Common Medical Problems in Pregnancy

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Objectives

- At the end of this talk, you will be able to
  - Act on evidence-based recommendations for evaluation and management of common medical problems in pregnancy
  - Confidently prescribe needed medications in pregnancy

Medical Disorders

- Asthma
- Cystic fibrosis
- Hypertension/PIH/PET
- Arrthymias
- Valvular disease
- Cardiomyopathy
- Cyanotic heart disease
- VSD/ASD
- Pulmonary hypertension
- Epilepsy
- Multiple sclerosis
- Intracranial hypertension
- Benign cranial tumours eg pit adenomas
- Obstetric Cholestasis
- Acute Fatty Liver of Pregnancy
- IBS
- Crohns/Ulceative colitis
- Thrombophilias
- VTE
- Antiphospholipid syndrome
- SLE
- Rheumatoid arthritis
- Sickle cell disease/thalassaemias
- Anaemia
- Diabetes
- Hypo/hyperthyroidism
- Adrenal disease
- Cancer

Pregnancy rates in women over 40 increased 65% between 1990-2008

--Ventura SJ et al; 3 National Vital Statistics Reports,Vol.60,No.7,June 20,2012

Pregnancy and chronic disease

- Pregnancy likely to unmask occult chronic disease
  - Glucose intolerance
  - Renal dysfunction
  - Hypercoaguable states
  - Valvular heart disease
  - Cerebral aneurysm
- Pregnancy as a “stress test for life”

Kaaja and Greer, JAMA 2006

Postpartum effects

- Increased rates of postpartum chronic disease
  - Women with GDM have up to 75% likelihood of developing Type II DM in subsequent five years
  - Women with preeclampsia more likely to develop CAD and stroke later in life
    - Higher rates of hypertension, insulin resistance, dyslipidemia and inflammatory markers
    - Primary prevention could play an important role

O'Sullivan, J, Diabetes 1991;
JAMA 1982; Kaaja, JAMA 2005

Approach to Medical Illness in Pregnancy

- Great need for primary providers to understand medical illness in pregnancy
  - Management of medical illness including appropriate contraception
  - Preconception counseling and patient education
  - Collaboration with subspecialists, MFM's

Approach to Medical Illness in Pregnancy

- The tools you need:
  - An understanding of the physiologic changes of pregnancy and how they affect disease
  - A basic knowledge of pregnancy specific illnesses
  - A strategy for evaluating drug safety in pregnancy

ASTHMA

- Commonest chronic medical illness to complicate pregnancy
- Up to 3-8%* of women of childbearing age
- Often undiagnosed or undertreated
  - A significant increase in complications of pregnancy in asthmatic women.
  - The largest study to date shows a 15 to 20 percent increased risk of perinatal mortality, preeclampsia, preterm delivery, or low birth weight infants compared to non-asthmatic women
  - Patients with more severe asthma have a 30 to 100 percent increased risk#

*Kwon HL, et al. Ann Epidemiol. 2003;13(5):317 # Kallen, B, et al. Eur J Epidem 2000; 16:167.

I am wheezing more often

- A 23-year-old non-smoking woman (gravida 1, para 0) referred to you at 11 weeks' gestation with an 8-year history of asthma, which has worsened over the past year.
- She reports symptoms requiring albuterol two or three times per day and interfering with sleep every night.
- Her forced expiratory volume in 1 second is 65% of the predicted value; it increases to 88% after administration of albuterol. How should her case be managed?

Answer?

A. Continue the current regimen
B. Add Budesonide
C. Add theophylline
D. Add salmeterol
E. Add inhaled cromolyn

Respiratory Changes in Pregnancy

- ↑O2 demand-20% increased consumption
- Tidal volume increases
- (and with small ↑ in respiratory rate= large increase on ventilation-40-50% ↑in minute ventilation)
- Inspiratory capacity increases
- Residual volume decreases
- Expiratory reserve decreases
- Marked reduction in functional residual capacity
  - Diaphragmatic elevation
  - Increase in subcostal angle and transverse thoracic diameter
- FEV1 and PEFR are unchanged

Respiratory Changes

- Progesterone effect probably underlies changes in ventilation and reduction in CO_2
  - Directly on respiratory centre
  - Increases carbonic anhydrase in maternal RBC
    - Increased breakdown of CO_2 and excretion of HCO_3 through maternal kidneys
- Functional changes facilitate airflow along bronchial tree
  - Women with chronic respiratory disease tend to deteriorate less in pregnancy
  - Peak expiratory flow and FEV1 can still be valid in pregnant asthmatics
- Shortness of breath is common symptom in pregnancy
  - Individual variations in chemoreceptors
  - Physiological increase in proportion of blood shunted away from functioning alveoli

Management

- Emphasis on prevention rather than treatment
- Treatment in pregnancy is no different to non-pregnant women
  - Optimise control prior to pregnancy
  - Achieve control asap in new diagnosis
  - Use of B2 agonist +/- inhaled corticosteroids mainstay

Medication Issues

- B2 agonists
  - Safe in pregnancy
  - Serevent experience growing and ALSO appears safe
- No adverse fetal effects reported with the use of the following inhaled drugs
  - Disodium chromoglycate
  - Nedocromil
  - Anticholinergics (ipratropium)
  - Inhaled cortocosteroids

Medication Issues

- Steroids
  - Inhaled:
    - minimal absorption
    - No evidence fetal malformations or adverse fetal effects
  - Oral
    - Should not be withheld in acute attacks
    - No strong evidence of fetal malformations, miscarriage, stillbirth or neonatal death
    - Will worsen glycaemic control in diabetics or may increase risks GDM with long-term use
    - Long-term high dose steroids ↑risk premature ROM

Wendel PJ et al; Am J Obstet Gynecol. 1996 Jul;175(1):150-4.

Acute Asthma Attack

- Manage as non-pregnant
  - IV rehydration
  - O_2
  - B_2 agonists as O_2 nebuliser (may be repeated)
  - CXR if suspicion pneuthorax/pneumonia or failure to improve
  - Give steroids JUST AS IF pt was not pregnant! (often inappropriately withheld)
  - If not improving, may need IV steroids or inhaled B_2 agonists +/- Magnesium sulfate

I have seizures and want to get pregnant

- A 25-year-old woman with epilepsy comes to the office seeking advice about pregnancy.
- She first developed seizures after sustaining a head injury in a motor vehicle collision at age 16 years.
- MRIs obtained since then have shown an area of encephalomalacia in the right temporal lobe. Her seizures were initially refractory to carbamazepine and valproic acid monotherapy. Carbamazepine was stopped, and lamotrigine was added to the valproic acid 1 year ago. She has not had any seizures since that time.

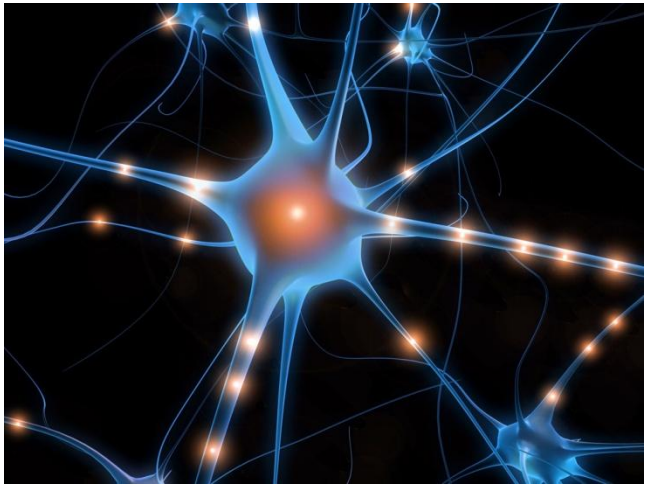
Answer?

Which of the following is the most appropriate management?

A. Advise the patient not to become pregnant
B. Continue the valproic acid and lamotrigine
C. Discontinue the valproic acid and continue the lamotrigine
D. Discontinue the valproic acid and lamotrigine
E. Substitute phenobarbital for her current medications

EPILEPSY

- About 0.5% women of childbearing age
- Most diagnosed (known) prior to pregnancy
- All seizure types may be affected by pregnancy
- Associated with risks maternal death due to aspiration and SUDEP



Effect of Pregnancy on Epilepsy

- 25-30% ↑seizure frequency
- 54% no change
- If seizure free unlikely to have seizures UNLESS stops medications
- Poorly-controlled (>1/month) likely to deteriorate in pregnancy
- Risk of seizures highest in peripartum period

Reasons for Deterioration of Control

- Pregnancy
- Poor compliance (Fears of teratogenesis)
- Decreased drug levels due to nausea and vomiting
- Decreased drug levels due to ↑volume of distribution and ↑drug clearance
- Lack of sleep towards term and during labour
- Lack of absorption of drugs during labour
- Hyperventilation during labour

Effects of Epilepsy on Pregnancy

- Fetus is relatively resistant to short-term hypoxia (during seizures)
    - No evidence adverse effects
- No increased risks of miscarriage or obstetric complications (IUGR, PTL, PET etc)
- Status Epilepticus <1% pregnancies BUT dangerous for mum and baby-TREAT VIGOROUSLY!
- Major risk is teratogenicity of drugs
    - Even women on no Rx have ↑risk malformations (4% vs 3% in general population)
- Risk of child developing epilepsy
    - 5% if either parent has epilepsy
    - 15-20% if both
    - 10% if affected sibling and <2 parents affected
    - 9-12% if parent has idiopathic generalised-only 3% if partial seizures

Teratogenic Risks of Anticonvulsants

- ALL are teratogenic-newer drugs thought to be safe but now shown to have risks associated with use
- Major malformations are:
  - Neural tube defects (esp valproate 1-2%) and carbamazepine (0.5-1%)
  - Orofacial clefts (especially phenytion)
  - Cardiac defects (esp phenytion and valproate)
- Minor malformations (fetal anticonvulsant syndrome)
  - Dysmorphic features (V-shaped eyebrows, lowset ears, broad nasal bridge, irregular teeth)
  - Hypertelorism
  - Hypoplastic nails and distal digits

Teratogenic Risks of Anticonvulsants

- Little difference in risk levels between drugs
- Risk for any one drug is 6-7% (2-3x↑)
- Risk increases with number of drugs (polypharmacy)- taking 2 or more: risk 15%
- If take phenytion, valproate AND carbamazepine, risk to fetus is up to 50%
- Benzodiazepines are not teratogenic
- Mechanism of teratogenesis though to be folate deficiency
  - All women should be on high dose folate (5mg/day) preconceptually and throughout pregnancy

Management in Pregnancy

- Preconceptually:
  - take folic acid 5mg/day from at least 12 weeks prior to conception
- Pregnancy
  - Continue **folic acid** throughout as risks folic deficiency anaemia
  - Continue current drugs if well controlled *except*
  - Wean off/change phenobarbitone due to risks of neonatal withdrawal convulsions
  - **Detailed fetal scan** at 18-20 weeks with detailed fetal cardiac scan at 22 weeks
  - Advise shallow bath or shower (risks of drowning if fit)
  - Relatives advised re: recovery position of seizures
  - If give steroids, ↑dose if enzyme inducing drugs (phenytoin, phenobarbitone, carbamazepine)
  - **Vit K 10-20mg orally from 34-36 weeks** if on enzyme inducers due to risks of fetal Vit K deficiency and Haemorrhagic Disease Newborn

“I get tired more easily; my feet are swollen”

- A 35-year-old black woman is evaluated for progressive dyspnea 3 weeks after delivery of her first child. Other than hypertension during pregnancy, the pregnancy and delivery were uncomplicated. She has no history of cardiovascular disease.
- On physical examination, the blood pressure is 110/70 mm Hg in both upper extremities, the heart rate is 105/min and regular, and the respiratory rate is 28/min. The estimated central venous pressure is 10 cm H_2O and there are no carotid bruits. The apical impulse is displaced and diffuse. There is a grade 2/6 holosystolic murmur noted at the apex. Third and fourth heart sounds are also noted at the apex. There is dullness to percussion at the posterior lung bases bilaterally, and there are crackles extending up half of the lung fields. Lower extremity pulses are normal and without delay, but pedal edema is present.
- The electrocardiogram demonstrates sinus tachycardia. There are no ST-segment or T-wave changes. The chest radiograph demonstrates bilateral pleural effusions and interstitial infiltrates. The aortic contour is unremarkable.

Diagnosis?

Which of the following is the most likely cause of the patient's current symptoms?

A. Acute myocardial infarction
B. Aortic dissection
C. Coarctation of the aorta
D. Acute pulmonary embolism
E. Peripartum cardiomyopathy

Peripartum cardiomyopathy

- Defined as heart failure with LVEF < 45%;
  - diagnosed from 3 months before upto 6 months PP in the absence of an identifiable cause.
- Usually diagnosed in month 1 postpartum.
- Typical features : time of onset, evidence of LV dilation (displaced and diffuse apical impulse), and typical signs of heart failure.
- Risk factors :Age (>30 years at the time of the pregnancy), race (black, African, Haitian), and the presence of gestational hypertension.
- Maternal mortality rate ~10%, peripartum cardiomyopathy is the major cause of pregnancy-related death in North America.
- Urgent confirmation of global ventricular systolic dysfunction by TTE; and treatment with standard heart failure therapy are critical.
- Improvement in LV function in ~ 50% of women within 6 months after delivery. Intravenous immune globulin and pentoxifylline have been shown to improve outcomes in some studies.
- Anticoagulation is recommended for thromboembolic prophylaxis when LVEF < 35%.

Key physiologic changes: cardiovascular

- Hemodynamic changes
  - Blood volume/cardiac output increase
    - 50% increase, with half of this by 8 weeks
    - Maximum blood volume expansion at 28 weeks
    - Labor may increase cardiac output another 50%
  - 10-20% increase in HR
  - 25% decrease in systemic vascular resistance
    - Systolic BP decreases by 5-10mmHg, diastolic by 10-15mmHg

Key physiologic changes: cardiovascular

- Oncotic changes:
  - Increased plasma volume by 50%
  - Increased red cell mass by 33%
  - Resulting dilutional anemia

Predictors of poor outcome in women with heart disease

- New York Heart Association Class III or IV
  - Symptoms with less than ordinary physical activity or at rest
- History of prior cardiac event or arrhythmia
- Left sided obstruction in mitral or aortic valve
- Ejection fraction less than 40%

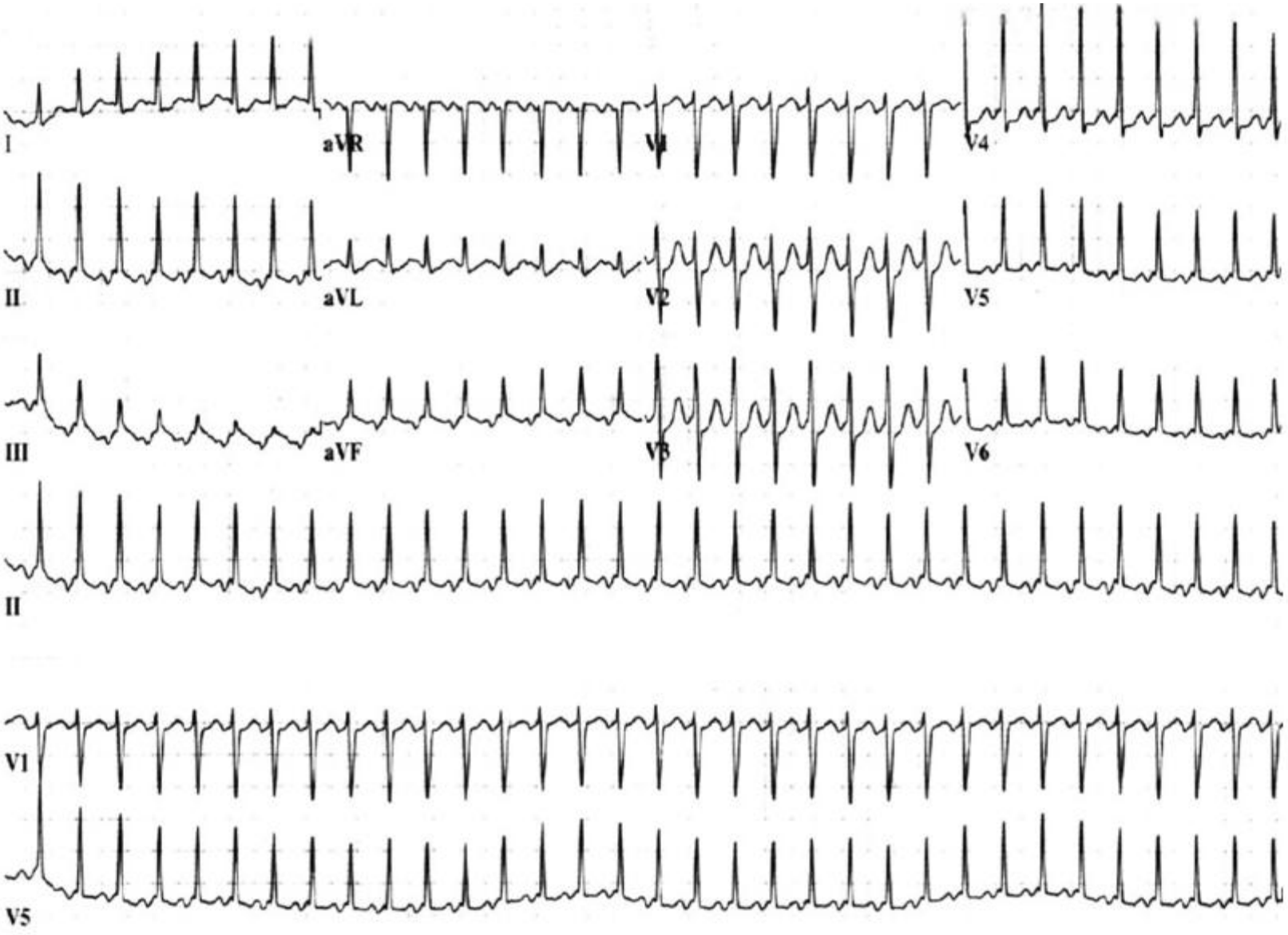
Siu, SC, Circulation 2001

“I feel dizzy ”

A 26-year-old woman who is 25 weeks pregnant is evaluated in the emergency department for palpitations and episodic lightheadedness. She has no history of cardiovascular disease or tachycardia.

- On physical examination, her blood pressure is 100/70 mm Hg and her pulse is 175/min. The estimated central venous pressure is normal and there are no carotid bruits. The apical impulse is not displaced. There are no murmurs or abnormal heart sounds detected. The examination is otherwise unremarkable.
- A Valsalva maneuver is performed by the patient and carotid sinus massage is performed by the attending physician, but the tachycardia continues.

Her Electrocardiogram



How would you treat?

Which of the following is the most appropriate intravenous medication to administer at this time?

A. Adenosine
B. Amiodarone
C. Digoxin
D. Diltiazem
E. Metoprolol

Pre-Pregnancy with Mechanical Mitral Valve

- A 29-year-old woman with a mechanical mitral valve prosthesis presents for pregnancy counseling. She has a history of mitral regurgitation and had mitral valve replacement for progressive left ventricular enlargement several years ago. She recently married and would like to start a family. She is asymptomatic and has been on a stable dose of warfarin (4 mg/d) for the past 2 years.
- On physical examination, her blood pressure is 120/70 mm Hg. The estimated central venous pressure is 3 cm H_2O. There is a crisp, mechanical S_1. No murmurs are detected. The remainder of the examination is unremarkable.
- Which of the following is the most appropriate anticoagulation regimen for this patient if she becomes pregnant?

Answer?

A. Continue warfarin, adjusted to INR
B. Stop warfarin; start aspirin and clopidogrel
C. Stop warfarin; start fondaparinux
D. Stop warfarin; start weight-based low-molecular-weight heparin
E. Stop warfarin; Start Dabigatran

A Conundrum: Anticoagulation for mechanical prosthetic valves in pregnancy

- Warfarin has a LMW: crosses placenta to cause poor fetal outcomes especially in 1st trimester (embryopathy; still birth, ICH, spontaneous abortion)
- Warfarin also has the lowest risk for maternal complications and death
  - Used in other countries outside the USA
- Fondaparinux approved for DVT/PE but not for anticoagulation for mechanical valves
- LMWH is the choice here. Weight-based dosing is not adequate.
  - Monitor anti Xa activity levels weekly or biweekly to guide dosing

Stout KK; Heart 2007; 93 (5):552-558

Prescribing in pregnancy

- Do not start any medication unless clearly indicated
- Do not discontinue medicines that successfully maintain the maternal condition unless there are clear indications to do so
- Ask about and document non-prescription meds

Lee R, 2000

Prescribing in pregnancy

- Have a pregnancy medication reference available
- Favor older medicines with longer record of use
- Check blood levels and consider increased and/or more frequent dosing
  - Increased volume of distribution, hepatic and renal clearance
  - Increased production of binding proteins—free drug levels are better

Powrie, R SGIM 2000

Prescribing in pregnancy

- Educate and negotiate with your patient
  - Pregnant women more likely to stop needed meds
- Report adverse outcomes
- Always consider the effect of not treating
- Remember that few drugs are absolutely contraindicated

FDA Drug Ratings in Pregnancy

Category	Interpretation
A	Controlled human studies show no risk
B	No evidence of risk in studies
C	Risk cannot be ruled out
D	Positive evidence of risk
X	Contraindicated in pregnancy

Limits of the FDA classification

- Hard to remember
- May be misleading
  - Up to 60% of category X drugs have no human data
  - No information on degree of risk
  - A drug may end up in category X simply if it has no utility in pregnancy
  - Rarely updated
  - Efforts underway to address these concerns

Sciali, 2004 accessed from www.reprotox.org

Drugs to avoid in pregnancy

- **ACE inhibitors**: renal dysgenesis
- **Tetracycline**: abnormalities of bone and teeth
- **Fluoroquinolones**: abnl cartilage development
- **Systemic retinoids**: CNS, craniofacial, CV defects
- **Warfarin**: skeletal and CNS defects
- **Valproic acid**: neural tube defects
- **NSAIDS**: bleeding, premature closure of the ductus arteriosis
- **Live vaccines (MMR, oral polio, varicella, yellow fever)**: may cross placenta

Lee, R 2000

Good References for Drug Prescribing

- Briggs, Freeman, and Yaffe: Drugs in Pregnancy and Lactation, 2005.
- Lee, Rosene-Montella, Barbour, Garner, Keely: Medical Care of the Pregnant Patient, 2000.
- www.reprotox.org
- www.motherisk.org
- www.micromedix.com (reprorisk)
- www.otispregnancy.org (free)
- Hale, T: Medications and Mother's Milk, 2004. Also www.ibreastfeeding.com

Example from Reprotox

- **Agent Summary—Citalopram (Celexa)**
  Quick take: Based on experimental animal studies and limited human reports, standard therapeutic use of citalopram is not expected to increase the risk of congenital anomalies. Use of serotonin reuptake inhibitors late in pregnancy can be associated with a mild transient neonatal syndrome of central nervous system, motor, respiratory, and gastrointestinal signs. In a small number of cases, the use of other serotonin reuptake inhibitors after 20 weeks gestation has been associated with an increased risk of neonatal pulmonary hypertension.

Reprotox website 2006

Case #2

- 39 yo G4P2 for new primary care appointment
- Obese
- History of pulmonary embolus in prior pregnancy
- Upreg positive today, 9 weeks by LMP
- Complaining of mild shortness of breath, O2 sat is 93%

Case #2

- What are some changes in the respiratory and hematologic systems in pregnancy?
- How might they affect this patient?
- What would you do next?

Key physiologic changes: pulmonary

- Increased minute ventilation
  - Mediated by progesterone
  - Increased tidal volume>>respiratory rate
  - Compensated respiratory alkalosis
  - Normal ABG in pregnancy: 7.43/29/100
    - $PaCO_2$ of 40mmHg is very abnormal in pregnancy
    - Fetus relies on high maternal PaO_2

Key physiologic changes: pulmonary

- Greater tendency to pulmonary edema
  - Increased cardiac output
  - Decreased oncotic pressure
  - Leaky capillaries
  - Aggressive IV fluids
  - Meds

Key physiologic changes in pregnancy: Hematologic

- Hematologic/Immunologic:
  - Procoagulant factors increase: factor VIII, vWF, fibrinogen
  - Protein S levels markedly reduced
  - Increased risk of venous clots
    - Greatest risk in post-partum period

Key physiologic changes: endocrine

- Endocrine:
  - Insulin resistance, dyslipidemia
  - Relative TSH suppression in first trimester
  - Other thyroid changes

Key physiologic changes: renal

- Increased glomerular filtration rate
  - Baseline proteinuria increases
  - Drugs metabolized more rapidly by kidney
- Creatinine falls
- Collecting system dilates

Case #2

- You want to order a chest x-ray for initial evaluation
- She is concerned about the effects on the fetus
- What would you say?

Principles of diagnostic imaging

- Greater risk of harm by **not** getting a needed study than getting one
- Little evidence that radiation exposures <5 rads have significant fetal effects
- Almost all imaging studies involve radiation well below this level
  - CXR <0.001 rad
  - Chest CT PE protocol 0.001-0.002 rads
  - CT abdomen/pelvis 0.64 rads

IV contrast

- Theoretical concern for effects on fetal thyroid
- Case reports of women receiving high dose iodine in pregnancy-->no adverse outcomes
- General advice: avoid if possible, but use contrast when clinically necessary

MRI

- Few studies
  - Animal evidence shows little risk
- NIH consensus statement
  - Recommends MRI be reserved for 2nd and 3rd trimester if possible, but can be performed in pregnancy
- Gadolinium
  - Little data—use if clinically warranted

Case #2

- CT with PE protocol done: PE
- Managed with treatment dose low molecular weight heparin, converted to subcutaneous unfractionated heparin at 36 weeks
- Vaginal delivery of healthy baby boy

A patient with intractable itching

- A 23-year-old woman gravida 2 para 1 at 35 weeks with a singleton gestation is referred from a dermatologist for intractable itching. The itching is primarily on the palms of her hands and soles of her feet. It is present day and night, and keeps her from sleeping. The patient also had itching during her first pregnancy in which the fetus died in utero in the third trimester. She states no explanation was given for the fetal demise and the pregnancy was otherwise uncomplicated. Autopsy and karyotype of the fetus were normal. She has no known prior history of liver disease or risk factors for viral hepatitis. Her physical examination is notable for numerous skin excoriations related to scratching and a gravid uterus. She has no abdominal pain and a nonpalpable liver or spleen.
- Laboratory evaluation is notable for elevations of serum aminotransferases, alkaline phosphatase, and total bilirubin (ALT 1201 IU/L, AST 910 IU/L total bilirubin 3.1 mg/dL alkaline phosphatase 400 IU/L). The GGTP is normal, but total serum bile acid concentrations are 10 times normal. Viral hepatitis serologies are negative. A right upper quadrant ultrasound is normal

Diagnosis?

A. Acute viral hepatitis
B. Choledocholithiasis
C. Primary biliary cirrhosis
D. Cholangitis
E. Intrahepatic cholestasis of pregnancy

Additional Information

- This patient's clinical presentation is consistent with intrahepatic cholestasis of pregnancy (ICP).
  - Serologic testing excluded viral hepatitis
  - the high level of aminotransferases with normal GGTP makes primary biliary cirrhosis unlikely.
  - The absence of abdominal pain, fever, or biliary duct dilation helped exclude choledocholithiasis and cholangitis.
  - The patient's prior history of itching during pregnancy is helpful, since intrahepatic cholestasis of pregnancy tends to recur.
  - Intrauterine demise during her prior pregnancy may reflect the adverse fetal outcomes associated with this condition and should prompt her clinician to advise increased fetal monitoring with consideration of early delivery.
  - **ursodeoxycholic** acid increases bile flow and has been used to relieve pruritus and improve liver biochemical tests in patients with ICP. no adverse effects in the mothers or babies
  - In a pooled analysis that compared UDCA with all controls, patients who received UDCA were more likely to report an improvement in pruritus (61 versus 27 percent;) and were more likely to have total resolution of pruritus (42 versus 6 percent). Patients who received UDCA were also more likely to have improvements in their transaminase and serum bile acid concentrations and had a lower premature delivery rate (16 versus 34 percent; OR 0.44).

Gurung V, Middleton P, Milan SJ, et al. Interventions for treating cholestasis in pregnancy. Cochrane Database Syst Rev 2013; 6:CD000493.

A patient with elevated aminotransferases

- A 26-year-old woman gravida 3 para 2 currently in her 14th week with a singleton gestation is hospitalized with intractable nausea, vomiting, and dehydration. During her two prior pregnancies, she also had severe nausea and vomiting, which resolved early in the second trimester. Her past medical history is otherwise unremarkable. She has not traveled in the past year, and does not take any medications (including over-the-counter agents and herbal compounds) other than prenatal vitamins and folate. Her physical examination is notable for dry mucus membranes, and a gravid uterus. She has no abdominal pain, and does not have a palpable liver or spleen.
- Her initial laboratory examination reveals elevations in serum aminotransferases ALT (175 IU/L), AST (122 IU/L), serum total bilirubin (2.1 mg/dL). Amylase and lipase are normal. The albumin is slightly decreased from normal values, but consistent with pregnancy. Liver biochemical tests prior to pregnancy are not available. A right upper quadrant ultrasound is normal. Urinalysis shows elevated ketones.

Diagnosis?

A. viral hepatitis
B. Autoimmune hepatitis
C. Drug toxicity
D. Hyperemesis gravidarum

Additional testing

- Serology for hepatitis A, B, and C is negative,
- antinuclear antibodies are absent
- serum protein electrophoresis is normal (making autoimmune hepatitis unlikely).
- TSH is normal.
- Obstetrical ultrasound examination demonstrates a normal singleton gestation.
- She was treated with antiemetics, IV fluids
- At 20 weeks of gestation, her symptoms completely abate, and her liver biochemical tests return to normal.

A patient with elevated aminotransferases and hypertension

- A 23-year-old woman gravida 1 para 0 currently with twin gestation at 30 weeks is hospitalized with hypertension, for which methyldopa had been prescribed at 28 weeks of gestation. Despite treatment, she continues to be mildly hypertensive and is developing a progressive rise in serum aminotransferases, which are over 85 IU/L. Hepatitis serology and markers for autoimmune hepatitis are negative. Her platelet count, peripheral blood smear, and right upper quadrant ultrasound are normal. Urinalysis is normal except for 1+ proteinuria.
- Within 36 hours, the patient develops progressive thrombocytopenia, worsening hypertension, and a headache; and her serum aminotransferase concentrations continue to rise

Diagnosis?

A. Toxicity due to methyldopa
B. Early acute fatty liver of pregnancy
C. Severe preeclampsia
D. Autoimmune hepatitis
E. Hyperemesis gravidarum

A patient with nausea and vomiting in the third trimester

- A 32 year-old woman gravida 1 para 0 with a singleton gestation at 34 weeks of gestation is admitted to the hospital with a three-day history of nausea and vomiting, malaise, and jaundice. Her blood pressure is mildly elevated. Urinalysis shows trace protein, serum aminotransferases range between 200 to 500 IU/L, serum glucose is in the low-normal range. White blood cell count and prothrombin time are elevated. She denies any recent travel. Hepatitis serologies were sent, but are unavailable

Diagnosis?

A. Acute fatty liver of pregnancy.
B. HELLP syndrome
C. Atypical preeclampsia
D. Viral hepatitis
E. Intrahepatic cholestasis of pregnancy

Clinical characteristics of liver diseases in pregnancy

Disease	Trimester (1 2 3 PP)	Laboratory studies: Amino-transferases, U/L	Laboratory studies: Total bili, mg/dL	Laboratory studies: Other	Differential diagnosis	Prognosis
Hyperemesis gravidarum		<200 (ALT>AST) may be as high as 1000	<4		Gastroenteritis, cholecystitis, hepatitis, intestinal obstruction, peptic ulcer disease, pancreatitis, appendicitis, diabetic ketoacidosis, hyperparathyroidism, hyperthyroidism, drug toxicity	Maternal and fetal mortality rare; disease may recur.
HELLP syndrome		<500 (median 250) unless hepatic infarction	↑ (median 1.5)	PLTS <100,000 LDH >600	Acute fatty liver of pregnancy, gastroenteritis, hepatitis, pyelonephritis, appendicitis, cholelithiasis, idiopathic thrombocytopenic purpura, hemolyticuremic syndrome	Maternal mortality low, but complications high; fetal mortality may be as high as 35 percent; recurs 3 to 27 percent
Intrahepatic cholestasis		<500 usually >1000 occasionally	<6	Bile acids ↑ AP 4x normal (out of proportion to GGT)	Cholelithiasis, viral hepatitis, primary biliary cirrhosis, primary sclerosing cholangitis, drug hepatoxicity	Maternal mortality rare; fetal mortality 1 to 2 percent; associated with prematurity and stillbirth, recurs in 60 to 70 percent.
Acute fatty liver of pregnancy		<500 may be as high as 1000	↑	WBC ↑ PT ↑ PLTS ↓ glucose ↓ uric acid ↑	HELLP, drug toxicity, fulminant hepatic failure	Maternal mortality <3 percent; fetal mortality as high as 35 to 45 percent; recurrence uncommon.

PLTS: platelet count; PT: prothrombin time; AP: alkaline phosphatase; GGT: gammaglutamyl transpeptidase; WBC: white blood cell count; LDH: lactate dehydrogenase; ALT: alanine aminotransferase; AST: aspartate aminotransferase; PP: Post partum.

How Common are these problems?

- Pregnant women with abnormal liver tests represent 3 percent of deliveries*
  - The majority of cases were attributed to pregnancy-specific disorders (preeclampsia, HELLP syndrome, obstetric cholestasis, hyperemesis gravidarum, acute fatty liver of pregnancy);
    - the reminder were attributed to other conditions (eg, sepsis, drug-related, bile duct stones, hepatitis) or of uncertain etiology

*Ch'ng CL. Et al; Prospective study of liver dysfunction in pregnancy in Southwest Wales. Gut 2002; 51:876.

Liver tests in normal pregnancy

Liver tests affected by pregnancy (these tests are increased or decreased in relation to values in non-pregnant women)
Albumin and total protein (decreased from the first trimester)
Alkaline phophatase levels (increased in second and third trimester)
Bilirubin levels (slightly decreased from the first trimester)
Gamma glutamyltransferase levels (slightly decreased in late pregnancy)
Liver tests not affected by pregnancy
Serum aminotransferase levels (ALT, AST)
Prothrombin time
Serum concentration of total bile acids (fasting state)
Lactate dehydrogenase (LDH)

Evaluation of Liver Disease in Pregnancy

History and ROS
Hx of Pruritus during previous pregnancies or while on OCPs, abdominal pain, nausea or vomiting, polyuria and polydypsia, drugs, travel, exposure to viral hepatitis, history of gallstones. Note trimester of pregancy
Physical Examination
Temperature, bloodpressure, proteinuria, liver examination
Blood tests
CBC including platelets; Routine LFTs including PT; serum creatinine, electrolytes, glucose and uric acid levels
Serology for viral hepatitis (A,B,C) and CMV. Test for Hepatitis E if suspected
Measure total serum bile acids if cholestasis suspected
Urinalysis and Culture
Ultrasound of the liver and bile ducts
Monitor evolution of symptoms and LFTs before and After delivery

Questions?