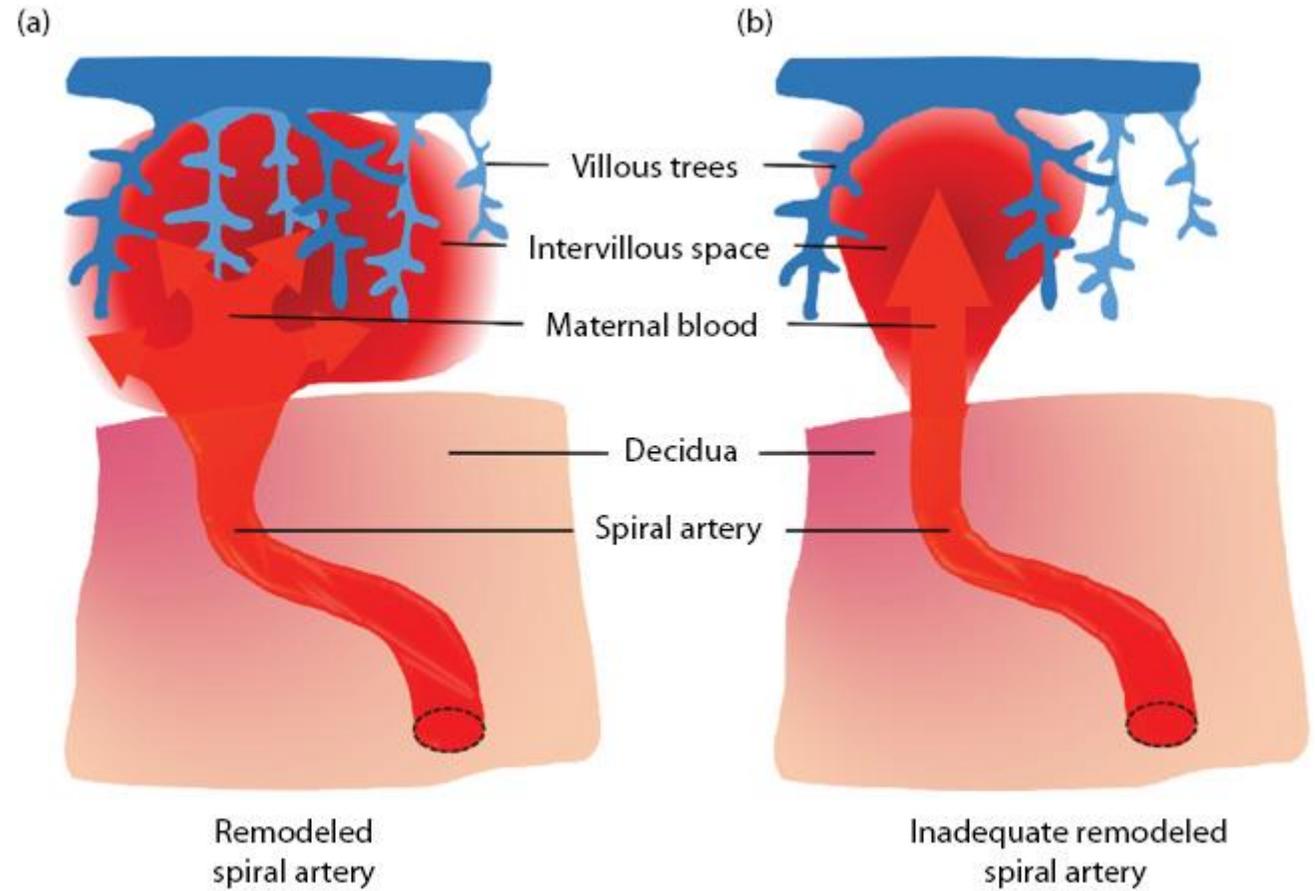
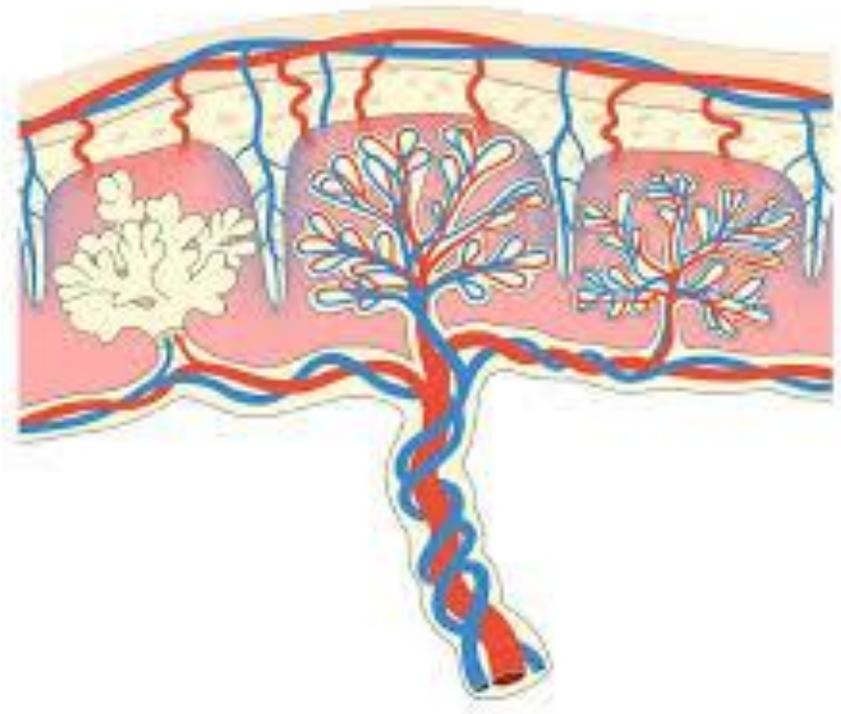
	Pre-pregnancy	Pregnancy
Weight	70 grams / 2.5 ounces	1100 grams / 2.5 lbs
Capacity	10ml	5,000ml



- Maternal position, maternal arterial pressure and uterine contractility influence uterine blood flow
  - Regulated by the BP and SVR (Systemic Vascular Resistance)
  - Supine position compresses inferior vena cava and aorta, ↓ blood flow

IMPORTANT TO  
REMEMBER IN A  
LABORING PATIENT  
RELATED TO THE  
UTERUS

# Placenta



<https://encrypted-tbn0.gstatic.com/images?q=tbn:ANd9GcQAQ0pYcPKUbluVursOloiBbX-hoO7YN2vOeA&usqp=CAU>

<https://i2.wp.com/obgynkey.com/wp-content/uploads/2020/05/101496.jpg?w=960>

# PHYSIOLOGY OF THE PLACENTA & SPIRAL ARTERIOLES

- During normal pregnancy – the uterine spiral arteries within the placenta and myometrium are transformed from small, high-resistant vessels to dilated, low resistant vessels
  - This helps ↑ placental circulation and is called “Angiogenesis”
  - See picture on next slide

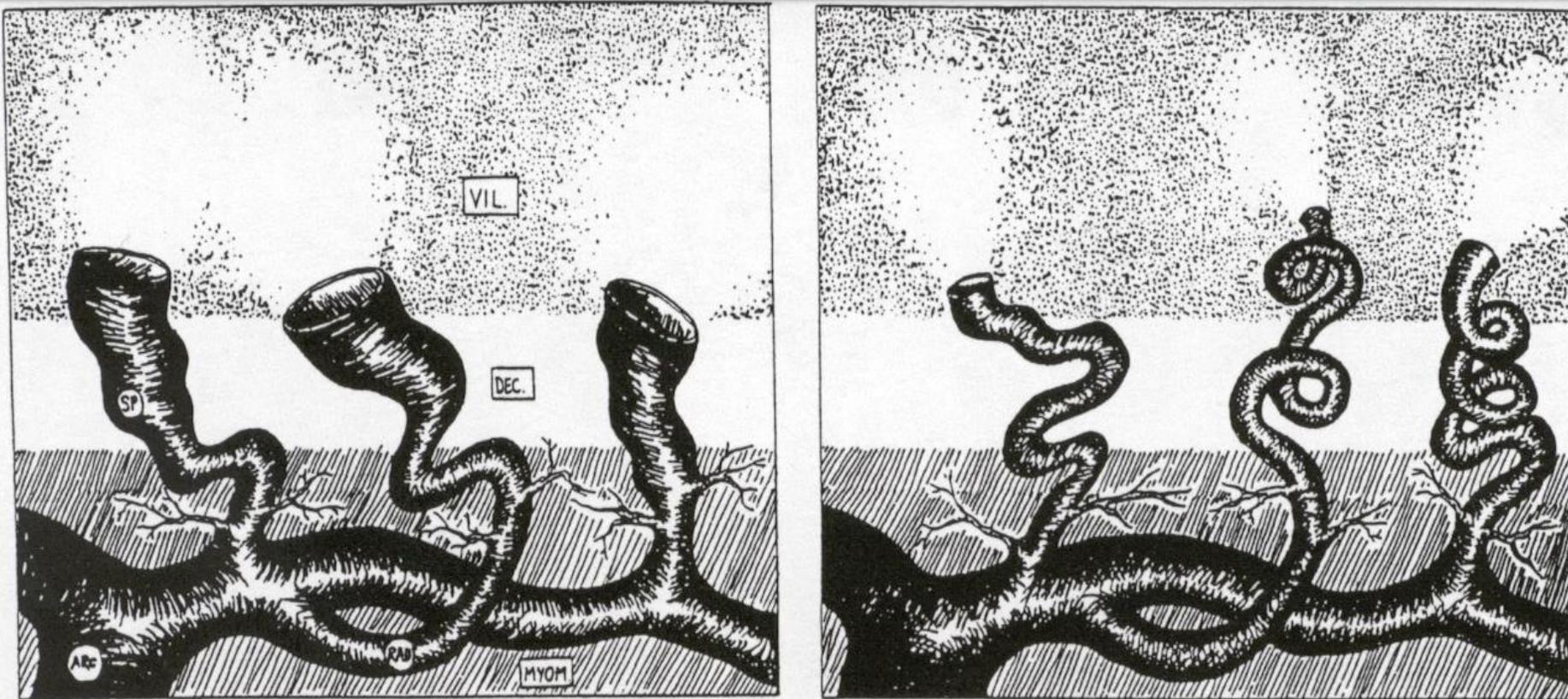


Fig. 1. Diagram illustrating defective placentation. The left side of the diagram shows normal adaptation of spiral arteries to pregnancy, whereas the right side depicts this process in preeclampsia. *Vil*, intervillous space; *sp*, spiral artery; *dec*, decidua; *rad*, radial artery; *arc*, arcuate artery; *myom*, myometrium.

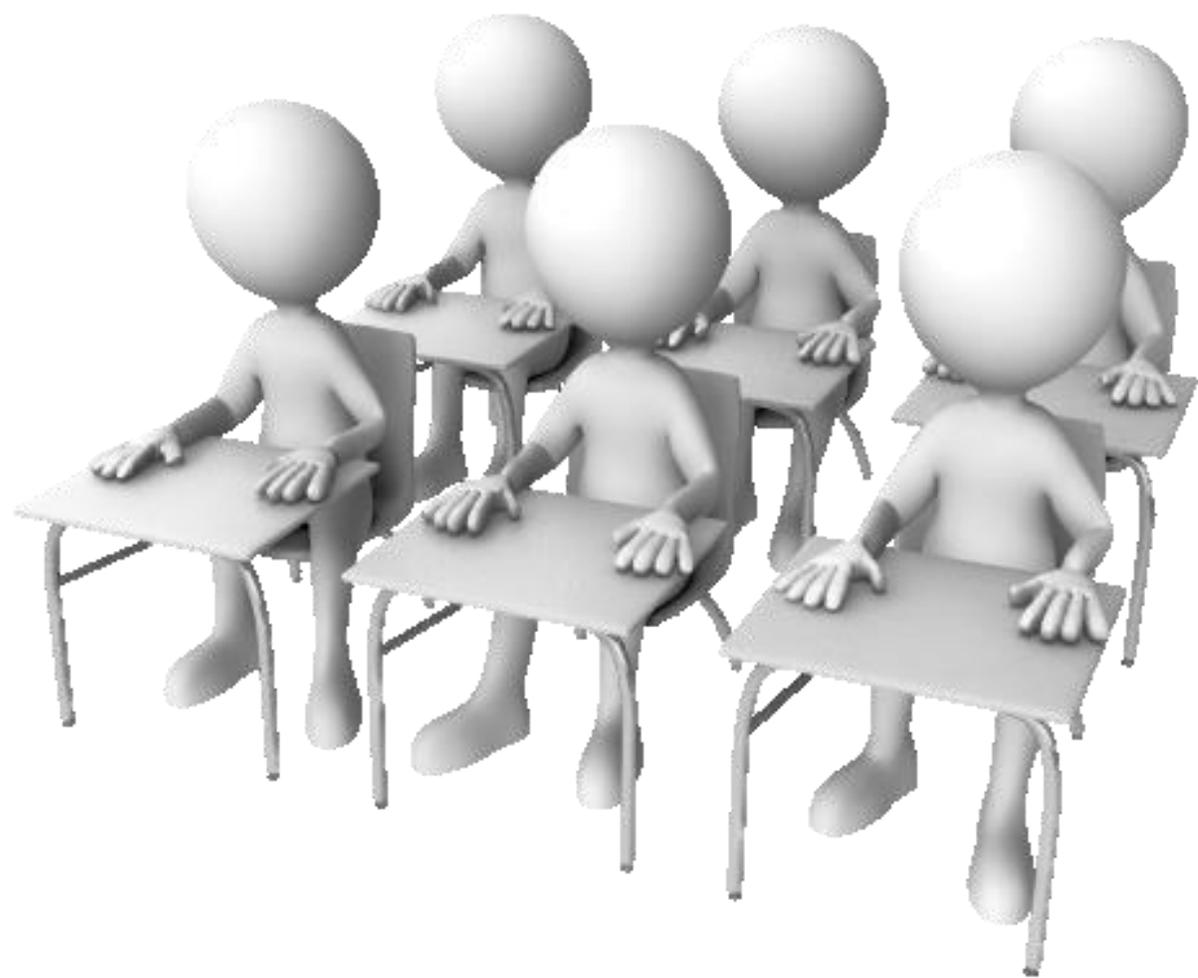
- Lack of Angiogenesis in pregnancy results in placental ischemia
- This leads to the production of placental factors that enter the maternal circulation
  - Maternal endothelia dysfunction occurs
  - Variety of manifestations of the disease of preeclampsia is from the reduced end organ perfusion



15 Minute  
YouTube Video  
on Physiological  
Changes in  
Pregnancy –  
Obtained  
January 2023

<https://www.youtube.com/watch?v=dLsy2pJjTEg>





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