**GUIDELINES
FOR STUDENTS
INDEPENDENT WORK
IN THE PRACTICAL CLASSES PREPARING**

Academic discipline	Internal medicine
Module	Current practice of internal medicine
Content module	Management of the patients with main symptoms and syndromes in pulmonology clinic
Study subject	**Management of the patients with chronic cough**
	Management of the patients with hemoptysis
Course	VI
Faculty	of foreign students training

1. The aims of the training course:

To Know:
1. Differential diagnosis the conditions that accompanied with the presence of pulmonary artery hypertension, hemoptysis (bronchiectasis, tumors, tuberculosis, pneumonia, pulmonary infarction, etc.).
2. Existing algorithms for diagnosis.
3. Test plan, the role of radiological, instrumental and laboratory methods of examination (radiography, bronhohrafy, CT, bronchoscopy, ultrasound, EhoCG, general and biochemical analysis).
4. Indications for consultation by other specialists (chest physician, oncologist, surgeon, etc.).
5. Drug and non-medicamentous treatment.

To be able to:
Conduct surveys and examination of patients with major Pulmonological syndromes
• draft examination of patients with major Pulmonological syndromes
• justify the use of basic diagnostic methods in pulmonology, identify indications and contraindications for their conduct, possible complications
• prescribe treatment, determine prognosis and to conduct primary and secondary prevention in the major respiratory diseases
• diagnose and assist in respiratory distress
• justify the need of pleural puncture
• Perform pikfluometry
Demonstrate knowledge of moral principles

The contents of topic:

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Last full review/revision May 2014 by Mark T. Gladwin, MD; Shilpa Jain, MD

Pulmonary artery hypertension

Pulmonary hypertension is increased pressure in the pulmonary circulation. It has many secondary causes; some cases are idiopathic. In pulmonary hypertension, pulmonary vessels become constricted. Severe pulmonary hypertension leads to right ventricular overload and failure. Symptoms are fatigue, exertional dyspnea, and, occasionally, chest discomfort and syncope. Diagnosis is made by finding elevated pulmonary artery pressure (estimated by echocardiography and confirmed by right heart catheterization). Treatment is with pulmonary vasodilators and diuretics. In some advanced cases, lung transplantation is an option. Prognosis is poor overall if a treatable secondary cause is not found.

Pulmonary hypertension is defined as a mean pulmonary arterial pressure ≥ 25 mm Hg at rest and a normal (≤ 15 mm Hg) pulmonary artery occlusion pressure (pulmonary capillary wedge pressure) as measured by right heart catheterization.

Etiology

Many conditions and drugs cause pulmonary hypertension. The most common overall causes of pulmonary hypertension are

- Left heart failure, including diastolic dysfunction
- Parenchymal lung disease with hypoxia
- Miscellaneous: Sleep apnea, connective tissue disorders, and recurrent pulmonary embolism

Pulmonary hypertension is currently classified into 5 groups based on a number of pathologic, physiologic, and clinical factors. In the first group (pulmonary arterial hypertension), the primary disorder affects the small pulmonary arterioles.

A small number of cases of pulmonary arterial hypertension occur sporadically, unrelated to any identifiable disorder; these cases are termed idiopathic pulmonary arterial hypertension. Hereditary forms of pulmonary arterial hypertension (autosomal dominant with incomplete penetrance) have been identified; 75% of cases are caused by mutations in bone morphogenetic protein receptor type 2 (*BMPR2*). Other identified mutations include activin-like kinase type 1 receptor (*ALK-1*), caveolin 1 (*CAV1*), endoglin (*ENG*), potassium channel subfamily K member 3 (*KCNK3*), and mothers against decapentaplegic homologue 9 (*SMAD9*) but are much less common, occurring in ~1% of cases. In about 20% of cases of hereditary pulmonary arterial hypertension, the causative mutations are unidentified.

Patients with hereditary causes of hemolytic anemia, such as sickle cell disease, are at high risk of developing pulmonary hypertension (10% of cases based on right heart catheterization criteria). The mechanism is related to intravascular hemolysis and release of cell-free Hb into the plasma, which scavenges nitric oxide, generates reactive oxygen species, and activates the hemostatic system. Other risk factors for pulmonary hypertension in sickle cell disease include iron overload, liver dysfunction, thrombotic disorders, and chronic kidney disease.

Pathophysiology

Pathophysiologic mechanisms that cause pulmonary hypertension include

- Increased pulmonary vascular resistance
- Increased pulmonary venous pressure

Increased pulmonary vascular resistance is caused by obliteration of the pulmonary vascular bed and/or by pathologic vasoconstriction. Pulmonary hypertension is characterized by variable and sometimes pathologic vasoconstriction and by endothelial and smooth muscle proliferation, hypertrophy, and chronic inflammation, resulting in vascular wall remodeling. Vasoconstriction

is thought to be due in part to enhanced activity of thromboxane and endothelin-1 (both vasoconstrictors) and reduced activity of prostacyclin and nitric oxide (both vasodilators). The increased pulmonary vascular pressure that results from vascular obstruction further injures the endothelium. Injury activates coagulation at the intimal surface, which may worsen the hypertension. Thrombotic coagulopathy due to platelet dysfunction, increased activity of plasminogen activator inhibitor type 1 and fibrinopeptide A, and decreased tissue plasminogen activator activity may also contribute. Platelets, when stimulated, may also play a key role by secreting substances that increase proliferation of fibroblasts and smooth muscle cells such as platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), and transforming growth factor-β (TGF-β). Focal coagulation at the endothelial surface should not be confused with chronic thromboembolic pulmonary hypertension, in which pulmonary hypertension is caused by organized pulmonary emboli.

Increased pulmonary venous pressure is typically caused by disorders that affect the left side of the heart and raise left chamber pressures, which ultimately lead to elevated pressure in the pulmonary veins. Elevated pulmonary venous pressures can cause acute damage to the alveolar-capillary wall and subsequent edema. Persistently high pressures may eventually lead to irreversible thickening of the walls of the alveolar-capillary membrane, decreasing lung diffusion capacity. The most common setting for pulmonary venous hypertension is in left heart failure with preserved ejection fraction (HF-PEF), typically in older women who have hypertension and the metabolic syndrome. When the transpulmonary gradient (mean pulmonary artery pressure to pulmonary artery occlusion pressure gradient) is > 12 mm Hg or the pulmonary artery diastolic pressure to pulmonary artery occlusion pressure gradient is > 6 mm Hg, prognosis is poor.

In most patients, pulmonary hypertension eventually leads to right ventricular hypertrophy followed by dilation and right ventricular failure. Right ventricular failure limits cardiac output during exertion.

Symptoms and Signs

Progressive exertional dyspnea and easy fatigability occur in almost all patients. Atypical chest discomfort and exertional light-headedness or presyncope may accompany dyspnea and indicate more severe disease. These symptoms are due primarily to insufficient cardiac output caused by right heart failure. Raynaud syndrome occurs in about 10% of patients with idiopathic pulmonary arterial hypertension; the majority are women. Hemoptysis is rare but may be fatal. Hoarseness due to recurrent laryngeal nerve compression by an enlarged pulmonary artery (ie, Ortner syndrome) also occurs rarely.

In advanced disease, signs of right heart failure may include right ventricular heave, widely split 2nd heart sound (S_2), an accentuated pulmonic component (P_2) of S_2, a pulmonary ejection click, a right ventricular 3rd heart sound (S_3), tricuspid regurgitation murmur, and jugular vein

distention. Liver congestion and peripheral edema are common late manifestations. Pulmonary auscultation is usually normal. Patients also may have manifestations of causative or associated disorders.

Diagnosis

- Exertional dyspnea
- Initial confirmation: Chest x-ray, spirometry, ECG, echocardiography, and CBC
- Identification of underlying disorder: Ventilation/perfusion scan or CT angiography, high-resolution CT (HRCT) of the chest, pulmonary function testing, polysomnography, HIV testing, liver function testing, and autoantibody testing
- Determination of severity: 6-min walk distance, plasma levels of N-terminal brain natriuretic peptide (BNP) or pro-BNP and right heart catheterization

Pulmonary hypertension is suspected in patients with significant exertional dyspnea who are otherwise relatively healthy and have no history or signs of other disorders known to cause pulmonary symptoms.

Patients initially undergo chest x-ray, spirometry, and ECG to identify more common causes of dyspnea, followed by transthoracic Doppler echocardiography to assess right ventricular function and pulmonary artery systolic pressures as well as to detect structural left heart disease that might be causing pulmonary hypertension. CBC is obtained to document the presence or absence of erythrocytosis, anemia, and thrombocytopenia.

The most common x-ray finding in pulmonary hypertension is enlarged hilar vessels that rapidly prune into the periphery and a right ventricle that fills the anterior airspace on lateral view. Spirometry and lung volumes may be normal or detect mild restriction, and diffusing capacity for carbon monoxide (DL_{CO}) is usually reduced. Common ECG findings include right axis deviation, $R > S$ in V_1, $S_1 Q_3 T_3$, (suggesting right ventricular hypertrophy) and peaked P waves (suggesting right atrial dilation).

Additional tests are obtained as indicated to diagnose secondary causes that are not apparent clinically. These tests can include

- Ventilation/perfusion scanning or CT angiography to detect thromboembolic disease
- HRCT for detailed information about lung parenchymal disorders
- Pulmonary function tests to identify obstructive or restrictive lung disease
- Serum autoantibody tests (eg, antinuclear antibodies [ANA], rheumatoid factor [RF], Scl-70 [topoisomerase I], anti-Ro (anti-SSA), antiribonucleoprotein [anti-RNP], and anticentromere antibodies) to gather evidence for or against associated autoimmune disorders

Chronic thromboembolic pulmonary hypertension is suggested by CT or lung scan findings and is confirmed by arteriography. CT angiography is useful to evaluate proximal clot and fibrotic encroachment of the vascular lumen. Other tests, such as HIV testing, liver function tests, and polysomnography, are done in the appropriate clinical context.

When the initial evaluation suggests a diagnosis of pulmonary hypertension, pulmonary artery catheterization is necessary to measure right atrial, right ventricular, pulmonary artery, and pulmonary artery occlusion pressures; cardiac output; and left ventricular diastolic pressure. Right-sided O_2 saturation should be measured to exclude atrial septal defect. Although finding a mean pulmonary arterial pressure of > 25 mm Hg and a pulmonary artery occlusion pressure ≤ 15 mm Hg in the absence of an underlying disorder identifies pulmonary arterial hypertension, most patients with pulmonary arterial hypertension present with substantially higher pressure (eg, mean of 60 mm Hg). Vasodilating drugs, such as inhaled nitric oxide, IV epoprostenol, or adenosine, are often given during catheterization. Decreasing right-sided pressures in response to these drugs may help in the choice of drugs for treatment. Lung biopsy, once widely done, is neither needed nor recommended because of its associated high morbidity and mortality. Echocardiography findings of right heart systolic dysfunction (eg, tricuspid annular plane systolic excursion) and certain right heart catheterization results (eg, low cardiac output, high mean pulmonary artery pressures and high right atrial pressures) indicate that pulmonary hypertension is severe. Other indicators of severity in pulmonary hypertension are assessed to evaluate prognosis and to help monitor responses to therapy. They include a low 6-min walk distance and high plasma levels of N-terminal pro-brain natriuretic peptide (NT-pro-BNP) or brain natriuretic peptide (BNP).

Once pulmonary hypertension is diagnosed, the patient's family history should be reviewed to detect possible genetic transmission (eg, premature deaths in otherwise healthy members of the extended family). In familial pulmonary arterial hypertension, genetic counseling is needed to advise mutation carriers of the risk of disease (about 20%) and to advocate serial screening with echocardiography. Testing for mutations in the *BMPR2* gene in idiopathic pulmonary arterial hypertension can help identify family members at risk.

Prognosis

Five-year survival for treated patients is about 50%. However, recent findings in some patient registries suggest lower mortality (eg, 20 to 30% at 3 to 5 yr in the French registry and 10 to 30% at 1 to 3 yr in the REVEAL registry), presumably because currently available treatments are superior. Indicators of a poorer prognosis include lack of response to vasodilators, hypoxemia, reduced overall physical functioning, low 6-min walk distance, high plasma levels of NT-pro-BNP or BNP, echocardiographic indicators of right heart systolic dysfunction (eg, tricuspid annular plane systolic excursion) and right heart catheterization showing low cardiac output, high mean pulmonary artery pressures, and high right atrial pressures. Patients with systemic

sclerosis, sickle cell anemia, or HIV infection with pulmonary arterial hypertension have a worse prognosis than those without pulmonary arterial hypertension. For example, patients with sickle cell disease and pulmonary hypertension have a 40% 4-yr mortality rate.

Treatment

- Avoidance of activities that may exacerbate the condition (eg, cigarette smoking,high altitude, pregnancy, use of sympathomimetics)
- Idiopathic and familial pulmonary arterial hypertension: IV epoprostenol; inhaled, oral, or sc prostacyclin analogs; oral endothelin-receptor antagonists; oral phosphodiesterase 5 inhibitors, and/or soluble guanylate cyclase stimulators
- Secondary pulmonary arterial hypertension: Treatment of the underlying disorder
- Lung transplantation
- Adjunctive therapy: Supplemental O $_2$, diuretics, and/or anticoagulants

Pulmonary arterial hypertension, group 1

Treatment is rapidly evolving.

IV epoprostenol, a prostacyclin analog, improves function and lengthens survival even in patients who are unresponsive to a vasodilator during catheterization. Epoprostenol is currently the most effective therapy for pulmonary arterial hypertension. Disadvantages are the need for continuous central catheter infusion and frequent, troubling adverse effects, including flushing, diarrhea, and bacteremia associated with the indwelling central catheter. Prostacyclin analogs that are inhaled (iloprost and treprostinil) or given sc or IV (treprostinil) are available.

Three oral endothelin-receptor antagonists, bosentan, ambrisentan, and macitentan, are now available.Sildenafil and tadalafil, oral phosphodiesterase 5 inhibitors, can also be used. Riociguat is the first available soluble guanylate cyclase stimulator. Drugs improve exercise capacity and reduce composite endpoints of clinical worsening, often defined by hospitalization for right heart failure. No studies have compared oral drugs to each other. Most patients prefer to begin treatment with an oral drug, adding a 2nd oral drug if necessary based on clinical response. Exercise capacity is improved if the second drug is from a different class (endothelin-receptor antagonist or phosphodiesterase 5 inhibitor). However, phosphodiesterase 5 inhibitors cannot be combined with riociguat because both drug classes increase cyclic guanosine monophosphate (cGMP) levels and the combination can lead to dangerous hypotension. Patients with severe right heart failure who are at high risk of sudden death may benefit from early therapy with an intravenous or subcutaneous prostacyclin analog.

Lung transplantation offers the only hope of cure but has high morbidity because of rejection (bronchiolitis obliterans syndrome) and infection. The 5-yr survival rate is 50%. Lung transplantation is reserved for patients with New York Heart Association class IV disease

(defined as dyspnea associated with minimal activity, leading to bed to chair limitations) or complex congenital heart disease in whom all therapies have failed and who meet other health criteria to be a transplant candidate.

Many patients require adjunctive therapies to treat heart failure, including diuretics, and most should receive warfarin unless there is a contraindication.

Pulmonary hypertension, groups 2 to 5

Primary treatment involves management of the underlying disorder. Patients with left-sided heart disease may need surgery for valvular disease. Patients with lung disorders and hypoxia benefit from supplemental O_2 as well as treatment of the primary disorder. Treatments for patients with severe pulmonary hypertension secondary to chronic thromboembolic disease include riociguat and surgical pulmonary thromboendarterectomy. During cardiopulmonary bypass, an organized endothelialized thrombus is dissected along the pulmonary vasculature in a procedure more complex than acute surgical embolectomy. This procedure cures pulmonary hypertension in a substantial percentage of patients and restores cardiopulmonary function; operative mortality is < 10% in patients treated in centers that have extensive experience.

Patients with **sickle cell disease** who have pulmonary hypertension are aggressively treated using hydroxyurea, iron chelation, and supplemental O_2 as indicated. In patients with pulmonary arterial hypertension and elevated pulmonary vascular resistance confirmed by right heart catheterization, selective pulmonary vasodilator therapy (with epoprostenol or an endothelin-receptor antagonist) can be considered. Sildenafil increases incidence of painful crises in patients with sickle cell disease and so should be used only if patients have limited vaso-occlusive crises and are being treated with hydroxyurea or transfusion therapy.

Key points

- Pulmonary hypertension is classified into 5 groups.
- Suspect pulmonary hypertension if patients have dyspnea unexplained by another clinically evident cardiac or pulmonary disorder.
- Begin diagnostic testing with chest x-ray, spirometry, ECG, and transthoracic Doppler echocardiography.
- Confirm the diagnosis by right heart catheterization.
- Treat group 1 by giving pulmonary vasodilators and, if these are ineffective, considering lung transplantation.
- Treat groups 2 to 5 by managing the underlying disorder, treating symptoms, and sometimes other measures.

Last full review/revision May 2014 by Mark T. Gladwin, MD; Shilpa Jain, MD

Hemoptysis is coughing up of blood from the respiratory tract. Massive hemoptysis is production of ≥ 600 mL of blood (about a full kidney basin's worth) within 24 h.

Pathophysiology

Most of the lung's blood (95%) circulates through low-pressure pulmonary arteries and ends up in the pulmonary capillary bed, where gas is exchanged. About 5% of the blood supply circulates through high-pressure bronchial arteries, which originate at the aorta and supply major airways and supporting structures. In hemoptysis, the blood generally arises from this bronchial circulation, except when pulmonary arteries are damaged by trauma, by erosion of a granulomatous or calcified lymph node or tumor, or, rarely, by pulmonary arterial catheterization or when pulmonary capillaries are affected by inflammation.

Etiology

Blood-streaked sputum is common in many minor respiratory illnesses, such as URI and viral bronchitis.

The differential diagnosis is broad.

In adults, 70 to 90% of cases are caused by

- Bronchitis
- Bronchiectasis
- Necrotizing pneumonia
- TB

Primary lung cancer is an important cause in smokers ≥ 40 yr, but metastatic cancer rarely causes hemoptysis. Cavitary *Aspergillus* infection is increasingly recognized as a cause but is not as common as cancer.

In children, common causes are

- Lower respiratory tract infection
- Foreign body aspiration

Massive hemoptysis

The most common causes have changed over time and vary by geographic region but include the following:

- Bronchogenic carcinoma
- Bronchiectasis
- TB and other pneumonias

Evaluation

History

History of present illness should cover the duration and temporal patterns (eg, abrupt onset, cyclical recurrence), provoking factors (eg, allergen exposure, cold, exertion, supine position), and approximate volume of hemoptysis (eg, streaking, teaspoon, cup). Patients may need specific prompting to differentiate between true hemoptysis, pseudohemoptysis (ie, bleeding originating in the nasopharynx that is subsequently coughed up), and hematemesis. A sensation of postnasal drip or any bleeding from the nares without coughing is suggestive of pseudohemoptysis. Concomitant nausea and vomiting with black, brown, or coffee-ground–colored blood is characteristic of hematemesis. Frothy sputum, bright red blood, and (if massive) a sensation of choking are characteristic of true hemoptysis.

Review of systems should seek symptoms suggesting possible causes, including fever and sputum production (pneumonia); night sweats, weight loss, and fatigue (cancer, TB); chest pain and dyspnea (pneumonia, pulmonary embolism); leg pain and leg swelling (pulmonary embolism); hematuria (Goodpasture syndrome); and bloody nasal discharge (granulomatosis with polyangiitis [Wegener granulomatosis]).

Patients should be asked about risk factors for causes. These risk factors include HIV infection, use of immunosuppressants (TB, fungal infection); exposure to TB; long smoking history (cancer); and recent immobilization or surgery, known cancer, prior or family history of clotting, pregnancy, use of estrogen -containing drugs, and recent long-distance travel (pulmonary embolism).

Past medical history should cover known conditions that can cause hemoptysis, including chronic lung disease (eg, COPD, bronchiectasis, TB, cystic fibrosis), cancer, bleeding disorders, heart failure, thoracic aortic aneurysm, and pulmonary-renal syndromes (eg, Goodpasture syndrome, granulomatosis with polyangiitis). Exposure to TB is important, particularly in patients with HIV infection or another immunocompromised state.

A history of frequent nosebleeds, easy bruising, or liver disease suggests possible coagulopathy. The drug profile should be reviewed for use of anticoagulants and antiplatelet drugs.

Physical examination

Vital signs are reviewed for fever, tachycardia, tachypnea, and low O_2 saturation. Constitutional signs (eg, cachexia) and level of patient distress (eg, accessory muscle use, pursed lip breathing, agitation, decreased level of consciousness) should also be noted.

A full lung examination is done, particularly including adequacy of air entry and exit, symmetry of breath sounds, and presence of crackles, rhonchi, stridor, and wheezing. Signs of consolidation (eg, egophony, dullness to percussion) should be sought. The cervical and supraclavicular areas should be inspected and palpated for lymphadenopathy (suggesting cancer or TB).

Neck veins should be inspected for distention, and the legs and presacral area should be palpated for pitting edema (suggesting heart failure). Heart sounds should be auscultated with notation of any extra heart sounds or murmur that might support a diagnosis of heart failure and elevated pulmonary pressure.

The abdominal examination should focus on signs of hepatic congestion or masses, which could suggest either cancer or hematemesis from potential esophageal varices.

The skin and mucous membranes should be examined for ecchymoses, petechiae, telangiectasia, gingivitis, or evidence of bleeding from the oral or nasal mucosa.

If the patient can reproduce hemoptysis during examination, the color and amount of blood should be noted.

Red flags

The following findings are of particular concern:

- Massive hemoptysis
- Back pain
- Presence of a pulmonary artery catheter or tracheostomy
- Malaise, weight loss, or fatigue
- Extensive smoking history
- Dyspnea at rest during examination or absent or decreased breath sounds

Interpretation of findings

The history and physical examination often suggest a diagnosis and guide further testing.

Despite the many possibilities, some generalities can be made. A previously healthy person with a normal examination and no risk factors (eg, for TB, pulmonary embolism) who presents with

acute-onset cough and fever most likely has hemoptysis due to an acute respiratory illness; chronic disorders are much lower on the list of possibilities. However, if risk factors are present, those specific disorders must be strongly suspected. A clinical prediction rule can help estimate the risk of pulmonary embolism. A normal O_2 saturation does not exclude pulmonary embolism.

Patients whose hemoptysis is due to a lung disorder (eg, COPD, cystic fibrosis, bronchiectasis) or heart disease (eg, heart failure) typically have a clear history of those disorders. Hemoptysis is not an initial manifestation.

Patients with known immunocompromise should be suspected of having TB or a fungal infection.

Patients with symptoms or signs of chronic illness but no known disorders should be suspected of having cancer or TB, although hemoptysis can be the initial manifestation of lung cancer in a patient who is otherwise asymptomatic.

Several specific findings are of note. Known renal failure or hematuria suggests a pulmonary-renal syndrome (eg, Goodpasture syndrome, granulomatosis with polyangiitis). Patients with granulomatosis with polyangiitis may have nasal mucosal lesions. Visible telangiectasias suggest arteriovenous malformations. Patients with hemoptysis due to a bleeding disorder usually have cutaneous findings (petechiae, purpura, or both) or a history of anticoagulant or antiplatelet drug use. Recurrent hemoptysis coinciding with menses strongly suggests pulmonary endometriosis.

Testing

Patients with massive hemoptysis require treatment and stabilization, usually in an ICU, before testing. Patients with minor hemoptysis can undergo outpatient testing.

Imaging is always done. A chest x-ray is mandatory. Patients with normal results, a consistent history, and nonmassive hemoptysis can undergo empiric treatment for bronchitis. Patients with abnormal results and patients without a supporting history should undergo CT and bronchoscopy. CT may reveal pulmonary lesions that are not apparent on the chest x-ray and can help locate lesions in anticipation of bronchoscopy and biopsy. CT angiography or, less commonly, ventilation/perfusion scanning with or without pulmonary arteriography can confirm the diagnosis of pulmonary embolism. CT and pulmonary angiography can also detect pulmonary arteriovenous fistulas.

Fiberoptic inspection of the pharynx, larynx, and airways may be indicated along with esophagogastric endoscopy when the etiology is obscure to distinguish hemoptysis from hematemesis and from nasopharyngeal or oropharyngeal bleeding.

Laboratory testing is also done. Patients usually should have a CBC, a platelet count, and measurement of PT and PTT. Anti-factor Xa testing can be used to detect supratherapeutic anticoagulation in patients receiving low molecular weight heparin. Urinalysis should be done to look for signs of glomerulonephritis (hematuria, proteinuria, casts). TB skin testing and sputum culture should be done as the initial tests for active TB, but negative results do not preclude the need to induce sputum or do fiberoptic bronchoscopy to obtain samples for further acid-fast bacillus testing if an alternative diagnosis is not found.

Cryptogenic hemoptysis

The cause of hemoptysis remains unknown in 30 to 40% of patients, but the prognosis for patients with cryptogenic hemoptysis is generally favorable, usually with resolution of bleeding within 6 mo of evaluation.

Treatment

Massive hemoptysis

Initial treatment of massive hemoptysis has two objectives:

- Prevent aspiration of blood into the uninvolved lung (which can cause asphyxiation)
- Prevent exsanguination from ongoing bleeding

It can be difficult to protect the uninvolved lung because it is often initially unclear which side is bleeding. Once the bleeding side is identified, strategies include positioning the patient with the bleeding lung in a dependent position and selectively intubating the uninvolved lung and/or obstructing the bronchus going to the bleeding lung.

Prevention of exsanguination involves reversal of any bleeding diathesis and direct efforts to stop the bleeding. Clotting deficiencies can be reversed with fresh frozen plasma and factor-specific or platelet transfusions. Laser therapy, cauterization, or direct injection with epinephrine or vasopressin can be done bronchoscopically.

Massive hemoptysis is one of the few indications for rigid (as opposed to flexible) bronchoscopy, which provides control of the airway, allows for a larger field of view than flexible bronchoscopy, allows better suctioning, and is more suited to therapeutic interventions, such as laser therapy.

Embolization via bronchial artery angiography is becoming the preferred method with which to stop massive hemoptysis, with reported success rates of up to 90%. Emergency surgery is indicated for massive hemoptysis not controlled by rigid bronchoscopy or embolization and is generally considered a last resort.

Once a diagnosis is made, further treatment is directed at the cause.

Minor hemoptysis

Treatment of minor hemoptysis is directed at the cause.

Early resection may be indicated for bronchial adenoma or carcinoma. Broncholithiasis (erosion of a calcified lymph node into an adjacent bronchus) may require pulmonary resection if the stone cannot be removed via rigid bronchoscopy. Bleeding secondary to heart failure or mitral stenosis usually responds to specific therapy for heart failure. In rare cases, emergency mitral valvulotomy is necessary for life-threatening hemoptysis due to mitral stenosis.

Bleeding from a pulmonary embolism is rarely massive and almost always stops spontaneously. If emboli recur and bleeding persists, anticoagulation may be contraindicated, and placement of an inferior vena cava filter is the treatment of choice.

Because bleeding from bronchiectatic areas usually results from infection, treatment of the infection with appropriate antibiotics and postural drainage is essential.

Key Points

- Hemoptysis needs to be distinguished from hematemesis and nasopharyngeal or oropharyngeal bleeding.
- Bronchitis, bronchiectasis, TB, and necrotizing pneumonia or lung abscess are the most common causes in adults.
- Lower respiratory tract infection and foreign body aspiration are the most common causes in children.
- Patients with massive hemoptysis require treatment and stabilization before testing.
- With massive hemoptysis, if the side of bleeding is known, patients should be positioned with the affected lung in the dependent position.
- Bronchial artery embolization is the preferred treatment for massive hemoptysis.

Last full review/revision July 2014 by Noah Lechtzin, MD, MHS

TABLE 1
Differential Diagnosis of Hemoptysis

Source other than the lower respiratory tract	Pulmonary parenchymal source	Primary vascular source
Upper airway (nasopharyngeal) bleeding	Lung abscess	Arteriovenous malformation
	Pneumonia	Pulmonary embolism
	Tuberculosis	Elevated pulmonary venous pressure (especially mitral

Gastrointestinal bleeding

Mycetoma ("fungus ball")

stenosis)

Tracheobronchial source

Goodpasture's syndrome

Idiopathic pulmonary hemosiderosis

Pulmonary artery rupture secondary to balloon-tip pulmonary artery catheter manipulation

Neoplasm (bronchogenic carcinoma, endobronchial metastatic tumor,

Wegener's granulomatosis

Lupus pneumonitis

Miscellaneous and rare causes

Kaposi's sarcoma, bronchial carcinoid)

Long contusion

Pulmonary endometriosis

Bronchitis (acute or chronic)

Systemic coagulopathy or use of anticoagulants or thrombolytic agents

Bronchiectasis

Broncholithiasis

Airway trauma

Foreign body

TABLE 2
Differentiating Features of Hemoptysis and Hematemesis

Hemoptysis	*Hematemesis*
History	
Absence of nausea and vomiting	Presence of nausea and vomiting
Lung disease	Gastric or hepatic disease
Asphyxia possible	Asphyxia unusual
Sputum examination	
Frothy	Rarely frothy
Liquid or clotted appearance	Coffee ground appearance
Bright red or pink	Brown to black
Laboratory	
Alkaline pH	Acidic pH
Mixed with macrophages and neutrophils	Mixed with food particles

TABLE 3
Diagnostic Clues in Hemoptysis: Physical History

Clinical clues	*Suggested diagnosis**
Anticoagulant use	Medication effect, coagulation disorder
Association with menses	Catamenial hemoptysis
Dyspnea on exertion, fatigue, orthopnea, paroxysmal nocturnal dyspnea, frothy pink sputum	Congestive heart failure, left ventricular dysfunction, mitral valve stenosis
Fever, productive cough	Upper respiratory infection, acute sinusitis, acute

Clinical clues	Suggested diagnosis*
	bronchitis, pneumonia, lung abscess
History of breast, colon, or renal cancers	Endobronchial metastatic disease of lungs
History of chronic lung disease, recurrent lower respiratory track infection, cough with copious purulent sputum	Bronchiectasis, lung abscess
HIV, immunosuppression	Neoplasia, tuberculosis, Kaposi's sarcoma
Nausea, vomiting, melena, alcoholism, chronic use of nonsteroidal anti-inflammatory drugs	Gastritis, gastric or peptic ulcer, esophageal varices
Pleuritic chest pain, calf tenderness	Pulmonary embolism or infarction
Tobacco use	Acute bronchitis, chronic bronchitis, lung cancer, pneumonia
Travel history	Tuberculosis, parasites (e.g., paragonimiasis, schistosomiasis, amebiasis, leptospirosis), biologic agents (e.g., plague, tularemia, T2 mycotoxin)
Weight loss	Emphysema, lung cancer, tuberculosis, bronchiectasis, lung abscess, HIV

HIV = human immunodeficiency virus.

—Arranged from most to least common diagnosis for each clinical clue.

TABLE 4
Diagnostic Clues in Hemoptysis: Physical Examination

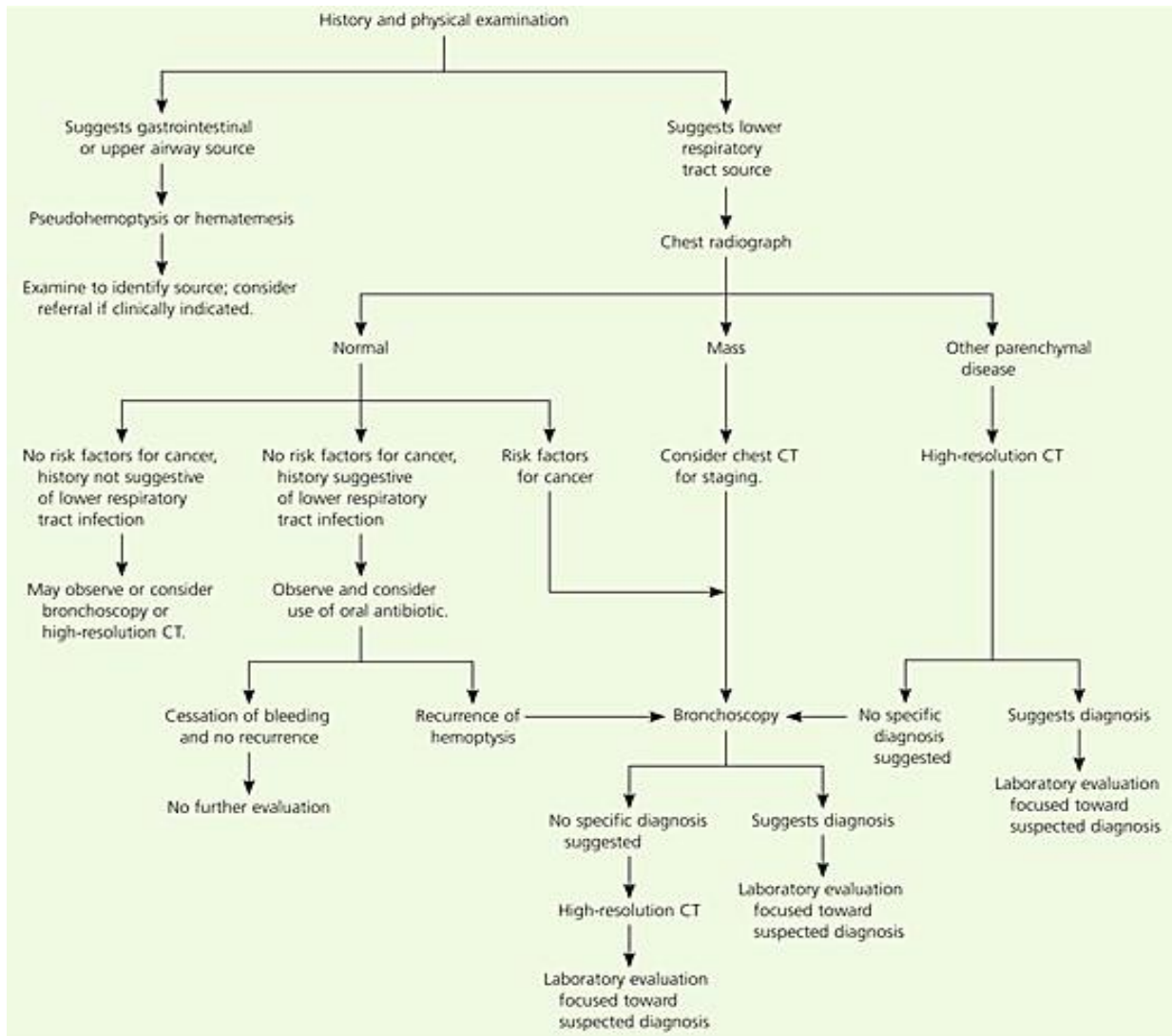| Clinical clues	Suggested diagnosis*
Cachexia, clubbing, voice hoarseness, Cushing's syndrome, hyperpigmentation, Horner's syndrome	Bronchogenic carcinoma, small cell lung cancer, other primary lung cancers
Clubbing	Primary lung cancer, bronchiectasis, lung abscess, severe chronic lung disease, secondary lung metastases
Dullness to percussion, fever, unilateral rales	Pneumonia
Facial tenderness, fever, mucopurulent nasal discharge, postnasal drainage	Acute upper respiratory infection, acute sinusitis
Fever, tachypnea, hypoxia, hypertrophied accessory respiratory muscles, barrel chest, intercostal retractions, pursed lip breathing, rhonchi, wheezing, tympani to percussion, distant heart sounds	Acute exacerbation of chronic bronchitis, primary lung cancer, pneumonia
Gingival thickening, mulberry gingivitis, saddle nose, nasal septum perforation	Wegener's granulomatosis
Heart murmur, pectus excavatum	Mitral valve stenosis
Lymph node enlargement, cachexia, violaceous tumors on skin	Kaposi's sarcoma secondary to human immunodeficiency virus infection
Orofacial and mucous membrane telangiectasia, epistaxis	Osler-Weber-Rendu disease
Tachycardia, tachypnea, hypoxia, jugulovenous distention, S3 gallop, decreased lung sounds, bilateral rales, dullness to percussion in lower lung fields	Congestive heart failure caused by left ventricular dysfunction or severe mitral valve stenosis
Tachypnea, tachycardia, dyspnea, fixed split S2, pleural friction rub, unilateral leg pain and edema	Pulmonary thromboembolic disease
Tympani to percussion over lung apices, cachexia	Tuberculosis

Diagnosing Nonmassive Hemoptysis

Figure 1.
Algorithm for diagnosing nonmassive hemoptysis. (CT = computed tomography.)

TABLE 5
Diagnostic Clues in Hemoptysis: Chest Radiograph

Chest radiograph finding	*Suggested diagnosis**
Cardiomegaly, increased pulmonary vascular distribution	Chronic heart failure, mitral valve stenosis
Cavitary lesions	Lung abscess, tuberculosis, necrotizing carcinoma
Diffuse alveolar infiltrates	Chronic heart failure, pulmonary edema, aspiration, toxic injury
Hilar adenopathy or mass	Carcinoma, metastatic disease, infectious process, sarcoid
Hyperinflation	Chronic obstructive pulmonary disease
Lobar or segmental infiltrates	Pneumonia, thromboembolism, obstructing carcinoma
Mass lesion, nodules, granulomas	Carcinoma, metastatic disease, Wegener's

Chest radiograph finding	Suggested diagnosis*
	granulomatosis, septic embolism, vasculitides
Normal or no change from baseline	Bronchitis, upper respiratory infection, sinusitis, pulmonary embolism
Patchy alveolar infiltrates (multiple bleeding sites)	Bleeding disorders, idiopathic pulmonary hemosiderosis, Goodpasture's syndrome

*—*Arranged from most to least common diagnosis for each clinical clue.*

TABLE 6
Diagnostic Clues in Hemoptysis: Laboratory Tests

Test	Diagnostic findings
White blood cell count and differential	Elevated cell count and differential shifts may be present in upper and lower respiratory tract infections
Hemoglobin, hematocrit	Decreased in anemia
Platelet count	Decreased in thrombocytopenia
Prothrombin time, International Normalized Ratio, partial thromboplastin time	Increased in anticoagulant use, disorders of coagulation
Arterial blood gases	Hypoxia, hypercarbia
D-dimer	Elevated in pulmonary embolism
Sputum Gram stain, culture, acid-fast bacillus smear and culture	Pneumonia, lung abscess, tuberculosis, mycobacterial infections
Sputum cytology	Neoplasm
Purified protein derivative skin test	Positive increases risk for tuberculosis
Human immunodeficiency virus test	Positive increases risk for tuberculosis, Kaposi's sarcoma
Erythrocyte sedimentation rate	Elevated in infection, autoimmune disorders (e.g., Wegener's syndrome, systemic lupus erythematosus, sarcoid, Goodpasture's syndrome), may be elevated in neoplasia

Self preparation at class:
Listen information;
Work with patients (with cardiac pathology);
Ask about the problems that have not been found in information given.
Self preparation at home:

Compose the plan of your answer;
Answer the questions to the topic;
Do the test given above.

1. What is the BEST position in which to place a patient with massive hemoptysis?
(A) Affected side up
(B) Affected side down
(C) Trendelenburg
(D) Reverse Trendelenburg
(E) None of the above

Recommended literature:

 A. Main:
1. ―Harrison's principles of internal medicine‖, Editors: Anthony S. Fauci, Dennis L. Kasper, Stephen L Hauser, Dan L. Longo, Joseph Loscalzo, McGraw-Hill Education / Medical; 19 edition (April 8, 2015), 1-2 volumes, 3000 p.
2. CURRENT Medical Diagnosis and Treatment 2012, Fifty-First Edition (LANGE CURRENT Series) by Stephen McPhee, Maxine Papadakis and Michael W. Rabow (Paperback - Sep 12, 2011)
3. Davidson's Principles and Practice of Medicine: With STUDENT CONSULT Online Access, 21e (Principles & Practice of Medicine (Davidson's)) by Nicki R. Colledge BSc FRCP(Ed), Brian R. Walker BSc MD FRCP(Ed) and Stuart H. Ralston MB ChB MD FRCP FMedSci FRSE (Paperback - Mar 11, 2010)Kumar and Clark's Clinical Medicine, 7e (Kumar, Kumar and Clark's Clinical Medicine) by Parveen J. Kumar (Paperback - Jul 2, 2009)
4. CURRENT Diagnosis and Treatment Emergency Medicine, Seventh Edition (LANGE CURRENT Series) by C. Keith Stone (May 23, 2011)
5. Goldman's Cecil medicine / [edited by] Lee Goldman, Andrew I. Schafer.—24th ed. Elsevier Sanders. Rev. ed. of: Cecil medicine. 23rd ed. – 2012. p.
6. Sonographer's Handbook of Diagnostic Ultrasound by Jason R. Young M.D. (Feb 23, 2011)

Additional literature:
1.Kovalyova O.M., Asheulova T.V. Propedeutics to internal medicine. Part 1, Diagnostics. Vinnytsya, Nova Knyha, 2006, 424 p

The answer is B. The optimal positioning for patients with massive hemoptysis is with the bleeding lung down. This minimizes contamination of blood from the affected to the unaffected lung and helps prevent compromise of oxygenation and ventilation. Tracheal intubation is indicated if there is respiratory failure or the patient is unable to clear blood from the airway.

Methodical recommendations consisted by   Kulishov S.K.

malignancy, suppurative lung disease, and congenital heart problems. Treatment is directed at the underlying disease process. While x-rays may suggest osteomyelitis, the process is usually bilateral and easily distinguishable from osteomyelitis. The first step in evaluation of this patient is to obtain a chest x-ray looking for lung infection and carcinoma.

2 The answer is c. When stupor and coma supervene in CO_2 retention, fatal arrhythmias, seizures, and death are likely to follow. Stopping oxygen is the worst course of action, as it will exacerbate life-threatening hypoxia. Intubation is the treatment of choice. Bicarbonate plays no role in this acidosis, which is respiratory and caused by hypoventilation.

Methodical recommendations consisted by   Kulishov S.K.