Pregnancy, CKD, and ESRD

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The 'Obstetric Nephrologist'

- Management/counseling of pregnant women with all forms of renal disease
  - How does pregnancy affect renal disease?
  - How does renal disease affect pregnancy?
- Evaluation of new onset hypertension, creat, or proteinuria during pregnancy
- Work with MFM team

Kidney Disease and Hypertension in Pregnancy: The Roadmap

- Physiologic adjustments to pregnancy
- CKD in pregnancy
- Acute kidney injury
- ESRD

Clinically Significant Hemodynamic Alterations in Pregnancy

- Vasodilation - Lower blood pressure – increased plasma volume
- Decreased afterload; increased cardiac output
- Increased heart rate
- Increased respiratory rate

\[ \text{GFR} = (\Delta P - \Delta \tau) \times k_f \]

↑ U Calcium

Renal Vasodilation
+ GFR
+ RBF
+ Scrat
+ Uprotein
+ Aldosterone
+ Na reabsorption
+ H₂O reabsorption
+ \( \Delta \text{Na} \)
+ \( \Delta \text{Sosm} \)
+ glucosuria
+ amino aciduria
Acid Base Changes in Pregnancy
- Lower PCO2, (progesterone mediated increased respiratory rate)
- Mild metabolic compensation for respiratory alkalosis
- Slightly lower serum bicarbonate

Summary: Renal Physiology in Pregnancy
- Increased kidney size
- Increased GFR
- Increased Renal blood flow
- Increased urinary protein excretion
- Physiologic ‘hyponatremia’ : resetting of osmostat
- Hypercapnea and compensatory increase in bicarbonate excretion

How Might Pregnancy Adversely Affect Renal Disease?
- ? Hyperfiltration – Limited evidence for increased GC Pressure
- ? Increased inflammatory response
- Increased urinary protein excretion
- Preeclampsia
- Possibility of permanent loss of function

Renal Outcomes After Pregnancy in Women with Moderate CKD
- 30% Irreversible ↓GFR
- Hypertension: Worse Outcomes

Baseline Creatinine Predicts Worsening of GFR in Pregnancy

How Does Renal Disease affect Pregnancy?
- The significant hemodynamic and hormonal adjustments made by the kidney are essential for fetal growth and development
- Women with impaired kidney function have adverse pregnancy outcomes in proportion to the degree of GFR reduction and hypertension

Healthy Kidneys – Healthy Pregnancy
Stage 1 and 2 CKD and Pregnancy Outcomes

<table>
<thead>
<tr>
<th>Stage 1 CKD N=127 (eGFR&gt;90)</th>
<th>Stage 2 CKD N=28 (eGFR 60-90)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delivery&lt;37 wks</td>
<td>28%</td>
</tr>
<tr>
<td>Delivery &lt;34 wks</td>
<td>10%</td>
</tr>
<tr>
<td>SGA</td>
<td>14%</td>
</tr>
</tbody>
</table>

Pregnancy Outcomes with Moderate to Severe CKD (Jones, Hayslett)

- 60% pre term delivery
- 37% IUGR
- 7% Fetal loss
- Maternal hypertension and proteinuria: 50%

Risk of Preeclampsia is Proportional to Severity of CKD

Pre Donation vs. Post Donation Pregnancy Outcomes (Ibrahim et al 2009)

<table>
<thead>
<tr>
<th></th>
<th>Pre Donation</th>
<th>Post Donation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre term Del</td>
<td>4%</td>
<td>7.1%</td>
</tr>
<tr>
<td>Fetal Loss</td>
<td>11.3%</td>
<td>19.2%</td>
</tr>
<tr>
<td>Gest DM</td>
<td>0.7%</td>
<td>2.7%</td>
</tr>
<tr>
<td>Maternal HTN</td>
<td>0.6%</td>
<td>5.7%</td>
</tr>
<tr>
<td>Preeclampsia</td>
<td>0.8%</td>
<td>5.5%</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>1.1%</td>
<td>5.3%</td>
</tr>
</tbody>
</table>

P = 0.0001

Summary

- Renal adjustments to pregnancy are profound, and apparently necessary for normal gestation
- There is a direct relationship between degree of renal dysfunction, hypertension, significant proteinuria and adverse pregnancy outcome
- Even mildly reduced GFR is associated with pre term birth, fetal loss, preeclampsia

CKD and Pregnancy

Take Home Message (Summary)

- Outcome related to GFR, Proteinuria, and BP:
  - Favorable (but not equal to ‘normal’) if Scr < 1.5 mg/dl, proteinuria < 1 g/d (Imbasciati et al 2007; Rene e Gravidanza)
  - Favorable in absence of hypertension
  - Little evidence for relationship between histologic diagnosis and outcome
**Type 1 Diabetes: Diabetic Nephropathy**

- **Maternal Risks**
  - accelerating hypertension/preeclampsia
  - worsening proteinuria
  - deterioration in renal function
  - maternal death

- **Fetal Risks**
  - Pre-term birth,
  - Death

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**Pregnancy Outcome in 240 Type 1 Diabetics**

(Ekbom et al, 2001)

<table>
<thead>
<tr>
<th>Pre Pregnancy Proteinuria</th>
<th>Albumin</th>
<th>Microalbumin (30-300 mg/24 h)</th>
<th>Nephropathy (&gt;300 mg/24 h)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>203</td>
<td>26</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Preeclampsia</td>
<td>12(6%)</td>
<td>11(42%)</td>
<td>7(64%)</td>
<td>.001</td>
</tr>
<tr>
<td>Del &lt; 37 wk</td>
<td>71(35)</td>
<td>16(62)</td>
<td>10(91)</td>
<td>.001</td>
</tr>
<tr>
<td>Del &lt; 34 wk</td>
<td>12(6)</td>
<td>6(23)</td>
<td>5(45)</td>
<td>.001</td>
</tr>
<tr>
<td>SGA</td>
<td>4(2)</td>
<td>1(4)</td>
<td>5(45)</td>
<td>.001</td>
</tr>
</tbody>
</table>

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**Renal Outcome** After Pregnancy with Diabetic Nephropathy (Rosing et al 2004)

- Prospective cohort of type 1 Diabetic women with normal GFR and microalbuminuria
- Compared women who became pregnant with those who did not
- Similar rate of decline of renal function in pregnant group
- Pregnancy does not adversely affect DN (normal baseline renal function)

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**Management of Diabetic Nephropathy**

Before and During Pregnancy

- Tight blood sugar control with multiple injections and dietary supervision
- DC ACE I/ARB; antihypertensive therapy with methyldopa, labetolol, calcium antagonists, diuretics
- Antepartum cardiac evaluation
- Laboratory assessment every month

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**Diabetic Nephropathy in Pregnancy: Summary**

- Improved outcomes with microalbuminuria alone
- Maternal mortality increased
- First trimester glycemic control is important
- ACE inhibitors and ARB’s are contraindicated

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**Lupus is Associated with Poor Pregnancy Outcomes**

- ‘Active’ SLE at conception doubles fetal loss (25%)
  triples pre term births (75%)
  (Clowse et al. 2005)

- 4 fold increase in stillbirth
  30% preterm birth, 28% LBW
  20-30 % Hypertension/preeclampsia
  (Dhar et al. 2005)
Lupus and Pregnancy
Risk Factors for Adverse Pregnancy Outcomes:
• Chronic, long duration of disease
• Disease active at conception
• Antiphospholipid antibodies
• Hypertension, ↓ GFR, proteinuria in 1st trimester
• Pregnancy may be associated with flares in disease: conflicting reports

* Course during pregnancy is unpredictable

Lupus Nephritis and Pregnancy
Case control studies (Piccoli 2004, Tandon 2004):
• No difference in exacerbation of renal activity in pregnant c/w non pregnant matched women: 30-40% had increased activity of nephritis throughout pregnancy; 25% deterioration in renal function

Pregnancy with Biopsy Confirmed Lupus Nephritis
Imbasciati et al; NDT, 2009
• 113 pregnancies: Nl baseline renal function
• Fetal loss – 13%
• 30% preterm birth; 25% IUGR

Pregnancy and Lupus Nephritis
Imbasciati et al.
• 34 renal flares; most treatable; 3 deterioration in GFR, one ESRD

Predictors of Pregnancy Outcomes:
• Hypocomplementemia, low dose aspirin

Predictors of Adverse Renal Outcomes:
• Proteinuria > 1g; GFR < 60 (OR 9)
• Partial remission (OR 3)

Treatment of Lupus Nephritis in Pregnancy
• High dose steroids; ? Pulse Rx
• Azathiaprine, hydroxychloroquine
• Cytoxan, cellcept rarely/never justified
• Delivery for worsening maternal or fetal condition: superimposed 'pregnancy component' may be indistinguishable from renal flare

Lupus Flare vs Preeclampsia?
Proteinuria SLE PE
Hypertension + +
↓ GFR + +
RBC Casts + -
Low C3,C4 + -
Abnl LFTs - +/-
Low platelets + +/-
Low WBC + -
Antiphospholipid Antibodies in Pregnancy

- Fetal loss: miscarriage, 2nd trimester loss, Stillbirth
- Arterial and venous thrombosis
- Renal vasculitis, thrombotic microangiopathy
- Severe, early preeclampsia
- Rx: LMW Heparin, hydroxychloroquine, ASA

Lupus Nephropathy: Summary

- Possibility of flare during pregnancy increases morbidity
- Conception should be discouraged when disease is ‘active’
- Antiphospholipid antibodies (LAC) are associated with poor pregnancy outcome
- Cytoxan and cellcept are contraindicated in pregnancy

CKD in Pregnancy

- Anatomic/congenital: Reflux, solitary kidney
- GN; IgA, FSGS, Vasculitis (SLE, Wegener’s)
- PKD
- Interstitial nephritis

Renal Disease First Diagnosed During Pregnancy

- Any mild renal disease may become clinically apparent for the first time during pregnancy because of hemodynamically mediated increase in proteinuria, closer monitoring of BP and U/A
- Examples: FSGS, Reflux nephropathy, chronic pyelo, ADPKD, SLE
- 40% of stage 1 CKD – diagnosis made during pregnancy (Piccoli et al 2012)

Renal Evaluation During Pregnancy

- GFR: serum creatinine, creat clearance
- Proteinuria: 24 hr urine, P:C ratio
- Serologies
- Ultrasound
- Biopsy: < 30-32 weeks deteriorating function morbid nephrotic syndrome; Bx may be associated with significant morbidity

Polycystic Kidney Disease and Pregnancy

- Increased incidence of UTI
- Maternal hypertension associated with poor outcome
- Extrarenal complications: SAH, liver cysts
Assessment of GFR and Proteinuria in Pregnancy

- GFR estimating equations (e.g. MDRD) are not valid for pregnancy
- Creatinine clearance is gold standard
  - Preeclampsia GFR (PGFR) — Alper et al.
- Serum creatinine is useful, although sensitivity for mildly reduced GFR is low

Protein Creatinine Ratios

- “…if validated for pregnancy, a messianic gift to clinical trials” Marshall Lindheimer 2010
- Data comparing PC ratio to 24 hour urine: > 15 studies — varying clinical circumstances, methodologies
- Cutoff for normal ranges from .19 to 1.1 gm/gm
  - for mmol/L urine protein \( \times 0.088 \div \) urine creatinine

Not Widely Used by Obstetricians

Intrinsic Renal Disease vs Preeclampsia (gestational age> 20 wks)

<table>
<thead>
<tr>
<th></th>
<th>Preeclampsia</th>
<th>Renal Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>BP</td>
<td>&gt; 140/90 mm Hg</td>
<td>variable</td>
</tr>
<tr>
<td>Uprot</td>
<td>&gt;300 mg/d</td>
<td>variable</td>
</tr>
<tr>
<td>Serum Cr</td>
<td>.8-1.2 mg/dl</td>
<td>&gt;1.0 mg/dl</td>
</tr>
<tr>
<td>Uric acid</td>
<td>&gt;5.5 mg/dl</td>
<td>variable</td>
</tr>
<tr>
<td>LFTs</td>
<td>may be increased</td>
<td>normal</td>
</tr>
<tr>
<td>Platelets</td>
<td>may be decreased</td>
<td>usually normal</td>
</tr>
<tr>
<td>UA</td>
<td>protein, +/- RBC, WBC</td>
<td>variable</td>
</tr>
</tbody>
</table>

Management of CKD During Pregnancy

- Preconception counseling; DC ACE-I, ARB’s
- Multidisciplinary Approach
- Frequent monitoring of BP (q 1-2 weeks) and renal function (q month)
- Balanced diet (moderate Na, protein)
- Maintain BP 120-140/80-90 mm Hg
- Watch for preeclampsia

Antihypertensive Therapy in Pregnancy

- Blood pressure may decrease: fewer medications may be needed
- Failure of blood pressure to decrease may be a poor prognostic sign
- Treatment targets should probably be lower than in essential hypertension; no clinical trial data available

Antihypertensive Drugs Safe in Pregnancy

- Methyldopa (clonidine, if side effects to MD)
  - Starting dose 250 BID
  - Maximum of 500 QID
- Labetolol (and other beta blockers)
  - Starting dose 100 BID
  - Maximum 200 QID
- Nifedipine XL (other NDHP CCBs have been used)
  - Starting dose 30 OD
  - Maximum 90 OD
- Diuretics: HCTZ, Furosemide, especially with reduced GFR
CKD in Pregnancy: Summary

- ADPKD may be diagnosed during pregnancy
- Kidney biopsy is rarely indicated during pregnancy
- Increased creatinine without proteinuria: CKD, not preeclampsia
- Proteinuria without hypertension: CKD, not preeclampsia

Acute Kidney Injury in Pregnancy and the Puerperium

- ATN: hemodynamic, NSAID's, toxins, septic, etc.
- AIN
- Acute fatty liver
- Preeclampsia/HELLP
- Microangiopathic syndromes
- Acute cortical necrosis: obstetric hemorrhage

HELLP Syndrome, Acute Fatty Liver of Pregnancy, HUS/TTP

- **Time of Onset:**
  - HELLP/AFLP: third trimester
  - TTP: any time
  - HUS: post partum
- All usually associated with hypertension

- **Laboratory Features:**
  - Decreased platelets, microangiopathy: all
  - Elevated LFT's: HELLP and AFLP
  - Hypoglycemia, coagulopathy: AFLP
  - Severe renal dysfunction: HUS
  - Moderate renal dysfunction: AFLP
  - Mild renal dysfunction: TTP/HELLP

Acute Fatty Liver of Pregnancy vs HELLP

- **AFLP**
  - anorexia, nausea, vomiting
  - early onset, moderate to severe AKI
  - Mitochondrial dysfunction due to inhibition of b-oxidations of fats; may be due to fetal genetic defect; Neonatal surveillance

- **HELLP**
  - headache, RUQ pain, chest pain
  - Severe AKI rare
  - pathogenesis similar to preeclampsia

Thrombotic Microangiopathy and Pregnancy

- Overall frequency: 2 in 25,000 pregnancies: 12-15% of cases of TTP/HUS occur in pregnancy
- TTP: Small decrease in ADAMTS 13 observed in late pregnancy and puerperium (Sanchez-Luceros et al; *Thromb Haemost* 2004)

Pregnancy Associated HUS (P-aHUS)

- 20% of pts with aHUS develop P-aHUS (*Fakhouri et al JASN 2010*)
- High prevalence of mutations in complement genes: CFH most common (FH deficiency)
- Post partum HUS may be due to loss of placental regulatory proteins that compensate for increased complement activation due to inherited mutations
P-aHUS: Clinical Implications

- Highest frequency in second pregnancies
- As many as 75% of pregnancies in patients with hX of aHUS and complement dysregulation have uneventful pregnancies: 20% have P-aHUS (75% ESRD), 7.4% preeclampsia, 4.6% fetal loss
- Non penetrance rate of complement mutations in aHUS ~ 50%; pregnancy is a triggering event

AKI: Summary

- Preeclampsia and HELLP syndrome are common causes of AKI in pregnancy, but AKI is a rare complication of preeclampsia and HELLP
- NSAIDs in the puerperium may cause AKI
- Pregnancy associated atypical HUS usually develops post partum and is associated with genetic alterations in alternate complement pathway (CFH deficiency)

Dialysis and Pregnancy

- Asamiya et al (KI 2009): 28 pregnancies; only 2 full term (average, 32 weeks)
  - 18 infants survived one year
  - BUN should be <= 48mg/dl
  - Hb should be 9-11
  - Better outcomes associated with increased dialysis, EPO, transfusions
- Luders et al (AJKD 2010): 52 pregnancies, 87% success rate (32 wks)
  - Preeclampsia major risk factor for adverse outcome

Dialysis and Pregnancy

- Successful pregnancy on Nocturnal HD (Banu et al; CJASN, 2008): 5 pts, 48 hours dialysis, gest age 36 weeks
- Early initiation of CAPD when GFR ~ 20 ml/min (Jeffreys et al, Nephrology 2008)

Transplantation and Pregnancy

- Prognosis depends on BP and baseline renal function (< 1.5 -2 mg/dL; nl BP)
- Controversy whether pregnancy accelerates graft loss
- Patients are advised to wait 1-2 years post transplant
- CN inhibitors associated with HT, prematurity
- Cell cept, Rapa: contraindicated
- Azathiaprine, prednisone: preferred regimen

Hypertension in Pregnancy: What Does the Nephrologist Need to Know?

- Differential diagnosis of hypertension in pregnancy - how to recognize preeclampsia
- Evaluation and treatment of chronic hypertension
- When should blood pressure be lowered?
- How should blood pressure be lowered?
**Preeclampsia: Morbidity**

- Leading cause of maternal death (15-20%, ~75,000 per year)
- About 1% of cases develop eclampsia
- CVA, Placental abruption, acute renal failure, bleeding, liver rupture

**Long Term 'Sequelae' of Preeclampsia**

- HTN (4 fold increase), heart disease (2 fold increase), stroke, VTE
- Insulin resistance, altered endothelial cell function
  - shared risk factors vs. cause and effect
- Preeclampsia with IUGR and preterm birth: 7 fold risk of hospitalization for ischemic heart disease
- Renal outcomes: Small but increased risk of later ESRD, microalbuminuria

**Classification**

- Chronic hypertension
- Preeclampsia-eclampsia
- Preeclampsia superimposed upon chronic hypertension
- Gestational hypertension

**Differential Diagnosis of Hypertension in Pregnancy**

- < 20 weeks gestation: Chronic hypertension (primary or secondary)
- > 20 weeks gestation: preeclampsia, chronic hypertension with or without superimposed preeclampsia, gestational hypertension
- Normal labs, multiparous: more likely gestational or chronic hypertension

**Preeclampsia: Clinical Features**

- A syndrome of pregnancy, diagnosed after 20 weeks, characterized by:
  - Hypertension: >= 140/90 mm Hg, proteinuria >=300 mg/day, OR evidence of organ dysfunction (LFTs, platelets).
  - Mild to moderate HTN – 140-159/90-109 mm Hg
  - Severe HTN- 160/110 mm Hg
- Headache, visual disturbances, abdominal or chest pain; Edema of hands and face; Sudden weight gain

**Lab Tests In Preeclampsia**

<table>
<thead>
<tr>
<th>Test</th>
<th>Normal Pregnant</th>
<th>Preeclampsia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine Protein</td>
<td>≤ 300 mg/day</td>
<td>&gt; 300 mg/day</td>
</tr>
<tr>
<td>Creatinine</td>
<td>.4-.6 mg/dl</td>
<td>&gt; .8 mg/dl</td>
</tr>
<tr>
<td>Uric Acid</td>
<td>&lt; 4.5 mg/dl</td>
<td>&gt;5.5 mg/dl</td>
</tr>
<tr>
<td>Urine calcium</td>
<td>Variable, &gt;200 mg/day</td>
<td>&lt; 150 mg/day</td>
</tr>
<tr>
<td>BUN</td>
<td>&lt;15 mg/dl</td>
<td>10-20 mg/dl</td>
</tr>
</tbody>
</table>
Laboratory Tests in Preeclampsia

- ↑ Hematocrit (> 36%)
- Thrombocytopenia (< 100,000)
- Elevated liver enzymes
- HELLP syndrome: hemolysis, elevated liver enzymes, low platelet count

Common Diagnostic Mistakes in Preeclampsia

- Ignoring high normal blood pressure or changes in BP (120-139/80-89 mm Hg)
- Ignoring subtle lab abnormalities (e.g. uric acid 6 mg/dl, creatinine .9 mg/dl, Hct 39, platelets 140 K)
- Ignoring 3rd trimester non specific complaints: headache, nausea

New onset HTN in 3rd trimester is Preeclampsia until proven otherwise

The Obstetric Nephrologist's Role in Management of Hypertensive Pregnancy

- Establishing an accurate diagnosis
- Management of blood pressure
- Timing of delivery

Maternal Deaths Due to Preeclampsia/Eclampsia per year (WHO)

- Incidence of preeclampsia: 1.3-6.7%
- Incidence of eclampsia: .8-2.3%
- Maternal deaths due to preeclampsia/eclampsia: ~ 50,000/year

Hypertension in Pregnancy: Maternal Morbidity

- Cerebrovascular accidents
- Placental abruption
- Acute renal failure
- Hepatic rupture
- Maternal death
Summary: Diagnosis of Hypertension in Pregnancy

- New onset Hypertension after 20 weeks is preeclampsia until proven otherwise
- Gestational hypertension is new onset hypertension in pregnancy without proteinuria and may develop into preeclampsia
- Important risk factors for preeclampsia include maternal hypertension, CKD, obesity, diabetes, previous (early) preeclampsia, multiple gestations, inherited or acquired thrombophilias

Uteroplacental Circulation in Normal and Preeclamptic Pregnancy

The Link Between Reduced Placental Perfusion and Maternal Disease ‘Toxemia’

Placental hypoxia may be a stimulus for:

- ↑ Syncytiotrophoblast debris: ↑ Reactive oxygen species, lipid peroxides
- Cytokines: ↑ TNF α, IL 6, IL 18, IFN
- Leptin
- Angiogenic factors: Increased s FLT-1; Endoglin, decreased PlGF

Preeclampsia: Pathophysiology

- Lipid peroxides
- Cytokines
- Leptin
- Maternal endothelial cell damage
- Platelet aggregation
- Thrombode A2
- Serotonin, PDGF
- Thrombin
- Systemic Vasopasm
- Organ flow
- Intravascular coagulation

Figure 2: An example of an arterial blood flow velocity, typical of preeclampsia nephropathy. A loss distal arterial capillaries typically found in the renal tubules. (Ishii et al., 1990).
**Preeclampsia Prevention 2014**

- Aspirin: 10-15% reduction in relative risk of adverse maternal and fetal outcomes. ASA should be used with high baseline risk.
- Calcium Supplementation: Beneficial in women on low calcium diet.
- Antioxidants: Vit C, Vit E: no beneficial effect RCT’s.
- Acquired thrombophilia, previous early severe PE: heparin, aspirin.

**Management of Preeclampsia**

- At term: delivery is always appropriate.
- Remote from term: close surveillance of maternal and fetal condition; bed rest, maintain maternal BP < 150/100, seizure prophylaxis with MgSO4.

**Lowering Blood Pressure in Women with Preeclampsia**

- Prevents maternal cardiovascular and cerebrovascular complications: 160/110 mm Hg.
- Lowering BP does not cure/reverse/prevent preeclampsia: it may permit prolongation of pregnancy.
- Decreased uteroplacental blood flow, placental ischemia are features of preeclampsia: aggressive lowering of BP is not recommended.
- For most women: 130-150/75-100 mm Hg.

**Additional Considerations for Antihypertensive Rx in Preeclampsia**

- Symptoms (headache).
- Baseline blood pressure.
- Rate of increase.
- Comorbid conditions (bleeding, cardiac, seizures, renal).
- Diuretics are almost never appropriate except for CHF.

**Antihypertensive Therapy in Preeclampsia**

**Imminent Delivery**
- IV labetalol
- IM or IV Hydralazine
- Calcium channel blockers
- Diazoxide

**Delayed Delivery**
- Methyldopa
- Labetalol
- Calcium channel blockers
- Beta blockers
- Alpha blockers
- Clonidine
- Hydralazine
Eclampsia- convulsions. 20% have a diastolic blood pressure below 90 mm Hg or no proteinuria

- 50% occur antepartum, 40% peripartum, but can occur up to two weeks post partum
- Worse maternal and fetal morbidity and mortality

Anticonvulsant Therapy in Preeclampsia

- Magnesium sulfate is superior to phenytoin or diazepam for prevention of recurrent seizures
- Magnesium sulfate is indicated for primary prevention of seizures in women with moderate to severe preeclampsia: May also reduce maternal mortality
- Some uncertainty regarding need for Mg in mild preeclampsia
- Avoid Mg when creatinine elevated; major toxicity respiratory failure

Indications for Delivery in Preeclampsia

Maternal
- Gestational age 38 weeks
- Platelet count <100 x 10^9 cells/mm^3
- Progressive deterioration in liver and renal function
- Suspected abruptio placenta
- Uncontrolled severe hypertension despite medication

Fetal
- Fetal growth restriction
- Non reassuring fetal testing results (e.g. bradycardia)
- Oligohydramnios

Post Partum Evaluation

- Who: early (<34 weeks), severe, recurrent preeclampsia
  Persistent hypertension, renal abnormalities
- How: secondary hypertension, renal disease
  ? Thrombophilia: Factor V L; PT20210; MTHFR; Prot S, Prot C; APA, LAC;

Management of Preeclampsia Summary

- Low dose aspirin has a modest (10%) benefit for prevention
- Calcium supplementation may prevent hypertension in women on low calcium diets.
- Delivery is treatment for preeclampsia at term
- Antihypertensive therapy prevents maternal hypertensive complications but does not cure preeclampsia
- Mg Sulfate is the anticonvulsant of choice for prevention of eclampsia

Chronic Hypertension

- 1-5% of pregnancies (older age, multiparous)
- Risk of Superimposed Preeclampsia: 15-25%
- Increased morbidity associated with Superimposed PE
Routine Evaluation for Chronic Hypertension in Pregnancy

- Comprehensive history and physical
- Biochem profile (not part of routine antepartum care), CBC
- Urinalysis, quantify proteinuria (24 hour urine or P:C ratio)

Secondary HTN in Pregnancy: ‘Pearls of Wisdom’

- Hyperaldosteronism is not rare: bp usually lower, K+ usually higher during pregnancy, but sometimes associated with preeclampsia. Postpartum - Low K+, resistant HTN
- Renovascular HTN: severe, resistant HTN early in pregnancy, poor outcome, may be treated in early 2nd trimester
- Pheo: very dangerous: severe resistant HTN, superimposed PE, maternal and fetal death

Treatment of Chronic Hypertension in Pregnancy

- Goals: Prevent maternal complications, follow closely to detect abnormal fetal growth and/or distress
- Antihypertensive therapy (lowering BP) prevents severe maternal hypertension, but not preeclampsia
- Absence of proof or proof of absence?: demonstrating a 50% reduction in outcomes would have required enrollment of 2000 women in each group- published trials are too small

Antihypertensive Drugs Safe in Pregnancy

- Methyldopa
  - Starting dose 250 BID
  - Maximum of 500 QID
- Labetolol
  - Starting dose 100 BID
  - Maximum 200 QID
- Nifedipine XL
  - Starting dose 30 OD
  - Maximum 90 OD
- Amlodipine
  - 2.5 to 10 mg OD

Management of Chronic Hypertension Prior to Pregnancy

- Pre conception: adjust medications
  - DC ACE inhibitors and AT II blockers –
  - Atenolol may be associated with smaller babies
- Recommend
  - methyldopa or labetolol (first line), calcium channel blockers (second line)
  - Continue diuretic (lower doses) in those already using

Treatment of Chronic Hypertension in Pregnancy

- Severe HTN (160/110 mm Hg) should always be treated
- Mild to moderate HTN - < 160/110; guidelines vary
  - U.S. Diastolic BP > 99
  - Canada Systolic >149, Diastolic > 94
  - Australia SPB > 159, DBP >89
- Treatment Targets
  - U.S. no current guideline
  - Canada 140/90
  - Australia DBP >110
Gestational Hypertension

- Hypertension without proteinuria or other signs of preeclampsia after 20 weeks in a previously normotensive woman
- May be early manifestation of preeclampsia or early unrecognized chronic hypertension
- 15-40% progress to preeclampsia (Risk factors: gestational age, severity of HTN, previous GH)
- Need to perform baseline urinalysis and blood chemistry to rule out preeclampsia

Risk Factors for PP HTN

- Older age
- Longer duration of antepartum HTN
- Use of NSAIDs for post partum analgesia
- Chronic hypertension
- Secondary HTN

Management of PP HTN

- DC NSAIDs
- Reduce IV fluids; DC if taking PO; Diuretics may be necessary short term
- Assess breast feeding plans: avoid diuretics, consult Pediatricians
- Use same drugs as antepartum; Particularly address volume
- Nifedipine may cause headaches – confound important clinical clue of worsening disease