

Thromboembolic Diseases in Pregnancy and Puerperium

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Raoul, the first case of deep vein thrombosis
(1271)



DVT: History

- During Renaissance, popular belief was-
 - Pregnancy related DVT was due to retention of 'evil humors'
 - Postpartum DVT was caused by retention of unconsumed milk in the legs ('milk leg')
- Popular treatment of DVT: To discharge evil humors by bloodletting

Introduction

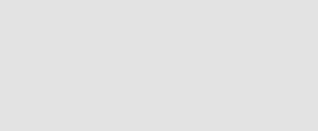
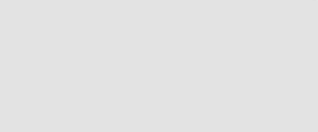
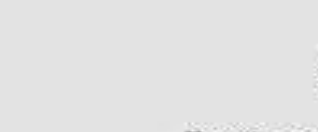
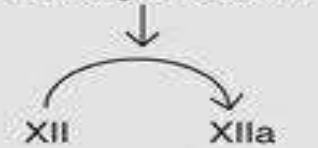
- Pregnancy or postpartum period is thrombophilic
- 4-5 fold increased risk of thromboembolism
- 80% are venous, rest arterial
- 75–80% of cases VTE : DVT and 20–25% are PE
- Approximately 50% during pregnancy and the rest during postpartum
- The risk greatest in the weeks immediately after delivery
- VTE accounts for 9.3% of all maternal deaths

Physiologic Changes

Coagulant Factors	Change in Pregnancy	
Procoagulants		
• Fibrinogen, Factor VII, VIII, X		
• Von Willebrand Factor		
• Plasminogen activator inhibitor-1, 2		
• Factor II, V, IX		No change
Anticoagulants		
• Free Protein S		
• Protein C		No change
• Anti-thrombin		No change

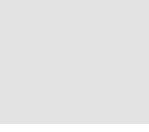
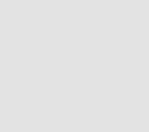
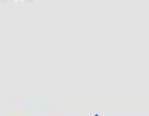
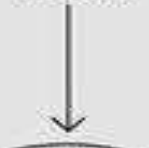
Contact activation (intrinsic) pathway

Damaged surface



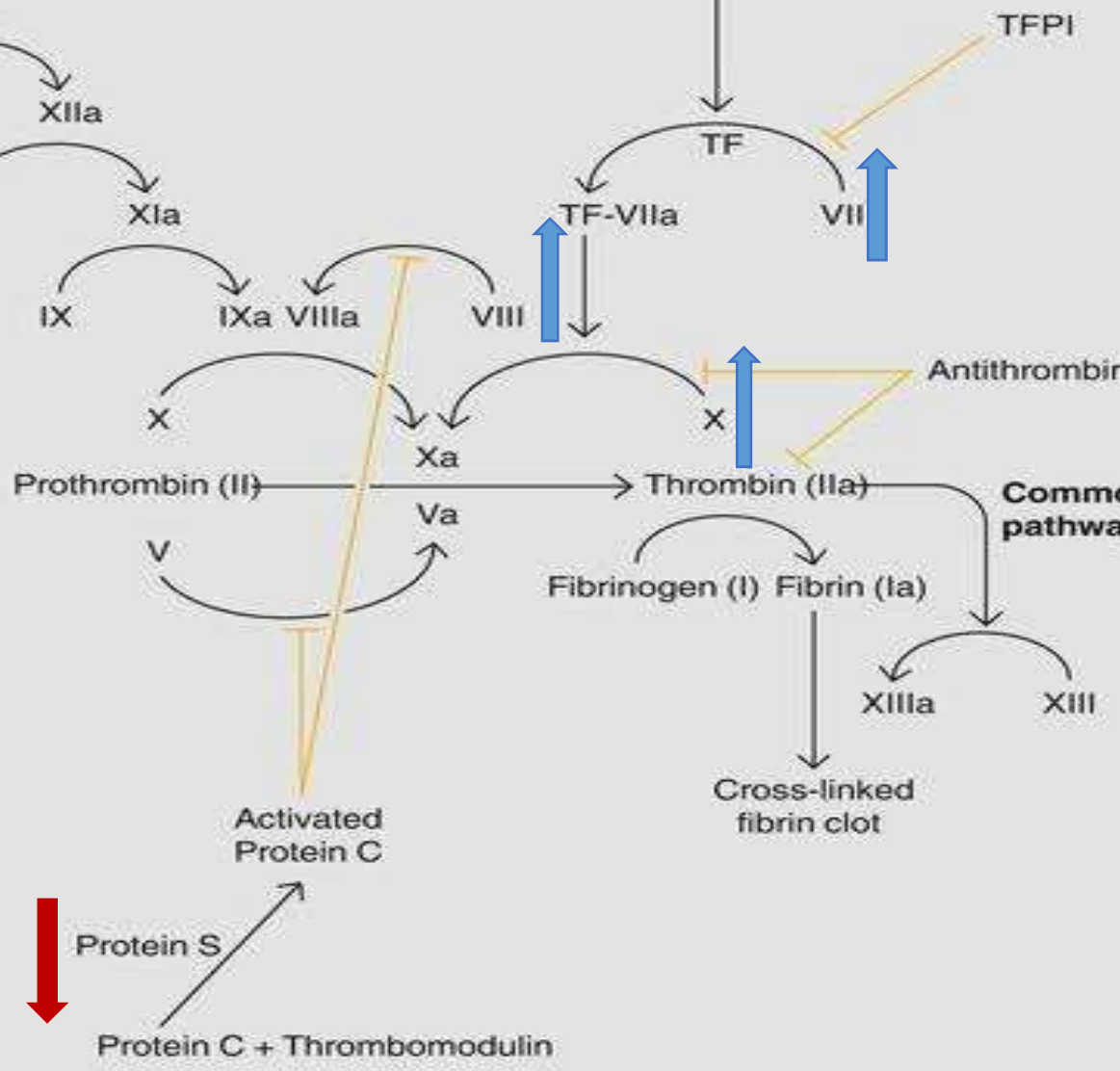
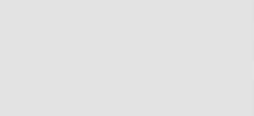
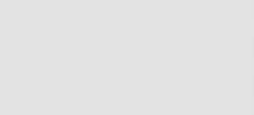
Tissue factor (extrinsic) pathway

Trauma



Common pathway

Thrombin (IIa)



Case 1

Mrs. X, 32 years, presented with

- severe headache for 2 days
- 2 episodes of seizure following delivery

On examination:

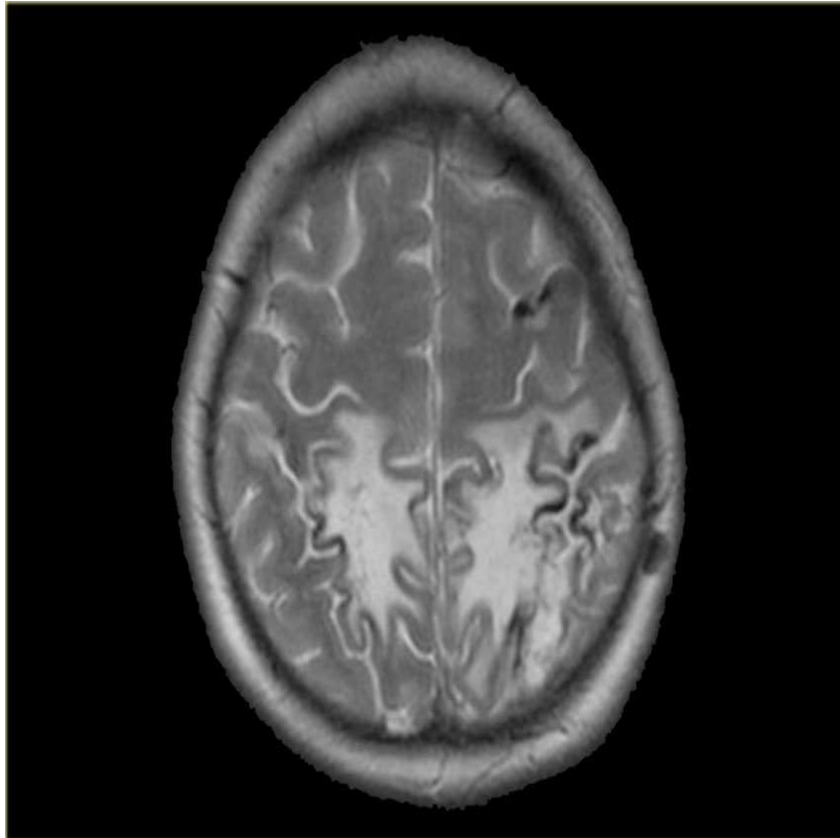
- BP: 160/90 mmHg

She was initially treated as post-partum eclampsia with no improvement.

What should be the next approach?



Case 1 cont.



T2 sequence showing hyperintense lesion in both parietal region



MRV of brain showing flow void in superior sagittal sinus

Thromboembolic Manifestations

Commonly:

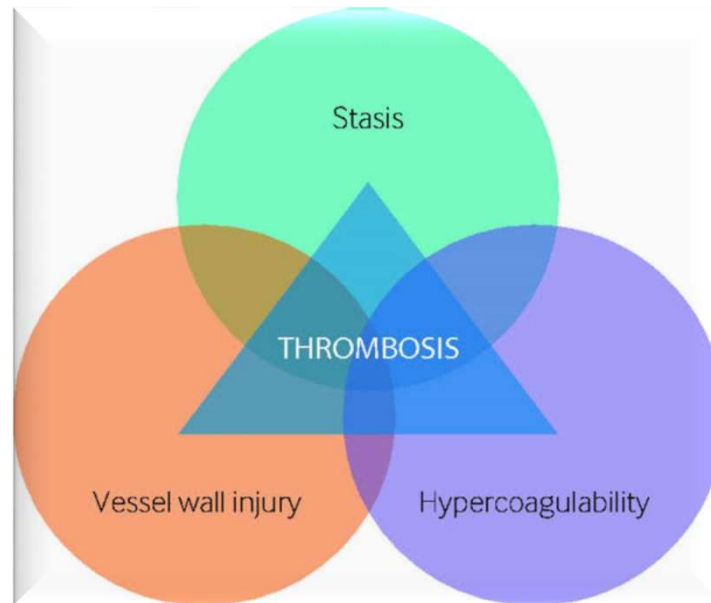
- Deep Vein Thrombosis
- Pulmonary embolism

Less commonly

- CVST
- Budd- Chiari syndrome
- Ischemic stroke
- Coronary artery disease
- Septic pelvic vein thrombophlebitis
- Portal vein thrombosis
- Renal vein thrombosis

Pathogenesis

Vasodilatation
Decreased flow
Compression of IVC,
pelvic veins by uterus



Trauma to
pelvic vein at
the time of
delivery

Physiological
hypercoagulable
state

Risk Factors

Pregestational Risk Factors	Gestational Risk Factors
Age > 35y	Multiple pregnancy
Obesity	Immobility
Smoking	Pregnancy following IVF
Sickle cell disease	Cesarean section (four fold)
Diabetes	PPH (>1 litre)
Hypertension	Prolonged labour (24 hr)
Personal/family history of VTE	
Thrombophilia	

Risk of VTE Complications

and

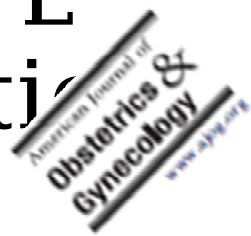


Table IV Medical conditions and thromboembolism

Complication (ICD-9 code)
Hypertension (401-405)
Heart disease (390-399, 412-417, 420)
Thrombophilia (273.8, 286.9, 289.8)
History of thrombosis (V12.51)
Antiphospholipid (286.5, 289.9)
Sickle cell disease (282.4, 282.8)
Lupus (695)
Diabetes
Obesity
Smoking
Substance use

Journal of Obstetrics and Gynecology (2009) 104, 1111-1114

GENERAL OBSTETRICS AND GYNECOLOGY: OBSTETRICS

Venous thromboembolism during pregnancy and the postpartum period: Incidence, risk factors, and mortality

Andra H. James, MD, PhD, Margaret G. Jamison, PhD, Leo R. Branchzio, MD, Evan R. Myers, MD

	OR	95% CI
	1.6	(1.2-2.1)
	2.6	(2.2-2.9)
	0.6	(0.8-4.1)
	2.5	(2.0-3.2)
	4.9	(4.1-5.9)
	0.9	(0.7-1.0)
	0.9	(0.7-9.5)
	2.3	(1.8-2.8)
	4.1	(2.9-5.7)
	1.3	(1.1-1.6)
	7.6	(6.2-9.4)
	2.1	(1.8-2.4)

Medical conditions and VTE

- Thrombophilia
- H/O thrombosis
- APS

Pregnancy complications and VTE

- Transfusion
- Fluid and electrolyte imbalance
- Puerperal infection

Pregnancy and Thrombophilia

Heritable	Acquired
▪ Antithrombin deficiency	▪ Antiphospholipid Syndrome
▪ Protein C deficiency	
▪ Protein S deficiency	
▪ Factor V leiden	
▪ Prothrombin Gene Mutation	

Pregnancy and Thrombophilia cont.

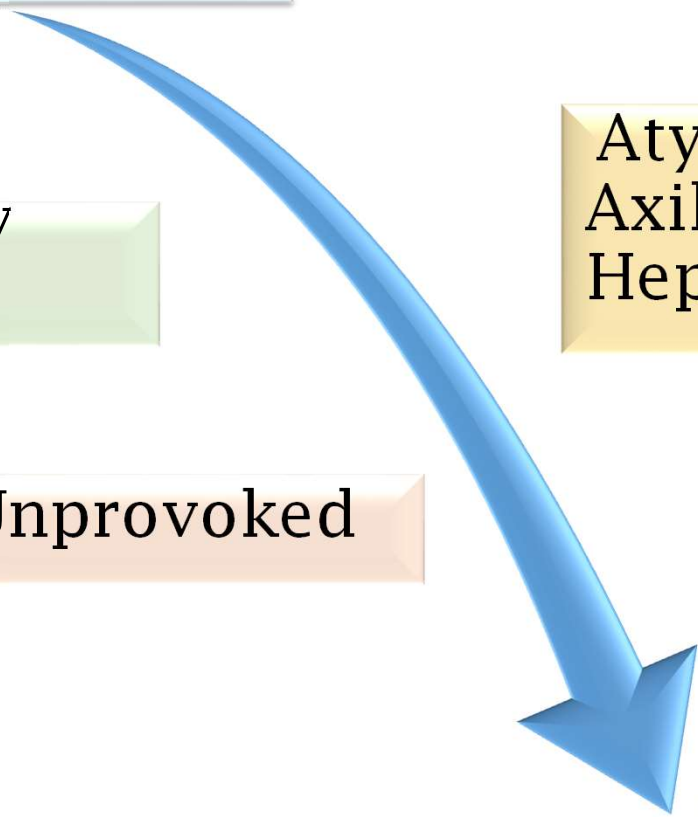
**Suspect thrombophilia
in pregnancy if**

Family
history

Atypical (i.e.
Axillary vein,
Hepatic vein)

Unprovoked

Recurrent



Pregnancy and DVT

Features:

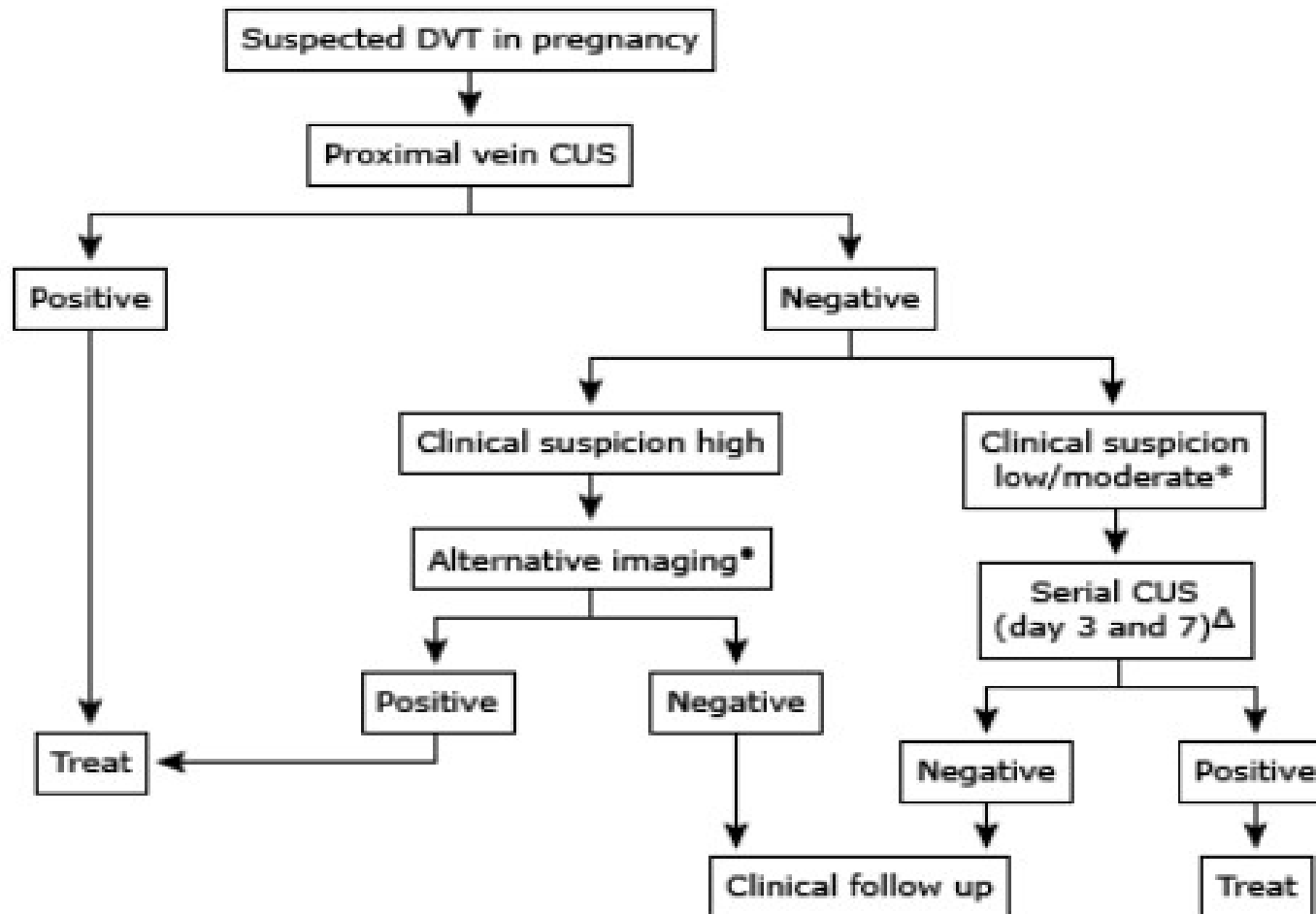
- Leg Swelling (often masked by physiological edema)
- Leg pain
- Highest in the first six weeks postpartum
- Predominantly left-sided in pregnancy (70 to 90 percent)
- Pelvic vein DVT is more common
 - Iliofemoral (64%)
 - Iliac thrombosis (17%)

Pregnancy and DVT cont.

Diagnostic tools:

- Compression duplex USG
- Magnetic resonance venography
- D-dimer: **Not recommended**

Approach to Pregnancy with DVT



Pulmonary Embolism

Clinical features

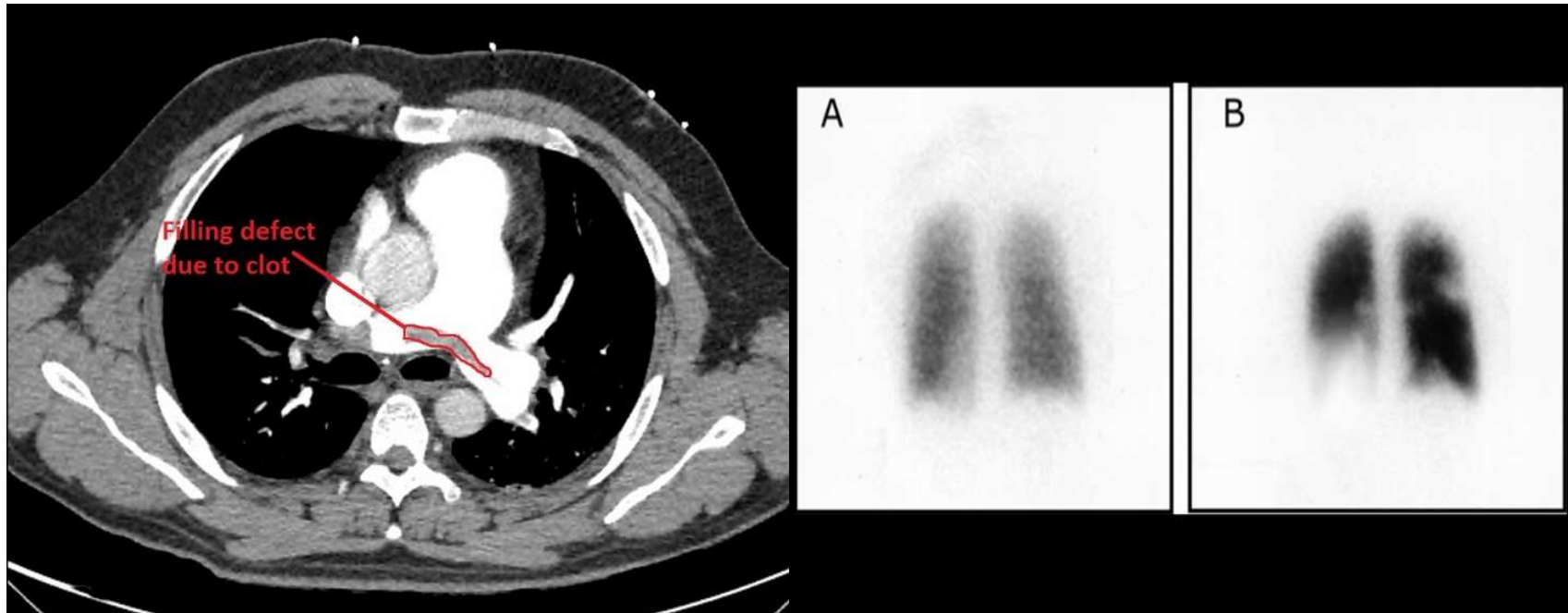
	Acute massive PE	Acute Small/Medium PE
Symptoms	<ul style="list-style-type: none"> • Faintness or collapse • Central chest pain • Apprehension • Severe dyspnoea 	<ul style="list-style-type: none"> • Pleuritic chest pain • Restricted breathing • Haemoptysis
Signs	<ul style="list-style-type: none"> • Circulatory collapse • Tachycardia • Hypotension • ↑JVP • RV gallop rhythm • loud P2 • severe cyanosis 	<ul style="list-style-type: none"> • Tachycardia • Pleural rub • Crackles • P. effusion (often blood-stained) • Low-grade fever

Pregnancy and Pulmonary Embolism

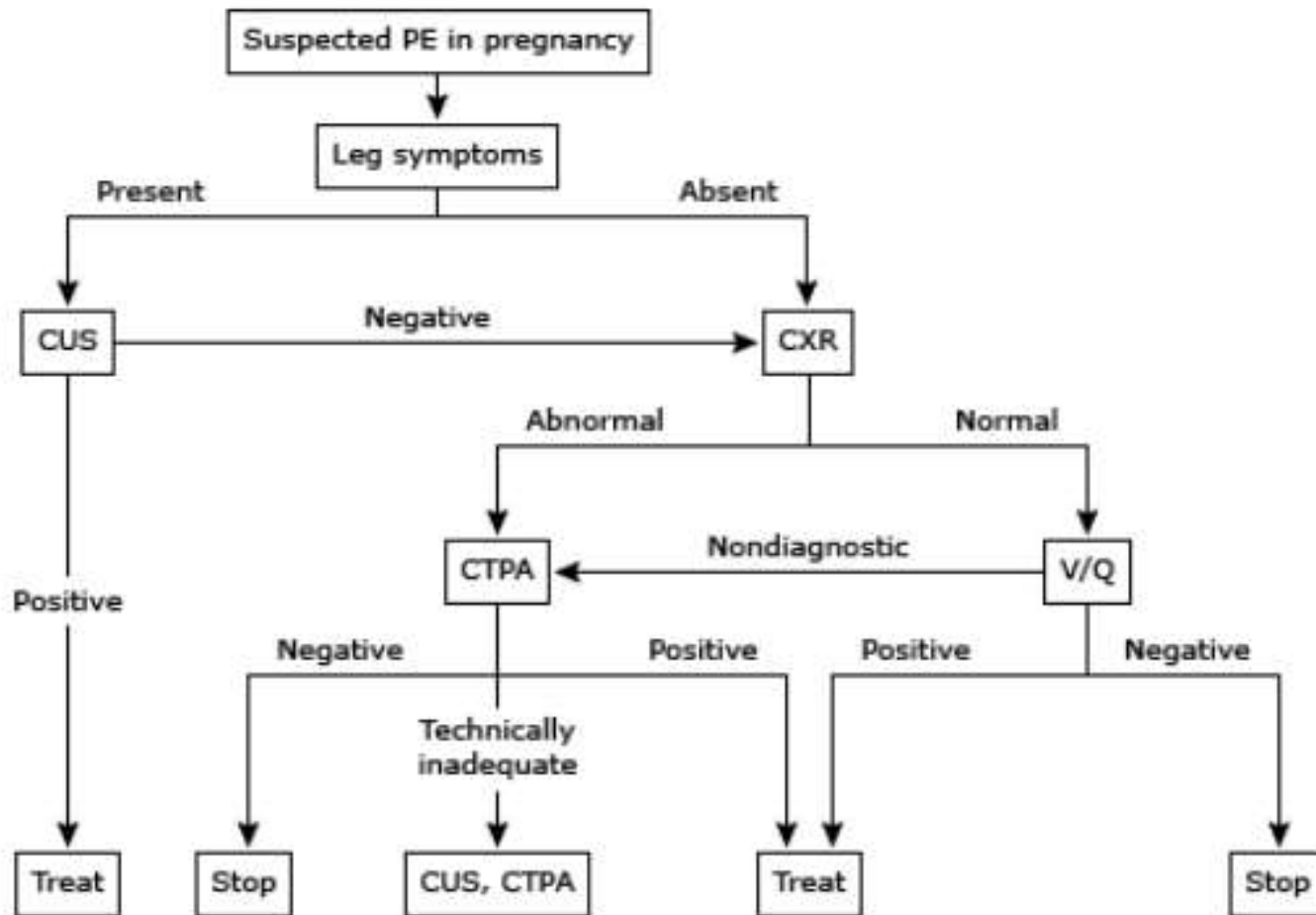
Diagnostic tools:

- Chest X-ray
- ECG
- Echocardiogram
- V/Q Scan (If CXR normal)
- CT pulmonary angiogram (If CXR abnormal or V/Q scan inconclusive or not available)

CTPA, VQ Scan



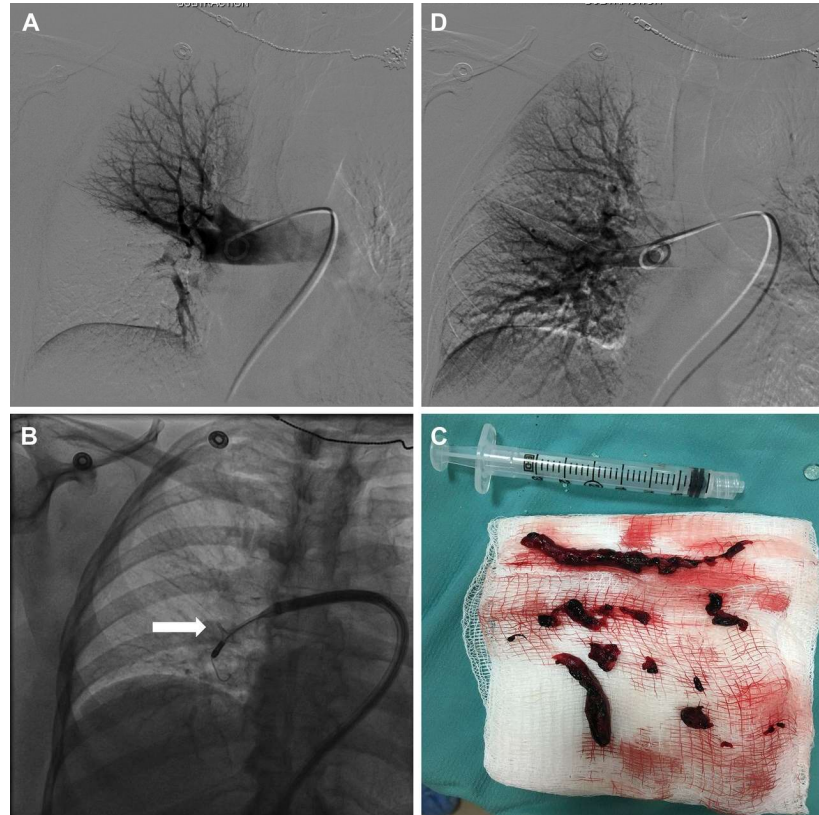
Approach to Pregnancy with PE



PE: pulmonary embolism; CUS: compression ultrasound; CXR: chest radiography; CTPA: computed-tomographic pulmonary angiography; V/Q: ventilation-perfusion.

Management options for Massive PE

- Anticoagulation
- Thrombolysis
- Pulmonary artery catheter break-up
- Embolectomy



Case 2

22 year old lady, 33 weeks pregnant

- Disproportionate abdominal distension for 2 weeks
- Abdominal pain (RUQ) for 2 weeks

Treated as a case of dyspepsia without any improvement

Case 2 cont.

Investigation:

- CBC: normal
- LFT: normal
- RFT: normal
- RBS: normal
- USG of W/A: Hepatomegaly with Ascites

- What may be the **diagnosis** ?

Case 2 cont.

- Duplex USG: Hepatic vein thrombosis
- **Diagnosis:** Budd Chiari Syndrome

Pregnancy and Budd Chiari

Pit-falls:

- Ascites- difficult to evaluate
- Abdominal pain, vomiting - Often overlooked
- Jaundice - misdiagnosed as AFLP/ICP/HELLP syn.
- So, High index of suspicion
- Search for other thrombophilia

Pregnancy and VTE Management Modalities

Management Proper

- Anticoagulants (heparin)
- Thrombolytic therapy (Massive PE with shock)
- Pulmonary artery catheter break up of thrombus & Embolectomy (life-threatening PE)
- IVC filter (recurrent PE in ileofemoral thrombus, despite full anticoagulation)

VTE Prophylaxis

Pregnancy and Anticoagulation

Therapeutic options:

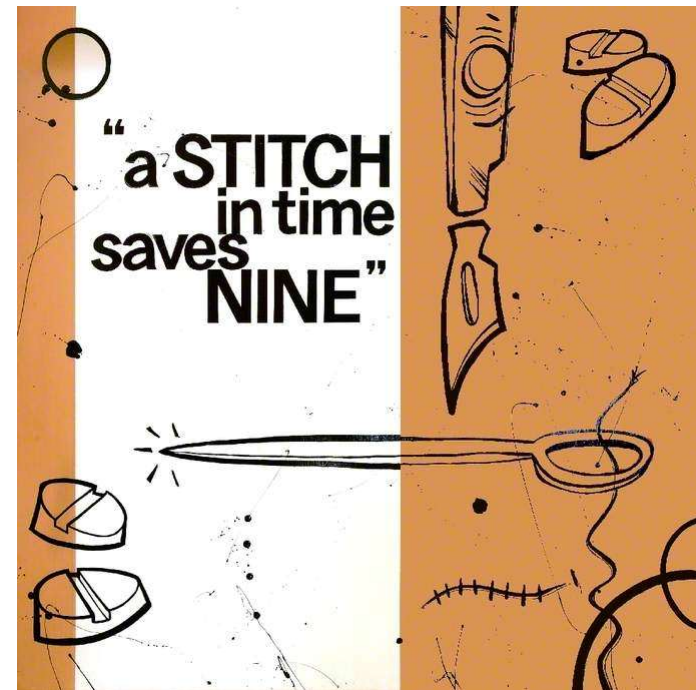
Therapeutic agents	Advantage/Disadvantages
LMWH	Drug of choice Less Osteopenia, HIT
Unfractionated Heparin	Easily reversible with Protamine sulfate
Warfarin	Teratogenic: Used in metallic valves only
Fondaparinux	Heparin intolerance (allergic reaction, HIT)
Aspirin	Limited role (adjunct in APS)
DOAC	CI in pregnancy and lactation
rTPA (i.e	Used in life threatening Pulmonary

Anticoagulation in Peripartum Period

- LMWH to unfractionated heparin before delivery if needed
- Prophylactic LMWH: discontinue 12 hours before delivery
- Therapeutic LMWH: discontinue 24 hours before delivery
- Resume after 4-6hrs (VD) or 6-12 hrs (CS)
- Warfarin not contraindicated in Breastfeeding, but needs supervision

Pregnancy and Thromboprophylaxis

- VTE are dangerous but potentially preventable
- Emphasis on prevention rather than cure
- Risk stratification to sort into different risk



Risk Stratification

Very High Risk

- Previous VTE on long-term warfarin
- AT deficiency
- APS with previous VTE

High risk

- Any previous VTE
- (except a single VTE related to major surgery)

Intermediate risk

- Group A: Asymptomatic high-risk thrombophilia
- Group A: Homozygous FVL/compound heterozygote
- Group A: Protein C or S deficiency
- Group B: Single previous VTE associated with major surgery without thrombophilia, family history or other risk factors

Low risk

- Asymptomatic low-risk thrombophilia (prothombin gene mutation or FVL)

Pharmacologic Thromboprophylaxis

Risk	Pregnancy	Puerperium
Very high risk	Recommend antenatal high-dose LMWH	At least 6 weeks post-natal LMWH/ warfarin
High Risk	Recommend antenatal LMWH	6 weeks post-natal prophylactic LMWH
Int. Risk	Consider antenatal LMWH	
<ul style="list-style-type: none"> Group A Group B 	Recommend LMWH from 28 weeks' gestation	
Low Risk	Surveillance	Surveillance or Recommend 10 days post-natal prophylactic LMWH if other risk factors

Management of aPL Positive Patients

Clinical	Treatment during pregnancy	Treatment after pregnancy
Any prior	Therapeutic dose LMWH+Aspirin	Warfarin indefinitely
No prior		
<ul style="list-style-type: none"> First pregnancy 	Aspirin	VD: Aspirin for 6weeks CS: Prophylactic LMWH+Aspirin for 6 weeks
<ul style="list-style-type: none"> Single pregnancy loss at <10 weeks 	Aspirin	VD: Aspirin for 6weeks CS: Prophylactic LMWH+Aspirin for 6 weeks

Management of aPL Positive Patients

Clinical Circumstances	Treatment during pregnancy	Treatment after pregnancy
<ul style="list-style-type: none"> ▪ ≥ 1 fetal deaths ≥ 10 weeks of gestation 	Prophylactic dose LMWH+ Aspirin	Prophylactic dose LMWH+ Aspirin
<ul style="list-style-type: none"> ▪ ≥ 1 preterm deliveries before 34 weeks of gestation due to severe preeclampsia, eclampsia, or placental insufficiency 	Aspirin	VD: Aspirin for 6 weeks CS: Prophylactic LMWH + Aspirin for 6 weeks
<ul style="list-style-type: none"> ▪ ≥ 3 pregnancy losses < 10 weeks of gestation 	Prophylactic LMWH+ Aspirin	Prophylactic dose LMWH+ Aspirin

Case 3



- 34 years married female housewife presented with lateral medullary syndrome due to APS
- She was on warfarin
- She wanted to conceive. After conception she was given prophylactic LMWH and Aspirin
- Her pregnancy was carried out successfully and puerperium was uneventful

Case 4

Mrs. Sharmin 25yr amenorrhoeic lady was admitted and diagnosed as-

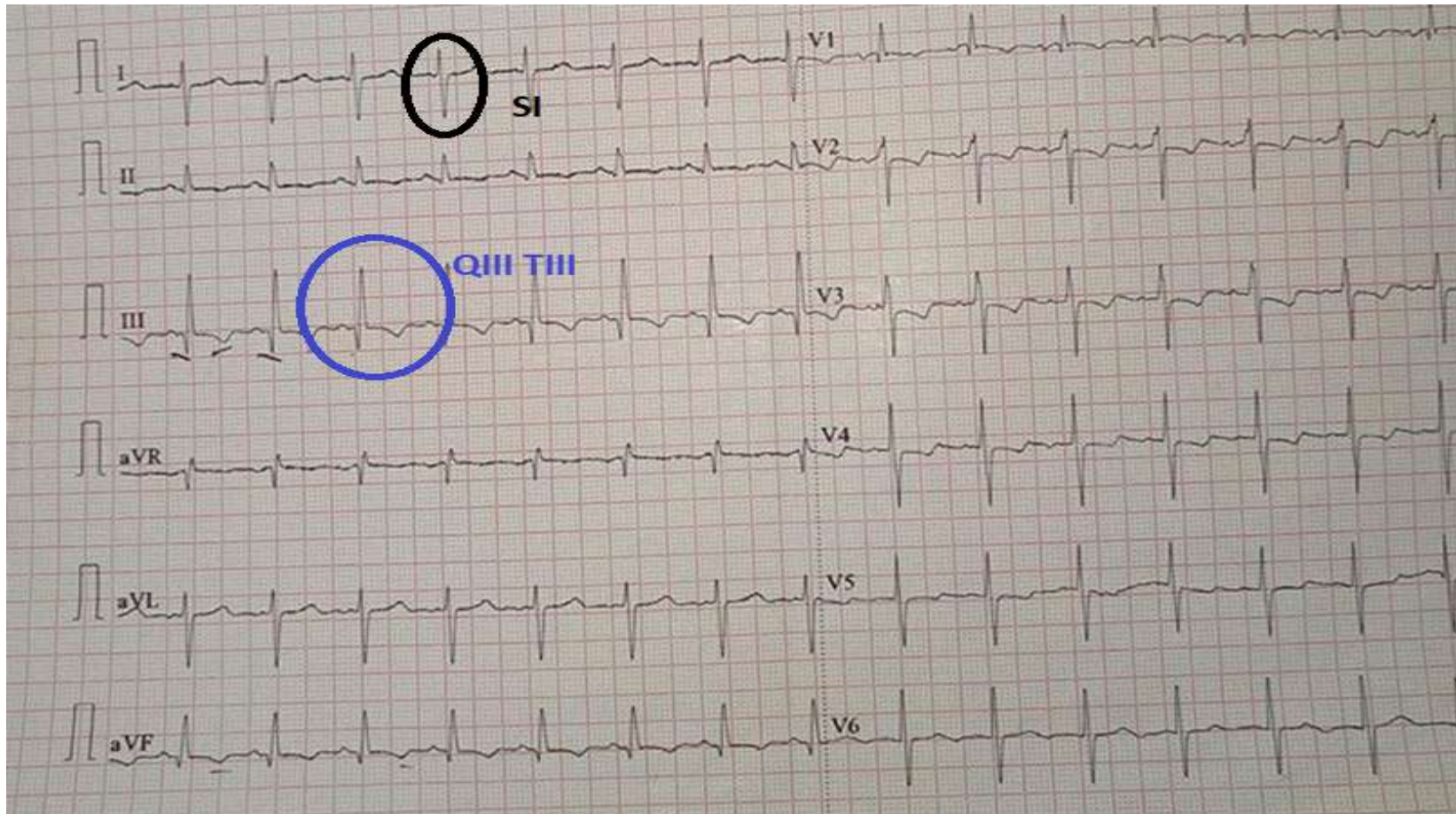
Septic abortion with **AKI** following D&C

5 days after admission, patient suddenly developed

- Severe breathlessness & Disorientation.
- On examination:
 - BP : **80/50** mmHg, Pulse : **110** bpm, Spo2 : **90%**
 - Heart: **Gallop rhythm** with **Loud P2** present

She was resuscitated, but passed away the next day.

Case 4 cont.



Take Home Message

1. VTE in pregnancy is not uncommon but often overlooked

2. High index of suspicion needed

3. This is an area where Physicians and Gynecologists

should complement each other to serve the patient in

a holistic way

4. Dangerous but potentially preventable and treatable.