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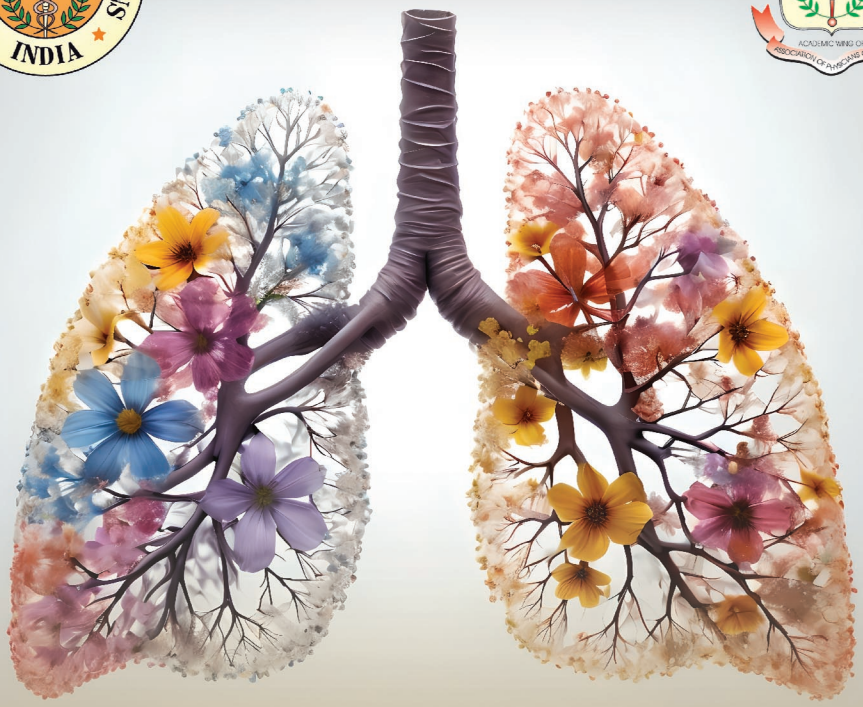

Clinical Methods in Respiratory Medicine

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CHAPTER

Clinical Approach and Analysis of Respiratory Symptoms

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A. CLINICAL APPROACH TO COUGH AND EXPECTORATION

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INTRODUCTION

Globally, cough is the most common reason for patients seeking medical attention. It is also one of the mechanisms by which infections can spread as droplets and most importantly it is one of many defense mechanisms that help clear excessive secretions and foreign material from the airways. Excessive cough is often a manifestation of various pulmonary and nonpulmonary diseases.

Estimates of prevalence of cough are scanty in our country. A population-based survey in rural India reports a prevalence of 3% among patients seeking medical care. Questionnaire-based estimates from the United States and Europe are between 9 and 33%. Cough, when chronic, can have serious impacts on various aspects of the patient's life. There can be problems with sleep, voice quality, musculoskeletal pain, and even rib fractures. Chronic cough can result in social problems such as relationship difficulties, decreased social interaction, and work-related problems, affecting physical, mental, and social health and even avoidance of public areas. Some patients, especially elderly women, also experience cough-related urinary incontinence with a dramatic impact on quality of life (QoL).

Cough is a reflex, and understanding its mechanism is of paramount importance in planning management and in future research. This chapter will discuss the main causes and outline a simple clinical approach to chronic cough.

WHAT ARE THE CAUSES OF COUGH?

Cough is commonly classified according to its duration as acute, subacute (lasting 3–5 weeks), and chronic (lasting more than 8 weeks). Such a classification is useful in framing the differential diagnoses and planning further management **(Table 4A.1)**.

The main concern in the management of acute cough is early recognition of life-threatening conditions which may be present such as pneumonia, severe exacerbations of preexisting lung diseases such as asthma and chronic obstructive pulmonary disease (COPD), pulmonary edema, and pulmonary embolism.

In cases of subacute onset cough, the most important task is to recognize the etiology as being infectious. When due to a noninfectious etiology, the approach is similar to chronic cough.

Chronic cough is a challenge to clinicians. Often cough is the only symptom in the absence of other clinical pointers to a specific disease.

In nonsmoker patients with chronic cough, normal chest radiology who are not in therapy with an angiotensin-converting enzyme (ACE) inhibitor, the most common causes are upper airway cough syndrome (UACS) (formerly called a postnasal drip syndrome), cough

Table 4A.1: Common causes of cough according to duration.

Common causes	Less common causes
Acute cough (<3 weeks)	
Upper respiratory infections (sinusitis)	Acute exacerbations of underlying pulmonary diseases (COPD, ILD, asthma, and bronchiectasis)
Allergic rhinitis	Heart failure
Pneumonia	Acute exposure to noxious gases (occupational or environmental)
Subacute cough (3–8 weeks)	
Upper respiratory infections	Chronic heart failure
Acute exacerbations of underlying pulmonary diseases (COPD, ILD, asthma, and bronchiectasis)	Postviral infection
Chronic cough (>8 weeks)	
Upper airway cough syndrome	Connective tissue diseases (rheumatoid arthritis, scleroderma, SLE, Wegener's granulomatosis, and Sjögren's syndrome)
Obstructive airway diseases (asthma, COPD, bronchiectasis, cystic fibrosis, ILD, and bronchiectasis)	Inflammatory bowel disease
Gastroesophageal reflux	Tracheobronchomegaly
Nonasthmatic eosinophilic bronchitis	Foreign bodies (includes airway stents)
Lung cancer	Broncholithiasis
Sarcoidosis	Tracheoesophageal fistula
Indolent infections (tuberculosis and endemic fungi)	Psychogenic or habit cough

(COPD: chronic obstructive pulmonary disease; ILD: interstitial lung diseases; SLE: systemic lupus erythematosus)

variant asthma, nonasthmatic eosinophilic bronchitis (NAEB), or gastroesophageal reflux disease (GERD), alone or in combination. In fact, chronic cough may be simultaneously caused by more than one condition (19–62% of cases). However, despite comprehensive evaluation and treatment, up to 20% of patients with cough continue to remain symptomatic.

History and Clinical Examination

The current diagnostic protocols for chronic cough are based on the work of Irwin and colleagues first reported over 20 years ago. The first step is gathering a detailed medical history.

The importance of medical history in chronic cough is limited to seeking information on ACE inhibitor intake, smoking (past or current), having pets or birds at home or work, resident of a geographic area where tuberculosis or certain fungal diseases are endemic, previous history of cancer, tuberculosis, or acquired immunodeficiency syndrome (AIDS), or any current symptoms of fever, sweats, or weight loss.

Other important symptoms that may be useful in narrowing down the differential diagnoses are history of episodic wheezes, chest tightness, and shortness of breath suggestive of airway diseases or UACS.

Surprisingly, medical history in cough evaluation has been held to be of little value as regards the patient's description of his or her cough (i.e., character, timing, and aggravating factors), or the presence or absence of sputum production. None of these characteristics are of diagnostic value in terms of a specific etiology. Even when significant bronchorrhea is present, a nonsmoker patient with cough who is not on ACE inhibitors and has a normal chest roentgenogram will usually have UACS, asthma, GERD, or some combination of these diagnoses. In fact, clinical practice guidelines for patients with chronic cough suggest that neither the patient's description of his or her cough in terms of its character or timing, nor the presence or absence of sputum production, should be used to rule in or rule out a diagnosis or to determine the clinical approach. However, the presence of hemoptysis is a red flag sign for urgent evaluation.

Clinical examination is nonspecific for any specific etiology of cough. However, ear, nose, and throat (ENT) examination for ruling in a diagnosis of sinusitis or UACS must not be forgotten. The presence of wheeze on chest auscultation directs further diagnostic tests and empiric treatment. Most commonly, however, clinical examination is entirely normal.

Investigations

Radiology: A chest radiograph is the most important investigation for chronic cough patients. If abnormal and consistent with an etiology capable of causing cough, further tests are directed at diagnosing the specific etiology. But more than often chronic cough patients have normal chest X-rays.

There is no role for high-resolution CT (HRCT) scan in routine investigation of chronic cough. Its only role is to identify parenchymal or interstitial lung diseases, which are not apparent on simple chest roentgen. When used routinely, bronchiectasis can be identified in nearly a quarter of cases. Targeted use of HRCT in patients with chest radiographic abnormalities and/or clinical findings on chest examination has a diagnostic yield of only 17%.

The exact role and timing of sinus imaging in patients with chronic cough have yet to be established. Intuitively, it should follow ear, nose, and throat inspection to confirm or identify abnormalities not appreciated on examination. Plain sinus radiographs are considered to be of little value in the evaluation of chronic cough. This stems from the results of a prospective study where abnormalities of the plain sinus radiograph were identified in only 29% of patients, while in another prospective evaluation routine CT sinus imaging was no better than a good clinical examination. Thus, sinus CT scanning should be reserved for refractory cases, which may require surgical intervention.

Spirometry, bronchoprovocation test, and peak expiratory flow (PEF) measurements: Asthma is one such cause of chronic cough which can easily be diagnosed by spirometry even in busy clinics. When available, it should be performed with reversibility testing in all patients with chronic cough. Baseline spirometry results are likely to be normal in patients with cough variant asthma. This is when a bronchoprovocation test is required to demonstrate variable airflow obstruction.

Bronchoprovocation tests or bronchial challenge tests can provide useful information in patients with chronic cough. This test can be done either with agents working directly on airway musculature (histamine and methacholine) or by indirect methods (hypertonic saline, exercise, mannitol, and adenosine), where bronchoconstriction is stimulated by mediators released from inflammatory cells.

Bronchial hyperreactivity or a positive bronchoprovocation test in a patient with cough and normal spirometry helps in the diagnosis of asthma (cough variant asthma) by demonstrating variable airflow obstruction. Airway hyperreactivity may develop during or following an acute viral respiratory illness and may persist for some months afterward. A positive challenge test in such circumstances may be diagnostically misleading. A negative bronchial challenge test effectively excludes the diagnosis of asthma but does not eliminate a cough that may respond to steroid treatment. In fact, a negative bronchial challenge should prompt the clinician to look for evidence of underlying uncontrolled airway inflammation.

Sometimes, PEF measurement in patients with persistent cough presenting helps in diagnosing airflow obstruction, especially if spirometry is not available. Otherwise, the use of PEF measurements to assess bronchodilator response appears to have limitations compared to conventional methods. The value of serial PEF measurements for determining diurnal variability has not been properly assessed and is infrequently requested by specialist cough clinics.

Measuring airway inflammation: The major role of measuring airway inflammation (bronchitis) in chronic cough is to demonstrate the presence and nature of bronchitis in patients without functional or radiologic abnormalities, especially bronchial hyperreactivity associated with asthma. If the underlying inflammation is eosinophilic, the clinical condition is that of eosinophilic bronchitis without asthma. This forms almost 15% of cases of chronic cough in referral clinics and is possibly an underestimate due to nonavailability of tools for measuring airway inflammation in most centers.

The most well-described method for measuring airway inflammation is by sputum quantitative assay. The test entails selection of a small quantity of sputum from either a spontaneous or induced sample, treatment with a sputolysin (dithiothreitol) or subsequent filtering to obtain a homogeneous suspension of cells. The total cell count and viability are

determined in a hemocytometer, while differential counts are obtained from Wright stained cytospins. According to the cellular nature, inflammation can be of four main types namely: (1) Eosinophilic, (2) neutrophilic, (3) combined eosinophilic and neutrophilic, and (4) paucigranulocytic.

Exhaled breath nitric oxide (FeNO) may be a simpler and operator friendly alternative to sputum quantitative assay, but currently it is not recommended routinely in the management of chronic cough. Its disadvantages are that it cannot distinguish between eosinophilic and noneosinophilic inflammation and has a wide normal range. However, a normal FeNO level can reliably rule out uncontrolled airway inflammation. The measurement of different inflammatory substances (e.g., hydrogen peroxide) in breath condensate, although currently a research procedure, may have a place in the diagnosis of chronic cough in the future.

Fiberoptic bronchoscopy: Despite a low diagnostic yield in the routine evaluation of chronic cough, bronchoscopy has significant diagnostic potential in patients where the more common causes have been rigorously excluded. In patients with refractory cough, bronchoscopic diagnoses included broncholithiasis, tracheobronchopathia, and laryngeal dyskinesia. Aspirated foreign bodies may go unrecognized for prolonged periods of time. Fiberoptic bronchoscopy may also sometimes be used for airway sampling either by mucosal biopsy or bronchial lavage in situations where the cause of cough remains undetected despite all noninvasive work-ups.

Gastrointestinal investigations: Since the association between gastroesophageal reflux and chronic cough has long been established, an empirical trial of antireflux therapy may be the best first-line approach for patients with cough with or without symptoms of heartburn. If a therapeutic trial fails, laboratory investigations such as 24-hour esophageal pH monitoring may be required. In fact, 24-hour esophageal pH monitoring is currently the best single test to help characterize any link between gastroesophageal reflux and cough. With the availability of dual probe technology, it is now possible to detect reflux to the hypopharynx and beyond (laryngopharyngeal reflux), which, though uncommon, occurs in some patients and may be the reason for their cough.

Another important concept that has evolved when evaluating patients who continue to cough despite complete acid suppression is that of nonacid refluxate. It is estimated that up to one-third of reflux episodes in patients with GERD are nonacid, and a recent development has been the simultaneous intraesophageal impedance and pH measurement of acid and nonacid reflux events. These patients with nonacid reflux might benefit from antireflux surgery.

Psychological assessment: A diagnosis of psychogenic cough (habit cough) in adults or children ("cough tic") warrants careful exclusion of organic causes. A psychological assessment is usually reserved as a last resort and, psychotherapy has shown favorable outcomes in such situations.

CASE VIGNETTE 1

A 73-year-old smoker developed high fever for 5 days associated with cough with blood stained purulent expectorant and pain in right lower chest aggravated with cough.

a. What are the types of pneumonia?

Ans. Community-acquired pneumonia (CAP) and hospital-acquired pneumonia (HAP). Ventilator-associated pneumonia is a part of HAP. Recently added type is healthcare-associated pneumonia (HCAP).

b. What are the likely organisms in CAP?

Ans. Common organisms causing CAP are *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Klebsiella pneumoniae*, *Chlamydia pneumoniae*, *Mycoplasma pneumoniae*, *Pseudomonas aeruginosa*, *Legionella* species. *Staphylococcus* is not a usual cause of CAP. Anaerobic infection occurs in setting of aspiration.

c. What are the CURB-65 criteria?

Ans. C for level of consciousness, U means blood urea nitrogen (more than 7 mmol/L), R means respiratory rate (≥30 breaths/min), B means blood pressure (systolic ≤ 90 mm Hg and/or diastolic ≤60 mm Hg), and 65 means age ≥ 65 years. Score 0 can be treated at home, score 1 and 2 should be admitted to a hospital and score ≥ 3 needs admission to intensive care unit (ICU).

d. What are the markers of severe pneumonia?

Ans. CURB-65 score 3 or more are indicators of severe pneumonia and need treatment at ICU. Multilobar involvement, hypoxemia [oxygen saturation (SpO_2) < 90%], acidosis (pH < 7.3), confusion, respiratory rate > 30 breaths/minute, neutropenia, thrombocytopenia, hypoalbuminemia, hyponatremia, and hypoglycemia are markers of severe pneumonia.

Other markers of severe pneumonia include complications of pneumonia such as parapneumonic effusion, empyema, septicemia, multiorgan failure, associated diseases such as diabetes, renal failure, and neurological diseases.

Another scoring system is pneumonia severity index (PSI) that includes 20 variables with age, coexisting illness, and abnormal physical and laboratory findings.

e. What are the antibiotic choices for CAP?

Ans. Beta-lactam antibiotics such as amoxycillin 1 g three times a day (TID), coamoxyclav 2 g two times a day (BID), cefuroxime 500 mg BID, cepodoxim 200 mg BID, and ceftriaxone 1–2 g intravenously (IV) BID.

Macrolide such as azithromycin 500 mg daily and clarithromycin 500 mg BID. Doxycycline 100 mg BID, levofloxacin 750 mg daily (fluoroquinolone should be avoided in CAP treatment).

Usual duration of treatment is 7 days.

Q1. What is your diagnosis?

Ans. Community-acquired pneumonia.

Q2. What are the points in favor?

Ans. Points in favor are high fever, cough, purulent/rusty expectoration, pleuritic chest pain along with findings of consolidation (high temperature, use of accessory muscles, diminished movement over the particular lobe, impaired to dull percussion notes, bronchial breath

sound, increased vocal resonance, egophony and whispering pectoriloquy, and absence of mediastinal shift.

Q3. What are the physical signs of pneumonia?

Ans. High temperature, use of accessory muscles, diminished movement over the particular lobe, impaired to dull percussion note, bronchial breath sound, increased vocal resonance, egophony and whispering pectoriloquy, and absence of mediastinal shift.

Q4. What are the radiological signs of consolidation?

Ans. Homogenous opacity usually confined to a lobe with peripheral alveolar filling pattern and the presence of air bronchogram.

Q5. Is it possible to have mediastinal shift to the same side of pneumonia?

Ans. Usually, there is no mediastinum shift. Mediastinum may be shifted toward diseased side in case of associated lung volume loss due to fibrosis or collapse. Fibrosis may occur due to delayed resolution of pneumonia. Collapse may be due to postobstructive pneumonia or collapse-consolidation (middle lobe syndrome).

Q6. What are the indications for hospitalization in pneumonia?

Ans. CURB-65 score 1 or more.

Q7. What are the complications of pneumonia?

Ans. Parapneumonic effusion, empyema, delayed resolution of pneumonia, superinfection, septicemia, and septic embolism.

Q8. How will you investigate pneumonia?

Ans. Routine peripheral blood examination, blood sugar, urea, creatinine, liver function test (LFT), chest X-ray, sputum gram-stain, sputum culture and sensitivity (C/S), sputum for acid-fast bacilli (AFB)/cartridge-based nucleic acid amplification test (CBNAAT), blood C/S; computed tomography (CT) of thorax and bronchoscopy in selected case (hemoptysis, delayed resolution, and mediastinum shifted to disease side), examination of pleural fluid; and urine antigen analysis for *Legionella* infection. Other tests such as polymerase chain reaction (PCR) and serology may be required.

Q9. How to suspect development of effusion with pneumonia?

Ans. Mediastinum shift toward opposite side, dullness/stony dullness/diminished or absent breath sound, and vocal resonance.

Q10. How will you investigate pneumonia?

Ans. Already given.

Q11. What is the line of management of pneumonia?

Ans. Appropriate antibiotic and supportive treatment with paracetamol for fever/chest pain, oxygen for hypoxemia, aspiration, and examination of pleural fluid. Hospitalized patients should be treated with intravenous antibiotics. Some cases may require invasive ventilation.

CASE VIGNETTE 2

A 65-year-old man presents with insidious onset of cough with mucoid to mucopurulent expectoration and sometimes hemoptysis for many years along with a past history of tuberculosis (TB) 15 years ago.

The outline of findings in this case:
Insidious onset of cough with mucoid to mucopurulent expectoration and occasional hemoptysis for more than 5 years; flattening of left hemithorax, scoliosis with concavity toward left, dropping left shoulder, winging of left scapula, diminished movement of left hemithorax, trachea shifted toward left, apical impulse at left anterior axillary line, rib crowding in left hemithorax, and crackles scattered over left hemithorax.

Q1. What is the diagnosis?

Ans. Left lung fibrosis.

Q2. What are the types of fibrosis of the lung?

Ans. Lung parenchymal fibrosis, pleural fibrosis, pleuropulmonary fibrosis, and interstitial fibrosis.

Q3. What is "diffuse fibrosis" of the lung?

Ans. This is interstitial fibrosis usually bilateral involving mainly lower parts of the lungs. That may be idiopathic interstitial disease (ILD), also called diffuse parenchymal lung disease (DPLD), or secondary to diseases such as collagen vascular disease, occupational and drug induced.

Q4. What are the classical features of fibrosing alveolitis at the bedside?

Ans. Progressive dyspnea, dry cough, bilateral disease, diminished movement of thorax, end inspiratory crackles predominantly at lung bases.

CASE VIGNETTE 3

A 65-year-old man presents with acute onset of cough, dyspnea, and two episodes of hemoptysis in the last 1 month.

He had been a heavy smoker for the last 30 years. On examination, there was shifting of the trachea to left side, the left side of chest is flattened, drooping of the shoulder present on the left, percussion note is impaired, the breath sound is diminished and impaired resonance on left hemithorax present.

Q1. What is the diagnosis?

Ans. It is a left-sided collapse of lung.

Q2. How do you classify collapse of the lung?

Ans. Absorption collapse (due to absorption of air distal to airway obstruction such as lung cancer and foreign body); relaxation collapse (due to release of negative pleural pressure

such as pneumothorax and pleural effusion); cicatricial collapse (due to stiffening of lung due to fibrosis); microatelectasis [adhesive atelectasis due to loss of surfactant found in acute respiratory distress syndrome (ARDS)].

Q3. What are the common causes of absorption collapse in relation to age?

Ans. In children—foreign body inhalation, and in elderly persons—bronchogenic carcinoma are the most important causes. Other causes include extraluminal obstruction as a result of compression by lymph nodes usually occurs in children; intraluminal disease such as malignant and benign diseases arising from the bronchus such as carcinoma (CA) or adenoma; and intraluminal obstruction due to foreign-body, blood clot, mucus clot, etc.

Q4. What is "middle lobe syndrome"?

Ans. Collapse consolidation of middle lobe without intraluminal obstruction.

Q5. What are the clinical features of bronchiectasis?

Ans. Cough with profuse mucoid/mucopurulent expectoration that will be separated into three layers while kept in a test tube and hemoptysis. There may be weight loss or failure to thrive, clubbing, and course/lathery biphasic crackles.

Q6. What are the clinical features of pulmonary tuberculosis (postprimary)?

Ans. Cough for more than 2 weeks, unexplained fever for more than 2 weeks, significant weight loss or no weight gain in children, hemoptysis, and abnormal chest X-ray. Signs are usually nonspecific or due to complications. Sign may be absent.

Q7. What are the clinical stigmata of evidence of past or present tuberculous infections?

Ans. The word stigmata should not be used with TB as this can lead to serious socioeconomic consequences and as a result increase the delay in contacting healthcare professional.

Q8. What are the effects of asbestos exposure in respiratory system?

Ans. Pleural plaque, benign pleural effusion, malignant pleural effusion, interstitial lung disease, bronchogenic carcinoma, and mesothelioma.

Q9. What is "pack year"?

Ans. The number of cigarette packets (20/pack) multiplied by years of smoking. If a patient smokes 10 cigarettes/day for 10 years then pack year will be $10/20 \times 10 = 5$.

Q10. What is the position of mediastinum in collapse of the lung?

Ans. Mediastinum will be shifted toward diseased side in whole lung collapse; trachea will be shifted in upper lobe collapse; whereas, heart will be shifted in lower lobe collapse.

Q11. What are the bronchopulmonary segments in the lung?

Ans. Collapse of bronchopulmonary segment is unlikely as there are communications among segments. There are 18–20 bronchopulmonary segments. In right side, upper lobe—apical, posterior and anterior; middle lobe—medial and lateral; lower lobe—apical and medial, anterior, lateral, posterior basal segments. In left side, upper lobe—apical and

posterior (or apicoposterior segment), anterior, superior, and inferior lingular; lower lobe—medial segment may be absent.

Q12. What investigations would you like to perform (fibrosis or collapse)?

Ans. Chest X-ray, HRCT thorax in fibrosis/contrast-enhanced computed tomography (CECT) in collapse; sputum for AFB, CBNAAT, and malignant cell; fiberoptic bronchoscopy (FOB) in selected cases; apart from routine blood examination and blood biochemistry.

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B. CLINICAL APPROACH TO HEMOPTYSIS

Surya Kant, Nandini Chatterjee

INTRODUCTION

Hemoptysis is the expectoration of blood that originates from the lower respiratory tract. Bleeding from the upper airways is excluded from this definition.

Pseudohemoptysis occurs due to infections with *Serratia marcescens*, which produces a red pigment. So, there is red expectoration, but there are no red blood cells (RBCs) in the sputum.

False hemoptysis/spurious hemoptysis is bleeding from the upper aerodigestive tract (gums, nose, or pharynx).

Hemoptysis is usually a self-limiting event, but in fewer than 5% of cases, it may be massive. Hemoptysis is mainly classified by the amount of blood expectorated into mild, moderate, and massive. Massive hemoptysis is either more than and equal to 500 mL of expectorated blood over a 24-hour period or bleeding at a rate more than and equal to 100 mL/h. A large volume of expectorated blood alone should not define massive hemoptysis, rather an amount of blood sufficient to threaten the patient's life can be a more correct and functional definition of severe hemoptysis. Massive hemoptysis is usually a life-threatening condition with mortality rate of more than 50%. Flooding of the airways with blood leads to asphyxiation, and this is usually the cause of death rather than exsanguination.

ETIOLOGY

Two arterial vascular systems supply blood to the lungs: (1) The pulmonary arteries and (2) the bronchial arteries. The pulmonary arteries provide 99% of the arterial blood to the lungs and are involved in gas exchange. The bronchial arteries supply nourishment to the extra- and intrapulmonary airways. The bronchial arteries are direct branches of the aorta; hence, blood flow is at systemic pressure, while pulmonary arteries have one-third systemic pressure. In cases of severe hemoptysis, the source of bleeding usually originates from bronchial vessels (in 90% cases) and pulmonary arteries in 5% cases.

Table 4B.1 shows the differentiation of hemoptysis from hematemesis. **Box 4B.1** shows the common causes that are to be searched for in a case of hemoptysis.

APPROACH TO PATIENT

History

The history should be directed toward the cause that is relevant to the setting as treatment is mainly treating the primary cause. The color, amount of blood, and associated symptoms should be asked to determine the cause of hemoptysis and to differentiate from upper gastrointestinal (GI) bleed or bleeding from nasal tract. Old age and smoking should warrant search for malignancy. Constitutional symptoms such as fever, fatigue, malaise,

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