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Pulmonary Embolism

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Author: **Craig Feied, MD, FACEP, FAAEM, FACPh**, Director, National Institute for Medical Informatics, Director, Federal Project ER One, Director of Informatics, Washington National Medical Center, [Director, National Center for Emergency Medicine Informatics](#)

Coauthor(s): **Jonathan A Handler, MD**, Director of Informatics, Assistant Professor, Department of Emergency Medicine, [Northwestern Memorial Hospital](#)

Craig Feied, MD, FACEP, FAAEM, FACPh, is a member of the following medical societies: [American Academy of Emergency Medicine](#), [American College of Emergency Physicians](#), [American College of Phlebology](#), [American College of Physicians](#), [American Medical Association](#), [American Medical Informatics Association](#), [Medical Society of the District of Columbia](#), [Society for Academic Emergency Medicine](#), and [Undersea and Hyperbaric Medical Society](#)

Editor(s): **Michael S Beeson, MD, MBA**, Program Director, Summa Health System; Professor of Clinical Emergency Medicine, Emergency Medicine, Northeastern Ohio Universities College of Medicine; **Francisco Talavera, PharmD, PhD**, Senior Pharmacy Editor, eMedicine; **Gary Setnik, MD**, Chair, Department of Emergency Medicine, Mount Auburn Hospital; Assistant Professor, Division of Emergency Medicine, Harvard Medical School; **John Halamka, MD**, Chief Information Officer, CareGroup Healthcare System, Assistant Professor of Medicine, Department of Emergency Medicine, Beth Israel Deaconess Medical Center; Assistant Professor of Medicine, Harvard Medical School; and **Robert E O'Connor, MD, MPH**, Director of Education and Research, Department of Emergency Medicine, Christiana Care Health System; Professor of Emergency Medicine, Thomas Jefferson University

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INTRODUCTION

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Background: Pulmonary embolism (PE) is an extremely common and highly lethal condition that is a leading cause of death in all age groups. A good clinician actively seeks the diagnosis as soon as any suspicion of PE whatsoever is warranted, because prompt diagnosis and treatment can dramatically reduce the mortality rate and morbidity of the disease. Unfortunately, the diagnosis is missed far more often than it is made, because PE often causes only vague and nonspecific symptoms.

The most sobering lessons about PE are those obtained from a careful study of the autopsy literature. Deep vein thrombosis (DVT) and PE are much more common than usually realized. Most patients with DVT develop PE and the majority of cases are unrecognized clinically. Untreated, approximately one third of patients who survive an initial PE die of a future embolic episode. This is true whether the initial embolism is small or large.

Most patients who die of PE have not had any diagnostic workup, nor have they received any prophylaxis for the disease. In most cases, the diagnosis has not even been considered, even when classic signs and symptoms are

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documented in the medical chart. Sadly, appropriate diagnostic and therapeutic management often is withheld even when the potential diagnosis of PE has been considered explicitly and documented in the chart.

Pathophysiology: Pulmonary thromboembolism is not a disease in and of itself. Rather, it is an often fatal complication of underlying venous thrombosis. Under normal conditions, microthrombi (tiny aggregates of red cells, platelets, and fibrin) are formed and lysed continually within the venous circulatory system. This dynamic equilibrium ensures local hemostasis in response to injury without permitting uncontrolled propagation of clot. Under pathological conditions, microthrombi may escape the normal fibrinolytic system to grow and propagate. PE occurs when these propagating clots break loose and embolize to block pulmonary blood vessels.

Thrombosis in the veins is triggered by venostasis, hypercoagulability, and vessel wall inflammation. These 3 underlying causes are known as the Virchow triad. All known clinical risk factors for DVT and PE have their basis in one or more of the triad.

Patients who have undergone gynecologic surgery, those with major trauma, and those with indwelling venous catheters may have DVTs that start at any location. For other patients, lower extremity venous thrombosis nearly always starts in the calf veins, which are involved in virtually 100% of all cases of symptomatic spontaneous lower extremity DVT. Although DVT starts in the calf veins, it already has propagated above the knee in 87% of symptomatic patients before the diagnosis is made.

Studies suggest that nearly every patient with thrombus in the upper leg or thigh will have a PE if a sensitive enough test is done to look for it. Current techniques allow us to demonstrate PE in 60-80% of these patients, even though about half have no clinical symptoms to suggest PE. Thrombus in the popliteal segment of the femoral vein (the segment behind the knee) is the cause of PE in more than 60% of cases.

PE can arise from DVT anywhere in the body. Fatal PE often results from thrombus that originates in the axillary or subclavian veins (deep veins of the arm or shoulder) or in veins of the pelvis. Thrombus that forms around indwelling central venous catheters is a common cause of fatal PE.

The belief that calf vein DVT is only a minor threat is outdated and inaccurate. DVT of the calf is a significant source of PE and often causes serious morbidity or death. In fact, one third of the cases of massive PE have their only identified source in the veins of the calf. One important autopsy study showed that more than 35% of patients who died from PE had isolated calf vein thrombosis. Other studies have shown that the overall frequency of PE from DVT isolated to the small deep veins of the calf is 33-46%. Most of the time, emboli from calf veins are of smaller caliber than those from more proximal venous segments, but not all emboli from calf veins are small. Even a very narrow vein can produce a long, sinuous clot that can cause hemodynamic collapse, and approximately 40% of PEs from calf veins produce perfusion scan defects that are large or massive.

Calf emboli that are very small carry their own special risks. In a 1993 study of patients with identifiable thrombi causing paradoxical embolization through a patent foramen ovale, the source was isolated to the calf veins in 15 of 24 cases.

Frequency:

- **In the US:** PE is the third most common cause of death in the US, with at least 650,000 cases occurring annually. It is the first or second most common cause of unexpected death in most age groups. The highest incidence of recognized PE occurs in hospitalized patients. Autopsy results show that as many as 60% of patients dying in the hospital have had a PE, but the diagnosis has been missed in about 70% of the cases. Surgical patients have long been recognized to be at special risk for DVT and PE, but the problem is not confined to surgical patients. Prospective studies show that acute DVT may be demonstrated in any of the following:
 - General medical patients placed at bed rest for a week (10-13%)
 - Patients in medical intensive care units (29-33%)
 - Patients with pulmonary disease kept in bed for 3 or more days (20-26%)
 - Patients admitted to a coronary care unit after myocardial infarction (27-33%)
 - Patients who are asymptomatic after coronary artery bypass graft (48%)

Not only are these patient groups at high risk for clinically unrecognized DVT, but half or more of the patients with DVT also can be shown to have suffered a PE, even though the majority have had none of the classic symptoms of PE.

- **Internationally:** Several papers suggest that the incidence of PE may differ substantially from country to country, but no prospective controlled studies lend support to this notion. The observed variance may be due more to differences in the rate of diagnosis than to differences in the frequency of the disease. If the differences are real, whether they are due to genetic variation or to population differences in diet and activity is not known.

Mortality/Morbidity:

- Massive PE is one of the most common causes of unexpected death, being second only to coronary artery

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disease as a cause of sudden unexpected natural death at any age. Most clinicians do not appreciate the extent of the problem, because the diagnosis is unsuspected until autopsy in approximately 80% of cases.

- Although PE often is fatal, prompt diagnosis and treatment can reduce the mortality rate dramatically.
 - Approximately 10% of patients in whom acute PE is diagnosed die within the first 60 minutes. Of the remainder, the condition eventually is diagnosed and treated in one third and remains undiagnosed in two thirds.
 - Among the group whose PEs are correctly diagnosed and treated, only about one twelfth die from massive PE or its complications. Among the group whose PEs are undiagnosed and therefore untreated, roughly one third die. The diagnosis of PE is missed more than 400,000 times in the US each year, and approximately 100,000 patients die who would have survived with the proper diagnosis and treatment.
- Patients who survive an acute PE are at high risk for recurrent PE and for the development of pulmonary hypertension and chronic cor pulmonale, which occurs in up to 70% of patients and carries its own attendant mortality and morbidity.

Race: Subtle population differences may exist in the incidence of DVT and PE, but the incidence is high in all racial groups.

Sex: PE is common in all trimesters of pregnancy and the puerperium, but sex alone is not an independent risk factor.

Age:

- Although the frequency of PE increases with age, age is not an independent risk factor. Rather, the accumulation of other risk factors, such as underlying illness and decreased mobility, causes the increased frequency of PE in older patients.
- Unfortunately, the diagnosis of PE is especially likely to be missed in older patients. The correct diagnosis of PE is made in 30% of all patients who die with massive PE but in only 10% of those who are 70 years of age or older. It is the most commonly missed diagnosis responsible for death in the elderly institutionalized patient.

CLINICAL

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History: PE is so common and so lethal that the diagnosis should be sought actively in every patient who presents with any chest symptoms that cannot be proven to have another cause.

- Symptoms that should provoke a suspicion of PE must include chest pain, chest wall tenderness, back pain, shoulder pain, upper abdominal pain, syncope, hemoptysis, shortness of breath, painful respiration, new onset of wheezing, any new cardiac arrhythmia, or any other unexplained symptom referable to the thorax.
- The classic triad of signs and symptoms of PE (hemoptysis, dyspnea, chest pain) are neither sensitive nor specific. They occur in fewer than 20% of patients in whom the diagnosis of PE is made, and most patients with those symptoms are found to have some etiology other than PE to account for them. Of patients who go on to die from massive PE, only 60% have dyspnea, 17% have chest pain, and 3% have hemoptysis.
- Many patients with PE are initially completely asymptomatic, and most of those who do have symptoms have an atypical presentation.
- Patients with PE often present with primary or isolated complaints of seizure, syncope, abdominal pain, high fever, productive cough, new onset of reactive airway disease ("adult-onset asthma"), or hiccoughs. They may present with new-onset atrial fibrillation, disseminated intravascular coagulation, or any of a host of other signs and symptoms.
- Pleuritic or respirophasic chest pain is a particularly worrisome symptom. PE can be proven in 21% of young, active patients who come to the ED complaining only of pleuritic chest pain. These patients usually lack any other classical signs, symptoms, or known risk factors for pulmonary thromboembolism. Such patients often are dismissed inappropriately with an inadequate workup and a nonspecific diagnosis, such as musculoskeletal chest pain or pleurisy.

Physical:

- Massive PE causes hypotension due to acute cor pulmonale, but the physical examination findings early in submassive PE may be completely normal. Initially, abnormal physical findings are absent in most patients with PE.

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- After 24-72 hours, loss of pulmonary surfactant often causes atelectasis and alveolar infiltrates that are indistinguishable from pneumonia on clinical examination and by x-ray.
- New wheezing may be appreciated. If pleural lung surfaces are affected, a pulmonary rub may be heard.
- The spontaneous onset of chest wall tenderness without a good history of trauma is always worrisome, because patients with PE may have chest wall tenderness as the only physical finding.
- In patients with massive PE, the incidence of physical signs has been reported as follows:
 - 96% have tachypnea (respiratory rate >16/min)
 - 58% develop rales
 - 53% have an accentuated second heart sound
 - 44% have tachycardia (heart rate >100/min)
 - 43% have fever (temperature >37.8° C)
 - 36% have diaphoresis
 - 34% have an S3 or S4 gallop
 - 32% have clinical signs and symptoms suggesting thrombophlebitis
 - 24% have lower extremity edema
 - 23% have a cardiac murmur
 - 19% have cyanosis

Causes:

- Hypercoagulable states
 - Prolonged venous stasis or significant injury to the veins can provoke DVT and PE in any person, but increasing evidence suggests that spontaneous DVT and PE nearly always are related to some underlying hypercoagulable state. Other identified "causes" most likely serve only as triggers for a system that is already out of balance.
 - Hypercoagulable states may be acquired or congenital. An inborn resistance to activated protein C is the most common congenital risk factor for DVT that has been identified to date. Most patients with this syndrome have a genetic mutation in factor V known as "factor V Leyden," although other mechanisms also can produce a resistance to activated protein C.
 - Primary or acquired deficiencies in protein C, protein S, or antithrombin III are also common underlying causes of DVT and PE.
- Risk markers: The most important clinically identifiable risk markers for DVT and PE are a prior history of DVT or PE, recent surgery or pregnancy, prolonged immobilization, or underlying malignancy. Many other recognized markers of risk for venous thromboembolic disease are listed here.
 - AIDS (lupus anticoagulant)
 - Antithrombin III deficiency
 - Behçet disease
 - Blood type A
 - Burns
 - Catheters (indwelling venous infusion catheters)
 - Chemotherapy
 - Congestive heart failure (CHF)
 - Drug abuse (intravenous [IV] drugs)

- Drug-induced lupus anticoagulant
- DVT in the past
- Estrogen replacements (high dose only)
- Fibrinogen abnormality
- Fractures
- Hemolytic anemias
- Heparin-associated thrombocytopenia
- Homocystinuria
- Hyperlipidemias
- Immobilization
- Malignancy
- Myocardial infarction
- Obesity
- Old age
- Oral contraceptives
- PE in the past
- Phenothiazines
- Plasminogen abnormality
- Plasminogen activator abnormality
- Polycythemia
- Postoperative
- Postpartum period
- Pregnancy
- Protein C deficiency
- Protein S deficiency
- Resistance to activated protein C
- Systemic lupus erythematosus
- Thrombocytosis
- Trauma
- Ulcerative colitis
- Varicose veins
- Venography
- Venous pacemakers
- Venous stasis
- Warfarin (first few days of therapy)

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Other Problems to be Considered:

Whether the presentation of the patient with pulmonary thromboembolism is typical or atypical, the list of differential diagnoses remains extensive and the true diagnosis must be sought actively.

Pneumonia
Musculoskeletal pain
Herpes zoster
Tuberculosis
Pleurisy
Costochondritis
Chronic obstructive pulmonary disease
Carcinoma
Rib fractures
Pericarditis
Asthma
Congestive heart failure
Angina or myocardial infarction
Hyperventilation
Pneumothorax
Hepatitis
Pancreatitis
Splenic flexure syndrome
Bronchitis
Salicylate intoxication
Hyperventilation
Myositis
Lung carcinoma
Tuberculosis
Sepsis
Pericardial tamponade

Lab Studies:

- Clinical variables alone lack sufficient power to permit a treatment decision, so patients in whom PE is suspected must undergo diagnostic tests until the diagnosis is proven or ruled out, or until some alternative diagnosis is proven.
- Unfortunately, no known blood or serum test can move a patient with a high clinical likelihood of pulmonary thromboembolism into a low likelihood category or vice versa.
- The PO₂ on arterial blood gases analysis (ABG) has a zero or even negative predictive value in a typical population of patients in whom PE is suspected clinically. This is contrary to what has been taught in many textbooks, and it seems counter-intuitive, but it is demonstrably true. The reason is as follows:
 - Other etiologies that masquerade as PE are more likely to lower the PO₂ than is PE. In fact, because other diseases that may masquerade as PE (eg, chronic obstructive pulmonary disease [COPD], pneumonia, CHF) affect oxygen exchange more than PE, the blood oxygen level often has an inverse predictive value for PE.
 - In most settings, fewer than half of all patients with symptoms suggestive of PE actually turn out to have PE as their diagnosis. In such a population, if any reasonable level of PaO₂ is chosen as a dividing line, the incidence of PE will be higher in the group with a PaO₂ above the dividing line than in the group whose PaO₂ is below the divider. This is a specific example of a general truth that may be demonstrated mathematically for any test finding with a Gaussian distribution and a population incidence of less than 50%.
 - Conversely, in a patient population with a very high incidence of PE and a lower incidence of other respiratory ailments (such as postoperative orthopedic patients with sudden onset of shortness of breath), a low PO₂ has a strongly positive predictive value for PE.
 - The discussion above holds true not only for arterial PO₂, but also for the alveolar-arterial oxygen gradient and for the oxygen saturation level as measured by pulse oximetry. In particular, pulse oximetry is extremely insensitive, is normal in the majority of patients with PE, and should not be used to direct a diagnostic workup.
- The white blood cell (WBC) count may be normal or elevated. A WBC count as high as 20,000 is not uncommon in patients with PE.
- Clotting study results are normal in most patients with pulmonary thromboembolism.
 - Prolongation of the prothrombin time (PT), activated partial thromboplastin time (aPTT), or clotting time have no prognostic value in the diagnosis of PE. DVT and PE can and often do recur in patients who are fully anticoagulated.
 - New PE in the hospital occurs in the following despite therapeutic anticoagulation:
 - Patients who have nonfloating DVT without PE at presentation (3%).
 - Patients who present with a floating thrombus but no PE (13%).
 - Patients who already had PE at presentation but had no floating thrombus (11%).
 - Patients presenting with PE who have a floating thrombus visible at venography (39%).
- D-dimer is a unique degradation product produced by plasmin-mediated proteolysis of cross-linked fibrin. D-dimer is measured by latex agglutination or by an enzyme-linked immunosorbent assay (ELISA) test that is considered positive if the level is greater than 500 ng/mL.
 - The latex agglutination test (one trade name is SimpliRED) is completely unreliable, with a sensitivity of only 50-60% for DVT and PE.
 - The ELISA test is more sensitive than the latex agglutination test, but in a population with a PE prevalence of 50%, the negative predictive value of the test is still only 79%. Under the best of circumstances, the D-dimer study misses 10% of patients with positive pulmonary angiograms, while only 30% of those with a positive D-dimer will have a positive angiogram.
 - At the present time, D-dimer is not sensitive or specific enough to change the course of diagnostic evaluation or treatment for patients with suspected PE. Complex theoretical algorithms that attempt to combine unreliable D-dimer results with unreliable guesses at clinical likelihood are not useful in guiding the workup of a live patient with signs or symptoms suggestive of DVT and PE.

Imaging Studies:

- The initial chest x-ray (CXR) findings of a patient with PE are virtually always normal.

- On rare occasions they may show the Westermark sign, a dilatation of the pulmonary vessels proximal to an embolism along with collapse of distal vessels, sometimes with a sharp cutoff.
 - Over time, an initially normal CXR often begins to show atelectasis, which may progress to cause a small pleural effusion and an elevated hemidiaphragm.
 - After 24-72 hours, one third of patients with proven PE develop focal infiltrates that are indistinguishable from an infectious pneumonia.
 - A rare late finding of pulmonary infarction is the Hampton hump, a triangular or rounded pleural-based infiltrate with the apex pointed toward the hilum, frequently located adjacent to the diaphragm.
- Nuclear scintigraphic ventilation-perfusion (V/Q) scanning of the lung is the single most important diagnostic modality for detecting pulmonary thromboembolism available to the clinician.
 - V/Q scan is indicated whenever the diagnosis of PE is suspected and no alternative diagnosis can be proved. V/Q also is indicated for most patients with DVT even without symptoms of PE.
 - A repeat V/Q scan is indicated before stopping anticoagulation in a patient with irreversible risk factors for DVT and PE, because recurrent symptoms are common and a reference "posttreatment" V/Q scan can serve as a new baseline for comparison, often sparing the patient the need for a future angiogram.
 - The Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) classification scheme allows interpretation of the results of the V/Q scan in a meaningful way, but this standard classification is not used in its entirety at every institution. At some institutions, V/Q scan findings are never reported as normal no matter what the actual pattern of perfusion. This is unfortunate, because normal perfusion is the scan pattern with the highest predictive value. Some institutions continue to report nondiagnostic V/Q patterns using obsolete and clinically confusing terminology, such as "indeterminate," "intermediate," or "low probability."
 - Diagnostic V/Q patterns classified as high probability or as normal perfusion may be relied upon to guide the clinical management of patients when the prior clinical assessment is concordant with the scan result.
 - No matter what language is used, a nondiagnostic V/Q pattern is not an acceptable endpoint in the workup for pulmonary thromboembolism. Pulmonary angiography or another definitive test must be performed when the diagnosis remains uncertain.
 - Thousands of patients die needlessly because of wishful thinking or confusion over this simple fact: unless the scan shows normal perfusion, the patient must not be abandoned without a definitive test to rule out PE or a definitive test to prove an alternative diagnosis.
- Normal V/Q scan
 - No perfusion defects are seen.
 - At least 2% of patients with PE have this pattern, and 4% of patients with this pattern have PE. This means that approximately 1 of every 25 patients sent home after a normal V/Q scan actually has a PE that has been missed. This is unfortunate, but risk-benefit analysis supports the idea that unless the presentation is highly convincing and no alternate diagnosis is demonstrable, a normal perfusion scan pattern often may be considered negative for PE.
- High-probability scan
 - This includes scans with any of the following findings:
 - Two or more segmental or larger perfusion defects with normal CXR and normal ventilation
 - Two or more segmental or larger perfusion defects where CXR abnormalities and ventilation defects are substantially smaller than the perfusion defects
 - Two or more subsegmental and one segmental perfusion defect with normal CXR and normal ventilation
 - Four or more subsegmental perfusion defects with normal CXR and normal ventilation
 - Forty-one percent of patients with PE have this pattern and 87% of patients with this pattern have PE.
 - In most clinical settings, a high-probability scan pattern may be considered positive for PE.
- Nondiagnostic scan (with a pattern type that was formerly graded as low probability)
 - This includes scans with any of the following findings:
 - Small perfusion defects, regardless of number, ventilation findings, or CXR findings
 - Perfusion defects substantially smaller than a CXR abnormality in the same area

- Matching perfusion and ventilation defects in less than 75% of one lung zone or in less than 50% of one lung, with a normal or nearly normal CXR
 - A single segmental perfusion defect with a normal CXR, regardless of ventilation match or mismatch
 - Nonsegmental perfusion defects
- Sixteen percent of patients with PE have this pattern and 14% of patients with this pattern have PE. This pattern often is called "low probability," but the term is a misnomer: in a typical population, 1 in 7 patients with this pattern turn out to have a PE.
- This scan pattern is an indication for pulmonary angiography or some other definitive test.
 - All patients suspected of PE who have a nondiagnostic scan must have PE definitively ruled out or some definitive alternative diagnosis made.
 - Discharging such patients without a definitive diagnostic outcome is highly inappropriate, as this leads to the deaths of many patients.
- Nondiagnostic scan (with a pattern type that was formerly graded as "intermediate probability")
 - Any V/Q abnormality not otherwise classified: Approximately 40% of patients with PE fall into this category and 30% of all patients with this pattern have PE.
 - This scan pattern is always an indication for pulmonary angiography or another definitive test to rule out PE. Failure to pursue the diagnosis further in these patients leads to disastrous outcomes.
- Pulmonary angiography remains the criterion standard for the diagnosis of PE.
 - When performed carefully and completely, a positive pulmonary angiogram provides virtually 100% certainty that an obstruction to pulmonary arterial blood flow does exist. A negative pulmonary angiogram provides greater than 90% certainty in the exclusion of PE.
 - A positive angiogram is an acceptable endpoint no matter how abbreviated the study. However, a complete negative study requires the visualization of the entire pulmonary tree bilaterally. This is accomplished via selective cannulation of each branch of the pulmonary artery and injection of contrast material into each branch, with multiple views of each area. Even then, emboli in vessels smaller than third order or lobular arteries are not seen.
 - Small emboli cannot be seen angiographically, yet embolic obstruction of these smaller pulmonary vessels is very common when postmortem examination follows a negative angiogram. These small emboli can produce pleuritic chest pain and a small sterile effusion even though the patient has a normal V/Q scan and a normal pulmonary angiogram.
 - In most patients, however, PE is a disease of multiple recurrences, with both large and small emboli already present by the time the diagnosis is first suspected. Under these circumstances, both the V/Q scan and the angiogram are likely to detect at least some of the emboli.
- High-resolution helical (spiral) computed tomographic angiography (CTA) is a promising technique that soon may replace ordinary contrast pulmonary angiography. In many patients, helical CT scans with intravenous contrast can resolve third-order pulmonary vessels without the need for invasive pulmonary artery catheters.
 - The absolute sensitivity and specificity of CTA are evolving over time. Today we can say safely that in a patient with hemodynamic collapse due to a large PE, CTA is unlikely to miss the lesion. In a patient with pleuritic chest pain due to multiple small emboli that have lodged in distal vessels, CTA is more likely to miss the lesions, but these lesions also may be difficult to detect using conventional angiography.
 - Ongoing studies will determine whether the sensitivity and specificity of CTA are high enough to displace invasive angiography for the diagnosis of PE.
- Duplex ultrasound
 - The diagnosis of PE can be proven by demonstrating the presence of a DVT at any site. Sometimes this may be accomplished noninvasively, by using duplex ultrasound.
 - To look for DVT using ultrasound, the ultrasound transducer is placed against the skin and then is pressed inward firmly enough to compress the vein being examined. In an area of normal veins, the veins are easily compressed completely closed, while the muscular arteries are extremely resistant to compression.
 - Where DVT is present, the veins do not collapse completely when pressure is applied using the ultrasound probe.
 - A negative ultrasound scan does not rule out DVT, because many DVTs occur in areas that are inaccessible to ultrasonic examination. Before an ultrasound scan can be considered negative, the entire deep venous system must be interrogated using centimeter-by-centimeter compression testing of every vessel.
 - In two thirds of patients with PE, the site of DVT cannot be visualized by ultrasound, so a negative duplex ultrasound does not

markedly reduce the likelihood of PE.

Other Tests:

- Electrocardiogram
 - The most common ECG abnormalities in the setting of PE are tachycardia and nonspecific ST-T wave abnormalities.
 - Any other ECG abnormality may appear with equal likelihood, but none are sensitive or specific for PE.
 - The classic findings of right heart strain and acute cor pulmonale are tall, peaked P waves in lead II (P pulmonale), right axis deviation, right bundle-branch block, an S1-Q3-T3 pattern, or atrial fibrillation. Unfortunately, only 20% of patients with proven PE have any of these classic ECG abnormalities.
 - If ECG abnormalities are present, they may be suggestive of PE, but the absence of ECG abnormalities has no significant predictive value.
 - One fourth of patients with proven PE have ECGs that are unchanged from their baseline state.

TREATMENT

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Prehospital Care:

- The most important thing that can be done in the prehospital setting is to transport the patient to a hospital. As long as no reliable method is available of making a clinical diagnosis of PE without diagnostic tests, treating PE in a meaningful way in the field will remain difficult.
- Isolated case reports exist of patients who have been resuscitated successfully after receiving fibrinolytic agents in the field for cardiac arrest strongly believed (and later proven) to be due to PE.
- Presumptive fibrinolysis in the field is aggressive, but it may be a reasonable course of action today when patients being treated as outpatients for known DVT suddenly become short of breath and hypotensive.
- Oxygen always should be started in the prehospital phase, and an IV line should be placed if it can be accomplished rapidly without delaying transport. Fluid loading should be avoided unless the patient's hemodynamic condition is deteriorating rapidly, because IV fluids may worsen the patient's condition. Without invasive testing or trial and surveillance, the physician cannot know whether additional preload will help or hurt a heart that is failing already because of high outflow pressures from pulmonary vascular obstruction.

Emergency Department Care:

- Fibrinolytic therapy has been the standard of care for all patients with massive or unstable PE since the 1970s. Unless overwhelming contraindications are evident, a rapidly acting fibrinolytic agent should be administered immediately to every patient who has suffered any degree of hypotension or is significantly hypoxemic from PE.
 - Improvement of hypotension in response to hydration or pressors does not remove the indication for immediate fibrinolysis. The fact that hypotension has occurred at all is a sufficient indication that the patient has exhausted his or her cardiopulmonary reserves and is at high risk for sudden collapse and death.
 - Fibrinolysis also is strongly indicated for patients with PE who have any evidence of right heart strain, because substantial evidence indicates that the mortality rate can be cut in half by early fibrinolysis in this patient population.
 - Today, fibrinolysis should be considered for all patients with PE who lack specific contraindications to the therapy. Many centers now regard fibrinolysis as the primary treatment of choice for all patients with PE and even for all patients who have DVT without evidence of PE. Over the past 20 years, a large number of small studies and a small number of large studies have demonstrated consistently that fibrinolytic therapy dramatically reduces the mortality rate, morbidity, and rate of recurrence of PE regardless of the size or type of PE at the time of presentation.
- Heparin reduces the mortality rate of PE because it slows or prevents clot progression and reduces the risk of further embolism.
 - Heparin does nothing to dissolve clot that has developed already, but it is still the single most important treatment that can be provided, because the greatest contribution to the mortality rate is the ongoing embolization of new thrombi. Prompt effective anticoagulation has been shown to reduce the overall mortality rate from 30% to less than 10%.
 - Early heparin anticoagulation is so essential that heparin should be started as soon as the diagnosis of pulmonary thromboembolism is considered seriously. Anticoagulation should not wait for the results of diagnostic tests: if anticoagulation is delayed, venous thrombosis and PE may progress rapidly.
- Oxygen should be administered to every patient with suspected PE, even when the arterial PO₂ is perfectly normal, because increased alveolar oxygen may help to promote pulmonary vascular dilatation.
- IV fluids may help or may hurt the patient who is hypotensive from PE depending on which point on the Starling curve describes the

patient's condition.

- A Swan-Ganz catheter is helpful to determine whether a fluid bolus is indicated; as an alternative, a cautious trial of a small fluid bolus may be attempted, with careful surveillance of the systolic and diastolic blood pressures and immediate cessation if the situation worsens after the fluid bolus.
- Improvement or normalization of blood pressure after fluid loading does not mean the patient has become hemodynamically stable.
- Fibrinolysis is indicated overwhelmingly for any patient with a PE large enough to cause hypotension, even if the hypotension is transient or correctable. As noted above, early fibrinolysis is expected to reduce the mortality rate by 50% for patients who have right ventricular dysfunction due to PE, even if they are hemodynamically stable.
- Cardiopulmonary resuscitation (CPR) and advanced cardiac life support (ACLS) protocols are of no value in patients whose cardiac arrest is due to PE, since obstruction of the pulmonary circuit prevents oxygenated blood from reaching the peripheral and cerebral circulation.
 - The only management approaches likely to be helpful in this situation are emergency cardiopulmonary bypass or emergency thoracotomy.
 - If cardiopulmonary bypass with extracorporeal membrane oxygenation is available, it may be lifesaving for patients with massive PE in whom cardiac arrest has occurred or appears imminent.
- Prior to the introduction of emergency cardiopulmonary bypass, the expected mortality rate after cardiac arrest from PE was 100%. Although experience with the technique is limited, one study reported the complete recovery of 7 of 9 patients when cardiopulmonary bypass was used to stabilize the patients for operative embolectomy.
- If emergency cardiopulmonary bypass is not available, several case reports suggest that immediate bilateral thoracotomy and massage of the pulmonary vessels may dislodge a saddle embolus and restore circulation to part of the pulmonary vascular tree.
 - This aggressive procedure is appropriate in patients with cardiac arrest from proven or highly likely PE, because the expected mortality rate without the procedure is 100%.
 - The procedure is not one to be used as a "last resort." Thoracotomy must be carried out immediately to be of any value, because in cardiac arrest from PE, closed-chest CPR is not able to provide any blood flow to the cerebral circulation.
- Compression stockings
 - Compression stockings that provide a 30-40 mm Hg compression gradient should be used, because they are a safe and effective adjunctive treatment that can limit or prevent extension of thrombus.
 - True gradient compression stockings (30-40 mm Hg or higher) are highly elastic, providing a gradient of compression that is highest at the toes and gradually decreases to the level of the thigh. This reduces capacitive venous volume by approximately 70% and increases the measured velocity of blood flow in the deep veins by a factor of 5 or more. Compression stockings of this type have been proven effective in the prophylaxis of thromboembolism and are also effective in preventing progression of thrombus in patients who already have DVT and PE.
 - A 1994 meta-analysis calculated a DVT risk odds ratio of 0.28 for gradient compression stockings (as compared to no prophylaxis) in patients undergoing abdominal surgery, gynecologic surgery, or neurosurgery.
 - Other studies have found that gradient compression stockings and low-molecular-weight heparin (LMWH) were the most effective modalities in reducing the incidence of DVT after hip surgery; they were more effective than subcutaneous unfractionated heparin, oral warfarin, dextran, or aspirin.
 - The ubiquitous white stockings known as "anti-embolic stockings" or "Ted hose" produce a maximum compression of 18 mm Hg. Ted hose rarely are fitted in such a way as to provide even that inadequate gradient compression. Because they provide such limited compression, they have no efficacy in the treatment of DVT and PE, nor have they been proven effective as prophylaxis against a recurrence.
 - True 30-40 mm Hg gradient compression pantyhose are available in sizes for pregnant women. They are recommended by many specialists for all pregnant women because they not only prevent DVT, but they also reduce or prevent the development of varicose veins during pregnancy.

Consultations:

- Fibrinolytic therapy should not be delayed while consultation is sought. The decision to treat PE by fibrinolysis is properly made by the responsible emergency physician alone, and fibrinolytic therapy is properly administered in the ED. No amount of contrary advice from a stay-at-home consultant can remove the duty to provide immediate effective treatment for this life-threatening condition.
- An interventional radiology consultation may be helpful for catheter-directed fibrinolysis in selected patients. In rare cases, arranging for placement of a venous filter may be appropriate, but recent prospective randomized studies suggest that venous filters probably increase the overall mortality rate slightly.

Immediate full anticoagulation is mandatory for all patients with suspected DVT or PE, because effective anticoagulation with heparin reduces the mortality rate of PE from 30% to less than 10%. Heparin works by activating antithrombin III to slow or prevent the progression of DVT and to reduce the size and frequency of PE. Heparin does not dissolve existing clot.

Anticoagulation is essential, but anticoagulation alone does not guarantee a successful outcome. DVT and PE may recur or extend despite full and effective heparin anticoagulation.

Fibrinolytic therapy is mandatory for 3 groups of patients: those who are hemodynamically unstable, those with right heart strain and exhausted cardiopulmonary reserves, and those who are expected to have multiple recurrences of pulmonary thromboembolism over a period of years. Patients with a prior history of PE and those with known deficiencies of protein C, protein S, or antithrombin III should be included in this latter group.

Besides those for whom it is mandatory, fibrinolysis should be considered as a potential therapy for every patient with proven PE.

Long-term anticoagulation is essential for patients who survive an initial DVT or PE. The optimum total duration of anticoagulation has been controversial in recent years, but general consensus holds that at least 6 months of anticoagulation is associated with significant reduction in recurrences and a net positive benefit.

Drug Category: *Fibrinolytics* -- Fibrinolysis is always indicated for hemodynamically unstable patients with PE, because no other medical therapy can improve acute cor pulmonale quickly enough to save the patient's life.

Because it is less invasive and has fewer complications, fibrinolytic therapy has replaced surgical embolectomy as the primary mode of treatment for hemodynamically unstable patients with pulmonary thromboembolism. Surgical thromboembolectomy now is reserved for patients in whom fibrinolysis has failed or cannot be tolerated.

Fibrinolytic regimens currently in common use for PE include 2 forms of recombinant tissue plasminogen activator, t-PA (alteplase) and r-PA (reteplase), along with urokinase and streptokinase. Alteplase usually is given as a front-loaded infusion over 90 or 120 minutes. Urokinase and streptokinase usually are given as infusions over 24 hours or more. Reteplase is a new-generation thrombolytic with a longer half-life that is given as a single bolus or as 2 boluses administered 30 minutes apart.

Of the 4, the faster-acting agents reteplase and alteplase are preferred for patients with PE, because the condition of patients with PE can deteriorate extremely rapidly.

Many comparative clinical studies have shown that administration of a 2-hour infusion of alteplase is more effective (and more rapidly effective) than urokinase or streptokinase over a 12-hour period. One prospective randomized study comparing reteplase and alteplase found that total pulmonary resistance (along with pulmonary artery pressure and cardiac index) improved significantly after just 0.5 hours in the reteplase group as compared to 2 hours in the alteplase group. Fibrinolytic agents do not seem to differ significantly with respect to safety or overall efficacy.

Streptokinase is least desirable of all the fibrinolytic agents because antigenic problems and other adverse reactions force the cessation of therapy in a large number of cases.

Empiric thrombolysis may be indicated in selected hemodynamically unstable patients, particularly when the clinical likelihood of PE is overwhelming and the patient's condition is deteriorating. The overall risk of severe complications from thrombolysis is low and the potential benefit in a deteriorating patient with PE is high. Empiric therapy especially is indicated when a patient is compromised so severely that he or she will not survive long enough to obtain a confirmatory study. Empiric thrombolysis should be reserved, however, for cases that truly meet these definitions, as many other clinical entities (including aortic dissection) may masquerade as PE, yet may not benefit from thrombolysis in any way.

If indicated, fibrinolysis may be used in pregnancy at the same dose used for nonpregnant patients. Fear of complications should never prevent the use of fibrinolytics when a pregnant patient has significant right ventricular dysfunction from PE, as the best predictor of fetal outcome in this setting remains maternal outcome.

Drug Name	<p>Reteplase (r-PA, Retavase) -- Second-generation recombinant tissue-type plasminogen activator. As fibrinolytic agent, seems to work faster than its forerunner, alteplase, and also may be more effective in patients with larger clot burden. Also has been reported more effective than other agents in lysis of older clots.</p> <p>Two major differences help explain these improvements. Compared to alteplase, reteplase does not bind fibrin so tightly, allowing drug to diffuse more freely through clot. Another advantage seems to be that reteplase does not compete with plasminogen for fibrin-binding sites, allowing plasminogen at site of clot to be transformed into clot-dissolving plasmin.</p> <p>FDA has not approved reteplase for use in PE.</p> <p>Studies of reteplase for PE have used same dose approved by FDA for coronary artery fibrinolysis.</p>
Adult Dose	<p>Two 10-unit IV boluses, given 30 min apart</p> <p>In setting of cardiac arrest or impending arrest due to PE, single IV bolus of 20 units has been used successfully in small number of cases</p>
Pediatric Dose	<p>Not established</p>

Contraindications	Active internal bleeding; history of cerebrovascular accident; recent intracranial or intraspinal surgery or trauma; intracranial neoplasm, arteriovenous malformation, or aneurysm; known bleeding diathesis; severe uncontrolled hypertension
Interactions	Antiplatelet agents or anticoagulants may increase risk of bleeding
Pregnancy	C - Safety for use during pregnancy has not been established.
Precautions	<p>In following conditions, risks of fibrinolytic therapy may be increased and should be weighed against anticipated benefits: recent major surgery; recent puncture of noncompressible vessels; cerebrovascular disease; recent GI or GU bleeding; recent trauma; hypertension: systolic BP >180 mm Hg and/or diastolic BP >110 mm Hg; high likelihood of left heart thrombus (eg, mitral stenosis with atrial fibrillation); acute pericarditis; subacute bacterial endocarditis; hemostatic defects including those secondary to severe hepatic or renal disease; significant hepatic dysfunction; pregnancy; diabetic hemorrhagic retinopathy or other hemorrhagic ophthalmic conditions; septic thrombophlebitis or occluded AV cannula at seriously infected site; advanced age (ie, >75 y); patients currently receiving oral anticoagulants (eg, warfarin sodium); any other condition in which bleeding would be particularly difficult to manage because of its location; documented hypersensitivity</p> <p>Combining fibrinolytic agents and heparin can be confusing; heparin never should be given concurrently with urokinase, streptokinase, or APSAC to treat any condition; instead, heparin is started when thrombin time or aPTT is at or below twice normal control value; heparin should be given concurrently with alteplase or reteplase for treatment of acute MI; neither heparin nor aspirin should be given concurrently when tissue plasminogen activator used for acute ischemic stroke; when tissue-type plasminogen activators used for PE, heparin may be given concurrently or may be held and restarted after end of fibrinolytic therapy or when thrombin time or aPTT is at or below twice normal control value</p> <p>Coagulation studies should be performed 4 h after initiation of fibrinolytic therapy</p>
Drug Name	Alteplase (rt-PA, Activase) -- Drug most often used to treat PE in ED. One advantage of alteplase is that FDA has approved it for this indication. Another advantage is that most ED personnel are familiar with alteplase because it is used so widely for treatment of patients with acute MI.
Adult Dose	<p>100 mg IV infusion over 2 h (FDA-approved regimen for PE)</p> <p>Accelerated 90-min regimen is used widely, and most authors believe it is both safer and more effective than 2-h infusion. For accelerated regimen, recommended total dose based upon patient weight, not to exceed 100 mg</p> <p><67 kg: drug administered as 15-mg IV bolus, followed by 0.75 mg/kg infused over next 30 min (not to exceed 50 mg) and then 0.50 mg/kg over next 60 min (not to exceed 35 mg)</p> <p>>67 kg: 100 mg given as 15-mg IV bolus followed by 50 mg infused over next 30 min and then 35 mg infused over next 60 min</p> <p>Heparin therapy should be instituted or reinstated near end of or immediately following alteplase infusion, when aPTT or thrombin time returns to twice normal or less.</p>
Pediatric Dose	Use weight-adjusted accelerated regimen as in adults
Contraindications	Active internal bleeding; history of cerebrovascular accident; recent intracranial or intraspinal surgery or trauma; intracranial neoplasm, arteriovenous malformation, or aneurysm; known bleeding diathesis; severe uncontrolled hypertension
Interactions	Antiplatelet agents or anticoagulants increase risk of bleeding
Pregnancy	C - Safety for use during pregnancy has not been established.
Precautions	<p>In following conditions, risks of fibrinolytic therapy may be increased and should be weighed against anticipated benefits:</p> <p>Recent major surgery; recent puncture of noncompressible vessels; cerebrovascular disease; recent GI or GU bleeding; recent trauma; hypertension: systolic BP >180 mm Hg and/or diastolic BP >110 mm Hg; high likelihood of left heart thrombus (eg, mitral stenosis with atrial fibrillation); acute pericarditis; subacute bacterial endocarditis; hemostatic defects including those secondary to severe hepatic or renal disease; significant hepatic dysfunction; pregnancy; diabetic hemorrhagic retinopathy or other hemorrhagic ophthalmic conditions; septic thrombophlebitis or occluded AV cannula at seriously infected site; advanced age (ie, >75 y); patients currently receiving oral anticoagulants (eg, warfarin sodium); any other condition in which bleeding would be particularly difficult to manage because of its location; documented hypersensitivity</p> <p>Combining fibrinolytic agents and heparin can be confusing; heparin never should be given with urokinase, streptokinase, or APSAC to treat any condition; instead, heparin started when thrombin time or aPTT is at or below twice normal control value; heparin should be given concurrently with alteplase or reteplase for treatment of acute MI; neither heparin nor aspirin should be given concurrently when tissue plasminogen activator used for acute ischemic stroke; when tissue-type plasminogen activators used for PE, heparin may be given concurrently or may be held and restarted after end of fibrinolytic therapy or when thrombin time or aPTT is at or below twice normal control value</p> <p>Coagulation studies should be performed 4 h after initiation of fibrinolytic therapy</p>

Drug Name	Urokinase (Abbokinase) -- Direct plasminogen activator produced by human fetal kidney cells grown in culture. Relatively low in antigenicity. At time of this writing, production of urokinase and many other human cell culture products has been put on hold because of concerns about viral infections that can colonize human cell production facilities. When used for localized fibrinolysis, given as local catheter-directed continuous infusion directly into area of thrombus with no loading dose. When used for PE, loading dose necessary.
Adult Dose	Loading dose: 2000 U/lb infused over 10 min Maintenance dose: 2000 U/lb/h for 24 h
Pediatric Dose	Loading dose: 4400 U/kg IV over 10 min Maintenance dose: 4400 U/kg/h IV for 12-72 h
Contraindications	Active internal bleeding; history of cerebrovascular accident; recent intracranial or intraspinal surgery or trauma; intracranial neoplasm, arteriovenous malformation, or aneurysm; known bleeding diathesis; severe uncontrolled hypertension
Interactions	Antiplatelet agents or anticoagulants increase risk of bleeding
Pregnancy	C - Safety for use during pregnancy has not been established.
Precautions	In following conditions, risks of fibrinolytic therapy may be increased and should be weighed against anticipated benefits: recent major surgery; recent puncture of noncompressible vessels; cerebrovascular disease; recent GI or GU bleeding; recent trauma; hypertension: systolic BP >180 mm Hg and/or diastolic BP >110 mm Hg; high likelihood of left heart thrombus (eg, mitral stenosis with atrial fibrillation); acute pericarditis; subacute bacterial endocarditis; hemostatic defects including those secondary to severe hepatic or renal disease; significant hepatic dysfunction; pregnancy; diabetic hemorrhagic retinopathy or other hemorrhagic ophthalmic conditions; septic thrombophlebitis or occluded AV cannula at seriously infected site; advanced age (ie, >75 y); patients currently receiving oral anticoagulants (eg, warfarin sodium); any other condition in which bleeding would be particularly difficult to manage because of its location; documented hypersensitivity Combining fibrinolytic agents and heparin can be confusing; heparin never should be given concurrently with urokinase, streptokinase, or APSAC to treat any condition; instead, heparin started when thrombin time or aPTT at or below twice normal control value; heparin should be given concurrently with alteplase or reteplase for treatment of acute MI; neither heparin nor aspirin should be given concurrently when tissue plasminogen activator used for acute ischemic stroke; when tissue-type plasminogen activators used for PE, heparin may be given concurrently or may be held and restarted after end of fibrinolytic therapy or when thrombin time or aPTT at or below twice normal control value Coagulation studies should be performed 4 h after initiation of fibrinolytic therapy
Drug Name	Streptokinase (Kabikinase, Streptase) -- Highly antigenic, with high likelihood that treatment will be interrupted because of allergic drug reactions.
Adult Dose	Loading dose: 250,000 U over 30 min Maintenance dose: 100,000 U/h for 12-72 h
Pediatric Dose	Not established; 3500-4000 U/kg IV over 30 min followed by 1000-1500 U/kg/h suggested
Contraindications	Exposure to streptokinase within past 4 y; recent streptococcal infection; active internal bleeding; history of cerebrovascular accident; recent intracranial or intraspinal surgery or trauma; intracranial neoplasm, arteriovenous malformation, or aneurysm; known bleeding diathesis; severe uncontrolled hypertension
Interactions	Antiplatelet agents or anticoagulants increase risk of bleeding
Pregnancy	C - Safety for use during pregnancy has not been established.
Precautions	In following conditions, risks of fibrinolytic therapy may be increased and should be weighed against anticipated benefits: recent major surgery; recent puncture of noncompressible vessels; cerebrovascular disease; recent GI or GU bleeding; recent trauma; hypertension: systolic BP >180 mm Hg and/or diastolic BP >110 mm Hg; high likelihood of left heart thrombus (eg, mitral stenosis with atrial fibrillation); acute pericarditis; subacute bacterial endocarditis; hemostatic defects including those secondary to severe hepatic or renal disease; significant hepatic dysfunction; pregnancy; diabetic hemorrhagic retinopathy or other hemorrhagic ophthalmic conditions; septic thrombophlebitis or occluded AV cannula at seriously infected site; advanced age (ie, >75 y); patients currently receiving oral anticoagulants (eg, warfarin sodium); any other condition in which bleeding would be particularly difficult to manage because of its location; documented hypersensitivity Chills, fever, nausea, and skin rashes are frequent (up to 20%); BP and heart rate drop in about 10% of cases during or shortly after treatment Late complications can include purpura, respiratory distress syndrome, serum sickness, Guillain-Barré syndrome, vasculitis, and renal or hepatic dysfunction Combining fibrinolytic agents and heparin can be confusing; heparin never should be given concurrently with urokinase, streptokinase, or APSAC to treat any condition; instead, heparin started when thrombin time or aPTT at or below twice normal control value; heparin should be given concurrently with alteplase or reteplase for treatment of acute MI; neither heparin nor aspirin should be given concurrently when tissue plasminogen activator used for acute ischemic stroke;

when tissue-type plasminogen activators used for PE, heparin may be given concurrently or may be held and restarted after end of fibrinolytic therapy or when thrombin time or aPTT at or below twice normal control value
Coagulation studies should be performed 4 h after initiation of fibrinolytic therapy

Drug Category: Anticoagulants -- Heparin augments the activity of antithrombin III and prevents the conversion of fibrinogen to fibrin. Full-dose LMWH or full-dose unfractionated IV heparin should be initiated at the first suspicion of DVT or PE.

With proper dosing, several LMWH products have been found safer and more effective than unfractionated heparin both for prophylaxis and for treatment of DVT and PE. Monitoring the aPTT is neither necessary nor useful when giving LMWH, because the drug is most active in a tissue phase and does not exert most of its effects on coagulation factor IIa.

Many different LMWH products are available around the world. Because of pharmacokinetic differences, dosing is highly product specific. At this writing, 3 LMWH products are available in the US: enoxaparin (Lovenox), dalteparin (Fragmin), and ardeparin (Normiflo). Enoxaparin is the only one of these currently labeled by the FDA for treatment of DVT. Each has been approved by the FDA at a lower dose for prophylaxis, but all appear to be safe and effective at some therapeutic dose in patients with active DVT or PE.

Fractionated LMWH administered subcutaneously is now the preferred choice for initial anticoagulation therapy. Unfractionated IV heparin can be nearly as effective but is more difficult to titrate for therapeutic effect. Warfarin maintenance therapy may be initiated after 1-3 d of effective heparinization.

The weight-adjusted heparin dosing regimens that are appropriate for prophylaxis and treatment of coronary artery thrombosis are too low to be used unmodified in the treatment of active DVT and PE. Coronary artery thrombosis does not result from hypercoagulability but rather from platelet adhesion to ruptured plaque. In contrast, patients with DVT and PE are in the midst of a hypercoagulable crisis, and aggressive countermeasures are essential to reduce mortality and morbidity rates.

In a hemodynamically unstable patient, heparin therapy alone is not adequate. Heparin is essential because it inhibits clot extension, but it is not sufficient because it is incapable of dissolving existing clot. The variable clot resolution that occurs in patients treated with heparin is due to natural fibrinolytic processes. Fibrinolytic agents, on the other hand, act directly and rapidly to dissolve existing clot. In hemodynamically unstable patients, use of anticoagulants alone (failure to administer a fibrinolytic agent) is associated with a high mortality rate.

Drug Name	Enoxaparin (Lovenox) -- First LMWH released in US. Only LMWH now approved by FDA for both treatment and prophylaxis of DVT and PE. LMWH has been used widely in pregnancy, although clinical trials not yet available to demonstrate that it is as safe as unfractionated heparin. Except in overdoses, checking PT or aPTT has no utility, as aPTT does not correlate with anticoagulant effect of fractionated LMWH.
Adult Dose	Treatment of DVT and PE: 1 mg/kg SC q12h or 1.5 mg/kg SC qd DVT prophylaxis: 30 mg SC q12h DVT prophylaxis in abdominal surgery: 40 mg SC qd, with first dose given 2 h prior to surgery
Pediatric Dose	For treatment of acute DVT or PE: 1 mg/kg SC q12h
Contraindications	Documented hypersensitivity; major bleeding; thrombocytopenia
Interactions	Platelet inhibitors or oral anticoagulants such as aspirin, NSAIDs, dipyridamole, salicylates, sulfipyrazone, and ticlopidine can potentiate risk of bleeding
Pregnancy	B - Usually safe but benefits must outweigh the risks.
Precautions	Reversible elevation of hepatic transaminases occasionally seen; heparin-associated thrombocytopenia has been seen with fractionated LMWH; for significant bleeding complications, 1 mg of protamine sulfate reverses effect of approximately 1 mg of enoxaparin
Drug Name	Dalteparin (Fragmin) -- LMWH with many similarities to enoxaparin but with different dosing schedule. Approved for DVT prophylaxis in patients undergoing abdominal surgery. Except in overdoses, checking PT or aPTT has no utility, as aPTT does not correlate with anticoagulant effect of fractionated LMWH.
Adult Dose	DVT prophylaxis in patients undergoing abdominal surgery: 2500 U SC qd
Contraindications	Documented hypersensitivity; major bleeding; thrombocytopenia
Interactions	Platelet inhibitors or oral anticoagulants such as aspirin, NSAIDs, dipyridamole, salicylates, sulfipyrazone, and ticlopidine can potentiate risk of bleeding
Pregnancy	B - Usually safe but benefits must outweigh the risks.
Precautions	Reversible elevation of hepatic transaminases occasionally seen; heparin-associated thrombocytopenia has been seen with fractionated LMWH If necessary, 1 mg protamine can neutralize 100 U of dalteparin
Drug Name	Ardeparin (Normiflo) -- LMWH that was recently released in US for DVT prophylaxis in patients undergoing hip and knee surgery. Except in overdoses, checking PT or aPTT has no utility, as aPTT does not correlate with anticoagulant effect of fractionated LMWH.
Adult Dose	DVT prophylaxis in patients undergoing hip and knee surgery: 50 U/kg SC q12h
Contraindications	Documented hypersensitivity; major bleeding; thrombocytopenia
Interactions	Platelet inhibitors or oral anticoagulants such as aspirin, NSAIDs, dipyridamole, salicylates, sulfipyrazone, and ticlopidine can potentiate risk of bleeding

Pregnancy	B - Usually safe but benefits must outweigh the risks.
Precautions	Reversible elevation of hepatic transaminases occasionally seen; heparin-associated thrombocytopenia has been seen with LMWH If necessary, 1 mg protamine can neutralize 100 units of ardeparin
Drug Name	Unfractionated heparin -- When unfractionated heparin used, aPTT should not be checked until 6 h after initial heparin bolus, as an extremely high or low value during this time should not provoke any action.
Adult Dose	Initial bolus: 120-140 U/kg IV or approximately 10,000 U/70-kg person Initial infusion: 20 U/kg/h IV After bolus, check aPTT q6h until stable, and heparin dosing should be adjusted as follows: If aPTT is low (<1.5 times control value), administer second bolus of 5000 U and increase drip by 10% If aPTT is high (>2.5 times control value), decrease drip 10% If aPTT is extremely high (>100 s), hold heparin drip for 1 h and decrease drip 10%
Pediatric Dose	Pediatric loading dose: 100 U/kg/h Maintenance infusion: 15-25 U/kg/h; increase dose by 2-4 U/kg/h q6-8h prn using aPTT results
Contraindications	Documented hypersensitivity; subacute bacterial endocarditis; active noncompressible bleeding; any history of heparin-induced thrombocytopenia
Interactions	Digoxin, nicotine, tetracycline, and antihistamines may decrease effects; NSAIDs, aspirin, dextran, dipyridamole, and hydroxychloroquine may increase toxicity and risks of bleeding
Pregnancy	B - Usually safe but benefits must outweigh the risks.
Precautions	Most important risk associated with unfractionated heparin is that it will be ineffective because of insufficient doses All forms of heparin may cause hemorrhagic complications and all can trigger immune thrombotic thrombocytopenia 1-2 wk after beginning of treatment; heparin-associated thrombocytopenia is very serious, causes widespread thrombosis that is refractory to treatment, and can be fatal if not recognized quickly and managed appropriately If significant bleeding complications develop, 15 mg of protamine sulfate (infused over 3 min) usually reverse anticoagulant effect Some preparations contain benzyl alcohol as preservative; benzyl alcohol, used in large amounts, has been associated with fetal toxicity (gasping syndrome); use of preservative-free heparin recommended in neonates Use with caution in patients with shock or severe hypotension
Drug Name	Warfarin (Coumadin) -- Interferes with hepatic synthesis of vitamin K-dependent coagulation factors. Never give to patient with thrombosis until after patient has been anticoagulated fully with heparin, because first few days of warfarin therapy produce hypercoagulable state. Failing to anticoagulate with heparin before starting warfarin will cause clot extension and recurrent thromboembolism in about 40% of patients, compared with 8% of those who receive full-dose heparin before starting warfarin. Heparin should be continued for first 5-7 d of oral warfarin therapy, regardless of PT, to allow time for depletion of procoagulant vitamin K-dependent proteins. Anticoagulant effect of warfarin adjusted by varying dose to keep INR within target range. An INR target range of 2.5 to 3.5 makes sense for DVT and PE because rate of recurrence increases dramatically when INR drops below 2.5 and decreases when INR is kept above 3.0. The risk of serious bleeding (including hemorrhagic stroke) is approximately constant when INR is between 2.5 and 4.5 but rises dramatically when INR is 5.0 or higher. In UK, higher INR target of 3.0 - 4.0 is recommended more often. Best evidence suggests that 6 mo of anticoagulation reduces rate of recurrence to half of that observed when only 6 wk of anticoagulation given. Long-term anticoagulation indicated for patients with irreversible underlying risk factor with recurrent DVT or recurrent PE. Procoagulant vitamin K-dependent proteins responsible for transient hypercoagulable state when warfarin first started and when stopped. This phenomenon occasionally causes warfarin-induced necrosis of large areas of skin or of distal appendages. Heparin always used to protect against this hypercoagulability when warfarin started, but when warfarin stopped, problem resurfaces, causing abrupt temporary rise in rate of recurrent venous thromboembolism. At least 186 different foods and drugs have been reported to interact with warfarin. Clinically significant interactions have been verified for a total of 26 common drugs and foods, including 6 antibiotics and 5 cardiac drugs. Every effort should be made to keep patient adequately anticoagulated at all times because procoagulant factors recover first when warfarin therapy is inadequate. Patients who have difficulty maintaining adequate anticoagulation while taking warfarin may be asked to limit their intake of foods that contain vitamin K. Foods that have moderate to high amounts of vitamin K include brussel sprouts, kale, green tea, asparagus, avocado, broccoli, cabbage, cauliflower, collard greens, liver, soybean oil, soybeans, certain beans, mustard greens, peas (blackeyed peas, split peas, chick peas), turnip greens, parsley, green onions, spinach, and lettuce.

Adult Dose	Initial dose: 5-15 mg/d PO qd After initial anticoagulation obtained, adjust dose according to desired INR
Pediatric Dose	Administer weight-based dose of 0.05-0.34 mg/kg/d and adjust dose according to desired INR Infants may require doses at high end of this range
Contraindications	Documented hypersensitivity; pregnancy; severe liver or kidney disease; gastrointestinal ulcers
Interactions	Many medications may affect warfarin activity Drugs that may decrease anticoagulant effects include griseofulvin, nafcillin, phenytoin, rifampin, barbiturates, carbamazepine, glutethimide, estrogens, cholestyramine, colestipol, spironolactone, oral contraceptives, vitamin K, and sucralfate Some medications that may increase anticoagulant effects include oral antibiotics, ethacrynic acid, miconazole, nalidixic acid, phenylbutazone, salicylates, sulfonamides, chloral hydrate, clofibrate, diazoxide, sulfonyleureas, allopurinol, chloramphenicol, phenylbutazone, phenytoin, propoxyphene, cimetidine, disulfiram, metronidazole, sulfonamides, gemfibrozil, acetaminophen, anabolic steroids, ketoconazole, and sulindac
Pregnancy	X - Contraindicated in pregnancy
Precautions	Avoid or use extreme caution in patients with hereditary or acquired deficiencies of protein C or protein S, because these deficiencies are associated with higher incidence of tissue necrosis following warfarin administration Do not switch brands after achieving satisfactory therapeutic response; use caution in patients with active TB or diabetes; exercise caution in patients with protein C or S deficiency, because they are at high risk of developing skin necrosis Warfarin teratogenic and contraindicated in pregnancy

FOLLOW-UP

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Further Inpatient Care:

- Any degree of hemodynamic compromise or hypoxemia is an indication that the patient should be assigned to an observation unit rather than to a regular floor bed. These patients have exhausted their cardiopulmonary reserves and, because PE is a condition of many frequent recurrences, many of these patients will worsen suddenly at some point during their hospitalization.

Complications:

- A large proportion of patients with PE develop recurrent PE and cor pulmonale.
- Most patients with PE that originated as leg vein thrombosis go on to develop permanent leg swelling, discomfort, discoloration, and atrophic skin changes; they have a high likelihood of chronic nonhealing ulcerations.

Patient Education:

- For excellent patient education resources, visit eMedicine's [Lung and Airway Center](#) and [Circulatory Problems Center](#). Also, see eMedicine's patient education articles [Pulmonary Embolism](#) and [Blood Clot in the Legs](#).

MISCELLANEOUS

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Medical/Legal Pitfalls:

- Because PE is both extremely common and fairly difficult to diagnose, many patients are seen in the ED and later die from undiagnosed PE. In fact, respiratory complaints are the most common complaints in patients who are seen alive in the ED and later die unexpectedly.
- A small number of often repeated mistakes in diagnosis and treatment are responsible for a large proportion of the bad outcomes with serious legal repercussions. The most common and most serious of these errors are as follows:
 - Dismissing complaints of unexplained shortness of breath as anxiety or hyperventilation without an adequate workup
 - Dismissing complaints of unexplained chest pain as musculoskeletal pain without an adequate workup
 - Failure to properly diagnose and treat symptomatic DVT
 - Failure to recognize that DVT below the knee is just as serious as more proximal DVT
 - Failure to order a V/Q scan when a patient has symptoms consistent with PE

- Failure to pursue the diagnosis after a V/Q scan that is not perfectly normal
- Failure to start full-dose heparin at the first real suspicion of PE, before the V/Q scan
- Failure to give fibrinolytic therapy immediately when a patient with PE becomes hemodynamically unstable

Special Concerns:

- Pregnancy
 - DVT and PE are common during all trimesters of pregnancy and for 6-12 weeks after delivery.
 - The diagnostic approach should be exactly the same in a pregnant patient as in a nonpregnant one. A nuclear perfusion lung scan is safe in pregnancy. Heparin is safe in pregnancy. Fibrinolysis is safe in pregnancy. Failure to treat the mother properly is the most common cause of fetal demise.
- Geriatric
 - PE becomes increasingly common with age, yet the diagnosis of PE is missed more often in the geriatric population, largely because respiratory symptoms often are dismissed as chronic in geriatric patients.
 - Even when the diagnosis is made, appropriate therapy more often is withheld inappropriately in this population than in any other group.

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- Feied CF: Pulmonary embolism. In: Rosen and Barkin, eds, Emergency Medicine Principles and Practice, 4th ed. 1998; 3: Chapter 111.
- Feied CF: Peripheral venous disease. In: Rosen and Barkin, eds, Emergency Medicine Principles and Practice, 4th ed. 1998; 3: Chapter 107.
- Feied CF: Pulmonary chest pain, cor pulmonale and pulmonary embolism. In: Gibler and Aufderheide, eds, Emergency Cardiac Care, 1st ed. 1994; 1: 243 - 303.

NOTE:

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Chronic Obstructive Pulmonary Disease and Emphysema

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Synonyms and related keywords: [COPD](#), [chronic bronchitis](#), cough, dyspnea, [pulmonary infections](#), [cardiac failure](#), [respiratory failure](#), edema, [weight gain](#), [obesity](#), [mucopurulent relapses](#), cachexia, blue bloater, pink puffer, [asthma](#), [wheeze](#), [wheezing](#), [emphysema](#), [tobacco abuse](#), [cystic fibrosis](#), [alpha-1 antitrypsin deficiency](#), [bronchiectasis](#), bullous lung disease, [excessive mucus production](#), hyperplasia of mucus-producing glands, [hypoxemia](#), [polycythemia](#), [hypercapnia](#), [respiratory acidosis](#), [cor pulmonale](#), [hypoxemia](#), [right heart failure](#), V/Q mismatch, progressive exercise intolerance, [recurrent pulmonary infections](#), [progressive cardiac failure](#), [progressive respiratory failure](#), progressive dyspnea, [coarse rhonchi](#), [wheezing](#), [cyanosis](#), [barrel chest](#), [air pollution](#)

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Author: [Paul Kleinschmidt, MD](#), Consulting Staff, Department of Emergency Medicine, Womack Army Medical Center

Paul Kleinschmidt, MD, is a member of the following medical societies: [American Academy of Emergency Medicine](#), and [Special Operations Medical Association](#)

Editor(s): **David FM Brown, MD**, Instructor, Department of Medicine, Division of Emergency Medicine, Harvard Medical School; Associate Chief, Department of Emergency Medicine, Massachusetts General Hospital; **Francisco Talavera, PharmD, PhD**, Senior Pharmacy Editor, eMedicine; **Paul Blackburn, DO**, Program Director, Department of Emergency Medicine, Maricopa Medical Center; Assistant Professor, Department of Surgery, University of Arizona; **John Halamka, MD**, Chief Information Officer, CareGroup Healthcare System, Assistant Professor of Medicine, Department of Emergency Medicine, Beth Israel Deaconess Medical Center; Assistant Professor of Medicine, Harvard Medical School; and **Barry Brenner, MD, PhD**, Professor of Emergency Medicine, Professor of Internal Medicine, and Professor of Anatomy and Neurobiology, Chairman, Department of Emergency Medicine, University of Arkansas for Medical Sciences

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Background: Chronic obstructive pulmonary disease (COPD) is estimated to affect 32 million persons in the United States and is the fourth leading cause of death in this country. Patients typically have symptoms of both chronic bronchitis and emphysema, but the classic triad also includes asthma. Most of the time COPD is secondary to tobacco abuse, although cystic fibrosis, alpha-1 antitrypsin deficiency, bronchiectasis, and some rare forms of bullous lung diseases may be causes as well.

Patients with COPD are susceptible to many insults that can lead rapidly to an acute deterioration superimposed on chronic disease. Quick and accurate recognition of these patients along with aggressive and prompt intervention may be the only action that prevents frank respiratory failure.

Pathophysiology: COPD is a mixture of 3 separate disease processes that together form the complete clinical and pathophysiological picture. These processes are chronic bronchitis, emphysema and, to a lesser extent, asthma. Each case of COPD is unique in the blend of processes; however, 2 main types of the disease are recognized.

Chronic bronchitis

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In this type, chronic bronchitis plays the major role. Chronic bronchitis is defined by excessive mucus production with airway obstruction and notable hyperplasia of mucus-producing glands.

Damage to the endothelium impairs the mucociliary response that clears bacteria and mucus. Inflammation and secretions provide the obstructive component of chronic bronchitis. In contrast to emphysema, chronic bronchitis is associated with a relatively undamaged pulmonary capillary bed. Emphysema is present to a variable degree but usually is centrilobular rather than panlobular. The body responds by decreasing ventilation and increasing cardiac output. This V/Q mismatch results in rapid circulation in a poorly ventilated lung, leading to hypoxemia and polycythemia.

Eventually, hypercapnia and respiratory acidosis develop, leading to pulmonary artery vasoconstriction and cor pulmonale. With the ensuing hypoxemia, polycythemia, and increased CO₂ retention, these patients have signs of right heart failure and are known as "blue bloaters."

Emphysema

The second major type is that in which emphysema is the primary underlying process. Emphysema is defined by destruction of airways distal to the terminal bronchiole.

Physiology of emphysema involves gradual destruction of alveolar septae and of the pulmonary capillary bed, leading to decreased ability to oxygenate blood. The body compensates with lowered cardiac output and hyperventilation. This V/Q mismatch results in relatively limited blood flow through a fairly well oxygenated lung with normal blood gases and pressures in the lung, in contrast to the situation in blue bloaters. Because of low cardiac output, however, the rest of the body suffers from tissue hypoxia and pulmonary cachexia. Eventually, these patients develop muscle wasting and weight loss and are identified as "pink puffers."

Frequency:

- **In the US:** Two thirds of men and one fourth of women have emphysema at death. Approximately 8 million people have chronic bronchitis and 2 million have emphysema.

Mortality/Morbidity: COPD is the fourth leading cause of death in the United States, affecting 32 million adults.

Sex: Men are more likely to have COPD than women.

Age: COPD occurs predominantly in individuals older than 40 years.

CLINICAL

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History: Patients with COPD present with a combination of signs and symptoms of chronic bronchitis, emphysema, and asthma. Symptoms include worsening dyspnea, progressive exercise intolerance, and alteration in mental status. In addition, some important clinical and historical differences can exist between the types of COPD.

- In the chronic bronchitis group, classic symptoms include the following:
 - Productive cough, with progression over time to intermittent dyspnea
 - Frequent and recurrent pulmonary infections
 - Progressive cardiac/respiratory failure over time, with edema and weight gain
- In the emphysema group, the history is somewhat different and may include the following set of classic symptoms:
 - A long history of progressive dyspnea with late onset of nonproductive cough
 - Occasional mucopurulent relapses
 - Eventual cachexia and respiratory failure

Physical: Depending on the type of COPD, physical examination may vary.

- Chronic bronchitis (blue bloaters)
 - Patients may be obese.
 - Frequent cough and expectoration are typical.

Continuing Education

CME available for this topic. Click [here](#) to take this CME.

Patient Education

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[Asthma Overview](#)

[Emphysema Overview](#)

- Use of accessory muscles of respiration is common.
 - Coarse rhonchi and wheezing may be heard on auscultation.
 - Patients may have signs of right heart failure (ie, cor pulmonale), such as edema and cyanosis.
 - Because they share many of the same physical signs, COPD may be difficult to distinguish from CHF. One crude bedside test for distinguishing COPD from CHF is peak expiratory flow. If patients blow 150-200 mL or less, they are probably having a COPD exacerbation; higher flows indicate a probable CHF exacerbation.
- Emphysema (pink puffers)
 - Patients may be very thin with a barrel chest.
 - They typically have little or no cough or expectoration.
 - Breathing may be assisted by pursed lips and use of accessory respiratory muscles; they may adopt the tripod sitting position.
 - The chest may be hyperresonant, and wheezing may be heard; heart sounds are very distant.
 - Overall appearance is more like classic COPD exacerbation.

Causes: In general, the vast majority of COPD cases are the direct result of tobacco abuse. While other causes are known, such as alpha-1 antitrypsin deficiency, cystic fibrosis, air pollution, occupational exposure (eg, firefighters), and bronchiectasis, this is a disease process that is somewhat unique in its direct correlation to a human activity.

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Lab Studies:

- Arterial blood gas
 - Arterial blood gas (ABG) analysis provides the best clues as to acuteness and severity.
 - In general, renal compensation occurs even in chronic CO₂ retainers (ie, bronchitics); thus, pH usually is near normal.
 - Generally, consider any pH below 7.3 a sign of acute respiratory compromise.
- Serum chemistry
 - These patients tend to retain sodium.
 - Diuretics, beta-adrenergic agonists, and theophylline act to lower potassium levels; thus, serum potassium should be monitored carefully.
 - Beta-adrenergic agonists also increase renal excretion of serum calcium and magnesium, which may be important in the

presence of hypokalemia.

- CBC - Polycythemia

Imaging Studies:

- Chest x-ray
 - Chronic bronchitis is associated with increased bronchovascular markings and cardiomegaly.
 - Emphysema is associated with a small heart, hyperinflation, flat hemidiaphragms, and possible bullous changes.

Other Tests:

- Pulse oximetry
 - Pulse oximetry does not offer as much information as ABG.
 - When combined with clinical observation, this test can be a powerful tool for instant feedback on the patient's status.
- Electrocardiogram
 - The presence of underlying cardiac disease is highly likely.
 - Establish that hypoxia is not resulting in ischemia.
 - Establish that the underlying cause of respiratory difficulty is not cardiac in nature.
- Pulmonary function tests
 - Decreased forced expiratory volume in 1 second (FEV₁) with concomitant reduction in FEV₁/forced vital capacity (FVC) ratio
 - Poor/absent reversibility with bronchodilators
 - FVC normal or reduced
 - Normal or increased total lung capacity (TLC)
 - Increased residual volume (RV)
 - Normal or reduced diffusing capacity

TREATMENT

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Prehospital Care: The mainstays of therapy for acute exacerbations of COPD are oxygen, bronchodilators, and definitive airway management.

- Oxygen
 - Adequate oxygen should be given to relieve hypoxia. A belief (ingrained from medical school) is held widely that too much oxygen causes significant respiratory depression. Multiple studies in the literature dispute this view. With administration of oxygen, PO₂ and PCO₂ rise but not in proportion to the very minor changes in respiratory drive.
 - The need for intubation can be established quickly at the bedside by asking the patient hold the nebulizer in his or her hand. If the patient becomes so sleepy that the nebulizer starts to fall away, the patient should be intubated regardless of PCO₂ level. The cause of increased CO₂ production is not decreased respiratory drive but probably reversal of hypoxic arterial vasoconstriction in areas of less-ventilated lung tissue, which increases the extent of ventilation/perfusion defects and thus CO₂. "Stated another way, there is probably no single value for arterial PCO₂, pH, or PO₂ that by itself constitutes and indication for [intermittent positive pressure ventilation (IPPV)]" (Pierson, 2002)
 - Occasionally, large increases in CO₂ can lead to deterioration of mental status, causing stupor and obtundation. In such cases, decreasing O₂ delivery is the wrong action. The CO₂ narcosis inhibits respiratory drive to the point that decreasing O₂ delivery leads only to worsening of hypoxia. The correct action is immediate intubation and oxygenation.
 - Supply the patient with enough oxygen to maintain a near normal saturation (above 90%) and do not be concerned about oxygen supplementation leading to clinical deterioration. If the patient's condition is that tenuous, intubation most likely is needed anyway.

- Bronchodilator

- In the prehospital setting, administer only beta-agonist nebulizer therapy, which should be given as needed.
- If necessary and available, continuous positive airway pressure (CPAP) may be used.
- Of course, in times of respiratory failure, patients may need intubation in the field.

Emergency Department Care: In addition to oxygen, proper ED care may comprise bronchodilators, antibiotics, magnesium, CPAP or biphasic positive airway pressure (BiPAP), Heliox (ie, mixture of helium and oxygen), and definitive airway management via intubation. All of these should be considered in the context of the individual patient's condition.

For more information, please see either [Medication](#) or [In/Out Patient Meds](#) in the Follow-up section.

Consultations:

- Pulmonology

MEDICATION

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Medicines available for ED treatment of COPD include bronchodilators, oxygen, theophylline, corticosteroids and, possibly, magnesium.

Terbutaline can be considered for patients with such significant exacerbations that they are not moving enough air to take full advantage of nebulizer therapy.

The greatest single problem that persists in this area is the underdosing of beta agonists and the nonutilization of anticholinergics. Although only a small subset of patients respond to beta agonists, a reasonable dose approaches continuous nebulization, as is seen in current asthma treatment.

Anticholinergics seem to have an important role in the acute treatment of COPD exacerbations.

The use of antibiotics is still controversial. These patients are almost uniformly heavily colonized with *Haemophilus influenzae*, streptococcal pneumonia, and others; however, researchers have not proven these organisms to be the cause of the exacerbation. In fact, viruses are thought to be the instigating factor in as many as half of the cases. In addition, the particular antibiotic chosen seems to have much less effect on outcome than the particular host factors of the patient. Although some meta-analyses have suggested statistically significant improvement in outcome in those patients who receive empiric antibiotic coverage, the lack of quality studies and power leaves the subject open for debate. If antibiotics are given, the choice should provide coverage against pneumococcus, *H influenzae*, *Legionella* species, and gram-negative enterics.

Drug Category: *Bronchodilators* -- These agents act to decrease muscle tone in both small and large airways in the lungs, thus increasing ventilation. Category includes subcutaneous medications, beta-adrenergic agonists, methylxanthines, and anticholinergics. Note that only 10-15% of all patients with COPD have a true reversible (ie, bronchospastic) component; however, because predicting response is impossible on presentation, all patients should be treated with aggressive bronchodilator therapy.

Drug Name	Terbutaline (Brethaire, Bricanyl) -- Acts directly on beta2-receptors to relax bronchial smooth muscle, relieving bronchospasm and reducing airway resistance.
Adult Dose	0.25 mg (0.25 mL of 1 mg/mL concentration) SC; not to exceed 0.5 mg SC q4h
Pediatric Dose	Not established
Contraindications	Documented hypersensitivity; tachycardia resulting from cardiac arrhythmias
Interactions	Beta-blockers may inhibit bronchodilating, cardiac, and vasodilating effects; concomitant MAOIs may result in a hypertensive crisis; concomitant oxytocic drugs such as ergonovine may result in severe hypotension
Pregnancy	B - Usually safe but benefits must outweigh the risks.
Precautions	Caution in coronary disease; through intracellular shunting, may decrease serum potassium levels, which can produce adverse cardiovascular effects (decrease usually transient and may not require supplementation)
Drug Name	Albuterol (Proventil) -- Beta-agonist useful in treatment of bronchospasm. Drug selectively stimulates beta2-adrenergic receptors of lungs. Bronchodilation results from relaxation of bronchial smooth muscle, which relieves bronchospasm and reduces airway resistance. Note that prior use of long-acting agents such as salmeterol does not seem to compromise response to albuterol during acute attacks. Use 5 mg/mL solution for nebulization; usually underdosed in acute settings. Many studies have demonstrated that high-dose therapy is most efficacious. Goal is continuous therapy in initial treatment phase. Note that properly used MDI with spacer is equal in effectiveness to nebulized therapy.
Adult Dose	5 mg/mL solution: 1 mL (5 mg) in 2-3 mL of saline solution minimum; give multiple nebs in succession; goal is continuous therapy in initial treatment phase Properly used MDI with spacer equal in effectiveness to nebulized therapy

Pediatric Dose	Not established
Contraindications	Documented hypersensitivity
Interactions	Beta-adrenergic blockers antagonize effects; inhaled ipratropium may increase duration of bronchodilatation by albuterol; cardiovascular effects may increase with MAOIs, inhaled anesthetics, TCAs, and sympathomimetic agents
Pregnancy	C - Safety for use during pregnancy has not been established.
Precautions	Caution in hyperthyroidism, diabetes mellitus, and cardiovascular disorders

Drug Name	Theophylline (Theo-Dur, Slo-bid, Theo-24) -- Acts to increase collateral ventilation, respiratory muscle function, mucociliary clearance, and central respiratory drive. Acts partly by inhibiting phosphodiesterase, elevating cellular cyclic AMP levels, or antagonizing adenosine receptors in bronchi, resulting in relaxation of smooth muscle. However, clinical efficacy is controversial, especially in acute setting. Author advocates this medicine only if patient was taking medicine already and had subtherapeutic level. Do not give IV form (aminophylline) because it can precipitate arrhythmias, especially in patients such as these who are already in an excess catecholamine state. Measure serum level to adjust dose. Note that most recent meta-analyses and other literature have failed to show a benefit from the use of methylxanthines in acute exacerbations.
Adult Dose	Target concentration: 10 mcg/mL Dosing = (target concentration - current level) x 0.5 (ideal body weight) Alternatively, 1 mg/kg results in approximately 2 mcg/mL increase in serum levels
Pediatric Dose	Not established
Contraindications	Documented hypersensitivity; uncontrolled arrhythmias; hyperthyroidism
Interactions	Aminoglutethimide, barbiturates, carbamazepine, ketoconazole, loop diuretics, charcoal, hydantoins, phenobarbital, phenytoin, rifampin, isoniazid, and sympathomimetics may decrease effects; effects may increase with allopurinol, beta-blockers, ciprofloxacin, corticosteroids, disulfiram, quinolones, thyroid hormones, ephedrine, carbamazepine, cimetidine, erythromycin, macrolides, propranolol, and interferon
Pregnancy	C - Safety for use during pregnancy has not been established.
Precautions	Caution in peptic ulcer, hypertension, tachyarrhythmias, hyperthyroidism, or compromised cardiac function; do not inject IV solution faster than 25 mg/min; patients diagnosed with pulmonary edema or liver dysfunction are at greater risk of toxicity because of reduced drug clearance Again, author recommends not giving the IV form at all

Drug Name	Ipratropium bromide (Atrovent) -- Anticholinergic medication that appears to inhibit vagally mediated reflexes by antagonizing action of acetylcholine specifically with muscarinic receptor on bronchial smooth muscle. Vagal tone can be increased by as much as 50% in patients with COPD, so this can have a profound effect. Dose can (and should) be mixed with first beta-agonist nebulizer because it can take up to 20 min to begin having effect. Admitted controversy exists regarding efficacy of ipratropium, but it still should be part of total treatment picture.
Adult Dose	0.5 mg/nebulizer treatment; can be mixed with albuterol and used as part of first nebulized treatment on presentation to hospital
Pediatric Dose	Not established
Contraindications	Documented hypersensitivity
Interactions	Drugs with anticholinergic properties, such as dronabinol, may increase toxicity; albuterol increases effects
Pregnancy	B - Usually safe but benefits must outweigh the risks.
Precautions	Not indicated for acute episodes of bronchospasm; caution in narrow-angle glaucoma, prostatic hypertrophy, and bladder neck obstruction

Drug Name	Ipratropium and albuterol (Combivent) -- Ipratropium is chemically related to atropine. It has anti-secretory properties and, when applied locally, inhibits secretions from serous and seromucous glands lining the nasal mucosa. Albuterol is a beta-agonist for bronchospasm refractory to epinephrine. It relaxes bronchial smooth muscle by action on beta2-receptors with little effect on cardiac muscle contractility. Recommended to "test spray" 3 times before using the first time and in cases where the aerosol has not be used for >24 h.
Adult Dose	2 inhalations qid; may take additional inhalations prn; not to exceed 12 inhalations/24 h
Pediatric Dose	Administer as in adults
Contraindications	Documented hypersensitivity

Interactions	Drugs with anticholinergic properties, such as dronabinol, may increase toxicity; albuterol increases effects of ipratropium Beta-adrenergic blockers antagonize effects; inhaled ipratropium may increase duration of bronchodilatation by albuterol; cardiovascular effects may increase with MAOIs, inhaled anesthetics, tricyclic antidepressants, and sympathomimetic agents
Pregnancy	C - Safety for use during pregnancy has not been established.
Precautions	Caution in hyperthyroidism, diabetes mellitus, and cardiovascular disorders; caution in narrow-angle glaucoma, prostatic hypertrophy, and bladder neck obstruction

Drug Name	Tiotropium (Spiriva) -- A quaternary ammonium compound. Elicits anticholinergic/antimuscarinic effects with inhibitory effects on M ₃ receptors on airway smooth muscles, leading to bronchodilation. Available as a capsule dosage form containing a dry powder for oral inhalation via the HandiHaler inhalation device. Helps COPD patients by dilating narrowed airways and keeping them open for 24 h.
Adult Dose	Inhale contents of 1 cap (18 mcg) via HandiHaler device qd
Pediatric Dose	Not established
Contraindications	Documented hypersensitivity
Interactions	Coadministration with other anticholinergic containing drugs (eg, ipratropium) may increase toxicity risk
Pregnancy	C - Safety for use during pregnancy has not been established.
Precautions	For maintenance treatment only; not effective for acute (rescue) therapy of bronchospasm; discontinue use and consider other treatments if immediate hypersensitivity reactions (including angioedema) or paradoxical bronchospasm occur; caution with narrow-angle glaucoma, prostatic hyperplasia, or bladder neck obstruction; commonly causes dry mouth; may also cause constipation, increased heart rate, blurred vision, glaucoma, and urinary difficulty or retention; monitor patients with moderate-to-severe renal impairment

Drug Category: *Corticosteroids* -- These agents have been shown to be effective in accelerating recovery from acute COPD exacerbations. Although they may not make a clinical difference in the ED, they have some effect by 6-8 h into therapy; therefore, early dosing is critical.

Some newer studies are suggesting that inhaled corticosteroids (eg, nebulized budesonide) may be equally effective as IV or PO steroids in the mild-to-moderate exacerbation; however, further studies are needed.

Drug Name	Methylprednisolone (Solu-Medrol, Depo-Medrol, Adlone) -- Usually given in IV form in ED for initiation of corticosteroid therapy, although PO form theoretically equally efficacious. Two forms equal in potency, time of onset, and adverse effects. Inhaled corticosteroids probably equally efficacious and have fewer adverse effects for patients discharged from ED.
Adult Dose	125 mg IV q6h recommended dose, but true optimal dose not known Alternative: 1-2 mg/kg IV q6h; not to exceed 125 mg; this dose often used in children
Pediatric Dose	Not established
Contraindications	Documented hypersensitivity; viral, fungal, or tubercular skin infections
Interactions	Coadministration with digoxin may increase digitalis toxicity secondary to hypokalemia; estrogens may increase levels; phenobarbital, phenytoin, and rifampin may decrease levels (adjust dose); monitor patients for hypokalemia when taking concurrent diuretics
Pregnancy	C - Safety for use during pregnancy has not been established.
Precautions	Hyperglycemia, edema, osteonecrosis, peptic ulcer disease, hypokalemia, osteoporosis, euphoria, psychosis, growth suppression, myopathy, and infections are possible complications

Drug Category: *Electrolyte supplements* -- Magnesium is used to replenish stores that become depleted in periods of adrenergic excess such as asthma attacks, COPD exacerbations, and diuretic use.

Drug Name	Magnesium sulfate -- Thought to produce bronchodilation through counteraction of calcium-mediated smooth muscle constriction. Again, for every study showing positive finding, probably another shows no benefit, but given properly, magnesium is safe and may have some benefit.
Adult Dose	1.2-2 g IV over 15 min; not to exceed 150 mg/min
Pediatric Dose	Not established
Contraindications	Documented hypersensitivity; heart block; Addison disease; myocardial damage; severe hepatitis
Interactions	Concurrent nifedipine may cause hypotension and neuromuscular blockade; may increase neuromuscular blockade seen with aminoglycosides and potentiate neuromuscular blockade produced by tubocurarine, vecuronium, or succinylcholine; may increase CNS effects and toxicity of CNS depressants and betamethasone; may increase cardiotoxicity of ritodrine

Pregnancy	A - Safe in pregnancy
Precautions	May alter cardiac conduction, leading to heart block in digitalized patients; respiratory rate, deep tendon reflexes, and renal function should be monitored when administered parenterally; caution when administering magnesium dose, since may produce significant hypertension or asystole; in overdose, calcium gluconate, 10-20 mL IV of 10% solution, can be given as antidote for clinically significant hypermagnesemia

FOLLOW-UP

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Further Inpatient Care:

- In cases in extremis, CPAP or BiPAP may be attempted prior to intubation. This can be started in the ED and continued for several hours in the hospital. Usual recommended settings are an inspiratory positive airway pressure (IPAP) of 10 cm H₂O and an expiratory positive airway pressure (EPAP) of 2 cm H₂O, with further adjustments based on the individual. This is contingent on the patient's ability to withstand the mask. This treatment is not a substitute for intubation; rather, it is a means of trying to avoid intubation.
- Heliox is an additional strategy that can be attempted prior to intubation. Whether Heliox or CPAP is used will depend on the individual patient and local hospital availability. Again, like several other therapies mentioned in this chapter, study results both for and against Heliox have been published. The current summation of that literature indicates that Heliox actually may decrease the work of breathing while the patient is breathing the mixture, but its effects are not long lasting once it is removed. The proper mixture of the gases and the ability to deliver enough oxygen to the patient also are issues.
- Inhaled nitric oxide has been suggested, but at this point does not seem to have a role in acute treatment.
- Lung volume reduction surgery has also been touted as effective, but most recent studies demonstrate varying levels of success.

Further Outpatient Care:

- Disposition from the ED depends on the clinical picture for each patient more than any single laboratory value or test. In general, the longer the exacerbation, the more airway edema and debris are present, making resolution in the ED increasingly more difficult. Patients who state that they "feel back to normal" and have no overt reason for admission can reasonably be discharged home with follow-up arrangements. The corollary to this is that patients who state they "do not feel comfortable," regardless of the numbers, are the best predictors of outcome and probably should be admitted. Data on risk factors for relapse and need for admission are limited at present.
- For patients who are sent home, nearly all should receive a short steroid burst and an increase in the frequency of inhaler therapy. Close follow-up should be arranged with the patient's regular care provider. Other therapies should be considered on a case by case basis.
- Patients with severe or unstable disease should be seen monthly.
- When their condition is stable, patients may be seen biannually.
- Check theophylline level with each dose adjustment, then every 6-12 months.
- For patients on home oxygen, check ABGs yearly or with any change in condition. Monitor oxygen saturation more frequently than ABGs.

In/Out Patient Meds:

- Bronchodilators
 - Epinephrine or terbutaline can be administered subcutaneously when intravenous access is not possible or the patient is moving so little air that nebulizer therapy is ineffective. Terbutaline is thought to be safer in older patients, and it has shown to be more efficacious than epinephrine.
 - Methylxanthines: Theophylline increases collateral ventilation, respiratory muscle function, mucociliary clearance, and central respiratory drive. Despite this, many questions exist as to its true efficacy. In general, if the patient is already on theophylline and has a subtherapeutic level, a mini-loading dose is appropriate. If the patient is not on theophylline, the delay before benefit of the oral form makes it not worth using. Intravenous aminophylline has a propensity to cause arrhythmias, especially in a population that already has cholinergic excess coupled with coronary disease.
 - Anticholinergics: These are as effective as beta-agonists in acute attacks and have synergistic properties with the beta-agonists. They act by antagonizing the vagal innervation of the tracheobronchial tree. Vagal tone can be increased by as much as 50% in patients with COPD.
 - Corticosteroids: These also have bronchodilatory properties, although they primarily act by decreasing inflammation in the tracheobronchial tree. While 8-12 hours are required for full effect, corticosteroids should be administered in the ED, as some mild improvements may be noted much earlier.
- Antibiotics

- Recent meta-analysis suggests that patients with COPD exacerbations who receive empiric broad-spectrum antibiotic coverage have significantly shorter ICU and hospital stays than patients treated only for documented infections.
- If administered, the antibiotic should provide broad-spectrum coverage against pneumococcus, *H influenza*, *Legionella* species, and gram-negative enterics.
- Magnesium
 - Though controversial, administration of magnesium is thought to produce bronchodilation through the counteraction of calcium-mediated smooth muscle constriction.
 - Magnesium depletion is known to occur in periods of adrenergic excess (eg, asthma exacerbations, diuretic use).
- CPAP and BiPAP
 - These devices help to decrease the work of breathing and maintain positive end-expiratory pressure (PEEP).
 - Patient must be alert with no excess secretions.
- Heliox
 - Heliox usually is a 60:40 mixture of helium and oxygen.
 - Helium is a smaller particle than oxygen and in small airways promotes laminar flow and facilitates both oxygen transport and carbon dioxide diffusion.
 - Many patients who seem to breathe better on Heliox return to a worsened respiratory state when removed from Heliox.

Deterrence/Prevention:

- For the vast majority of patients, cessation of smoking is the only true means of prevention.

Complications:

- Some complications that must be anticipated in COPD treatment include the following:
 - Incidence of pneumothorax due to bleb formation is relatively high; consider pneumothorax in all patients with COPD who have increased shortness of breath.
 - In patients who require long-term steroid use, the possibility of adrenal crisis is very real; at a minimum, patients with steroid-dependent COPD should receive stress dosing in the event of an exacerbation or any other stressor.
 - Infection (common)
 - Cor pulmonale
 - Secondary polycythemia
 - Bullous lung disease
 - Acute or chronic respiratory failure
 - Pulmonary hypertension
 - Malnutrition

Prognosis:

- Patient's age and postbronchodilator FEV₁ are the most important predictors of prognosis. Young age and FEV₁ greater than 50% of predicted are associated with a good prognosis. Older patients and those with more severe lung disease do worse.
- Supplemental oxygen (when indicated) has been shown to increase survival rates.
- Smoking cessation improves prognosis.
- Cor pulmonale, hypercapnia, tachycardia, and malnutrition indicate a poor prognosis.

Patient Education:

- The best education comes in 2 forms.

- Educate patients to the dangers of smoking and the improvement in quality of life attainable with smoking cessation.
- Instruct patients with COPD to present early during an exacerbation and not wait until they are in distress.
- Printed material is available from the National Jewish Hospital in Denver, Colorado, as well as the American Lung Association.
- Instruct patients concerning appropriate pulmonary toilet.
- For excellent patient education resources, visit eMedicine's [Lung and Airway Center](#). Also, see eMedicine's patient education articles [Chronic Obstructive Pulmonary Disease \(COPD\)](#), [Cigarette Smoking](#), [Asthma](#), and [Emphysema](#).

MISCELLANEOUS

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Medical/Legal Pitfalls:

- Be wary of discharging patients with exacerbations when they do not feel comfortable with their breathing, regardless of their oxygen saturation, ABG, or other test results.
- Always look for underlying cardiac ischemia with acute exacerbations. With hypoxia and distress, many of these patients can have unrecognized underlying ischemia.
- Administer as much oxygen as necessary to avoid hypoxia. If the patient retains excessive carbon dioxide, intubate.
- A common mistake is utilizing a high respiratory rate after intubation. The patient most likely is acidotic and has marginally normal or low potassium due to diuretic and bronchodilator therapy. With a too rapid respiratory rate, the patient will become alkalotic, causing an intracellular shift in potassium with potentially dangerous hypokalemia as a result.

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- Aaron SD, Vandemheen KL, Hebert P, et al: Outpatient oral prednisone after emergency treatment of chronic obstructive pulmonary disease. *N Engl J Med* 2003 Jun 26; 348(26): 2618-25[[Medline](#)].
- Alter HJ, Koepsell TD, Hilty WM: Intravenous magnesium as an adjuvant in acute bronchospasm: a meta-analysis. *Ann Emerg Med* 2000 Sep; 36(3): 191-7[[Medline](#)].
- Baigorri F, Joseph D, Artigas A, Blanch L: Inhaled nitric oxide does not improve cardiac or pulmonary function in patients with an exacerbation of chronic obstructive pulmonary disease. *Crit Care Med* 1999 Oct; 27(10): 2153-8[[Medline](#)].
- Balter MS, La Forge J, Low DE, et al: Canadian guidelines for the management of acute exacerbations of chronic bronchitis. *Can Respir J* 2003 Jul-Aug; 10 Suppl B: 3B-32B[[Medline](#)].
- Barr RG, Rowe BH, Camargo CA: Methyl-xanthines for exacerbations of chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2001; CD002168[[Medline](#)].
- Cydulka RK, Emerman CL: Effects of combined treatment with glycopyrrolate and albuterol in acute exacerbation of chronic obstructive pulmonary disease. *Ann Emerg Med* 1995 Apr; 25(4): 470-3[[Medline](#)].
- Dailey RH: Chronic obstructive pulmonary disease. In: Rosen P, et al, eds. *Emergency Medicine Concepts and Clinical Practice*. 3rd ed. Mosby-Year Book Inc; 1992:1093-1111.
- De Palo VA: Pulmonary disease: pneumonia, chronic obstructive pulmonary disease, asthma, and thromboembolic disease. *J Am Podiatr Med Assoc* 2004 Mar-Apr; 94(2): 157-67[[Medline](#)].
- Dewan NA, Daniels A, Ziemann G, Kramer T: The National Outcomes Management Project: a benchmarking collaborative. *J Behav Health Serv Res* 2000 Nov; 27(4): 431-6[[Medline](#)].
- Faulkner MA, Hilleman DE: Pharmacologic treatment of chronic obstructive pulmonary disease: past, present, and future. *Pharmacotherapy* 2003 Oct; 23(10): 1300-15[[Medline](#)].
- Ferguson GT, Cherniack RM: Management of chronic obstructive pulmonary disease. *N Engl J Med* 1993 Apr 8; 328(14): 1017-22[[Medline](#)].
- FitzGerald JM, Shragge D, Haddon J, et al: A randomized, controlled trial of high dose, inhaled budesonide versus oral prednisone in patients discharged from the emergency department following an acute asthma exacerbation. *Can Respir J* 2000 Jan-Feb; 7(1): 61-7[[Medline](#)].
- Fromm RE Jr, Varon J: Acute exacerbations of obstructive lung disease: What to do when immediate care is critical. *Postgraduate Medicine* 1994; 95(8): 101-6[[Medline](#)].
- Greenfield RH: Pulmonary disease in the elderly. Lecture presented at the ACEP Scientific Assembly. 1994.
- Hirschmann JV: Do bacteria cause exacerbations of COPD?. *Chest* 2000 Jul; 118(1): 193-203[[Medline](#)].
- Hirshberg AJ, Dupper RL: Use of doxapram hydrochloride injection as an alternative to intubation to treat chronic obstructive pulmonary disease patients with hypercapnia. *Ann Emerg Med* 1994 Oct; 24(4): 701-3[[Medline](#)].
- Ingram RH: Chronic bronchitis, emphysema, and airway obstruction. In: Fauci AS, et al, eds. *Harrison's Principles of Internal Medicine*. McGraw-Hill Companies; 1991: 1074-1082.
- Jaber S, Fodil R, Carlucci A, et al: Noninvasive ventilation with helium-oxygen in acute exacerbations of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2000 Apr; 161(4 Pt 1): 1191-200[[Medline](#)].
- Kino RJ: The difficult COPD patient: Alternative therapy regimens. Lecture presented at the ACEP Scientific Assembly. 1996.
- Korosec M, Novak RD, Myers E, et al: Salmeterol does not compromise the bronchodilator response to albuterol during acute episodes of asthma. *Am J Med* 1999 Sep; 107(3): 209-13[[Medline](#)].
- Lieberman D, Lieberman D, Ben-Yaakov M, et al: Infectious etiologies in acute exacerbation of COPD. *Diagn Microbiol Infect Dis* 2001

Jul; 40(3): 95-102[[Medline](#)].

- Maltais F, Ostinelli J, Bourbeau J, et al: Comparison of nebulized budesonide and oral prednisolone with placebo in the treatment of acute exacerbations of chronic obstructive pulmonary disease: a randomized controlled trial. Am J Respir Crit Care Med 2002 Mar 1; 165(5): 698-703[[Medline](#)].
- Peng CC, Aspinall SL, Good CB, et al: Equal effectiveness of older traditional antibiotics and newer broad-spectrum antibiotics in treating patients with acute exacerbations of chronic bronchitis. South Med J 2003 Oct; 96(10): 986-91[[Medline](#)].
- Pierson DJ: Indications for mechanical ventilation in adults with acute respiratory failure. Respir Care 2002 Mar; 47(3): 249-62; discussion 262-5[[Medline](#)].
- Saint S, Bent S, Vittinghoff E, Grady D: Antibiotics in chronic obstructive pulmonary disease exacerbations. A meta-analysis. JAMA 1995 Mar 22-29; 273(12): 957-60[[Medline](#)].
- Schmidt GA, Hall JB: Acute chronic respiratory failure: Assessment and management of patients with COPD in the emergent setting. JAMA 1989; 261(23): 3444-3453[[Medline](#)].
- Sclar DA, Legg RF, Skaer TL, et al: Ipratropium bromide in the management of chronic obstructive pulmonary disease: effect on health service expenditures. Clin Ther 1994 May-Jun; 16(3): 595-601; discussion 594[[Medline](#)].
- Siedman JC: Chronic obstructive pulmonary disease. In: Tintinalli J, et al, eds. Emergency Medicine: A Comprehensive Study Guide. McGraw-Hill Com; 1992: 298-302.
- Skorodin MS, Tenholder MF, Yetter B, et al: Magnesium sulfate in exacerbations of chronic obstructive pulmonary disease. Arch Intern Med 1995 Mar 13; 155(5): 496-500[[Medline](#)].
- Skorodin MS: Pharmacotherapy for asthma and chronic obstructive pulmonary disease. Current thinking, practices, and controversies. Arch Intern Med 1993 Apr 12; 153(7): 814-28[[Medline](#)].
- Sohy C, Pilette C: Acute exacerbation of chronic obstructive pulmonary disease and antibiotics: what studies are still needed? European Respiratory Journal 2002; 19: 966-75.
- Stewart AG, Waterhouse JC, Billings CG, et al: Effects of angiotensin converting enzyme inhibition on sodium excretion in patients with hypoxemic chronic obstructive pulmonary disease. Thorax 1994; 49(10): 995-8[[Medline](#)].
- Varkey B: Obstructive, occupational, and environmental diseases. Curr Opin Pulm Med 2004 Mar; 10(2): 97[[Medline](#)].
- Whittle A: COPD guidelines. Thorax.
- Zehner WJ, Scott JM, Iannolo PM, et al: Terbutaline vs albuterol for out-of-hospital respiratory distress: randomized, double-blind trial. Acad Emerg Med 1995 Aug; 2(8): 686-91[[Medline](#)].

NOTE:

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