Diagnosis of Venous Thromboembolism During Pregnancy & Postpartum

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Objectives

- **To review evidence-based strategies for diagnosing VTE during pregnancy and postpartum**
- **To understand why CT and V/Q imaging perform differently in pregnant and postpartum women compared to nonpregnant populations**
- **To feel comfortable counseling women regarding risks and benefits of CT and V/Q imaging during pregnancy and postpartum**

Case

- **38 yo G1 P0 @ 20 weeks with trichorionic triplets presents to the ED complaining of shortness of breath and pleuritic chest pain for the last hour.**

Case

- **This pregnancy was conceived via IVF after many failed cycles.**
- **The patient has significant anxiety related to this pregnancy, and has been on self-prescribed bedrest.**
- **No personal or family history of clotting.**

Case

- **Vitals: HR 120, BP 100/70, RR 30, SaO2 94% on room air**
- **Appears to be in mild distress**
- **Tachycardic on exam**
- **Lungs clear to auscultation bilaterally**
- **Mild symmetric lower extremity edema.**

Case

- **ED provider calls you for help.**
- **“I think she may have a PE. How do I work this up?”**

VTE during pregnancy and postpartum

- **Definition**
  - **VTE = DVT + PE**
- **Incidence**
  - **0.76 to 1.72 per 1000 pregnancies**
  - **4 times the risk of nonpregnant population**
  - **2/3 of DVTs occur antepartum**
    - **Distributed relatively equally among all 3 trimesters**
  - **43-60% of PEs occur postpartum**
  - **PE is leading cause of maternal death in developed countries**
    - **1.1 to 1.5 deaths per 100,000 deliveries in U.S. and Europe**
    - **Accounts for 1/3 of all maternal deaths in the U.K.**

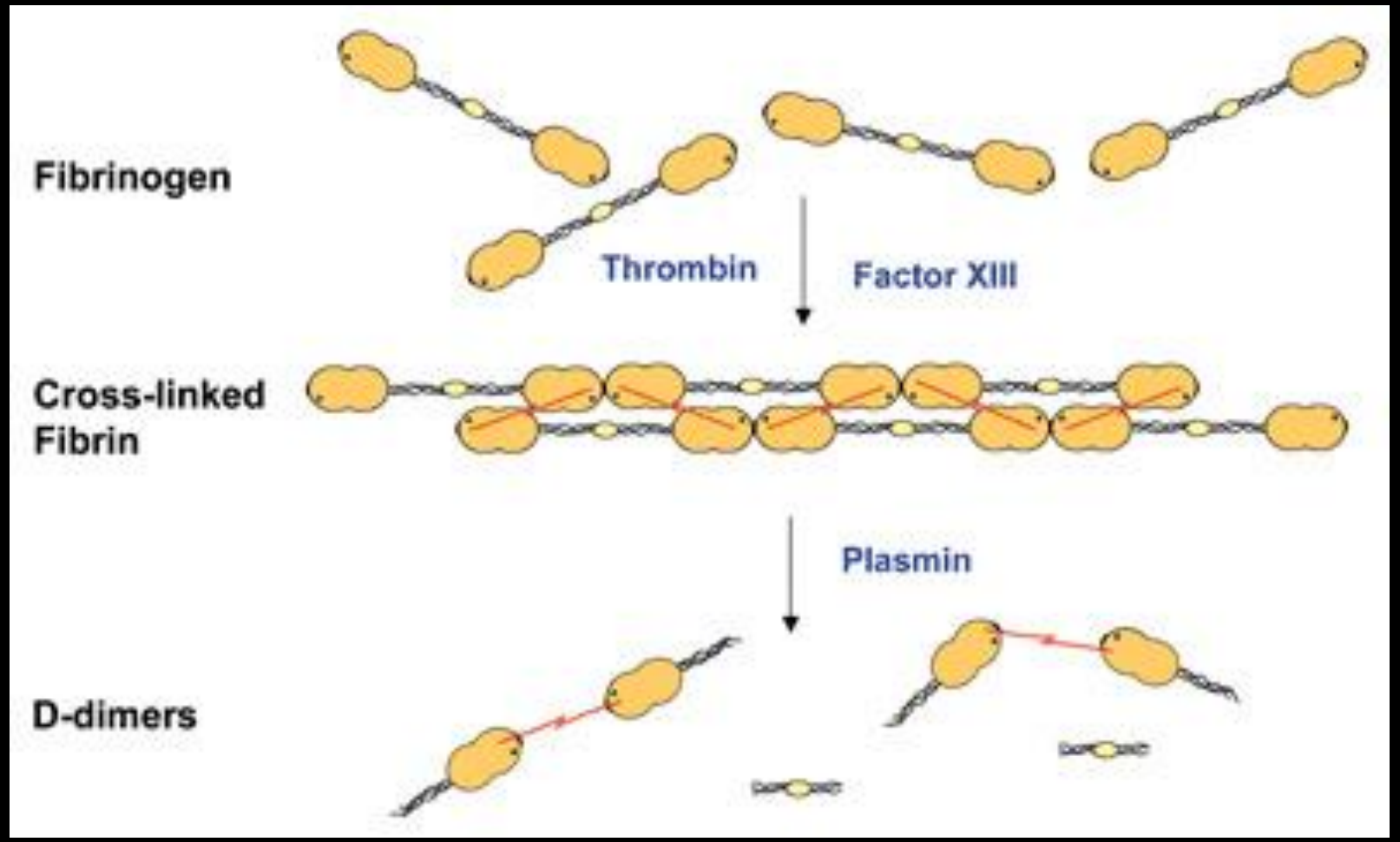
VTE during pregnancy and postpartum

- **Risk factors**
  - **History of VTE**
  - **Inherited or acquired thrombophilias**
  - **Black race**
  - **Heart disease**
  - **Sickle cell disease**
  - **Diabetes**
  - **Lupus**
  - **Smoking**
  - **Multiple gestation**
  - **Age >35 years**
  - **Obesity**
  - **Cesarean delivery (especially emergent during labor)**

VTE during pregnancy and postpartum

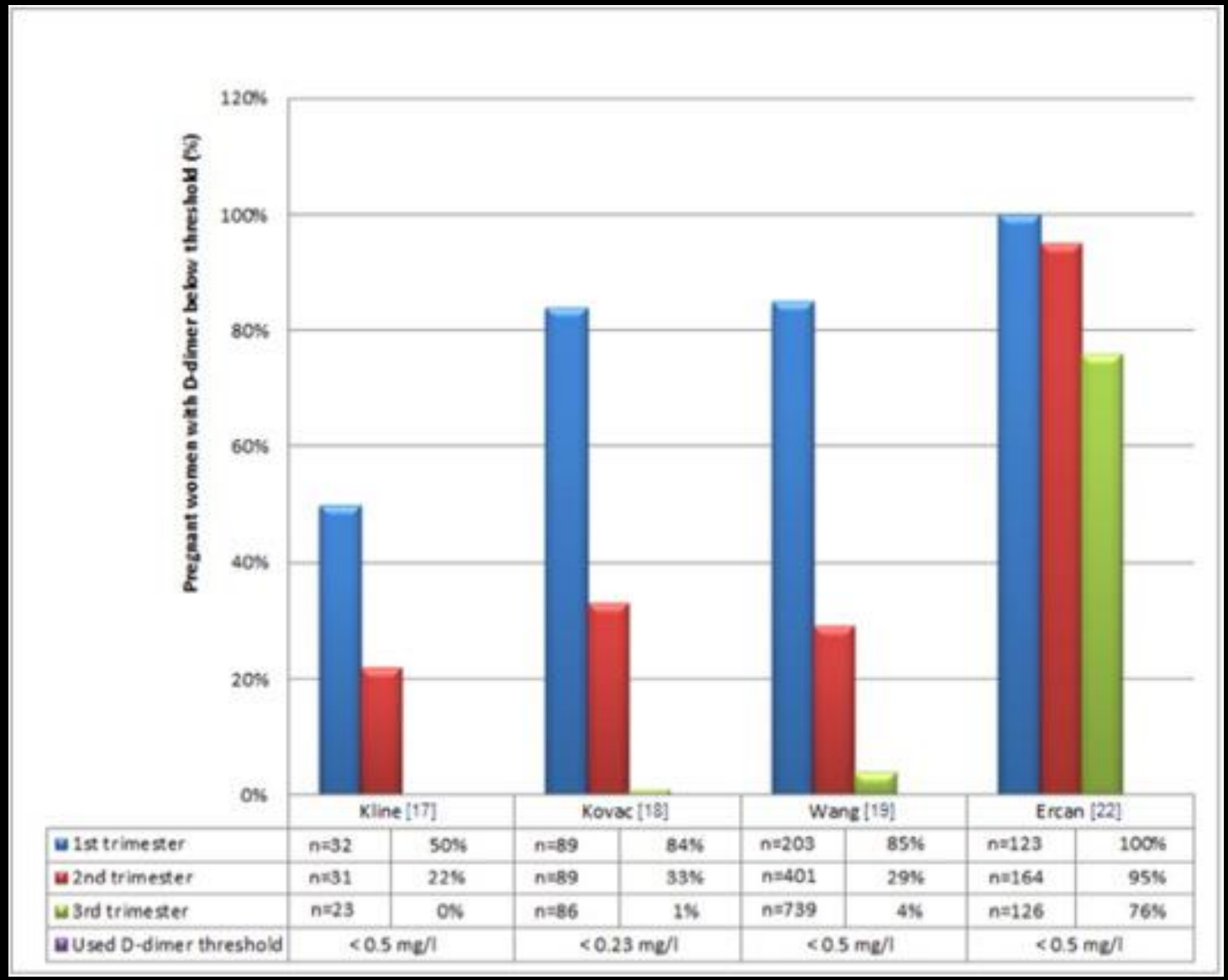
- **Classic signs/symptoms may be associated with normal pregnancy**
  - **Leg swelling**
  - **Tachycardia**
  - **Tachypnea**
  - **Dyspnea**
- **VTE confirmed in <10% of pregnant women in whom VTE suspected**
- **Objective testing should be performed expeditiously because of risk for sudden death**
- **Initiating treatment pending test results may be prudent**

D-dimer



https://www.labmedic.org/bs/strucni-radovi/530-3-dimer

D-dimer



	Kline [17]		Kovac [18]		Wang [19]		Ercan [22]	
1st trimester	n=32	50%	n=89	84%	n=203	85%	n=123	100%
2nd trimester	n=31	22%	n=89	33%	n=401	29%	n=164	95%
3rd trimester	n=23	0%	n=86	1%	n=739	4%	n=126	76%
Used D-dimer threshold	< 0.5 mg/l		< 0.23 mg/l		< 0.5 mg/l		< 0.5 mg/l	

Van der Pol et al. Blood Reviews 2016.

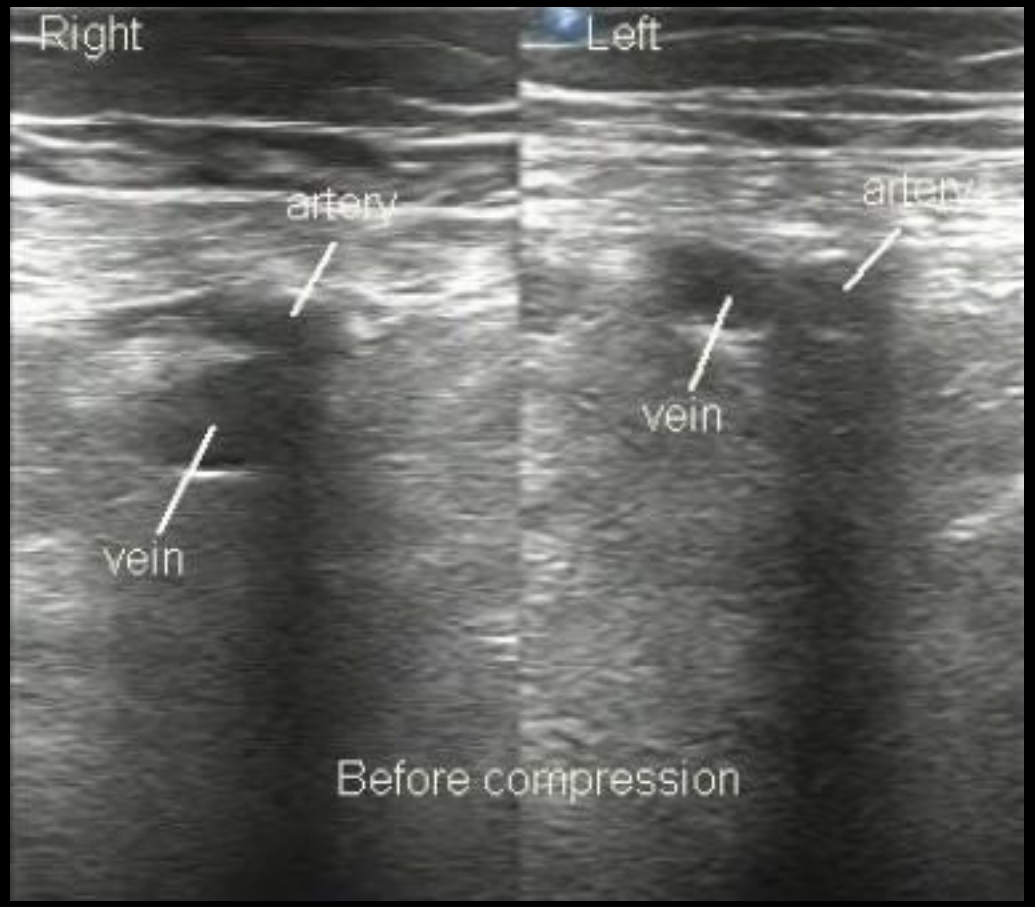
D-dimer

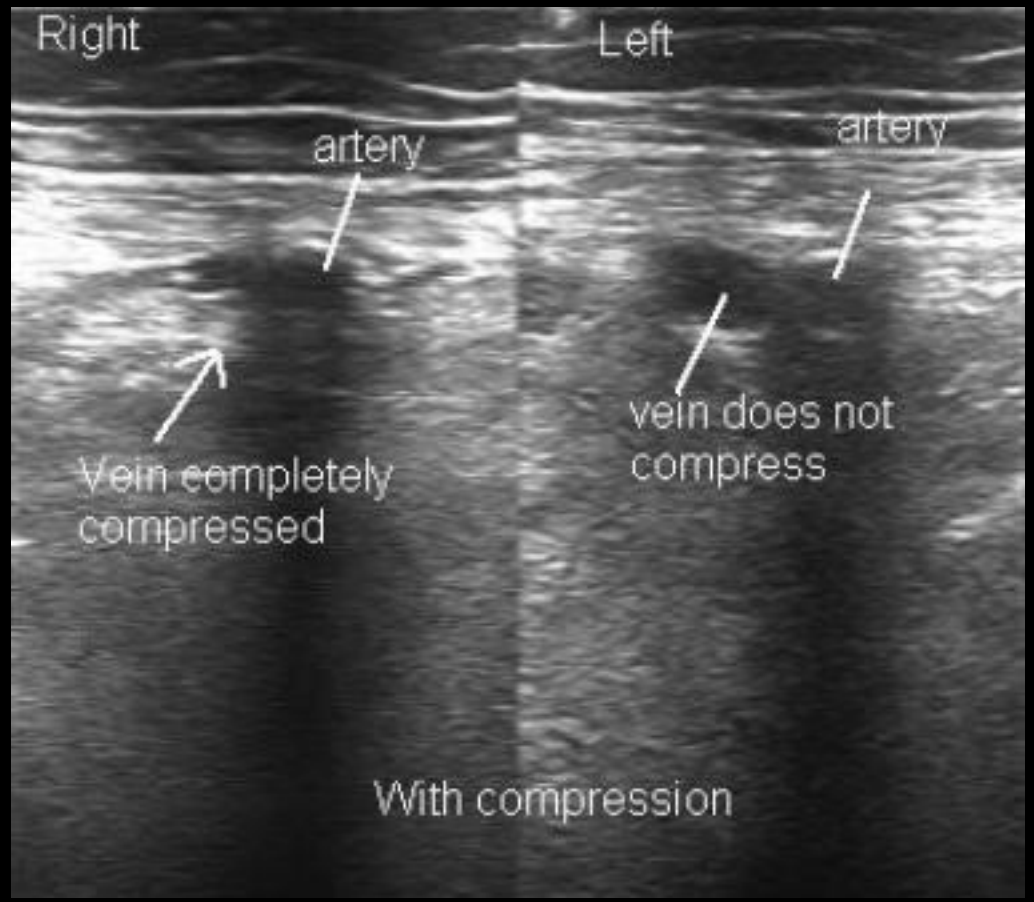
- Increases with advancing gestational age
- Relative increase with multiple gestation
- A negative result may spare a pregnant woman expensive imaging studies and radiation exposure (negative predictive value 100%)
- Cost analysis would be helpful
  - Would perform a lot of relatively cheap blood tests to avoid obtaining one relatively expensive imaging study

Compression ultrasonography

- **Noninvasive, no radiation, risk-free**
- **97% sensitivity, 94% specificity in the general population with symptomatic, proximal DVT**
  - **Less accurate for isolated calf and iliac vein DVTs**
- **Recommended in women with signs/symptoms of lower extremity DVT**
- **Consider in women with suspected PE and no signs/symptoms of lower extremity DVT**
  - **30% of apparently isolated PEs associated with “silent” DVT**

Compression ultrasonography





Emedicine.medscape.com/article/1362989-overview

Chest imaging

- **Plain film**
- **Computed tomography (CT)**
- **Ventilation/perfusion (V/Q, scintigraphy)**
- **All require use of ionizing radiation**

Radiation exposure

Table 2. Effects of Gestational Age and Radiation Dose on Radiation-Induced Teratogenesis

Gestational Period	Effects	Estimated Threshold Dose*
Before implantation (0–2 weeks after conception)	Death of embryo or no consequence (all or none)	50–100 mGy
Organogenesis (2–8 weeks after conception)	Congenital anomalies (skeleton, eyes, genitals)	200 mGy
	Growth restriction	200–250 mGy
Fetal period	**Effects**	**Estimated Threshold Dose***
8–15 weeks	Severe intellectual disability (high risk)†	60–310 mGy
	Intellectual deficit	25 IQ-point loss per 1,000 mGy
	Microcephaly	200 mGy
16–25 weeks	Severe intellectual disability (low risk)	250–280 mGy*

*Data based on results of animal studies, epidemiologic studies of survivors of the atomic bombings in Japan, and studies of groups exposed to radiation for medical reasons (eg, radiation therapy for carcinoma of the uterus).

†Because this is a period of rapid neuronal development and migration.

Reprinted from Patel SJ, Reede DL, Katz DS, Subramaniam R, Amorosa JK. Imaging the pregnant patient for nonobstetric conditions: algorithms and radiation dose considerations. Radiographics 2007;27:1705–22.

ACOG CO 656. Guidelines for diagnostic imaging during pregnancy and lactation. 2016.

Radiation exposure

Table 3. Fetal Radiation Doses Associated With Common Radiologic Examinations

Type of Examination	Fetal Dose* (mGy)
Very low-dose examinations (<0.1 mGy)	
Cervical spine radiography (anteroposterior and lateral views)	<0.001
Radiography of any extremity	<0.001
Mammography (two views)	0.001–0.01
Chest radiography (two views)	0.0005–0.01
Low- to moderate-dose examinations (0.1–10 mGy)	
Radiography	
Abdominal radiography	0.1–3.0
Lumbar spine radiography	1.0–10
Intravenous pyelography	5–10
Double-contrast barium enema	1.0–20
CT	
Head or neck CT	1.0–10
Chest CT or CT pulmonary angiography	0.01–0.66
Limited CT pelvimetry (single axial section through the femoral heads)	<1
Nuclear medicine	
Low-dose perfusion scintigraphy	0.1–0.5
Technetium-99m bone scintigraphy	4–5
Pulmonary digital subtraction angiography	0.5
Higher-dose examinations (10–50 mGy)	
Abdominal CT	1.3–35
Pelvic CT	10–50
^{18}F PET/CT whole-body scintigraphy	10–50

Abbreviations: CT, computed tomography; PET, positron emission tomography.

*Fetal exposure varies with gestational age, maternal body habitus, and exact acquisition parameters.

Note: Annual average background radiation = 1.1–2.5 mGy, ^{18}F = 2-[fluorine-18]fluoro-2-deoxy-D-glucose.

Reprinted from Tremblay E, Therasse E, Thomassin-Naggara I, Trop I. Quality initiatives: guidelines for use of medical imaging during pregnancy and lactation. Radiographics 2012;32:897–911.

ACOG CO 656. Guidelines for diagnostic imaging during pregnancy and lactation. 2016.

Radiation exposure

"With few exceptions, radiation exposure through radiography, computed tomography scan, or nuclear medicine imaging techniques is at a dose much lower than the exposure associated with fetal harm. If these techniques are necessary in addition to ultrasonography or magnetic resonance imaging or are more readily available for the diagnosis in question, they should not be withheld from a pregnant patient."

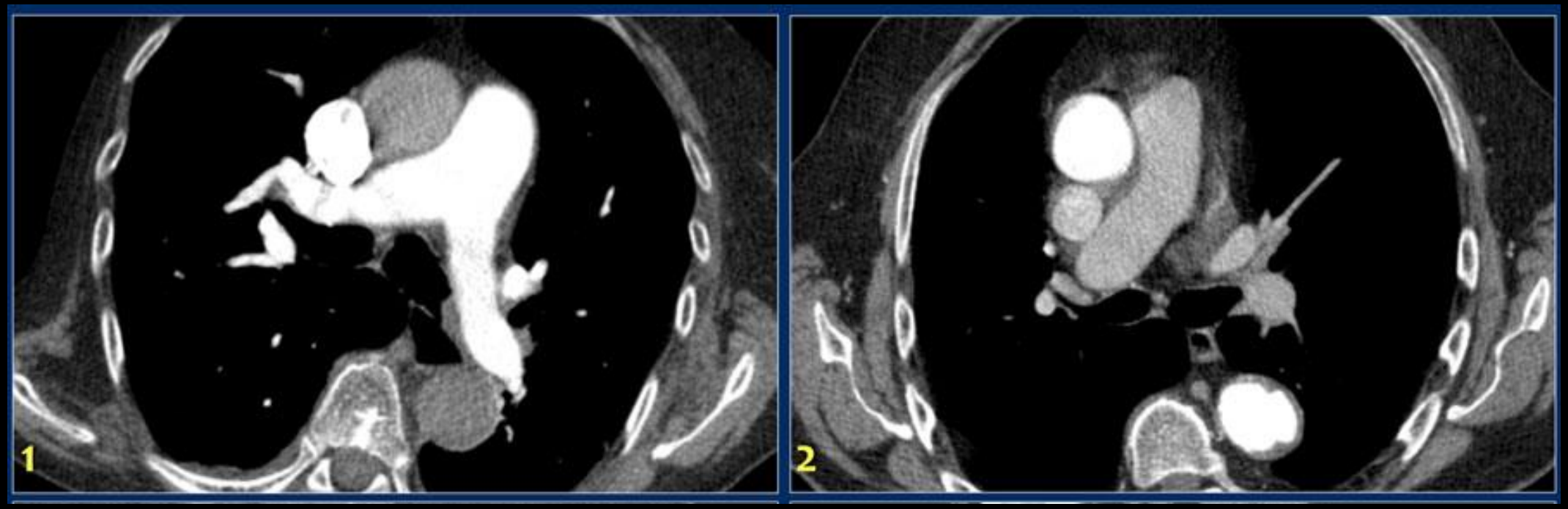
-ACOG

ACOG CO 656. Guidelines for diagnostic imaging during pregnancy and lactation. 2016.

Computed tomography

- **Test of choice for imaging pulmonary vasculature in nonpregnant population**
- **Involves injection of iodinated contrast into a peripheral vein, then timing the scan so that contrast is passing through the pulmonary arteries while images are obtained**
- **The quality of CT depends on good contrast delivery and PERFECT TIMING**
  - **Frequently poor quality in young patients, ESPECIALLY PREGNANT WOMEN, because high cardiac output results in dilution of contrast and poor enhancement**

Computed tomography



1. Optimal contrast timing.

2. Too late!

www.radiologyassistant.nl/en/p52c04470dbd5c/ct-contrast-injection-and-protocols.html

Computed tomography

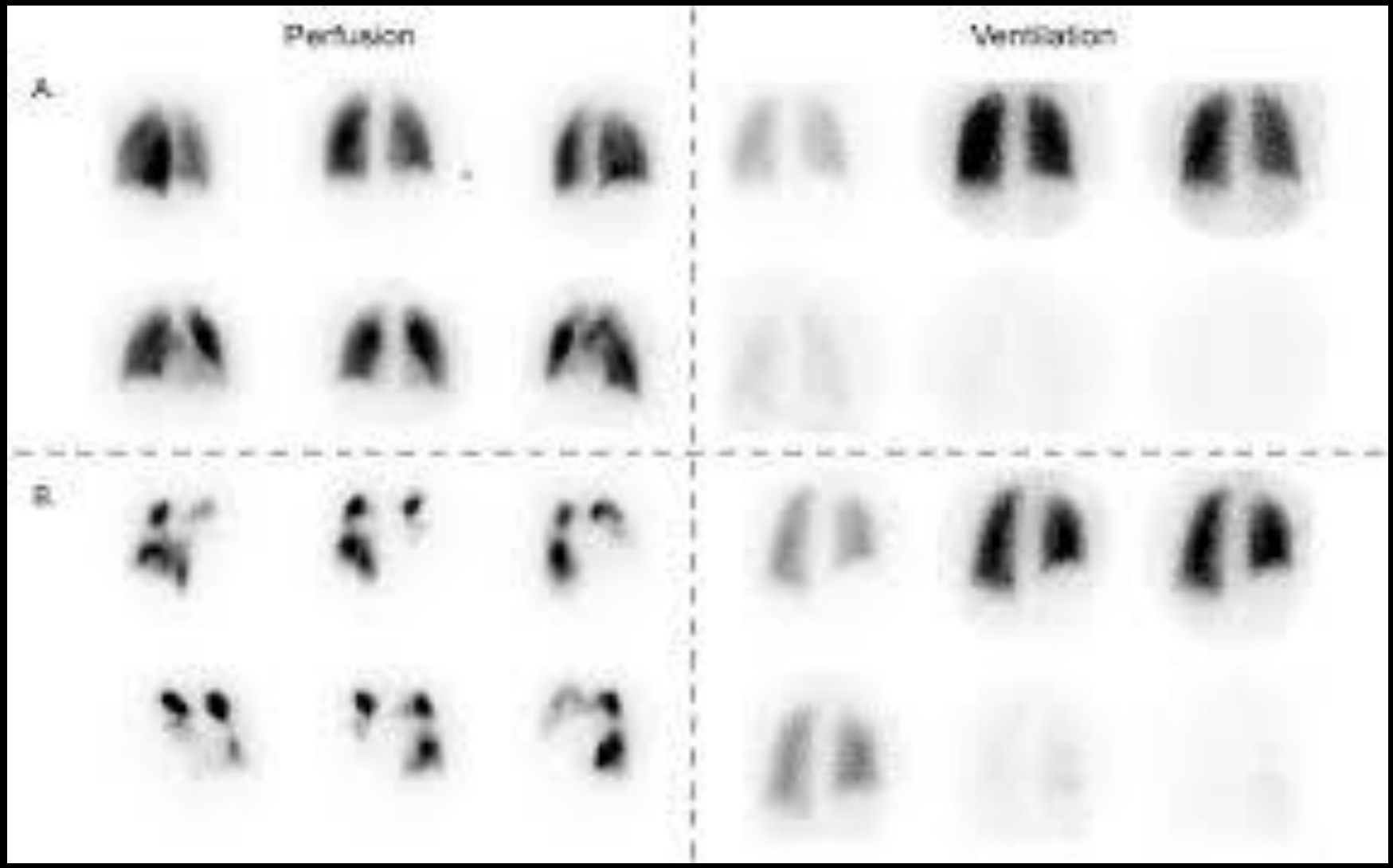
- **Modified protocol in pregnancy can improve adequacy of study from 64% to 90%**
- **Modifications include**
  - **Shallow inspiration breath-hold**
  - **High concentration/high rate of injection**
  - **High volume of contrast material**

Ridge CA et al. AJR 2011.

Ventilation/perfusion

- **Performs poorly in nonpregnant population**
- **Involves injection of radiolabeled chemical into maternal vein and inhalation of radiolabeled gas into maternal airway, then comparing distribution of radioisotope via ventilation and perfusion to look for a mismatch**
  - **Technetium 99m**
  - **Perfusion-only imaging can lower fetal radiation dose**
- **Adequacy of study adversely affected by respiratory comorbidities, which are relatively uncommon in pregnant population**
  - **V/Q MAY OUTPERFORM CT IN PREGNANT WOMEN as long as a chest X-ray is normal**

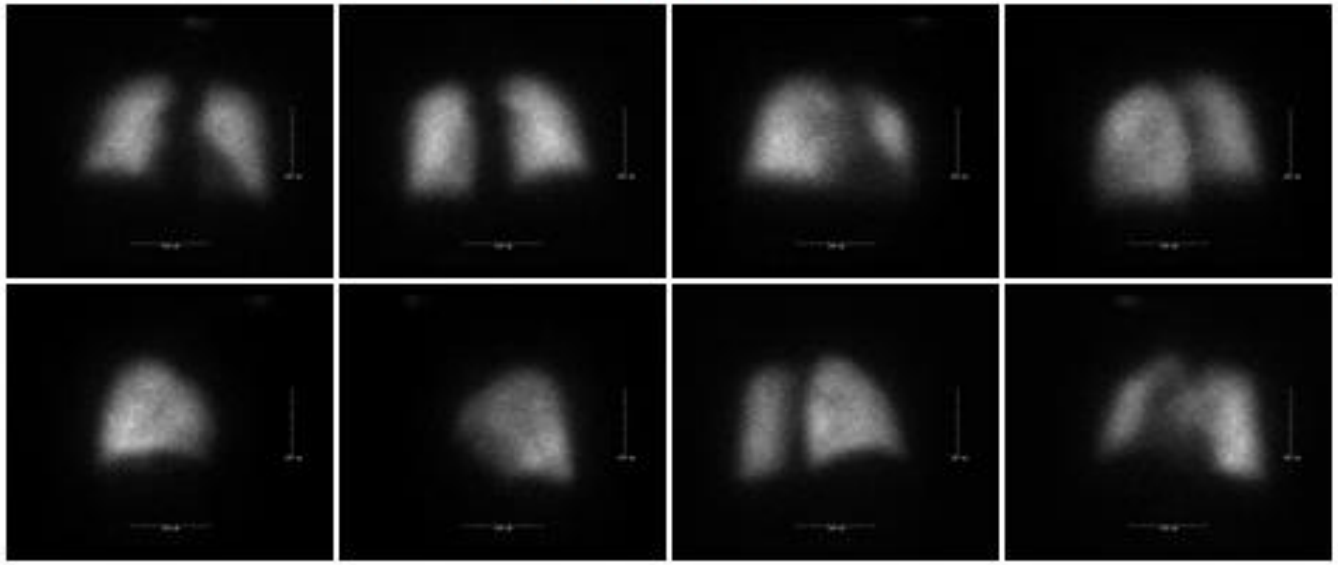
Ventilation/perfusion



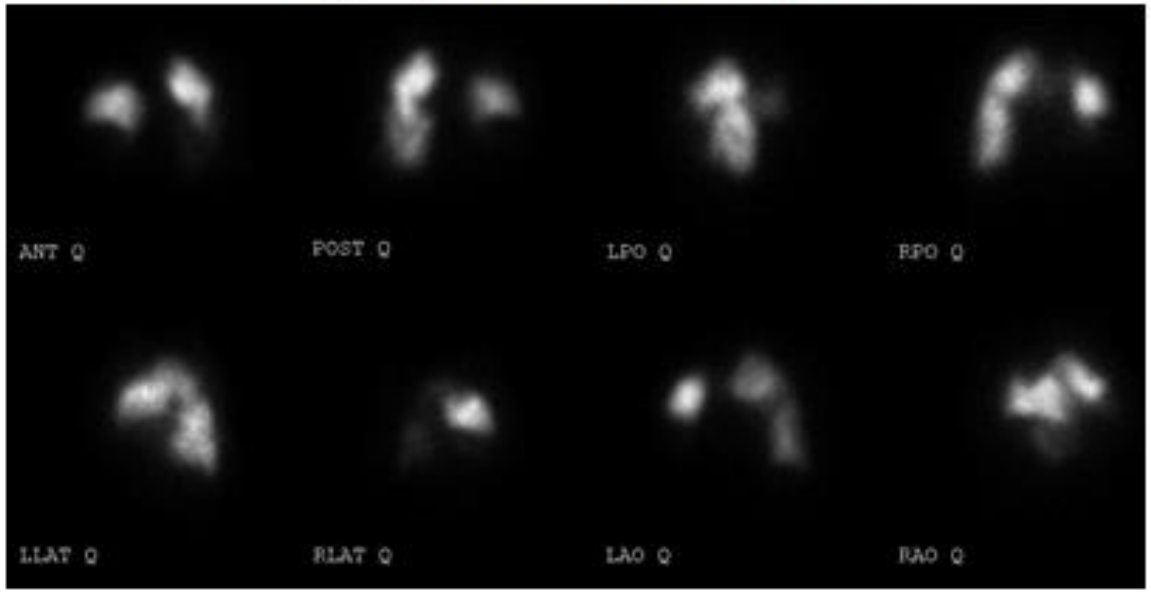
www.radiology.umn.edu/sites/radiology.umn.edu/files

Perfusion-only imaging

Normal



Large perfusion defects



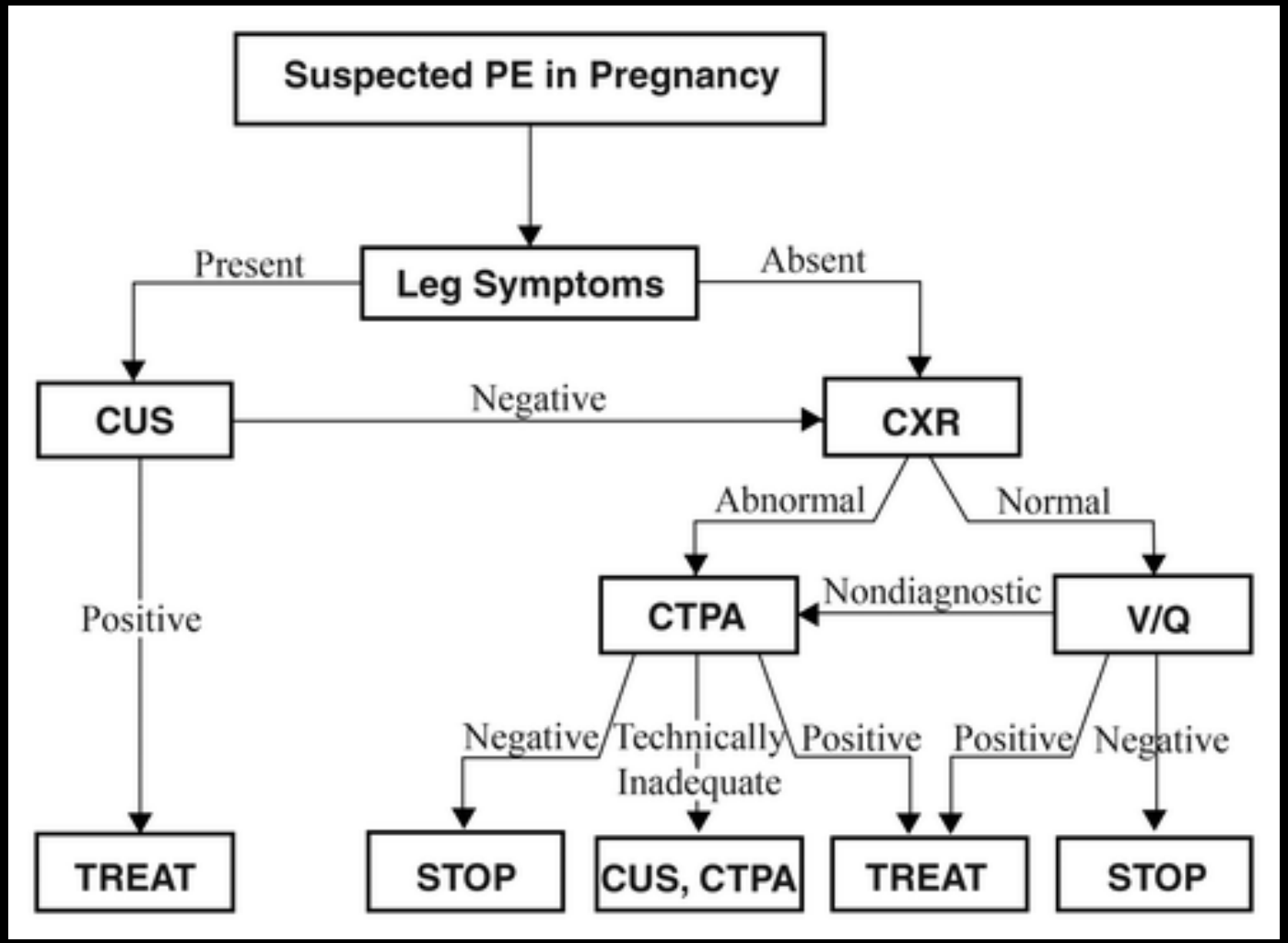
Hcp.cteph.com/diagnosis/v-q-scan

CT vs V/Q

Characteristic	CT	V/Q
Nondiagnostic rate	6%	4%
Maternal radiation dose	2.2-6.0 mSv	1.4 mSv
Radiation-related maternal breast cancer risk	13% increase (1 in 8 baseline risk)	No increase (1 in 8 baseline risk)
Fetal radiation dose	3-131 uGy	640-800 uGy
Radiation-related childhood cancer risk	<1 in 1 million	1 in 280,000
Breastfeeding	No interruption	May recommend interruption for 6 hours

Cochrane Review 2017.
Marik & Plante. NEJM 2009.
Toxnet.nlm.nih.gov.

Published algorithm



American Thoracic Society/Society of Thoracic Radiology. Radiology 2012.
Cahill et al. Obstet Gynecol 2009.

Summary

- **Role of D-dimer in evaluation of pregnant and postpartum women is unclear (cost analysis)**
- **Compression ultrasonography recommended if clinical concern for DVT, but negative result does not exclude possibility of clot (pelvis)**
- **Can also consider compression ultrasonography if clinical concern for PE but not DVT (30% incidence of “silent” DVT)**
- **V/Q performs better in pregnant and postpartum women than in nonpregnant populations, and has a lower nondiagnostic rate than CT**
- **Tradeoffs in risk for radiation-associated cancers for mother and child with CT and V/Q**

Case

- **I would start with a CXR**
- **If normal, consider V/Q**
  - **Talk to the radiologist at your institution before ordering an exam**
- **If abnormal, proceed with CT**
- **Consider a standardized protocol agreed upon by obstetricians and radiologists to improve efficiency**

Questions?