Pregnancy – What a Hospitalist Needs to Know

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My Background

- Internal medicine residency at Brigham and Women's Hospital
- 2 year fellowship in Obstetric and Consultative Medicine at Women & Infants Hospital affiliated with Brown University
- Obstetric Internal Medicine consult clinic at Brigham and Women's Hospital

Disclosures and Disclaimers

I have no disclosures

I do have a few disclaimers…

1. This discussion will focus on care of cisgender pregnant women.
2. This is a broad field! I will focus on the specific topics that were requested for this talk.
3. I use the terms “fetus” and “baby” interchangeably.

General Principles

1

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2. Uninvestigated symptoms → progression of untreated disease
3. Uncontrolled maternal disease → compromised fetal safety, growth and development
4. Generally, withholding treatment/diagnostic testing = more harmful
5. With medications, imaging, procedures, think "justifiable vs not justifiable" rather than "safe vs not safe"

Topics to be covered

- Hyperemesis gravidarum
- Hypertensive disorders of pregnancy
- Pyelonephritis
- Pulmonary embolism
- Procedures during pregnancy
- Diabetes

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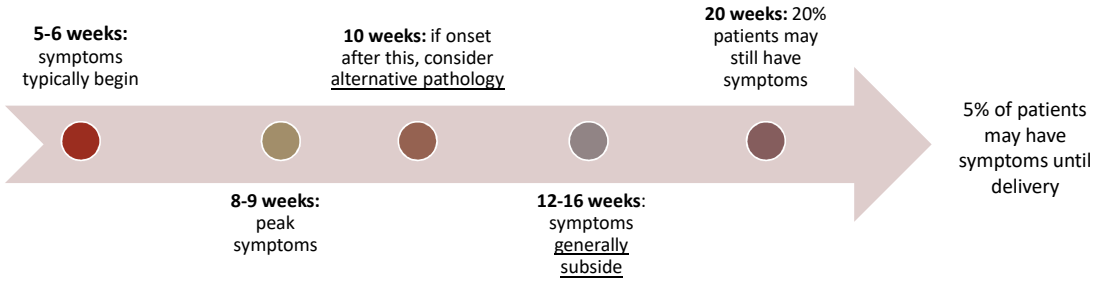
Nausea and Vomiting of Pregnancy

- Nausea +/- vomiting affects **80-90% of pregnancies**
- Nausea and vomiting of pregnancy (NVP): nausea/vomiting **due to pregnancy, rather than other pathology**
  - Vital signs, physical exam, and labs are **normal**
  - Follows **typical timeline** below



- Higher hCG (multifetal gestation, molar pregnancies) associated with more prevalent/severe nausea and vomiting

Matthews A, et al. Cochrane Database Syst Rev. 2015 Sep 8;2015(9):CD007575.
ACOG Practice Bulletin No. 189: Nausea And Vomiting Of Pregnancy. Obstet Gynecol. 2018 Jan;131(1):e15-e30..

Hyperemesis gravidarum

- Hyperemesis gravidarum = severe end of the nausea and vomiting spectrum

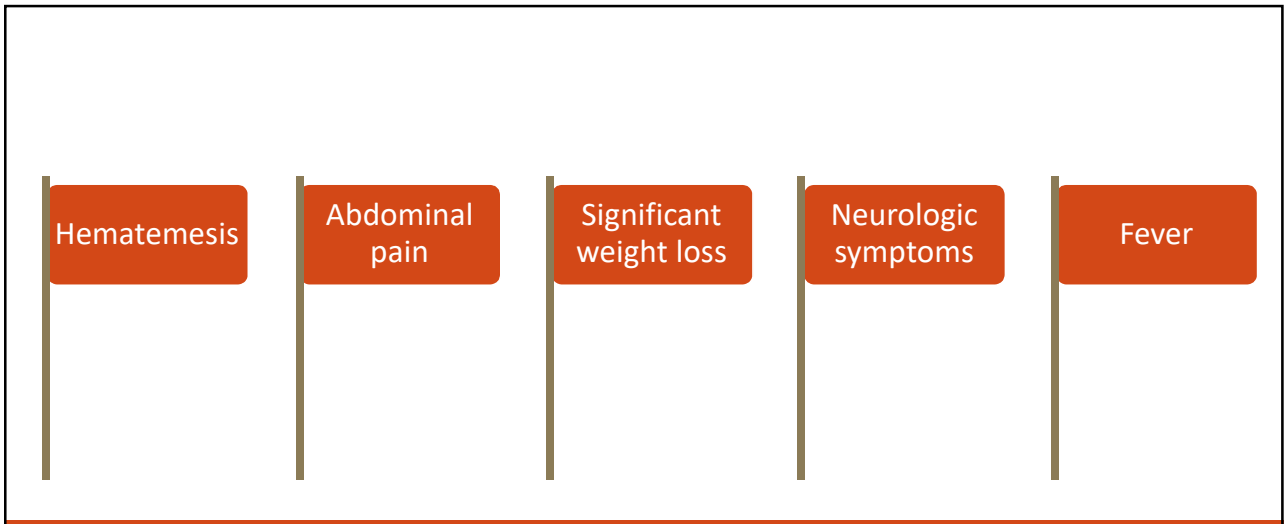
Less common, affects 0.3-3.6% of pregnancies

No single consensus definition, commonly:

- Weight loss (general
- ate
- day

- Symptoms start <16 weeks
- Nausea and/or vomiting is severe
- Unable to eat and/or drink normally
- Daily activities strongly limited

Goodwin TM. Hyperemesis gravidarum. Obstet Gynecol Clin North Am. 2008 Sep;35(3):401-17, viii.
Jansen et al. European J of Obstet Gynceol Rep Biology. 2021 Nov; 266(15-22).



Atypical features / red flags

Differential diagnosis

Gastrointestinal	Genitourinary	Metabolic	Neurologic	Miscellaneous	Pregnancy-related
• Gastroenteritis • Gastroparesis • Achalasia • Biliary tract disease • Hepatitis • Obstruction • PUD • Pancreatitis • Appendicitis	• Pyelonephritis • Uremia • Ovarian torsion • Nephrolithiasis • Degenerating uterine leiomyoma	• DKA • Addison's disease • Hyperthyroid • Hyperparathyroid • Porphyria	• Increased intracranial pressure (IIH) • Vestibular lesions • Migraine • CNS tumor • Lymphocytic hypophysitis	• Drug toxicity or intolerance • Psychiatric conditions • Cannabis hyperemesis	• Acute fatty liver of pregnancy (consider >20 weeks) • Preeclampsia (consider >20 weeks)

Differential diagnosis

Gastrointestinal	Genitourinary	Metabolic	Neurologic	Miscellaneous	Pregnancy-related
• **Gastroenteritis** • **Gastroparesis** • Achalasia • **Biliary tract disease** • Hepatitis • Obstruction • PUD • **Pancreatitis** • **Appendicitis**	• **Pyelonephritis** • Uremia • Ovarian torsion • **Nephrolithiasis** • Degenerating uterine leiomyoma	• **DKA** • **Addison's disease** • **Hyperthyroid** • Hyperparathyroid • Porphyria	• Increased intracranial pressure (IIH) • Vestibular lesions • **Migraine** • CNS tumor • Lymphocytic hypophysitis	• Drug toxicity or intolerance • Psychiatric conditions • **Cannabis hyperemesis**	• Acute fatty liver of pregnancy • Preeclampsia

Initial testing

BMP, Mg, phos

LFTs

UA

CBC w/diff

TSH

Lipase

VBG, lactate, beta hydroxybutyrate

EKG

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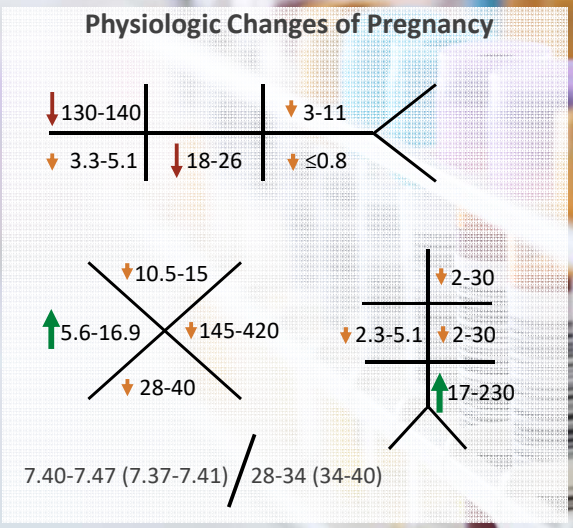
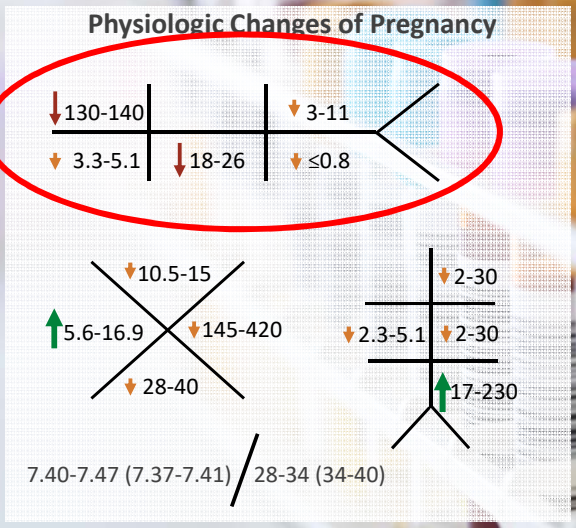


Initial testing

BMP, Mg, phos

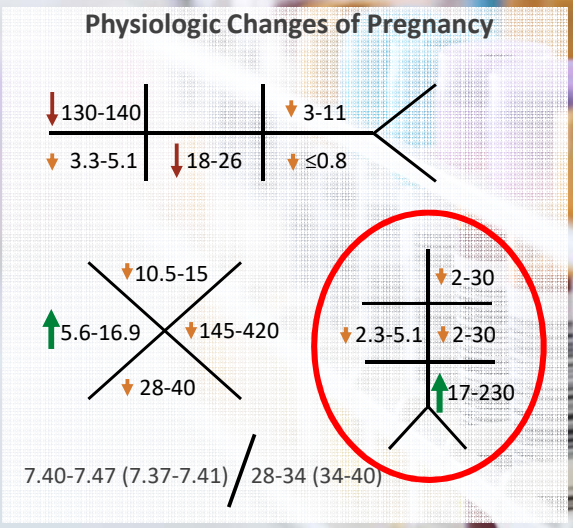
- Mostly attention to correcting deficiencies
- Stay attuned to inconsistencies in derangement (ie high-normal K, suggestive of alternative etiology ie Addison's)
- Assess anion gap *corrected for albumin*
- Often see hypochloremic metabolic alkalosis, check for concomitant metabolic acidosis (think about starvation ketosis)



Initial testing

LFTs

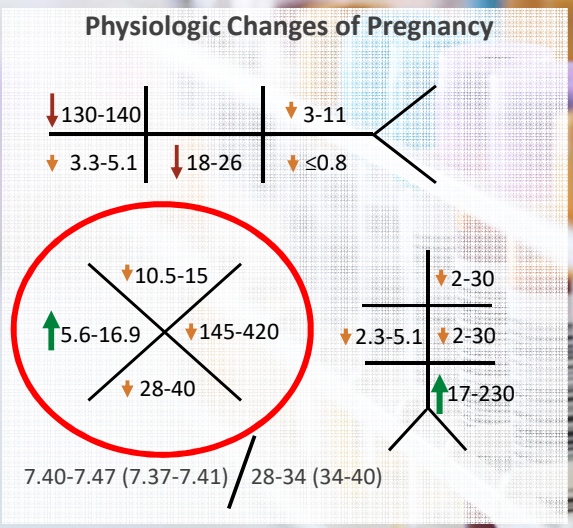
- Abnormal in up to 50% of patients hospitalized for hyperemesis
- ALT > AST
- Mild elevation 2-3x ULN, into low 100s
- Total bilirubin may be elevated (direct and indirect), rarely exceeds 4



Initial testing

CBC

- Physiologic leukocytosis in pregnancy – usually normal diff or neutrophil predominant
- Lymphocyte count may be higher in hyperemesis
- Physiologic decrease in hgb and plt may mask hemoconcentration



Initial testing

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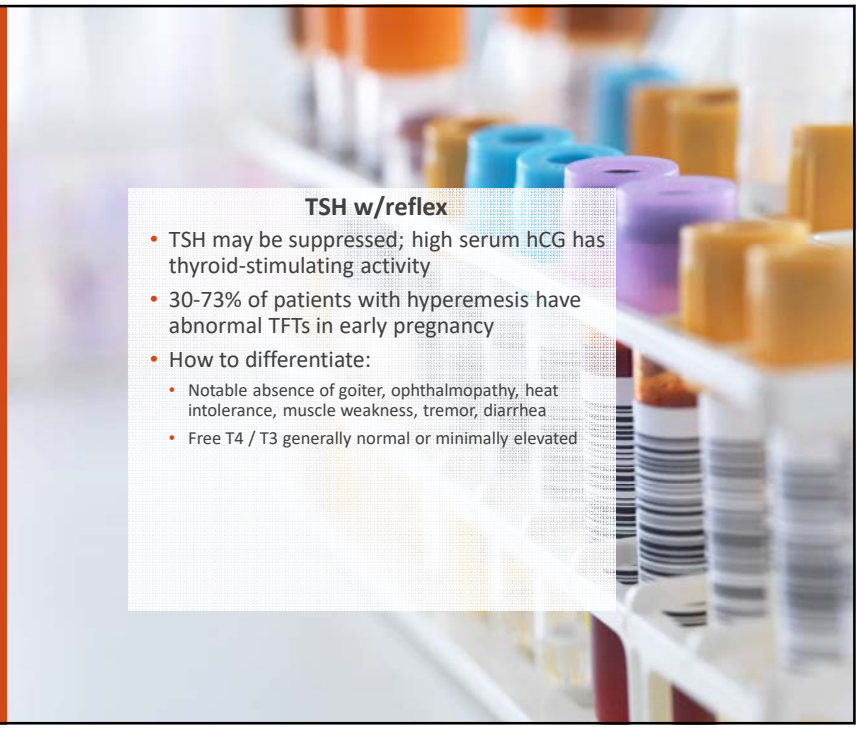

TSH w/reflex

- TSH may be suppressed; high serum hCG has thyroid-stimulating activity
- 30-73% of patients with hyperemesis have abnormal TFTs in early pregnancy
- How to differentiate:
  - Notable absence of goiter, ophthalmopathy, heat intolerance, muscle weakness, tremor, diarrhea
  - Free T4 / T3 generally normal or minimally elevated

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BMP, Mg, phos

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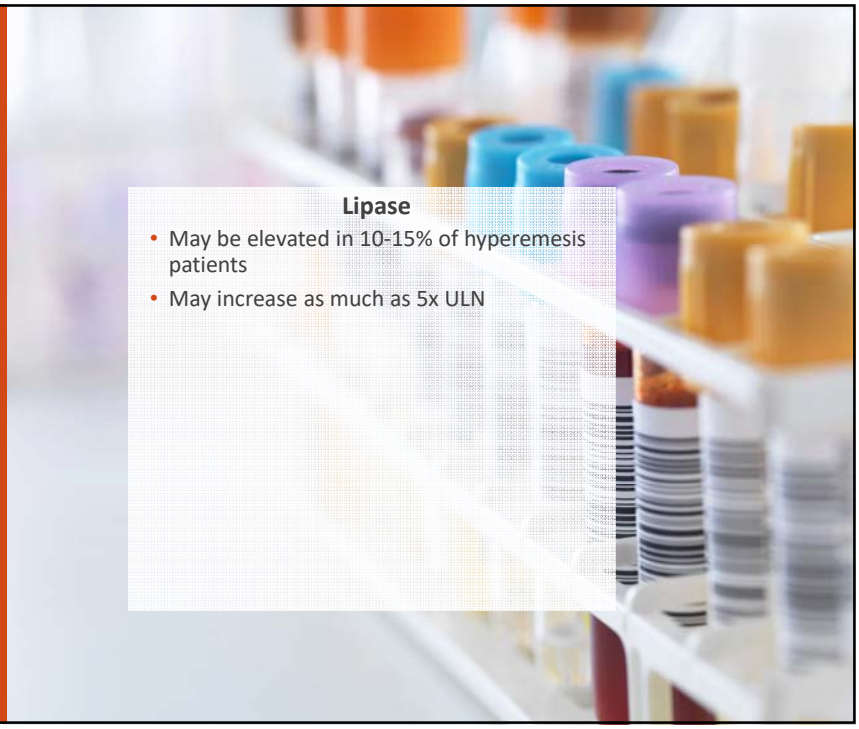


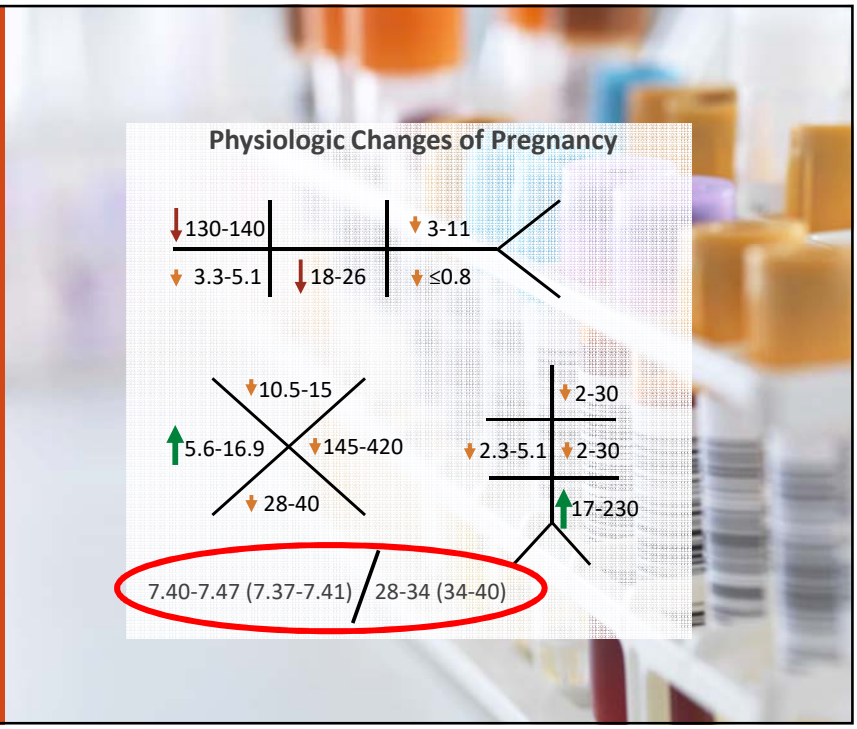
Lipase

- May be elevated in 10-15% of hyperemesis patients
- May increase as much as 5x ULN

Initial testing

VBG, lactate, beta hydroxybutyrate

- VBG if evidence of metabolic acidosis, to assess degree of acidemia
- If investigating a gap acidosis, consider lactate AND beta hydroxybutyrate
- Ketoacidosis occurs in absence of DM due to starvation ketosis (more common in 3rd trimester and if s/p RYGB)



Volume resuscitation with IVF without dextrose (as you would in a nonpregnant patient)

↓

Replete electrolytes IV (as you would in a nonpregnant patient)

↓

Give thiamine 100-200mg IV daily x 3 days or until tolerating PO

↓

Once volume status, electrolytes, and thiamine given, can switch to mIVF w/ 5% dextrose 125-150cc/h

↓

IV MVI + 0.6mg folic acid + B6 25mg daily

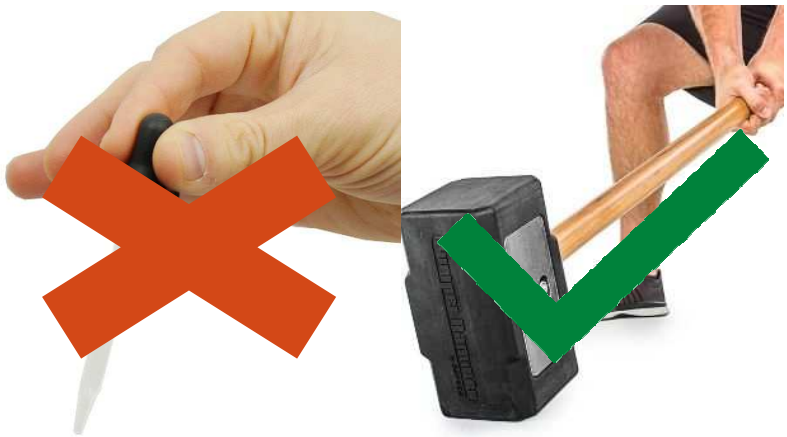
↓

Short period of gut rest (if helpful for patient), monitor for refeeding

Management – fluid and electrolytes

Jarvis S, Nelson-Piercy C. Management of nausea and vomiting in pregnancy. BMJ. 2011 Jun 17;342:d3606.
Tan P et al. Obstet Gynecol. 2013 Feb;121(2 Pt 1):291-298.

Management - pharmacologic



Lowest **EFFECTIVE** dose

Avoid exposure to subtherapeutic doses/regimens = fetal risk without maternal/fetal benefit

Management - pharmacologic

Antihistamine (H1 antagonist)

- **Diphenhydramine** 25mg IV or IM Q6 hours
- Dimenhydrinate 50mg IV Q4-6 hours

Dopamine antagonist

- **Metoclopramide** 5-10mg IV Q8h
- **Prochlorperazine** 5-10mg IV/IM Q6-8 hours OR 25mg PR Q12 hours
- Promethazine 12.5-25mg PR/IM Q4-6 hours
  - Mostly H1 antagonist, but also weak dopamine antagonist)
  - IV is route of last resort

Serotonin antagonist

- **Ondansetron** 4-8mg IV Q8h
- (Granisetron)

Adjunctive therapy

- Famotidine 20mg IV BID
- Pantoprazole 40mg IV daily
- Sucralfate

ACOG Practice Bulletin No. 189: Nausea And Vomiting Of Pregnancy. Obstet Gynecol. 2018 Jan;131(1):e15-e30.
Huybrechts KF, et al. JAMA. 2020 Jan 28;323(4):372-374.

Management – when all else fails

Corticosteroids

- **Be sure **alternative etiologies** for n/v have been **ruled out**
- Methylprednisolone 16mg IV Q8h for 48-72 hours
- Prednisone taper 40mg daily x 1-2 days, 20mg x 3 days, 10mg x 3 days, 5mg x 7 days

TPN/NGT

- Discuss with **nutrition** and **primary OBGYN**
- TPN confers high risk for venous thrombotic complications given prothrombotic nature of pregnancy, dehydration/hemoconcentration
- Hydration > nutrition in acute phase

McParlin C, et al. JAMA. 2016 Oct 4;316(13):1392-1401.
Cape AV, et al. JPEN J Parenter Enteral Nutr. 2014 Jul;38(5):595-601.

Management – when tolerating PO

- ***Slowly*** cross-titrate from standing IV to standing PO/PR **ONE** medication at a time
- Keep **PRN IV** antiemetics **available**
- Continue **standing PO + PRN IV** regimen until reliably eating without vomiting
- Add doxylamine 20mg QHS + pyridoxine 25mg Q8h
- Discharge on **standing PO + PRN PO regimen** for at least 1 week
- Wait for **at least 1 week of reliable PO intake** before transition to PRN PO antiemetics (or continue through 1st trimester)

Management – resuming a diet

- Get nutrition involved
- Consistent protein intake is key
- Avoid an empty stomach
- Small, frequent snacks
- Eat slowly
- Consume liquids and solids at least 30 minutes apart

Bischoff SC, Renzer C. Nausea and nutrition. Auton Neurosci. 2006 Oct 30;129(1-2):22-7
Newman V, et al. J Obstet Gynecol Neonatal Nurs. 1993 Nov-Dec;22(6):483-90.

Hyperemesis – key points

- Not all nausea/vomiting in pregnancy is due to pregnancy- have a differential for nausea/vomiting in a pregnant patient
- Prioritize volume resuscitation, electrolyte correction, and thiamine supplementation
- Treatment usually includes multiple IV/IM/PR antiemetics and SLOW transition to PO antiemetics
- Expect patients will need at least 1 week of standing PO antiemetics after discharge
- Involve nutrition early and often!
- Pregnant patients are at higher risk for starvation ketoacidosis

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Multisystem inflammatory disorder occurring *during pregnancy* or within *~6 weeks postpartum* characterized by:

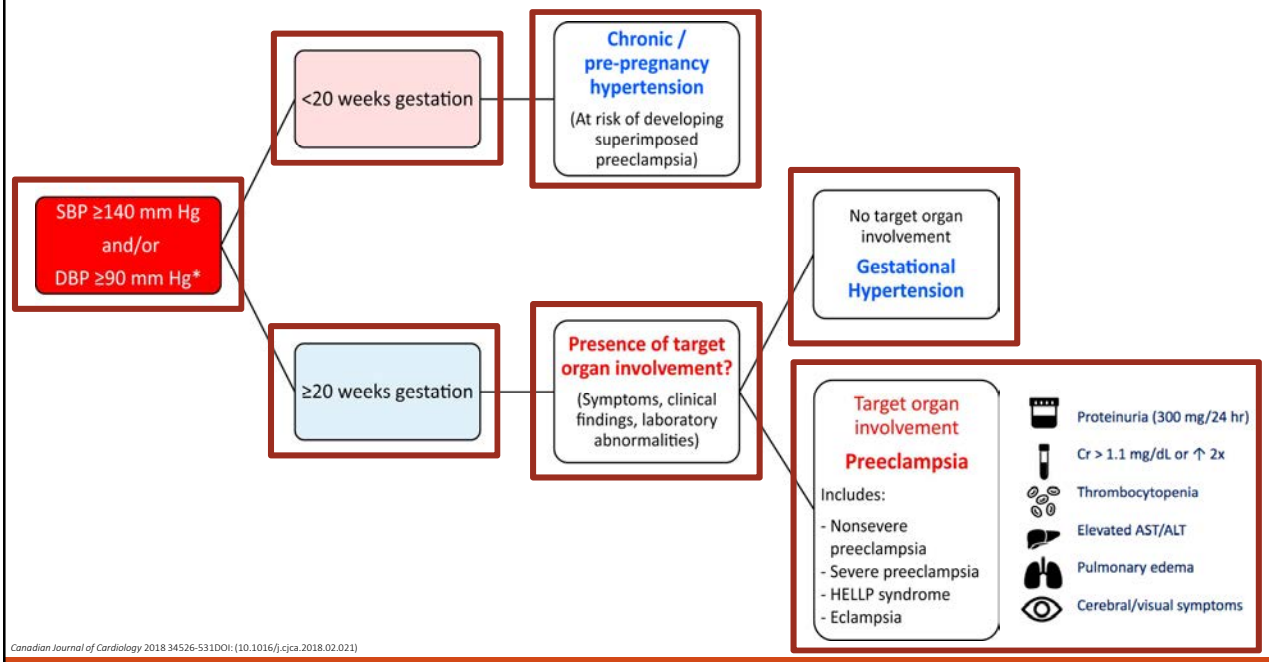
- Vasospasm
- Endothelial dysfunction
- Microthrombi

Can think of it like hypertensive emergency: easier to identify the systems preeclampsia can affect

BRAIN (HEADACHE, STROKE, EDEMA, SEIZURE, RCVS, PRES) | EYES (RETINAL HEMORRHAGE, MACULAR EDEMA) | HEART (HEART FAILURE, TROP LEAK) | LUNGS (EDEMA, PE) | LIVER (SUBCAPSULAR HEMATOMA/RUPTURE THROMBUS) | KIDNEYS (PROTEINURIA, AKI, ATN) | BABY (IUGR, ABRUPTION, OLIGOHYDRAMNIOS, IUFD)

Gestational Hypertension and Preeclampsia: ACOG Practice Bulletin, Number 222. Obstet Gynecol. 2020 Jun;135(6):e237-e260.

Preeclampsia



Canadian Journal of Cardiology 2018 34526-531DOI: (10.1016/j.cjca.2018.02.021)

Hypertensive disorder	Definition
Chronic hypertension	• SBP ≥140 or DBP ≥90 on ≥2 occasions ≥4 hours apart AND • Pre-pregnancy or <20 weeks
Gestational hypertension	• SBP ≥ 140 or DBP ≥ 90 on ≥2 occasions ≥4 hours apart at ≥20 weeks AND • Absence of proteinuria or end-organ dysfunction
Preeclampsia	• SBP ≥140 or DBP ≥90 on ≥2 occasions ≥4 hours apart AND (1 or 2) 1. Proteinuria +/- end-organ dysfunction OR 2. Signs/symptoms of end-organ dysfunction w/o proteinuria
Chronic hypertension with superimposed preeclampsia	• Preeclampsia in a patient with chronic hypertension (as defined above)

Preeclampsia with severe features	• SBP ≥ 160 or DBP ≥ 110 (confirmed w/in a short interval to facilitate timely therapy) in patient with preeclampsia (as defined above), OR
	• Preeclampsia (as defined above), AND more severe end-organ dysfunction:
	  • Thrombocytopenia (**plt <100,000**) OR
	  • Impaired liver function (**AST or ALT > 2x ULN**) not accounted for by alt dx, or severe persistent **RUQ/epigastric pain** unresponsive to medications OR
	  • Renal insufficiency (**Cr > 1.1 or 2x pt's normal Cr**) OR
	  • **Pulmonary edema** OR
	  • New-onset **headache** unresponsive to medication and not accounted for by alt dx OR
	  • **Visual disturbances**

Imitators of Severe Preeclampsia

- HELLP
- AFLP
- Secondary hypertension
- TTP
- aHUS
- SLE flare
- Catastrophic APLS
- HSV hepatitis
- Arboviral disease
- Drug use

Morton, A. Pregnancy Hypertension. 6(1):2016, pp. 1–9.

Feature	Preeclampsia	HELLP	AFLP	aHUS	TTP	CAPS	SLE
Hypertension	+++	+++	+	++	+	+/–	++
Proteinuria	+++	++	+/–	+++	+/–	+	+++
Nausea/vomiting	+	+	++	+/–	+/–	+/–	+/–
Abdominal pain	+/–	++	++	+/–	+/–	+/–	+/–
Jaundice	+/–	+/–	++	+/–	+/–	+/–	+/–
Neurologic symptoms	+	+	+	+/–	++	++	+
Thrombocytopenia	+	+++	+	+++	+++	+	+
Hemolysis	+/–	+++	+	+++	+++	+/–	+
Raised bilirubin	+/–	+++	+++	+++	+++	+/–	+/–
Renal impairment	+/–	+	++	+++	+	++	++
DIC	+/–	++	+++	+/–	+/–	+/–	+/–
Hypoglycemia	+/–	+/–	+++	+/–	+/–	+/–	+/–
Elevated ammonia	+/–	+/–	+	+/–	+/–	+/–	+/–
Elevated transaminases	+	+++	+++	+/–	+/–	+/–	+
Peak time of onset	Third trimester	Third trimester	Third trimester	Postpartum	Second or third trimester	Anytime	Anytime

Gernsheimer, Terry, et al. "How I Treat Thrombocytopenia in Pregnancy." Blood, vol. 121, no. 1, 2013, pp. 38–47, https://doi.org/10.1182/blood-2012-08-448944.

Hemolysis with Elevated Liver Enzymes and Low Platelets (HELLP)

ACOG acknowledges absence of clinical consensus among experts and suggests:

- LDH ≥600 AND
- AST and ALT ≥2x ULN AND
- Thrombocytopenia <100,000

Others use the **Tennessee Classification**:

- Hemolysis, established by at least two of the following:
  - Peripheral smear with schistocytes / burr cells
  - Serum bilirubin ≥1.2 mg/dL
  - Low serum haptoglobin (≤25 mg/dL) OR lactate dehydrogenase (LDH) ≥2x ULN
  - Severe anemia, unrelated to blood loss (hgb <8 to 10)
    **more useful to look for significant drop in hgb
- Elevated liver enzymes:
  - AST OR ALT ≥2x ULN
  - Thrombocytopenia <100,000

Gestational Hypertension and Preeclampsia: ACOG Practice Bulletin, Number 222. Obstet Gynecol. 2020 Jun;135(6):e237-e260.
Ditisheim A, Sibai BM. Clin Obstet Gynecol. 2017 Mar;60(1):190-197

Acute Fatty Liver of Pregnancy (AFLP)

Don't let the name confuse you – this is essentially pregnancy-induced **acute liver failure**

Swansea criteria for diagnosis (# criteria needed has varied from 6-9 in research studies)

Signs and symptoms

- Vomiting
- **Abdominal pain**
- Polydipsia/polyuria
- **Encephalopathy**

Laboratory findings

- Elevated bilirubin (>0.8 mg/dL)
- **Hypoglycemia** (glucose <72 mg/dL)
- Leukocytosis (>11,000 cells/microL)
- Elevated transaminases (AST or ALT) (usually **5-10x ULN**)
- Elevated **ammonia** (>47 micromol/L)
- Elevated uric acid (5.7 mg/dL)
- Acute kidney injury, or creatinine >1.7 mg/dL (150 micromol/L)
- **Coagulopathy** or prothrombin time >14 seconds

Imaging: Ascites or hyperechoic (bright) liver on ultrasound scan

Histology: Microvesicular steatosis on liver biopsy

Initial diagnostics

CMP

CBC

Urine protein:Cr ratio

--

RUQUS

CXR

Head imaging

Peripheral smear

Initial diagnostics

CMP

CBC

Urine protein:Cr ratio

--

RUQUS

CXR

Head imaging

Peripheral smear

CMP

- Creatinine generally decreases in pregnancy, threshold for preeclampsia is:
  - > 1.1 or
  - 2x patient's baseline
- Diagnostic threshold for preeclampsia is AST or ALT >2x ULN
  - Remember ULN AST and ALT in young, healthy women is ~20-30

Initial diagnostics

CMP

CBC

Urine protein:Cr ratio

--

RUQUS

CXR

Head imaging

Peripheral smear

CBC

- Hemoconcentration
  - 3rd spacing from increased hydrostatic pressure
  - decreased oncotic pressure due to albuminuria
- Thrombocytopenia
  - increased consumption, platelet aggregation, microthrombi formation
  - Diagnostic threshold for thrombocytopenia in preeclampsia is **<100K**

Initial diagnostics

CMP

CBC

Urine protein:Cr ratio

--

RUQUS

CXR

Head imaging

Peripheral smear

Urine protein:Cr ratio

- There is physiologic increase in proteinuria in pregnancy
- Diagnostic threshold for preeclampsia is UPC ≥ 0.3 ie 300mg/day

Initial diagnostics

CMP

CBC

Urine protein:Cr ratio

--

RUQUS

CXR

Head imaging

Peripheral smear

RUQUS

- If intractable RUQ pain, assess for:
  - subcapsular hematoma
  - hepatic or portal venous thrombosis
  - bright liver/ascites
- May also use to rule out other pathologies for elevated LFTs

Initial diagnostics

CMP

CBC

Urine protein:Cr ratio

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RUQUS

CXR

Head imaging

Peripheral smear

CXR

- To assess for pulmonary edema if any respiratory symptoms or findings on exam
- If there is pulmonary edema, consider echo as preeclampsia is risk factor for peripartum cardiomyopathy

Initial diagnostics

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CBC

Urine protein:Cr ratio

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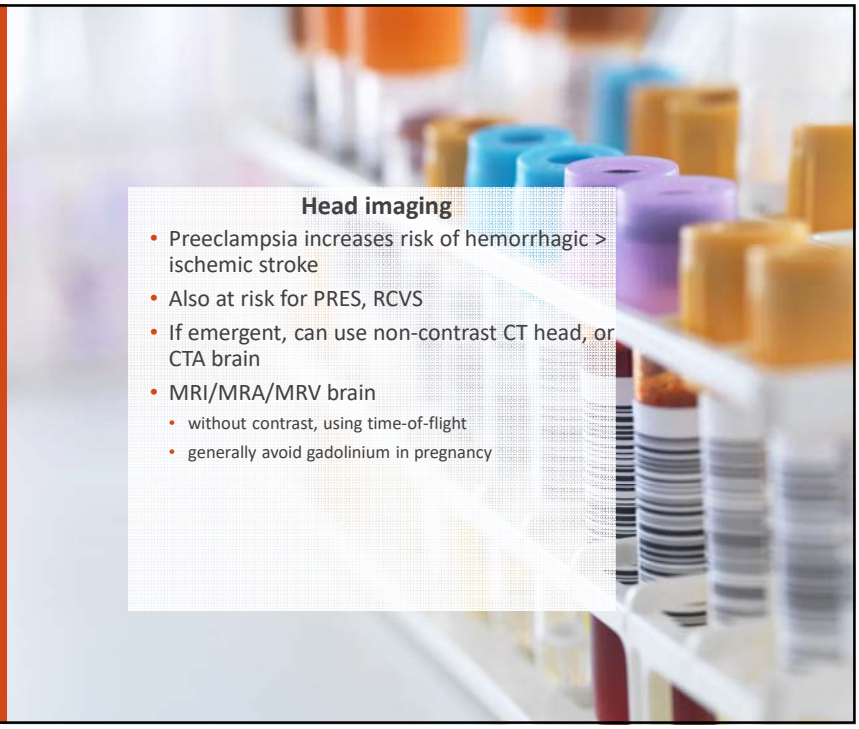
RUQUS

CXR

Head imaging

Peripheral smear



Head imaging

- Preeclampsia increases risk of hemorrhagic > ischemic stroke
- Also at risk for PRES, RCVS
- If emergent, can use non-contrast CT head, or CTA brain
- MRI/MRA/MRV brain
  - without contrast, using time-of-flight
  - generally avoid gadolinium in pregnancy

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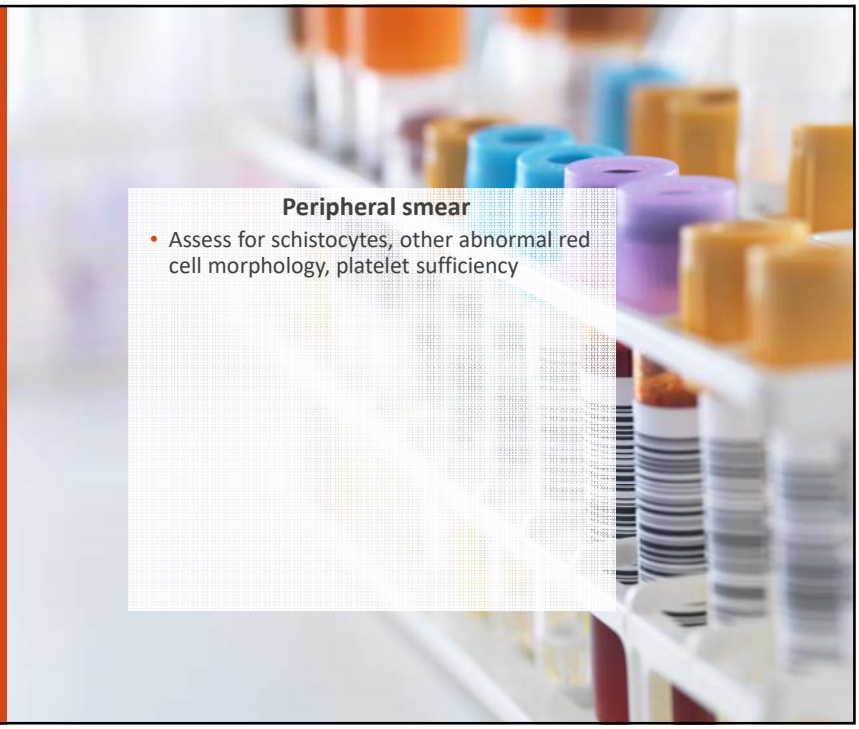
Peripheral smear



Maternal Complications of Preeclampsia

- Seizure
- Hemorrhagic or ischemic stroke
- PRES, RCVS
- Retinal edema
- Pulmonary Edema
- DIC
- Acute renal failure
- HELLP
- AFLP
- Hepatic infarct, rupture, hemorrhage
- Diabetes insipidus

Management in preeclampsia

Delivery (indication, timing, mode)

Blood pressure control

Seizure prophylaxis/treatment

Evaluation, monitoring, and treatment of complications

Severe Hypertension (≥160/110) Management = EMERGENCY

Antihypertensives

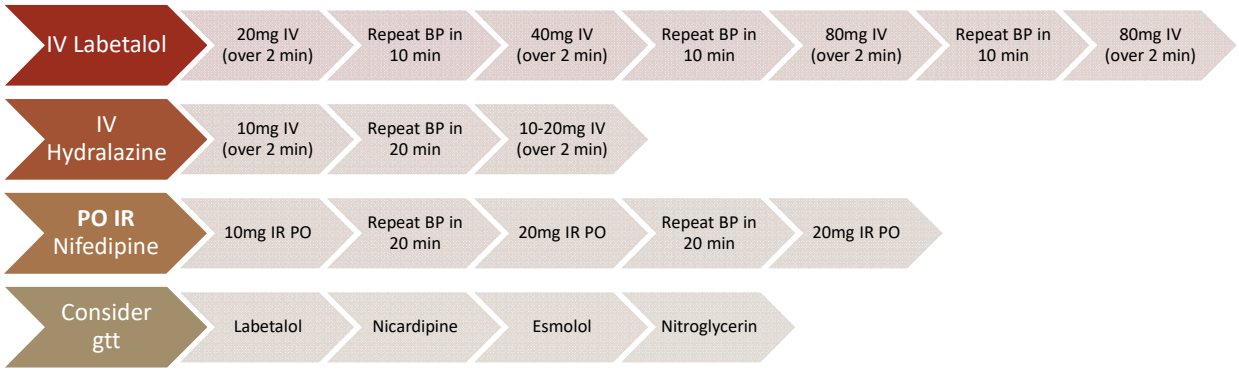
- IV labetalol
- IV hydralazine
- PO IR nifedipine (if no IV)

Magnesium sulfate

- Not recommended as antihypertensive agent
- **Should be used for**: seizure prophylaxis and **controlling seizures in eclampsia**
  - IV bolus of 4-6g in 100mL over 20 minutes, then IV infusion of 1-2g/h (continued for 24h postpartum)
  - If no IV access, 10g of 50% solution IM (5g in each buttock)
  - If no magnesium, benzos can be used
  - Contraindications: pulmonary edema, renal failure, myasthenia gravis
- *Historical* concern of low BP with magnesium + nifedipine **BUT** has **NOT** borne out in trials

Gestational Hypertension and Preeclampsia. Obstetrics & Gynecology. 2020; 135 (6): e237-e260. .

Severe Hypertension (≥160/110) Management Algorithm



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Oral Antihypertensives

Once BP non-severe (<160/110), begin oral therapies

- I tend to think of it like afib w/RVR
- Just be careful of stacking, keeping in mind total IV and IR PO medications received and respective time to peak/half-lives

Goal BP *(controversial)*

- If still pregnant = initial: 130-150/80-100 → subsequent: 130-140/80-90
- If postpartum = 110-140/70-90

Oral antihypertensives

- Often more frequent dosing (BID for nifedipine, TID for labetalol) is helpful given increased hepatic and renal clearance in pregnancy and postpartum
- Nifedipine 30mg XR daily or BID → can uptitrate to total 120mg/day
- Labetalol 200mg BID or TID → can uptitrate to total of 2400mg/day **often diminishing returns beyond 1200mg/day*
- Captopril or enalapril **if postpartum (okay in breastfeeding)*
- Hydralazine or second line agents (ie thiazide diuretics) **if still pregnant and maxed on nifedipine + labetalol*

Gestational Hypertension and Preeclampsia. Obstetrics & Gynecology. 2020; 135 (6): e237-e260. .

Preeclampsia – key points

- Preeclampsia is a multisystem inflammatory disorder that affects pregnant and postpartum patients
- Not all new hypertension in pregnancy is preeclampsia
- Severe hypertension (≥160/110) needs to be treated emergently with fast-acting antihypertensives
- Generally, IV antihypertensives need to be followed by long-acting oral antihypertensives
- Magnesium is for seizure prophylaxis/treatment, not for blood pressure control
- Pregnancy-related hypertension can persist for up to 12 weeks postpartum

Topics to be covered

- Hyperemesis gravidarum
- Hypertensive disorders of pregnancy
- Pyelonephritis
- Pulmonary embolism
- Procedures during pregnancy
- Diabetes

Topics to be covered

- Hyperemesis gravidarum
- Hypertensive disorders of pregnancy
- **Pyelonephritis**
- Pulmonary embolism
- Procedures during pregnancy
- Diabetes

Pyelonephritis in Pregnancy

- Incidence estimated 0.5-2% pregnancies; higher than in general population
- Most cases occur in 2nd and 3rd trimesters
- Often **not** preceded by recognized symptoms of cystitis
- General presentation: fever, nausea/vomiting, flank pain/CVA tenderness
- Similar organisms to nonpregnant women: E coli, Klebsiella, Enterobacter, Proteus, GBS
- 20% have co-existing structural disease (ie obstruction)

Gilstrap LC 3rd, Ramin SM. Obstet Gynecol Clin North Am. 2001 Sep;28(3):581-91.
Hill JB, et al.. Obstet Gynecol. 2005 Jan;105(1):18-23.
Frise, Charlotte; Collins, Sally. Obstetric Medicine. Oxford University Press. 2020. 1(193).

Pyelonephritis - Differential

Nephrolithiasis	Intraamniotic infection	Placental abruption	Appendicitis
Pancreatitis	Biliary tract disease	MSK back pain + bacteriuria	NVP + bacteriuria

Initial diagnostics

UA, Ucx

Blood cxs

CMP

CBC w/diff

--

Lactic acid

Renal US

CXR

Initial diagnostics

UA, Ucx

Blood cxs

CMP

CBC w/diff

--

Lactic acid

Renal US

CXR

UA, Ucx

- Remember we treat asymptomatic bacteriuria in pregnancy because of the risk of pyelo

Initial diagnostics

UA, Ucx

Blood cxs

CMP

CBC w/diff

--

Lactic acid

Renal US

CXR

Lactic acid

- No change in normal range in pregnancy, except during labor when ULN is 4 mmol/L

Initial diagnostics

UA, Ucx

Blood cxs

CMP

CBC w/diff

--

Lactic acid

Renal US

CXR

Renal US

- Generally, obtain if:
  - Inappropriate clinical response to antibiotics
  - Severe illness/urosepsis
  - Renal colic, hx nephrolithiasis, DM, hx GU surgery, immunosuppression, pyelo recurrence
- Look for perinephric abscess, obstruction
- *Remember, there is physiologic hydronephrosis in pregnancy, often R>L, so need to ask the US tech/radiologist look for **ureteral jets** bilaterally

Pyelonephritis - Management

Site of care

- Hospitalization with IV antibiotics
- Until 48h afebrile + symptomatically improved

Empiric antibiotics

- Broad spectrum beta-lactams
  - ceftriaxone, piperacillin-tazobactam, cefepime
  - amp/gent (less preferred 2/2 risk fetal ototoxicity w/aminoglycosides)
  - carbapenem if prior ESBL: - mero- or ertapenem (imipenem generally avoided given animal data)
- If beta-lactam allergy: aztreonam
- Choose based on local antibiogram + patient's prior culture data

Antimicrobial therapy for obstetric patients. ACOG educational bulletin 245. 1998; Washington, DC.
Wing DA, et al. Obstet Gynecol. 1998 Aug;92(2):249-53..

Pyelonephritis - Management

Tailored antibiotic therapy

- Once afebrile x48h, can switch to PO therapy to complete 10-14 day course
  - Beta-lactams based on culture data
  - Bactrim if in the 2nd trimester
- Need **test of cure** at end of treatment

Recurrence

- Recurrence reported in 6-25% of pregnancies
- Low-dose **antimicrobial therapy** generally used for **rest of pregnancy and 4-6 weeks postpartum** to prevent recurrence
  - Macrobid 100mg PO nightly
  - Cephalexin 250-500mg PO nightly

But she is still febrile…

Antibiotic failure is not particularly common (2.2% of inpatients) given lower rates of resistant organisms in pregnant patients

Pyelonephritis is **extremely inflammatory** in pregnancy

Often **takes true 48-72h** of appropriate antibiotic therapy for significant improvement (75-95% will be afebrile x 24h within 48-72h)

Still, **up to 20%** of patients may develop **complications**

Hill JB, et al. Obstet Gynecol. 2005 Jan;105(1):18-23.
Cunningham FG, Lucas MJ. Baillieres Clin Obstet Gynaecol. 1994 Jun;8(2):353-73.

Pyelonephritis – Complications

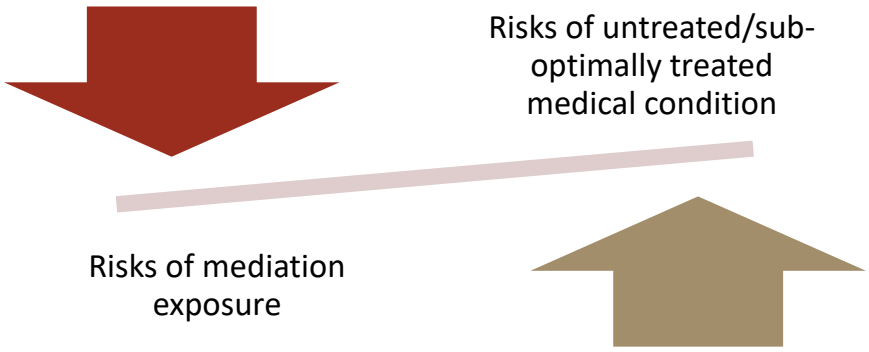
Perinephric or renal abscess	Obstructing stone	Respiratory insufficiency / pulmonary edema	Sepsis and septic shock	Obstetric risks
• Assess with renal US • Discuss with urology/IR re: percutaneous drainage	• Assess with renal US • May need retrieval by urology vs percutaneous nephrostomy tube • No extracorporeal lithotripsy, intra-ureteral okay in pregnancy	• Up to 7% w/ARDS • Caution with volume resuscitation • Often responds to small dose of diuretics	• Treat as you would sepsis / septic shock in nonpregnant patients • 30 cc/kg volume resuscitation • If no longer volume responsive, start norepinephrine	• Preterm labor • Low birth weight • Intrauterine fetal demise • NICU admission • Management per OB

Hill JB, et al. Obstet Gynecol. 2005 Jan;105(1):18-23.
Cunningham FG, et al. Am J Obstet Gynecol. 1987 Apr;156(4):797-807.
Towers CV, et al. Am J Obstet Gynecol. 1991 Apr;164(4):974-8

Use justifiable when indicated	Use may be justifiable in unique circumstances	Rarely justifiable
• Penicillins (w/ or w/o beta-lactamase inhibitors) • Cephalosporins • Nitrofurantoin (use alternative options if available in 1st trimester) • Clindamycin • Certain macrolides (azithromycin, erythromycin) • Metronidazole (avoid in 1st trimester) • Carbapenems (mero-, erta-) • Vancomycin • Aztreonam	• Aminoglycosides (human experience limited; theoretical concern for nephrotoxicity / ototoxicity but not born out clinically) • Trimethoprim (folate antagonist, avoid in 1st trimester) • Sulfamethoxazole (may displace bilirubin, caution in 3rd trimester) • Certain macrolides (clarithromycin)	• Tetracyclines (bone growth inhibition, teeth staining) • Fluoroquinolones (toxic to developing cartilage in animal models) • Imipenem

Bookstaver PB, et al. Pharmacotherapy. 2015 Nov;35(11):1052-62.

General antibiotic guidance



Clinicians and patients must weigh risks and avoid a false "safe vs not safe" dichotomy

Old FDA letter "grading" system is **OUT**

Risk narratives and risk/benefit discussion are **IN**

Roca C, US Food and Drug Administration. An evolution of labeling information for pregnant women: PLLR history and background. March 5, 2018.

Drug safety in pregnancy

Information sources for providers

FDA Drug Labels
https://labels.fda.gov/

FDA Pregnancy Registry Listing
www.fda.gov/ScienceResearch/SpecialTopics/WomensHealthResearch/ucm251314.htm

Briggs Drugs in Pregnancy and Lactation

TERIS (Teratogen Information System)
https://deohs.washington.edu/teris/

ReproTox
https://reprotox.org/

LactMed
https://www.ncbi.nlm.nih.gov/books/NBK501922/

Pyelonephritis – key points

- Pyelo is more common among pregnant patients than the general population
- Pyelo in pregnancy is often **not** preceded by typical cystitis symptoms
- Broad spectrum beta lactams are appropriate empiric treatment, choose by local antibiogram and prior cultures
- Treatment of sepsis in pregnancy is the same as in nonpregnant patients
- Pyelo in pregnancy is INFLAMMATORY, complications are common including respiratory failure
- Maintain a low threshold to get renal US to look for obstruction or perinephric abscess

Topics to be covered

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Pulmonary Embolism in Pregnancy

- Accounts for 10–15% of pregnancy-associated mortality in high-income countries
- Affects 0.45-2 per 1000 pregnancies (4x nonpregnant population) – more common postpartum
- Presentation of PE in pregnancy is often more subtle
- Signs/symptoms of physiologic changes of pregnancy overlap with those of PE (tachycardia, lower extremity edema, dyspnea)
- Left leg predominance for DVT

Chang J, et al. Pregnancy-related mortality surveillance--United States, 1991--1999. MMWR Surveill Summ. 2003 Feb 21;52(2):1-8.
Elgendy IY, et al. Mayo Clin Proc. 2021 Aug;96(8):2102-2113.
James AH, et al. Am J Obstet Gynecol. 2006 May;194(5):1311-5.
Morris JM, et al.. J Thromb Haemost. 2010 May;8(5):998-1003.
Marik PE, Plante LA. N Engl J Med. 2008 Nov 6;359(19):2025-33.

Similar symptoms to nonpregnant patients

54% dyspnea at rest

52% pleuritic chest pain

9% cough

7% hemoptysis

Goodacre S, et al. The DiPEP study. BJOG. 2019 Feb;126(3):383-392.

Clinical pr[illegible] probability

D-dimer testing

Imaging studies

Diagnosis of PE in n[illegible]-pregnant patients

Diagnostics

Pulse oximetry

ABG

EKG

CXR

D-dimer

LE US

VQ scan/CTPA

Diagnostics

Pulse oximetry

ABG

EKG

CXR

D-dimer

LE US

VQ scan/CTPA

Pulse oximetry

- Not sensitive or specific
- Can get ambulatory O2 sats as well
- Concern if SpO2 falls while walking or if <95% (though newer studies suggest concern if <94%)

Diagnostics

Pulse oximetry

ABG

EKG

CXR

D-dimer

LE US

VQ scan/CTPA

ABG

- ABG is neither sensitive nor specific
- Respiratory alkalosis is a very common feature of both pregnancy and PE

Diagnostics

Pulse oximetry

ABG

EKG

CXR

D-dimer

LE US

VQ scan/CTPA

EKG

- Not sensitive or specific
- Look for RH strain
- Tachycardia is common in normal pregnancy up to 110

Diagnostics

Pulse oximetry

ABG

EKG

CXR

D-dimer

LE US

VQ scan/CTPA

CXR

- May be helpful if obvious other parenchymal abnormality
- May also be helpful if you plan to get V/Q scan
- Otherwise not sensitive or specific

Diagnostics

Pulse oximetry

ABG

EKG

CXR

D-dimer

LE US

VQ scan/CTPA

D-dimer

- Rises over the course of normal pregnancy
- No established "normal ranges" in pregnancy
  - 1st: 167-721ng/mL
  - 2nd: 298-1653ng/mL
  - 3rd: 83-2256ng/mL

Diagnostics

Pulse oximetry

ABG

EKG

CXR

D-dimer

LE US

VQ scan/CTPA

LE US

- If signs/symptoms concerning for LE VTE
- Absence does not mean much, VTE at/above common femoral vein is more common in pregnancy

Diagnostics

Pulse oximetry

ABG

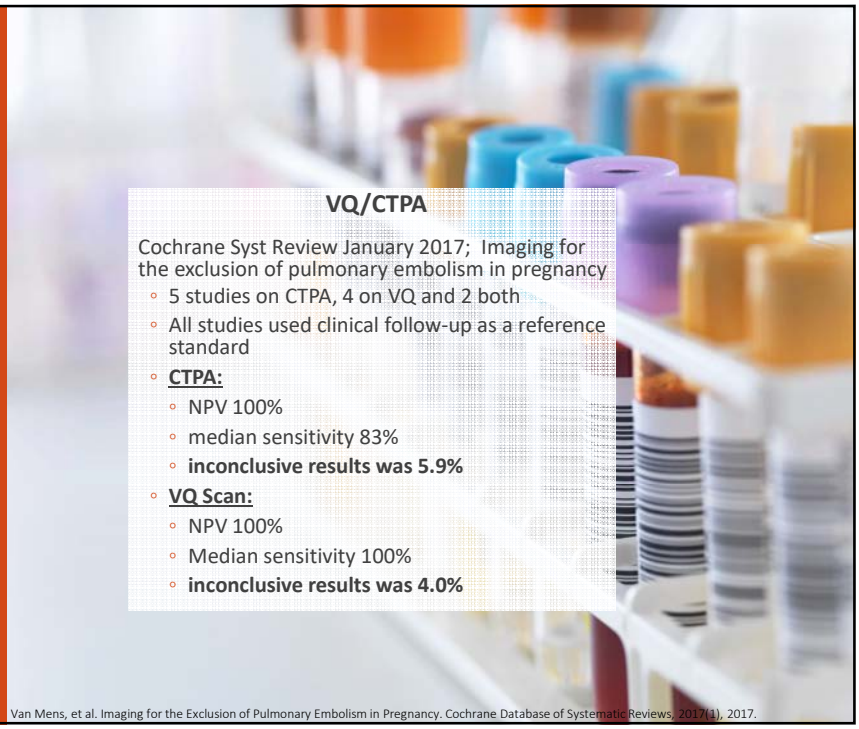
EKG

CXR

D-dimer

LE US

VQ scan/CTPA



VQ/CTPA

Cochrane Syst Review January 2017; Imaging for the exclusion of pulmonary embolism in pregnancy

- 5 studies on CTPA, 4 on VQ and 2 both
- All studies used clinical follow-up as a reference standard
- **CTPA:**
  - NPV 100%
  - median sensitivity 83%
  - **inconclusive results was 5.9%**
- **VQ Scan:**
  - NPV 100%
  - Median sensitivity 100%
  - **inconclusive results was 4.0%**

Van Mens, et al. Imaging for the Exclusion of Pulmonary Embolism in Pregnancy. Cochrane Database of Systematic Reviews, 2017(1), 2017.

Diagnostics

Pulse oximetry

ABG

EKG

CXR

D-dimer

LE US

VQ scan/CTPA

CTPA

- Advantages
  - May offer an alternative diagnosis (13% cases)
  - Fetal radiation exposure lower than V/Q
  - Better availability than V/Q
- Disadvantages:
  - Reduced vascular enhancement related to increased plasma volume, increased cardiac output and heart rate
- Be sure to note pregnant status and gestational age to appropriately protocol
  - Bolus timing/rate
  - Contrast dose

Radiation

Radiation in very high doses can lead to:

- Miscarriage
- Growth restriction
- Small head size
- Lower intellect
- Increased risk of childhood cancers

US National Council on Radiation Protection

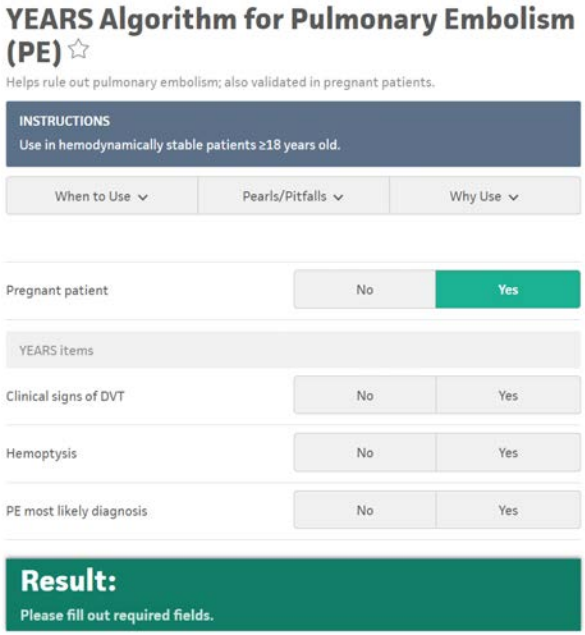
- No evidence of adverse effects from exposures <5 rads (50 mGy)
- Almost all commonly used diagnostic imaging involves fetal radiation exposure <<1 rad (10 mGy)
  - CTA chest 0.01-0.51 mGy
  - VQ scan 0.2-0.7 mGy
  - CXR (2 views) 0.0005-0.01 mGy
  - CT Abdomen 1.3-35 mGy
  - Head/neck CT 0.001-0.01 mGy

"natural" background radiation exposure to fetus is **~1mGy**

Tremblay, E et al. Radiographics, 32(3); 2012, pp. 897–911.

Pregnancy-Adapted YEARS algorithm

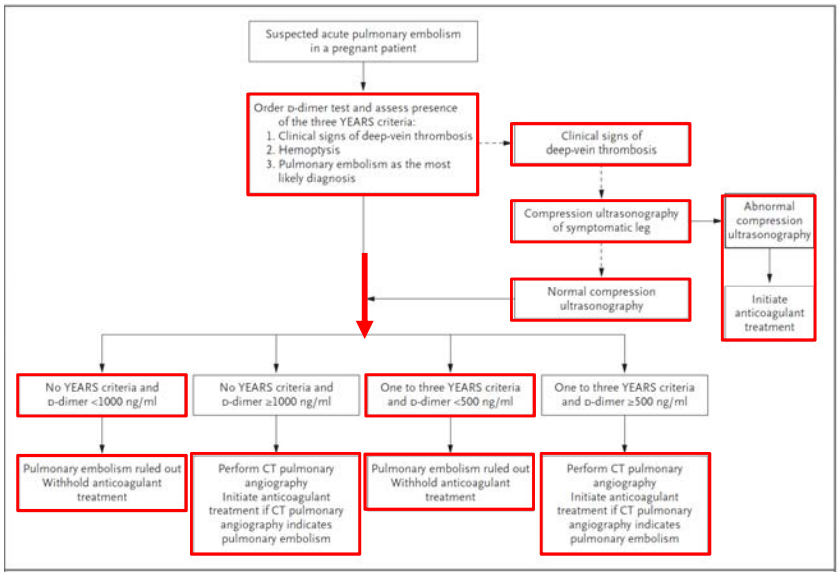
- Prospective study
- 498 **pregnant** women with suspected PE in ED or OB triage
- Suspected PE was defined by new onset or worsening of chest pain or dyspnea, with or without hemoptysis or tachycardia
- Used adapted YEARS algorithm + D-dimer to exclude PE
- If PE could not be excluded, underwent CTA
- Primary outcome: number of VTE events during 3-month follow-up
- Secondary outcome: number of required CTA examinations



Van der Pol et al. NEJM, 2019; *380*(12), 1139–1149.

Pregnancy-Adapted YEARS algorithm

- PE is considered excluded if:
  - Zero YEARS criteria + D-Dimer <1,000 ng/mL
  - ≥1 YEARS items and D-dimer <500 ng/mL
- All other patients will be referred for CTPA



Van der Pol et al. NEJM, 2019; *380*(12), 1139–1149.

PE was diagnosed in 4% of patients

CTA was avoided in 39% of all patients

- One patient not initially diagnosed with VTE was diagnosed with DVT during the 3-month follow-up
- No patients were diagnosed with subsequent PE during follow-up

The efficiency of the algorithm was **highest in the 1st trimester**, lowest in the 3rd – CTA was avoided in:

- 65% of patients in the first trimester
- 46% in the second trimester
- 32% in the third trimester

Van der Pol et al. NEJM, 2019: *380*(12), 1139–1149.

Pregnancy-Adapted YEARS algorithm

Pulmonary Embolism – Management

LMWH

- 1mg/kg Q12h
- 1.5mg/kg daily also endorsed by 2018 ASH guidelines

Unfractionated heparin

- Less preferred: difficult dosing, worse safety profile, lower efficacy
- Used if GFR <30
- Reasonable initial dose 17,500 U Q12, titrate to aPTT/anti-Xa

Duration and intensity are not well established in pregnant populations

- Some recommendations allow step down to intermediate intensity or prophylactic dosing after 3-6 months of full-dose treatment – to be continued for at least 6 weeks postpartum
- Others recommend continuing 3-6 months of full-dose anticoagulation or until 6 weeks postpartum, whichever is **longer**

Planned induction recommended for patients on **therapeutic** anticoagulation

Direct oral thrombin and Xa inhibitors have **inadequate safety data** in pregnancy or breastfeeding to justify use

Coumadin is generally avoided in pregnancy (teratogen) but can be used in breastfeeding

Bates, S et al. ASH 2018 Guidelines for Management of VTE in the Context of Pregnancy. Blood Advances, vol. 2, no. 22, 2018, pp. 3317–59.
ACOG Practice Bulletin No. 196: Thromboembolism in Pregnancy. Obstetrics and Gynecology. 132(1), 2018, pp. e1–e17,
Bates SM, et al. 9th ed: Chest. 2012 Feb;141(2 Suppl):e691S-e736S

Pulmonary Embolism – Peripartum Management

Timing of clot in relation to labor	Plan for peri-partum therapy
<2 weeks	Consider retrievable IVC filter
2-4 weeks	IV heparin to be stopped 4-6 hours prior to anticipated delivery Restart IV heparin after delivery Consider retrievable IVC filter if HD significant PE
>1 month	Time anticoagulant offset prior to induction of labor or CS Restart anticoagulation following delivery with LMWH (dose and timing tailored to risk/benefit) https://med.stanford.edu/content/dam/sm/pain/documents/neuraxial-procedure-v2-3.26.19.pdf

Physiologic Changes in Coagulation in Pregnancy

Table 1. Changes in the Normal Functioning of the Coagulation System During Pregnancy

Coagulant Factors	Change in Pregnancy
Procoagulants	
Fibrinogen	Increased
Factor VII	Increased
Factor VIII	Increased
Factor X	Increased
Von Willebrand factor	Increased
Plasminogen activator inhibitor-1	Increased
Plasminogen activator inhibitor-2	Increased
Factor II	No change
Factor V	No change
Factor IX	No change
Anticoagulants	
Free Protein S	Decreased
Protein C	No change
Antithrombin	No change

Data from Bremme KA. Haemostatic changes in pregnancy. Best Pract Res Clin Haematol 2003;16:153–68 *and* Medcalf RL, Stasinopoulos SJ. The undecided serpin. The ins and outs of plasminogen activator inhibitor type 2. Febs J 2005;272:4858–67.

Pulmonary embolism – key points

- PE is more common in pregnancy/postpartum compared to general population
- PE remains a leading cause of maternal morbidity/mortality
- Signs/symptoms of PE have considerable overlap with physiologic changes in pregnancy
- Benefits of imaging often outweigh risks in pregnant patients with suspected PE
- There are emerging algorithms which allow incorporation of D-dimer testing for pregnant patients
- Low molecular weight heparin is first line treatment

Topics to be covered

- Hyperemesis gravidarum
- Hypertensive disorders of pregnancy
- Pyelonephritis
- Pulmonary embolism
- Procedures during pregnancy
- Diabetes

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- Hypertensive disorders of pregnancy
- Pyelonephritis
- Pulmonary embolism
- Procedures during pregnancy
- Diabetes

Procedures during pregnancy – key points

1. Pregnant patients should **never be denied/have delayed medically necessary surgery** regardless of trimester
2. **Elective** surgery should be postponed until after delivery
3. No currently used, standardly dosed anesthetics have demonstrated human teratogenicity
4. No human evidence that in utero anesthetic/sedative exposure affects fetal brain development
5. When considering non-obstetric surgery, the **primary OB care provider should be involved**
6. **Fetal monitoring** may help in maternal positioning and cardiorespiratory management, and delivery decision making
7. **Screen for VTE risk** and administer appropriate perioperative thromboprophylaxis

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Management of diabetes in pregnancy is different

- Inpatient management of diabetes in pregnancy should include **endocrine consultation**
- **Insulin resistance increases** over gestation, often week over week
- **Glycemic targets are MUCH tighter**:
  - fasting 70-90
  - 1h PP 110-140
  - 2h PP 100-120
- Measurement is different:
  - fasting
  - 1 or 2h PP
  - QHS
  - sometimes pre-meal (if mealtime insulin is based on this)
- **Insulin is first-line treatment**, metformin used selectively

ACOG Practice Bulletin No. 201: Pregestational Diabetes Mellitus. (2018). *Obstetrics and Gynecology (New York. 1953), 132*(6), e228–e248.

Pre-pregnancy T1DM and T2DM

DKA occurs in up to 3% of pregnant patients with pre-existing diabetes

- Mostly T1DM but can occur in T2DM (particularly those who are "ketosis prone")
- Occurs at lower glucose levels in pregnancy; 30% patients had BG <200 mg/dL
- Mostly 2nd and 3rd trimesters, but can happen in 1st
- Symptoms similar to nonpregnant patients
- Triggers similar to nonpregnant patients + a few pregnancy specific (steroids for fetus, tocolytics)
- Lab findings similar to nonpregnant patients (attn to hidden metabolic acidosis i/s/o respiratory alkalosis, hidden AG from low albumin)
- DKA is an obstetric emergency → fetal hypoxemia/acidosis + maternal morbidity, rarely mortality

ACOG Practice Bulletin No. 201: Pregestational Diabetes Mellitus. (2018). *Obstetrics and Gynecology (New York. 1953)*, *132*(6), e228–e248.

If **ON** insulin prior to pregnancy:

- Use 60-70% of PRE-PREGNANCY dose (1/2 as basal)
- Use 30-40% of most recent pregnancy dose (1/2 as basal)

If **NOT** on insulin prior to pregnancy:

- Generally do not need insulin postpartum
- Can resume metformin in lactation

Insulin requirements decrease RAPIDLY and SUBSTANTIALLY after delivery

ACOG Practice Bulletin No. 201: Pregestational Diabetes Mellitus. (2018). *Obstetrics and Gynecology (New York. 1953)*, *132*(6), e228–e248.

Diabetes – key points

- Endocrine consult is appropriate for pregnant patients admitted with pre-existing diabetes
- Treatment targets for blood sugars in pregnancy are much tighter
- Blood sugar monitoring in pregnancy is different than in nonpregnant patients
- DKA occurs in T1 and T2DM in pregnancy and at lower blood glucose levels
- DKA is an obstetric emergency
- Insulin requirements decrease rapidly and substantially after delivery

General Principles

1. Fetal well being depends on maternal well being
2. Uninvestigated symptoms → progression of untreated disease
3. Uncontrolled maternal disease → compromised fetal safety, growth and development
4. Generally, more harm in withholding treatment/diagnostic testing in pregnancy than using these
5. Think of medications, radiologic studies, and procedures as "justifiable vs not justifiable" rather than "safe vs not safe"

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