PHYSIOLOGICAL CHANGES DURING PREGNANCY

From many references

PHYSIOLOGICAL CHANGES DURING PREGNANCY

CHANGES IN MAMMARY GLANDS

- BREASTS ARE ENLARGED.
- THE AREOLA AND NIPPLES ARE DARKENED & SWOLLEN.

CHANGES IN REPRODUCTIVE ORGANS

- PROFOUND CHANGES OCCUR.
- UTERUS INCREASES IN WEIGHT & SIZE.
- BOTH HYPERPLASIA & HYPERTROPHY OCCUR OF BOTH ENDO & MYOMETRIA.
- WEAK CONTRACTIONS OCCUR IN THE UTERUS

CHANGES IN REPRODUCTIVE ORGANS CONTD.

- CERVIX BEGINS TO SOFTEN.
- OVARIES: NO OVULATION
- CORPUS LUTEUM OF PREGNANCY INCREASES IN SIZE WITHIN THE OVARY.
- VAGINA BECOMES HYPERVASCULAR.
- MUCOSA BECOMES PURPLISH
- ↑ ACIDITY IN THE VAGINA.

CXR

- ☐ Elevation of diaphragm
- ☐ Heart to be displaced to the left and upward
- ☐ Increase in the cardiac silhouette
- ☐ benign pericardial effusion

Echocardiogram

- ☐ Increased left ventricular wall mass
- ☐ Increased end diastolic dimensions
- ☐ Increase in EDV and therefore inc in SV

Electrocardiogram

- ☐ Slight left axis deviation

Total body water

- Increases 6-8 L
- Increases by 40 %
- Normal body water
  - 2/3 intracellular
  - 1/3 extracellular
    - ¾ interstitial
    - ¼ intravasular
- 2/3 increase is extravascular

Cardiac output (CO=HR X SV)

- Begins to increase by the 5th wk
- Rise of 40 % by 20-24 wks
- Initial increase is a function of
  - The increase in heart rate
  - Reduced systemic vascular resistance
- By 10- 20 wks the increase in CO is reflected mainly by the increase in SV
- The notable increase in plasma volume or preload contributes to the increase SV
- As pregnancy advances to term, the HR continues to increase but the SV falls to close to normal levels, this accounts for the fall in CO to near non-pregnant levels at term

Cardiac Physiology

- Major changes affecting function:
  - Total body water increase 6.5-8.5 L
    - Fetus, placenta 3.5 L
    - Maternal blood volume 1.5 L
  - Lowered osmotic thresholds (278-280)
  - Sodium accumulation 900 mEq
  - Increased plasma renin activity
  - Increased atrial natriuretic peptide

Cardiac Physiologic changes

- During pregnancy, cardiac output increases by?
  - 30-50% vs. non-pregnant
- Steepest?
  - First trimester
- Peaks?
  - 20 weeks

Cardiac Output

- Maternal cardiac output is highest in which position?
  - Knee-chest or lateral recumbent
- Lowest?
    - Standing

Respiratory Physiology

- Elevated diaphragm
  - TLC reduced 5%
  - FRC reduced 20%
    - Both ERV and RV are reduced
- IC increases 5-10% as a consequence of reduced FRC
- VC does not change

Respiratory Physiology

- FEV1 is unchanged
- TV increases about 40%; since RR is unchanged, that increases minute ventilation 40%
- Increased MV leads to:
  - Increased alveolar oxygen
  - Slightly increased arterial oxygen (101-108)
  - Decreased alveolar and arterial CO2 (27-32)

Physiologic anemia of pregnancy

- Physiologic intravascular change
- Plasma volume increases 50-70 %
  - Beginning by the 6th wk
- RBC mass increases 20-35 %
  - Beginning by the 12th wk
- Disproportionate increase in plasma volume over RBC volume----Hemodilution
- Despite erythrocyte production there is a physiologic fall in the hemoglobin and hematocrit readings

Hematologic Changes

- Blood Volume increases by?
  - 40-50%
- Peaks at?
  - 30-34 weeks
- RBC Mass increases?
  - 20% without iron supplementation
  - 30% with iron supplementation

Normal Iron Requirements

- Total body iron content average in normal adult females is 2gm
- Iron requirement for normal pregnancy is 1 gm
  - 200 mg is excreted
  - 300 mg is transferred to fetus
  - 500 mg is need for mom
    - Total volume of RBC inc is 450 ml
    - 1 ml of RBCs contains 1.1 mg of iron
    - 450 ml X 1.1 mg/ml = 500 mg
- Daily average is 6-7 mg/day
- Small intervals between pregnancies are most concerning

Hematologic Changes

- What are the total iron demands for a normal term pregnancy in a woman without preexisting iron depletion?
- 1000 mg
  - 300 mg fetus and placenta
  - 500 mg maternal red cell increase
  - 200 mg compensate for normal daily losses
- Translates into required daily absorption of 3.5 mg.

Hematologic Changes

- Iron demands increase in later gestation (6-7 mg/day near term)
- About 10% of ingested iron is absorbed under conditions of normal iron demands; can increase when depleted
- Iron supplementation is needed to avoid iron depletion during pregnancy

Hematologic Changes

- Without Iron Supplement
  - Hemoglobin falls
  - Serum iron falls
  - Ferritin falls
  - TIBC increases
- With Iron Supplementation
  - Hemoglobin is unchanged
  - Serum iron is unchanged
  - Ferritin is unchanged
  - TIBC increases, but by a smaller degree

Hematologic Changes

- Mild decrease in mean platelet count
  - 322 → 278
  - Increased platelet destruction
- Up to 8% will have gestational thrombocytopenia
  - Platelet count 70-150,000/mm^3
  - No increased bleeding complications
  - Return to normal after delivery

Hematologic Changes

- Mean WBC count increases
  - 1st trimester 8000 (5100-9900)
  - 2nd and 3rd trimester 8500 (5600-12200)
  - In labor may rise to 26,000-30,000
- T helper 1 and natural killer cells decrease, T helper 2 increase (cell-mediated immunity → humoral immunity)
- Decreased concentrations of IgG, IgM, IgA

Coagulation System

- Procoagulant factors increased
  - (factors I, VII, VIII, IX, X).
- Natural inhibitors of coagulation decreased
- Decreased fibrinolysis
  - Reduced plasminogen activator
- Defense against puerperal hemorrhage
- Increased risk of thromboembolism

GI Physiology

- Common symptoms: heartburn, increased appetite
- Constipation may be increased - typically responds to fluids, fiber, MOM, senna
- Overall inhibition of GI motility
- Many physiologic changes attributed to progesterone

GI Physiology

- Esophagus
  - no change in motility
  - reduced LES resting pressure (decreases with gestational age)
  - reduced LES response to agonists
  - Changes may be progesterone-mediated but evidence circumstantial; no correlation with progesterone levels in one study

GI Physiology

- Stomach
  - Conflicting data on acid production, gastric emptying
  - Davison (1970) showed a longer total emptying time but no difference in 30 minute volume; changes more pronounced in women with heartburn or in labor
  - Slowed emptying during labor due in part to analgesic and sedative use

GI Physiology

- Intestines
  - Increased transit time shown in multiple studies, probably progesterone-mediated
  - Theoretical changes in absorption related to slower transit time and longer exposure of intestinal contents to the mucosa
    - could be beneficial - allow more time for absorption
    - could be detrimental - allow bacterial overgrowth
    - No studies to confirm

Hepatic Physiology

- Increased protein synthesis (estrogen effect)
  - increased clotting factors, binding globulins
  - hemodilution decreases albumin concentration
- 50% of normal pregnancies have dilated esophageal veins (portal-systemic shunt)
- Hepatomegaly is abnormal; palmar erythema and spider veins common

Hepatic Physiology

- Girling (1997) - normal values for AST, ALT, GGT, and bilirubin are lower in uncomplicated pregnancies than the normal non-pregnant laboratory reference range
- Abnormal LFT seen in 54% with preeclampsia and 14% with PIH
- Higher LFT: more proteinuria, lower platelets, more maternal complications

Hepatic Physiology

	NP	1st	2nd	3rd
AST (U/L)	7-40	10-28	11-29	11-30
ALT (U/L)	0-40	6-32	6-32	6-32
Bili (µmol/L)	0-17	4-16	3-13	3-14
GGT (U/L)	11-50	5-37	5-43	3-41

Genital Tract

- Uterine hypertrophy of the myocytes
- Hypertrophy can cause venouscompression
  - Can result in fall in venous return
  - Furthermore a fall in CO

- Physiologic compensation
  - Rise in peripheral resistance to minimize fall in blood pressure

Insulin resistance

- Anti-insulin environment is aided by:
- placental lactogen
  - Like growth hormone
  - Increases lipolysis and FFA
  - Increases tissue resistance to insulin
- Increased unbound cortisol
- Estrogen and Progesterone may also
- exert some anti-insulin effects

Melasma

Striae

Linea nigra

Estrogen and progesterone

- Some melanocyte stimulating effect

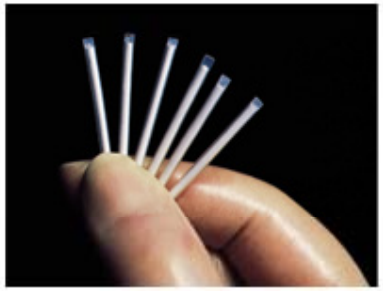
Various Birth Control Devices

a.

b.

c.

d.



e.

f.

Gonadal Dysfunction

- Gonads fail to develop properly. Alterations of the SRY gene (by point mutation or deletions) can lead to a gonadal dysgenesis (XY female) also called Swyer's syndrome.
- **Gonadal Dysgenesis:** 46,XX, Swyer's syndrome
- **Mixed Gonadal Dysgenesis:** 45,X/46,XY
- **Primary Hypogonadism:** 46,XX, affected females
- **Primary Hypogonadism:** Defective anterior pituitary production of gonadotropin, lack of gonadotropin-releasing hormone

Spermatogenesis Abnormalities

- These are male abnormalities that generally become apparent late postnatally after puberty or when reproduction is planned.
- These conditions would not be detected (unless with a genetic history) in prenatal and early postnatal development.

Oligospermia (Low Sperm Count)

- Less than 20 million sperm after 72 hour abstinence from sex

Azoospermia (Absent Sperm)

- Two main forms identified as:
- Obstructive azoospermia (OA) - blockage of duct network
- Non-obstructive azoospermia (NOA) - ADP-ribosyltransferase 3 gene (ART3) recently described as a susceptibility gene.

EXTRA TO READ

Sexual Desire/Drive

subjective experience - wishes, fantasies - measured by behaviors (e.g., masturbation) that arise as a result of wishes and fantasies

sexual desire involves activity within the central nervous system and endocrine system

Sexual Desire: Nervous System

- Serotonin:
  - important for sexual desire in both men and women
  - Common side effect of SSRIs (e.g., Prozac) is diminished sexual desire
- Dopamine:
  - important for sexual desire in men and women
  - increased dopamine levels (e.g., medication for Parkinson's disease) associated with increased sexual desire
  - dosage and duration of use dependent

Sexual Desire: Endocrine Functions

- Testosterone
  - Men & Women:
    - necessary for sexual drive in both men and women - threshold level required
    - above threshold, testosterone levels not associated with degree of sexual desire
    - taking supplemental testosterone not shown to increase sexual drive in those with normal levels of testosterone
  - Men:
    - above threshold, testosterone levels not associated with degree of sexual desire
      - exception: handful of studies found levels of testosterone associated with frequency of sexual thoughts, initiation of sexual activities in males
      - possible reason: sexual thoughts/fantasies may stimulate testosterone production

Sexual Desire: Endocrine Functions

- Testosterone
  - Women:
    - above threshold, testosterone levels not associated with degree of sexual desire
      - inconsistent findings:
        - T levels associated with masturbation frequency
        - T levels associated with intercourse frequency, initiation of intercourse
        - T levels associated with drive levels in post-menopausal women
      - As with males, sexual thoughts/fantasies may stimulate T production

Sexual Desire: Endocrine Functions

- Estrogen
  - Men:
    - play minimal role in normal males
    - administration of high levels of E may inhibit sexual desire
  - Women:
    - play only minimal role
    - administration of E does not affect desire
- Progesterone:
  - Men:
    - very little research
  - Women:
    - play only minimal role
- Oxytocin: may promote sexual desire by promoting positive mood

Sexual Arousal

- subjective arousal
  - female: "turned on," tingling, warm sensation (most women unable to accurately estimate level of vaginal lubrication)
  - male: "turned on," tingling, warm sensation, erection
- physiological arousal
  - female: vaginal lubrication
  - male: erection

Involves activity in the central and peripheral nervous systems and endocrine system

Sexual Arousal

- Male - parasympathetic cholinergic nerves
  - mediate erection
    - acetylcholine
    - vasoactive intestinal polypeptide
    - nitric oxide synthase
  - stimulates secretions from
    - seminal vesicles
    - prostate
    - Cowper's glands

Andersson et al. (2000)

Sexual Arousal

- Female - sympathetic nervous system involved in sexual arousal/vaginal lubrication
  - Meston & Gorzalka (1996)
    - 36 healthy women engaged in vigorous exercise (activating SNS) and no exercise prior to watching an erotic film
    - vaginal responses monitored with vaginal photoplethysmography
    - Finding:
      - viewing erotic film produced greater vaginal vasocongestion if preceded by exercise versus no exercise

Sexual Arousal: Nervous System

- Serotonin:
  - may be involved in regulation of blood flow to the genitals
- Dopamine:
  - important for erectile functioning
  - medications that increase D, produce erections (e.g., Parkinson's medication)
  - medications that decrease D, may inhibit erections or produce prolonged erections (e.g., antipsychotic medication)
  - dosage and duration of use dependent

Sexual Arousal: Nervous System

- Epinephrine:
  - Men:
    - maintains penis in flaccid state
    - involved in detumescence
  - Women:
    - active as women become physiologically sexually aroused
      - increase prior to viewing erotic film
      - increase with masturbation
    - levels remain elevated for up to 23 hours following sexual activity
    - activities that stimulate sympathetic nervous system function (such as exercise), promote physiological sexual arousal

Sexual Arousal: Nervous System

- Norepinephrine:
  - Men:
    - blood levels positively correlated with arousal and erection during masturbation and intercourse
    - medications that increase NE levels less likely to cause erectile problems
  - Women:
    - blood levels increase in anticipation of intercourse
    - blood levels increase with masturbation

Sexual Arousal: Endocrine Function

- Testosterone
  - Men:
    - may help enhance subjective sexual arousal in men
    - threshold level required to achieve erection in men
    - when levels normal, supplements do not improve erection
  - Women:
    - mixed findings: some studies show greater vaginal blood flow response among women with higher T, other studies find no relationship

Sexual Arousal: Endocrine Function

- Estrogen
  - Women:
    - necessary for maintenance of the vaginal tissue
    - necessary for vaginal lubrication
    - indirectly affect subjective experience (I.e., increased depression, pain affects sexual pleasure)
- Oxytocin
  - oxytocin levels increase during sexual arousal for both men and women

Orgasm

- Orgasm
  - Male:
    - subjective pleasure
    - physical response - spinal cord reflex
      - rhythmic muscular contraction
      - ejaculation
      - detumescence - veins dilate and blood flows out of penis

Involves activity in the central and peripheral nervous system and endocrine system

Orgasm

- Male - sympathetic nervous system
  - involved in ejaculation of semen
    - stimulates contractions of smooth muscles in the vas deferens, seminal vesicles, and prostate -> semen into urethra
    - stimulates rhythmic contractions of bulbocavernosus and ischiocavernosus -> semen ejected out of urethra

Orgasm

- Orgasm
  - Female:
    - subjective pleasure
    - physical response - spinal cord reflex
      - rhythmic, synchronized vaginal, anal and uterine contractions (Masters & Johnson, 1966)
        - vaginal blood volume (VBV) drops during orgasm
        - VBV returns, post-orgasm, to approx. 1/2 levels pre-orgasm
        - 10 minutes post-orgasm, VBV remain elevated above baseline levels.
        - rhythmic contraction, dipping, "sucking" cervix?
      - G-spot and female ejaculation?

Involves activity in the central and peripheral nervous system and endocrine system

Orgasm

Joseph R. Beck, physician, 1872, upon examining a women with uterine prolapse, who warned the physician to be careful, as she could reached orgasm very easily, even with the pressure of his finger.

"separating the labia with my left hand, so that the os was brought clearly into view in the sunlight, I now swept my right forefinger quickly three or four times across the space between the cervix and the pubic arch, when almost immediately the orgasm occurred…Instantly the height of the excitement was at hand, the os opened itself to the extent of fully and inch, as nearly as my eye could judge, made five or six successive gasps, as it were, drawing the external os into the cervix each time powerfully, and, it seemed to me, with a regular rhythmical action, at the same time losing its former density and hardness, and becoming quite soft to the touch. All the phenomena occurred within the space of twelve seconds of time certainly, and in an instant all was as before. At the near approach of the orgastic excitement the os and cervix became intensely congested, assuming almost a livid purple color, but upon the cessation of the action, as related, the os suddenly closed, the cervix again hardened itself, the intense congestion was dissipated, the organs concerned resolved themselves into their normal condition."

Joseph R. Beck, "How Do Spermatoxoa Enter the Uterus?" *St. Louis Medical and Sergical Journal 9* (September 1872): 449.

Orgasm

- Do women ejaculate?
- Darling et al. (1990)
  - surveyed 1230 professional women, 22-82 yrs
  - Findings:
    - 40% reported ejaculation at orgasm following stimulation to the g-spot
    - women who reported ejaculation indicated greater sexual responsiveness, no difference in sexual satisfaction

Orgasm

- Is female ejaculate merely urine expelled during orgasm?
- Belzer et al. (1984)
  - 7 women who reported that they ejaculate at orgasm
  - collected urine samples and ejaculate samples
  - Finding:
    - the urine sample and ejaculate sample markedly differed

Orgasm: Nervous System

- Serotonin:
  - important for orgasm in both men and women
  - Common side effect of SSRIs (e.g., Prozac) is delayed orgasm, inability to reach orgasm
- Dopamine:
  - medications that increase D, may increase or decrease latency to orgasm
  - medications that decrease D, increase latency to orgasm, and/or inhibit orgasm in men and women
  - dosage and duration of use dependent

Orgasm: Nervous System

- Epinephrine:
  - Women: levels peak at orgasm, diminish to baseline levels within minutes of orgasm
- Norepinephrine:
  - Men:
    - up to a 12-fold increase at orgasm in men, return to baseline levels within 2 minutes post orgasm
    - medications that increase NE levels less likely to cause erectile problems
  - Women:
    - levels peak at orgasm, slowly decline after orgasm
    - levels remain elevated up to 23 hours after intercourse

Orgasm: Endocrine Function

- Oxytocin:
  - levels increase during orgasm in both men and women
  - related to myotonia, rhythmic orgasmic contractions

Q&A

- 21 YO G0 referred for preconception counseling – has idiopathic dilated cardiomyopathy, current LVEF 30%. The physiologic change most likely to cause decompensation of her cardiac status in pregnancy is?

Q&A

- A. Decreased SVR
- B. Increased intravascular volume
- C. Hypercoagulability
- D. Decreased PVR

Q&A

- B. Increased intravascular volume
  - Unable to increase left ventricular work in response to increased pre-load
  - Result: pulmonary edema

Q&A

- 30 YO G1 had a thyroidectomy for Graves' and takes levothyroxine 0.125 mg daily. She takes calcium carbonate tablets for GERD. Her third trimester labs shoe a microcytic anemia and you plan FeSO4 325 mg BID. Her TSH is 5.4mIU/mL. Regarding her medications, you recommend?

Q&A

- A. Increase levothyroxine
- B. No change
- C. Decrease levothyroxine
- D. Separate levothyroxine and iron by 4-6 hours
- E. Separate levothyroxine and calcium carbonate by 2-4 hours

Q&A

- D. Separate levothyroxine and iron by 4-6 hours
  - Other agents including aluminum hydroxide, cholestyramine, and sucralfate can affect absorption of levothyroxine
  - Anticonvulsants (phenytoin, carbamazepine, phenobarbital) may increase hepatic metabolism of levothyroxine

Q&A

- 34 YO G3P2 at 13 weeks tells you she stopped her treatment for Graves' when she learned she was pregnant. Complains of palpitations. HR 105. TSH undetectable, free T4 markedly elevated. Next step?

Q&A

- A. beta blocker
- B. propylthiouracil
- C. Lugol's solution
- D. methimazole
- E. subtotal thyroidectomy

Q&A

- B. propylthiouracil
  - Inhibits organification and coupling during thyroid hormone biosynthesis; also inhibits peripheral conversion of T4 to T3 (which methimazole does not do)
  - Iodides temporarily suppress release of stored thyroxine; may cause fetal goiter; used for storm

Q&A

- Glucose intolerance in gestational diabetes mellitus is caused by:
- A. low fasting insulin levels
- B. low post-prandial insulin levels
- C. increased insulin resistance
- D. increased post-prandial hepatic glucose production

Q&A

- C. insulin resistance
  - Insulin resistance rises in direct proportion to increases in estrogen, progesterone and HPL.
  - Insulin receptor number and function do not increase in pregnancy, even in the face of increased circulating insulin concentrations

Q&A

- 19 YO G2P1 presents to the ED at 20 weeks with an asthma exacerbation. She complains of upper respiratory symptoms and ran out of her inhaler 2 weeks ago. Her exam includes a T38, P 110, RR 40 and FHR 150. Which of the following statements about asthma in pregnancy is true?

Q&A

- A. Asthma exacerbations are more common in pregnant women than in non-pregnant women of similar age
- B. Influenza vaccination is contraindicated in pregnancy.
- C. Peak expiratory flow rate monitoring is unreliable for monitoring disease state during pregnancy.
- D. In pregnant women, the arterial partial pressure of carbon dioxide (PaCO2) is decreased on arterial blood gases compared to non-pregnant individuals.
- E. Due to potential risks of fetal radiation exposure, chest radiography should not be performed to evaluate for underlying pneumonia in women with asthma exacerbation.

Q&A

- D. In pregnant women, the arterial partial pressure of carbon dioxide (PaCO2) is decreased (28-32) on arterial blood gases compared to non-pregnant individuals (37-40).