Episode Overview:

1) Describe the treatment of asthma exacerbation during pregnancy.
   What are potential side effects of systemic corticosteroids?
2) What anti-HTN meds are not safe in pregnancy? How is a hypertensive emergency treated?
3) How are prosthetic heart valves management in pregnancy?
4) Should anti-epileptics be discontinued in pregnancy? What are the risks of common antiepileptics?
   a. What complications are associated with the treatment of epilepsy during pregnancy?
5) How does pregnancy affect a patient with myasthenia gravis?
6) What is neonatal myasthenic syndrome? How is it treated?
7) What are the unique complications of pregnancy in a patient with a spinal cord injury?
8) What is autonomic dysreflexia? How is it managed?
9) List 4 maternal and 4 fetal complications of maternal diabetes
10) List 3 mechanisms of vertical transmission of HIV

Wisecracks:

1. How do the agents used to treat an asthma exacerbation affect labour?
2. Which types of valvular heart disease cause the most significant problems during pregnancy?
3. How is maternal Hepatitis B managed in the peripartum period? What treatments are indicated for the fetus?

Key Concepts:

- The physiologic demands of pregnancy may cause previously occult medical conditions to become apparent and known problems to deteriorate rapidly.
- The physiologic adjustments of pregnancy alter the normal ranges for certain laboratory values. The adjusted values need to be considered in the interpretation of results.
- The possibility of pregnancy should be considered in the differential diagnosis of certain conditions, including new-onset seizures or status epilepticus (eclampsia), glucose intolerance (GDM), persistent vomiting (hypermesis gravidarum), and thyroid disorders.
- The immunosuppressive effects of pregnancy may cause temporary improvement in inflammatory and autoimmune conditions. This beneficial effect is lost in the postpartum period, resulting in exacerbations of asthma, thyroid disorders, and myasthenia gravis.
• Medication requirements can change drastically during pregnancy and the postpartum period.

• Certain medical conditions in the mother result in neonatal complications that require special resuscitative measures. This is particularly true of many chemical dependency states, and anticipatory management of these patients is essential.

Rosen’s in Perspective:

The enormous breadth of physical and physiologic changes that occur in pregnancy may overwhelm a woman’s compensatory mechanisms and lead to deterioration of pre-existing disease. This has implications for the mother, the fetus and for the puerperium.

[1] Describe the treatment of asthma exacerbation during pregnancy. What are the potential side effects of systemic glucocorticoids?

Very common problem in pregnancy; associated with maternal and fetal morbidity. Controlling asthma during pregnancy leads to less intrauterine growth retardation and fewer adverse perinatal outcomes. It has been well documented that asthma may worsen, improve, or remain the same during pregnancy.

Remember that a compensated respiratory alkalosis is normal in pregnancy: 7.40/32/-/19. Don’t let that pseudonormal ABG fool you. Also, remember that we must keep the SP02 > 95%! Anyone with a PEF < 50% predicted is having a severe asthma exacerbation.

Tidal volume and minute ventilation increase by 45% over the course of pregnancy resulting in an average Pco2 of 32 mm Hg. The kidneys compensate and maintain an average bicarbonate level of 19 mEq/mL, which results in a compensated respiratory alkalosis with a serum pH between 7.40 and 7.45.

An initial fetal assessment should be performed, including fetal heart tones and continuous electronic fetal monitoring with a biophysical profile if the pregnancy has reached viability.

Really, the treatment is the same!

1. Inhaled beta 2 agonists:
   a. Ventolin 5 mg q 20 mins (x3 in first hr or continuous neb if severe)
   b. MDI puffs 8-10 q 20 mins x3 also an option
   c. IV doses have no proven benefit to inhaled

2. Systemic steroids
   a. Prednisone PO (unless in impending resp.failure or unable to take PO)
   b. May increase risk of preterm delivery and low-birth-weight infants; there is also conflicting evidence of an increased risk of orofacial clefts. However the benefits of oral corticosteroid use for avoiding fetal hypoxia outweighs the risk of adverse perinatal outcomes.

3. Epinephrine 0.3–0.5 mg IM (1 :1000 or 1 mg/mL) every 20 min for SEVERE cases
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a. May decrease placental blood flow

4. Additional therapies
   a. Inhaled anticholinergics Ipratropium bromide 0.5 mg every 20 min Not first-line therapy; should be used with beta agonists. Consider for use in patients with severe exacerbations
   b. Smooth muscle relaxation -
      i. MgSO4 - limited data supports its use
   c. Maintenance inhaled steroids and LRTA’s

[2] What anti-hypertensives are not safe in pregnancy? How is a hypertensive emergency treated?

The increase in blood volume due to pregnancy, along with the increases in preload, cardiac output, and oxygen consumption, can worsen or reveal cardiac disease in pregnant women. Because the signs and symptoms of acute coronary syndromes and heart failure (eg, shortness of breath, mild chest pain, edema) can be seen in normal pregnancies, these entities are especially difficult to diagnose.

Chronic hypertension is defined as hypertension (>140 mm Hg systolic or >90 mm Hg diastolic) diagnosed prior to pregnancy or before 20 weeks’ gestation. The key question in the ER is: Does that patient have any end organ dysfunction? (head, eyes, heart, lungs, liver, kidney, bone marrow)

Medical treatment of uncomplicated chronic hypertension in pregnancy without evidence of end-organ damage has demonstrated no benefit in reducing adverse perinatal outcomes as compared to placebo in multiple studies.

Additionally, antihypertensive medications pose a risk of hypotension and decreased fetal blood flow. Thus, the ACOG recommends that antihypertensive treatment should be started when blood pressures are consistently higher than 160 mm Hg systolic and/or higher than 105 mm Hg diastolic.

NOT safe:
   ● ACE and ARBs are teratogenic
   ● Spironolactone is not safe
   ● Avoid BB’s in first trimester (risk of small for gestational age)

The most commonly used agents include methyldopa (preferred agent), labetalol, and hydralazine.

A hypertensive emergency (>160/110 mmHg) is treated urgently:
   ● First line choices for preeclampsia and eclampsia = labetalol, hydralazine

See Table 179.4 in Rosen’s 9th Edition

[3] How are prosthetic heart valves managed during pregnancy?
The European Registry on Pregnancy and Heart Disease has reported that mitral stenosis and regurgitation are the most common types of valvular disease (63%), followed by aortic valve disease (23%). The most common valvular complication in pregnancy is heart failure (challenging dx to make in pregnancy!)

When it comes to prosthetic valves, these women are at high risk for clotting (hypercoagulable state) as well as thromboembolic phenomenon! Pregnant patients with prosthetic heart valves who are not anticoagulated have a maternal mortality as high as 5%, and thromboembolic events can occur in up to 24% of cases. Patients with mechanical and bioprosthetic valves remain on low dose ASA throughout the pregnancy.

For those with mechanical heart valves, things are more complicated…
- There is a major risk-benefit discussion needed between physician and patient:
  - Vitamin K antagonist use is associated with an increased risk of fetal anomalies (particularly with warfarin doses >5 mg/day) and a high risk of late fetal loss. LMWH use is associated with low fetal risk but higher risk of maternal mortality and thromboembolism than with VKA. - Uptodate
  - The final decision is way too complex for us because there are multiple factors to consider:
    - Value on maternal risk vs. value on unborn risk
    - Risk factors are valve thrombosis (e.g. A fib, multiple valves)
    - First vs. second and third trimester
    - Peripartum phase (at 36 weeks the VKA is usually switched to SC LMWH)

Warfarin is the most effective anticoagulant in preventing maternal thromboembolic events. However, warfarin is considered teratogenic in the first trimester.

Neither unfractionated heparin (UFH) nor low-molecular-weight heparin (LMWH) crosses the placenta and are not teratogenic. However, their use throughout pregnancy is not recommended due to the increased risk of thromboembolic events as compared to using UFH or LMWH in the first trimester, followed by warfarin for the remainder of pregnancy.

Current anticoagulation recommendations in pregnant patients with prosthetic heart valves are to continue using warfarin until pregnancy has been achieved. If an international normalized ratio of 2.5 to 3.5 can be achieved with a warfarin dose less than or equal to 5 mg, warfarin may be used throughout pregnancy after a full discussion with the patient about the benefits and risks of the therapy. If a dose more than 5 mg is required, UFH or LMWH should be used in the first trimester, with warfarin being resumed for the second and third trimesters. Warfarin should again be replaced by UFH or LMWH several weeks before delivery.

[4] Should anti-epileptics be continued during pregnancy? What are the risks of common anti-epileptics?

Maybe.
This isn’t really our decision in the ER, but women with non-convulsive seizures who have been seizure free for a long period of time may be able to have a period of non-pharmacologic observation.

But for the remaining patients with epilepsy they should probably continue their medication in consultation with their neurologist; the primary complication of AED use in pregnancy is congenital malformations.

Of primary concern is the risk for neural tube defects, facial clefts, cardiac anomalies, and cognitive defects with the older generation agents (eg, valproate, carbamazepine, phenytoin) and the newer generation agents (eg, lamotrigine, topiramate, levetiracetam).

There is a two- to three-fold increase in the incidence of serious congenital malformations in offspring of epileptic mothers taking these agents.

The risk is greatest with valproate and is also increased with AED polypharmacy and increased dose of individual agents. Of all the older agents, carbamazepine appears to be the safest for use as monotherapy. Recent studies have looked at the risk of major congenital malformations of the newer AEDs and have found that in monotherapy with lamotrigine or levetiracetam, the risks are lower than those in the older agents.

What complications are associated with the treatment of epilepsy during pregnancy?

Fetal—various congenital malformations associated with AEMs, fetal hypoxia and bradycardia, fetal loss.

Maternal—variable changes in seizure frequency; alterations in AEM levels; increased seizure frequency secondary to voluntary medication noncompliance; abruption, anemia, hyperemesis gravidarum, preeclampsia, possible need for labor induction and cesarean section, premature rupture of membranes. (AEM = antiepileptic medications)

Management of status epilepticus is the same as for the nonpregnant patient. The newer AEM levetiracetam has demonstrated a lower incidence of birth defects and has equal to better efficacy as older AEMs. Folate supplementation (at least 0.4 mg/day) is indicated for patients taking AEMs.

How does pregnancy affect a patient with myasthenia gravis?

Unpredictably….At risk for muscle arrest in labour and disease exacerbation postpartum, but some women have not change in their disease….and others have an exacerbation of the disease postpartum as the immunosuppressive effect of pregnancy wanes.

Patients receiving maintenance corticosteroids require “stress dose” hydrocortisone during labor and delivery.
[6] What is neonatal myasthenic syndrome? How is it treated?

Up to 30% of neonates born to mothers with myasthenia gravis have a transient neonatal myasthenia syndrome through the placental transport of acetylcholine receptor antibodies.

The onset of neonatal myasthenia is typically within the first hours of life but may be delayed by a period of days. Manifestations include poor feeding and suck, diminished reflexes, hypotonia, and bulbar and respiratory muscle weakness.

Management = supportive care. Small, frequent feeds; assisted ventilation. Neostigmine can be given prior to feeds and then gradually weaned. Most recover by two months.

There is no correlation between the severity of maternal disease and occurrence of neonatal myasthenia.

[7] What are the unique complications of pregnancy in a patient with a spinal cord injury?

- DVT’s / thrombosis
- UTI’s
- Autonomic dysreflexia

The hypercoagulable state of pregnancy, combined with chronic immobilization, results in an increased incidence of thromboembolic disease, with the incidence of deep vein thrombosis (DVT) reported as high as 8% in pregnant women with SCI.

The incidence of urinary tract infection is also markedly increased as a result of neurogenic complications and the need for catheterization. Infections are even more likely during pregnancy and may progress to pyelonephritis, with the subsequent increased risk of fetal loss, prematurity, and maternal sepsis.

[8] What is autonomic dysreflexia? How is it managed?

Autonomic dysreflexia is the most serious complication of SCI and occurs in up to 85% of women with high lesions (above T5-T6); it occurs with increased frequency during pregnancy.

Autonomic dysreflexia is manifested as severe paroxysmal hypertension, headache, tachycardia, diaphoresis, piloerection, mydriasis, and nasal congestion.

It is often precipitated by afferent stimuli from the hollow viscus such as the bladder, bowel, or uterus.

Symptoms of autonomic dysreflexia often occur with uterine contractions during labor.
However, labor may be difficult to detect because patients with spinal cord lesions below T10 to T12 have an intact uterine nerve supply and will experience labor pains; however, with lesions above T10, labor may be imperceptible or experienced as only mild abdominal discomfort.

Pregnant patients with SCI with symptoms of autonomic dysreflexia should be assessed for cervical dilation and have uterine contractions monitored. ED treatment is directed at the restoration of normal blood pressure with standard agents. Definitive therapy is with regional anesthesia. Spinal anesthesia and epidural anesthesia obliterate and prevent this response and should be used as soon as possible during labor for all women with SCI.

Tricky question: AD vs. eclampsia?

Difficult to differentiate between the symptoms of autonomic dysreflexia and preeclampsia. In autonomic dysreflexia, symptoms such as hypertension will resolve once the stimuli to the skin or hollow viscus have been relieved; in preeclampsia, the symptoms and laboratory abnormalities are more likely to persist.


These women with either type 2 DM or type 1 DM seem to be at equal risk for these complications! Complications relate to inadequate glycemic control and to the presence of vascular complications or severe renal insufficiency more than to the type of diabetes.

Maternal
- CV: silent ischemia, CHF,
- Diabetic nephropathy, preeclampsia
- Retinopathy
- DKA (can present in subtle ways, with pseudonormal pH)
- Increased need for C-section (macrosomia)

Fetal
- congenital malformations;
- macrosomia;
- IUGR;
- fetal loss;
- neonatal hypoglycemia,
- jaundice,
- Hypomagnesemia,
- hypocalcemia

[10] List 3 mechanisms of vertical transmission of HIV

Thought to be multifactorial:
- during delivery through exposure to maternal blood and secretions
- infected in utero
● through breast-feeding.

Wiscracks:

[1] How do the agents used to treat an asthma exacerbation affect labor?

Beta agonists are tocolytics and often halt labour.

[2] Which types of valvular heart disease cause the most problems during pregnancy?

● Mitral stenosis > class 1 for
● Advanced aortic stenosis
● Aortic or mitral lesions associated with pulmonary hypertension or ventricular dysfunction
● Mechanical prosthetic valves requiring anticoagulation

See Table 179.5 in Rosen’s 9th Edition

Ddx of chest pain in pregnancy:
Pulmonary embolus, reflux esophagitis, biliary colic, and aortic dissection are all more common than myocardial ischemia during pregnancy and should be considered in the differential diagnosis of the pregnant patient who presents with chest pain.

[3] How is maternal Hepatitis B managed in the peripartum period? What treatments are indicated for the fetus?

Perinatal transmission is approximately 10% to 20% in women seropositive for HBV surface antigen (HBsAg) alone but approaches 90% in mothers who are seropositive for HBsAg and HBV envelope antigen (HBeAg); it is also more likely if the mother has acute infection during the third trimester.

Of infants who have HBV infection, up to 90% become chronic carriers as adults and are at risk for complications such as cirrhosis and hepatocellular carcinoma.

Studies have suggested that lamivudine given in late pregnancy to women with high viral loads of HBV DNA reduces viral transmission when given in conjunction with HBV vaccine and immune globulin.

Infants of HBsAg-positive mothers should receive hepatitis B immune globulin and the first dose of vaccine within 12 hours of birth. Two additional doses of vaccine are administered at a later date.