Pregnancy – What a Hospitalist Needs to Know

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Training

- Medical school at Harvard Medical School
- 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

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 in this talk.

General Principles

1. Fetal well being depends on maternal well being
2. Uninvestigated symptoms may lead to progression of untreated disease
3. Uncontrolled maternal disease may compromise fetal safety, growth and development
4. Generally, more harm is done by withholding treatment/diagnostic testing from pregnant patients than by pursuing it
5. Medications and radiologic studies, and procedures in pregnancy should be thought of as “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

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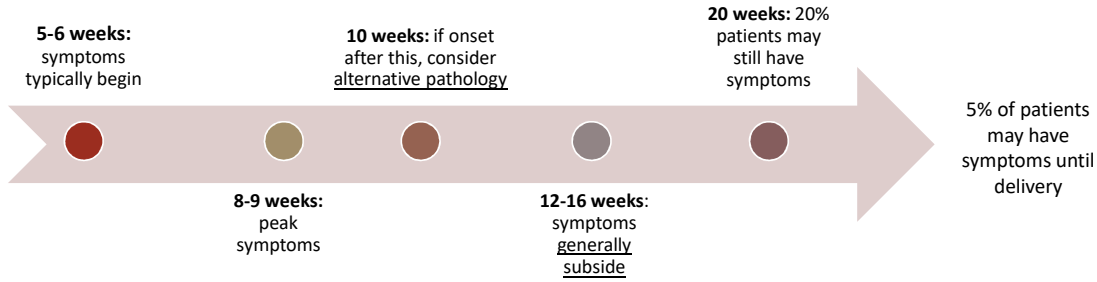
Nausea and Vomiting of Pregnancy

- Nausea with or without vomiting affects up to **90% of pregnancies**
- Nausea and vomiting of pregnancy (NVP): nausea/vomiting that appears to be **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..

Hematemesis

Epigastric pain

Significant weight loss

Atypical features / red flags

Hyperemesis gravidarum

•Hyperemesis gravidarum is considered the severe end of the nausea and vomiting spectrum

Less common, affects 0.3-3% of pregnancies

No single consensus definition, commonly:

- Weight loss (generally >5% body weight)
- Hypovolemia
  - **OR**
- Weight loss >3kg or 5% body weight
- Pregnancy-related vomiting occurring >3 times per day
- Ketonuria

Goodwin TM. Hyperemesis gravidarum. Obstet Gynecol Clin North Am. 2008 Sep;35(3):401-17, viii.

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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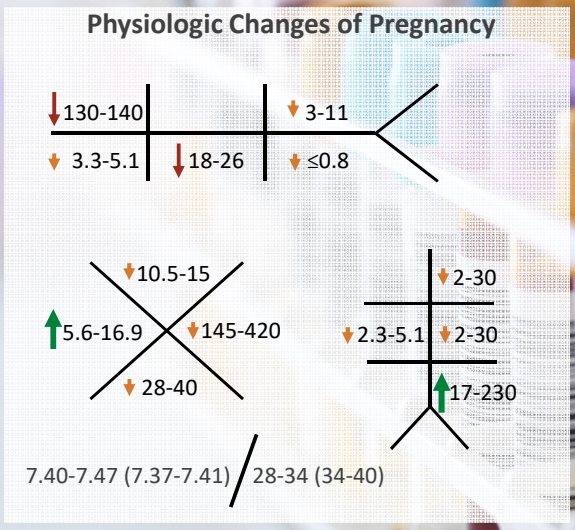
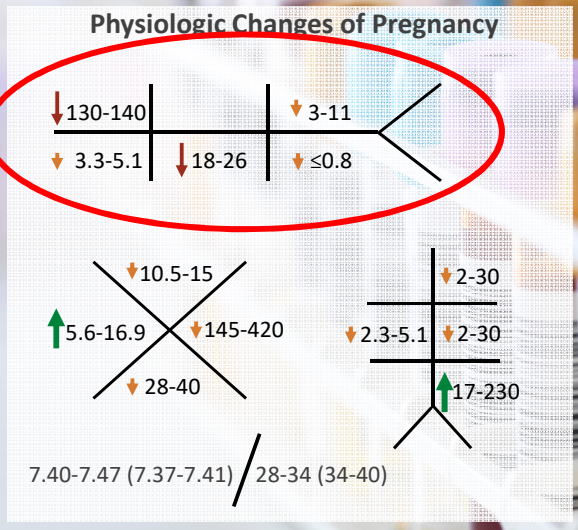


Initial testing

BMP, Mg, phos

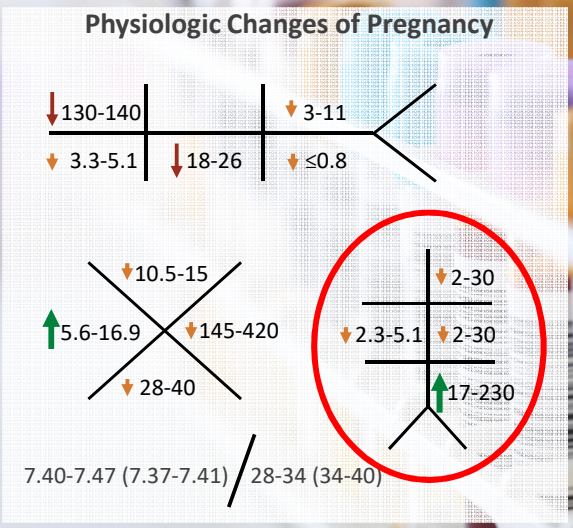
- Mostly attention to correcting deficiencies
- Stay attuned to inconsistencies in derangement (ie high-normal K, suggestive of alternative etiology ie Addison's)
- Assess anion gap *corrected for albumin*
- Often see hypochloremic metabolic alkalosis, check for concomitant metabolic acidosis (think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



Initial testing

LFTs

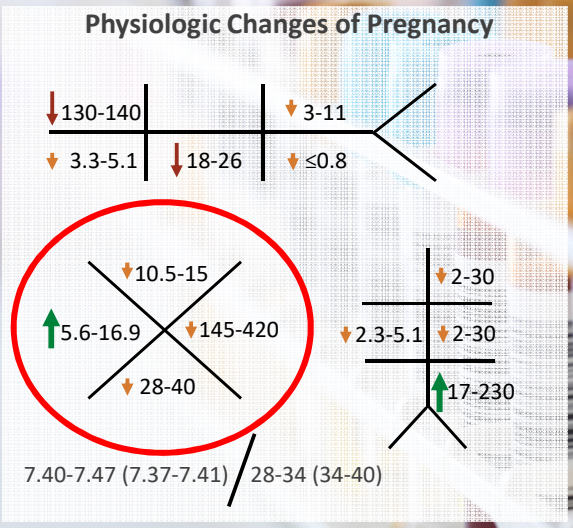
- Abnormal in up to 50% of patients hospitalized for hyperemesis
- ALT > AST
- Mild elevation 2-3x ULN, into low 100s
- Total bilirubin may be elevated (direct and indirect), rarely exceeds 4



Initial testing

CBC

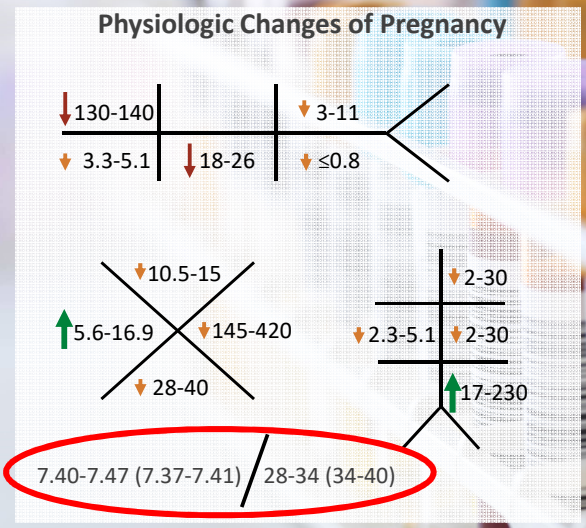
- Physiologic leukocytosis in pregnancy – usually normal diff or neutrophil predominant
- Lymphocyte count may be higher in hyperemesis
- Physiologic decrease in hgb and plt may mask hemoconcentration



Initial testing

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)



Initial testing

BMP, Mg, phos

LFTs

UA

CBC w/diff

TSH

Lipase

VBG, lactate, beta hydroxybutyrate

EKG

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

Initial testing

BMP, Mg, phos

LFTs

UA

CBC w/diff

TSH

Lipase

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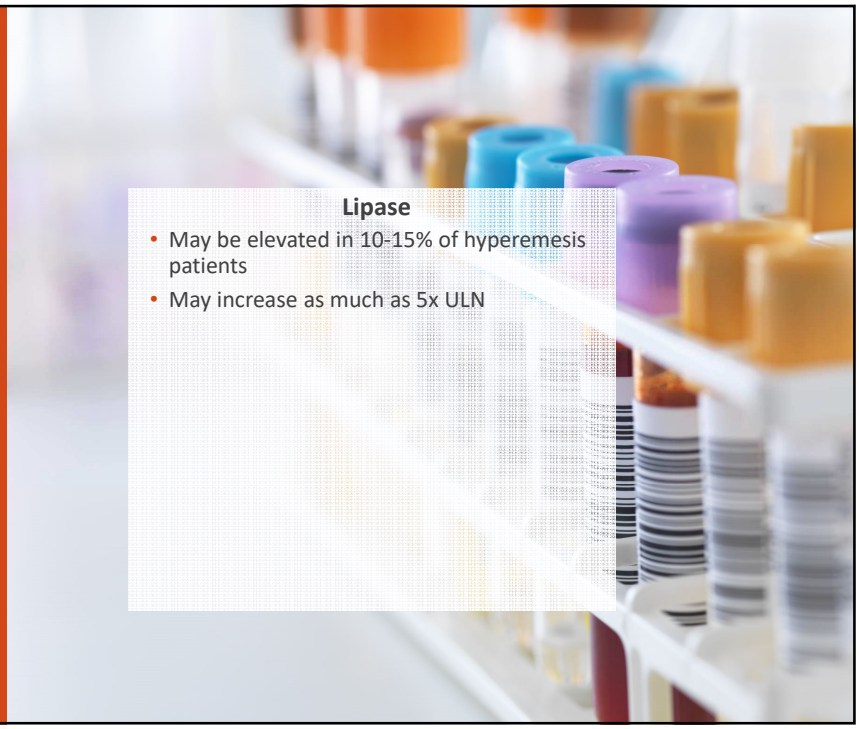

Lipase

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

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 100mg IV daily x 3 days

Once volume status, electrolytes, and thiamine replete, can switch to mIVF w/ 5% dextrose 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

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

Glucocorticoids

- **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 1 medication at a time (can also transition to PR medications)
- Keep PRN IV antiemetics available
- Continue standing PO regimen until patient is reliably eating without vomiting
- Add doxylamine 20mg QHS + pyridoxine 25mg Q8h
- Generally, patients will be discharged on a standing PO regimen + PRN POs for at least 1 week
- Transition to PRN PO antiemetics after 1 week of stability in tolerating PO intake

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

- Pregnant women can have medical problems - 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 women are at higher risk for starvation ketoacidosis

Topics to be covered

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- Pyelonephritis
- Pulmonary embolism
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- **Hypertensive disorders of pregnancy**
- Pyelonephritis
- Pulmonary embolism
- Tachycardia

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

- Vasospasm
- Endothelial dysfunction
- Microthrombi

Can be thought of like hypertensive emergency: this makes it 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

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, EITHER
	  • Proteinuria +/- end-organ dysfunction OR
	  • 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
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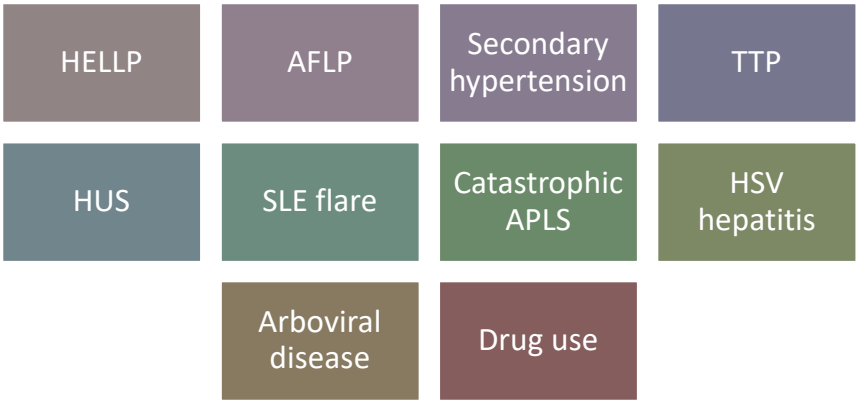
Imitators of Severe Preeclampsia



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

The Swansea criteria have been used (# 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

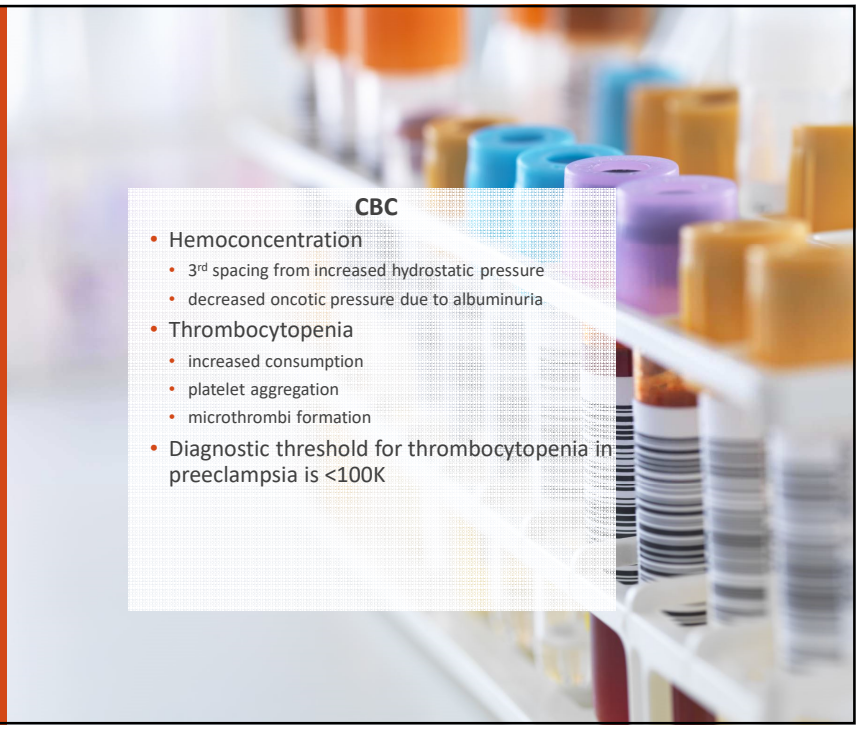
--

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 thrombus, bright liver/ascites
- May also use to rule out other pathologies for elevated LFTs

Initial diagnostics

CMP

CBC

Urine protein:Cr ratio

--

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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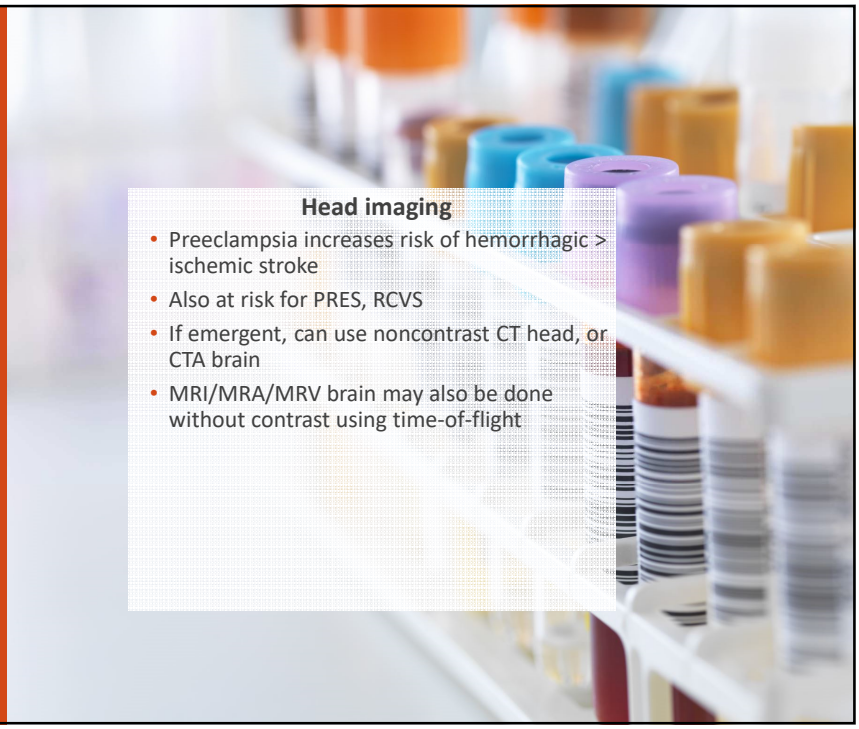
RUQUS

CXR

Head imaging

Peripheral smear



Head imaging

- Preeclampsia increases risk of hemorrhagic > ischemic stroke
- Also at risk for PRES, RCVS
- If emergent, can use noncontrast CT head, or CTA brain
- MRI/MRA/MRV brain may also be done without contrast using time-of-flight

Initial diagnostics

CMP

CBC

Urine protein:Cr ratio

--

RUQUS

CXR

Head imaging

Peripheral smear

Peripheral smear

- Assess for schistocytes, other abnormal red cell morphology, platelet sufficiency

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

Antihypertensives

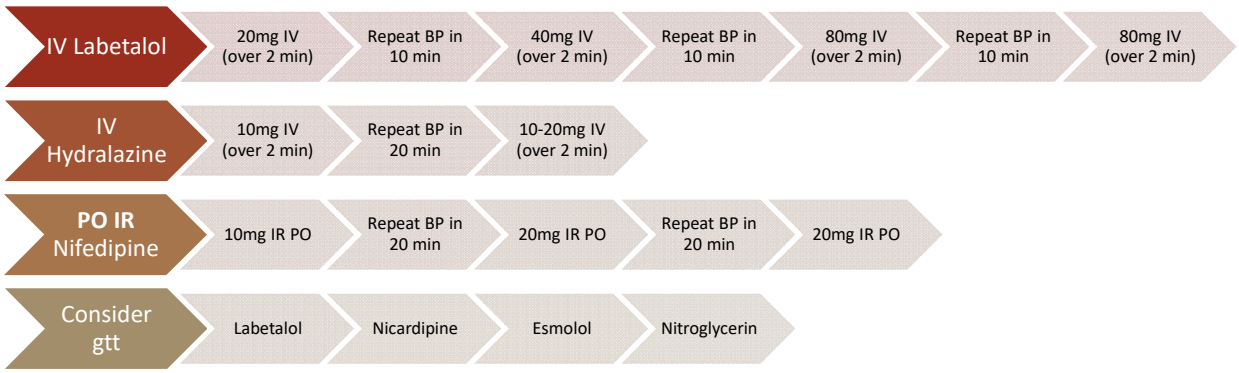
- IV labetalol
- IV hydralazine
- PO IR nifedipine

Magnesium sulfate

- Not recommended as antihypertensive agent
- **Should be used for**: seizure prophylaxis and **controlling seizures in eclampsia**
  - IV bolus of 4-6 grams in 100 ml over 20 minutes, followed by IV infusion of 1-2 grams per hour. Continue for 24 hours postpartum
  - If no IV access, 10 grams of 50% solution IM (5 g 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 has not borne out in trials

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

Severe Hypertension (≥ 160/110) Management Algorithm



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

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 = 130-150/80-95
- If postpartum = 120-140/70-90

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 methyldopa **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

Topics to be covered

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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).

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, prior 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
- Determine choice 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 to perform **test of cure** at the end of treatment

Recurrence

- Pyelonephritis recurs in 6-8% of pregnancies
- Low-dose **antimicrobial therapy** is generally used for the **remainder 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 given lower rates of resistant organisms in (generally young, healthy) pregnant patients

Pyelonephritis is **extremely inflammatory** in pregnancy

Should see the fever curve starting to bend, but often **takes true 48h** of appropriate antibiotic therapy to see significant improvement

But, **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	Preterm labor
• 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	• Occurs in up to 7% • 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	• Be aware of this risk • 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) • Cephalos • Nitrofura available in 1 • Clindamy • Certain n erythromycin • Metronid • Carbaper • Vancomycin • Aztreonam	• Aminoglycosides (human experience	• Tetracyclines (bone growth inhibition, to developing

Briggs Drugs in Pregnancy and Lactation
Reprotox
Lactmed

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

General antibiotic guidance

Pyelonephritis – key points

- Pyelo is more common among pregnant patients than the general population
- Pyelo in pregnancy is often **not** preceded by typical symptoms of cystitis
- Broad spectrum beta lactams are appropriate for empiric treatment, with choice driven 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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- Pyelonephritis
- Pulmonary embolism
- Procedures during pregnancy

Topics to be covered

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

Pulmonary Embolism in Pregnancy

- PE is the 6th leading cause of maternal mortality in US (1991-2005)
- Overall incidence 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 probability

D-dimer testing

Imaging studies

Diagnosis of PE in non-pregnant patients

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 radiation exposure well below 1 rad
- CTA chest 0.01-0.66 mGy
- VQ scan 0.1-0.7 mGy
- CXR (2 views) 0.0005-0.01 mGy
- CT Abdomen 1.3-35 mGy
- Head/neck CT 0.001-0.01 mGy

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

Diagnostics

Pulse oximetry

ABG

EKG

CXR

D-dimer

LE US

VQ scan/CTA

Diagnostics

Pulse oximetry

ABG

EKG

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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/CTA

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/CTA

EKG

- Not sensitive or specific
- Look for RH strain
- Tachycardia is common in normal pregnancy up to 110
- S1Q3T3 can be seen more commonly in pregnancy due to positional changes of the heart

Diagnostics

Pulse oximetry

ABG

EKG

CXR

D-dimer

LE US

VQ scan/CTA

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/CTA

D-dimer

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

Diagnostics

Pulse oximetry

ABG

EKG

CXR

D-dimer

LE US

VQ scan/CTA

LE US

- If signs/symptoms concerning for LE VTE
- Absence does not mean much, clots may originate at/above common femoral vein

Diagnostics

Pulse oximetry

ABG

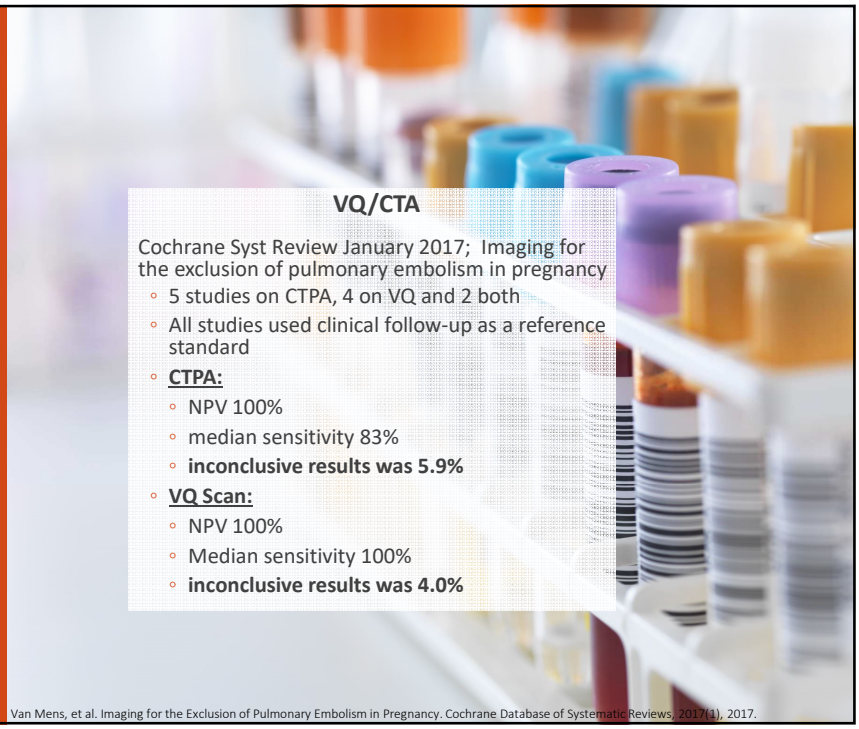
EKG

CXR

D-dimer

LE US

VQ scan/CTA



VQ/CTA

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/CTA

CTA

- Advantages
  - May offer an alternative diagnosis
  - Low dose of fetal radiation exposure
  - 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

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

YEARS Algorithm for Pulmonary Embolism (PE) ☆

Helps rule out pulmonary embolism; also validated in pregnant patients.

INSTRUCTIONS
Use in hemodynamically stable patients ≥18 years old.

When to Use ⌄ | Pearls/Pitfalls ⌄ | Why Use ⌄

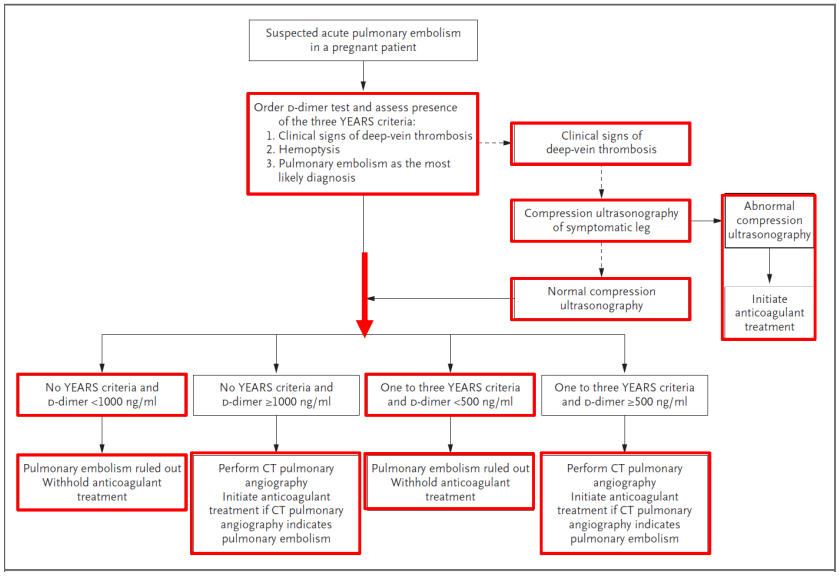
Pregnant patient	No	**Yes**
YEARS items		
Clinical signs of DVT	No	Yes
Hemoptysis	No	Yes
PE most likely diagnosis	No	Yes

Result:
Please fill out required fields.

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; re-start IV heparin after delivery
>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 and the postpartum period compared to general population
- PE is the 6th leading cause of maternal mortality in the US
- Signs and symptoms of PE have considerable overlap with physiologic changes in pregnancy
- Benefits of imaging often outweigh risks in pregnancy 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

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 anesthetic agents have demonstrated teratogenic effects in humans at any gestational age

4. No human evidence that in utero anesthetic or sedative exposure affects fetal brain development; animal data show no effect with exposure <3 hours

5. When non-obstetric surgery is being considered, 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

Tolcher, et al. Nonobstetric Surgery During Pregnancy. Obstetrics & Gynecology, 2018 ;132 (2), 395-403.

Procedures during pregnancy – general principles

Questions

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