Management of Pregnant Patients in the Hospital

Karen Rosene-Montella, MD
SVP Women’s Services, Lifespan
Professor and Vice Chair of Medicine
Director of Obstetric Medicine
Alpert Medical School at Brown University
Tonight’s Goal

- When called by the OB service or ED to see a sick pregnant patient you have a framework to do so
- You know the FDA drug classification limitations
- You feel comfortable with diagnostic testing because
- You understand that fetal well being is dependent on maternal well being
- And..........
Physiologic changes in Pregnancy

Remember Pregnancy is an altered but normal physiologic state
**Hemodynamic Changes in Pregnancy**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Change</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood volume</td>
<td>↑</td>
<td>30-50% increase</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>↓</td>
<td>&lt;120/80</td>
</tr>
<tr>
<td>Cardiac output</td>
<td>↑↑↑</td>
<td>5 to 7 L/m²/min (40% increase)</td>
</tr>
<tr>
<td>Colloid oncotic pressure</td>
<td>↓</td>
<td>10-15% decrease</td>
</tr>
<tr>
<td>EF</td>
<td>↔</td>
<td>70%</td>
</tr>
<tr>
<td>Heart rate</td>
<td>↑</td>
<td>Increase by 10-20 bpm</td>
</tr>
<tr>
<td>Pulmonary artery pressure</td>
<td>↔</td>
<td>&lt;25/12mmHg</td>
</tr>
<tr>
<td>Systemic vascular resistance</td>
<td>↓↓</td>
<td>25-30% decrease</td>
</tr>
</tbody>
</table>
Physiologic Changes of Pregnancy

Gravid uterus can dramatically effect venous return to the heart (preload) in some positions
Physiologic Changes of Pregnancy

- Particular periods of high risk for cardiac decompensation are:
  - when blood volume peaks at the end of the second trimester
  - during the work of labor
  - with postpartum fluid shifts.
Ventilation

- Minute Ventilation increased to 50% over baseline by term (progesterone and increase demand)
- $\text{PaCO}_2$ between 28-32
- Mild respiratory alkalosis
- Increased respiratory rate is never normal!
- $\text{Ph}$ 7.40-7.45 with a mean of 7.44
- Increase in renal excretion of bicarbonate
Altered Pharmacokinetics

- **Increased renal clearance**
  - glomerular filtration rates increase in pregnancy to 150% of normal range and many medications that are renally cleared require dosage alterations in pregnancy.

- **Increased volume of distribution**
  - Plasma volume increases to 150% of normal by 24-28 weeks gestation so that the volume of distribution is increased and therefore drugs may require dosage adjustments.

- **Altered absorption**
  - slowed gastrointestinal motility may delay absorption of oral agents.

- **Altered protein binding**
  - physiological dilutional hypoalbuminemia may lead to an increase in free drug levels for a particular total serum level.
Drug Use in Pregnancy

More harm is caused by withholding treatment from pregnant women than by providing indicated care.
U.S. Food and Drug Administration (FDA) Pregnancy Categories

- **Category A**
  - Controlled studies show no risk

- **Category B**
  - No evidence of risk in humans

- **Category C**
  - Risk cannot be ruled out

- **Category D**
  - Positive evidence of risk

- **Category X**
  - Contraindicated in pregnancy
General Rules

Medications to Avoid

- ACE inhibitors
- Angiotensin Receptor Blockers
- Tetracyclines
- Warfarin
- Isotretinoin
- Fluoroquinolones
Case

- A 24 year old woman at 38 weeks gestation develops marked dyspnea and is found to have a chest x-ray consistent with pulmonary edema.
- The ED admits her to the hospitalist service after OB, Cardiology, the CCU and the MICU have said no thank you.

What is the differential diagnosis and how will you manage her?
Pulmonary edema in pregnancy

- Noncardiogenic pulmonary edema
  - Pre-eclampsia
  - Sepsis (especially pyelonephritis)
  - Tocolytics
  - Aspiration or other pneumonia
  - Amniotic fluid embolism

- Cardiogenic pulmonary edema
  - Occult structural disease (especially MS)
  - Ischemic Heart Disease
  - Peripartum Cardiomyopathy (PPCM)
Pulmonary Edema in Pregnancy


- Tocolytic: 27%
- PIH: 18%
- Cardiac: 26%
- Fluid overload: 22%
- Infection: 4%
- Other: 3%

[Diagram showing the distribution of causes of pulmonary edema in pregnancy]
Preeclampsia/Eclampsia

- Misnomer – can present with Eclampsia
- HTN (BP > 140/90) plus Proteinuria – but much more
Preeclampsia/Eclampsia

- ENDOTHELIAL DYSFUNCTION and VASOSPASM
  - Cardiovascular System – Htn, edema (nonspecific)
  - Neurologic – Brain/retina – headache, visual symptoms
  - Liver – epigastric/RUQ pain, nausea/vomiting
  - Kidneys – decreased urine output
  - Heme
  - Pulmonary

- Treatment is delivery (removal of placenta)
Abnormal placentation and maternal vascular remodeling leads to:

- decreased placental perfusion
- inadequate nutrition/hypoxia
- placental release of factors
- endothelial dysfunction and preeclampsia
Preeclampsia/Eclampsia

- Imbalance between angiogenic factors (PlGF, VEGF) and antiangiogenic factors (sFlt, soluble endoglin)
- Activating immune cells releasing inflammatory cytokines
- Oxidative stress

## Diagnosis of preeclampsia

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Signs</th>
<th>Labs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visual disturbance</td>
<td>Hypertension</td>
<td>&gt; 300 mg protein</td>
</tr>
<tr>
<td>Headache</td>
<td>Retinal disease</td>
<td>Cr &gt; 0.8</td>
</tr>
<tr>
<td>Epigastric/RUQ pain</td>
<td>RUQ tenderness</td>
<td>Uric acid &gt; 0.5</td>
</tr>
<tr>
<td>(Edema)</td>
<td>Clonus</td>
<td>↑ AST</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ Hb</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Plt &lt; 150 k</td>
</tr>
</tbody>
</table>
Preeclampsia Evaluation

- CBC (plts, hgb)
- AST
- Creatinine, Uric Acid, Urinalysis
  - Protein/Creatinine ratio (<0.1 or >0.4 most helpful)
  - 24 hour urine for total protein and creatinine clearance
- Consider full LFTs, coags, DIC screen, LDH, haptoglobin

- Fetal Assessment - Obstetrician
  - NST/Biophysical Profile as indicated
  - Ultrasound for fetal growth
  - Possible Umbilical artery dopplers
Complications of Preeclampsia

- Maternal complications
  - Pulmonary Edema
  - HTN
  - Cardiac
  - Neurologic – Seizure, CVA
  - DIC
  - ARF
  - HELLP
  - Hepatic Infarct, rupture, hemorrhage
  - DI
Pulmonary Preeclampsia/Eclampsia

- Pulmonary edema (2-4% of preeclampsia)
  - Endothelial damage - capillary leak
  - Decreased oncotic pressure associated with pregnancy, further decreased with significant proteinuria
  - Decreased urinary output
  - IV fluids – magnesium
  - Steroids for fetal lung maturity contributes to Na retention
  - Preeclampsia related LV dysfunction
BP Control in Preeclampsia

- Goal = BP 140-155/90-105
- Medications for acute treatment of hypertension

<table>
<thead>
<tr>
<th>Drug</th>
<th>Initial dose</th>
<th>Onset of action</th>
<th>Duration of action</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Labetalol</td>
<td>10 mg IV</td>
<td>5-10 min</td>
<td>3-6 hrs</td>
<td>Contraindications: Asthma, bradycardia, cocaine, AV block</td>
</tr>
<tr>
<td>Hydralazine</td>
<td>2.5 – 10 mg IV</td>
<td>10-20 min</td>
<td>3-6 hrs</td>
<td>Watch for hypotension</td>
</tr>
<tr>
<td>Nifedipine</td>
<td>10 mg po</td>
<td>&lt; 30 min</td>
<td>4-5 hrs</td>
<td>May cause headache</td>
</tr>
</tbody>
</table>
Cardiovascular – Preeclampsia/Eclampsia

- Htn – often severe including Hypertensive Crisis, can be labile
  - Labetolol
  - Hydralazine
  - Nifedipine
  - Ace-inhibitors if postpartum
  - Nitroglycerin
  - Nitroprusside

- Goal BP <160/110 (+/-) but >140/90
Cardiovascular
Preeclampsia/Eclampsia

- HTN
- Left ventricular dysfunction
  - Secondary severe htn/afterload
  - Small vessel vasospasm
- Intravascular volume depletion – 3rd spacing
An echocardiogram is done which shows a structurally normal heart with an ejection fraction of 30%.
Peripartum Cardiomyopathy

- **Incidence**
  - Reports range from 1/1000 to 1/15000
  - 1000 women per year in USA

- **NHLBI Diagnostic Criteria**
  - Development of cardiac failure in last month of pregnancy or up to 5 months postpartum
  - No other identifiable cause
  - Absence of recognizable heart disease prior to last month of pregnancy
  - Evidence of LV dysfunction by echocardiogram
Peripartum Cardiomyopathy

- Treatment is the same as for any dilated cardiomyopathy except:
  - Avoid ACE-I and ARBs until after delivery
  - Treatment may need to include anticoagulation because of the high risk of thromboembolism.
- Heart failure treatment includes:
  - Diuretics
  - Vasodilator, eg Hydralazine
Ischemic Heart Disease

- Low dose ASA, nitrates, beta-blockers, heparins and thrombolytics (remote from delivery) okay to use.
- Coronary angioplasty and bypass have been safely performed in pregnancy.
Management of Acute Arrhythmias in Pregnancy

- Fetal well-being depends on maternal well-being
- Pregnancy does not significantly alter the approach to arrhythmia. ACLS protocols should be followed as in the nonpregnant
- DC cardioversion can be safely carried out during pregnancy.
  - Fetal monitoring devices should be removed to prevent arcing
  - Use appropriate maternal analgesia
Complications of Preeclampsia

- Our patient next complains of feeling “foggy” and is having trouble focusing on the book she is trying to read.
- Listen closely diagnostic clues as this population is basically young and healthy and always looks less sick than they are
Brain – Preeclampsia/Eclampsia

- Vasospasm and Endothelial Damage to Brain
- Cerebral edema
- Petechial hemorrhage
- Fibrinoid necrosis of the cerebral arterioles
Seizure = Eclampsia

- Occurs 1 in 200 untreated patients
- Rare in developed world
- Associated with 5% maternal mortality, 13%-30% perinatal mortality
- Onset antepartum (38-53%), intrapartum (18-36%), postpartum (11-44%)
- Usually preceded by signs of neuromuscular irritability
Treatment of Eclamptic Seizure

- Ensure airway protection and maternal oxygenation
- IV lorazepam or diazepam to stop sz
- Initiate fetal monitoring
- Magnesium bolus 4-6 g, then 1-4 g/hr
- Keep BP > 140/90 <155/105
- Check preeclampsia labs
- Initiate plans for delivery
- Head CT, timing to be determined by clinical status
Eyes – Preeclampsia/Eclampsia

- Visual disturbances (central or peripheral causes) common: scotomata, scintillations, blurred vision, visual loss
  - Cortical blindness – generally resolves
  - Vasospasm – segmental or diffuse
  - Serous retinal detachment
  - Retinal hemorrhages
Figure 2. Complete (irreversible) cerebral infarctions in a 24-year-old woman who developed cortical blindness after difficult labor. (a) Axial diffusion-weighted MR image shows restricted diffusion in both occipital lobes, primarily in the arterial watershed zones. (b) Axial FLAIR MR image shows corresponding edema and mass effect. MR imaging performed 7 weeks later showed corresponding laminar necrosis and cortical atrophy.
Lab Results

- The patients labs come back and her 24 hour urine shows 3 grams of protein.
- While you are thinking about how low her antithrombin must be and considering if she needs thromboprophylaxis the nurse calls to say that her left leg is markedly swollen and she is complaining of increased SOB
Pregnancy is a Hypercoagulable State

- Increased Clotting Factors
- Decreased Fibrinolysis
- Venous Stasis
Virchow’s Triad

Stasis
- Compression iliac veins
  - Rt. iliac artery over left iliac vein
  - Gravid uterus
- Hormonally mediated vein dilation
- Immobilization

Vascular Damage
- Vascular compression at delivery
- Assisted or operative delivery

Hypercoagulable Blood
- ↑ Procoagulant factors:
  - ↑ fibrinogen, ↑ factor V, IX, X XII and VIII levels
- ↓ Anticoagulant activity:
  - ↓ Protein S levels and ↑ activated protein C resistance
- ↓ Fibrinolytic activity:
  - ↑ PAI-1 and 2 and ↓-PA activity
= more thrombin generation + less clot dissolution
Epidemiology of VTE:

- VTE is 5-10X more common in the pregnant vs nonpregnant state
- VTE occurs in 5-13/10,000 pregnancies antepartum and 3-7/10,000 postpartum
- The risk is further increased by the presence of an additional risk factor
Other Risk Factors During Pregnancy

- Prolonged bedrest
- Cesarean Section
- Ovarian Hyperstimulation
- Preeclampsia
- Parity $\geq 3$
- Previous VTE, Thrombophilia or Family Hx
- Lifestyle: Tobacco Use, Obesity, Maternal Age
- Previous Superficial Thrombophlebitis
Significance

- PE is the leading medical cause of Maternal Mortality
- Fifty percent of VTE in women under 40 occur in association with Pregnancy
- Post Phlebitic Syndrome in 80%
- Objectively confirmed deep venous insufficiency in 65%
When In Pregnancy Does VTE Occur?

- Most DVT occurs antepartum
- Events are evenly distributed throughout gestation
- PE may be more common post partum
- Day to day risk greatest post partum
VTE incidence

- Incidence of DVT is 3 times higher than incidence of PE in pregnancy
- DVT is left sided in close to 85% of cases
- Isolated pelvic DVT much more common in pregnancy (11%* vs 1%#)

*James AH. AJOG 2005
#Goldhaber SZ. Am J Cardiol 2004
Diagnosis of Acute Thrombosis

- Clinical signs unreliable
- ≥90% of DVT occurs in the left leg
- LEFt clinical predictors
- A-a gradient/ABG’s normal in 60% of documented PE’s
Diagnosis of Acute Thrombosis

- Use Compression Ultrasonography
- Ventilation/Perfusion Scan has been diagnostic test of choice for PE
- CT Angio *limited pregnancy data*
  - Concern re maternal breast radiation exposure (2-3.5 rads)
Leg Studies

- **Ultrasound**
  - Test of choice
  - Protocol includes iliac veins and IVC at level of liver pregnant and postpartum

**MRI/MRV**

In patients with suspected iliac or pelvic vein thrombosis
Advantages and disadvantages of imaging techniques in pregnancy

Ventilation perfusion scans

**Advantages**
- Low radiation exposure to breast
- Low radiation exposure to fetus
- High rate of normal scans in pregnancy 70%

**Disadvantages**
- Interpretation of test strongly linked to clinical pretest probability. No clinical decision rules validated in pregnancy
- Does not offer alternative diagnosis
Advantages
• Could offer an alternative diagnosis
• Low radiation exposure to fetus
• Better availability than ventilation perfusion scintigraphy
• More cost effective than other approaches

Disadvantages
• Radiation exposure to breast (can be reduced with breast shields)
• Technical limitations in pregnancy. Need to modify imaging and injection protocol
• No accuracy or outcome studies available
• High rate of detection of subsegmental emboli (the clinical significance of subsegmental emboli is unclear, so the rate of detection needs to be low)
• Theoretical concern about the effect of iodinated contrast on fetal thyroid
UK Confidential Inquiry on Maternal Mortality

- Most common error leading to death was failure to diagnose VTE
- Occurred in over half of the 28 cases reviewed
- Typical errors were:
  - to only consider infection as a cause of symptoms and
  - *Failure to investigate because of mistaken belief that radiological testing is contraindicated in pregnancy*
Diagnostic Imaging

- US National Council on Radiation Protection
  - No evidence of adverse effects from exposures <5 rads (0.05 Gy)
  - Almost all commonly used diagnostic imaging involves radiation exposure well below 1 rad
<table>
<thead>
<tr>
<th>STUDY</th>
<th>RADIATION EXPOSURE (RADS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest X-ray</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Lung Scan</td>
<td>0.01-0.02 ventilation</td>
</tr>
<tr>
<td></td>
<td>0.01-0.03 perfusion</td>
</tr>
<tr>
<td>Pulmonary Angiogram</td>
<td>&lt;.050 via brachial route</td>
</tr>
<tr>
<td></td>
<td>0.2-0.3 via femoral route</td>
</tr>
<tr>
<td>CT angiogram</td>
<td>0.2-0.3</td>
</tr>
</tbody>
</table>
Treatment of Acute Thrombosis

- The safety of both UFH and LMWH for the Fetus have been established
- There is less thrombocytopenia and osteoporosis with LMWH
- Dosing Requirements for both Increase with Increasing Gestation
Treatment of Acute Thrombosis*

- Initial IV Heparin followed by subcutaneous adjusted dose UFH or LMWH or
- Initial adjusted dose (1mg/kg q 12 h) LMWH which is then continued
- Consider change to UF heparin for epidural
- Duration and Intensity of Treatment not well established but needs to continue at least six weeks post partum
Vena cava filters

- Temporary filters can be placed in the supra-renal IVC
- Risk of complications in supra-renal likely similar to infra-renal (1)
- Potential technical difficulties in pregnancy

Kalva AP. J Vasc Interv Radiol 2008
Providence, Rhode Island
Subscription Based Service for Hospitals

A single annual fee provides ....

- Professional Education on Pregnancy and Medical Complications of the Mother
  - Onsite medical education
  - Topical webinars
  - Additional online information for specific conditions
  - Care modules

- Physician to Physician Consult Service
  - Ob Med maintains a 24/7 on call service
  - Phone or on site

Principal goal is to increase capacity of a hospital to support medical admissions of pregnant women

Back up service for hospitalists or OB GYNs dealing with a complex medical case involving the mother
How it would work

A pregnant woman with medical complication is admitted

Refer back to educational materials

Seek real-time consult with Team Member