Physiologic Changes in Pregnancy

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Case

28 year old G2T1L1 at 24^{+3} weeks GA presents to ER with nausea, vomiting and right lower quadrant pain,

- *Pregnancy history*- Uneventful, with early nausea treated with Diclectin, U/S at 18 weeks- normal, Blood type- A Rh+, VDRL/HbsAg/HIV- negative
- *PMHx*- Nil, no surgeries
- *Medications*- Prenatal vitamins, NKDA
- *Physical Exam*- AVSS, CVS and Resp- normal, Abdominal exam reveals tenderness and guarding in the right lower quadrant

- **Differential Diagnosis-** ?, During workup must understand what is normal in a pregnancy

Pregnancy is a normal **healthy condition** and simultaneously the **most common altered physiologic state** to which human beings are subject to

Objectives

- Identify the common physiologic changes of each organ system in pregnancy
- Identify the pathologic vs. physiologic changes
- What to expect when ordering diagnostic tests
- Understand how to proceed with a pregnant surgical patient
- Special considerations

Introduction

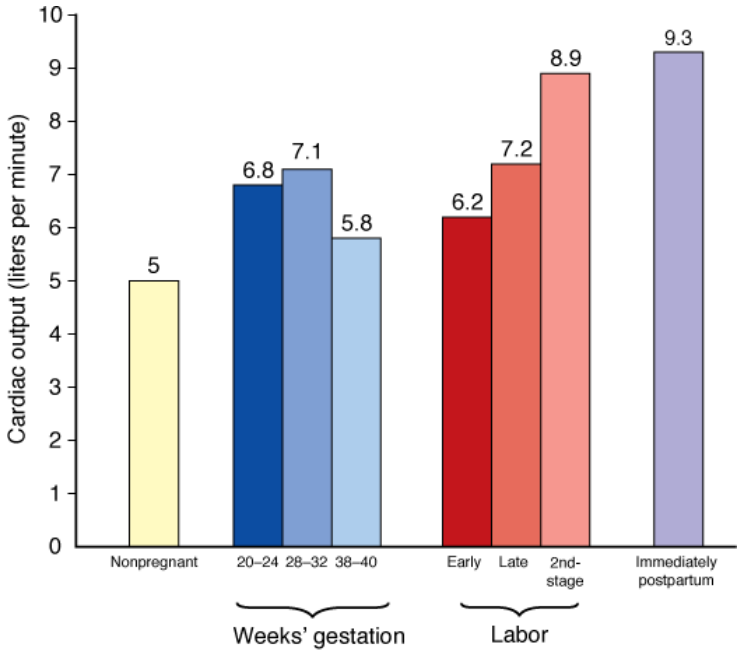
- Maternal physiologic adjustments in pregnancy occur to support the requirements of fetal homeostasis without jeopardizing maternal well being
- Maternal systems remodel to deliver substantial energy to the fetus and remove inappropriate waste products
- The normal values for many hematologic, biochemical and physiologic indices during pregnancy differ markedly from those in the non-pregnant range
- Important to understand these changes as pregnant patients can present with non-pregnancy related surgical emergencies
- Unique challenge as two patients to be cared for

Cardiovascular System

- **Cardiac output** and **blood volume** increase to meet maternal and fetal metabolic demands

- At term the blood volume has increased by 1000-1500 ml in most women
  - Each additional multiplet (twin/triplet) adds 500 cc of blood volume

- Cardiac chambers enlarge and myocardial hypertrophy is often noted on echocardiogram



Cardiovascular System specifics

- Increased **cardiac output** (40 % at term) is due to both increase in **HR** (15-30%) and **SV** (30%)
  - Resting tachycardia needs assessment

- **Blood pressure-** increase in CO, but **decrease in systemic vascular resistance** will result in decrease in **mean arterial pressure**
  - Decrease in **systemic vascular resistance** by the second trimester decreases both diastolic and, to lesser degree, systolic blood pressure
  - Beware of a high blood pressure in pregnancy

- Enlarging uterus compresses IVC and pelvic veins
  - Decreased venous return (hypotension)
  - Increased venous pressure (varicose veins, **hemorrhoids** and leg edema)

CVS physical exam findings/Investigations

Physical Exam

- Decreased BP- postural hypotension can occurs
- Increased HR
- Heart sounds
  - Systolic flow murmurs
  - Diastolic murmurs should be considered potentially pathologic
  - 3rd heart sound can occur after mid pregnancy
- Peripheral edema

EKG changes

- Increased HR, LAD, Inverted T waves in Lead III, Q waves in Lead III and AVF and unspecific ST changes

Echocardiogram

- Myocardial hypertrophy

Respiratory System

Major respiratory changes in pregnancy involve three factors:

1. **Mechanical-** Effects of the enlarging uterus with diaphragm displacement

2. **Consumption-** Increased need for oxygen

3. **Stimulation-** Progesterone acts as a respiratory stimulant

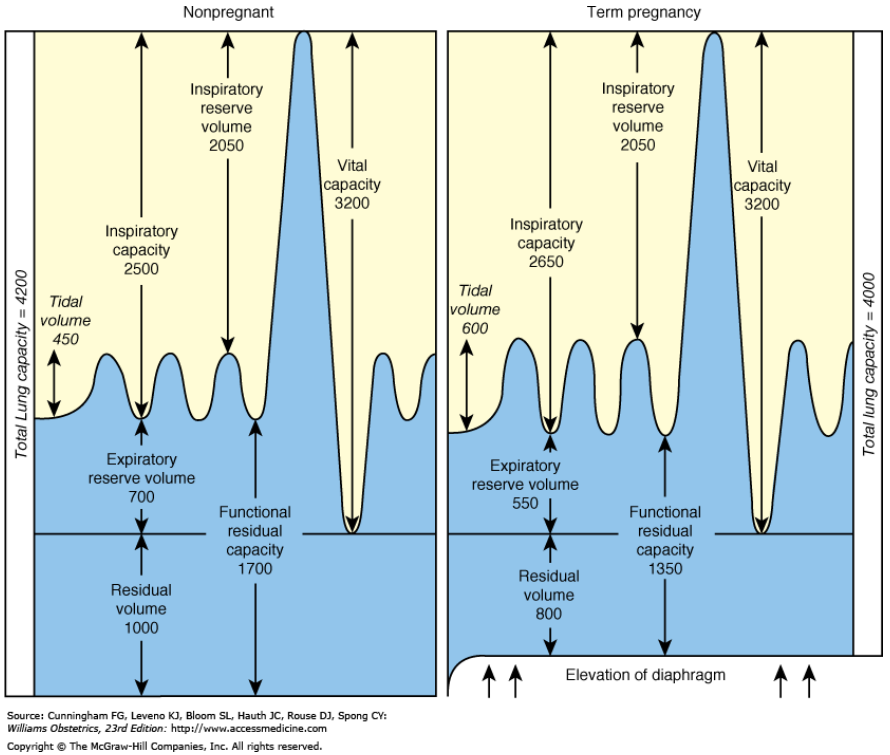
Respiratory mechanics in pregnancy

Diaphragm rises 4 cm

- Less negative intrathoracic pressure
- Decreased Functional Residual Capacity
- Decreased Expiratory Reserve Volume
- Decreased Residual Volume

No impairments in diaphragmatic or thoracic muscle motion

- Lung compliance remains unaffected



Consumption

- Oxygen consumption increases by 15-20%
- 50% of this increase is required by uterus
- Despite increase in oxygen requirements with the increase in CO and increase in alveolar ventilation oxygen consumption exceeds the requirements
- Arterial PCO_2 falls

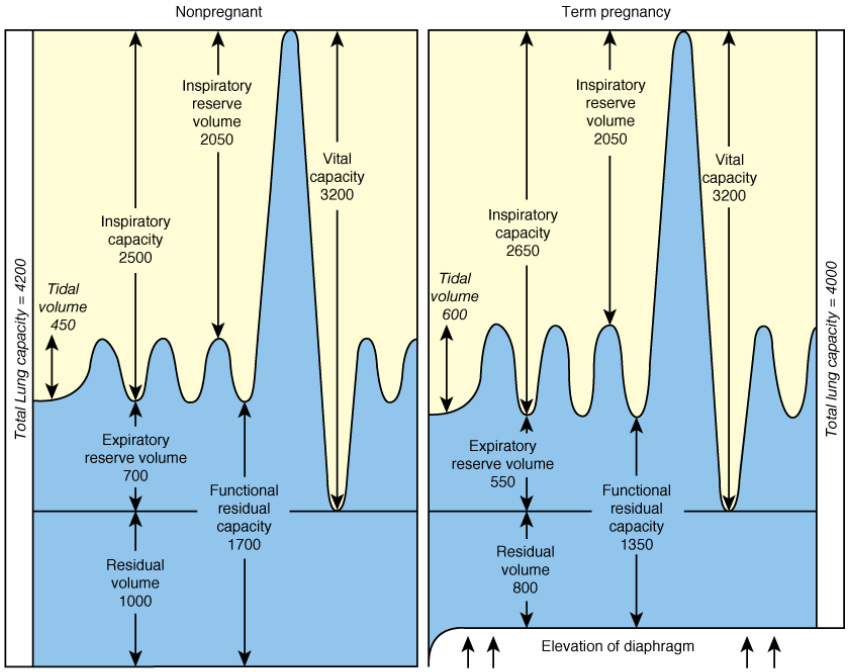
Stimulation

- Progesterone directly stimulates ventilation
- It also increases the sensitivity of the respiratory centers to CO_2

Additional respiratory points

Minute ventilation=Respiratory rate x Tidal Volume

- Tidal volume increases and RR stays same, so therefore minute ventilation increases
- Vital capacity- remains unchanged



Dyspnea of pregnancy

- Common symptom in pregnancy
- Up to 60-70% of women will experience at some point in their pregnancy
- Mechanism not established but may involve increased sensitivity and lower threshold to PCO_2

Hematological System

Pregnancy leads to a **hypercoagulable state** and **increased risk of thromboembolic disease**, due to

- Increased factors VII, VIII, X and XII
- Increased fibrinogen and FDPs
- Decreased fibrinolytic activity
- Decreased antithrombin III

Other hematologic changes:

- Increased WBC (up to 21)
- Platelets decrease by 10-20%

*In addition to hypercoaguable state **venous stasis** occurs- DVT/PE

Parameter	Nonpregnant	Pregnant
Activated PTT (sec)	31.6 +/- 4.9	31.9 +/- 2.9
Thrombin time (sec)	18.9 +/- 2.0	22.4 +/- 4.1
Fibrinogen (mg/dL)	256 +/- 58	473 +/- 72
Factor VII (%)	99.3 +/- 19.4	181.4 +/- 48.0
Factor X (%)	97.7 +/- 15.4	144.5 +/- 20.1
Plasminogen (%)	105.5 +/- 14.1	136.2 +/- 19.5
Antithrombin III (%)	98.9 +/- 13.2	97.5 +/- 33.3
Protein C (%)	77.2 +/- 12.0	62.9 +/- 20.5
Total Protein S (%)	75.6 +/- 14.0	49.9 +/- 10.2

Dilutional Anemia

- Increase in plasma volume
- **Increase in red blood cell mass** (lesser degree than increase in plasma volume)
- Results in a physiologically lowered hemoglobin, hematocrit and red blood cell count (no change in MCV)- different thresholds during pregnancy

Fe deficiency anemia- make up majority of causes of anemia in pregnant women- can start women on Fe replacement

Genitourinary System

Anatomical Changes

- Kidneys increase in length by 1-1.5cm
- Dilatation of renal calyces, renal pelvices and ureters
- Uterus can compress ureters at pelvic brim
- Due to dextrrotation of the uterus the right sided collecting system tends to be more dilated than left
- These changes lead to physiologic obstruction and urinary stasis, which results in an elevated risk for pyelonephritis, even in asymptomatic bacteriuria

* **Pyelonephritis** is the number one cause of non-pregnancy related hospital admission in a pregnant patient

Hydronephrosis. Plain film from the 15-minute image of an intravenous pyelogram (IVP). Moderate hydronephrosis on the right (*arrows) and mild hydronephrosis on the left (arrowheads) are both normal for this 35-week gestation.*

Genitourinary System

Physiologic Changes

- **GFR** increases
- Decrease in BUN and CR
- Increase in **urinary protein excretion**
- Although filtered load of sodium increases, the increase in tubular reabsorption leads to a net retention of sodium
- Glucosuria occurs because of increased GFR and decreased distal reabsorption
- Significant water retention- intravascular volume expands by 1-2L and extravascular by 4-7L. This results in a decrease in plasma sodium and in plasma osmolality

Gastrointestinal System

- Anatomic alterations secondary to displacement from uterus
- Increased intragastric pressure resulting in heartburn and hiatus hernia
- Appendix displaced superiorly and laterally (T2/T3)
- Increased incidence of hemorrhoids

- Physiologic changes are mediated by the smooth muscle relaxant effects of **progesterone**
- Decreased LES tone--> GERD and heartburn
- Decreased gastric and small bowel motility resulting in delayed gastric emptying
- Increased anesthetic risk--> regurgitation and aspiration

Hepatobiliary Changes

Anatomic

- Liver is shifted up and posteriorly
- Spider nevi and palmar erythema may be normal findings
- Dilation of the gallbladder and biliary duct system caused by progesterone
- Progesterone also inhibits cholecystokinin resulting in decreased gallbladder motility and bile stasis
- Increased incidence cholelithiasis

Laboratory Changes

- AST, ALT, GGT, bili are normal or slightly decreased
- PT and LDH levels are unchanged
- Albumin levels are decreased
- ALP levels increase

Endocrine and Metabolic Changes

Pituitary Gland

- Enlarges up to 135%
- Increased production of plasma growth hormone and prolactin

Thyroid

- Relative **iodine deficiency**
- Glandular hypertrophy (frank goiter however is not normal)
- Thyroid binding globulin increases due to estrogen effects
- Increase in total and bound T3 and T4 (free remains normal)
- TSH levels fall slightly in 1st trimester then recover later in pregnancy (changes in TSH due to α-HCG subunit)
- Practically this means that T3 and T4 is less helpful during pregnancy, use TSH

Endocrine and Metabolic Changes

Adrenal Glands

- Increased serum cortisol
- Increased serum aldosterone
- Increased adrenal androgens

Pancreas

- Beta cells undergo hyperplasia resulting in increased insulin secretion
- Peripheral insulin resistance increases throughout pregnancy

Immune System

- Decreased cellular immunity, with increase in humoral, or antibody mediated immunity
- This results in increased susceptibility to intracellular pathogens
- Cell mediated auto-immune diseases often improve during pregnancy

Musculoskeletal Changes

- Average 25-35 pound weight gain (vary depending on pre pregnancy weight)
- Increased force across joints
- Low back lordosis, forward neck flexion, widened stance
- Joint laxity
- Fluid retention can result in compression of nerves (eg carpal tunnel syndrome)
- These changes frequently result in pain, especially in the lower back

"The Faberge Egg"

aka The pregnant patient requiring non-obstetrical surgery

- 2 patients with unique vulnerabilities
- Need a heightened sense of awareness and avoid indecision or delay in treatment
- Delay in treatment can be the greatest danger in relation to morbidity and mortality
- Need to be aware of unique circumstances associated with each trimester of pregnancy
- Weigh the possible adverse effects on the fetus against the maternal risks of delaying the surgery
- Preop consultation between surgeon, anaesthesiologist, obstetrician and neonatologist

Common Indications for Surgery

- **Acute appendicitis**
- **Biliary Disease**
- **Trauma**
- **Breast**
- **Bowel obstruction**
- **Ureteric stenting**

Diagnostic imaging during pregnancy

- Safety of radiation to fetus is often concern but risk of delayed diagnosis can be greater risk
- Ultrasound and MRI are preferred if appropriate for confirmation of diagnosis
- Effects on fetus depend on gestational age, dose of radiation and fetal cellular repair mechanisms
- Radiation exposure of up to 5 rads is not associated with increased fetal anomalies, intellectual disability, growth restriction, or pregnancy loss

Fetal Radiation Exposure

Procedure	Fetal Dose (mrads)
Chest Xray (PA and lateral)	<1
Abdominal plain film	200 to 300
Intravenous pyelogram	400 to 900
Barium enema	700 to 1600
Cervical spine Xray	<1
Dorsal spine Xray	<1
Lumbar spine Xray	400 to 1600
Upper GI series	50 to 400
Hip and femur Xray	100 to 400
Dental Xray	0.01
Mammography	negligible
Cerbral angiography	<10
CT of Chest	30
CT of the abdomen	250
Perfusion of Lung scan	6-12
Ventilation lung scan	1-19
Pulmonary angiography via femoral route	221 to 374
Pulmonary angiography via brachial route	<50

Surgical Issues

- Potential concerns include teratogenesis, miscarriage, hemorrhage, infection, aspiration, preterm labor/delivery
- Data is based off of observational studies, expert opinion and extrapolation from trials in nonpregnant individuals
- If fetus is at viable gestation, staff should be on hand in case an emergent c-section be necessary

Timing

- **If possible wait until pregnancy is over**

- **If not possible....**
  - **Second trimester is optimal**
    - Uterus is smaller
    - Organogensis is complete
    - Lower rate of pre-term labour - 1% vs 9% in third
  - **First trimester**
    - Risk of miscarriage
      - Not clear if risk is increased due to underlying process itself or surgery but delay if possible
    - Organogenesis is ongoing
    - Teratogenesis
  - **Third trimester**
    - Increased risk of pre-term labour and delivery

Glucocorticoids

- Any surgery performed between 24-34 weeks should be considered for antenatal glucocorticoides
- Reduce perinatal morbidity/mortality if pre-term delivery should occur
- 12 mg doses of betamethasone given IM 24 hours apart
- Avoid in systemic infection - sepsis or ruptured appendix *

Positioning

- Gravid uterus causes aortocaval compression
  - Decreases venous return
  - Cardiovascular compromise

- Over 18 - 20 weeks

- Keep patient in 15 percent lateral tilt if possible
  or
- Right hip wedge

Surgical Approach

- Laparoscopic carries the same benefits as in the non-gravid patient (uterine perforation with veress and trochar a concern)
- If open to be preformed - vertical incision generally allows for better exposure
- Also depends on the skills of the surgeon

Fetal Heart Rate Monitoring

- In non-viable fetus
  - Document pre and post op FHR

- Viable fetus
  - Intraoperative FHR monitoring should be individualized (not used most often)
  - Recommend in those greater then 23-24 weeks

- Can be helpful for anesthesia to optimize uteroplacental oxygen
  - Ensure no aortocaval compression
  - Increase maternal hypoxia
  - Normocarbia
  - Correct hypovolemia and hypotension

- FHR shows decreased variability during anesthesia and may demonstrate baseline decrease in rate

Thromboprophylaxis

- Pregnancy is a hypercoagulable state

- Pneumatic compression devices

- Determine need for medical thromboprophylaxis based on specific case
  - surgery
  - thrombophilia
  - length of surgery
  - immobilization
  - previous history of DVT
  - malignancy
  - DM
  - varicose veins
  - paralysis
  - obesity
  - what would you do for a non-gravid patient?

- Safe to use heparin/fragmin in pregnancy

Anesthesia Issues

- Regional if possible
- Avoid hypotension
- Maintain oxygentation
  - risk of desaturation
    - 9 min vs 3 min (100%-90%), made worse with obesity 98sec
  - preoxygenate
- Avoid hypercarbia
- Higher rate of failed intubation due to changes in airway and edema
- Increased risk of aspiration
  - prophylaxis
    - sodium citrate to maintain gastric pH >3
    - histamine receptor antagonists
    - metoclopramide
    - nonparticulate antacids
  - no solid food x6h, liquids x2h
  - cricoid pressure and RSI

Appendicitis Case Considerations

- Most common cause of acute abdomen in pregnancy (1:1500)
- Typical presentation: colicky epigastric or periumbilical pain localizing to right side of abdomen
- Appendix migration during pregnancy needs to considered when evaluating pain location
- Anorexia and vomiting are non-specific indicators and fever is often not present
- Laboratory values not reliably predictive but WBC <10 gives reassurance
- Ultrasound is accurate for diagnosis in 1st and 2nd trimester but technically difficult 3rd trimester
- If think that appendicitis has occurred - operate
- If perforation occurs, fetal loss rate may be as high as 36% allowing for a higher negative exploration rate

Conclusions

- Many changes occur in the pregnant patient- important to understand the normal changes so can workup patient and interpret investigations as well as provide optimal care

- Pregnant patients can definitely have **non-pregnancy related issues-** may have to provide care for pregnant patient!

- Multidisciplinary approach will be necessary

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