MINISTRY OF PUBLIC HEALTH OF UKRAINE

Vinnitsa National Pirogov Memorial Medical University

"**Approved**"
by Methodical Council
Department of Tuberculosis, Clinical Immunology
and Allergy
Chair of Department
Ass Prof of HEI L.Kulyk

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Self-Study Modules on Tuberculosis

for preparing students to practical classes

(in English)

Subject	Phthisiology (Tuberculosis)
Module №1	Curation of patients with respiratory diseases.
Topic of practical class №4	Assessment and management of massive and non – massive haemoptysis. Diagnostics algorithm. How to rule out other reasons of bleeding. Drugs for critical care. Invasive therapeutic procedures.
Course	6th
Faculty	General medicine

1. Background

Hemoptysis is the spitting of blood that originated in the lungs or bronchial tubes. The patient's history should help determine the amount of blood and differentiate between hemoptysis, pseudohemoptysis, and hematemesis. A focused physical examination can lead to the diagnosis in most cases.

In children, lower respiratory tract infection and foreign body aspiration are common causes. In adults, bronchitis, bronchogenic carcinoma, and pneumonia are the major causes. Chest radiographs often aid in diagnosis and assist in using two complementary diagnostic procedures, fiberoptic bronchoscopy and high-resolution computed tomography, which are useful in difficult cases and when malignancy is suspected. The goals of management are threefold: bleeding cessation, aspiration prevention, and treatment of the underlying cause. Mild hemoptysis often is caused by an infection that can be managed on an outpatient basis with close monitoring. If hemoptysis persists, consulting with a pulmonologist should be considered. Patients with risk factors for malignancy or recurrent hemoptysis also require further evaluation with fiberoptic bronchoscopy or high-resolution computed tomography. In up to 34 percent of patients, no cause of hemoptysis can be found.

Hemoptysis is classified as nonmassive or massive based on the volume of blood loss; however, there are no uniform definitions for these categories. In this booklet, hemoptysis is considered nonmassive if blood loss is less than 50 mL per day. The lungs receive blood from the pulmonary and bronchial arterial systems. The low-pressure pulmonary system tends to produce small-volume hemoptysis, whereas bleeding from the bronchial system, which is at systemic pressure, tends to be profuse. Blood loss volume is more useful in directing management than in reaching a diagnosis.

After confirming the presence of blood, an initial task is differentiating between hemoptysis, pseudohemoptysis (i.e., the spitting of blood that does not come from the lungs or bronchial tubes), and hematemesis (i.e., the vomiting of blood).

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	*Evidence rating*
Patients with evidence of parenchymal disease should have high-resolution CT, and those with a mass should be considered for bronchoscopy.	C
Patients with normal chest radiograph, no risk factors for cancer, and findings not suggestive for infection should be considered for bronchoscopy or high-resolution CT.	C
After extensive initial investigation, closely follow smokers older than 40 years who have unexplained hemoptysis.	C

CT=computed tomography.

The common types of "coughing up blood"

Blood-tinged sputum: The blood in sputum is common, but it is usually not of concern. In most cases, the coughing up blood is in the form of blood streaks, blood spots or even blood clots in sputum, which may be either white mucus sputum, or yellow purulent sputum. Fortunately, it is harmless most of the time as a consequence of pneumonia, bronchitis or laryngitis, although the coughing up blood may be usually recurrent, especially after getting up in the morning.

Rusty sputum (prune-juice sputum): It is the reddish-brown sputum containing changed blood or blood pigments, as well as bacteria, mucus, and sloughed necrotic lung tissues; It is typical of the lobar pneumonia, a pneumonia caused by Streptococcus pneumoniae. In advanced pneumococcal pneumonia, the sputum appears as prune juice sputum: watery, dark brown, hemorrhagic sputum.

Gelatinous bloody sputum (currant-jelly sputum): It is a thick, bloody, mucoid sputum, characterized by brick red, jelly, like red currant jelly. This sputum is formed by an endobronchial plug of blood, mucus, debris and bacteria, and typical of pneumonia caused by Klebsiella pneumoniae. This is just a typical, but rare bloody sputum.

Pink frothy sputum: It is a type of coughing up blood, and usually results from blood (pink) and air (frothy) mixing with secretions in the alveoli. The pink frothy sputum typically occurs in acute pulmonary edema and any heart disease leading to acute left heart failure.

Pure coughing up blood: It is also a very common type of coughing up blood, without sputum. Vascular rupture and hemorrhage of the bronchi are the most common causes of coughing up pure blood. Many respiratory diseases can cause a "coughing up blood" with pure blood no sputum or mucus. The common causes of pure coughing up blood are pulmonary tuberculosis, bronchial tuberculosis, bronchiectasis, bronchial stones.

Large amounts of coughing up blood: Vascular rupture and hemorrhage of the bronchi are the most common respiratory tract bleeding. That can lead to a massive bleeding, and thus you may have a severe "coughing up blood". Through an erosion to the bronchial blood vessels, the cavitary pulmonary tuberculosis, chronic lung abscess and bronchiectasis often cause a massive bleeding, and may have a coughing up blood more than 500 ml per day, or one-time >100 ml. Patients with severe mitral stenosis may also have "coughing up blood" with a lot of bright red blood. Rare causes leading to coughing up a lot of blood, may be pulmonary infarction, pulmonary embolism, bronchogenic carcinoma, aspergilloma, others.

Causes of Hemoptysis

In the primary care setting, the most common causes of hemoptysis are acute and chronic bronchitis, pneumonia, tuberculosis, and lung cancer.

INFECTION

Infection is the most common cause of hemoptysis, accounting for 60 to 70 percent of cases. Infection causes superficial mucosal inflammation and edema that can lead to the rupture of the superficial blood vessels. In a retrospective study of inpatient and outpatient hemoptysis in the United States, bronchitis caused 26 percent of cases, pneumonia caused 10 percent, and tuberculosis accounted for 8 percent. Invasive bacteria (e.g., Staphylococcus aureus, Pseudomonas aeruginosa) or fungi (e.g., Aspergillus species) are the most common infectious causes of hemoptysis. Viruses such as influenza also may cause severe hemoptysis. Human immunodeficiency virus (HIV) infection predisposes patients to several conditions that may produce hemoptysis, including pulmonary Kaposi's sarcoma.

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
Gastrointestinal bleeding	Pneumonia	Pulmonary embolism
Tracheobronchial source	Tuberculosis	Elevated pulmonary venous pressure (especially mitral stenosis)
Neoplasm (bronchogenic carcinoma, endobronchial metastatic tumor, Kaposi's sarcoma, bronchial carcinoid)	Mycetoma ("fungus ball")	Pulmonary artery rupture secondary to balloon-tip pulmonary artery catheter manipulation
Bronchitis (acute or chronic)	Goodpasture's syndrome	**Miscellaneous and rare causes**
Bronchiectasis	Idiopathic pulmonary hemosiderosis	Pulmonary endometriosis
Broncholithiasis	Wegener's granulomatosis	Systemic coagulopathy or use of anticoagulants or thrombolytic agents
Airway trauma	Lupus pneumonitis	
Foreign body	Long contusion	

Adapted with permission from Weinberger SE. Principles of pulmonary medicine. 3d ed. Philadelphia: Saunders, 1998.

CANCER

Primary lung cancers account for 23 percent of cases of hemoptysis in the United States. Bronchogenic carcinoma is a common lung cancer responsible for hemoptysis in 5 to 44 percent of all cases. Bleeding from malignant or benign tumors can be secondary to superficial mucosal invasion, erosion into blood vessels, or highly vascular lesions. Breast, renal, and colon cancers have a predilection for lung metastasis; however, metastatic lung carcinoma rarely results in bleeding.[6] Obstructive lesions may cause a secondary infection, resulting in hemoptysis.

PULMONARY VENOUS HYPERTENSION

Cardiovascular conditions that result in pulmonary venous hypertension can cause cardiac hemoptysis. The most common of these is left ventricular systolic heart failure. Other cardiovascular causes include severe mitral stenosis and pulmonary embolism. Although hemoptysis is a recognized pulmonary

embolism symptom, pulmonary embolism is an uncommon cause of hemoptysis. For example, in a patient without underlying cardiopulmonary disease, the positive and negative likelihood ratios for hemoptysis in pulmonary embolism are 1.6 and 0.95, respectively. Therefore, the presence or absence of hemoptysis alone has no significant effect on the likelihood of pulmonary embolism.

IDIOPATHY

Idiopathic hemoptysis is a diagnosis of exclusion. In 7 to 34 percent of patients with hemoptysis, no identifiable cause can be found after careful evaluation. Prognosis for idiopathic hemoptysis usually is good, and the majority of patients have resolution of bleeding within six months of evaluation. However, results from one study found an increasing incidence of lung cancer in smokers older than 40 years with idiopathic hemoptysis, and suggested that these patients may warrant close monitoring.

ALVEOLAR HAEMORRHAGE (AH) is a rare and potentially lifethreatening condition characterised by diffuse blood leakage from the pulmonary microcirculation into the alveolar spaces due to microvascular damage.

The terms AH, diffuse AH and intrapulmonary haemorrhage are considered synonymous. AH designates bleeding from the pulmonary microcirculation (pulmonary arterioles, alveolar capillaries and pulmonary venules) as a result of microvascular damage leading to blood leakage into the alveolar spaces.

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

Box 1. Aetiology of alveolar haemorrhage syndromes

Diagnostic category	Common causes of AH	Rare causes of AH
Systemic vasculitis[#]	Granulomatosis with polyangiitis (Wegener's)[¶] [2, 10], microscopic polyangiitis[¶] [2, 3]	Henoch–Schoenlein purpura[¶] [11], Churg–Strauss syndrome[¶] [2, 12–14], Behçet syndrome [15], mixed cryoglobulinemia due to hepatitis C virus [16], pauci-immune pulmonary capillaritis (with or without anti-neutrophil cytoplasmic antibodies), polyarteritis nodosa related to hepatitis B virus, Takayasu disease [17]
Connective tissue diseases[#]	Systemic lupus erythematosus[¶] [5, 6, 18]	Rheumatoid arthritis [19], systemic sclerosis, idiopathic inflammatory myopathies [20], mixed connective tissue disease [19]
Other immune causes[#]	Anti-basement membrane antibody disease[¶] [21]	Pauci-immune glomerulonephritis[¶], immune complex glomerulonephritis[¶], haemolytic uraemic syndrome[¶], immunoglobulin A nephropathy[¶], coeliac disease [22], inflammatory bowel diseases, cows' milk intolerance [23]
Infections	Leptospirosis[#,¶] [24]	Invasive aspergillosis, systemic candidiasis, strongyloidiasis, staphylococci (including *Staphylococcus aureus* producing Panton–Valentine leukocidin), legionellosis, *Mycoplasma*, *Cytomegalovirus*, Herpes simplex virus, *Hantavirus*, AIDS, H1N1 influenza [25], malaria, *Strongyloides stercoralis*, *Stachybotrys chartarum* [26–28]
Drugs	Propylthiouracil[#] [29, 30]	Alemtuzumab [31], abciximab [32], transretinoic acid[#] [33], aminoglutethimide [34], amiodarone [35, 36], azathioprine[#], carbamazepine, carbimazole, cyclosporine, clomifen, cytarabine, dextran, dihydralazine[#], dimethylsulfoxide, D-penicillamine[#] [37], everolimus[#] [38], fludarabine, gemcitabine, glibenclamide[#], methotrexate[#], mitomycin [39], moxalactam, nitrofurantoin[#] [40], nitric oxide, phenytoin[#] [41], quinidine, rituximab[#], sirolimus[#] [42], sunitinib [43], tirofiban [32, 44]; see also haemostasis disorders
Toxic	Cocaine[#] [45]	Trimellitic anhydride[#] [46, 47], pyromellitic dianhydride [48], isocyanates [49], hydrocarbon derivatives
Intravascular metastasis		Angiosarcoma, Kaposi sarcoma [50], choriocarcinoma, epithelioid haemangioendothelioma, multiple myeloma, renal cell carcinoma [7]
Transplantation	Bone marrow transplant [51, 52]	Solid organ transplantation
Haemostasis disorders		Disseminated intravascular coagulation [7], thrombocytopenia, anti-phospholipid syndrome[#] [53], thrombotic thrombocytopenic purpura[#], haemophilia [54], drugs (oral anticoagulants [55], anti-aggregants [56], anti-glycoprotein IIb/IIIa [32], fibrinolytic agents [57])
Pulmonary vascular disease		Idiopathic and thromboembolic pulmonary hypertension, pulmonary veno-occlusive disease, pulmonary capillary haemangiomatosis
Heart disease		Mitral stenosis [58], left heart failure [58], left atrial myxoma

HEMOPTYSIS IN CHILDREN

The major cause of hemoptysis in children is lower respiratory tract infection. The second most common cause is foreign body aspiration, with most cases occurring in children younger than four years. Another important cause is bronchiectasis, which often is secondary to cystic fibrosis. Primary pulmonary tuberculosis is a rare cause estimated to occur in less than 1 percent of cases. Although uncommon, trauma is another possible cause. Blunt-force trauma may result in hemoptysis secondary to pulmonary contusion and hemorrhage. Bleeding caused by suffocation, deliberate or accidental, also should be considered.

Patient History

Historic clues are useful for differentiating hemoptysis from hematemesis. Patient history also can help identify the anatomic site of bleeding, differentiate between hemoptysis and pseudohemoptysis, and narrow the differential diagnosis. Factors such as age, nutrition status, and comorbid conditions can assist in the diagnosis and management of hemoptysis.

Once true hemoptysis is suspected, the investigation should focus on the respiratory system. Blood from the lower bronchial tree typically induces cough, whereas a history of epistaxis or expectorating without cough would be consistent with an upper respiratory source but does not exclude a lower tract site.

Bleeding is difficult to quantify clinically. Patients may find it difficult to discern whether they are throwing up, coughing, or spitting out bloody material. The amount of blood loss usually is overestimated by patients and physicians, but an attempt to determine the volume and rate of blood loss should be made. Methods of determination include observing as the patient coughs and the use of a graduated container. Blood-streaked sputum deserves the same diagnostic consideration as blood alone. The amount or frequency of bleeding does not correlate with the diagnosis or incidence of cancer.

It is helpful to determine whether there have been previous episodes of hemoptysis and what diagnostic assessments have been done. Mild hemoptysis recurring sporadically over a few years is common in smokers who have chronic bronchitis punctuated with superimposed acute bronchitis. Because smoking is an important risk factor, these patients are at higher risk for lung cancer. Chronic obstructive pulmonary disease also is an independent risk factor for hemoptysis.

Environmental exposure to asbestos, arsenic, chromium, nickel, and certain ethers increases risk for hemoptysis. Bronchial adenomas, although malignant, are slow growing and may present with occasional bleeding over many years. Malignancy in general, especially adenocarcinomas, can induce a hypercoagulable state, thereby increasing the risk for a pulmonary embolism. A history of chronic, purulent sputum production and frequent pneumonias, including tuberculosis, may represent bronchiectasis. Association of hemoptysis with menses (i.e., catamenial hemoptysis) may represent intrathoracic endometriosis.

A travel history may be helpful. Tuberculosis is endemic in many parts of the world, and parasitic etiologies should be considered. In regions where drinking from springs is common, there are case reports of hemoptysis caused by leeches attaching to the upper respiratory tract mucosa. Also, biologic weapons such as plague may cause hemoptysis.

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 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.*

Physical Examination

Historic clues often will narrow the differential diagnosis and help focus the physical examination. Examining the expectoration may help localize the source of bleeding. The physician should record vital signs, including pulse oximetry levels, to document fever, tachycardia, tachypnea, weight changes, and hypoxia. Constitutional signs such as cachexia and level of patient distress also should be noted. The skin and mucous membranes should be inspected for cyanosis, pallor, ecchymoses, telangiectasia, gingivitis, or evidence of bleeding from the oral or nasal mucosa.

The examination for lymph node enlargement should include the neck, supraclavicular region, and axillae. The cardiovascular examination includes an evaluation for jugular venous distention, abnormal heart sounds, and edema. The physician should check the chest and lungs for signs of consolidation, wheezing, rales, and trauma. The abdominal examination should focus on signs of hepatic congestion or masses, with an inspection of the extremities for signs of edema, cyanosis, or clubbing.

Box 2. Proposed evaluation of a patient with hemorrhage

In all cases	Depending on the clinical context
Targeted history and clinical examination: Review of exposures and inhaled agents Review of medication and illicit drugs Search for features of systemic vasculitis: general symptoms (fever, asthenia, weight loss), nasal symptoms (crusty rhinitis, septal erosions), ocular symptoms (episcleritis, retinal vasculitis), skin changes (palpable purpura, subcutaneous nodules, erythema, livedo), musculoskeletal symptoms (arthralgias, myalgias), neurological symptoms (mono- or multinevritis) Search for connective tissue disease Exposure to infected animals or their urine, immersion in contaminated water (swimming, fishing, floods), bites; recent stay in tropical areas	
Chest radiography, HRCT, echocardiography	
Complete blood picture, coagulation studies, urea, creatinine, urinary dipstick and sediment, creatinine clearance, 24-h proteinuria, NT-pro-BNP (limited value in renal failure)	
Arterial blood gases or pulse oxymetry	Lung function tests
Anti-nuclear antibodies, anti-double-strand DNA antibodies, anti-basement membrane antibodies, anti-neutrophil cytoplasmic antibodies	Rheumatoid factor, anti-cyclic citrullinated peptide antibodies, anti-nucleoproteins, serology for leptospirosis (IgM ELISA, microscopic agglutination test), cryoglobulin, complement, anti-cardiolipin antibodies, immunoelectrophoresis, anti-gliadin, anti-endomysial and anti-transglutaminase antibodies
Bronchoscopy with BAL: macroscopic appearance, cytology with differential cell count, Perls staining with percentage of haemosiderin-laden macrophages and Golde score, routine bacteriology, fungi, mycobacteria, *Pneumocystis jiroveci*	Viruses (in immunosuppressed patients)
	Biopsies: renal (with immunofluorescence), other (nasal), rarely lung biopsy

Diagnostic Evaluation

After a careful history and examination, a chest radiograph should be obtained. If a diagnosis remains unclear, further imaging with chest computed tomography (CT) or direct visualization with bronchoscopy often is indicated. In high-risk patients with a normal chest radiograph, fiberoptic bronchoscopy should be considered to rule out malignancy. Risk factors that increase the likelihood of finding lung cancer on bronchoscopy include male sex, older than 40 years, a smoking history of more than 40 pack-years, and duration of hemoptysis for more than one week.

Fiberoptic bronchoscopy is preferred if neoplasia is suspected; it is diagnostic for central endobronchial disease and allows for direct visualization of the bleeding site. It also permits tissue biopsy, bronchial lavage, or brushings for pathologic diagnosis. Fiberoptic bronchoscopy also can provide direct therapy in cases of continued bleeding. Rigid bronchoscopy is the preferred tool for cases of massive bleeding because of its greater suctioning and airway maintenance capabilities.

High-resolution CT has become increasingly useful in the initial evaluation of hemoptysis and is preferred if parenchymal disease is suspected. Its complementary use with bronchoscopy gives a

greater positive yield of pathology and is useful for excluding malignancy in high-risk patients. Its role in hemoptysis continues to evolve, and further studies are needed to evaluate its effect on patient management and outcome. Patients with recurrent or unexplained hemoptysis may need additional laboratory evaluation to establish a diagnosis.

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

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

Management

NONMASSIVE HEMOPTYSIS

The overall goals of management of the patient with hemoptysis are threefold: bleeding cessation, aspiration prevention, and treatment of the underlying cause. As with any potentially serious condition, evaluation of the "ABCs" (i.e., airway, breathing, and circulation) is the initial step.

The most common presentation is acute, mild hemoptysis caused by bronchitis. Low-risk patients with normal chest radiographs can be treated on an outpatient basis with close monitoring and appropriate oral antibiotics, if clinically indicated. If hemoptysis persists or remains unexplained, an outpatient evaluation by a pulmonologist should be considered.

An abnormal mass on a chest radiograph warrants an outpatient bronchoscopic examination. For patients with a normal chest radiograph and risk factors for lung cancer or recurrent hemoptysis, outpatient fiberoptic bronchoscopy also is indicated to rule out neoplasm. High-resolution CT is indicated when clinical suspicion for malignancy exists and sputum and bronchoscopy do not yield any

pathology. High-resolution CT also is indicated when chest radiography reveals peripheral or other parenchymal disease.

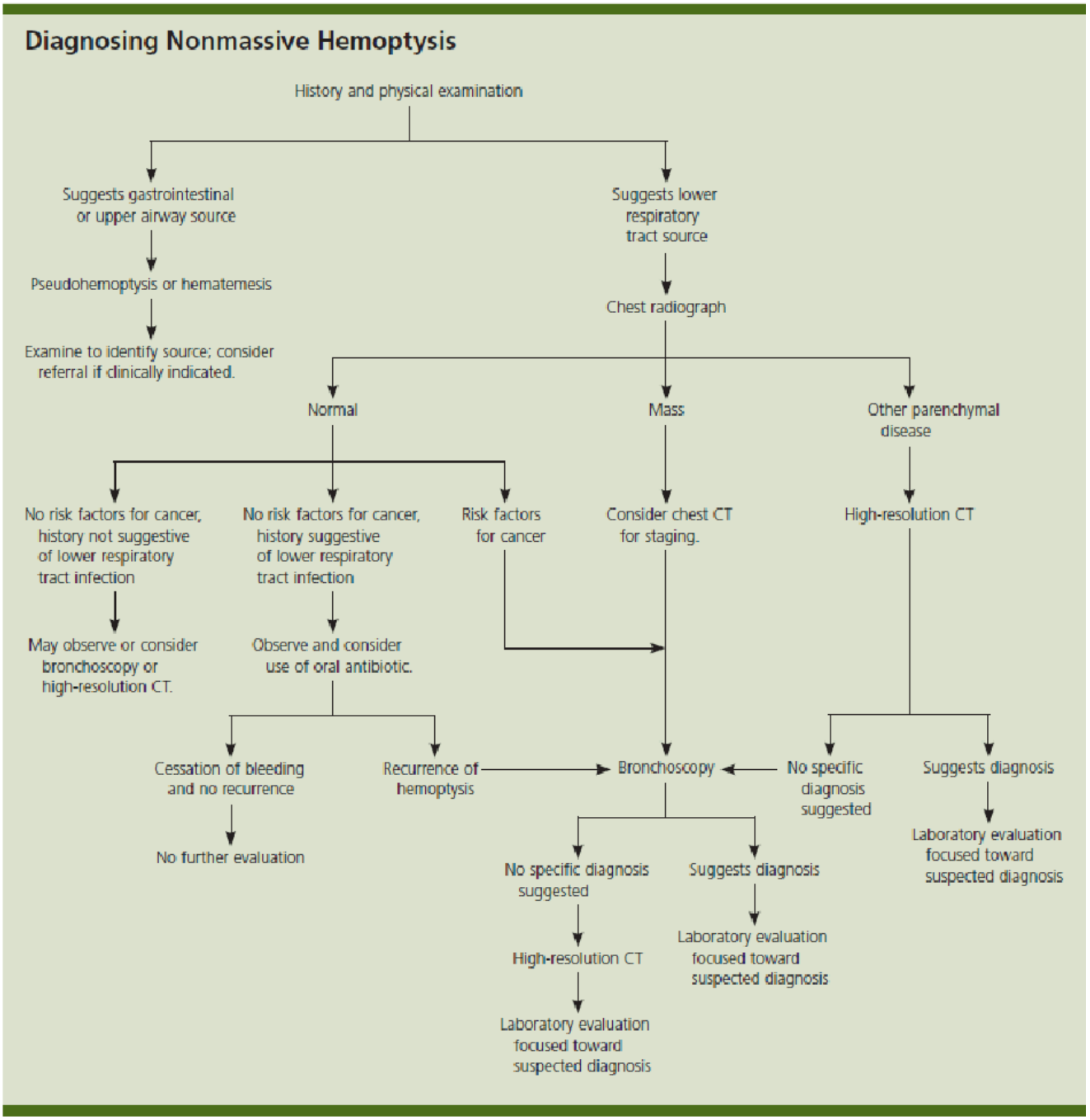


Figure 1. Algorithm for diagnosing nonmassive hemoptysis. (CT = computed tomography.)

Adapted with permission from Harrison TR, Braunwald E. Cough and hemoptysis. In: Harrison's Principles of internal medicine. 15th ed. New York: McGraw-Hill, 2001:208.

MASSIVE HEMOPTYSIS

The mortality rate from massive hemoptysis depends on the bleeding rate and etiology. Hemoptysis greater than 1,000 mL per 24 hours in the presence of malignancy carries a mortality rate of 80 percent; therefore, massive hemoptysis warrants a more aggressive, expedient approach. These patients require intensive care and early consultation with a pulmonologist. In cases of massive or life-threatening hemoptysis, diagnosis and therapy must occur simultaneously. Airway maintenance is vital because the primary mechanism of death is asphyxiation, not exsanguination. Supplemental

oxygen and fluid resuscitation are essential. Assistance by a cardiothoracic surgeon should be considered because emergency surgical intervention may be needed.

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 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

HEMOPTYSIS

Definition and pathophysiology

- Expectoration of blood or blood-streaked sputum
- **Massive hemoptysis**: ~>600 mL/24–48 h; gas exchange more important than blood loss
- Massive hemoptysis usually from tortuous or invaded **bronchial arteries**

Etiologies (*Crit Care Med* 2000;28:1642)	
Infection/ Inflammation	**Bronchitis** (most common cause of trivial hemoptysis) **Bronchiectasis** incl. **CF** (common cause of massive hemoptysis) Tuberculosis or aspergilloma (can be massive) Pneumonia or lung abscess
Neoplasm	Usually primary **lung cancer**, sometimes metastasis (can be massive)
Cardiovascular	**PE** (can be massive), pulmonary artery rupture (2° to instrumentation), CHF, mitral stenosis, trauma/foreign body, bronchovascular fistula
Other	**Vasculitis** (Wegener's, Goodpasture's, Behçet's; can be massive), AVM, anticoag (w/ underlying lung dis), coagulopathy, cocaine, idiopathic pulm hemosiderosis, catamenial (lung endometriosis)

Diagnostic workup

- Localize bleeding site
  - **Rule out GI or ENT source** by exam, history; may require endoscopy
  - Pulmonary source: determine whether **unilateral or bilateral, localized or diffuse, parenchymal or airway** by CXR or chest CT, bronchoscopy if necessary
- PT, PTT, CBC to rule out **coagulopathy**
- Sputum culture/stain for bacteria, fungi and AFB; cytology to **r/o malignancy**
- ANCA, anti-GBM, urinalysis to ✓ for **vasculitis** or **pulmonary-renal syndrome**

Treatment

- Mechanism of death is asphyxiation not exsanguination; maintain gas exchange, reverse coagulation and treat underlying condition; cough supp. may ↑ risk of asphyxiation
- Massive hemoptysis: put bleeding side dependent; selectively intubate nl lung if needed
  - *Angiography*: Dx & Rx (vascular occlusion balloons or **selective embol of bronchial art**)
  - *Rigid bronchoscopy*: allows more interventional options (electrocautery, laser) than flex.

2. Educational aims

1. Diagnosis and Management of Hemoptysis

Students should be able to:

- To collect history and examine the patients with hemoptysis.
- To distinguish hemoptysis with blood up sputum of other etiologies.
- To interpret results of laboratory tests
- To prescribe treatment of patients with hemoptysis.

3. Interdisciplinary integration

Name of discipline	Necessary skills
Human Anatomy	Segments of the lungs. Pulmonary lymphatic system. Structure of hilum. Large *and* small circulation.
Pathological Physiology	Inflammation. Tuberculous inflammation. Exudative and productive processes. Ways of spread mycobacteria in humans body.
Pathological Anatomy	Morphological manifestations of tuberculous inflammation in organs and tissues, residual tuberculous changes.
General and Clinical Pharmacology	TB chemotherapy, classification, dosage, methods of administration. Pharmacokinetics of antituberculosis drugs. Adverse reactions to antibacterial drugs, prevention and elimination.
Radiology	Methods of lung imaging. Interpretation of CT and CXR films.

4. Educational questions

1. Which one of the following statements is true? Treatment of EPTB:
() Should always be longer than for pulmonary TB. () Is usually combined with surgery. () Should include corticosteroids in TB pleurisy. () Can be shortened to 4 months in TB osteoarthritis. () Is prolonged in severe TB meningitis.

2. Which one of the following statements is true? The treatment of MDR-TB:
() Should include an earlier generation fluoroquinolone, if possible according to DST. () Should not include amikacin, capreomycin or kanamycin because of the toxicity profile of these injectable drugs. () Should not include PZA because of the likelihood of PZA drug resistance. () Should include a later-generation fluoroquinolone, if possible according to DST. () Should always include high-dose isoniazid to overcome the drug resistance.

3. Which one of the following statements about TB treatment is true?
() If rifampicin is not included in a regimen, the total treatment duration should be at least 18 months.
() Cycloserin and meropenem are WHO Group 4 drugs. () Up to 90–95% of isoniazid-resistant ***M. tuberculosis*** are MDR-TB. () Treatment of TB in HIV-positive patients should be at least twice as long as in HIV patients.
() Surgery should be avoided in the treatment of MDR-TB.

4. Which one of the following are risk factors for adverse effects during treatment of TB?
() Advanced age. () HIV infection. () Malnutrition. () Advanced age and malnutrition. () Advanced age, HIV infection and malnutrition.

5. In the treatment of DR-TB among HIV-infected patients, additive toxicity may occur between antiretroviral therapy and anti-TB drugs with respect to which one of the following:
() Depression. () Lipodystrophy. () Dysglycaemia. () Depression and dysglycaemia. () Lipodystrophy and dysglycaemia.

6. Which of the following statements is not true in relation to the management of cutaneous hypersensitivity reactions?
() For mild skin reactions, it may be possible to continue anti-TB drugs with symptomatic treatment and close clinical monitoring. () After resolution of skin rashes, serial reintroduction of drugs one by one aims to identify the causative drug. () During re-challenge, each drug should be reintroduced at gradually increasing doses over 1 week. () Re-challenge of a strongly suspected drug should be avoided for very severe reactions. () If a reaction occurs during drug re-challenge, drug desensitisation may be considered if the causative drug cannot be readily replaced.

7. Adjustment of dose and/or dosing frequency is required for which one of the following drug(s) in patients with a creatinine clearance <30 $mL \cdot min^{-1}$ or receiving haemodialysis:
() Levofloxacin. () Rifampicin. () Cycloserine. () Levofloxacin and cycloserine. () Levofloxacin, rifampicin and cycloserine.

8. Which one of the following statements regarding the use of injectables (aminoglycosides and capreomycin) is false?
() Nephrotoxicity of the injectables usually involves renal tubules and may present with non-oliguric acute renal failure. () The serum potassium level should be monitored with prolonged use of capreomycin. () Risk factors include old age, renal impairment, dehydration, high trough concentration, prolonged use, use of loop diuretics and liver disease. () Injectables are absolutely contraindicated in patients on haemodialysis. () None of these.

9. Which one of the following statements is true? Neuropsychiatric reactions may occur with:
() Isoniazid. () Cycloserine. () Fluoroquionolone. () Isoniazid and cycloserine. () Isoniazid, cycloserine and fuoroquionolone.

10. Which one of the following statements concerning the use of fluoroquionolones is false?
() Of the commonly used fluoroquinolones, the risk of prolonged QT interval is highest with moxifloxacin. () The prolonged QT interval occurs through blockade of the voltage-gated calcium channels. () Moxifloxacin should be used with caution in patients at risk of Torsades de pointes. () Caution is warranted with the concomitant use of methadone, levomethadyl or other opiods. () None of these.

11. Which one of the following statements regarding hepatotoxicity related to anti-TB drugs is false?
() Pyrazinamide appears to be the most hepatotoxic agent among the first-line drugs. () Risk factors include old age, malnutrition, alcoholism, hepatitis B and C infections, and HIV infection. () Aspartate transaminase elevation may indicate abnormalities in the liver, muscle, heart or kidney. () There is considerable mortality risk amongst patients with concurrent elevations of alanine transaminase that are more than three times the upper limit of normal and of bilirubin more than two times the upper limit of normal. () None of these.

12. Which one of the following statements regarding the epidemiology of childhood TB is true?
() All children diagnosed with TB should be tested for HIV infection. () As children rarely transmit disease, household contact tracing is not necessary. () School-age children are at the highest risk of progression from infection with ***M. tuberculosis*** to clinical disease. () BCG vaccination has had little impact on the TB epidemic in the majority of the world; therefore, it no longer has a role to play in the prevention of TB. () The majority of cases of childhood TB are microbiologyically confirmed.

13. Which of the following statements about the diagnosis of pulmonary TB in children is true?
() Negative cultures exclude the diagnosis of TB. () Induced sputum specimens can only be used in children >7 yrs of age. () A negative TST rules out disease in children. () Fine-needle aspiration of cervical lymph nodes may be diagnostic in suspected TB. () Chest CT is never indicated for the diagnosis of TB in children.

14. Which one of the following statements is true? In the treatment of childhood TB:
() Children should receive the same duration of treatment as adults. () The doses of anti-TB treatment (per kg) are the same for children and adults. () Children are more likely to get hepatic toxicity. () In children, drug-resistant TB usually develops due to poor adherence to therapy. () Children with HIV-TB co-infection and low CD4 counts should start ATT and ART concurrently.

15. The most severe form of childhood TB is TB meningitis. Which one of the following statements is true?
() The risk of developing TB meningitis can be up to 10% in infants compared with 1% in adults. () Steroids are contraindicated for the treatment of TB meningitis. () Blood brain penetration of ethambutol is better than that of isoniazid. () An LP typically shows low protein and high glucose in TB meningitis. () Magnetic resonance imaging of the brain is rarely helpful in diagnosis.

16. Contact tracing is very important in childhood TB. Which of the following statements are true? (Select

all that apply.)
○ The TST is a nonspecific test and the results may be influenced by BCG vaccination, non-tuberculous mycobacteria, immunosuppression and HIV. ○ Children under 2 yrs of age should be screened clinically and radiologically for TB regardless of TST or IGRA result. ○ A negative IGRA result rules out TB infection. ○ BCG vaccination can cause a false-positive IGRA result. ○ An indeterminate IGRA result in a child should be treated as a negative result.

17. Childhood TB should be suspected in which of the following clinical scenarios? (Select all that apply.)
○ A 12 year old with a cough for >2 weeks, fever and night sweats. ○ A 2-yr-old Somali infant admitted with fever and respiratory illness of 3 days' duration; chest radiograph shows hilar adenopathy. ○ A 4 year old who presents with focal seizure and low-grade fever; LP is unremarkable; magnetic resonance imaging of the brain shows basal enhancement. ○ A 6 year old with a 3-month history of weight loss and abdominal discomfort, and a 2-week history of low-grade fever. Ultrasound of the abdomen shows abdominal lymph nodes. The child's grandmother (who is from India) came to live with the family 9 months ago. ○ A 4 year old referred from the GP with cervical lymphadenopathy of 3 weeks' duration and with no response to a 10-day course of augmentin.

18. How do IGRA differentiate between BCG vaccination, ***M. tuberculosis*** infection and ***M. tuberculosis*** disease in children? (Select all that apply.)
○ They are the same as the TST, but are based on a blood sample. ○ They are a test for active TB.
○ They can distinguish between ***M. tuberculosis*** infection and disease. ○ They have antigens that will elicit a response only if the person is sensitised to ***M. tuberculosis*** but not to BCG. ○ They cannot differentiate between active and latent TB.

5. CASE PRESENTATION

Created By: Molly E. Billings

Case 1:

A 38 year-old man presents to clinic complaining of a two week history of cough. It started following a bad cold and is occasionally productive of yellow sputum. He denies any sinus pain, headaches, fevers, pleuritic chest pain, or shortness or breath. He has no medical problems and only uses acetaminophen on an occasional basis. He does not smoke. On exam, he is a well appearing man, with intermittent coughing. His vitals are normal and he has a normal lung exam.

He asks whether he can have some antibiotics to help treat the cough.

Should you give him the antibiotics? What would be the most useful therapy for his cough?

You see him for follow-up two months later and he is still coughing, although now with much less sputum production. What are the three most likely causes of his nagging cough?

1.

2.

3.

What other questions can you ask to sort through this differential?

Upon further history, he tells you that he has nasal congestion and finds himself clearing his throat on a frequent basis. What would be your next step in your evaluation and treatment?

You start a course of empiric therapy but when he returns in two months, he states that although his nasal congestion has improved, his cough is still present. He complains of periodic coughing spells, especially after exercising and exposure to cold air. Spirometry in your office shows FEV_1 of 104% predicted, FVC of 98% predicted and a ratio of 82%; there are no changes with bronchodilator administration. What should be the next step in your evaluation and management of his cough?

Case 2:

A 49 year-old woman presents to your clinic complaining of a nagging cough that has persisted for several months following an upper respiratory tract infection during the winter. Her cough is non-productive, worse at night-time and makes it difficult for her to remain asleep. She finds she has to prop herself up on pillows to sleep. On review of systems, she notes that she has occasional chest tightness and dyspnea on exertion. Her medical history includes obesity, diabetes and hypertension. Her medications include metformin, metoprolol, lisinopril, aspirin, atorvastatin as well as frequent maalox. She has no drug allergies. She also smokes one pack a day of cigarettes. What aspects of her history could suggest a cause for her cough? What other questions or exam information could help narrow the differential?

You obtain office spiromety which shows a FEV_1 of 2.2L 78% predicted, FVC 2.6L 73% predicted, and FEV_1/FVC ratio of 85%; There is no improvement in the FEV_1 or FVC with bronchodilator administration. How do you interpret these results?

You treat her with a proton-pump inhibitor, stop her lisinopril, but her cough does not improve. Although her reflux has improved, she is still coughing every day and is unable to sleep at night when you see her for follow-up two weeks later. You obtain full PFTs: her FEV_1 and FVC are as above, her TLC is 72% predicted, FRC of 70%, RV of 84% and DLCO is 54% predicted. You also obtain a CXR which is shown below.

What does your work-up suggest?

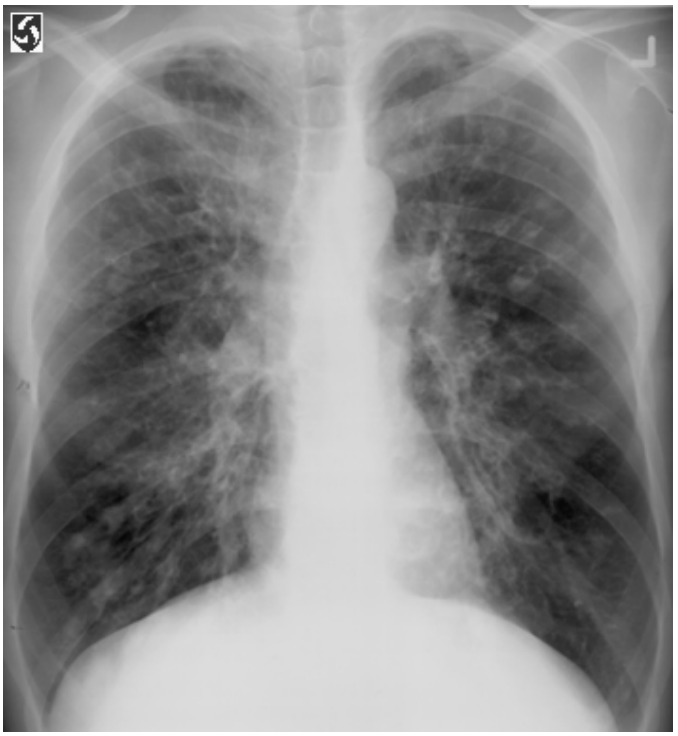
What further diagnostic and management steps should you take at this point?

Case 3:

A 26 year-old man presents to your office with persistent productive cough over the past several years. He states that every day he coughs up large amounts of thick, yellow sputum, perhaps as much as one-third to one-half of a cup daily, with occasional blood-tinging. He also notes some dyspnea on exertion as he gets short of breath with walking up hills. He is no longer able to play basketball due to severe dyspnea. When you review his past medical history, he states that he had frequent severe respiratory infections as a child and was even hospitalized on one occasion for pneumonia. On exam, he is a thin man with clubbing of his fingers. His lung exam is notable for bronchiolar breath sounds and occasional wheezing. What are the potential etiologies for his symptoms?

You obtain a full set of PFTs which reveal: FEV_1 of 2.2 L (42% predicted), FVC of 3.8L (65% predicted), FEV_1/ FVC ratio of 58%, TLC of 5.3L (87% predicted), RV of 2.1L (112%) and DLCO of 64% predicted. How would you interpret these PFT results?

You also get a chest X-ray.



What is the differential diagnosis for the observed findings on the CXR**?**

What further diagnostic testing should you do at this point?

What are the most likely pathogens in his sputum?

What treatment regimen should you start at this time?

Case 4:

A 58 year-old man who immigrated from Cambodia presents to the emergency room with a three day history of hemoptysis. He reports having a bad cough for the past week. Initially, the cough was productive of greenish-yellow sputum but a few days ago he noticed some blood tinging. Today, however, he has been coughing up large amount of frank blood clots, perhaps as much as one coffee cup-full. On review of systems, he reports some fevers, sweats and weight loss in the past few months. He has smoked 2 packs of cigarettes a day for the past 25 years.

What is the differential diagnosis for his hemoptysis?

What are your immediate diagnostic and management priorities as you are seeing him in the emergency room?

His ABG is pH 7.49, PCO_2 28, PO_2 54 on room air. You obtain a chest x-ray, which is shown below.

Does the imaging reveal any clues as to the cause of his hemoptysis**?**

As you are planning these tests he proceeds to cough up another cup of fresh blood and desaturates to 82% on high flow oxygen.

How should you proceed now?

Case 5:

A 72 year-old man with a 70 pack-year history of smoking and a long-standing history of a chronic productive cough presents to the VA urgent care clinic complaining of a two week history of blood tinged sputum. The blood tinging is present primarily in the mornings and is increased after severe coughing spells. His wife made him come in after it seemed as if he was coughing up more blood than normal today. He denies weight loss or fevers but states he has dyspnea on exertion that is unchanged from baseline. He takes aspirin daily and is no longer actively smoking.

What is the differential diagnosis for his hemoptysis?

His PFTs done 3 years ago show: FEV1 1.32L (56% predicted), FVC 2.42 L (61% predicted), FEV1/FVC ratio of 54%. TLC of 132%, RV of 158% and DLCO of 61% predicted. How would you interpret his PFTs**?**

His chest x-ray is shown below.

Does this film reveal any clues to the etiology of his hemoptysis?

You perform some initial laboratory studies in urgent care. His ABG shows: pH 7.36, PCO_2 48, PO_2 66 His Hct is 42%, platelets 341, and INR of 1.2. What further diagnostic and management steps should you pursue at this time?

Suppose the patient was 30 years old and was a non-smoker, how might that change your diagnostic and management approach?

6. Practical skills

- Interview (collection) complaints, all histories (present, past), inspectation and physical examination of the patient (revealing of abnormalities in organs and systems).
- To analyze and interpret results of the patient examination, data of chest X-ray, laboratory & instrument investigation.
- Defense of clinical point of view on diagnosis, prescribe adequate chemotherapy, detection of life prognosis and recovery.

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Prepared methodical recommendations associate Professor of HEI Oksana Litvinyuk MD, PhD