Hematologic Disease in Pregnancy & Hemoglobinopathies

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• No financial interests to disclose.
Objectives

• Cases
• Physiology
• Sickle cell disease
Case 1

- 25 yo P0000
- Sickle cell disease (hx of multiple transfusions/admissions for pain crisis)
- Presents at 28 weeks – pain crisis, Hb 6.5g/dL
Case 2 - Sickle cell disease

- 25 yo P0000 - 12 weeks pregnant, hx of sickle cell disease –
- FOB – unknown if carrier – ethnicity – African American
- Inheritance pattern?
- Carrier rate in general population?
- Chance fetus – is carrier? Is affected with sickle cell disease?
Physiologic changes in pregnancy

- Anemia in pregnancy
- First/third trimester – Hb <11g/dL
- Second trim – Hb <10.5g/dL

Iron requirements in pregnancy
  - Total 1000mg
    - 300mg (fetus/placenta)
    - 500mg (expansion of maternal Hb mass)
    - 200mg (shed through gut, urine, skin)
Pregnancy associated changes in coagulation

- Increased concentration of all clotting factors except for XI, XIII, and Protein S free levels which decrease
  - Fibrinogen, II, V, VII, VIII, IX, X, XII, PAI-1, 2
    - 200% increase
  - Von Willebrand factor increases 100-150%
- Decrease – XI, XIII, protein S
- Unchanged - Protein C, Antithrombin (ATIII)
- Levels of thrombin-ATIII complex increase, suggesting coagulation activation is consistent with elevated fibrinopeptides
Coagulation changes

- Fibrinogen level (increased concentration with increased plasma volume)
  - Avg nonpregnancy 300mg/dL (200-400)
  - Avg pregnancy increase is 50%; 450mg/dL late in pregnancy (300-600)
    - End product of coagulation cascade is fibrin formation
- Prothrombin time – no change
- Partial thromboplastin time – no change
Figure 18. Diagnostic assessment of anemia in pregnancy. Abbreviation: Hb indicates hemoglobin.
Fig. 1. Specialized antepartum evaluation for hematologic assessment of patients of African, Southeast Asian, or Mediterranean descent. Patients of Southeast Asian or Mediterranean descent should undergo electrophoresis if their blood test results reveal anemia. Abbreviations: CBC = complete blood count; RBC = red blood cell; MCV = mean corpuscular volume; Hb = hemoglobin.
• IV iron
  – Iron Dextran (0.6-1% rate of anaphylaxis)
  – Iron sucrose (lower rate of anaphylaxis and fatality rates)
  – Ferric gluconate

Autologous transfusion – Hct >32% at 32 weeks
Severe anemia

- Severe anemia with maternal Hb <6g/dL has been associated with abnormal fetal oxygenation resulting in NR FHR patterns, oligohydramnios, fetal cerebral vasodilatation and fetal death. Thus maternal transfusion should be considered for fetal indications. ACOG
**Hemoglobinopathies**

- **Definition** –
  - qualitative (sickle cell – Beta globin gene mutation)
  - quantitative (thalassemia, unbalance of alpha or beta globin chains) abnormality in the hemoglobin molecule

- **Incidence** – allele frequency depends on ethnicity;
  - worldwide > 270 million heterozygous carriers;
  - > 300,000 affected homozygotes or compound heterozygotes born each year (ACOG 2007)
Sickle cell anemia – Overview

• Definition – AR hemoglobin disease due βglobin chain (chromosome 11) missense mutation that substitutes valine for glutamic acid at amino acid 6 (β-globin glu6val mutation)
• Incidence – 1 in 700 (African), carrier rate -~1 in 10
• Pathogenesis – the glu6val mutation DECREASES the solubility and deformability of the βglobin chain so that after repeated cycles oxygenation and attendant sickling, the chains become permanently ‘sickled’ and occlude capillaries causing infarctions (painful crisis, acute chest syndrome, asplenia); irreversible sickled cells are removed by the spleen and the rate of removal of erythrocytes from the circulation exceeds the production capacity of the bone marrow and causes a hemolytic anemia
• Diagnosis – Peripheral smear; Hemoglobin electrophoresis identifying Hb SS (p100 Gehleter) – normal adult A (97.5%), A2 (2%), F (0.5%)
Peripheral smear from a patient with sickle cell anemia shows multiple spindly sickle cells (blue arrows), a nucleated red blood cell in the upper left, and a Howell-Jolly body (black arrow), which is a nuclear fragment normally removed by the spleen. Target cells are also present (red arrow). This patient has functional asplenia because of repeated splenic infarctions. Courtesy of Carola von Kapff, SH (ASCP).
Hgb electrophoresis
Electric field
Sickle (glu6val) valine in place of glutamine
Glutamine has a more Negative charge thus it travels further than Valine (S) or lysine (C)
-A = glutamine has the most negative charge – thus it goes far on the gel
-S = glutamine to valine (middle charge b/n +/-)
-C = glutamine to lysine (more + charge thus it does not goes as far on the gel)
-A2 (most positive charge, thus it does not go far on the gel)
Sickle Cell Disease and genetic principles

- Heterozygote advantage, plays role in ethnic variation in allele frequency
- Novel property mutation - sickle cell disease is an exception to the allelic heterogeneity rule in that one specific mutation is responsible for the unique ‘novel’ properties of sickle Hb; Hb C is less soluble than Hb A and tends to crystallize in red cells, decreasing the deformability in capillaries and this also creates mild hemolysis, but Hb C does not sickle or form the rod shaped polymers like Hb S
- Ethnic variation in allele frequency
## Sickle cell allele/mutation frequencies (Nussbaum 4<sup>th</sup> ed) — California cohort data

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>HB SS</th>
<th>Hb AS</th>
</tr>
</thead>
<tbody>
<tr>
<td>African American</td>
<td>1/700</td>
<td>1/14</td>
</tr>
<tr>
<td>Asian Indian</td>
<td>0/1600</td>
<td>1/700</td>
</tr>
<tr>
<td>Hispanic</td>
<td>1/46,000</td>
<td>1/180</td>
</tr>
<tr>
<td>Middle Eastern</td>
<td>0/22,000</td>
<td>1/360</td>
</tr>
<tr>
<td>Native American</td>
<td>1/17,000</td>
<td>1/180</td>
</tr>
<tr>
<td>White</td>
<td>1/160,000</td>
<td>1/600</td>
</tr>
<tr>
<td>Asian</td>
<td>0/200,000</td>
<td>1/1300</td>
</tr>
</tbody>
</table>
Hardy-Weinberg Principle & Assumptions

(T/T Genetics in Medicine)

• 2 components

• 1 – Under certain ideal conditions a simple relationship exists between allele frequencies and genotype frequencies in a population
  – The HW Law states that the frequency of the three genotypes AA, Aa, and aa is given by the terms of the binomial expansion of $(p+q)^2 = p^2 + 2pq + q^2$

• 2 – If allele frequencies do not change from generation to generation, the relative proportion of the genotypes will not change either; that is the population genotype frequencies from generation to generation will remain constant, at equilibrium, if the allele frequencies $p$ and $q$ remain constant. More specifically, when there is random mating in a population that is at equilibrium and genotypes AA, Aa, and aa are present in the proportions $p^2 : 2pq : q^2$, then genotype frequencies in the next generation will remain in the same relative proportions, $p^2 : 2pq : q^2$
HW Assumptions

(T/T Genetics in Medicine)

- The population is large and matings are random with respect to the locus in question
- Allele frequencies remain constant over time because:
  - There is no appreciable rate of mutation
  - Individuals with all genotypes are equally capable of mating and passing on their genes, that is, there is no selection against any particular genotype
  - There has been no significant immigration of individuals from a population with allele frequencies very different from the endogenous population
Hardy-Weinberg example

- Williams quest – What is approximate incidence of sickle cell anemia in African Americans if carrier rate is 1/12?

- $1 = p+q$
- $1 = p^2 + 2pq + q^2$
- $p = \text{dominant allele}$
- $q = \text{recessive allele}$
- $q = 1/12; q^2 \times \frac{1}{4} (\text{chance that 2 carriers would have affected child})$
- $\frac{1}{12} \times \frac{1}{12} \times \frac{1}{4} = 1 \text{ in 576}$
HW – PKU example

- PKU
- Frequency of affected homozygotes in the population can be determined accurately through newborn screening programs
- Heterozygotes – asymptomatic silent carriers, population incidence is impossible to measure directly from phenotype
- HW law allows estimate of heterozygote frequency to be made and used subsequently for counseling
- Frequency of PKU 1 in 4500 – 1/4500 in Ireland
  - Frequency of affected individuals = 1/4500 = \( q^2 \), \( q =0.015 \), and \( 2pq = 0.029 \) or approx ~3%
- Carrier frequency in the Irish population ~3%
- If pt is a known carrier – Partner is Irish (3% heterozygote rate)
  - Chance of affected offspring = \( 0.5 \times 0.03 \times 0.25 = 1 \) in 267
  - Chance of carrier offspring = \( 0.5 \times 0.03 \times 0.5 = 1 \) in 133
- If pt is known carrier – Partner is from Finland (PKU frequency 1/200,000)
  - Frequency of affected individuals = 1/200,000 = \( q^2 \), \( q =0.002 \), and \( 2pq = 0.004 = 0.4\% \) = carrier rate
  - Chance of affected offspring = \( 0.5 \times 0.004 \times 0.25 = 1 \) in 2000
  - Chance of carrier offspring = \( 0.5 \times 0.004 \times 0.5 = 1 \) in 1000
Sickle Cell Disease & Pregnancy

- Increased risk of morbidity/mortality – depends on severity of anemia
  - Hb SS and to lesser extent Hb SC - Risks include infection, acute chest syndrome, pain crises, dehydration, severe anemia, cholecystitis, preterm birth, low-birth weight infants (<2500g), fetal growth restriction, hospitalization, IUFD
  - Folic acid supplementation – 4mg/day
  - Painful crisis (tx with pain control, oxygen, IV hydration) – avoid cold temp, heavy exertion, dehydration, stress
  - Acute chest syndrome (fever, tachypnea, chest pain, hypoxia)
  - Autosomal recessive implications for offspring
  - Prophylactic or exchange transfusion – goal of Hct >21% (ideal ~30%) – decreases risk of painful crises, severe anemia, not necessarily associated with improved pregnancy outcome, less crises, less anemia (ACOG 2007)
  - Vaccinations – Pneumococcal vaccine and Meningococcal (ACWY/MPSV 4) and Haemophilus influenza type B - all ok in pregnancy
  - Serial Urine cultures -
Pregnancy and Sickle Cell Disease - Risks

- Maternal death – Mortality 72 deaths per 100,000 deliveries versus 12.7 deaths per 100,000 deliveries in women without SCD.
- Transfusion (OR 22.5; 95% CI 18.7-27.0)
- Systemic inflammatory response syndrome (SIRS; OR 12.6; 95% CI 2.1-13.6)
- Pneumonia (OR 9.8; 95% CI 8.0-12.0)
- Sepsis (OR 6.8; 95% CI 4.4-10.5)
- Asymptomatic bacteriuria (OR 6.8, 95% CI 3.1-14.9)
- Cerebral vein thrombosis (OR 4.9; 95% CI 2.2-10.9)
- Deep vein thrombosis (OR 2.5; 95% CI 1.5-4.1)
- Genitourinary tract infection (OR 2.3, 95% CI 1.9-2.7)
- No difference in stroke, PE, MI, pyelonephritis

The largest data set of SCD outcomes in pregnant women is the Nationwide Inpatient Sample from the Healthcare Cost and Utilization Project of the US Agency for Healthcare Research and Quality, which analyzed all pregnancy-related discharges with a diagnosis of SCD for the years 2000 to 2003, and included almost 18,000 deliveries to women with SCD and 17 million deliveries to women without the disease - Villers 2008
Pregnancy and Sickle Cell Disease - Risks

- Villers – 2008 - N = 286 SCD pregnancies
- Risks increased of
  - Intrauterine growth restriction (OR 2.2; 95% CI 1.8-2.6)
  - Eclampsia (OR 3.2; 95% CI 1.8-6.0)
  - Gestational hypertension and preeclampsia (OR 1.2; 95% CI 1.1-1.3)
  - Preterm labor (OR 1.4; 95% CI 1.3-1.6)
  - Postpartum infection (OR 1.4; 95% CI 1.1-1.7)
  - Abruption (OR 1.6; 95% CI 1.2-2.1)
  - Antepartum bleeding (OR 1.7; 95% CI 1.2-2.2)
  - Lower rate of PPH
- No difference in GDM rates. Inadequate number to assess risk of IUFD.

Villers 2008
Complications

• **Secondary organ system effects**
  - >80% of sickle cell patients have cardiomegaly (baseline echocardiogram, EF)
  - Prolongation of PR interval

• **Crisis**
  - Hematologic – Pediatric pop, rare in pregnancy
  - Vaso-occlusive -
Evaluation

- Diagnosis
- Echocardiogram
- PFTs
- Partner Carrier screening
- Hep B, C testing
- Retinal evaluation (retinopathy can worsen)
- Serial urine cultures
Sickle crisis

- **Hematologic**
  - Aplastic crisis – usually due to infection (bacterial, viral), human parvo (also risk to fetus)
    - Risk of stroke with severe anemia
    - Transfusion if HCT <25%

- **Vaso-occlusive**
  - Splenic sequestration
  - Hepatic sequestration
  - Hyperhemolytic sequestration
Sickle crisis - Pain

- Acute pain crisis
- 1/3 are associated with infection
- Management – Rest, hydration, oxygenation, pain control, antibiotics if infection is suspected
Algorithm – CCO

Critical Care OB - Dildy
Algorithm – CCO

Critical Care OB - Dildy
Sickle crisis – Pulmonary crisis

- Acute chest syndrome – potentially fatal
- Fever, pleuritic cp, tachypnea, pulmonary infiltrates
- DDX – PE, fat embolism, AFE
- Tx – oxygenation, hydration, treatment of infection, pain control
- Transfusion to increase HbA >40%, Hct <30%, HBS <60%
The diagram illustrates changes in lung capacities and volumes throughout pregnancy. The y-axis represents various lung capacities, including:

- Total lung capacity
- Inspiratory capacity
- Vital capacity
- Functional residual capacity
- Residual volume
- Expiratory reserve volume

The x-axis represents months pregnant, from 3 to 9 months. The columns show the relative changes in capacities from control to different months of pregnancy.
Pathophysiologic Implications

• Mom is able to hold her breath less
  – 1 vs 2 lung example

• Decreased FRC
  – Closing capacity – amount of volume that has to be behind to keep small airways open - diminished

• Develop hypoxemia quicker than when not pregnant (at greater risk of hypoxemia)

• Pulmonary insults are tolerated less well
### ABG Changes in Pregnancy

<table>
<thead>
<tr>
<th>Variable</th>
<th>Nonpregnant</th>
<th>Pregnant</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.35-7.43</td>
<td>7.4-7.47</td>
</tr>
<tr>
<td>pCO₂ (mmHg)*</td>
<td>37-40</td>
<td>27-31</td>
</tr>
<tr>
<td>pO₂ (mmHg)**</td>
<td>103</td>
<td>101-104</td>
</tr>
<tr>
<td>P(A-a)O₂ (mmHg)**</td>
<td>14</td>
<td>20</td>
</tr>
<tr>
<td>HCO₃⁻ (mEq/L)</td>
<td>22-26</td>
<td>18-22</td>
</tr>
<tr>
<td>Base deficit (mEq/L)</td>
<td>1</td>
<td>3</td>
</tr>
</tbody>
</table>

- *compensatory increase in renal bicarbonate excretion*
- **decreased in supine position and 3rd trimester**
- ***increased by 6 in supine position and 3rd trimester***
ACS

- Diagnostic criteria for ACS — ACS is defined as radiographic evidence of consolidation: a new segmental (involving at least one complete segment) radiographic pulmonary infiltrate [3], AND at least one of the following:
  - Temperature ≥38.5°C
  - >2 percent decrease in SpO₂ (O₂ saturation) from a documented steady-state value on room air (FiO₂ = 0.21)
  - PaO₂ <60 mmHg
  - Tachypnea (per age-adjusted normal)
  - Intercostal retractions, nasal flaring, or use of accessory muscles of respiration
  - Chest pain
  - Cough
  - Wheezing
  - Râles
- Of importance, the presence of pneumonia can formally be considered as meeting the criteria for ACS, since the two cannot be reliably distinguished from one another.
ACS severity index — Severity of ACS is considered mild, moderate, severe, or very severe,

- **Mild ACS** — Meets the diagnostic criteria for ACS plus ALL of the following:
  - Transcutaneous oxygen saturation >90 percent on room air (FiO₂ = 0.21)
  - Segmental or lobar infiltrates that involve no more than one lobe by chest radiography
  - Responsive to simple transfusion of no more than 2 units of red blood cells (or 15 mL/kg of packed RBCs)

- **Moderate ACS** — Meets the diagnostic criteria for ACS plus ALL of the following:
  - Transcutaneous oxygen saturation ≥85 percent on room air (FiO₂ = 0.21)
  - Segmental or lobar infiltrates that involve no more than two lobes by chest radiography
  - Responsive to transfusion of ≥3 units of red cells (or >20 mL/kg packed RBCs)
ACS severity index — Severity of ACS is considered mild, moderate, severe, or very severe,

- **Severe ACS** — Meets the diagnostic criteria for ACS plus one or more of the following:
  - Respiratory failure present (PaO$_2$ <60 mmHg or PCO$_2$ >50 mmHg)
  - Mechanical ventilatory support required
  - Transcutaneous oxygen saturation <85 percent on room air or ≤90 percent despite maximal supplemental O$_2$
  - Segmental or lobar infiltrates that involve three or more lobes by chest radiography
  - Requiring transfusion or exchange transfusion of RBCs to achieve hemoglobin A levels ≥70 percent

- **Very severe ACS** — Acute respiratory distress syndrome (ARDS) present or sudden, life-threatening lung failure. ARDS is defined by the following three criteria of the American-European Consensus Conference and includes:
  - Acute onset of bilateral infiltrates on chest radiography
  - Pulmonary artery wedge pressure <19 mmHg or the absence of clinical evidence of left atrial hypertension
  - PaO$_2$/FiO$_2$ ≤200 regardless of positive end expiratory pressure (PEEP) level
Hepatic crisis

• Vaso-occlusion of hepatic vasculature
• Fever, RUQ pain, leukocytosis, elevated LFTs, bilirubin
• DDX – choleycystitis, HELLP sd
• Management – hydration, pain control, antibiotics, serial labs
Exchange transfusion

- Prophylactic partial exchange transfusions prior to onset of vaso-occlusive crisis
- Decreased incidence of pain crisis, less maternal anemia, no consistent improvement in perinatal outcome
- Transfusion to increase HbA >40%, Hct <30%, HBS<60%
  - Standard exchange of 6 units of washed packed RBCs, increases HbA to 70%
  - Tables used to calculate required volume of transfusion given % of Hb A, Hct of transfused blood, patient weight (kg)
- Alloimmunization is main risk, thus prophylactic transfusions are not recommended
Simple transfusion

• Hb/Hct <6-7g/dL, 18-21%
• Goal of HCT <30% so as to avoid increased viscosity of blood which can precipitate a crisis

• Improved blood counts, risks of alloimmunization, etc, does not improve time of pain crisis or symptoms of pain crisis acutely
Medical therapy

- **Hydroxyurea** (increases amount of HbF)
  - Selectively cytotoxic in bone marrow, increases # of erythroblasts producing HbF
  - Cytotoxic – risk of teratogenicity and carcinogenicity
  - Case reports/series with favorable outcomes, no long term follow up
  - Not recommended in pregnancy
Medical therapy

- **EPO** – erythropoietin – hormone that stimulates red cell production
  - Possible stimulation of HbF production
  - Not used for HbF induction in sickle patients
  - May be used in sickle patients with renal insufficiency – (A/E HTN)
Medical therapy

• Prophylactic PCN – OK to continue during pregnancy if on PPX prior to pregnancy
  – Do not need to initiate PPX due to pregnancy
• Deferoxamine - D/c with pregnancy
• ACE inhibitors/ARBs – D/c with pregnancy
• Folate 4mg/day in pregnancy
Case 1

- 25 yo P0000
- Sickle cell disease (hx of multiple transfusions/admissions for pain crisis)
- Presents at 28 weeks – pain crisis, Hb 6.5g/dL
Simple transfusion

- Hb/Hct <6-7g/dL, 18-21%
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Case 2 - Sickle cell disease

- 25 yo P0000- 12 weeks pregnant, hx of sickle cell disease –
- FOB – unknown if carrier – ethnicity – African American
- Inheritance pattern? -- AR
- Carrier rate in general population? Depends on ethnicity – 1 in 12 in this case
- Chance fetus – is carrier? – Obligate carriers
  - Is affected with sickle cell disease?
    - $(1/12 \times 1/2) = 1 \text{ in } 24$
Take home points/Conclusions

• Care in Pregnancy- folate 4mg/day, serial urine cultures
• Crisis management
• Keep inheritance patterns and recurrence risk straight
• Use OMIM, GeneTest for review and options for prenatal diagnosis and counseling
End Sickle Cell Disease in Pregnancy

• Following slides – further hemoglobinopathy review
Thalassemias
Thalassemias –
Beta globin gene -- chromosome 11
Alpha globin gene -- chromosome 16

Life span
Of RBC 120d
## Classification of α/β-Thalassemias (ACOG bulletin, Nussbaum, Gelehter)

<table>
<thead>
<tr>
<th>Number of functional Globin Genes (ratio of α/β globin)</th>
<th>Genotype</th>
<th>Description</th>
<th>Clinical Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 (1)</td>
<td>αα/αα</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>3 (0.8)</td>
<td>α-/αα</td>
<td>Heterozygous α-thal trait (silent carrier)</td>
<td>Asymptomatic (silent carrier)</td>
</tr>
<tr>
<td>2 (0.6)</td>
<td>α-/α- αα/--</td>
<td>“α-thal trait” affected</td>
<td>Mild anemia</td>
</tr>
<tr>
<td>1 (0.3)</td>
<td>α-/-- 1α, rest β</td>
<td>Hb H disease (β4 tetramers detected)</td>
<td>Hb H – marked hemolytic anemia at birth (MCV &lt;50mm3)</td>
</tr>
<tr>
<td>0 (0)</td>
<td>--/-- All 4 γ</td>
<td>Hb Bart’s – no alpha globin</td>
<td>Hb Bart's (hydrops fetalis)</td>
</tr>
</tbody>
</table>

α thalassemia – diagnosed by DNA based testing (S. blot, PCR, ASO)

β thalassemia - βchain deficiency (Hb electrophoresis - >0.5% F, >3.5%% A2)
**α-thalassemia**

- Autosomal recessive; Classification table
- Chromosome 16 – 2 functioning α genes
  - Heterozygous α thal 2 (α-/αα) – silent carrier
  - ‘α thal trait’ – α thal 1 (2 of 4 α globin genes deleted)
    - Southeast Asians – (αα/--heterozygous for α 1, 2
    - Blacks – (α-/α-) – homozygous for α thal 2 chromosome
      - MCV slightly reduced, asymptomatic
  - Hb H → α-/-- essentially all 4 Beta chains, severe anemia
  - Hb Barts – hydrops (--/-- all gamma chains
- Most common abnormality – leads to loss of 1 α-globin gene on a chromosome – unequal crossing over of α-globin cluster on chromosome 16
  - High degree of homology of nucleotide sequences around α1 and α2 genes

Gelehrter p107-109
β thalassemia

- Autosomal recessive; β-globin gene Chromosome 11
- Large number of mutations that can result in decreased or absent function of β-globin gene
- Due to 1 β globin gene per chromosome 11, chance for unequal crossing over is much reduced (vs α thal)
- Classes
  - Minor – 1 normal β-gene, 1 nonfunctional gene
  - Intermedia – abnormality of both β-globin chains, anemic, symptomatic, but not transfusion dependent
  - Major – No β-globin made (both genes mutated), no Hb A made, severe anemia, transfusion dependent
Thalassemia (α/β) – overview

• Definition – quantitative abnormality of the globin chains
• Incidence – α-thal trait - 0.01% in nonmalarial exposed populations Iceland, UK, Japan; 49% in southwest Pacific islanders
  – Hb H disease, hydrops fetalis – restricted to Mediterranean and SE Asia
  – β-thal trait – 1-2% Africans and African Americans; 30% in Sardinia
• Pathogenesis - deficient synthesis of α-globin or β-globin chain that forms the hemoglobin molecule, unbalanced accumulation of alpha/beta subunits (Gelehrter, p96); childhood onset, hypochromic microcytic anemia, HSM, extramedullary hematopoiesis
  – ~80% untreated pts die within 5 years;
  – Transfusion therapy alone – death <30yo (due to infection, hemochromotosis)
  – Iron chelation therapy can reduce chance of hemochromotosis and cardiac, hepatic complications - from repeated transfusions

(OMIM)
Thalassemia – genetic principles

- Heterozygote advantage – carriers of trait display resistance to malaria; prevalence in an ethnic group reflects past and present exposure of a population to malaria
  - Ethnic variation in allele frequencies
- Gene dosage – amount of gene present affects degree of symptoms
Thalassemia & Pregnancy

- Thalassemia trait not increased risk
- Autosomal recessive implications, Screening at risk ethnic groups (Asians, Mediterranean, Blacks)
- Thalassemia major (little to no $\beta$ chain production)- pregnancy is recommended if normal cardiac function, Hb > 10g/dL after hypertransfusion and iron chelation therapy (ACOG 2007)
  - During pregnancy Hb goal >10 g/dL ; Deferoxamine stopped
  - Fetal testing (serial growth scans, weekly testing); CD for obstetric indications
  - Echocardiogram prepregnancy
- $\beta$-thalassemia minor – mild anemia; only ppx iron; fetal testing (ACOG 2007)
- Supportive therapy – Hct >21% (Hb >6g/dL); ideal Hct > 30%
Conclusions

• Keep inheritance patterns and recurrence risk straight

• Use OMIM, GeneTest for review and options for prenatal diagnosis and counseling
Questions -
• QUESTIONS ??
Texas Newborn Screening
http://www.dshs.state.tx.us/LAB/NBSdisorderList.pdf

- Amino Acid Disorders - Phenylketonuria (PKU), Maple Syrup Urine Disease (MSUD), Homocystinuria (HCY), Tyrosinemia Type I (TYR I), Argininosuccinic acidemia (ASA), Citrullinemia (CIT)
- Fatty Acid Disorders - Medium chain Acyl-CoA dehydrogenase deficiency (MCAD), Very Long chain Acyl-CoA dehydrogenase deficiency (VLCAD), Long Chain Hydroxy Acyl-CoA dehydrogenase deficiency (LCHAD), Trifunctional protein deficiency (TFP), Carnitine uptake defect (CUD),
- Organic Acid Disorders - Isovaleric Acidemia (IVA), Glutaric Aciduria Type I (GA-I), 3-hydroxy-3-methylglutaryl CoA lyase deficiency (HMG), Multiple carboxylase deficiency(MCD), Methylmalonic Acidemia/Methylmalonyl-CoA mutase (MUT), Methylmalonic Acidemia/Vitamin B12 Disorders (Cbl A,B), 3-methylcrotonyl-CoA carboxylase deficiency (3MCC), Propionic Acidemia (PROP), Beta ketothiolase deficiency (BKT),
- Hemoglobinopathies - Sickle Cell Anemia (SCA), Sickle C Disease (HB S/C), Sickle Beta Thalassemia (HB S/Th)
- Other Disorders - Hypothyroidism (HYPOTH), Biotinidase deficiency (BIO), Congenital Adrenal Hyperplasia (CAH), Transferase Deficient Galactosemia (GALT), Cystic Fibrosis (CF), Hearing (HEAR)
Kansas Newborn Screening
http://www.kdheks.gov/newborn_screening/disorder_listing.htm

- Amino Acid Disorders - Phenylketonuria (PKU), Maple Syrup Urine Disease (MSUD), Homocystinuria (HCY), Tyrosinemia Type I (TYR I), Argininosuccinic acidemia (ASA), Citrullinemia (CIT)
- Fatty Acid Disorders - Medium chain Acyl-CoA dehydrogenase deficiency (MCAD), Very Long chain Acyl-CoA dehydrogenase deficiency (VLCAD), Long Chain Hydroxy Acyl-CoA dehydrogenase deficiency (LCHAD), Trifunctional protein deficiency (TFP), Carnitine uptake defect (CUD),
- Organic Acid Disorders - Isovaleric Acidemia (IVA), Glutaric Aciduria Type I (GA-I), 3-hydroxy-3-methylglutaryl CoA lyase deficiency (HMG), Multiple carboxylase deficiency (MCD), Methylmalonic Acidemia/Methylmalonyl-CoA mutase (MUT), Methylmalonic Acidemia/Vitamin B12 Disorders (Cbl A,B), 3-methylcrotonyl-CoA carboxylase deficiency (3MCC), Propionic Acidemia (PROP), Beta ketothiolase deficiency (BKT),
- Hemoglobinopathies - Sickle Cell Anemia (SCA), Sickle C Disease (HB S/C), Sickle Beta Thalassemia (HB S/Th)
- Other Disorders - Hypothyroidism (HYPOTH), Biotinidase deficiency (BIO), Congenital Adrenal Hyperplasia (CAH), Transferase Deficient Galactosemia (GALT), Cystic Fibrosis (CF), Hearing (HEAR)
References

- Genetic in Medicine – Thompson/Thompson
- ACOG PB
- MFM Principles – Creasy
- Critical Care OB - Dildy
Notes

• – G3P2 30 weeks – Fatigue complaints. Hb 8g/dL. Peripheral smear, RBC indices c/w hypochromic microcytic anemia. Next step in management –

• Spherocytosis

• 23yo 16wks – c/o fatigue, n/v, yellow eyes. CBC – severe anemia; peripheral smear c/s spherocytosis
Notes

- Case – 22 yo P2002; SCA; Hx of 2 days of bone pain, typical of past bone crisis; CBC – Hb 6.5g/dL; Transfusion will increase blood count, but not decrease duration of the acute pain crisis or improve her pain symptoms.

- Complications include stroke

- Case 18yo P0000, hx sickle cell anemia – 19 weeks with fever shortness of breath and chest pain; CXR with pulmonary consolidation; CT with consolidation/infiltrate – what can precipitate this condition?

- What is condition –

- PPTs- infection, bone marrow emboli, atelectasis, VTE; vaso occlusive crisis of sickle cell disease, pulmonary infarcts; VTE
Notes

• 28yo P2002 at 8 weeks – Hx of ITP – Counseling/evaluation/management
• 28yo P0000 at 28 weeks, no known hx of ITP; platelet count –
  – 105k (DDX, counseling, management),
  – 65k (DDX, counseling, management),
  – 15k (DDX, counseling, management)
ACS

- Diagnostic criteria for ACS — ACS is defined as radiographic evidence of consolidation: a new segmental (involving at least one complete segment) radiographic pulmonary infiltrate \(^3\), AND at least one of the following:
  - Temperature \(\geq 38.5^\circ C\)
  - \(>2\) percent decrease in \(\text{SpO}_2\) (\(\text{O}_2\) saturation) from a documented steady-state value on room air (\(\text{FiO}_2 = 0.21\))
  - \(\text{PaO}_2 < 60\) mmHg
  - Tachypnea (per age-adjusted normal)
  - Intercostal retractions, nasal flaring, or use of accessory muscles of respiration
  - Chest pain
  - Cough
  - Wheezing
  - Râles
- Of importance, the presence of pneumonia can formally be considered as meeting the criteria for ACS, since the two cannot be reliably distinguished from one another.
ACS severity index — Severity of ACS is considered mild, moderate, severe, or very severe,

- Mild ACS — Meets the diagnostic criteria for ACS plus ALL of the following:
  - Transcutaneous oxygen saturation >90 percent on room air (FiO$_2$ = 0.21)
  - Segmental or lobar infiltrates that involve no more than one lobe by chest radiography
  - Responsive to simple transfusion of no more than 2 units of red blood cells (or 15 mL/kg of packed RBCs)
- Moderate ACS — Meets the diagnostic criteria for ACS plus ALL of the following:
  - Transcutaneous oxygen saturation ≥85 percent on room air (FiO$_2$ = 0.21)
  - Segmental or lobar infiltrates that involve no more than two lobes by chest radiography
  - Responsive to transfusion of ≥3 units of red cells (or >20 mL/kg packed RBCs)
ACS severity index — Severity of ACS is considered mild, moderate, severe, or very severe,

- **Severe ACS** — Meets the diagnostic criteria for ACS plus one or more of the following:
  - Respiratory failure present ($\text{PaO}_2 < 60 \text{ mmHg}$ or $\text{PCO}_2 > 50 \text{ mmHg}$)
  - Mechanical ventilatory support required
  - Transcutaneous oxygen saturation $<85$ percent on room air or $\leq 90$ percent despite maximal supplemental $\text{O}_2$
  - Segmental or lobar infiltrates that involve three or more lobes by chest radiography
  - Requiring transfusion or exchange transfusion of RBCs to achieve hemoglobin A levels $\geq 70$ percent
- **Very severe ACS** — Acute respiratory distress syndrome (ARDS) present or sudden, life-threatening lung failure. ARDS is defined by the following three criteria of the American-European Consensus Conference and includes:
  - Acute onset of bilateral infiltrates on chest radiography
  - Pulmonary artery wedge pressure $<19 \text{ mmHg}$ or the absence of clinical evidence of left atrial hypertension
  - $\text{PaO}_2/\text{FiO}_2 \leq 200$ regardless of positive end expiratory pressure (PEEP) level
Uptodate chest sd
Uptodate SCD in preg
Pregnancy and Sickle Cell Disease: Risks

- Maternal death – Mortality 72 deaths per 100,000 deliveries versus 12.7 deaths per 100,000 deliveries in women without SCD.
- Transfusion (OR 22.5; 95% CI 18.7-27.0)
- Systemic inflammatory response syndrome (SIRS; OR 12.6; 95% CI 2.1-13.6)
- Pneumonia (OR 9.8; 95% CI 8.0-12.0)
- Sepsis (OR 6.8; 95% CI 4.4-10.5)
- Asymptomatic bacteriuria (OR 6.8, 95% CI 3.1-14.9)
- Cerebral vein thrombosis (OR 4.9; 95% CI 2.2-10.9)
- Deep vein thrombosis (OR 2.5; 95% CI 1.5-4.1)
- Genitourinary tract infection (OR 2.3, 95% CI 1.9-2.7)
Evaluation

- Diagnosis
- Echocardiogram
- PFTs
- Partner Carrier screening
- Hep B, C testing
- Retinal evaluation (retinopathy can worsen)
- Serial urine cultures
Peripheral smear from a patient with sickle cell anemia shows multiple spindly sickle cells (blue arrows), a nucleated red blood cell in the upper left, and a Howell-Jolly body (black arrow), which is a nuclear fragment normally removed by the spleen. Target cells are also present (red arrow). This patient has functional asplenia because of repeated splenic infarctions. Courtesy of Carola von Kapff, SH (ASCP).
Hgb electrophoresis
Electric field
Sickle (glu6val) valine in place of glutamine
Glutamine has a more Negative charge thus it travels further than Valine (S) or lysine (C)
- A = glutamine has the most negative charge – thus it goes far on the gel
- S = glutamine to valine (middle charge b/n +/-)
- C = glutamine to lysine (more + charge thus it does not go as far on the gel)
- A2 (most positive charge, thus it does not go far on the gel)
Sickle Cell Disease and genetic principles

• Heterozygote advantage, plays role in ethnic variation in allele frequency
• Novel property mutation - sickle cell disease is an exception to the allelic heterogeneity rule in that one specific mutation is responsible for the unique ‘novel’ properties of sickle Hb; Hb C is less soluble than Hb A and tends to crystallize in red cells, decreasing the deformability in capillaries and this also creates mild hemolysis, but Hb C does not sickle or form the rod shaped polymers like Hb S
<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>HB SS</th>
<th>Hb AS</th>
</tr>
</thead>
<tbody>
<tr>
<td>African American</td>
<td>1/700</td>
<td>1/14</td>
</tr>
<tr>
<td>Asian Indian</td>
<td>0/1600</td>
<td>1/700</td>
</tr>
<tr>
<td>Hispanic</td>
<td>1/46,000</td>
<td>1/180</td>
</tr>
<tr>
<td>Middle Eastern</td>
<td>0/22,000</td>
<td>1/360</td>
</tr>
<tr>
<td>Native American</td>
<td>1/17,000</td>
<td>1/180</td>
</tr>
<tr>
<td>White</td>
<td>1/160,000</td>
<td>1/600</td>
</tr>
<tr>
<td>Asian</td>
<td>0/200,000</td>
<td>1/1300</td>
</tr>
</tbody>
</table>
Sickle cell disease & Pregnancy

- Increased risk of morbidity/mortality – depends on severity of anemia
  - Hb SS and to lesser extent Hb SC - Risks include infection, acute chest syndrome, pain crises, dehydration, severe anemia, cholecystitis, preterm birth, low-birth weight infants (<2500g), fetal growth restriction, hospitalization
  - Folic acid supplementation – 4mg/day
  - Painful crisis (tx with pain control, oxygen, IV hydration) – avoid cold temp, heavy exertion, dehydration, stress
  - Acute chest syndrome (fever, tachypnea, chest pain, hypoxia)
  - Autosomal recessive implications for offspring
  - Prophylactic or exchange transfusion – goal of Hct - >21% (ideal ~30%) – decreases risk of painful crises, severe anemia, not necessarily associated with improved pregnancy outcome, less crises, less anemia (ACOG 2007)
Screening in pregnancy (ACOG, 2007)

- CBC, hemoglobin electrophoresis, ferritin (<10 mcg/dL – iron deficiency)
- Individuals of African, Southeast Asian, and Mediterranean descent are at increased risk for being carriers of hemoglobinopathies and should be screened
- Carriers or affected patients – genetic counseling, prenatal diagnosis if mutations have been defined in the parents for thalassemia – DNA mutation analysis for sickle cell disease is available 2 carriers or affected patients
- MCV < 80fL, normal ferritin – screen with hemoglobin electrophoresis
Fig. 1. Specialized antepartum evaluation for hematologic assessment of patients of African, Southeast Asian, or Mediterranean descent. Patients of Southeast Asian or Mediterranean descent should undergo electrophoresis if their blood test results reveal anemia. Abbreviations: CBC = complete blood count; RBC = red blood cell; MCV = mean corpuscular volume; Hb = hemoglobin.
Conclusions

• Keep inheritance patterns and recurrence risk straight
• Use OMIM, GeneTest for review and options for prenatal diagnosis and counseling
Hematology

• END
Renal Disease in Pregnancy

- October 22, 2014
- See ppt slides in folder of renal disease in preg

- Physiology
- DM nephropathy
- Lupus nephritis
- Renal transplant
- Indications for Dialysis
- Oliguria in severe preeclampsia
Renal Disease in Pregnancy

• END
GI Disease in Preg

• Jan 28 2015
• See notes, ppt
• See notes from previous Williams Review
GI Disease in Pregnancy

• END
Endocrinology Emergencies/Disease in Pregnancy

- DIABETES
- Mar 25 2015
• See notes, ppt – see ppt on this talk – from Mar 2012

• See notes from previous Williams Review
Endocrinology Emergencies/Disease in Pregnancy

• END
Endocrinology
Emergencies/Disease in Pregnancy

• THYROID
• MAY 20, 2015
• See notes, ppt – see ppt on this talk – from Mar 2012
• See notes from previous Williams Review
Endocrinology Emergencies/Disease in Pregnancy

• END
YEAR 2
AUTOIMMUNE Disease

- Lupus, RA, APLS
PULMONARY
CARDIAC
ID/Fetal Infections/Genetics/
NEUROLOGIC Disease in Pregnancy
Dermatologic Disease in Preg
• See notes, ppt
• See notes from previous Williams Review
Dermatologic Disease in Preg

- END
Following slides are notes from 2010-2014
Kidney disease

- 24 yo  P0000
- PKD, Cr 3.5
- Prepregnancy evaluation
  - Counseling
  - Management
- Pregnancy counseling
  - Management
- Inheritance of PKD, AD, variable expressivity/penetrance
<table>
<thead>
<tr>
<th>Outcome</th>
<th>Cr&lt;1.5</th>
<th>Cr 1.5-3</th>
<th>Cr &gt;3</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTB</td>
<td>13%</td>
<td>50%</td>
<td>100%</td>
</tr>
<tr>
<td>Perinatal death</td>
<td>5%</td>
<td>17%</td>
<td>33%</td>
</tr>
<tr>
<td>IUGR</td>
<td>10%</td>
<td>20%</td>
<td>100%</td>
</tr>
<tr>
<td>Abortion</td>
<td>11%</td>
<td>21%</td>
<td>25%</td>
</tr>
<tr>
<td>Surviving infants</td>
<td>84%</td>
<td>62%</td>
<td>50%</td>
</tr>
</tbody>
</table>
Multifactorial inheritance

- 24 yo G2P1001
- Previous child with NTD
- Recurrence risk counseling
- Folic acid 4mg
  - Risk reduction by 70%
- Epileptics
  - Prepregnancy counseling/eval/management
CF

- Hardy Weinberg eq
- \( p^2 + 2pq + q^2 \)
- \( 1 = p + q \)
- Obligate carrier example
- Calc of carrier frequency when given disease incidence, v/v
# Wt gain recommendations

**TABLE 1** NEW RECOMMENDATIONS FOR TOTAL AND RATE OF WEIGHT GAIN DURING PREGNANCY, BY PREPREGNANCY BMI

<table>
<thead>
<tr>
<th>Prepregnancy BMI</th>
<th>BMI* (kg/m²) (WHO)</th>
<th>Total Weight Gain Range (lbs)</th>
<th>Rates of Weight Gain* 2nd and 3rd Trimester (Mean Range in lbs/wk)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>&lt;18.5</td>
<td>28–40</td>
<td>1 (1–1.3)</td>
</tr>
<tr>
<td>Normal weight</td>
<td>18.5-24.9</td>
<td>25–35</td>
<td>1 (0.8–1)</td>
</tr>
<tr>
<td>Overweight</td>
<td>25.0-29.9</td>
<td>15–25</td>
<td>0.6 (0.5–0.7)</td>
</tr>
<tr>
<td>Obese (includes all classes)</td>
<td>≥30.0</td>
<td>11–20</td>
<td>0.5 (0.4–0.6)</td>
</tr>
</tbody>
</table>

+ To calculate BMI go to www.nhlbisupport.com/bmi/

* Calculations assume a 0.5–2 kg (1.1–4.4 lbs) weight gain in the first trimester (based on Siega-Riz et al., 1994; Abrams et al., 1995; Carmichael et al., 1997)

The recommended weight gain ranges for short women and for racial or ethnic groups are the same as those for the whole population. In addition, teenagers who are pregnant should use the adult BMI categories to determine their weight gain range until more research is done to determine whether special categories are needed for them. Women who are pregnant with twins are given provisional guidelines. Those in the normal BMI category should aim to gain 37-54 pounds; overweight women, 31-50 pounds; and obese women, 25-42 pounds.
Pulmonary Disease in Pregnancy
Lung Volumes

- **Respiratory rate (# breaths/minute)** – no change
- **Total lung capacity** – total amount of volume you can breathe in after max inspiration
  - decreased
- **Vital capacity** – expired vol with maximal exhalation - NC
- **Residual volume** – what is left after maximal exhalation
  - volume in lungs after VC
- **FRC** – functional residual capacity – volume remaining after normal expiration (take normal breath out – how much vol is left in lungs)
  - Decreased 20%, by 300-500 mL – due to elevation of diaphragm
  - Changing from sitting to supine at term causes another 25% decrease in FRC
    - may increase closure of small airways especially in obese patients in the supine or lithotomy position
- **ERV** – expiratory reserve volume – (FRC – RV)
  - (Vol left after normal breath) – (Vol left after maximal breath)
Other variables

• Airway function – unchanged
• Diffusing capacity – unchanged
• Oxygen delivery – dependent on Hb
  – O₂ delivery = CO x CaO₂ x 10
  – CaO₂ = (Hgb x 1.34 x SaO₂) + (PaO₂ x 0.0031)
  – CaO₂ is thus much more dependant on Hgb function than diffusion of O₂ into serum
  – O₂ delivery can be significantly affected by maternal anemia or CO poisoning
  – Physiologic anemia of pregnancy is compensated by a 50% increase in CO (increases in both HR and SV)
Minute Ventilation is Increased

- **Minute ventilation** – RR x TV
  - Increases 40% to 100-200cc during early pregnancy and remains constant

- **More ventilation at the expense of reserves**
  - Increased AP diameter expansion
    - **Chest circumference increases** 2cm
    - **Diaphragm excursion not impaired, rather increases**
  - **Use up FRC, VC**
Respiratory physiology in pregnancy

• **Residual volume**
  - volume of air remaining in the lungs after maximal expiration
  - decreases 20% due to elevation of diaphragm

• **Functional residual capacity (volume of air in lungs at resting expiratory level)**
  - decreases 20% due to elevation of diaphragm
  - decreases 300-500mL
  - changing from sitting to supine at term causes another 25% decrease in FRC
    • may increase closure of small airways especially in obese patients in the supine or lithotomy position
<table>
<thead>
<tr>
<th>Term</th>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inspiratory</td>
<td>IRV</td>
<td>Capacity (IC)</td>
</tr>
<tr>
<td>Capacity (IC)</td>
<td>VC</td>
<td>Vital Capacity (VC)</td>
</tr>
<tr>
<td>Expiratory Reserve</td>
<td>ERV</td>
<td>Volume (ERV)</td>
</tr>
<tr>
<td>Volume (ERV)</td>
<td>FRC</td>
<td>Residual Volume (RV)</td>
</tr>
<tr>
<td>Residual Volume (RV)</td>
<td></td>
<td>Residual Volume (RV)</td>
</tr>
<tr>
<td>Inspiratory Reserve Volume (IRV)</td>
<td></td>
<td>Total Lung Capacity (TLC)</td>
</tr>
</tbody>
</table>
Pathophysiologic Implications

• Mom is able to hold her breath less
  – 1 vs 2 lung example

• Decreased FRC
  – Closing capacity – amount of volume that has to be behind to keep small airways open - diminished

• Develop hypoxemia quicker than when not pregnant (at greater risk of hypoxemia)

• Pulmonary insults are tolerated less well
# ABG Changes in Pregnancy

<table>
<thead>
<tr>
<th>Variable</th>
<th>Nonpregnant</th>
<th>Pregnant</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.35-7.43</td>
<td>7.4-7.47</td>
</tr>
<tr>
<td>pCO2 (mmHg)*</td>
<td>37-40</td>
<td>27-31</td>
</tr>
<tr>
<td>pO2 (mmHg)**</td>
<td>103</td>
<td>101-104</td>
</tr>
<tr>
<td>P(A-a)O2 (mmHg)**</td>
<td>14</td>
<td>20</td>
</tr>
<tr>
<td>HCO3- (mEq/L)</td>
<td>22-26</td>
<td>18-22</td>
</tr>
<tr>
<td>Base deficit (mEq/L)</td>
<td>1</td>
<td>3</td>
</tr>
</tbody>
</table>

- *compensatory increase in renal bicarbonate excretion*
- **decreased in supine position and 3rd trimester**
- ***increased by 6 in supine position and 3rd trimester***
## Blood Gas Interpretation – Pregnant Women

<table>
<thead>
<tr>
<th>pO2</th>
<th>pCO2</th>
<th>pH</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Decreased</td>
<td>Increased</td>
<td>Mild distress, compensated</td>
</tr>
<tr>
<td>Decreased</td>
<td>Decreased</td>
<td>Increased</td>
<td>Moderate distress, compensated</td>
</tr>
<tr>
<td>Decreased</td>
<td>Normal (~27-31)</td>
<td>Normal</td>
<td>Danger – Impaired Ventilation</td>
</tr>
<tr>
<td>Decreased</td>
<td>Increased (&gt;40)</td>
<td>Decreased</td>
<td>Respiratory Failure</td>
</tr>
</tbody>
</table>
CXR changes in pregnancy

- apparent cardiomegaly (enlarged transverse diameter)
- enlarged left atrium (lateral views)
- increased vascular markings
- straightening of left heart border
- postpartum pleural effusion (right sided)
Oxygen dissociation

- Right shift causes decreased maternal affinity for O2 (increased levels of 2,3-DPG)
- HbF is unable to react to 2,3-DPG, and so maintains high affinity for O2 despite relative acidemia
Cardiac Manifestations of Preeclampsia

- Wedge and CVP Do Not Correlate
- SVR is Low Initially, and then Becomes Very High (along with BP)
- Pulmonary Artery Catheter Findings
  - Elevated SBP, SVR
  - Hyperdynamic LV Function
  - Normal to Increased PCWP
  - Low CVP
  - High Wedge with Low CVP May be Due to Increased Afterload with Volume Depletion
Pulmonary Edema in Preeclampsia

- Occurs in 3% of Women with Preeclampsia
- 70% Occurs Postpartum (Fluid Overload)
- Antepartum Pulmonary Edema Associated with Chronic HTN in 90% Cases
- Risk Factors: Older Women, Multigravidas, Chronic Hypertension
- Associated with Fluid Overload, either Colloid or Crystalloid
Pulmonary Edema in Preeclampsia

• Pathophysiology of Pulmonary Edema
  – Reduced COP
  – Alteration of Capillary Membrane Permeability and Integrity
  – Elevated Pulmonary Vascular Hydrostatic Pressures

• Extravasation of Fluids in Pulmonary Interstitium
Pulmonary Edema in Preeclampsia

- Etiology of Pulmonary Edema
  - Abnormal COP-Wedge Gradient
  - Capillary Leak
  - LV Failure

- Non-hydrostatic Forces can Cause Pulmonary Edema

- Fluid Overload is Common, Presenting with Preeclampsia in Pulmonary Edema is Not (If you see it, think LV failure and know that you are in trouble)
Pulmonary Edema in Preeclampsia

- **Risk factors** – fluid overload, preeclampsia, tocolysis, uncontrolled hypertension

- **Diagnosis of Pulmonary Edema**
  - Clinical Diagnosis: Progressive Dyspnea and Chest Discomfort
  - Tachypnea, Tachycardia, Bilateral crackles
  - Confirm with CXR and ABG
  - Don’t Forget about Pulmonary Embolism
Case

- 34 yo P0, admitted for preeclampsia
  - IVF pregnancy
- HD #3, developed progressive dyspnea, crackles on physical exam, oxygen requirements
  - CXR revealed bilateral pleural effusions
- Fluid restriction, diuretics (Lasix 20mgIV), delivery, seizure prophylaxis
CXR of pulmonary edema
Pulmonary Edema in Preeclampsia

- **Management**
  - Oxygen, Fluid Restriction, Semi-Fowler
  - Accurate intake/output
  - If Fluid Overload, then Lasix, Increasing Doses as Needed
  - Consider PA Catheter: Fluid Overload vs. LV Dysfunction vs. Nonhydrostatic Pulmonary Edema
Indications for PA Catheter in Hypertensive Disease

- Severe preeclampsia with refractory oliguria or pulmonary edema
- Ineffective IV antihypertensive therapy
- Intraoperative or intrapartum cardiac failure
Pulmonary Edema in Preeclampsia – 3 subsets

• Management
  – Intravascular volume depletion (oliguria), low PCWP, high CO, high SVR, low CVP –
    • fluids
  – Renal Vasoconstriction (High PCWP, Normal CO and SVR, uroconcentration):
    • Dopamine – 1-5µg/kg/min; furosemide
  – LV Dysfunction/Failure with Vasospasm (high PCWP, high SVR, low CO <5 L/min):
    • Needs Afterload Reduction (Sodium nitroprusside 0.25-0.5µg/kg/min IV infusion)
    • Volume Restriction
    • Diuretics (max acute dose of furosemide is 120mg, start with 20-40mg)
  – Mechanical Ventilation for Respiratory Failure (If still Pregnant, Intubate Early rather than Late)