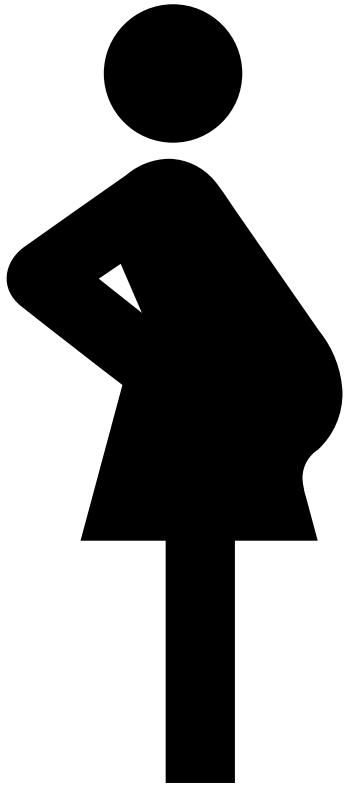


Common medical complications in pregnancy – inpatient edition

MEGHAN RUDDER, MD

MRUDDER@MGB.ORG

OBSTETRIC INTERNAL MEDICINE

7.24.2024

What has been your experience caring for pregnant patients in IM training?

https://redcap.link/OBIM

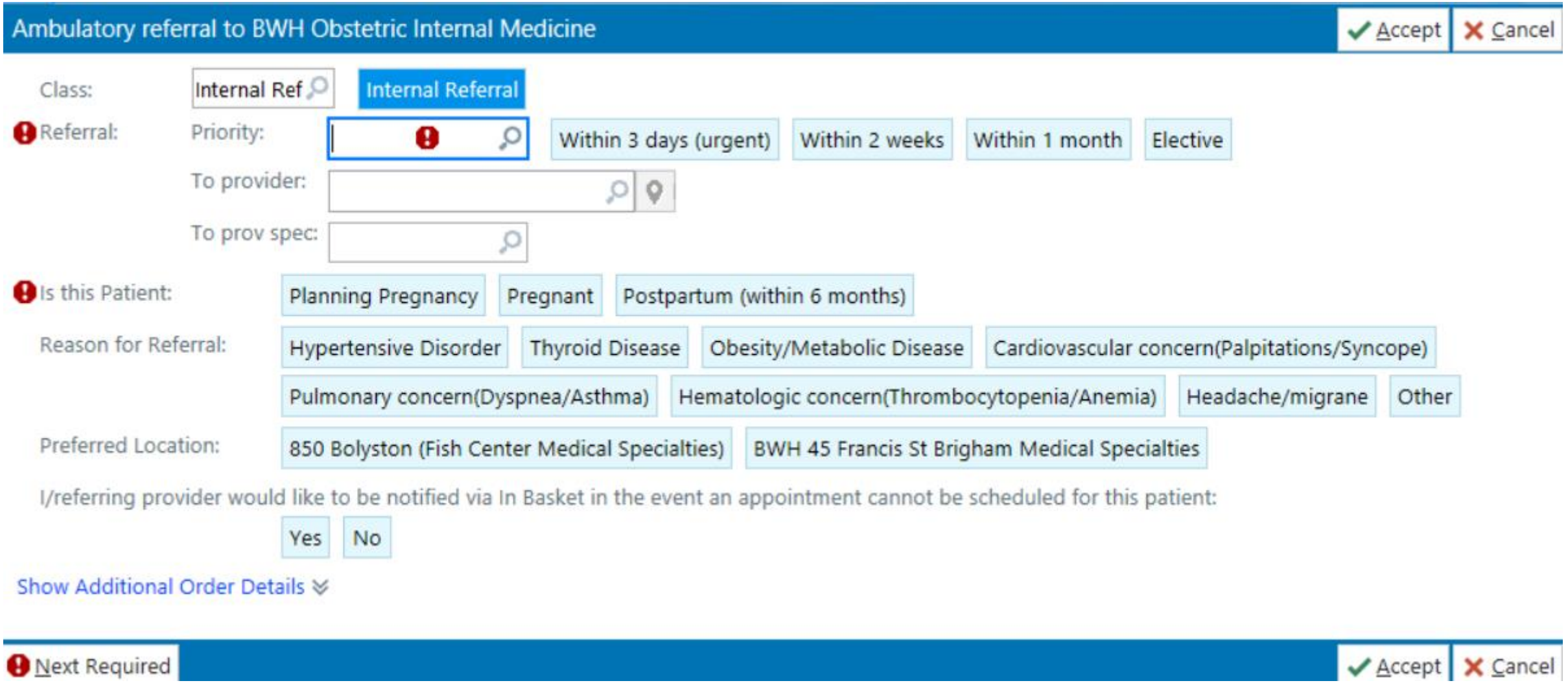
Who I am and why I am talking about pregnancy

Training

- Internal medicine residency at BWH
- Obstetric and Consultative Medicine fellowship at Women & Infants Hospital affiliated with Brown University

Now

- **Obstetric Internal Medicine (OBIM) consultative clinic**
- **Locations**:
  - Fish Center for Women's Health (850 Boylston St, Chestnut Hill)
  - Brigham Medical Specialties (45 Francis St, Boston)
- **Referrals**: Epic referral to Obstetric Internal Medicine (OBIM)
- **E-consult**: Epic E-consult to OBGYN → OB Internal Medicine (OBIM)
- **Contact**:
  - mrudder@mgb.org
  - Cell: 978 500 8510
- **More information**: Obstetric Internal Medicine (OBIM) – BWH WHR (harvard.edu)


Ambulatory referral to BWH Obstetric Internal Medicine
Accept
Cancel
Class:
Internal Ref
Internal Referral
Referral:
Priority:
Within 3 days (urgent)
Within 2 weeks
Within 1 month
Elective
To provider:
To prov spec:
Is this Patient:
Planning Pregnancy
Pregnant
Postpartum (within 6 months)
Reason for Referral:
Hypertensive Disorder
Thyroid Disease
Obesity/Metabolic Disease
Cardiovascular concern(Palpitations/Syncope)
Pulmonary concern(Dyspnea/Asthma)
Hematologic concern(Thrombocytopenia/Anemia)
Headache/migrane
Other
Preferred Location:
850 Bolyston (Fish Center Medical Specialties)
BWH 45 Francis St Brigham Medical Specialties
I/referring provider would like to be notified via In Basket in the event an appointment cannot be scheduled for this patient:
Yes
No
Show Additional Order Details
Next Required
Accept
Cancel

Ambulatory BWH OBGYN E-Consult

Accept | Cancel

Ordering Information

Gynecology: Gynecology E-consults are for general, benign, non-pregnant gynecologic concerns. These consults are not for gyn malignancies, complex infertility management or patients with established obstetric care, but may include management of possible miscarriage, ectopic pregnancy or pregnancy termination. Gyn e-consults are generally most helpful to primary care physicians, medical specialists and non-gyn surgeons.

Obstetric Internal Medicine (OBIM): OBIM e-consults provide medical consultation for patients with preexisting or newly developed medical conditions or concerns during preconception, pregnancy, or postpartum. Providers are trained in Internal Medicine with additional training in medical care of the pregnant patient. This consult may be appropriate for medical providers who have specific management questions, or obstetric providers who have medical questions about their patients, including pre-conception questions focused on optimization of medical problems. We do not make recommendations about prenatal care, fetal monitoring, or delivery decisions.

Maternal Fetal Medicine (MFM): This e-consult is intended for obstetric management questions and will be most useful to general obstetricians and midwives for established obstetric patients. The MFM e-consult may include management of fetal monitoring and delivery recommendations as well as pre-conception questions focused on future obstetric or genetic risk, and whether pre-pregnancy testing or evaluation is indicated.

Process Inst.: E-Consults are a quick and easy way to receive feedback on non-urgent, discrete questions to specialists about patient care. If you intend to order a traditional (in-person) OB referral, please select AMB Referral to BWH OB/GYN

Specialty: Gynecology | Obstetric Internal Medicine (OBIM) | Maternal Fetal Medicine (MFM)

Reason for E-Consult:
- ☐ Medications/imaging in pregnancy/lactation
- ☐ Laboratory abnormality in pregnancy/postpartum
- ☐ Thyroid Disease
- ☐ Obesity
- ☐ Diabetes
- ☐ Hypertension
- ☐ Hematologic Concern
- ☐ Headache/Migrane
- ☐ Add Free Text

Specific Patient Care Question:

Additional Comments:

Show Additional Order Details

Next Required

Accept | Cancel

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 a few of the more common medical reasons for hospitalization during pregnancy.
3. I use the terms “fetus” and “baby” interchangeably in this talk.


TREATING A PREGNANT WOMAN

General Principles

General Principles

1

Fetal well being depends on maternal well being

General Principles

1

Fetal well being depends on maternal well being

2

Uninvestigated symptoms → progression of untreated disease

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

General Principles

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3. Uncontrolled maternal disease → compromised fetal safety, growth and development
4. Generally, withholding treatment/diagnostic testing = more harmful

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, 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
- Asthma exacerbation

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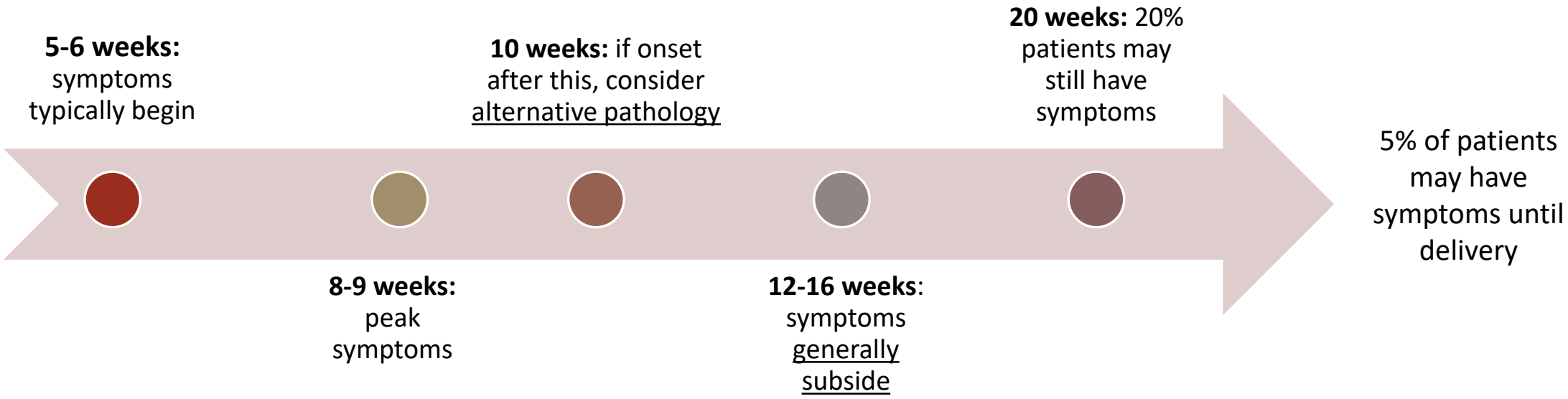
Nausea and Vomiting of Pregnancy

- 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



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 (genera
- 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

Initial testing

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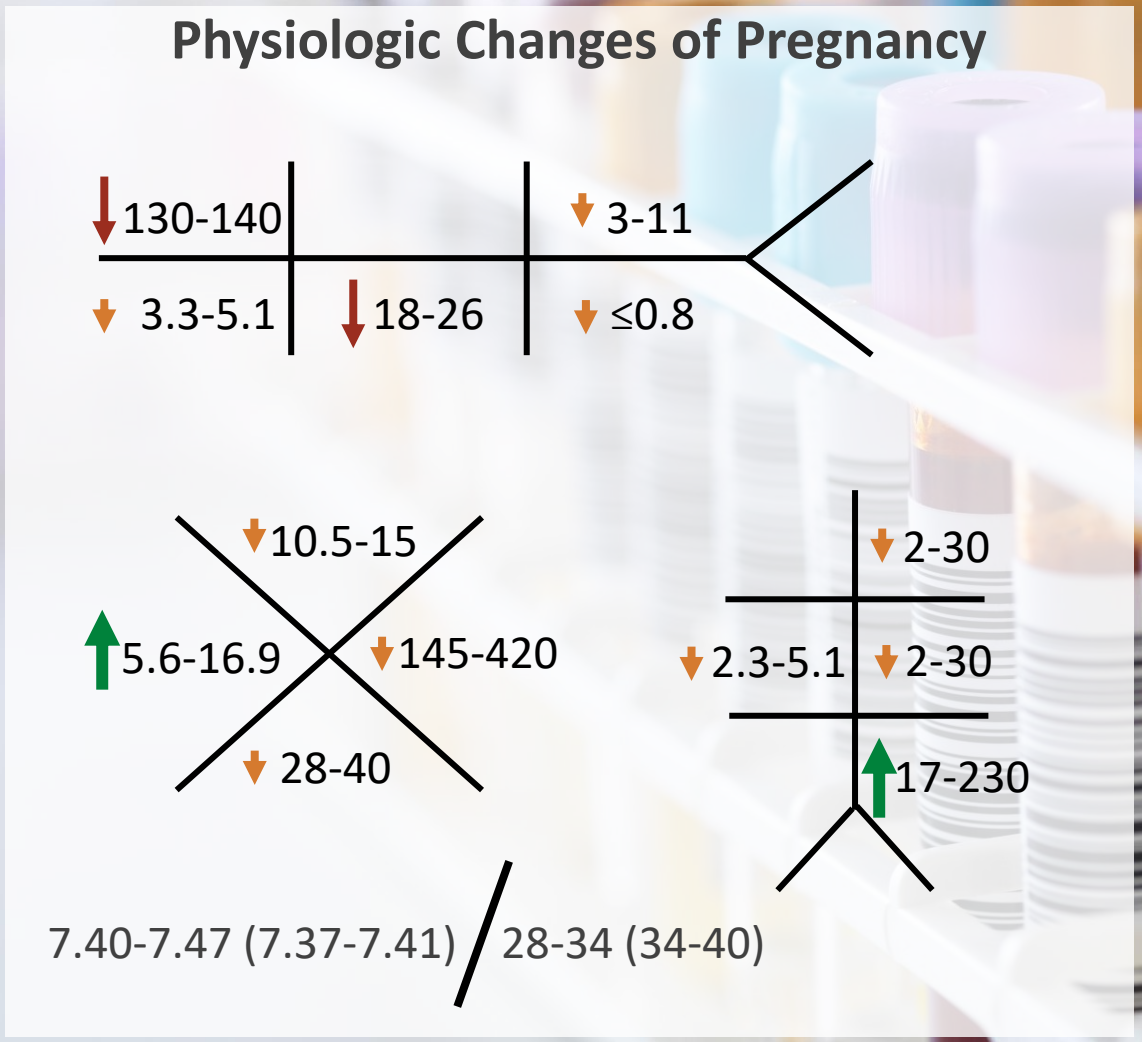
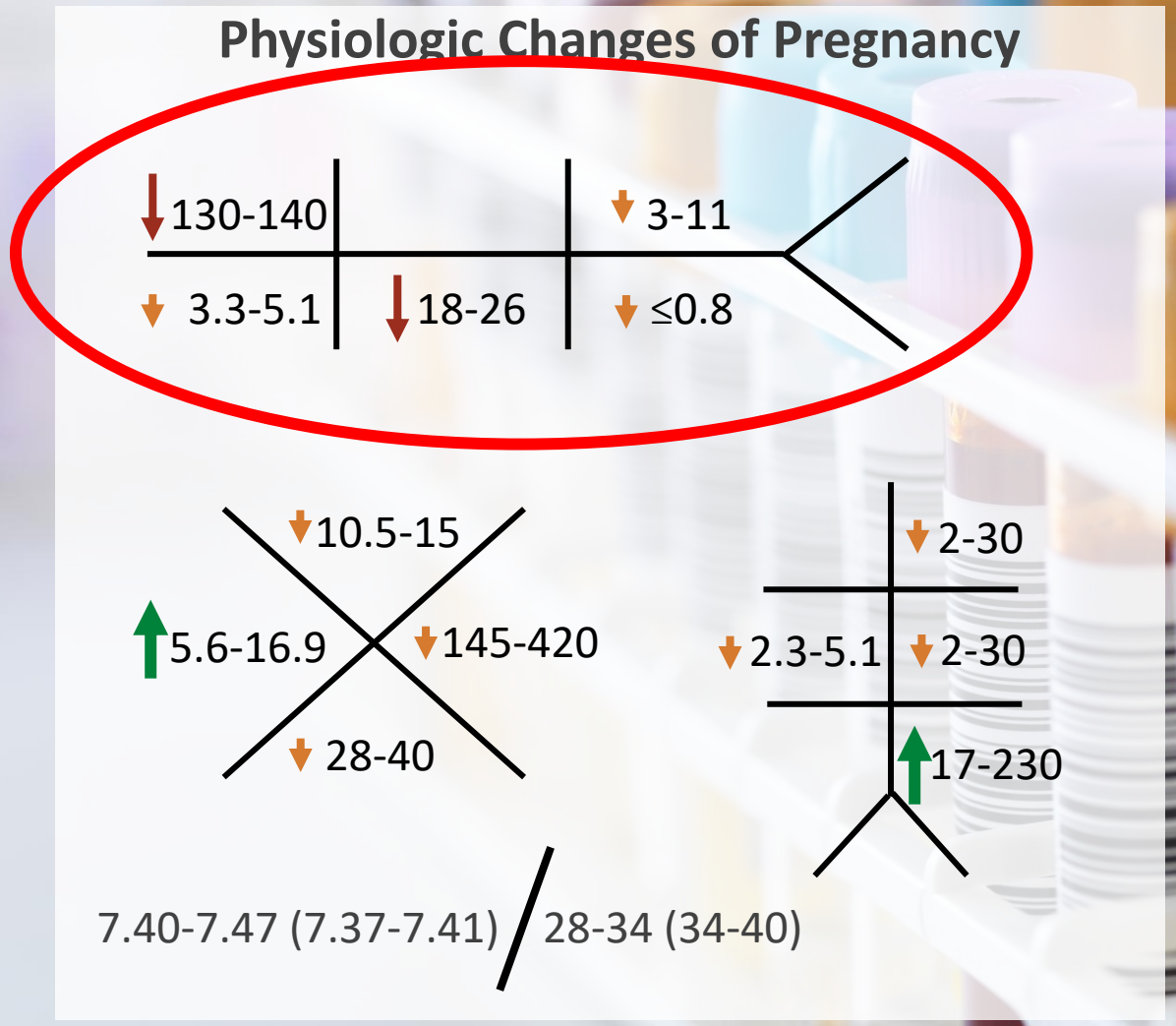


Initial testing

BMP, Mg, phos

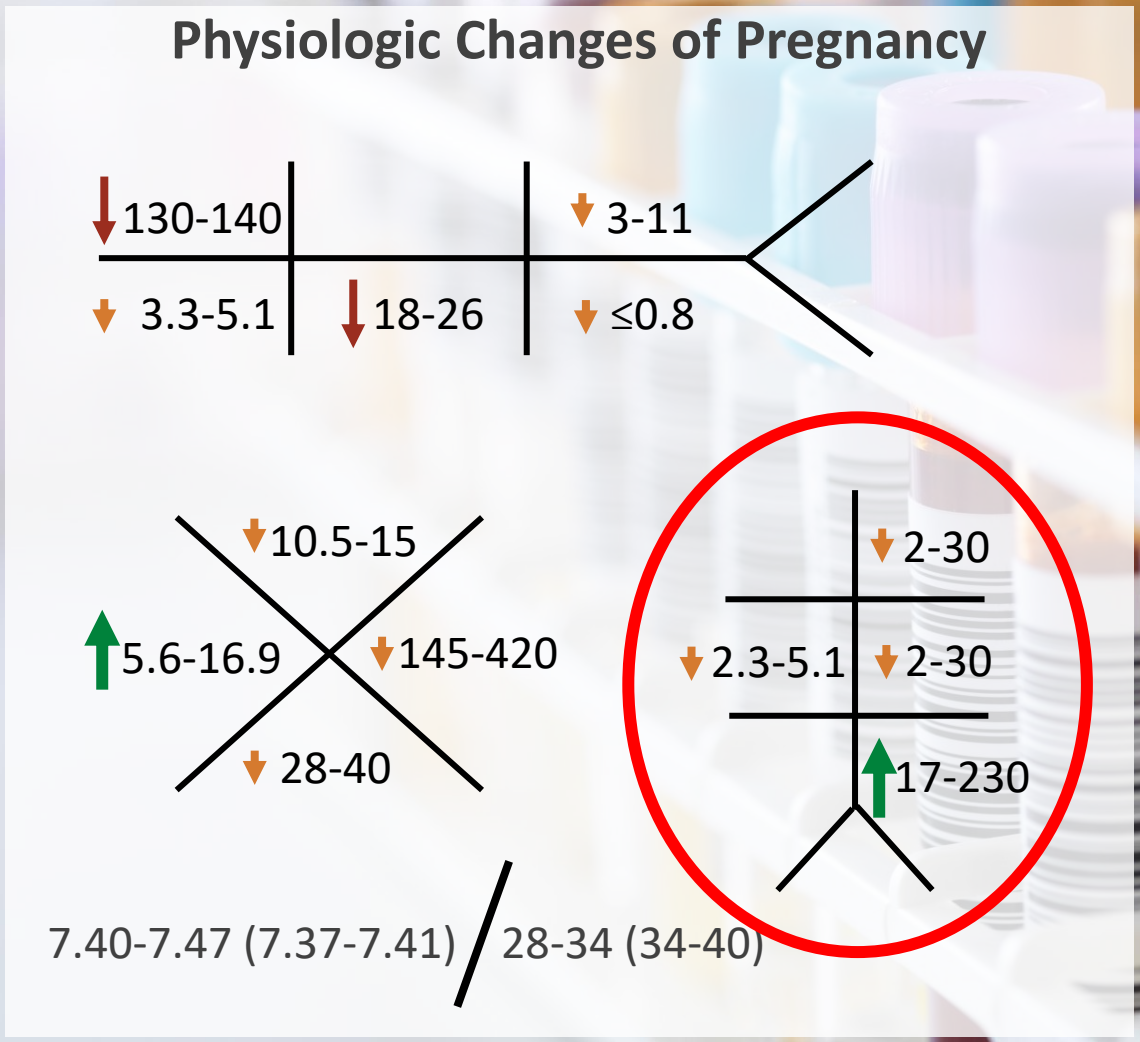
- Mostly attention to correcting deficiencies
- Stay attuned to inconsistencies in derangement (ie high-normal K, suggestive of alternative etiology ie Addison's)
- Assess anion gap *corrected for albumin*
- Often see hypochloremic metabolic alkalosis, check for concomitant metabolic acidosis (think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



Initial testing

LFTs

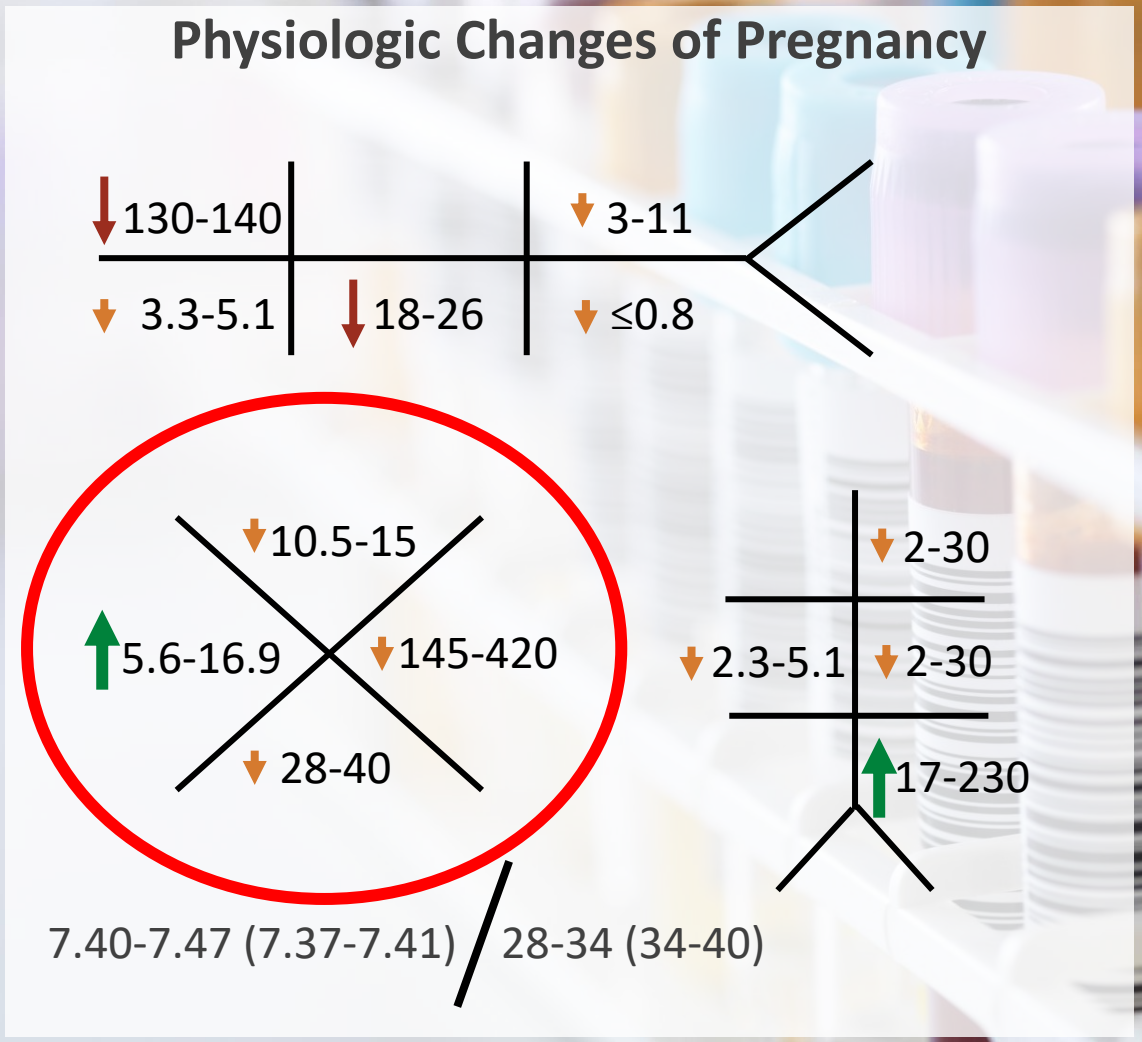
- Abnormal in up to 50% of patients hospitalized for hyperemesis
- ALT > AST
- Mild elevation 2-3x ULN, into low 100s
- Total bilirubin may be elevated (direct and indirect), rarely exceeds 4



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

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

VBG, lactate, beta hydroxybutyrate

EKG

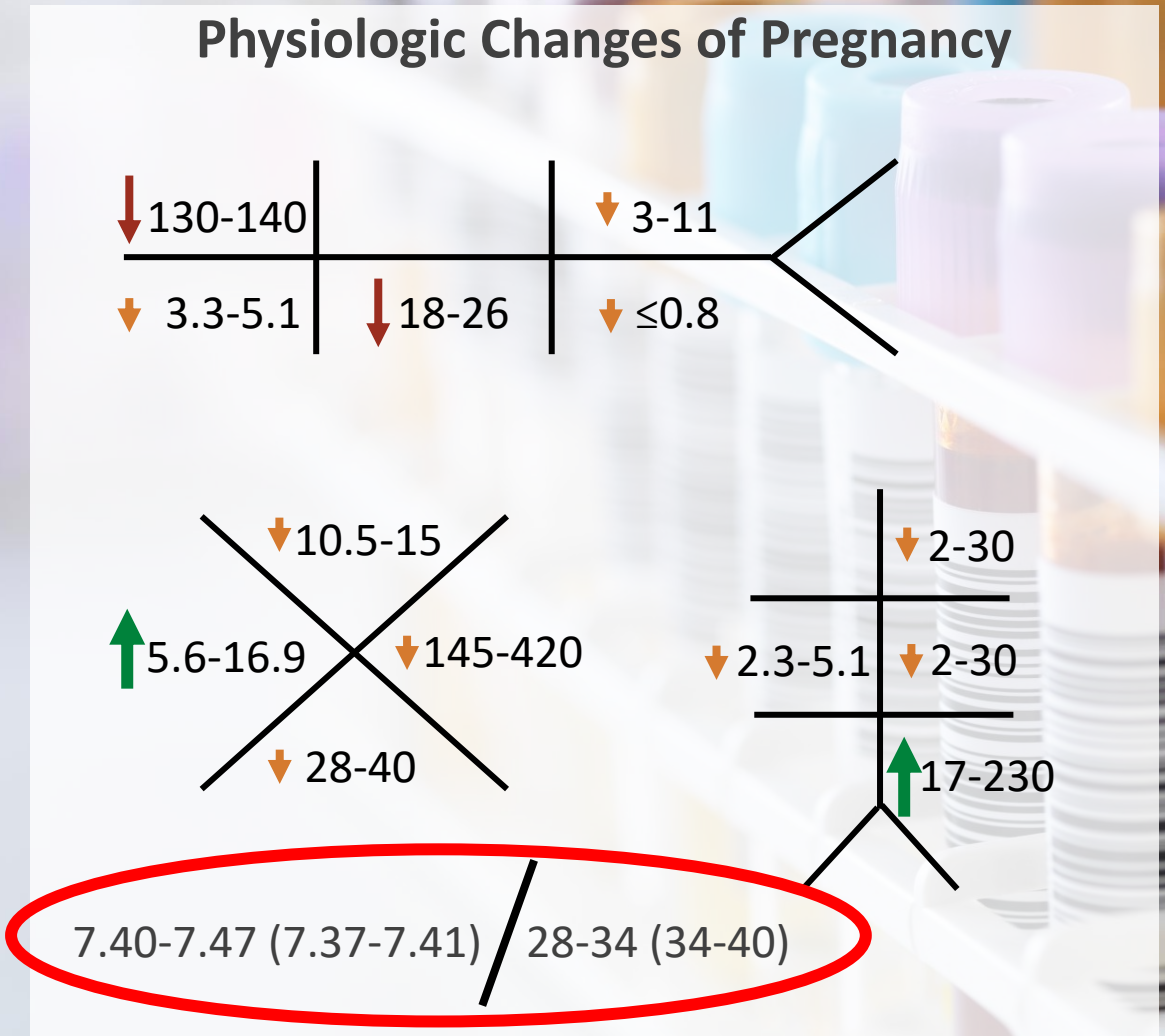
Lipase

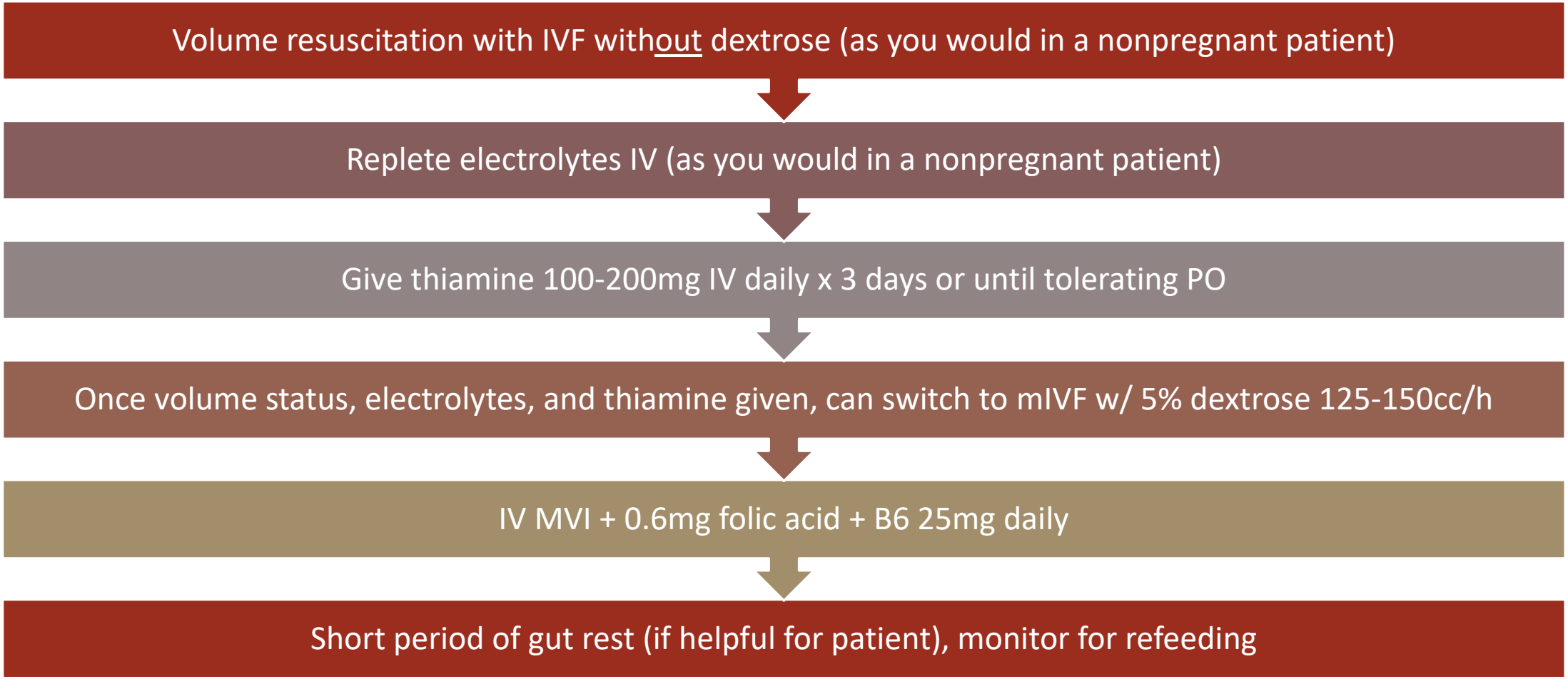
- May be elevated in 10-15% of hyperemesis patients
- May increase as much as 5x ULN

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)

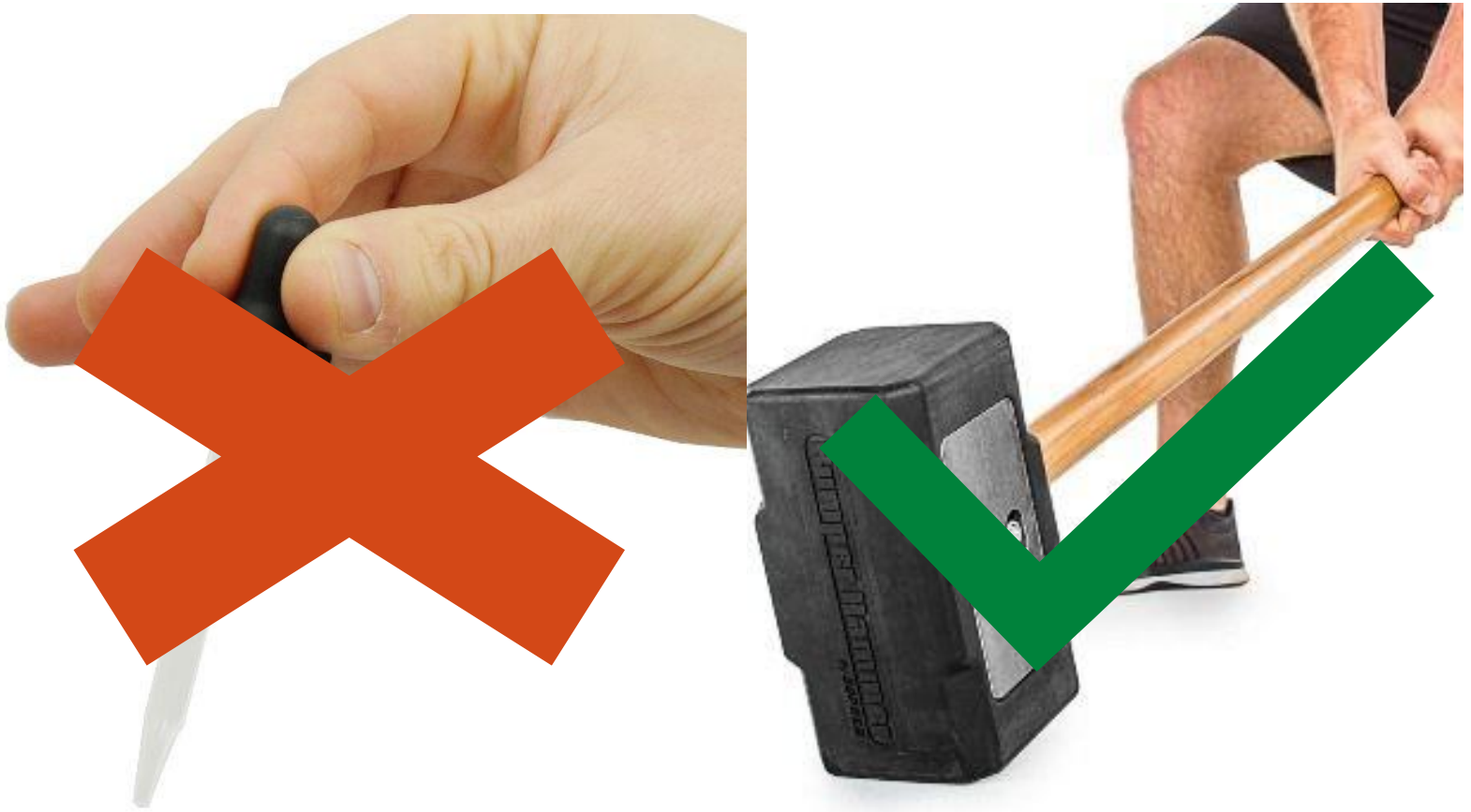




Management – fluid and electrolytes

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

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/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 women are at higher risk for starvation ketoacidosis

Topics to be covered

- Hyperemesis gravidarum
- Hypertensive disorders of pregnancy
- Pyelonephritis
- Pulmonary embolism
- Asthma exacerbation

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Multisystem inflammatory disorder beginning *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

SBP ≥140 mm Hg and/or DBP ≥90 mm Hg*

<20 weeks gestation

Chronic / pre-pregnancy hypertension

(At risk of developing superimposed preeclampsia)

≥20 weeks gestation

Presence of target organ involvement?

(Symptoms, clinical findings, laboratory abnormalities)

No target organ involvement

Gestational Hypertension

Target organ involvement

Preeclampsia

Includes:

- Nonsevere preeclampsia
- Severe preeclampsia
- HELLP syndrome
- Eclampsia


Proteinuria (300 mg/24 hr)


Cr > 1.1 mg/dL or ↑ 2x


Thrombocytopenia


Elevated AST/ALT


Pulmonary edema


Cerebral/visual symptoms

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

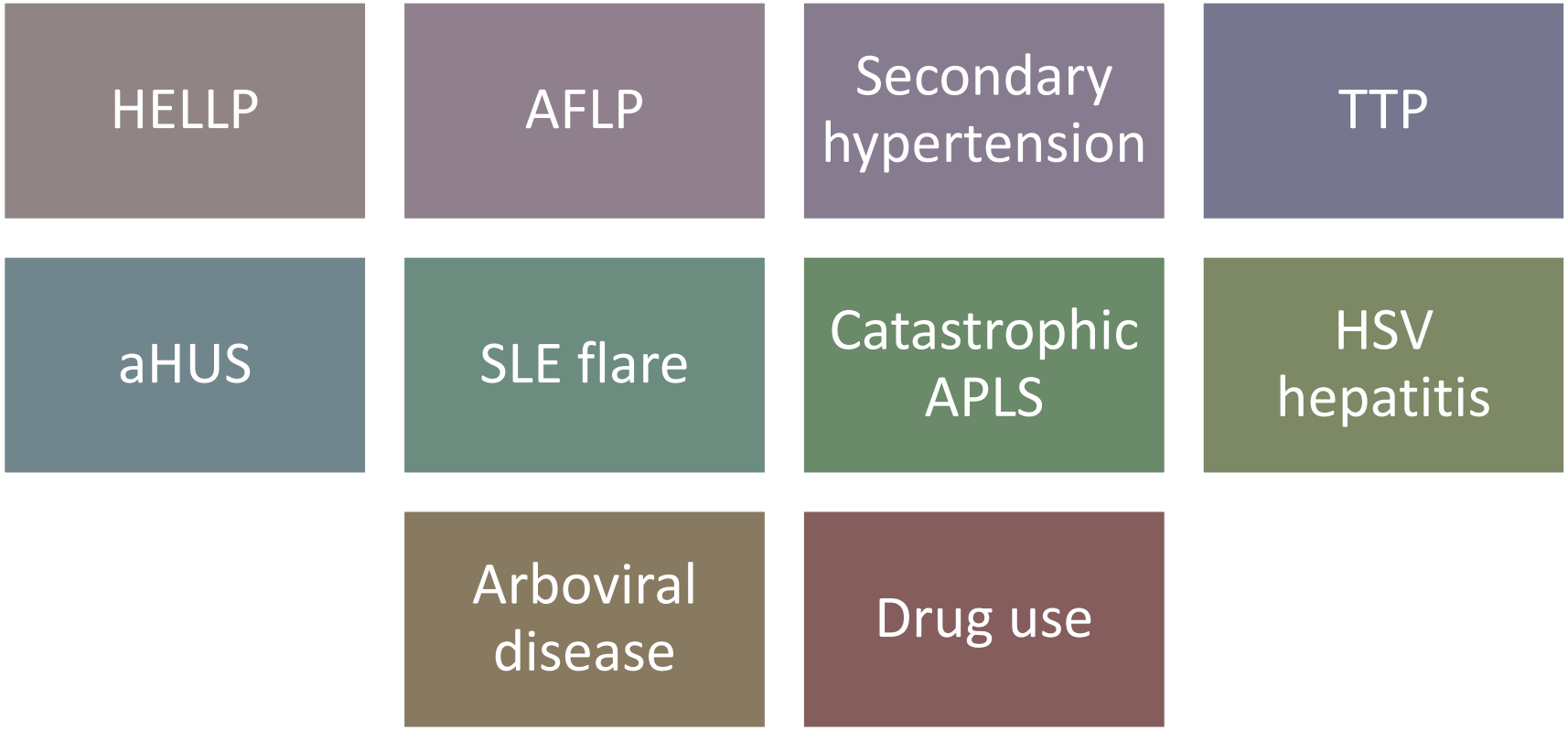
Hypertensive disorder	Definition
Chronic hypertension	• SBP ≥140 or DBP ≥90 on ≥2 occasions ≥4 hours apart AND • Pre-pregnancy or <20 weeks
Gestational hypertension	• SBP ≥ 140 or DBP ≥ 90 on ≥2 occasions ≥4 hours apart at ≥20 weeks AND • Absence of proteinuria or end-organ dysfunction

Preeclampsia	• SBP ≥140 or DBP ≥90 on ≥2 occasions ≥4 hours apart AND, 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
	  • **Pulmonary edema** OR
	  • New-onset **headache** unresponsive to medication and not accounted for by alt dx OR
	  • **Visual disturbances**

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	3rd trimester	3rd trimester	3rd trimester	Postpartum	2nd or 3rd 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/µL)
- Elevated transaminases (AST or ALT) (usually **5-10x ULN**)
- Elevated **ammonia** (>47 µmol/L)
- Elevated uric acid (5.7 mg/dL)
- Acute kidney injury, or creatinine >1.7 mg/dL (150 µmol/L)
- **Coagulopathy** or prothrombin time >14 seconds

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

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

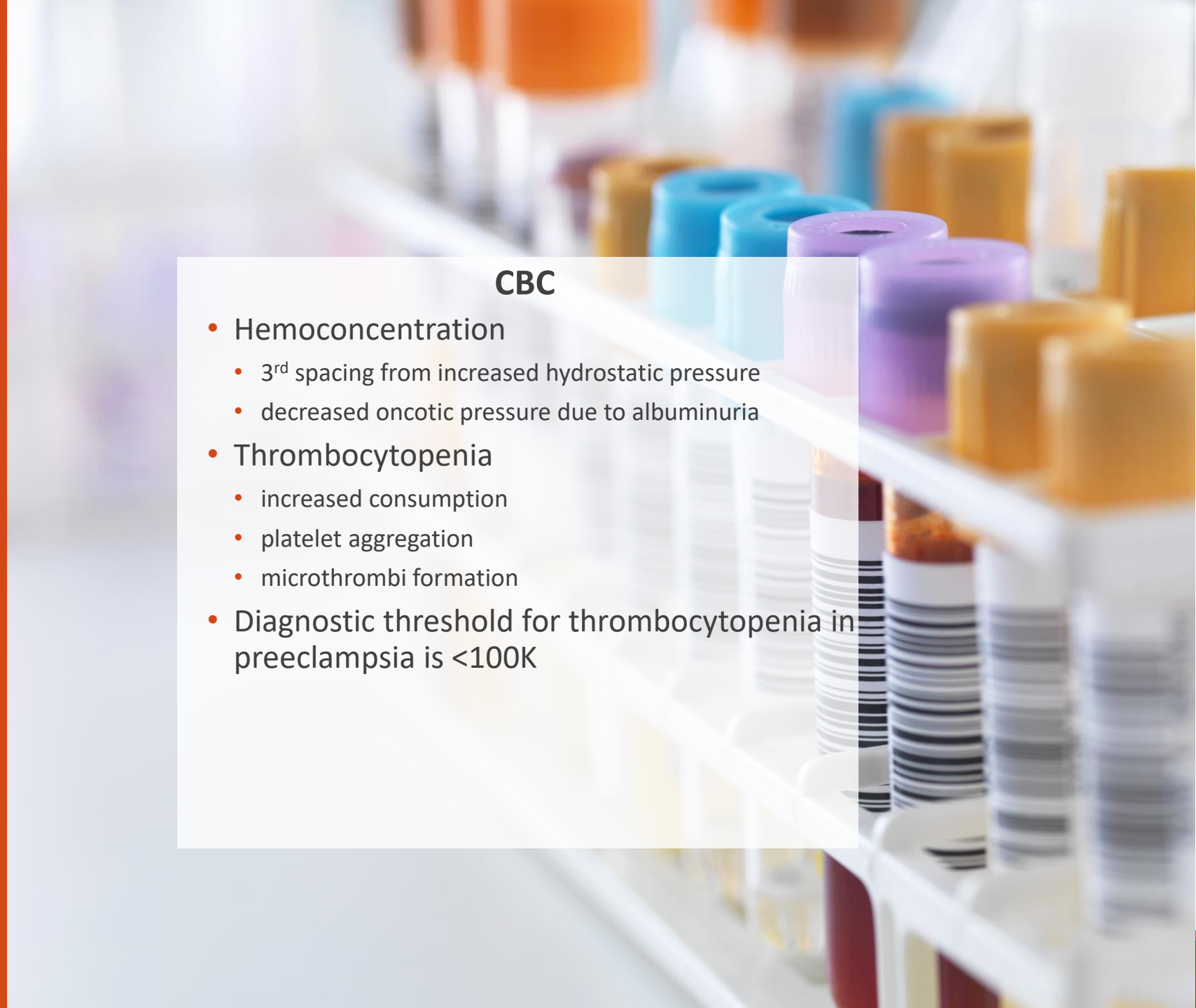
--

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

--

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

CMP

CBC

Urine protein:Cr ratio

--

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

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 = **EMERGENCY**

Antihypertensives

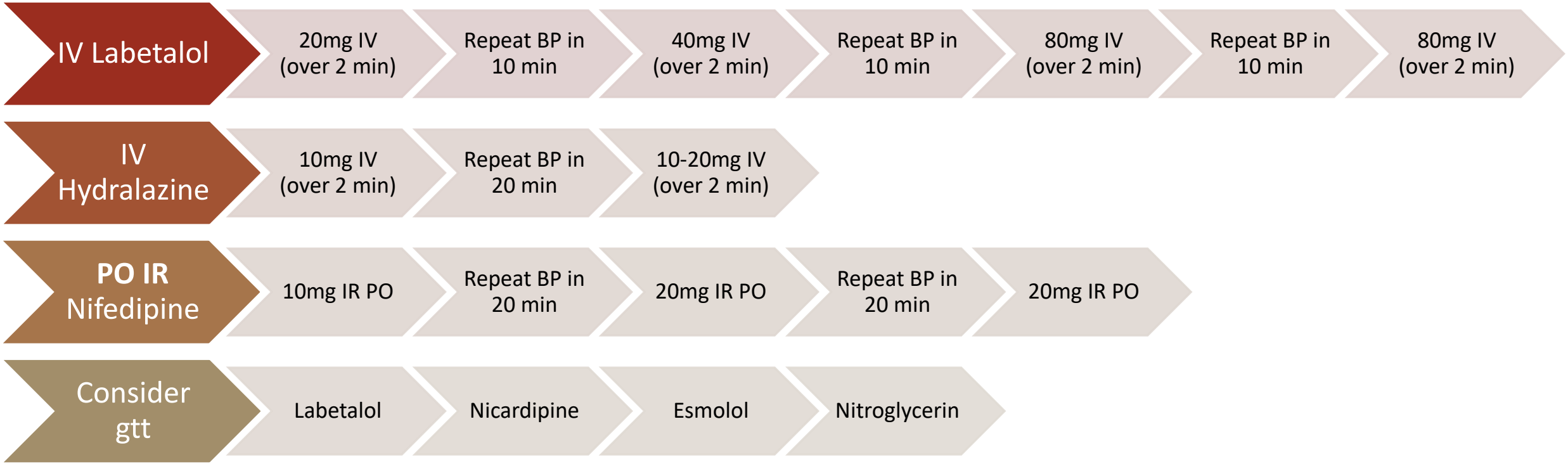
- IV labetalol
- IV hydralazine
- PO IR nifedipine

Magnesium sulfate

- Not recommended as antihypertensive agent
- **Should be used for**: seizure prophylaxis and **controlling seizures in eclampsia**
  - IV bolus of 4-6g 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



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 = initial: 130-150/80-100 → subsequent: 130-140/80-90
- 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 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
- Asthma exacerbation

Topics to be covered

- Hyperemesis gravidarum
- Hypertensive disorders of pregnancy
- **Pyelonephritis**
- Pulmonary embolism
- Asthma exacerbation

Pyelonephritis in Pregnancy

- Incidence 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 24-48h 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 to complete 10 day course
  - Beta-lactams based on culture data
  - Bactrim if in the 2nd trimester
- Need **test of cure** at the end of treatment

Recurrence

- Recurrence reported in 6-25%
- 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 (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

- 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

Use may be justifiable in unique circumstances

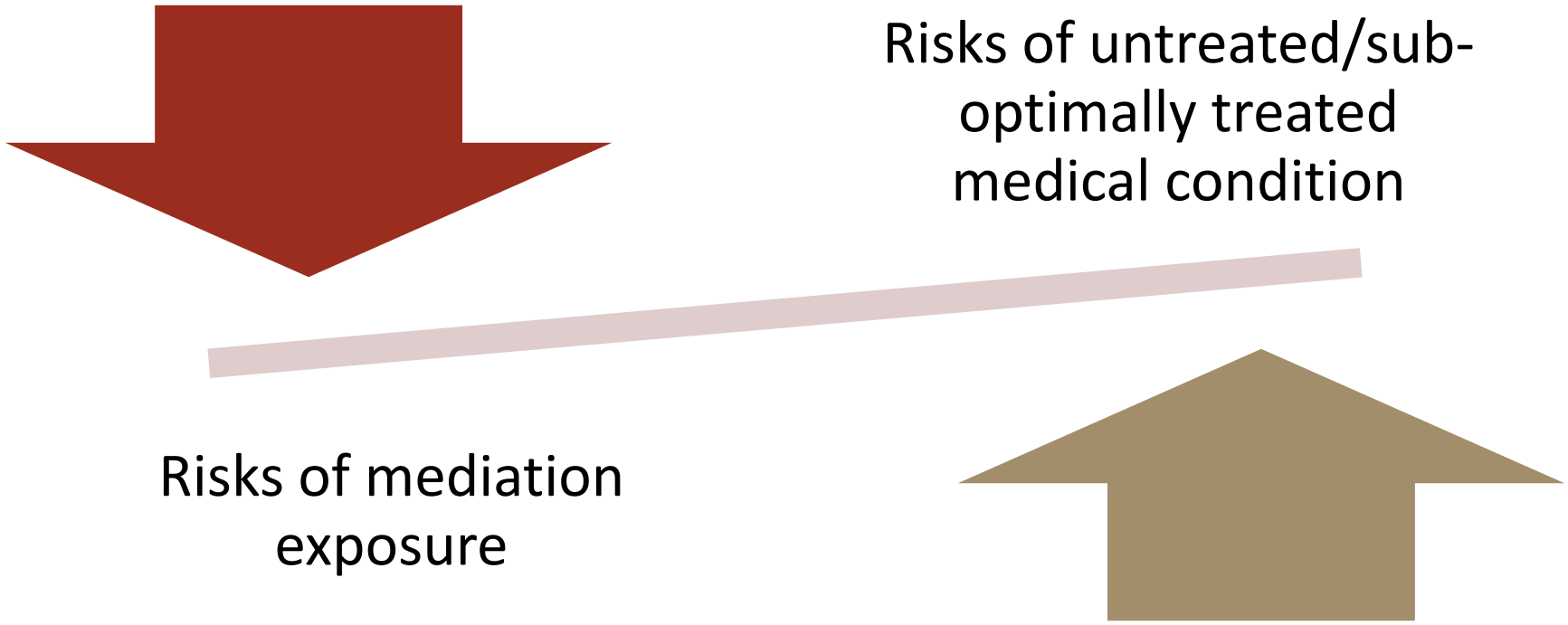
- Aminoglycosides (human experience limited; theoretical concern for nephrotoxicity / ototoxicity but not born out clinically)
- Trimethoprim (folate antagonist, avoid in 1st trimester)
- Sulfamethoxazole (may displace bilirubin, caution in 3rd trimester)
- Certain macrolides (clarithromycin)

Rarely justifiable

- 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/

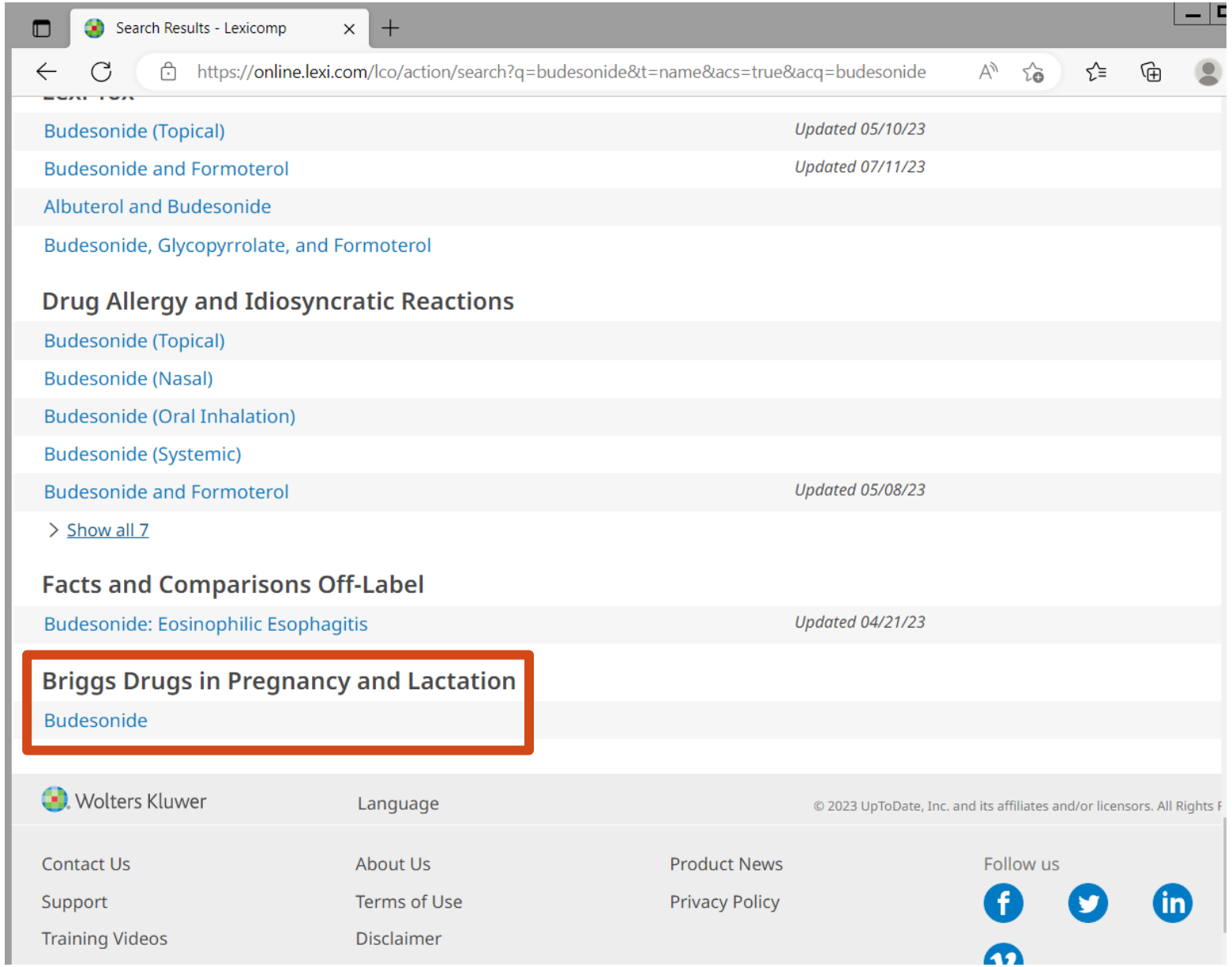
FDA Pregnancy Registry Listing
www.fda.gov/ScienceResearch/SpecialTopics/WomensHealthResearch/ucm251314.htm

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/


Search Results - Lexicomp
https://online.lexi.com/lco/action/search?q=budesonide&t=name&acs=true&acq=budesonide
Budesonide (Topical) Updated 05/10/23
Budesonide and Formoterol Updated 07/11/23
Albuterol and Budesonide
Budesonide, Glycopyrrolate, and Formoterol
Drug Allergy and Idiosyncratic Reactions
Budesonide (Topical)
Budesonide (Nasal)
Budesonide (Oral Inhalation)
Budesonide (Systemic)
Budesonide and Formoterol Updated 05/08/23
Show all 7
Facts and Comparisons Off-Label
Budesonide: Eosinophilic Esophagitis Updated 04/21/23
Briggs Drugs in Pregnancy and Lactation
Budesonide
Wolters Kluwer
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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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- Hypertensive disorders of pregnancy
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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

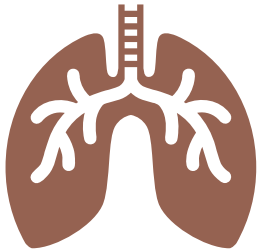
9% cough

7% hemoptysis

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

Clinical 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 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.

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

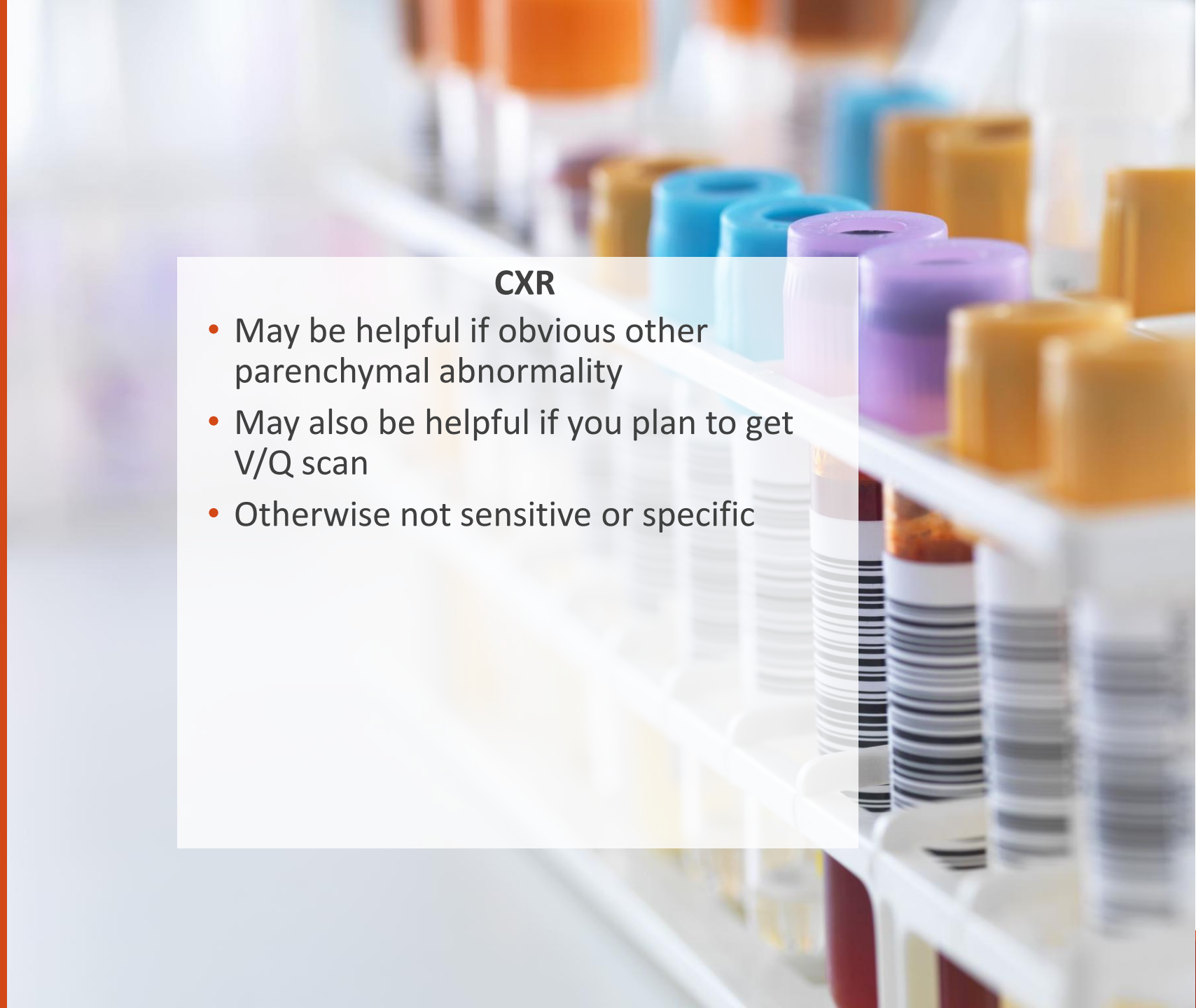
EKG

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

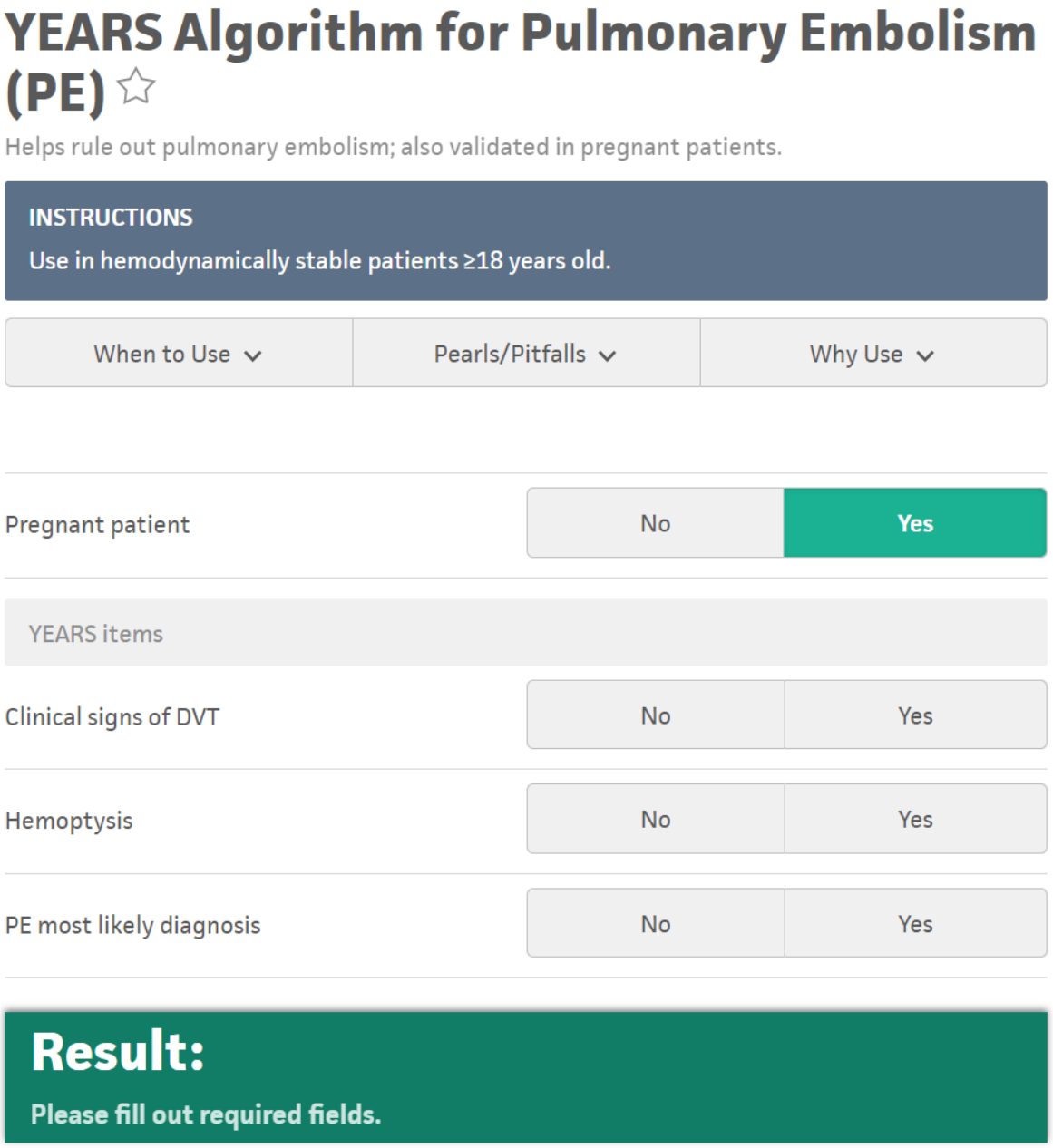
VQ scan/CTPA

CTPA

- Advantages
  - May offer an alternative diagnosis (12-13% 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

Pregnancy-Adapted YEARS algorithm

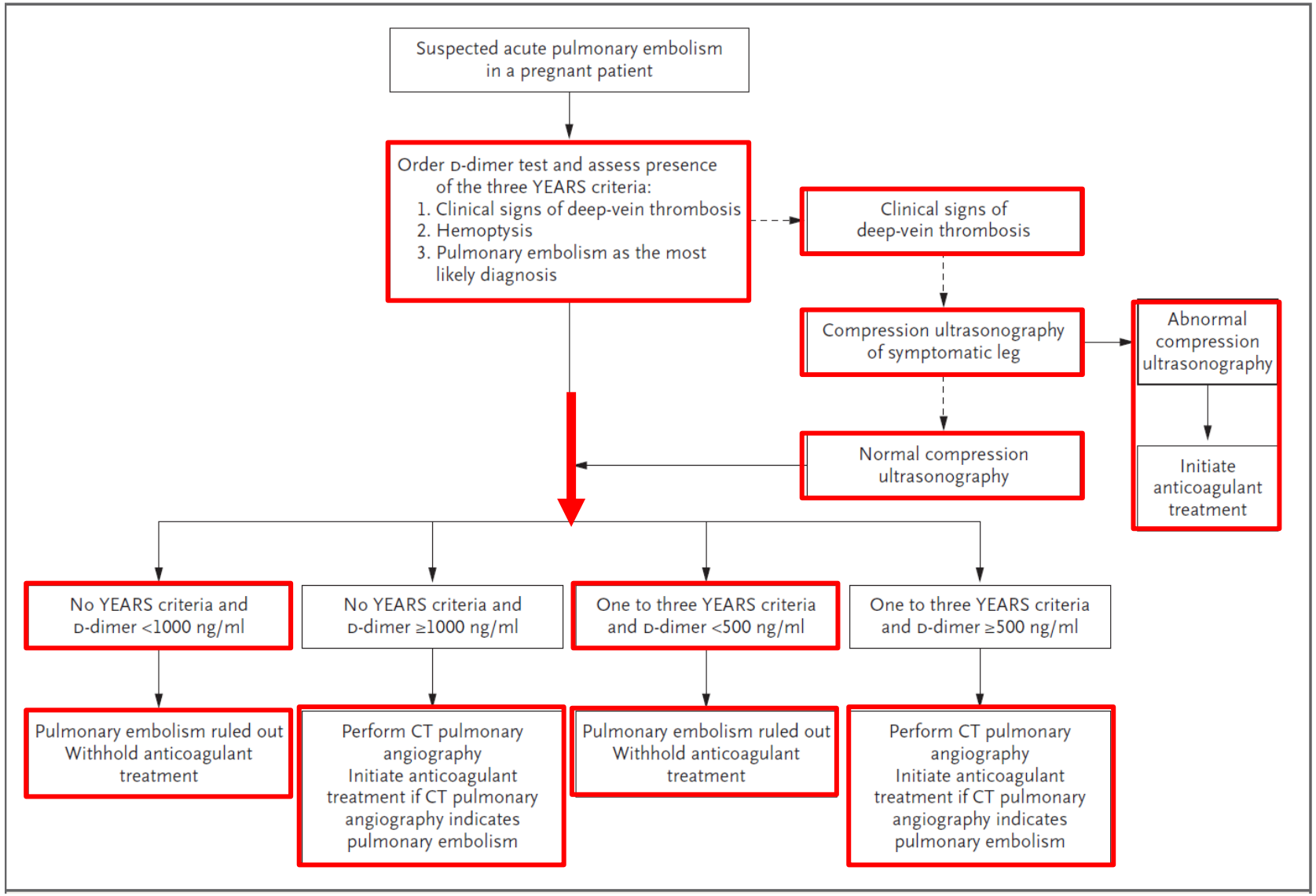
- Prospective study
- 498 **pregnant** women with suspected PE in ED or OB triage
- Suspected PE: new onset or worsening of chest pain or dyspnea, with or without hemoptysis or tachycardia
- Used adapted YEARS algorithm + D-dimer to exclude PE
- If PE could not be excluded, underwent CTA
- Primary outcome: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



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 17,500U Q12h, 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 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

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- Hypertensive disorders of pregnancy
- Pyelonephritis
- Pulmonary embolism
- Asthma exacerbation

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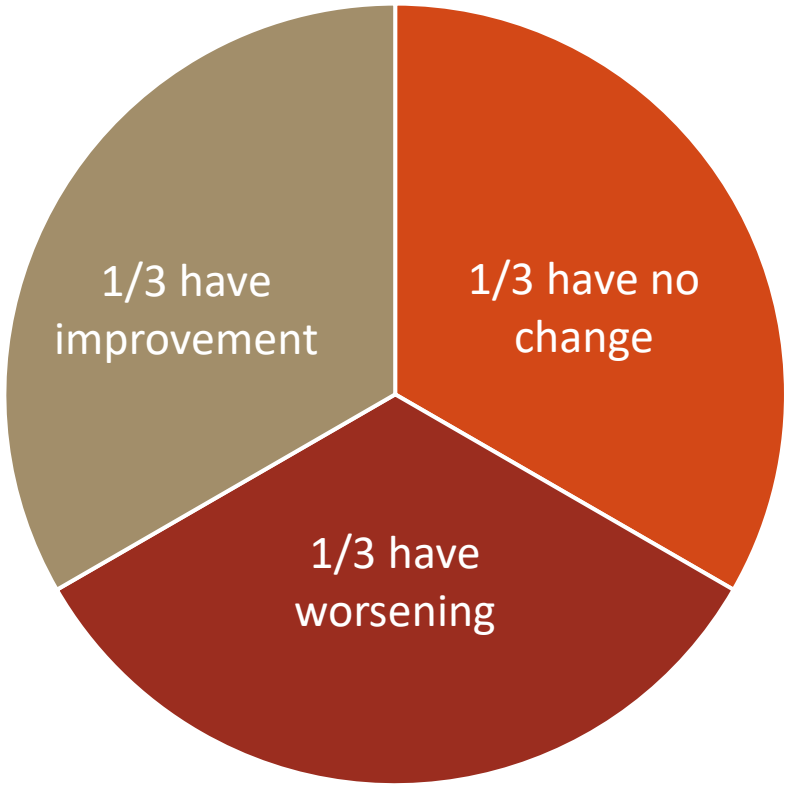


Asthma in pregnancy

Asthma affects ~4-8% of all pregnancies

Control of asthma before pregnancy and/or control in prior pregnancies may predict control in future pregnancy

For those who have worsening, tends to be in the 2nd and 3rd trimester

Risk factors for exacerbation in pregnancy:

- Overweight, obesity, excessive 1st trimester weight gain
- Smoking
- Maternal anxiety
- Discontinuation of inhaled corticosteroids
- Gestational rhinitis
- GERD
- Viral infection

Schatz et al, 1988

Diagnostics

Respiratory rate

Peak flow

ABG/ABG

Pulse oximetry

CXR

RPP

CBC w/diff

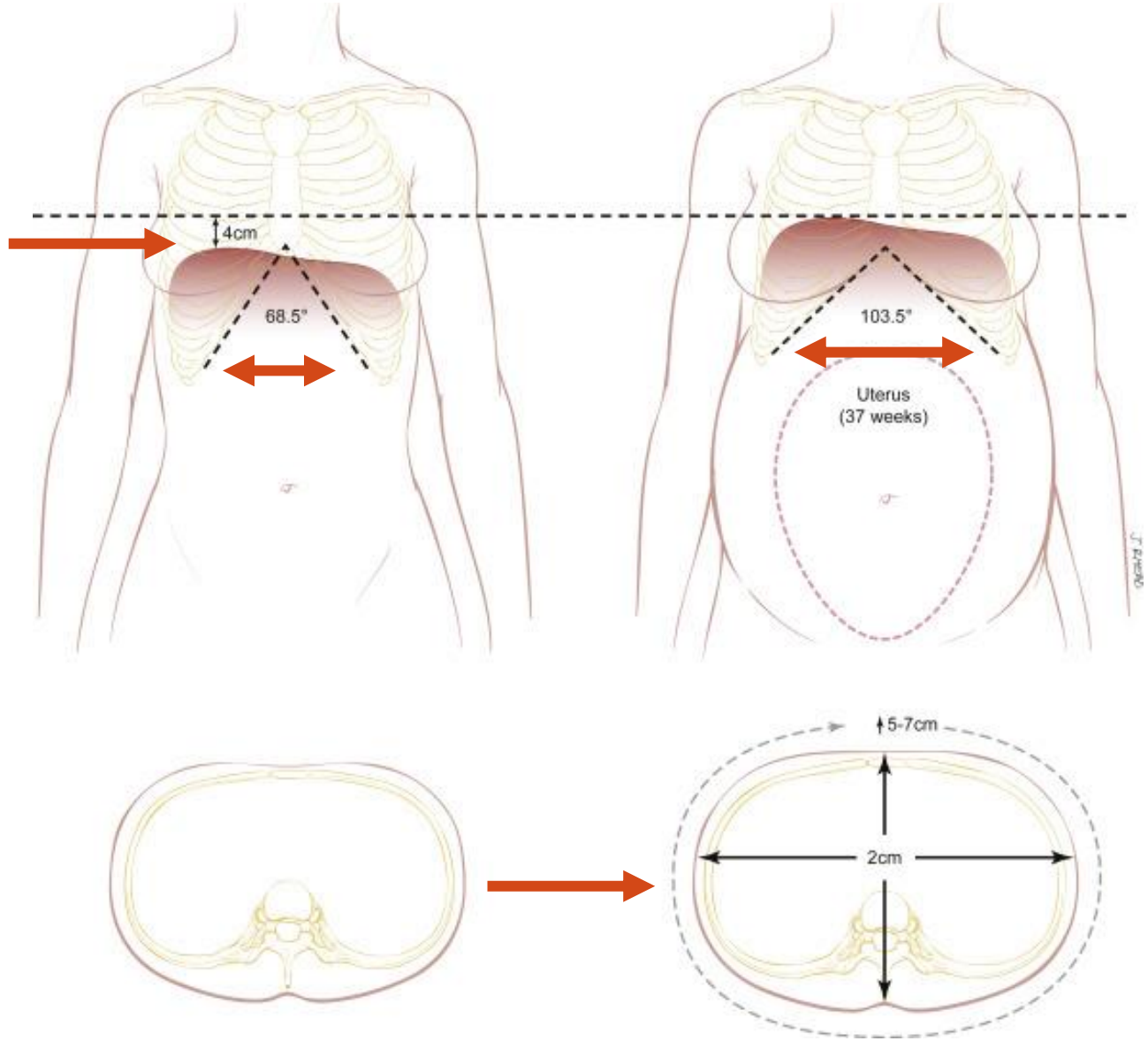
Procalcitonin

D-dimer

VQ scan/CTA

Chest wall

- Ribs flare outward
- Subcostal angle widens
- Diaphragm raises up to 4cm
- Diaphragmatic excursion increases up to 2cm
- Chest diameter increases



Hegewald MJ, Crapo RO. Respiratory physiology in pregnancy. Clin Chest Med. 2011 Mar;32(1):1-13.

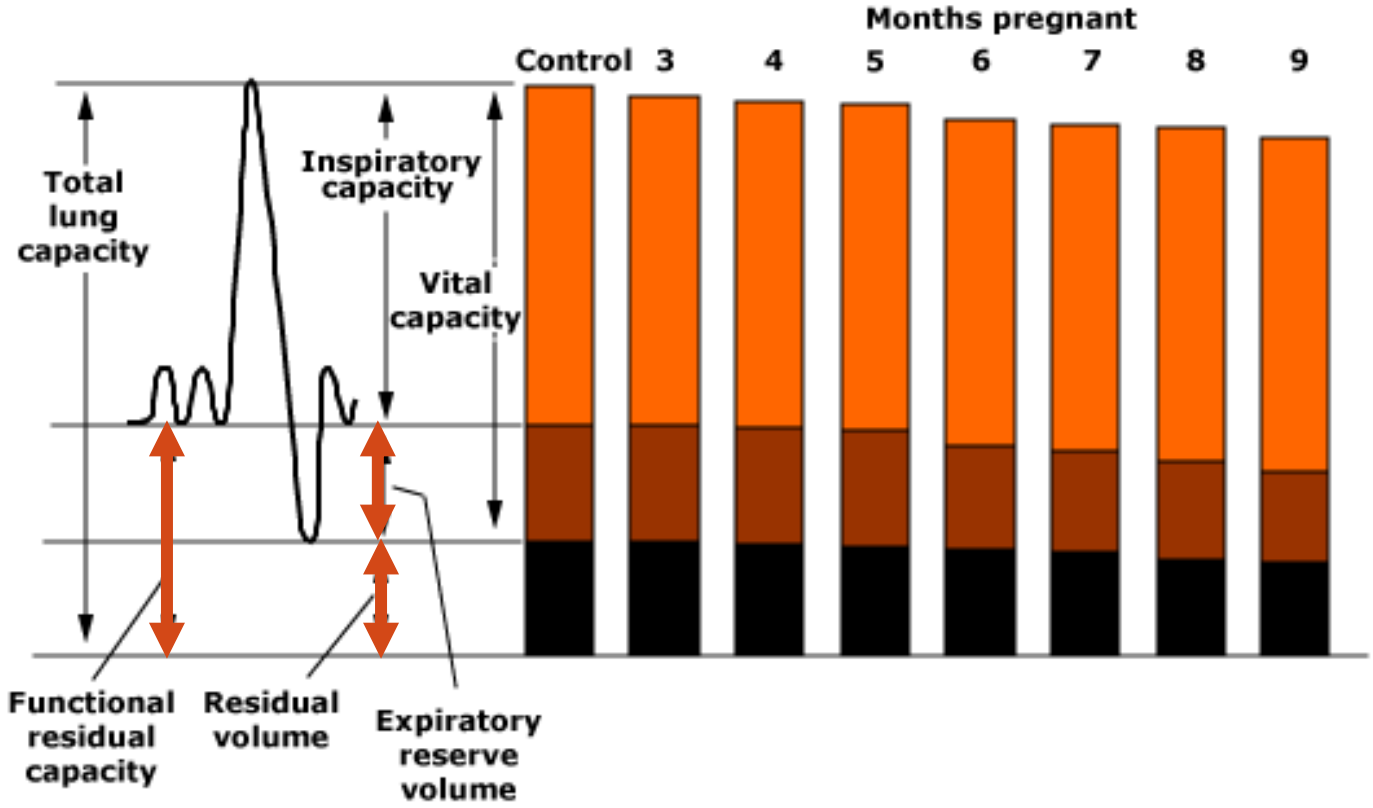
Lung volumes/flow

Functional residual capacity decreases

Due to decrease in both

- Residual volume
- Expiratory reserve volume

Function/flow are preserved = unchanged FEV1 + FEV1/FVC ratio

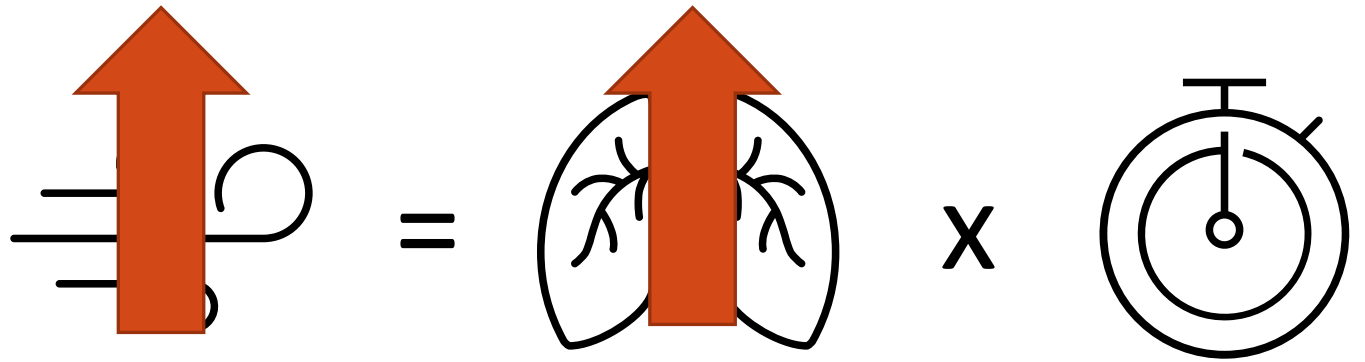


Ventilation

Minute ventilation increases by ~40-50% at term

Tidal volume increases

Respiratory rate stays same



Minute ventilation = Tidal volume x Respiratory rate

Tachypnea is NOT NORMAL in pregnancy

Diagnostics

Respiratory rate

Peak flow

ABG/ABG

Pulse oximetry

CXR

RPP

CBC w/diff

Procalcitonin

D-dimer

VQ scan/CTA

RR, PEF, VBG/ABG

- Respiratory rate should be unchanged
- Flow rates are relatively unchanged in pregnancy
  - FEV1 is generally not affected by pregnancy
  - Peak expiratory flow rates are unchanged
- Ventilation exceeds metabolic requirements

↑ ↓ ↑

pH / PaCO2 / PaO2

primary respiratory alkalosis
7.40-7.47 /28-34 / 100-110

Powrie et al. Medical Disorders in Obstetric Practice. 5th ed. 2010. pp 1-10

Diagnostics

Respiratory rate

Peak flow

ABG/ABG

Pulse oximetry

CXR

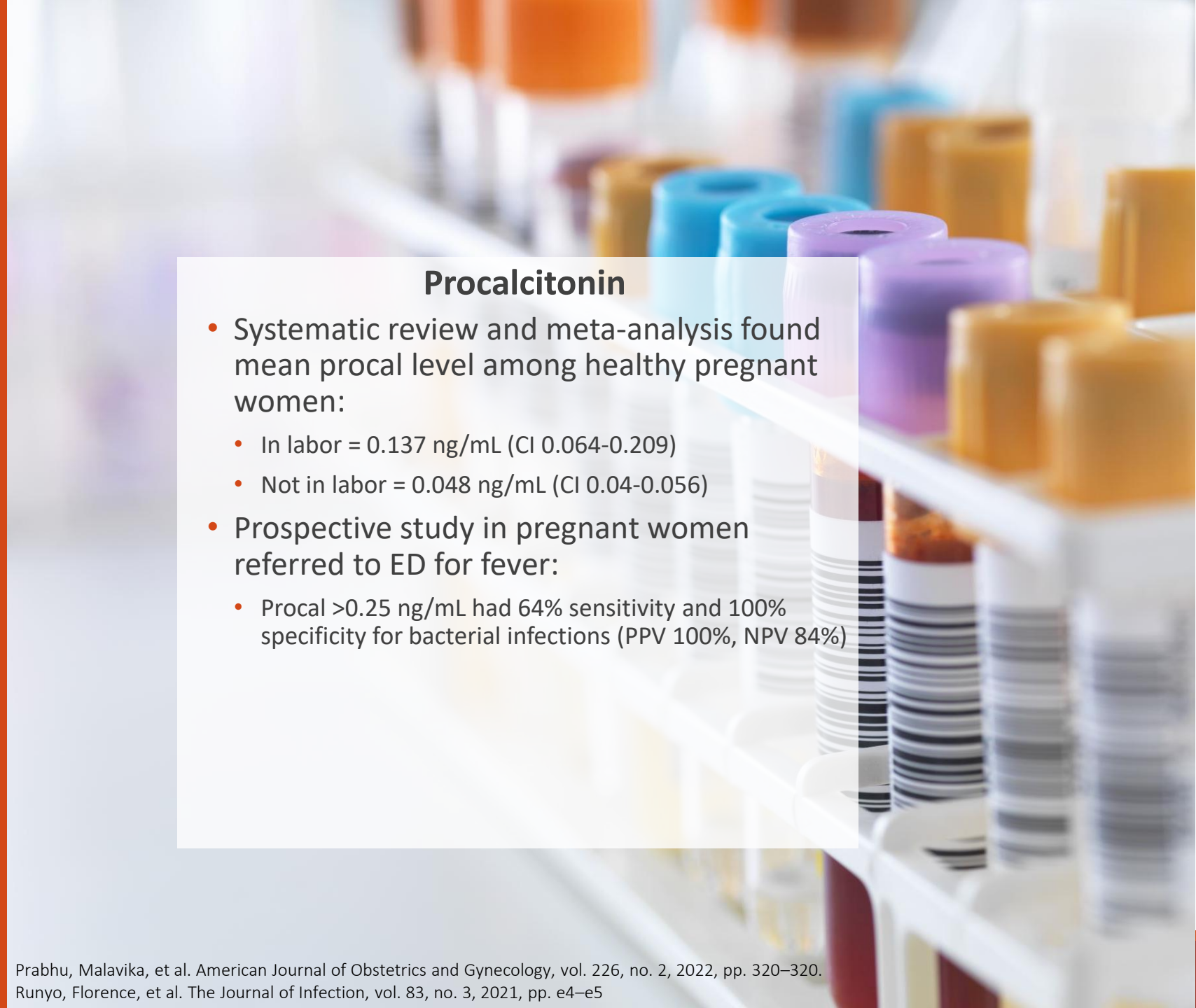
RPP

CBC w/diff

Procalcitonin

D-dimer

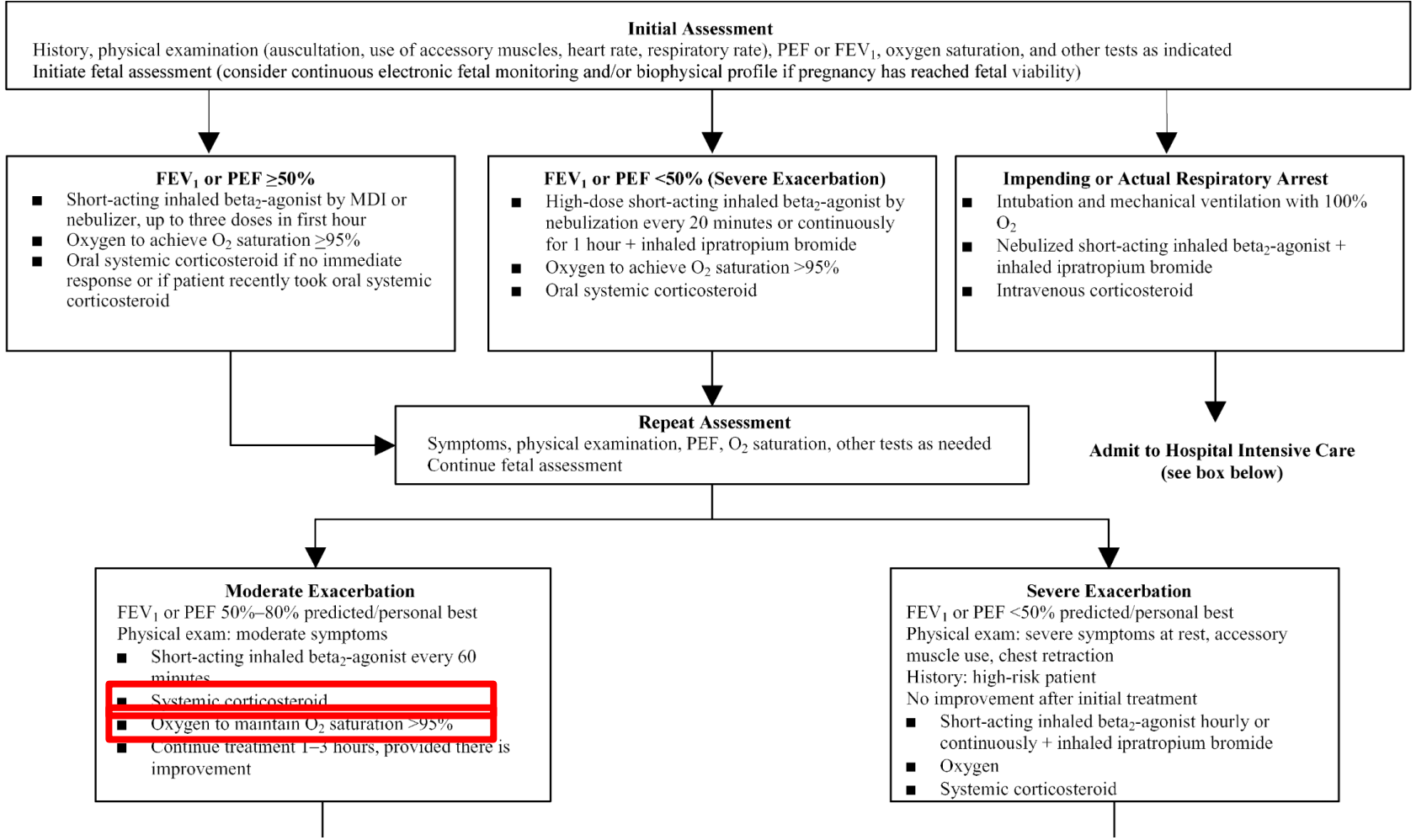
VQ scan/CTA



Procalcitonin

- Systematic review and meta-analysis found mean procal level among healthy pregnant women:
  - In labor = 0.137 ng/mL (CI 0.064-0.209)
  - Not in labor = 0.048 ng/mL (CI 0.04-0.056)
- Prospective study in pregnant women referred to ED for fever:
  - Procal >0.25 ng/mL had 64% sensitivity and 100% specificity for bacterial infections (PPV 100%, NPV 84%)

Prabhu, Malavika, et al. American Journal of Obstetrics and Gynecology, vol. 226, no. 2, 2022, pp. 320–320.
Runyo, Florence, et al. The Journal of Infection, vol. 83, no. 3, 2021, pp. e4–e5



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NAEPP guidelines for acute exacerbation management in pregnancy

Can you use steroids in pregnancy?

You may have read about fetal risks

- IUGR
- HPA axis suppression
- Premature rupture of membranes
- Orofacial clefts

You may be considering maternal risks

- Hyperglycemia
- Hypertension
- HPA axis suppression
- Infection
- Behavioral effects
- Dermatologic effects (striae gravidarum)
- Osteoporosis

TERATOLOGY 62:385–392 (2000)

RESEA

Corticosteroi

Anders Hviid MSc DM

Competing interests: None declared.

This article has been peer reviewed.

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CMAJ 2011. DOI:10.1503/cmaj.101063

OBSTETRICS

Maternal

Suzan L. Carmichae
Edward J. Lammer,

OBJECTIVE: The purp
nal corticosteroid use
an infant with an orof

STUDY DESIGN: This
tional Birth Defects F
case-control study. E
for mothers of 1141 c
cleft palate (CP), and

RESULTS: Mothers of
with CP (1.0%), and

Cite this article as: Carm

Corticosteroids
are a class of n
antiinflammatory
pressive properties
ful in the treatment
including asthma,
allergic reactions, a
methylprednisolon
mended as an alter
hyperemesis gravi
pregnancy.[1] Cortic
riety of malformati
ent animal models
clusion of a review
were published in 1

From the March of D
Birth Defects Monito
Slone Epidemiology
Center on Birth Defe
Prevention, Atlanta,
Institute, Oakland, C

nancy. Corticosteroid use
been associated with orc
mals, and similar risks
pected.[2] The available epidemiologic evidence

Corticosteroid Use and Risk of Orofacial Clefts

Hildur Skuladottir*[1,2], Allen J. Wilcox[3], Chen Ma[4], Edward J. Lammer[5], Sonja A. Rasmussen[6], Martha M. Werler[7], Gary M. Shaw[4], and Suzan L. Carmichael[4]

Background: Maternal use of corticosteroids during early pregnancy has been inconsistently associated with orofacial clefts in the offspring. A previous report from the National Bi
from 1997 to 2002, found
1.7; 95% confidence inter
ratio, 0.5, 95%CI, 0.2–1.3)
than doubled in size, and
more recent data. Methods
based case-control study o
controls born since 1997.
orofacial clefts using data f
2003 to 2009. Maternal co
interviews. Results: The ov
palate in the new data was 1.0 (95% CI, 0.7–1.4). There was little evidence of associations between specific corticosteroid components or timing and
om the NBDPS, the
corticosteroid use
cal and Molecular
roids; birth defects;

- Overall association of corticosteroids and cleft lip and palate was **1.0 (95% CI, 0.7-1.4)**
- Little evidence of associations between **specific corticosteroid components or timing** and clefts

Introduction

Orofacial clefts are one of the most common birth defects in humans, with a world birth prevalence of 1.7 per 1000 live births (Mossey et al., 2009). Orofacial clefts occur when the fusion of the lip and/or palate, which takes place during the first-trimester of pregnancy, is disrupted (Dixon et al., 2011). Corticosteroids are well-established as an experimental teratogen in animal models, causing cleft palate in mice (Fraser and Fainstat, 1951; Walker and

and Mølgaard-Nielsen, 2011).

The anti-inflammatory and immune modulating functions of corticosteroids are effective in the treatment of conditions such as asthma, allergic reactions, eczema, psoriasis, rheumatoid arthritis, and inflammatory bowel disease. These conditions are common and often affect women of reproductive age; however, the safety of corticosteroid medication during pregnancy is uncertain.

malformations, but the majority is isolated, nonsyndromic. Nu-

MATERIALS AND METHODS

re to
Study
l Studies

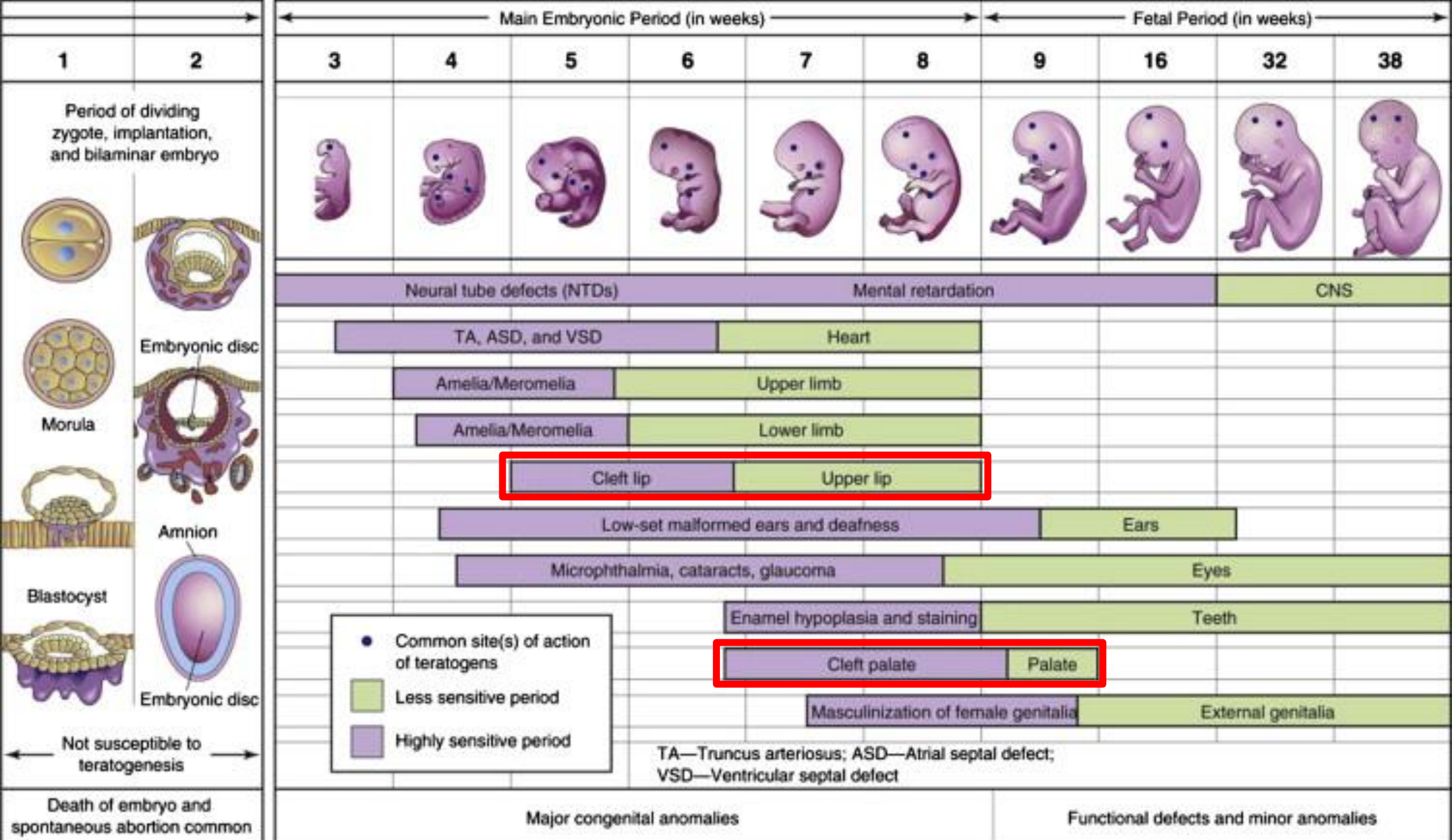
E. MORETTI,[2]
ACOBSON,[2]
YAT,[4]

stitute, Hospital
search and

RODUCTION

orticoid used in the treatment of
on, collagen vascular, and other
own to cross the human placenta
Beitins et al., '72; Levitz et al.,
Crowley et al., '95). Large doses
nt mice, rats and rabbits during
used cleft palate in the exposed
64; Pinsky and DiGeorge, '65;
e same teratogenic effect on the
bserved in mice given the natu-
orticoid, cortisone (Baxter and

from animals to humans is ten-
eports, women were treated dur-
with prednisone for a plethora of
dgkin's disease (Schilsky et al.,
n and Kaplan, '62; Dara et al.,
tion (Nolan et al., '74; Coulam et
t al., '93), systemic lupus ery-
man et al., '80; Jones et al., '86),
bodies (Tabbutt et al., '94),
et al., '86), rheumatoid arthritis
gional enteritis (Kraus, '75), glo-


Main Embryonic Period (in weeks)
Fetal Period (in weeks)
1
2
3
4
5
6
7
8
9
16
32
38
Period of dividing zygote, implantation, and bilaminar embryo
Morula
Blastocyst
Embryonic disc
Amnion
Embryonic disc
Neural tube defects (NTDs)
Mental retardation
CNS
TA, ASD, and VSD
Heart
Amelia/Meromelia
Upper limb
Amelia/Meromelia
Lower limb
Cleft lip
Upper lip
Low-set malformed ears and deafness
Ears
Microphthalmia, cataracts, glaucoma
Eyes
Enamel hypoplasia and staining
Teeth
Cleft palate
Palate
Masculinization of female genitalia
External genitalia
Common site(s) of action of teratogens
Less sensitive period
Highly sensitive period
TA—Truncus arteriosus; ASD—Atrial septal defect;
VSD—Ventricular septal defect
Not susceptible to teratogenesis
Death of embryo and spontaneous abortion common
Major congenital anomalies
Functional defects and minor anomalies

Can you use steroids in pregnancy?

You may have read about fetal risks

You may be considering maternal risks

YES

RISK UNCONTROLLED ASTHMA >>> RISK OF STEROIDS

- Dermatologic effects (striae gravidarum)
- Osteoporosis

salmeterol

budesonide

What are the preferred inhaled agents in pregnancy?

Asthma Severity	Symptoms	PEF (% of Personal Best) or FEV_1 (% Predicted)	Drug Class	Comments
Mild intermittent	≤ 2 d/wk or ≤ 2 nights/mo	≥ 80%	SABA	Use as rescue therapy in all categories of asthma Most safety data available for albuterol
Mild persistent	3-6 d/wk or ≥ 3 nights/mo	≥ 80%	Low-dose ICS	Most safety data available for budesonide, but no evidence that other ICS are less safe or efficacious
Moderate persistent	Intermittent daily or ≥ 4 nights/mo	61%-79%	Medium-dose ICS or ICS/ LABA combination	Increasing ICS dose vs adding LABA to ICS has been shown to be equally safe LABA should not be used as monotherapy Most safety data available for salmeterol, but no evidence that other LABA are less safe or efficacious
Severe persistent	Continuous daily or nightly	≤ 60%	High-dose ICS/ LABA Oral steroid if needed	Chronic oral steroids should be administered at the lowest dose and for the shortest period needed, particularly in the first trimester

A brief word on treatment

(Bonham et al, 2017)

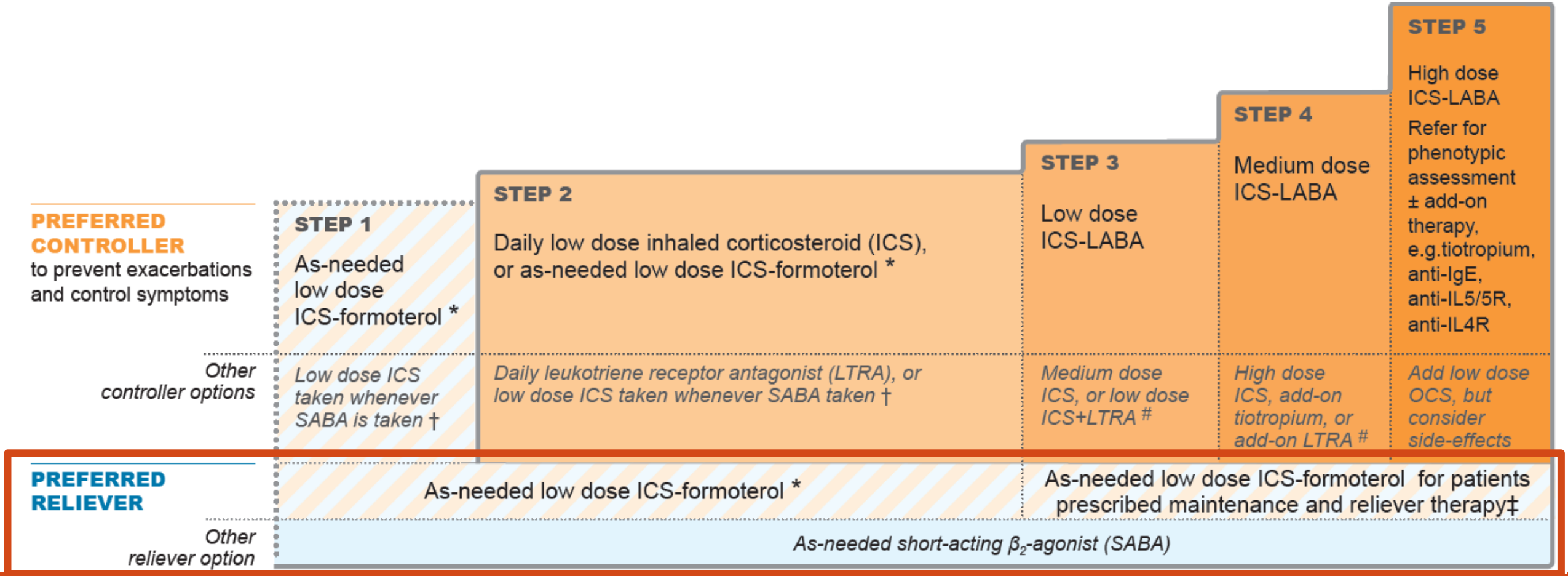
WHATEVER INSURANCE WILL COVER

salmeterol

budesonide

What are the preferred inhaled agents in pregnancy?

GINA strategy, updated 2020



WARNING: SERIOUS NEUROPSYCHIATRIC EVENTS

See full prescribing information for complete boxed warning.

- **Serious neuropsychiatric events have been reported in patients taking SINGULAIR (5.1).**
- **Discuss benefits and risks of SINGULAIR with patients and caregivers (5.1).**
- **Monitor for neuropsychiatric symptoms in patients taking SINGULAIR (5.1).**
- **Discontinue SINGULAIR immediately if neuropsychiatric symptoms occur (5.1).**
- **Because the benefits of SINGULAIR may not outweigh the potential risk of neuropsychiatric symptoms in patients with allergic rhinitis, reserve use for patients who have an inadequate response or intolerance to alternative therapies (1.3, 5.1).**

mately 4 to 8% of pregnant women carry a diagnosis of Rocklin, 2011; Namazy and Schatz, 2011). Some studies

What about LTRAs in pregnancy?

Pregnancy outcomes in the omalizumab pregnancy registry and a disease-matched comparator cohort

Jennifer A. Namazy, MD, FAAAAI,[a] Lucie Blais, PhD,[b] Elizabeth B. Andrews, PhD, MPH, FISPE,[c] Angela E. Scheuerle, MD,[d] Michael D. Cabana, MD, MPH,[e] John M. Thorp, MD,[f] Dale T. Umetsu, MD, PhD, FAAAAI,[g] Joachim H. Veith, MD, MS,[g] Diana Sun, PhD,[g] Derrick G. Kaufman, PhD, MS,[g] Deborah L. Covington, DrPH, FISPE,[h] Santanu Mukhopadhyay, MD,[i] Robert B. Fogel, MD,[j] Sandra Lopez-Leon, MD, PhD,[j] and C. Victor Spain, DVM, PhD[g]

San Diego, San Francisco, and South San Francisco, Calif; Montreal, Quebec, Canada; Research Triangle Park, Chapel Hill, and Wilmington, NC; Dallas, Tex; Basel, Switzerland; and East Hanover, NJ

Background: The Observational Study of the Use and Safety of Xolair (omalizumab) during Pregnancy (EXPECT) pregnancy registry was a prospective observational study established in 2006 to evaluate perinatal outcomes in pregnant women exposed to omalizumab and their infants.

Objective: This analysis compares EXPECT outcomes with those from a disease-matched population of pregnant women not treated with omalizumab. Data from a substudy of platelet counts among newborns are also presented.

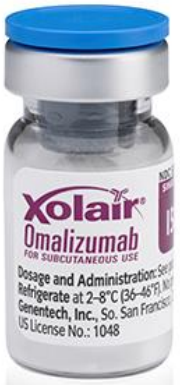
Methods: The EXPECT study enrolled 250 women with asthma exposed to omalizumab during pregnancy. The disease-matched external comparator cohort of women with moderate-to-severe asthma (n = 1153), termed the Quebec External Comparator Cohort (QECC), was created by using data from health care databases in Quebec, Canada. Outcome estimates were age adjusted based on the maternal age distribution of the EXPECT study.

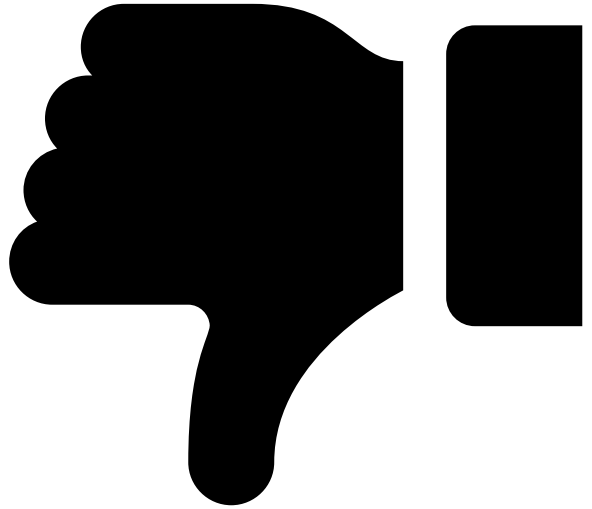
Results: Among singleton infants in the EXPECT study, the prevalence of major congenital anomalies was 8.1%, which was similar to the 8.9% seen in the QECC. In the EXPECT study 99.1% of pregnancies resulted in live births, which was similar to 99.3% in the QECC. Premature birth was identified in 15.0%

From [a]Division of Allergy and Immunology, Scripps Clinic, San Diego; [b]Université de Montréal, Faculty of Pharmacy, Montreal; [c]RTI Health Solutions, RTI International, Research Triangle Park; [d]Department of Pediatrics, Division of Genetics and Metabolism, University of Texas Southwestern Medical Center, Dallas; [e]Division of General Pediatrics, Departments of Pediatrics, Epidemiology & Biostatistics, University of California, San Francisco, San Francisco; [f]Department of Obstetrics and Gynecology, University of North Carolina School of Medicine, Chapel Hill; [g]Genentech, South San Francisco; [h]Real World Evidence, Evidera, Wilmington; [i]Novartis Pharma AG, Basel;

What about biologics in pregnancy?

Okay to continue





Do NOT start

What about biologics in pregnancy?

Asthma – key points

- FEV1 and PEF should be unchanged in pregnancy
- Pregnancy induces primary respiratory alkalosis, “normal” pCO_2 in exacerbation should be looked at critically
- Target SpO_2 is ≥95% in pregnancy
- Pregnancy alone does not increase procalcitonin or BNP
- Benefit >>> risk of systemic corticosteroid use in asthma exacerbation
- Prescribe the ICS/LABA covered by the patient’s insurance
- Montelukast and omalizumab may be used in pregnancy

Thank you! Questions?

https://redcap.link/OBIM

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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