MEDICINE

432 Team

8 Pulmonary Embolism

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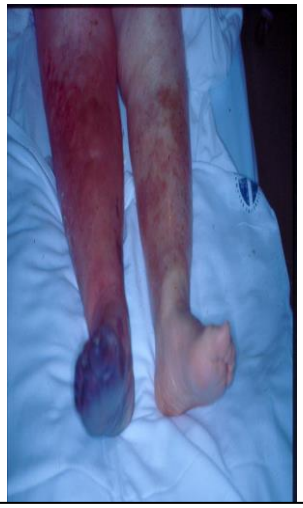
COLOR GUIDE: • Females' Notes • Males' Notes • Important • Additional

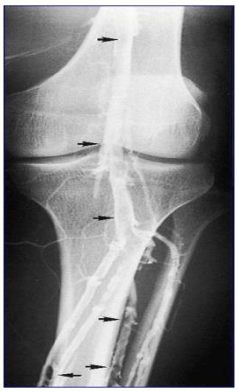
Objectives

1. To know etiology & risk factors for pulmonary embolism
2. How to diagnose pulmonary embolism & its major clinical presentations
3. Lines of treatment of pulmonary embolism

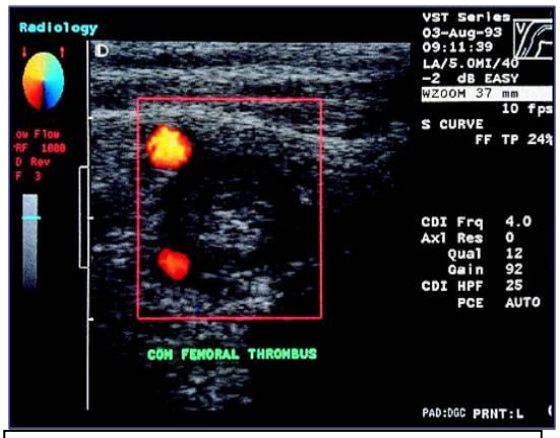
Deep Vein Thrombosis (DVT):



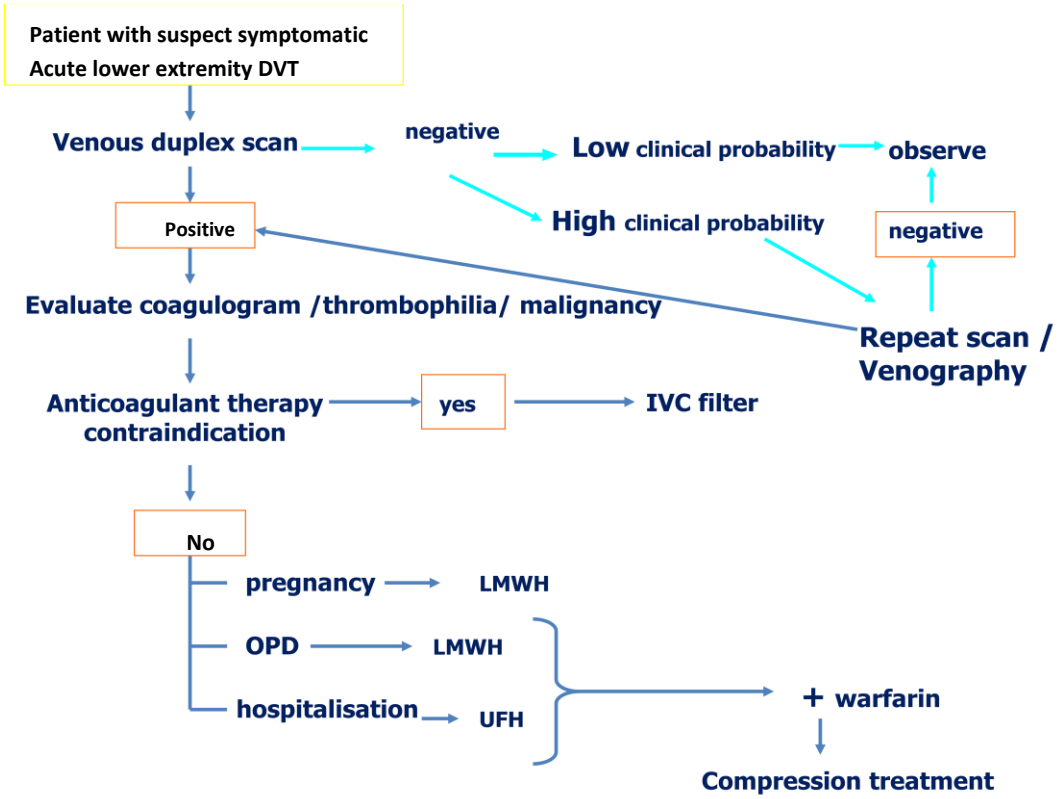
Phlegmasiaceruleadolens Venous gangrene (this is a severe case but most patients present with normal legs)



Venogram shows DVT



Color duplex scan of DVT (the blackish area within the red circle is the blood flow inside the vein and the white shadow represents the clot)



Thrombophilia screening (for Factor V leiden, Prot C/S deficiency, Antithrombin III deficiency) in case of:

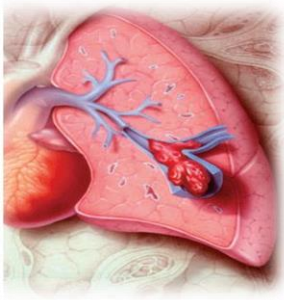
1. Idiopathic DVT < 50 years(with unknown risk factors)
2. Family history of DVT
3. Thrombosis in an unusual site(e.g. upper limb(which occur in IV drug abusers)
4. Recurrent DVT

Recommendation for duration of warfarin

1. 3-6 months first DVT with reversible risk factors
2. At least 6 months for first idiopathic DVT
3. 12 months to lifelong for recurrent DVT or first DVT with irreversible risk factors (malignancy or thrombophilicstate)

Catheter directed-thrombolysis

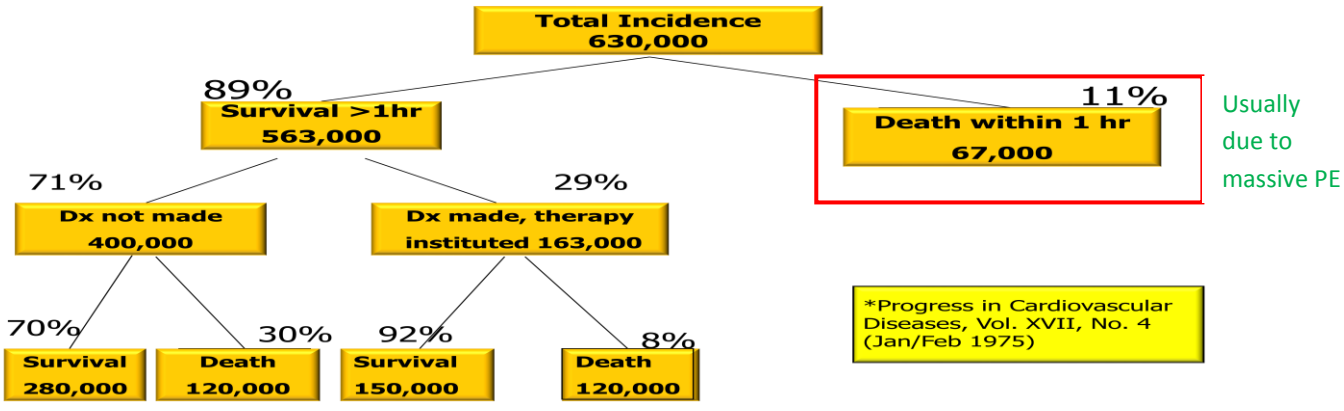
1. Consider in: Acute< 10 days iliofemoral DVT.
2. Long-term benefit in preventing post-phebitic syndrome isunknown.



Pulmonary Embolism (PE):

1. 50,000 individuals die from PE each year in USA
2. The incidence of PE in USA is 500,000 per year

Incidence of Pulmonary Embolism per Year in the United States*



Pulmonary embolism is a medical emergency, most of the cases are undiagnosed. Some patients come with shortness of breath, and other remain subclinical manifestations, and some may die immediately. PE is one of the causes of sudden death.

Risk factor for venous thrombosisVirchow's triad

1. Stasis(e.g. heart failure)
2. Injury to venous intima
3. Alterations in the coagulation-fibrinolytic system

Source of emboli

1. Deep venous thrombosis in the lower extremities(>95%)(iliofemoral vein isthe most common site)
2. Other veins: (Renal, Uterine, Right cardiac chambers)

Risk factors for DVT

1. General anesthesia – especially with long surgery (muscles relaxants are used during anesthesia leading to decrease blood from flowing back to the heart causing stasis)
2. Lower limb or pelvic injury or surgery
3. Congestive heart failure
4. Prolonged immobility
5. Pregnancy
6. Postpartum
7. Oral contraceptive pills
8. Malignancy
9. Obesity
10. Advanced age
11. Coagulation problems

Clinical features

1. Sudden onset dyspnea
2. Pleuritic chest pain(pain increases with breathing while muscular pain increases with breathing and movement)
3. Hemoptysis
4. Clinical clues cannot make the diagnosis of PE; their main value lies in suggesting the diagnosis

   Unlike asthma, asthmatic patient presents with shortness of breath that increases with dusts of and wheezing and can make the diagnosis clinically. Pneumonia is an easy case too, patient will present with fever and cough. Simple chest x-ray will confirm it.

Note(s):

*Sudden onset of unexplained **dyspnoea** is the most common and often the only symptom of pulmonary embolism (Kumar)*

Corpulmonale is defined as right ventricular hypertrophy and dilatation secondary to pulmonary hypertension caused by diseases of the lung parenchyma and/or pulmonary vessels, unrelated to the left side of the heart (right ventricle fails to pump blood to the pulmonary artery due to pressure difference)

Signs and Symptoms

Signs or symptoms observed in patients with thromboembolism			
		Study	
		Stein et al., % (n= 117)	Anderson et al., % (n= 131)
Pulmonary embolism	Dyspnea	73	77
	Tachypnea	70	70
	Chest pain	66	55
	Cough	37	—
	Tachycardia	30	43
Not common →	Cyanosis	1	18
	Hemoptysis	13	13
	Wheezing	9	—
	Hypotension	—	10
	Syncope	—	10
	Elevated jugular venous pulse	—	8
	Temperature >38.5°C	7	—
	S-3 gallop	3	5
	Pleural friction rub	3	2
Deep vein thrombosis	Swelling	28	88*
	Pain	26	56
	Tenderness	—	55
	Warmth	—	42
	Redness	—	34
	Homan's sign	4	13
	Palpable cord	—	6

Massive Pulmonary Embolism:

1. It is a catastrophic entity which often results in acute right ventricular failure and death(Massive PE depends on whether it causes shock (hemodynamically compromised) or not, not on its size)
2. Frequently undiscovered until autopsy
3. Fatal PE typically leads to death within one to two hours of the event

Pathophysiology:

1. Massive PE causes an increase in PVR → right ventricular outflow obstruction → decrease left ventricular preload → Decrease COCO= stroke volume ×HR
2. In patients without cardiopulmonary disease, occlusion of 25-30 % of the vascular bed → increase in Pulmonary artery pressure (PAP)normally 25/10 mmHg
3. Hypoxemia ensues → stimulating vasoconstriction → increase in PAP
4. More than 50% of the vascular bed has to be occluded before PAP becomes substantially elevated
5. When obstruction approaches 75%, the RV must generate systolic pressure in excess of 50mmHg to preserve pulmonary circulation
6. The normal RV is unable to accomplish this acutely and eventually fails(going to obstructive shock and death)

Note(s):

#Left ventricle is called (pressure chamber) because it pumps blood against high pressure
#Right ventricle is called (volume chamber)
 # PVR = pulmonary arterial resistance
 # preload depends on End Diastolic Volume (EDV)
SV=EDV – ESV
If EDV is decreased the stroke volume will decrease leading to decrease CO
 # Shock is a state of hypoperfusion from left ventricle

Note(s):

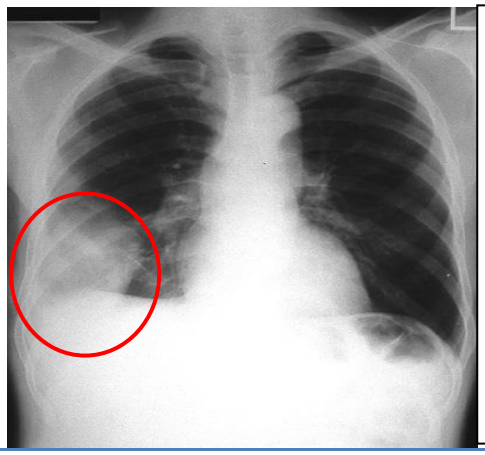
(Step up): Pathophysiology
a. Emboli block a portion of pulmonary vasculature, leading to increased pulmonary vascular resistance, pulmonary artery pressure, and right ventricular pressure. If it is severe (large blockage), acute corpulmonale may result. b. Blood flow decreases in some areas of the lung. Dead space is created in areas of the lung in which there is ventilation but no perfusion. The resulting hypoxemia andhypercarbia drive respiratory effort, which leads to tachypnea.
b. If the size of the dead space is large (large PE), clinical signs are more overt (SOB, tachypnea).

Lung filters the tiny clots in healthy individuals, the clot must occlude up to 20% of vascular bed to raise the pulmonary arterial pressure

(Danish):
Multiple micro emboli:
Large numbers of tiny emboli occlude the capillary beds of the lung. Due to collateral vascular supply there is no pulmonary infarction but there is insidious loss of the microvascular bed supplying the gas exchange units of lungs leading to pulmonary hypertension and right ventricular failure. (No sudden death Unlike the massive where there is no time for collateral)

Diagnosis: (The diagnosis of massive PE should be explored whenever oxygenation or hemodynamic parameters are severely compromised without explanation)

1. CXR



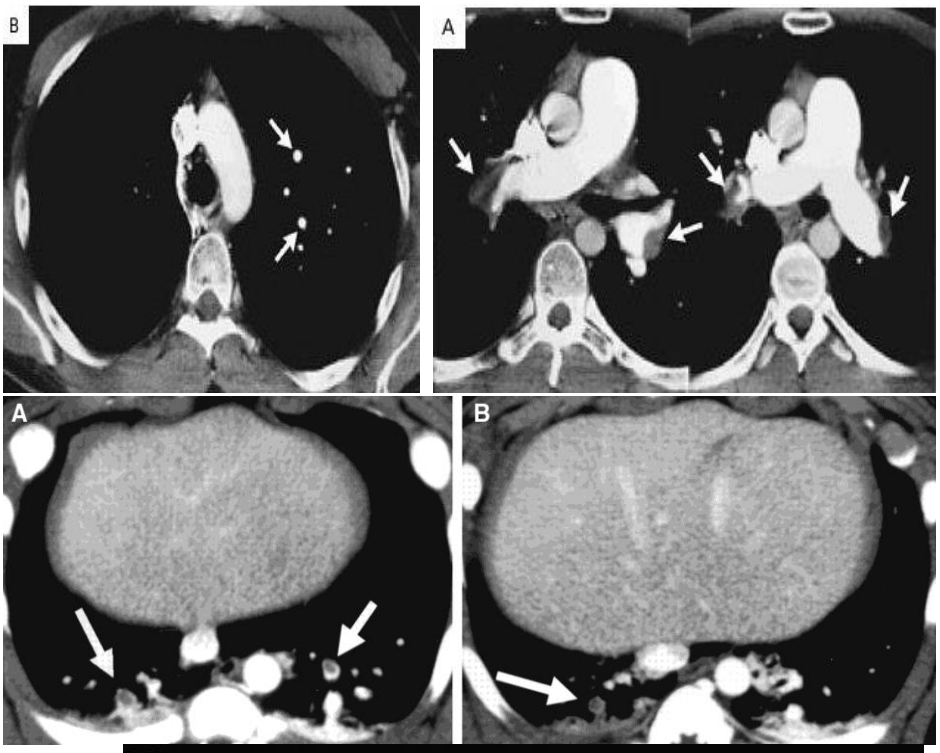
''CXR usually normal'' Chest radiograph showing pulmonary infarct in the right lower lobe. This patient had low-grade fever, hemoptysis, and pleuritic chest pain. The ventilation-perfusion scan was read as high probability for pulmonary embolism. A pleural-based density in the lower lobe with the convexity directed toward the hilum signifies pulmonary infarction. This sign is also known as? Hampton's hump." = wedge infarction

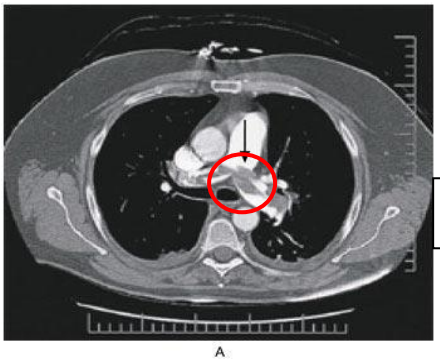
Chest radiographic findings in patients with pulmonary embolism

	COPD, % (n= 21)	No prior cardiopulmonary disease, % (n= 117)
Atelectasis or pulmonary parenchymal abnormality	76	68
Pleural effusion	52	48
Pleural-based opacity	33	35
Elevated diaphragm	14	24
Decreased pulmonary vascularity	38	21
Prominent central pulmonary artery	29	15
Cardiomegaly	19	12
Westermark's sign*	5	7
Pulmonary edema	14	4

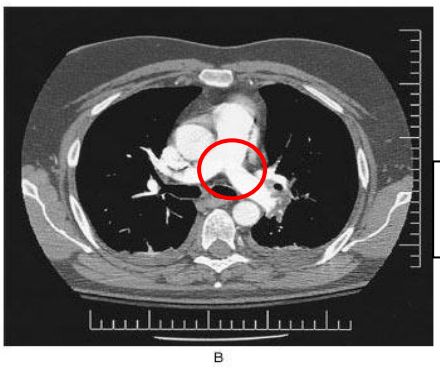
Chest radiographic findings in patients with pulmonary embolism. Although frequently abnormal, the chest radiograph is nonspecific for the diagnosis of pulmonary embolism and cannot be used to confirm the diagnosis. The existence of underlying lung disease may also influence the chest radiographic appearance of pulmonary embolism.

2. Spiral CT (diagnostic)

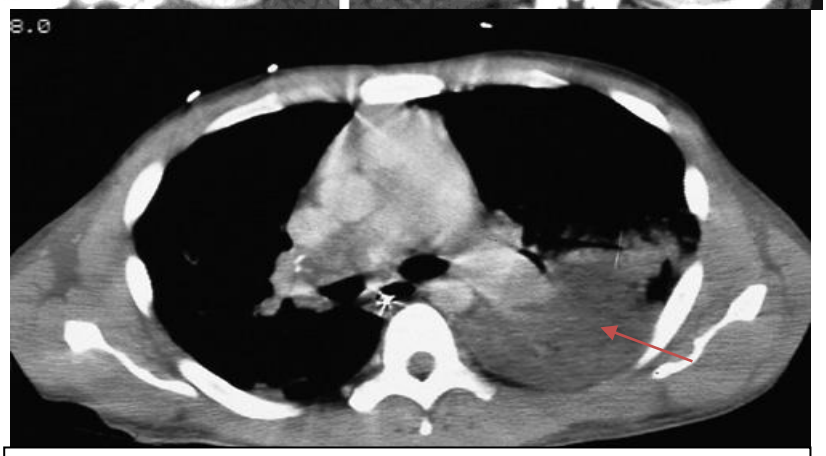




Before



After thrombolytic therapy



A, Computed tomographic scan demonstrating infarcted lung on left and large clot in the right main pulmonary artery.

3. ABG(Significant hypoxemia is almost uniformly present when there is a hemodynamically significant PE)

Normal Values:

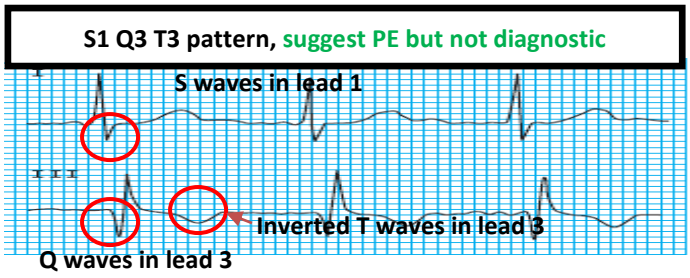
PH: 7.35-7.45 PO_2: 75-100 mmHg O_2 saturation: 95-100%

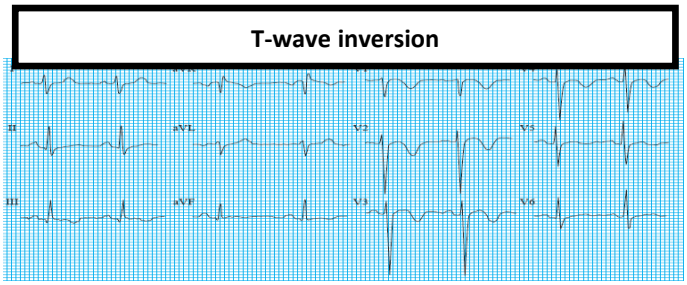
Note(s):

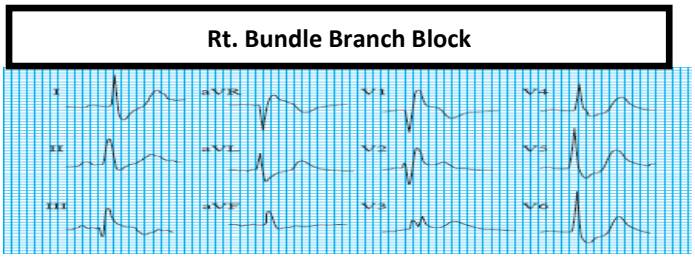
(Step up)

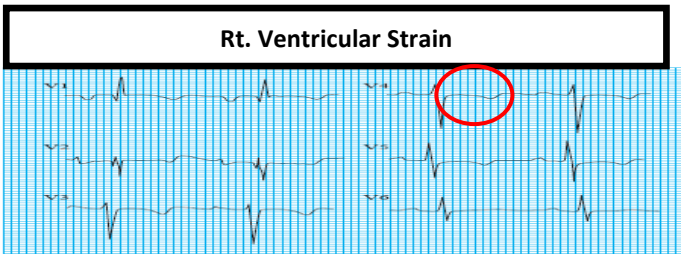
ABG levels are not diagnostic for PE.
a. PaO_2 and $PaCO_2$ are low (the latter due to hyperventilation) and pH is high; thus, there is typically a respiratory alkalosis.

ECG







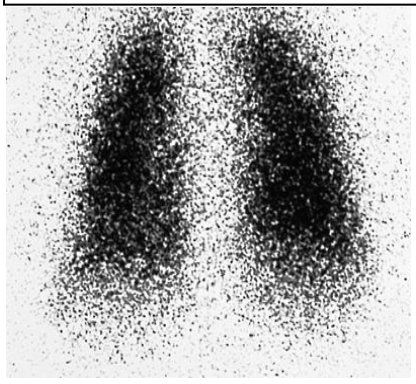


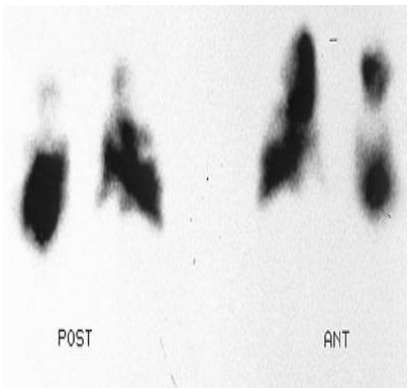
4. V/Q(rarely used, spiral CT is faster and easier) (used when CT is contraindicated e.g. pregnancy)

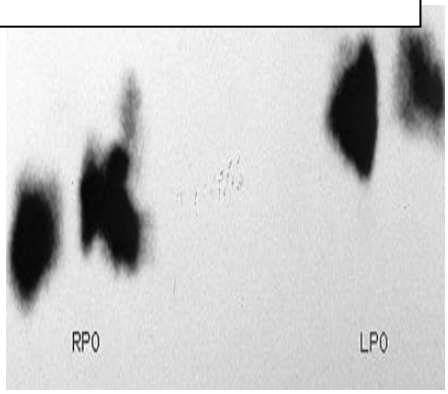
The use of ventilation perfusion scan in diagnosing pulmonary embolism
High probability= PE
=2 large segmental (>75% of a segment) perfusion defects without corresponding ventilation or radiographic abnormalities or substantially larger than matching ventilation or radiologic abnormalities
OR
=2 moderate segmental (>25% and <75% of a segment) perfusion defects without matching ventilation or chest radiographic abnormalities plus one large unmatched segmental defect
OR
=4 moderate segmental perfusion defects without matching ventilation or chest radiologic abnormalities
Intermediate probability
Scans that do not fall into normal, very low, low, or high probability categories
Low probability
Non-segmental perfusion defects
OR

Single moderate mismatched segmental perfusion defect with normal chest radiograph
OR
Any perfusion defect with a substantially larger abnormality on chest radiograph
OR
Large or moderate segmental perfusion defects involving no more than four segments in one lung and no more than three segments in one lung region with matching or larger ventilation/radiographic abnormalities
OR
More than three small segmental perfusion defects (<25% of a segment) with a normal chest radiograph
Very low probability
Three or fewer small segmental perfusion defects with a normal chest radiograph
Normal
No perfusion defects present

The use of ventilation-perfusion scan in diagnosing pulmonary embolism. The criteria used for interpreting ventilation-perfusion scans are listed in the figure. In patients suspected to have pulmonary embolism, this study is ordered routinely. The perfusion scan is usually performed first. Macroaggregates of albumin labeled with technetium-99m are injected, and images are obtained in anterior, posterior, and right and left lateral and oblique views. If the perfusion scan is normal, there is no need to perform a ventilation scan. Defects in perfusion are assessed and quantified. The ventilation scan is performed by inhalation of a radioactive gas, usually 133 Xe is mixed with air. The patient breathes this radioactive mixture until a state of equilibrium has been reached between the spirometer and lungs, then the patientbreathes room air. Images taken in this wash-out phase are useful in detecting ventilation abnormalities.





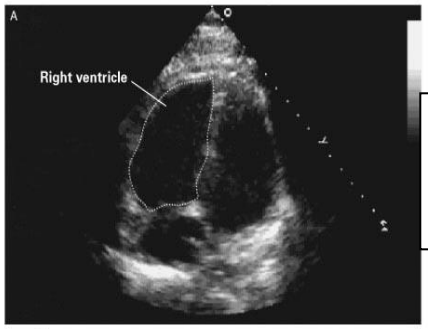


High-probability ventilation- perfusion scan

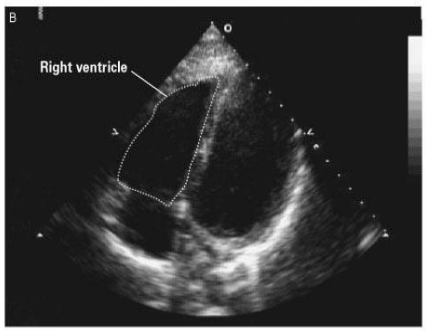
Prospective investigation of pulmonary embolism diagnosis results					
Scan category	PE present	PE absent	PE uncertain	No angiogram	Total
High probability	102	14	1	7	124
Intermediate probability	105	217	9	33	364
Low probability	39	199	12	62	312
Near normal or normal	5	50	2	74	131
Total	251	480	24	176	931

Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) results. This prospective study was designed to study the accuracy of ventilation-perfusion (õ/õ) scan in the diagnosis of pulmonary embolism. Results of õ/õ scan were compared with pulmonary angiography, which was used as a gold standard. From the results it is obvious that more than two thirds of patients have scans of low or intermediate probability that are non-diagnostic. Although a high-probability scan usually indicates pulmonary embolism, only a minority of patients with pulmonary embolism have a high-probability scan. Near-normal lung scans make the diagnosis of pulmonary embolism very unlikely.

5. Echocardiography

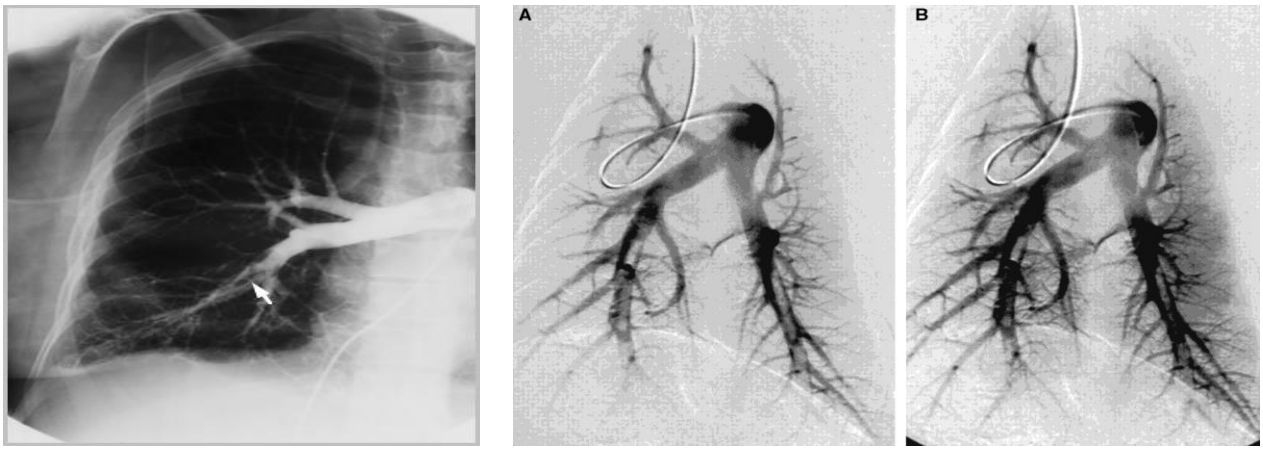


Before thrombolytic therapy, dilatation of right heart and pushing of the septa to left side of the heart



After the thrombolytic therapy

6. Angiogram



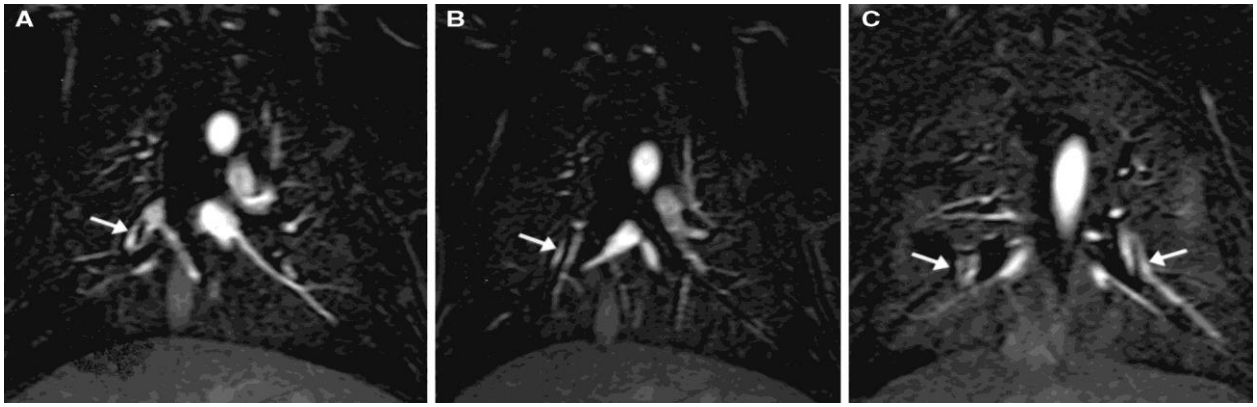
Pulmonary angiogram showing pulmonary embolism. Pulmonary angiography remains the diagnostic gold standard for pulmonary embolism. Access to the pulmonary artery is obtained via transvenous catheter placement. The diagnosis is confirmed by persistent filling defect or abrupt cut-off of flow. Abrupt cut-off of flow to the right and left upper lobe vessels is seen in this patient.

7. Fibrin Split Products/D-dimer
8. BNP
9. Troponin

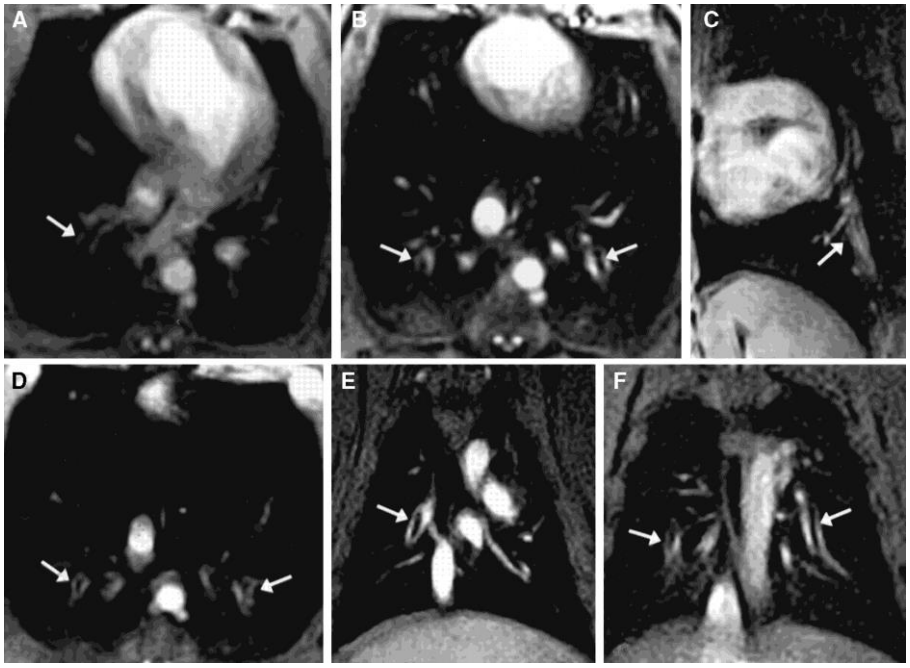
Note(s):

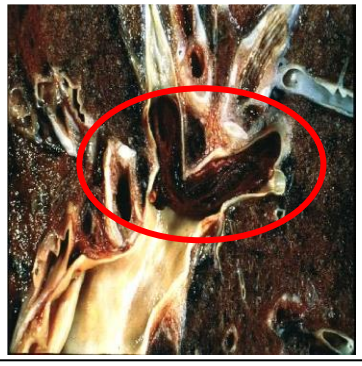
(Davidson's):
D-dimer and other circulating markers:
D- dimer is a specific degradation product released into the circulation when cross-linked fibrin undergoes endogenous fibrinolysis. An elevated D- dimer is of limited value, as it occurs in a number of conditions including PE, myocardial infarction, pneumonia and sepsis. However, low D-dimer levels (<500 ng/ml measured by ELISA), particularly where clinical risk is low, have a high negative predictive value and further investigation is unnecessary. The D- dimer result should be disregarded in high risk patients, as further investigation is mandatory even if it normal.
Other circulating markers that reflect right ventricular micro-infarction, such as troponin I and Brain Natriuretic Peptide (BNP)

10. MRA with contrast



MRA real time



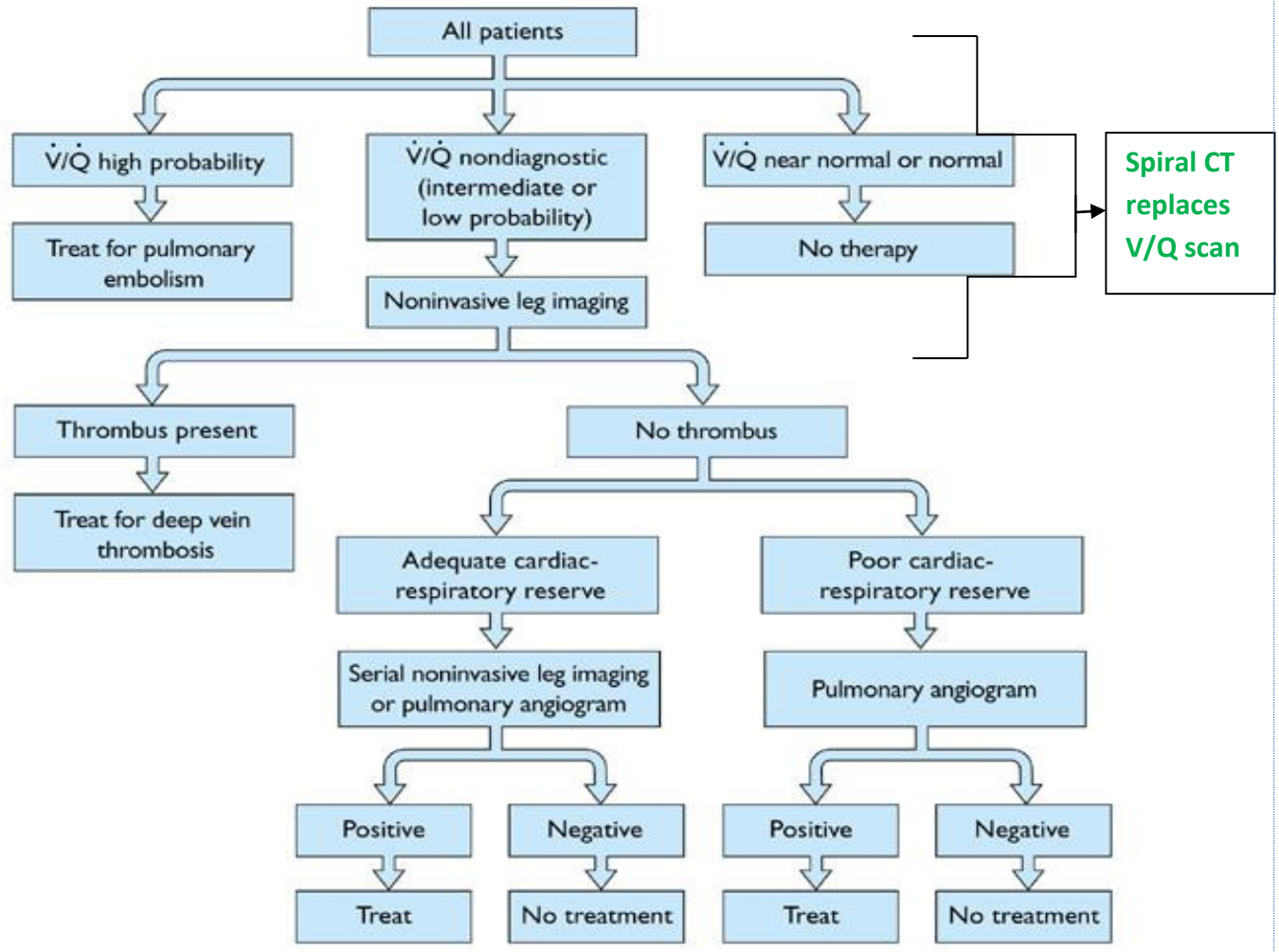


Saddle Embolus
A large embolism that straddles the arterial bifurcation and thus blocks both branches.

Sensitivity of spiral computed tomography, magnetic resonance angiography, and real-time magnetic resonance angiography, for detecting pulmonary emboli

Reader	CT	MRA	RT-MRA
1	72.1	79.1	**97.7**
2	69.8	81.4	**97.7**
Mean	71.0	80.3	**97.7**
K	0.86	0.84	**1**

Suggested diagnostic strategy for venous thromboembolism



Suggested diagnostic strategy for venous thromboembolism. The PIOPED study revealed that results of ventilation-perfusion (õ/õ) scans are nondiagnostic in more than 70% of the cases. The diagnostic strategy proposed in the figure provides a rational approach to work up patients with suspected thromboembolic disease. The role of spiral CT scan in the diagnosis of pulmonary embolism remains controversial with a wide range of reported sensitivities (53%–100%) and specificities (81%–100%)

Treatment

1. Respiratory support(Oxygen support)
2. Hemodynamic Support (e.g. If the patient is hypotensive, should be given fluid replacement)
3. Anticoagulation(Heparin IV should be started soon based on the clinical suspicion of PE without waiting for results, unless there is an absolute contraindication for anticoagulation) (we starte with heparin because warfrin takes time)

Dosage and monitoring of anticoagulant therapy

1. After initiating heparin therapy, repeat APTT every 6 h for first 24 h and then every 24 h when therapeutic APTT is achieved
2. Warfarin 5 mg/d can be started on day 1 of therapy; there is no benefit from higher starting doses
3. Platelet count should be monitored at least every 3 d during initial heparin therapy
4. Therapeutic APTT should correspond to plasma heparin level of 0.2–0.4 IU/mL
5. Heparin is usually continued for 5–7 d
6. Heparin can be stopped after 4–5 d of warfarin therapy when INR is in 2.0–3.0 rang

Note(s):

 # We start with heparin because warfarin takes time
 # IV Heparin needs monitoring by APTT
 # Low molecular weight heparin may be used instead of standard unfractioned heparin, but no need for APTT because its effect is predicted and it is given

Important drug interactions with warfarin	
Drugs that decrease warfarin requirement	Drugs that increase warfarin requirement
Phenylbutazone	Barbiturates
Metronidazole	Carbamazepine
Trimethoprim-sulfamethoxazole	Rifampin
Amiodarone	Penicillin
2nd and 3rd generation cephalosporins	Griseofulvin
Clofibrate	Cholestyramine
Erythromycin	
Anabolic steroids	
Thyroxine	

Complications of anticoagulation		
	Complication	Management
Heparine	Bleeding	Stop heparin infusion. For severe bleeding, the anticoagulant effect of heparin can be reversed with intravenous protamine sulfate 1 mg/100 units of heparin bolus or 0.5 mg for the number of units given by constant infusion over the past hour; provide supportive care including transfusion and clot evacuation from closed body cavities as needed.
	Heparin-induced thrombocytopenia and thrombosis	Carefully monitor platelet count during therapy. Stop-heparin for platelet counts <75,000. Replace heparin with direct inhibitors of thrombin-like desirudin if necessary. These agents do not cause heparin-induced thrombocytopenia. Avoid platelet transfusion because of the risk for thrombosis.**Cauld cause gangren**

	Heparin-induced osteoporosis (therapy >1 mo)	LMWHs may have lower propensity to cause osteoporosis as compared with unfractionated heparin; consider LMWH if prolonged heparin therapy is necessary.
	Complication	Management
Warfarin	Bleeding	Stop therapy. Administer vitamin K and fresh-frozen plasma for severe bleeding; provide supportive care including transfusion and clot evacuation from closed body cavities as needed
	Skin necrosis (rare)	Supportive care.
	Teratogenicity	Do not use in pregnancy or in patients planning to become pregnant.

Risks and benefits of thrombolytics vs heparin therapy for pulmonary embolism			
	Thrombolytic therapy	No difference	Heparin
Improved resolution at 2-4 h after onset of therapy			
Angiography	+	-	-
Pulmonary artery pressure	+	-	-
Echocardiography	+	-	-
Resolution at 24 h			
Lung scan	+	-	-
Angiography	+	-	-
Resolution at 1 wk and 30 d			
(lung scan)	-	+	-
Rate of confirmed recurrent PE	-	+	-
Hospital mortality	-	+	-
Late mortality	-	+	-
Less severe bleeding	-	-	+
Less intracranial hemorrhage	-	-	+
Lower cost	-	-	+

Approved thrombolytics for pulmonary embolism

1. Streptokinase
   250,000 IU as loading dose over 30 min, followed by 100,000 U/h for 24 h
2. Urokinase
   4400 IU/kg as a loading dose over 10 min, followed by 4400 IU/kg/h for 12-24 h
3. Recombinant tissue-plasminogen activator
   100 mg as a continuous peripheral intravenous infusion administered over 2 h

Indications for thrombolytic therapy in pulmonary embolism:

1. Hemodynamic instability
2. Hypoxia on 100% oxygen
3. Right ventricular dysfunction by echocardiography

Contraindications

Relative:

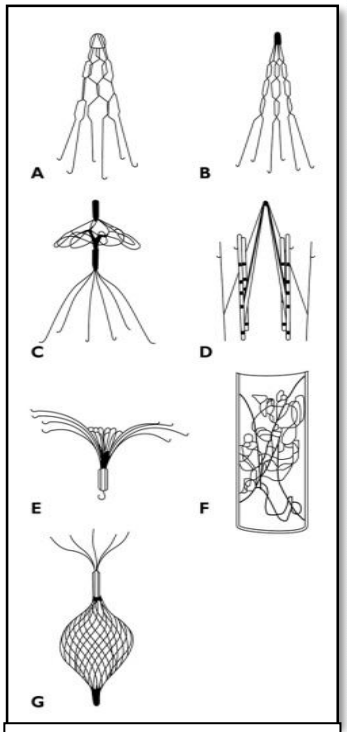
1. Recent surgery within last 10 d Previous arterial punctures within 10 d
2. Neurosurgery within 6 mo
3. Bleeding disorder (thrombocytopenia, renal failure, liver failure)
4. Ophthalmologic surgery within 6 wk
5. Hypertension >200 mm Hg systolic or 110 mm Hg diastolic Placement of central venous catheter within 48 h
6. Hypertensive retinopathy with hemorrhages or exudates Intracerebral aneurysm or malignancy
7. Cardiopulmonary resuscitation within 2 wk
8. Cerebrovascular disease
9. Major internal bleeding within the last 6 mo
10. Pregnancy and the 1st 10 d postpartum
11. Infectious endocarditis
12. Severe trauma within 2 mo
13. Pericarditis

Absolute

Active internal bleeding

Indications for inferior vena caval (IVC) filters

1. Absolute contraindication to anticoagulation (eg, active bleeding)
2. Recurrent PE despite adequate anticoagulant therapy
3. Complication of anticoagulation (eg, severe bleeding)
4. Hemodynamic or respiratory compromise that is severe enough that another PE may be lethal



Various Inferior vena caval filters

EMBOLECTOMY

1. Embolectomy (ie, removal of the emboli) can be performed using catheters or surgically.
2. It should be considered when a patient's presentation is severe enough to warrant thrombolysis (eg, persistent hypotension due to PE), but this approach either fails or is contraindicated.

Key points

1. Most pulmonary emboli arise from thrombosis in the deep veins of the legs, which is common in the immobilized patients and patients in the medical, surgical and obstetrics wards.
2. Assessment of patients with suspected pulmonary embolism involves proper assessment of suggestive clinical symptoms and risk factors and exclusion of alternative diagnoses.
3. Spiral CT scan of the chest is currently used as the main imaging modality for the diagnosis of PE.
4. Heparin is used to achieve rapid anti-coagulation followed by warfarin.
5. Thrombolytic therapy is reserved for patients with massive PE resulting in circulatory compromise.

Conclusions

1. PE is common and under-recognized serious medical problem
2. Early diagnosis and treatment is essential for good outcome
3. High index of suspicion is needed in high risk patients

SUMMARY

1) A PE occurs when a thrombus in another region of the body embolizes to the pulmonary vascular tree via the right ventricle and pulmonary artery. 2) DVT in lower extremities are the main source of emboli.
3) Clinical features of PE: sudden onset of dyspnea, pleuritic chest pain and hemoptysis.
4) Most often PE is clinically silent.
5) Recurrences are common, which can lead to development of chronic pulmonary HTN and chronic corpulmonale.
6) Spiral CT is the test of choice in diagnosing PE.
7) V/Q (Ventilation- Perfusion lung) scan : plays an important role in diagnosis when there is a contraindication to spiral CT.
8) treatment of PE :
A) supplement oxygen to correct hypoxemia
B) Hemodynamic support
C) acute anticoagulation therapy with either unfractionated or low-molecular-weight heparin to prevent another PE. “Heparin is used to achieve rapid anti-coagulation followed by warfarin"
9) Thrombolytic therapy is reserved for patients with massive PE resulting in circulatory compromise.

Questions

Case 1: You are a hospitalist called to evaluate 74-year-old female with dementia for SOB and increasing oxygen requirements. The patient was admitted to the hospital 4 days ago with dehydration. She has not been out of bed since being hospitalized because of her generalized weakness. She denies chest pain or any other symptoms. Temperature = 99.4, BP = 116/74, pulse = 112, RR = 26, oxygen saturation = 91% on 5 L of oxygen via nasal cannula. She is moderately tachypneic. Physical examination of heart and lungs is normal. What is the likely diagnosis in this patient? What is the appropriate management?

Case 2: A 39-year-old female is brought to the ED by her husband with the chief complaint of acute SOB and anxiety that started suddenly 2 to 3 hours ago while she was working around the house. She denies chest pain. Her PMH is unremarkable. She takes oral contraceptives but no other medications. Vital signs are: Temperature=99.1, RR=34, BP=148/90, pulse=100. Oxygen saturation is 94% on room air. On examination, the patient appears healthy although in moderate respiratory distress. Her examination is otherwise unremarkable. Laboratory tests reveal: WBC=7.1, Hgb=12.2, Hct=37.3, Na+=138, K+=4.7, Cl−=109, HCO3−=25, BUN=14, Cr=0.9, glucose=106. ABGs are obtained and reveal: pH=7.52, HCO3−=20, PaCO2=26, PaO2=70. CXR and ECG are normal. What is the acid–base disorder? What is the appropriate management of this patient?

Answers:

Case 1: A sudden increase in oxygen requirement should raise the suspicion of a pulmonary embolus. A history of recent immobilization is a classic risk factor for a DVT with conversion to PE. A V/Q scan or helical CT scan should be obtained. Iodinated contrast agents are needed for helical CT scans, and therefore one should inquire about a history of allergy to contrast material and know the patient's renal function before ordering this test, because its use may be contraindicated in such cases.

Case 2: This patient has respiratory alkalosis. Her hyperventilation may result from pulmonary embolism, or from a number of other conditions, including panic attacks. Given the high clinical suspicion for pulmonary embolism (sudden onset of dyspnea, oral contraceptive use, and hypoxemia), start the patient on heparin and obtain a V/Q scan or a spiral CT scan.