GI Disease in Pregnancy

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• No financial interests to disclose.
Objectives

• Physiology
• Hyperemesis
• Inflammatory Bowel Disease in Pregnancy
  – UC, Crohn Disease
• Appendicitis
• Medications
• Questions
• Misc – P4 – Parkland study
Case

- 36 yo P2012 – TSVD x1, CD x1 (significant postoperative infection)
- Hx of Crohn Disease
- No hx of perianal Crohn Disease that is reported
- Stopped her maintenance medications
- Recs?
Case

- 25 yo P1001
- 10 weeks –
- Admitted for refractory n/v/HEG-
- Management?
- When to add Dobhoff tube?
- When to move to TPN?
Physiologic changes during pregnancy

- Gastro-intestinal motility inhibited during pregnancy mediated by progesterone
Esophagus

• Physiology changes
  – Reduction in LES pressure
  – Reduction in responsiveness of LES to pharmacologic and physiologic stimulation

• Clinical implications
  – Gastroesophageal reflux
  – Heartburn
  – Risk of erosive esophagitis, strictures
What is mechanism behind symptoms of reflux esophagitis in pregnancy?
• Relaxation of LES – lower esophageal sphincter
• Not – relaxation of upper esophageal sphincter, decreased peristalsis, excess gastric acid production
Stomach

• Physiology changes
  – Slow gastric emptying with increased residual volume (term)
    • Increased risk of GERD, N/V, aspiration with GETA for delivery
  – Equivocal changes in acid + pepsin secretion
    • Decreased incidence of duodenal ulcers
Small intestine

- Physiologic changes (clinical implications)
- Increased transit time (stasis and bacterial overgrowth)
- Changes in propulsive motility (sequestration of bile acids)
- Reduced contractile responsiveness of intestinal muscle, in vitro (pseudo-obstruction syndrome)
- Increased activity of brush border enzymes, gut hypertrophy, and increased villus height (enhanced efficiency of absorption of some nutrients)
- Folate malabsorption (megaloblastic anemia, neural tube defects)
  - Folate Absorbed in jejunum (if needed – supp 1-4mg /day folate)
  - Iron absorbed in duodenum;
  - B12 absorbed in ileum (with IF from stomach)- supp/injections if hx of surgery of ileum

- Folate Absorbed in jejunum (if needed – supp 1-4mg /day folate)
- Iron absorbed in duodenum;
- B12 absorbed in ileum (with IF from stomach)- supp/injections if hx of surgery of ileum
Colon

• Physiologic changes (clinical implications)
• Increased transit time (constipation, other symptoms)
• Contractile responsiveness of colonic smooth muscle reduced (pseudo-obstruction syndrome)
• Increased sodium and water absorption
N/V of Pregnancy - ACOG
The most commonly cited criteria include persistent vomiting not related to other causes, a measure of acute starvation (usually large ketonuria), and some discrete measure of weight loss, most often at least 5% of prepregnancy weight (11). Electrolyte, thyroid, and liver abnormalities also may be present.

0.5-2% of all pregnancies
N/V -- Differential Diagnosis

- **GI** - Gastroenteritis, Gastroparesis, Achalasia, Biliary tract disease, Hepatitis, Intestinal obstruction, Peptic ulcer disease, Pancreatitis, Appendicitis
- **GU** - Pyelonephritis, Uremia, Ovarian torsion, Nephrolithiasis, Degenerating uterine leiomyoma
- **Metabolic Disease** - DKA, Porphyria, Addison's disease, Hyperthyroidism
- **Neurologic** - Pseudotumor cerebri, Vestibular lesions, Migraines, Tumors of the central nervous system
- **Miscellaneous** - Drug toxicity or intolerance, Psychologic
- **Pregnancy-Related Conditions** - Acute fatty liver of pregnancy, Preeclampsia


Williams Obstetrics
Diabetic Ketoacidosis
Diagnosis

- DKA -

- D – Diabetic - >180mg/dL
- K – serum acetone, Ketones 1:2 or greater
- A – Acidosis – arterial pH<7.3, HCO3- <15, anion gap [Na – (Cl +HCO3)] >12
Management

• Maternal Resuscitation
  – IV fluids
  – Insulin
  – Search for underlying cause – infection, noncompliance, etc
  – I/Os, monitoring glucose (q1-2hr),
  – ABG, pH, anion gap, electrolytes (q2-4hr)
  – Fetal monitoring*
    • Withhold intervention toward delivery on behalf of the fetus until maternal metabolic disturbances are corrected
    • Oxygen and correct maternal positioning while correcting disturbances
Management -

- **Fluid replacement**
  - Fluid deficit is 100cc/kg (7-10L for total deficit)
    - Accurate I/Os, BUN, Creatinine
    - Replace 75% of deficit in 1st 24 hrs, remainder over the hospitalization
  - NS (use isotonic solution to prevent rapid decline in plasma osmolarity and resultant cellular swelling and cerebral edema)
  - 1L NS in first hour, 500 mL/hr hours 2 and 3 (NS 1st 3 hrs)
  - LR or ½ NS at 250cc/hr in initial 24 hr until 75% of volume deficit is replaced
    - LR is used to avoid further acidosis (LR pH 6.5, vs 5.0 of NS)
    - Sodium load with NS – possible hypernatremia, switch to LR or ½ NS if Na >150meq/L
Insulin (0.1)

- **Insulin therapy** (inhibits lipolysis and ketogenesis, leads to suppression of hepatic glucose production)
  - Loading dose 0.1U/kg regular insulin
    - 50 units / 500 mL NS (1cc = 0.1units, 10 cc = 1unit)
  - Infusion 0.1units/kg/hour
  - If plasma glucose does not decrease by 10% in first hour or by 20% in second hour – repeat loading dose or double infusion rate
  - When glucose ~250mg/dL or less, add D5 to the fluids and reduce the hourly rate by 1/2
  - Continue infusion of insulin until serum bicarbonate and anion gap normalize
Potassium administration

- Anticipated potassium deficit in a pregnant patient with DKA is 5-10 meq/kg.
- Replacement usually delayed for the first 2-4hr of therapy, since K+ is usually elevated until patient diuresis has been established (at least 0.5cc/kg/h).
- Once IV fluids and insulin therapy are started serum K+ may drop quickly as a result of urinary loss and intracellular shift. When K+ is <5 and adequate diuresis has been established (0.5cc/kg/h) then K administration should begin.
- 40-60meq KCl/liter of NS
- If K+ is ≥4, give 10-20meq
- If K+ is <4, give 30-40 meq
- Replace K cautiously, watching UOP and serum K+ frequently, every 4hr
- Replace entire K+ deficit (5-10meq/kg) over the span of the patient’s entire hospitalization
- Alternatively – with DKA induced maternal phosphate deficiency, K2PO4 (KPhos) may be given as K replacement instead of KCL
Bicarbonate therapy

- Only if arterial pH <6.9-7.0 and HCO3 < 5meq/L
- Rapid undiluted correction of metabolic acidosis with NaHCO3 is unwarranted and may lead to severe hypokalemia, hypernatremia, impaired oxygen delivery, and a paradoxical fall in CSF pH
- One ampule (44meq NaHCO3) is diluted in 1000mL of ½NS
- Total deficit of bicarbonate can be calculated (obtain the base deficit on the ABG)
  - Bicarb (meq) regained to fully correct metabolic acidosis = Base deficit (meq/L) x patient weight (kg) / 4
- Since oxygen hemoglobin affinity is augmented in the presence of an alkalotic shift of the oxygen-hemoglobin disassociation curve to the left, it is prudent not to fully correct the patient’s metabolic acidosis, ensuring better oxygen delivery to the fetus
HEG
Pharmacologic treatment of nausea and vomiting of pregnancy* (if no improvement, proceed to the next step)

Monotherapy: Vitamin B₆, 10–25 mg, 3 or 4 times per day

Add: Doxylamine, 12.5 mg, 3 or 4 times per day†
Adjust schedule and dose according to severity of patient’s symptoms

Add: Promethazine, 12.5–25 mg every 4 hours, orally or rectally
Or
Dimenhydrinate, 50–100 mg every 4–6 hours, orally or rectally (not to exceed 400 mg per day; not to exceed 200 mg per day if patient also is taking doxylamine)

No dehydration

Dehydration

Add any of the following (presented here in alphabetical order):
Metoclopramide, 5–10 mg every 8 hours, intramuscularly or orally
Or
Promethazine, 12.5–25 mg every 4 hours, intramuscularly, orally, or rectally
Or
Trimethobenzamide, 200 mg every 6–8 hours, rectally

Intravenous fluid replacement‡

Add any of the following (presented here in alphabetical order):
Dimenhydrinate, 50 mg (in 50 mL saline, over 20 min) every 4–6 hours, intravenously
Or
Metoclopramide, 5–10 mg every 8 hours, intravenously
Or
Promethazine, 12.5–25 mg every 4 hours, intravenously

Add: Methylprednisolone§, 16 mg every 8 hours, orally or intravenously, for 3 days. Taper over 2 weeks to lowest effective dose.
If beneficial, limit total duration of use to 6 weeks.
Add: Methylprednisolone\textsuperscript{5}, 16 mg every 8 hours, orally or intravenously, for 3 days. Taper over 2 weeks to lowest effective dose. If beneficial, limit total duration of use to 6 weeks.

Or

Ondansetron\textsuperscript{11}, 8 mg, over 15 minutes, every 12 hours, intravenously

*This algorithm assumes other causes of nausea and vomiting have been ruled out. At any step, consider parenteral nutrition if dehydration or persistent weight loss is noted. Alternative therapies may be added at any time during the sequence depending on patient acceptance and clinician familiarity; consider P6 acupressure with wrist bands or acustimulation or ginger capsules, 250 mg 4 times daily.

\textsuperscript{4}In the United States, doxylamine is available as the active ingredient in some over-the-counter sleep aids; one half of a scored 25-mg tablet can be used to provide a 12.5-mg dose of doxylamine.

\textsuperscript{4}Thiamine, intravenously, 100 mg daily for 2–3 days (followed by intravenous multivitamins), is recommended for every woman who requires intravenous hydration and has vomited for more than 3 weeks. No study has compared different fluid replacements for nausea and vomiting of pregnancy.

\textsuperscript{5}Corticosteroids appear to increase risk for oral clefts in the first 10 weeks of gestation.

\textsuperscript{11}Safety, particularly in the first trimester of pregnancy, not yet determined; less effect on nausea.

Life threatening complications of HEG

- Life threatening complications of HEG
- Acute kidney injury—may require dialysis
- Depression—cause versus effect?
- Diaphragmatic rupture
- Esophageal rupture—Boerhaave syndrome
- Hypoprothrombinemia—vitamin K deficiency
- Hyperalimentation complications
- Mallory-Weiss tears—bleeding, pneumothorax, pneumomediastinum, pneumopericardium
- Wernicke encephalopathy—thiamine deficiency
Legend:
Endoscopic view of Mallory-Weiss tear. (From Song, 2012, with permission.)
• Endoscopic view – Mallory-Weiss tear
• Tx – IV fluids
• Bowel rest
• H2 blocker/PPI
• Transfusion as indicated
• Endoscopy/surgery
• Other complications that can arise – esophagus rupture, Borhavee syndrome

Williams Obstetrics
• Enteral nutrition preferred in most cases
• Dobhoff tubes placement with electromagnetic confirmation – novasource, nutren – 15cc/hr, increase to 30cc/h

– No radiation risk; risks – 2% tracheopulmonary

A nasogastric tube or a "dobhoff tube" is a small, thin tube that is inserted through the nose and down into the stomach or small intestine. A gastrostomy (or "PEG") tube or a jejunostomy (or "J") tube is placed surgically and is often used when feedings are going to be required for two months or more. All these tubes are temporary and are removed when they are no longer needed.

http://www.mcancer.org/living-with-cancer/mind-body-side-effects/nutrition/helping-hand
Indications for feeding tube

• Suspected to have or have had a total of 7-14 days of inadequate oral intake
• 10% weight loss on admission from previous admission
• 10% weight loss from beginning of pregnancy – if suspected to have inadequate oral intake/
CI to Dobhoff tubes

• Bariatric surgery
• Nasal /basilar skull fractures
• Esophageal tears
• Recent stomach/bowel surgery in last 7 days
• Recent thyroid surgery

• *If candidate - Place order for feeding tube, automatically goes to procedure team or call
Possible Indications for TPN in Pregnancy

- Achalasia
- Anorexia nervosa
- Appendiceal rupture
- Bowel obstruction
- Burns
- Cholecystitis
- Crohn disease
- Diabetic gastropathy
- Esophageal injury
- Hyperemesis gravidarum
- Jejunoileal bypass
- Malignancies
- Pancreatitis
- Short gut syndrome
- Stroke

Suspected to have or have had a total of 7-14 days of inadequate oral intake

10% weight loss on admission from previous admission

10% weight loss from beginning of pregnancy – if suspected to have inadequate oral intake/

Williams Obstetrics
TPN - complications

- Infection, sepsis
- Thrombosis
- Fluid overload
- Hypercapnia
- Hyperglycemia
- Non-anion gap metabolic acidosis
- Cholestasis
- Gallstones
- Hepatitis
- Pancreatitis
- Azotemia
- Bacteremia
- Lipid CI – pancreatitis with lipemia
- Dextrose CI – hypersensitivity, hypertonic solution with intracranial hemorrhage
- AA CI – Liver disease

Hypoglycemia is impending sepsis until proven otherwise
Discontinuation of TPN - +/- tapering, decrease to ½ rate for 4h then d/c; OK to d/c once enteral feeding is at 50% of goal
Refeeding syndrome – Medical ER
Electrolytes abnormalities (PO4, Mag, K+, glucose), check at initiation of refeeding
Respiratory distress
Arrhythmias
Cardiac arrest
Usually in long-standing, severe malnourishment
Initiate, refeed slow, do not overfeed
Supportive care, treatment of medical complications
Issues with TPN in Pregnancy

- Risks – infection, sepsis, central line risks (arrhythmias, pneumothorax), thromboembolism
- Calorie goal – 35kcal/kg/d + 300kcal/d (pregnancy)
- Protein – (stressed) – 1.2gm/kg/day +15g/day (pregnancy)
- Fat – 30% of total calories
- CHO – Total cal – TP – TF
- TPN - 75cc/hr
- IV fluids – 30mL/kg/d
- Insulin – SSI day 1-2, calculate total dose needed to keep at goal, then put that in the TPN bags on following days
- Composition – example calculation – caselist – had prepared – was asked re: calorie goal, how much protein (above)
- Base, electrolytes, additives – consult nutrition
- Monitoring -
TPN example

- See Wesley Intranet – order set
Which of the following is the most common complications of TPN?

A – Hemothorax
B – Catheter sepsis – 25%
C – Brachial plexus injury
D – Fetal subdural hematoma caused by vitamin K deficiency
Inflammatory Bowel Disease
Inflammatory Bowel Disease and Fertility

- Normal fertility rates unless severe disease that requires surgery
- Active Crohn Disease decreases female fertility, then returns to normal with remission (Alstead, 2003)
- If surgery is needed, laparoscopic anastomosis has higher subsequent fertility rates than laparotomy approach
- Fertility can improve with colectomy, but up to 50% will still be infertile
- Sulfasalazine – Reversible sperm abnormalities

Williams Obstetrics
Inflammatory Bowel Disease and Pregnancy

• Common in young women
• Pregnancy does not increase the likelihood of an inflammatory bowel disease flare.
• 10-year surveillance of women in the European Collaborative on Inflammatory Bowel Disease, the likelihood of a flare during pregnancy was decreased compared with the preconceptional rate (Riis, 2006). This diminished rate persisted for years after pregnancy and was attributed to close attention and monitoring of enrolled women.
• Quiescent disease in early pregnancy uncommonly have relapses, when a flare develops, it may be severe.
• Active disease in early pregnancy increases the likelihood of poor pregnancy outcome – PTB, LBW, IUGR, IUFD
  – Especially Crohn Disease – mostly with severe disease and multiple recurrences
  – Epicom study – Case /control study in Europe, prospective – 332 women – similar outcomes to normal pregnant women - studied UC and Crohn disease
• Most usual treatment regimens may be continued during pregnancy; diagnostic evaluations should be done ; Surgery if indicated
• If successful pregnancy - half experience improvement in their health-related quality of life (Ananthakrishnan, 2012)
• Calcium 1200mg/d, folate 1mg/day, Vitamin D 800U/d

Williams Obstetrics
Ulcerative Colitis

- Mucosal disease, confined to superficial layers of colon
- Begins at rectum and extends proximal
- 40% have disease confined to rectum and rectosigmoid
  - 20% with pancolitis
- Endoscopic findings - mucosal granularity and friability that is interspersed with mucosal ulcerations and a mucopurulent exudate
- Symptoms - diarrhea, rectal bleeding, tenesmus, and abdominal cramps.
- Intermittent, or acute with exacerbations and remissions
- Prior appendectomy protects against development of ulcerative colitis (Friedman, 2012, Selby 2002)
- Toxic megacolon and catastrophic hemorrhage are particularly dangerous complications that may necessitate colectomy.
- Extraintestinal manifestations include arthritis, uveitis, and erythema nodosum.
- Colon cancer risk – 1% per year
- UC and Crohn disease – increased risk of VTE

Williams Obstetrics
Ulcerative Colitis and Pregnancy

- Pregnancy has no significant effects on ulcerative colitis.
- Metaanalysis of 755 pregnancies (Fonage 1998)
  - Quiescent UC at conception – 1/3 of patients worsened during pregnancy
  - Active disease at conception – 45% worsened, 25% unchanged, 25% unchanged

- Calcium supplementation – osteoporosis prevention
- Folate – counteract antifolate actions of sulfasalazine
Ulcerative Colitis and Pregnancy

- Flares can be due to stress
- Active colitis –
  - Sulfasalazine – Delivers 5-ASA or mesalamine to mucosa and the 5-ASA moiety inhibits prostaglandin synthase in colonic mucosa
  - Olsalazine, coated 5-ASA derivatives (Asacol)
  - Glucocorticoids- PO, IV, or by enema for more severe disease that does not respond to 5-ASA.
  - Recalcitrant disease - immunomodulating drugs – azathioprine, 6-mercaptopurine, cyclosporine (Briggs, 2011, Moskovitz 2004)
  - Methotrexate is contraindicated
  - Cyclosporine - High-dose IV may help with severe disease vs colectomy
  - TPN if prolonged exacerbations.
  - Endoscopy used as needed
  - Fulminate colitis – colectomy and ostomy creation - has been reported in each trimester (Dozois, 2006, N=42 – outcomes are good)
- Nonpregnant women – proctocolectomy, ileal pouch, anal anastomosis – improved sexual function and fertility rates (Cornish, 2007) ; frequent bowel movements, fecal incontinence, nocturnal soilage.; pouchitis – inflammation of ileoanal pouch – tx cephalosporin, metronidazole
  - Temporarily worsen during pregnancy, they typically abate postpartum; case report of adhesions to the growing uterus led to ileal pouch perforation (Aouthmany, 2004)
  - OK to deliver vaginally (Ravid, 2002)
  - Hahnloser, 2004 – N= 235 pregnancies before and 232 pregnancies after ileoanal pouch surgery – outcomes similar – concluded to use CD for OB indications ; post cesarean ileoanal pouch obstruction has been reported (Maecki, 2010)
  - No reported increased risks of fistula
Ulcerative colitis and Pregnancy

- Adverse pregnancy outcomes – minimal risks (Modigliani, 2000; Bortoli, 2011; Dominitz 2002)
- Increased risks of congenital malformations, increased CD rates, increased PTB and LBW rates in some studies (Bortoli, 2011; Emerson, 2013)
Crohn Disease

- AKA Regional enteritis, Crohn ileitis, and granulomatous colitis
- Involves bowel mucosa, deeper layers, transmural
- Lesions throughout entire GI tract
- Segmental
  - Small bowel (30%)
  - Isolated colonic involvement (25%)
  - Small and Large Bowel (40%), with terminal ileum and colon involved
Crohn Disease

- Perirectal fistulas, abscesses develop in 33% of patients with colonic disease
- Symptoms – RLQ pain, cramping, diarrhea, weight loss, low-grade fever, and obstructive symptoms.
- Chronic disease with exacerbations and remissions, and importantly, it cannot be cured medically or surgically
- 1/3 of patients require surgery in 1st year in 1st year after diagnosis, then 5% per year thereafter
- Reactive arthritis is common
- GI cancer risk increased (but not as high as with UC)
Crohn Disease and Pregnancy

- Disease activity during pregnancy related to periconceptional disease status
- Fonage 1998 - Cohort study, N=279
  - Of 186 women with inactive disease at conception, 25% relapsed during pregnancy
  - Of 94 women with active disease at conception, 2/3 remained active or worsened
  - Findings similar to Miller, 1986, Oron, 2012
- Calcium 1200mg/d; folic acid 1mg/d, Vitamin D 800U/d
Crohn Disease in Pregnancy

• Parenteral hyperalimentation has been used successfully during severe recurrences

• Endoscopy or conservative surgery is indicated for complications. Patients with small-bowel involvement more likely will require surgery for complications that include fistulas, strictures, abscesses, and intractable disease.

• Surgery required in 5% of patients with Crohn Disease in pregnancy (Woolfson, 1990)

• Pts with ileal loop colostomy may have significant problems

• Pt with perianal fistula—unless these are rectovaginal—usually can undergo vaginal delivery without complications

• Perinatal outcomes worse with Crohn disease vs UC; especially when comparing controlled Crohn Disease to controlled UC and uncontrolled Crohn Disease and uncontrolled UC

• Increased rates of PTB, LBW infants, IUFD, Cesarean rates (Dominitz 2002)

• Prospective ECCO-EpiCom study found outcomes to be similar to those for normal pregnancies.

Williams Obstetrics
Crohn Disease - Medical Management

- No clear regimen known for asymptomatic periods to maintain remission
- Sulfasalazine effective
  - Newer 5-ASA formulations better tolerated
  - Safe in pregnancy
- Prednisone – controls moderate to severe disease, less effective for small bowel involvement
  - Clefts, osteoporosis, HTN,
  - Need for stress dose steroids
- Immunomodulators – Azathioprine, 6-mercaptopurine, cyclosporine used for active disease, safe in pregnancy
- Methotrexate, mycophenolate mofetil, mycophenolic acid – CI in pregnancy
- Anti-tumor necrosis factor (TNF)-α antibodies, which include infliximab (remicade), adalimumab, certolizumab – effective for active Crohn disease and maintenance
  - Safe in pregnancy,
  - D/c at 32 weeks to prevent neonatal immunosuppression and maternal immunosuppression

Williams Obstetrics
Mode of Delivery in Crohn Disease

- Elective cesarean section (CS) is a standard recommendation for pregnant women with perianal Crohn's disease.
- % risk of fistula formation in perianal disease, with rectovaginal fistula - unknown

Diagnosis of Perianal Crohn Disease

• Incidence 25-80% in some series
• Some reports of fistulizing PCD give incidence of 17-43%
• Def - inflammation at or near the anus, including tags, fissures, fistulae, abscesses, or stenosis.
• Symptoms - pain, itching, bleeding, purulent discharge, and incontinence of stool.

Zoeten 2014
Diagnosis

- **Exam**
- **Imaging/Endoscopy**
Crohn disease (PCD)
Case

- 36 yo P2012 – TSVD x1, CD x1 (significant postoperative infection)
- Hx of Crohn Disease
- No hx of perianal Crohn Disease that is reported
- Stopped her maintenance medications
- Recs – Resume maintenance medications to avoid flares/exacerbations
• UC and Crohn disease share all of the features below except?

• A – Genetic predisposition – chromosome 16

• B – Cured by proctocolectomy*

• C – Periods of exacerbation/remission

• D – Can be associated with erythema nodosum, arthritis

Williams Obstetrics
• Which feature is typical of Crohn disease?

• A – Rectum is usually spared* (UC involves rectum)

• B – Affected areas of bowel are contiguous (UC is continuous, Crohn Disease has skip lesions)

• C – Associated with ANCA (antineutrophil cytoplasm antibodies)

• D – Risk of cancer is greater than with UC (UC is 1% per year, higher)
Medications
Immunosuppressants (Scott CC OB)

• All drugs cross placenta, diffuse to fetus
• No convincing evidence that prednisone, azathioprine, cyclosporine, tacrolimus produce congenital abnormalities;
• Drugs of choice in preg transplant pts
• A/e IUGR, PTB , o/w neonates do well
  – Short term ‘prematurity issues of infection, hypoglycemia, bone marrow hypoplasia, leukopenia, reduced IGM, IGG, elevated serum cr’ hard to know if it’s the drug or prematurity
• Long term – poss infertility, autoimmune disease, neoplasia – need for long term f/u
Medication

- MOA -
- CI -
- Pregnancy -
- Breast feeding -
Sulfasalazine (Azulfidine)

- **MOA** – Sulfasalazine, metabolites (5-ASA, sulfapyridine) - anti-inflammatory and/or immunomodulatory properties, main effect in UC is from 5-ASA

- **CI** – Intestinal or urinary obstruction, patients with porphyria, allergy to sulfasalazine, metabolites, sulfonamides, salicylates

- **Pregnancy** – Class B, crosses placenta;; no increased rate of defects
  - Impairs folate absorption/metabolism – so take 1-4mg folate /day, esp periconceptionally

- **Breastfeeding** – Excreted; unsafe, especially if infant is preterm, <1month old, or FHX of G6PD deficiency

Drugs.com
Critical Care Obstetrics, 4th Ed (Dr. Scott)
Azathioprine (Imuran)

• MOA – inhibits T-lymphocytes; More toxic metabolite 6-mercaptopurine- purine analog that decreases delayed hypersensitivity and cellular cytotoxicity

• CI – Hypersensitivity, relative (pregnancy), increased risk of cancer, esp if previously used alkylating agents (eg, chlorambucil, cyclophosphamide, melphalan), liver disease, need to follow CBC, CMP

• Pregnancy – Class D - D b/c increased anomaly rate of 9 and 6.4%, not found in recent series, no specific pattern, possible bone marrow suppression in fetus, with anemia, leukopenia, thrombocytopenia
  • 64-90% of azathioprine crosses the placenta, majority is inactive thiouric acid

• Breast feeding – Excreted; UK, unsafe; US – Caution is rec ;Relative CI – Neutropenia, unknown risk of carcinogenesis; Women with decreased activity of enzyme that detoxifies azathioprine metabolites may pass on higher levels of drug to their infants via breast milk; if used, check CBC/diff, CMP in exclusively breastfed infants; wait to breastfeed 4-6hr after dose

Drugs.com
Critical Care Obstetrics, 4th Ed (Dr. Scott)
Tacrolimus (Prograf)

- MOA – Inhibits T-lymphocytes; macrolide antibiotic from streptomyces
- CI – Hypersensitivity, Kidney disease (relative)
- Pregnancy – Class C – Risk of PTB, neonatal hyperkalemia, renal dysfunction; animal studies show increased risk of anomalies, APO
- Breast feeding – Excreted; Unsafe

Drugs.com
Critical Care Obstetrics, 4th Ed (Dr. Scott)
Cyclosporine

• MOA – inhibits T-lymphocytes
  – Fungal metabolite, inhibits T-cell response by inhibiting IL2, inhibits cell mediated immunity

• CI - Hypersensitivity, Renal dysfunction, liver dysfunction, severe HTN; A/E lymphoma

• Pregnancy – C, PTB, LBW; crosses, no evidence of teratogenicity; levels drop in pregnancy

• Breast feeding – Excreted; unsafe; immunosuppression, neutropenia, growth impairment, carcinogenesis

Drugs.com
Critical Care Obstetrics, 4th Ed (Dr. Scott)
Infliximab (Remicade)

- **MOA** – Infliximab is a chimeric monoclonal antibody that binds to human tumor necrosis factor alpha (TNFα), thereby interfering with endogenous TNFα activity
- **CI** – Hypersensitivity to infliximab, murine proteins, or any component of the formulation; doses >5 mg/kg in patients with moderate or severe heart failure (NYHA Class III/IV)
- **Canadian labeling:** Additional contraindications (not in US labeling): Severe infections (e.g., sepsis, abscesses, tuberculosis, and opportunistic infections); use in patients with moderate or severe heart failure (NYHA Class III/IV)

- Pregnancy – Class B/C – stop at 32 wk to avoid immunosuppression for delivery, neonate
- Breastfeeding- Infliximab Breastfeeding Warnings
- Use is not recommended. Excreted into human milk: Unknown Excreted into animal milk: Data not available Comments: - Because human immunoglobulins are excreted in milk, women should not breast feed for at least 6 months after treatment is discontinued.
Prednisone

• MOA – inhibit humoral and cell mediated immune response

• CI – Uncontrolled DM, hypersensitivity

• Pregnancy – C; Prolonged courses of fluorinated steroids (dexta, beta) may cause decreased brain, somatic growth, adrenal suppression, neonatal sepsis, CLD, psychomotor delay, behavioral prob; metabolized by 11B HSD, fetus exposed to 10%
  – Vitamin D/calcium
  – Stress dosing at delivery

• Breast feeding – Risks increased

Drugs.com
Critical Care Obstetrics, 4th Ed (Dr. Scott)
Glucocorticoids

- Glucocorticoids (antiinflammatory, glucocorticoid, mineralocorticoid)
- Preg class C
- Avoid fluorinated glucocorticoids b/c they cross the placenta
  - Hydrocortisone, prednisone, prednisolone inactivated by 11-beta hydroxysteroid dehydrogenase in the placenta allowing <10% of active drug to reach fetus
- High dose associated with maternal/fetal A/E
  - Osteoporosis (tx with vit D, ca2+); glucose intolerance, sodium, h2o retention; hypertension, infection; avascular necrosis
  - Preg complications – GDM, preeclampsia, PPROM, IUGR
  - Incidence of fetal adrenal suppression with maternal tx is low
- Avoid empiric treatment, use at lowest possible dose
  
- Stress dose steroids (hydrocortisone 100mg IV q8hr in labor and for 24 hr PP)
  - Use if chronic steroids (>5mg/day for >2-4 weeks prior to delivery)
Immunosuppressants-

Cyclophosphamide per Dr. Scott in CC in OB book 4th ed

- Cyclophosphamide – MOA – alkylating agent; D
  - cancer chemotherapy and as an immunosuppressant
  - In human pregnancies, cyclophosphamide exposures that occurred during the first trimester have been associated with skeletal and palate defects, as well as malformations of the limbs and eyes
  - Cyclophosphamide is excreted into human milk (34). Two reports indicates that the platelet and leukocyte counts of a nursing infants were reversibly depressed during maternal cyclophosphamide therapy (35,48). Cyclophosphamide was classified among the cytotoxic drugs that may interfere with cellular metabolism of a nursing infant by the American Academy of Pediatrics (36).
Cyclophosphamide

- Cyclophosphamide (alkylates and cross links DNA)
- Preg class D
  - Cleft palate, skeletal abnormalities, abnormal renal function
  - Avoid, esp in first trimester
  - May be needed in cases of severe proliferative nephritis (drug of choice in nonpregnant patients with proliferative lupus nephritis)
  - Crosses placenta
• Which is not safe to use in pregnancy for reflux esophagitis?
• Cimetidine, PPIs, calcium carbonate – OK
   NO misoprostol – –
• What is constellation of defects that misoprostol is associated with if it does not cause SAB? – Moebius sequence –
Pregnancy - FDA classes

- **A** – controlled studies show no fetal risk in any trimester, probability of fetal harm is remote
- **B** – animal studies, no risk; if risk in animal studies, controlled human studies do not confirm harm
- **C** – harm in animal studies with no controlled human studies; no available human or animal studies
- **D** – human studies show fetal risk but r/b relative to medical state of mother may support use
- **X** – animal/human studies show fetal risk or abnormalities, use is contraindicated during pregnancy or in women who may become pregnant
Appendicitis

- Diagnosis
- Sonogram vs CT vs MRI
- Patient counseling re: surgery in pregnancy
Appendicitis

- Common indication for exploration
- Swedish registry – Suspected appendicitis – 1 in 1000, confirmed disease in 65%, overall rate 1 in 1500 of true disease (Mazze, 1991)
- Danish registry – confirmed appendicitis rate 1 in 5500 (Hee, 1999)
- Difficult diagnosis in pregnancy
  - N/v of normal pregnancy
  - As uterus enlarges, appendix moves upward and outward from RLQ
  - Leukocytosis of pregnancy
  - DDX – cholecystitis, PTL, pyelonephritis, renal colic, placental abruption, uterine leiomyoma degeneration
  - Increased morbidity and mortality rates as gestational age advances, due to delayed diagnosis and surgery
  - Appendiceal perforation incidence increases with gestational age – 1st trimester (8%), 2nd trimester (12%), 3rd trimester (20%) (Andersson 2001; Ueberrueck, 2004)
Appendicitis - Diagnosis

• Persistent abdominal pain/tenderness
• Mild leukocytosis with pregnancy makes WBC less reliable
• Sonogram – 1st line test; graded compression sonography – difficult to cecal displacement; uterine distorts anatomy
• CT - radiation risks ; more sensitive, accurate re: diagnosis
• Negative appendectomy rate
  – 54% with clinical diagnosis alone
  – 8 % if sonogram and CT used (Wallace, 2008)
  – MRI – metaanalysis, Blumenfeld, 2011 – PPV 90%, NPV 99.5%
  – MRI depends on experience of Radiologist with MRI in diagnosis of appendicitis
Radiation risks

• Radiation risks
• Ionizing radiation can break chemical bonds or create free radicals or ions capable of causing tissue damage

• External radiation –
• High levels of ionizing radiation – lethal to preblastocyst during pre-implantation
• Cell death, chromosome injury, anomalies, MR
• Human effect
• Greatest risk for microcephaly/severe MR – 8-15 weeks from observation of Japanese bomb survivors – larger doses needed at 16-25 weeks for equivalent proportion of mR

• Conversion
• Rad = rem
• 1Gray (1Gy) = 100rad
• <5rad – no increase r/o anomalies, SAB, MR, IUGR
• CXR <1 mrad
Radiation risks

- 2 weeks after fertilization – 10 rads needed to produce effect
- 1\textsuperscript{st} trimester 25 rads needed to produce effect
- 2\textsuperscript{nd}, 3\textsuperscript{rd} trimesters – 100 rads needed
- Threshold – 5 rads
- Exposure
  - Environmental 125 mrad
  - CT abdomen, spine 3.5 rad
  - Barium enema (SBFT) – 2-4 rads
  - IVP – 1-2 rad
  - CT head or CT chest – 1 rad
  - CT pelvimetry – 250 mrad
  - Hip Xray – 200 mrad
  - Abdominal plain film /KUB – 100 mrad
  - Mammography – 7-20 mrad
  - CXR – 0.05 mrad
  - MRI – zero rad
Appendicitis - Management

- Surgical – Regardless of trimester
- Antibiotics are to prevent risk of appendiceal rupture while waiting for surgery
When counseling a patient who needs nonobstetric surgery in pregnancy, which of the following should be disclosed?

A – there is an increased risk of IUFD
B – there is an increased risk of cerebral palsy
C – There is an increased risk of preterm delivery
D - There is no increased in long-term risks to the fetus or the mother*
Case

• 36 yo P2012 – TSVD x1, CD x1 (significant postoperative infection)
• Hx of Crohn Disease
• No hx of perianal Crohn Disease that is reported
• Stopped her maintenance medications
• Recs – Resume maintenance medications to avoid flares/exacerbations
Case

- 25 yo P1001
- 10 weeks –
- Admitted for refractory n/v/HEG-
- Management?
- When to add Dobhoff tube?
- When to move to TPN?
Indications for feeding tube

- Suspected to have or have had a total of 7-14 days of inadequate oral intake
- 10% weight loss on admission from previous admission
- 10% weight loss from beginning of pregnancy – if suspected to have inadequate oral intake/
CI to Dobhoff tubes

- Bariatric surgery
- Nasal /basilar skull fractures
- Esophageal tears
- Recent stomach/bowel surgery in last 7 days
- Recent thyroid surgery

*If candidate - Place order for feeding tube, automatically goes to procedure team or call
Possible Indications for TPN in Pregnancy

- Achalasia
- Anorexia nervosa
- Appendiceal rupture
- Bowel obstruction
- Burns
- Cholecystitis
- Crohn disease
- Diabetic gastropathy
- Esophageal injury
- Hyperemesis gravidarum
- Jejunoileal bypass
- Malignancies
- Pancreatitis
- Short gut syndrome
- Stroke

Suspected to have or have had a total of 7-14 days of inadequate oral intake
10% weight loss on admission from previous admission
10% weight loss from beginning of pregnancy – if suspected to have inadequate oral intake/
Summary

- N/V – Don’t forget to give thiamine
- Enteral feeding is best
- Crohn Disease – CD for perianal disease or uncontrolled disease
- Appendicitis – 50% negative appendectomy rate acceptable with clinical diagnosis
17P and prevention of PTB

- 2017 Trial
OBSTETRICS

17-alpha Hydroxyprogesterone caproate did not reduce the rate of recurrent preterm birth in a prospective cohort study

David B. Nelson, MD; Donald D. McIntire, PhD; Jeffrey McDonald, PhD; John Gard, PharmD; Paula Turricchi, BSBA, MS; Kenneth J. Leveno, MD

BACKGROUND: 17-alpha Hydroxyprogesterone caproate for prevention of recurrent preterm birth is recommended for use in the United States.

OBJECTIVE: We sought to assess the clinical effectiveness of 17-alpha hydroxyprogesterone caproate to prevent recurrent preterm birth ≤35 weeks compared to similar births in our obstetric population prior to the implementation of 17-alpha hydroxyprogesterone caproate.

STUDY DESIGN: This was a prospective cohort study of 17-alpha hydroxyprogesterone caproate in our obstetric population. The primary outcome was the recurrence of birth ≤35 weeks for the entire study cohort compared to a historical referent rate of 16.8% of recurrent preterm birth in our population. There were 3 secondary outcomes. First, did 17-alpha hydroxyprogesterone caproate modify a woman’s history of preterm birth when taking into account her prior number and sequence of preterm and term births? Second, was recurrence of preterm birth related to 17-alpha hydroxyprogesterone caproate plasma concentration? Third, was duration of pregnancy modified by 17-alpha hydroxyprogesterone caproate treatment compared to a prior preterm birth?

RESULTS: From January 2012 through March 2016, 430 consecutive women with prior births ≤35 weeks were treated with 17-alpha hydroxyprogesterone caproate. Nearly two thirds of the women (N = 267) began injections ≤18 weeks and 394 (92%) received a scheduled weekly injection within 10 days of reaching 35 weeks or delivery.

The overall rate of recurrent preterm birth was 25% (N = 106) for the entire cohort compared to the 16.8% expected rate (P = 1.0). The 3 secondary outcomes were also negative. First, 17-alpha hydroxyprogesterone caproate did not significantly reduce the rates of recurrence regardless of prior preterm birth number or sequence. Second, plasma concentrations of 17-alpha hydroxyprogesterone caproate were not different (P = .17 at 24 weeks; P = .38 at 32 weeks) between women delivered ≤35 weeks and those delivered later in pregnancy. Third, the mean (±SD) interval in weeks of recurrent preterm birth before 17-alpha hydroxyprogesterone caproate use was 0.4 ± 5.3 weeks and the interval of recurrent preterm birth after 17-alpha hydroxyprogesterone caproate treatment was 0.1 ± 4.7 weeks (P = .63). A side effect of weekly 17-alpha hydroxyprogesterone caproate injections was an increase in gestational diabetes. Specifically, the rate of gestational diabetes was 13.4% in 17-alpha hydroxyprogesterone caproate—treated women compared to 8% in case-matched controls (P = .001).

CONCLUSION: 17-alpha Hydroxyprogesterone caproate was ineffective for prevention of recurrent preterm birth and was associated with an increased rate of gestational diabetes.

Key words: efficacy, external validity, gestational diabetes, neonatal morbidity, prematurity, preterm birth, progesterone, progestogen, randomized trial
**TABLE 2**

Obstetric history of 430 women with births ≤35 weeks and recurrence rates after 17-alpha hydroxyprogesterone caproate treatment compared to historical cohort of 5787 women with prior preterm birth at Parkland Hospital

| Prior birth <35 wk | No 170HP-C | 170HP-C treated | Recurrence | Rate  | \(P\) value
|-------------------|------------|-----------------|------------|-------|----------------
|                   | Historical cohort recurrence rate | No. of women | Recurrence | No. of women | Rate  | 
| Overall           | 16.8%      | 430             | 106        | 25%   | 1.0            |
| Para 1            | 18%        | 141             | 44         | 31%   | 1.0            |
| Para 2            |            |                 |            |       |                |
| Both <35 wk       | 43%        | 48              | 20         | 42%   | .49            |
| Only second birth <35 wk | 17% | 52             | 11         | 21%   | .84            |
| Only first birth <35 wk | 11% | 39             | 2          | 5%    | .18            |
| Para ≥3           |            |                 |            |       |                |
| All <35 wk        | 45%        | 27              | 12         | 44%   | .56            |
| Other sequences of ≤35 wk | 12% | 123            | 17         | 14%   | .78            |

170HP-C, 17-alpha hydroxyprogesterone caproate.

\(^{a}\) Derived from Parkland obstetric population for 1988 through 2011 prior to introduction of 170HP-C; \(^{b}\) \(P\) values are 1-sided.

Recurrent preterm births according to 17-alpha hydroxyprogesterone caproate (17OHP-C) plasma drug concentrations measured at 24 and 32 weeks' gestation. Data are shown as median for treated women delivered ≤35 weeks (shaded) and >35 weeks (not shaded) on therapy.

March of Dimes
2014 Premature Birth Report Card

The March of Dimes is leading the Prematurity Campaign to reduce the nation’s preterm birth rate to 9.6 percent or less by 2020. This annual Premature Birth Report Card measures progress by comparing each state’s rate to the goal of 9.6 percent. The March of Dimes and the Association of State and Territorial Health Officials (ASTHO) have also established an interim goal to reduce premature birth by a minimum of 8 percent by 2014. In addition to improvements in public health, more research is needed to understand all the factors that contribute to premature birth.

All states, the District of Columbia and Puerto Rico pledged to reduce the preterm birth rate by 8% by 2014.
March of Dimes – PTB rate – US-2016-9.6% (1st increase in last 8yr)
March of Dimes - Peristats

March of Dimes 2014 Premature Birth Report Card

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<table>
<thead>
<tr>
<th>Grade</th>
<th>Preterm birth rate range/Scoring criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Preterm birth rate less than or equal to 9.6% (Score less than or equal to 0)</td>
</tr>
<tr>
<td>B</td>
<td>Preterm birth rate greater than 9.6%, but less than 11.3% (Score greater than 0, but less than 1)</td>
</tr>
<tr>
<td>C</td>
<td>Preterm birth rate greater than or equal to 11.3%, but less than 12.9% (Score greater than or equal to 1, but less than 2)</td>
</tr>
<tr>
<td>D</td>
<td>Preterm birth rate greater than or equal to 12.9%, but less than 14.6% (Score greater than or equal to 2, but less than 3)</td>
</tr>
<tr>
<td>F</td>
<td>Preterm birth rate greater than or equal to 14.6% (Score greater than or equal to 3)</td>
</tr>
</tbody>
</table>

Preterm birth rates by race and ethnicity

- Hispanic 12.1%
- White 10.2%
- Black 16.5%
- Native American 14.0%
- Asian 11.7%

The March of Dimes is concerned about inequities in health and health care that contribute to higher rates of preterm birth among different racial and ethnic groups. We urge state and federal governments to support funding and innovative practices that address the complex medical and social factors underlying racial and ethnic disparities in premature birth.
KS PTB rate – 2016 -8.8%

- **County Preterm birth rate**  **Grade**
  - Douglas 9.1% B
  - Johnson 7.9% A
  - Riley 7.6% A
  - Sedgwick 9.7% C
  - Shawnee 9.5% C
  - Wyandotte 9.8% C

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<td>A</td>
<td>Preterm birth rate less than or equal to 8.1%</td>
<td>Score less than or equal to 0.0</td>
</tr>
<tr>
<td>B</td>
<td>Preterm birth rate of 8.2% to 9.2%</td>
<td>Score greater than 0.0, but less than or equal to 1.0</td>
</tr>
<tr>
<td>C</td>
<td>Preterm birth rate of 9.3% to 10.3%</td>
<td>Score greater than 1.0, but less than or equal to 2.0</td>
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<td>D</td>
<td>Preterm birth rate of 10.4% to 11.4%</td>
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17-α-OH-progesterone

- 17-αOH progesterone - 250 mg IM from 16-36 weeks given to women with a prior history of prior spontaneous preterm birth between 20 and 36 6/7 weeks
- Reduction of risk of preterm birth by 30-35%
- Not useful in multifetal pregnancies without history of preterm birth
- Thought to be safe for mothers and infants

**Proposed mechanisms of action reported for progestogens to prevent preterm birth**

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Stimulate transcription of ZEB1 and ZEB2, which inhibit connexin 43 (gap-junction protein that helps synchronize contractile activity) and oxytocin-receptor gene</td>
</tr>
<tr>
<td>Decrease prostaglandin synthesis, infection-mediated cytokine production (antiinflammatory effects) by fetal membranes/placenta</td>
</tr>
<tr>
<td>Changes in PR-A and PR-B expression (decreased PR-A/PR-B ratio keeps uterus quiescent)</td>
</tr>
<tr>
<td>Membrane-bound PR in myometrium</td>
</tr>
<tr>
<td>PRs, when stimulated by progesterone, help selected gene promotion, or prevent binding of other factors</td>
</tr>
<tr>
<td>Interfere with cortisol-mediated regulation of placental gene expression</td>
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<tr>
<td>Nongenomic pathways</td>
</tr>
<tr>
<td>Reduce cervical stromal degradation in cervix</td>
</tr>
<tr>
<td>Alter barrier to ascending inflammation/infection in cervix</td>
</tr>
<tr>
<td>Reduce contraction frequency in myometrium</td>
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<tr>
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<td>Alter estrogen synthesis in fetal membranes/placenta</td>
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**MOA**

*PR*, progesterone receptor; *ZEB1*, zinc finger E-box binding homeobox protein 1; *ZEB2*, zinc finger E-box binding homeobox protein 2.

Conclusion

• Continue to recommend P4/17P to women at risk for PTB due to hx of spontaneous PTB/PPROM

• Continue to recommend vaginal P4 in women that have a short cervix in 2nd trimester
GI Disease in Pregnancy

• END
Appendicitis

• Diagnosis
• Sonogram vs CT vs MRI
• Patient counseling re: surgery in pregnancy
Appendicitis

- Common indication for exploration
- Swedish registry – Suspected appendicitis – 1 in 1000, confirmed disease in 65%, overall rate 1 in 1500 of true disease (Mazze, 1991)
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  - MRI – zero rad
Appendicitis - Management

- **Surgical** – Regardless of trimester
- **Antibiotics** are to prevent risk of appendiceal rupture while waiting for surgery
When counseling a patient who needs nonobstetric surgery in pregnancy, which of the following should be disclosed?

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C – There is an increased risk of preterm delivery
D - There is no increased in long-term risks to the fetus or the mother*
Questions -
Williams text
• See notes, ppt
• See notes from previous Williams Review
TPN example

• See Wesley Intranet – order set
Medications
NSAIDS

- NSAIDS – inhibits cyclooxygenase, lipoxygenase, reduces prostaglandin synthesis
- Class D
- Avoid especially in 3rd trimester
  - Cross placenta, blocks prostaglandin synthesis in fetal tissue
  - Premature closure of ductus arteriosus, fetal pulmonary hypertension, NEC, fetal renal insufficiency
  - Occurs with selective COX-II inhibitors
  - ASA crosses placenta and can affect fetal platelet function and is associated with intracranial fetal hemorrhage in 3rd trimester; avoid in pregnancy
- Used outside of pregnancy – most common anti-inflammatory agent
Hydroxychloroquine

- Hydroxychloroquine (antimalarial/antirheumatic; binds DNA, interferes with vesicle functions, inhibits phospholipid metabolism; immunosuppressive by inhibiting rheumatoid factor, acute phase reactants, enzymes)
  - Stopping this in pregnancy is associated with increased risk of lupus flares, continuing this drug is recommended if needed to control lupus (prospective study by cortes-hernandez showed the increased risk)
  - Large series show no increased risk of anomalies
  - Used in prevention of malaria with increase of fetal anomalies
  - Not associated with increased r/o fetal malformations

- Class C

- Chloroquine possible teratogenic in initial studies
  - Ototoxicity, eye development

Buchanan, 1996; Khamashta 1996
Klinger 2001; Motta 2002
Glucocorticoids

- Glucocorticoids (antiinflammatory, glucocorticoid, mineralocorticoid)
- Preg class C
- Avoid fluorinated glucocorticoids b/c they cross the placenta
  - Hydrocortisone, prednisone, prednisolone inactivated by 11-beta hydroxysteroid dehydrogenase in the placenta allowing <10% of active drug to reach fetus
- High dose associated with maternal/fetal A/E
  - Osteoporosis (tx with vit D, ca2+); glucose intolerance, sodium, h2o retention; hypertension, infection; avascular necrosis
  - Preg complications – GDM, preeclampsia, PPROM, IUGR
  - Incidence of fetal adrenal suppression with maternal tx is low
- Avoid empiric treatment, use at lowest possible dose
- Stress dose steroids (hydrocortisone 100mg IV q8hr in labor and for 24 hr PP)
  - Use if chronic steroids (>5mg/day for >2-4 weeks prior to delivery)
Azathioprine

- Azathioprine (inhibits T lymphocytes)
- Class D
- Teratogenic in animals, appears safe in humans
- Associated with IUGR
- Neonatal immunosuppression
- Indicated in pregnancy if chronic high doses of steroids is not controlling symptoms or to lower steroid dose
Cyclophosphamide

- Cyclophosphamide (alkylates and cross links DNA)
- Preg class D
  - Cleft palate, skeletal abnormalities, abnormal renal function
  - Avoid, esp in first trimester
  - May be needed in cases of severe proliferative nephritis (drug of choice in nonpregnant patients with proliferative lupus nephritis)
  - Crosses placenta
Methotrexate

- Methotrexate (inhibits dihydrofolate reductase; inhibits lymphocyte proliferation) (folate antagonist)
- Preg class X
- Avoid
- Embryolethal, IUFD
- Congenital anomalies
Cyclosporine

- Cyclosporine A (inhibits T lymphocytes)
- Preg class C
- Data comes from use in renal transplant patients, not an animal teratogen, appears safe in humans, long term follow up studies are limited
Tacrolimus

• Tacrolimus (inhibits T lymphocyte activation, immunosuppressant)
• Dose in liver transplant
  – 0.1-0.15mg/kg/d po divide q12 hr
• Preg class C
• Therapeutic drug levels 5-20 ng/ml just before next dose; time to steady state 3 days
• Monitor creatinine, K, fasting blood glucose, serum drug levels