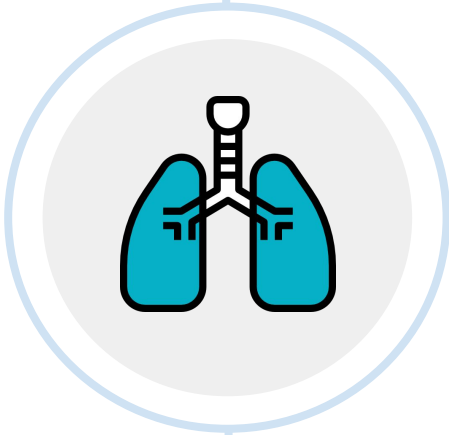




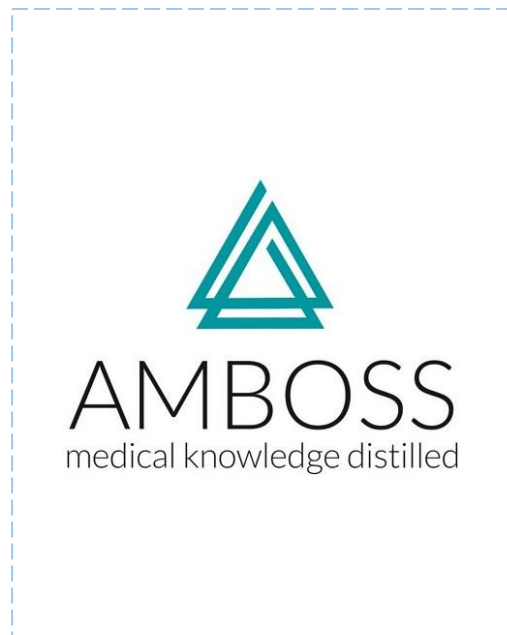
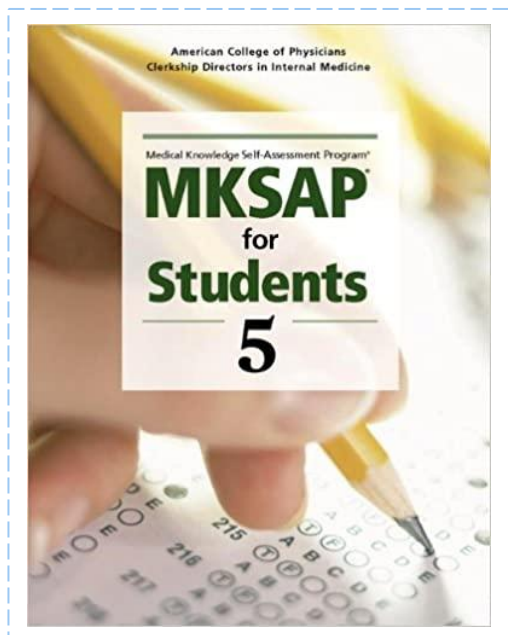
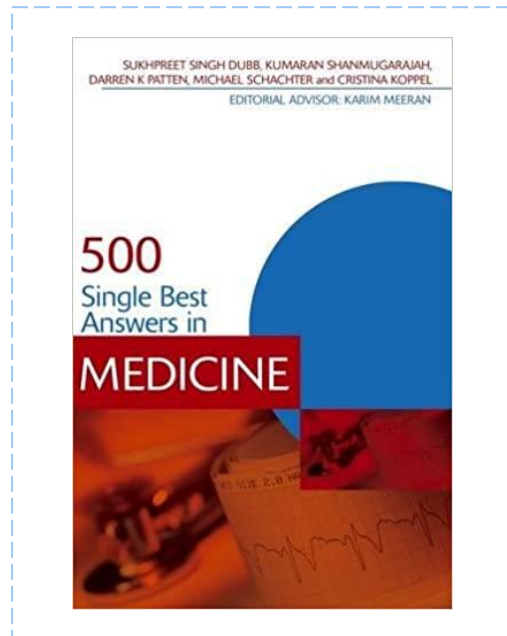
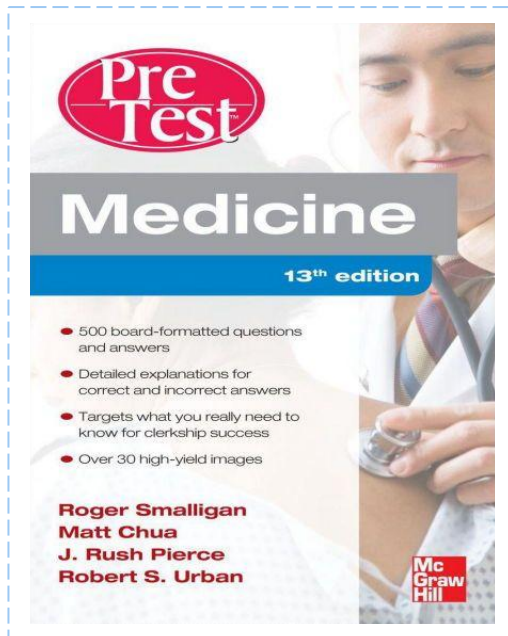
Practice file



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Resources



Asthma

Q1: A 28-year-old man has been newly diagnosed with asthma. He has never been admitted to hospital with an asthma exacerbation and experiences symptoms once or twice a week. You discuss the treatment options with him. His peak expiratory flow reading is currently 85 per cent of the normal predicted value expected for his age and height. Which of the following is the most appropriate first step in treatment?

- A. Short-acting beta-2 agonist inhaler
- B. Long-acting beta-2 agonist inhaler
- C. Low-dose steroid inhaler
- D. Leukotriene receptor antagonists
- E. High-dose steroid inhaler

Explanation: The British Thoracic Society has introduced a five step approach in the management of chronic asthma (2008 guidelines). Step 1: The use of short-acting beta-2 agonists in mild intermittent asthma. Step 2: If the patient is using beta-2 agonists three times a week or more or is symptomatic or has required oral corticosteroids in the last two years, then regular preventer therapy is required with an inhaled steroid (C) (e.g. 400 µg beclomethasone inhaler twice a day). The dose of steroid inhaler should be titrated according to disease severity. Step 3: Add-on therapy is usually instituted if the patient is symptomatic despite being on steroid inhalers. Long-acting beta-2 agonists (B) (e.g. salmeterol) can be used and the dose of steroid inhaler can be increased (E) if there is still poor asthma control. Step 4: If control remains inadequate despite additions used in step 3, the use of leukotriene receptor antagonists (D) (e.g. montelukast), theophyllines or slow release beta-2 agonist tablets is advised. Step 5: If control remains poor, then the addition of oral low dose steroids can be used.

Q2: A 33-year-old woman is evaluated in the emergency department for a 6-hour history of worsening asthma symptoms. Her medications include albuterol and an inhaled corticosteroid. She is treated with intravenous corticosteroids and albuterol. After 4 hours of treatment, she remains symptomatic and can speak only one to two words between breaths. On physical examination, she appears uncomfortable and tired. Temperature is 36.8°C (98.2°F), blood pressure is 150/90 mm Hg, heart rate is 124/min, and respiration rate is 32/min. Oxygen saturation by pulse oximetry is 92% with oxygen 2 L/min by nasal cannula. Lung examination reveals poor air movement and diffuse expiratory wheezes. Results of arterial blood gas studies: pH, 7.2; PCO₂, 45 mm Hg (6.0 kPa); PO₂, 70 mm Hg (9.3 kPa). Peak flow is 30% of best performance. Which of the following the most appropriate management for this patient?

- A. Admission to the hospital ward
- B. Intubation and mechanical ventilation
- C. Continued therapy in the emergency department
- D. Discharge home

Explanation: The most appropriate management for this patient is intubation and mechanical ventilation and admission to the intensive care unit. The cause of acute ventilatory failure in patients with exacerbations of asthma is increased airway resistance and also dynamic hyperinflation that reduces chest-wall compliance. Both contribute to excessive work of breathing. Bronchospasm, airway edema, and secretions, as well as excessive expiratory airway collapse, can severely reduce airway diameter, resulting in markedly prolonged expiration. Increased respiratory drive and high metabolic demands increase minute ventilation, and expiration between breaths is incomplete. Progressive stacking of breaths leads to an equilibration at a higher lung volume with higher positive end-expiratory alveolar pressure (auto-PEEP or intrinsic PEEP), associated with dynamic air trapping and hyperinflation. The associated flattening of the diaphragm decreases its function and forces greater reliance on accessory muscles, further increasing carbon dioxide production and oxygen consumption as a result of the inefficiency of these muscles compared with a properly functioning diaphragm. Severe air trapping can also cause alveolar rupture and marked reductions in venous return to the right heart, resulting in pneumothorax and hypotension, respectively. Typically, patients with an asthma exacerbation initially present with respiratory alkalosis. Slightly elevated or even normal PaCO₂ levels often indicate impending respiratory failure rather than recovery, and clinical correlation is critical for interpreting arterial blood gas findings in this setting. Additional features that suggest respiratory failure in this patient include pulse oximetry less than 95%, PO₂ less than 75 mm Hg (10.0 kPa), respiration rate greater than 30/min, and heart rate greater than 120/min.

Asthma

Q3: A 40-year-old woman is evaluated for worsening asthma symptoms after resolution of an acute respiratory tract infection that was treated with supportive measures. The patient has a 15-year history of asthma that has been well controlled on moderate-dose inhaled corticosteroids plus as-needed inhaled albuterol. Since her respiratory tract infection 10 days ago, her asthma symptoms have worsened; she has had frequent nighttime episodes of wheezing and has used her albuterol inhaler six to eight times a day. On physical examination, the patient is afebrile and has no chest pain or significant sputum production. Her peak flow is more than 40% below her baseline value. Which of the following is the most appropriate management for this patient?

- A. 7-Day course of a fluoroquinolone
- B. Leukotriene-modifying agent
- C. Long-acting β -agonist
- D. Nebulized albuterol at home
- E. Short course of an oral corticosteroid

Explanation: The most appropriate management for this patient is a short course of oral corticosteroids. This patient with previously well-controlled asthma has had "loss of control" after a respiratory tract infection. A short course of an oral corticosteroid (for example, prednisone, 0.5 mg/kg daily, for 5 to 7 days) can resolve the asthma symptoms and enable the patient to regain control of her disease. It is unclear whether doubling (or even quadrupling) the dose of inhaled corticosteroids is an effective strategy in place of oral corticosteroids. Antibiotics are generally not recommended for acute respiratory infections in asthma because most of these infections are viral and the routine use of antibiotics in patients with an asthma exacerbation is not recommended. Nebulized therapy at home should be reserved for patients who cannot use a metered-dose inhaler appropriately. Although nebulized bronchodilator therapy can be more effective in reversing bronchoconstriction than metered-dose inhaled bronchodilators, nebulized therapy should not be used as a substitute for oral corticosteroid therapy in patients with asthma exacerbations. Adding a leukotriene-modifying agent can be considered in patients who cannot or will not take oral corticosteroids; however, leukotriene receptor antagonists are less potent anti-inflammatory agents than corticosteroids and are not effective in patients with significant exacerbations. Adding a long-acting β -agonist would be reasonable in this patient if her symptoms persist after the oral corticosteroid therapy, but the persistence and severity of the patient's current symptoms suggest that there is ongoing airway inflammation and that a systemic corticosteroid is warranted.

Q4: A 75-year-old woman with long-standing asthma is evaluated for a 1-month history of nocturnal asthma symptoms at least weekly and the need to use an albuterol inhaler daily. Her asthma therapy is a moderate-dose inhaled corticosteroid. The patient is otherwise healthy. On physical examination, she has occasional wheezing, but the rest of the examination is unremarkable. On office spirometry, the FEV1 is 70% of predicted and FVC is 85% of predicted. Which of the following is the most appropriate management?

- A. Adding a leukotriene-modifying agent
- B. Adding a long-acting anticholinergic agent
- C. Adding a long-acting β -agonist
- D. Adding theophylline
- E. Doubling the corticosteroid dose

Explanation: The most appropriate management for this patient is the addition of a long-acting β -agonist. She has persistent asthma, which is defined as asthma symptoms occurring 2 or more days per week or 2 or more nights per month. Patients with persistent asthma should be treated with daily inhaled corticosteroid therapy. When asthma is not adequately controlled on low- or moderate-dose inhaled corticosteroid therapy, adding a long-acting β -agonist (salmeterol or formoterol) has been shown to be superior to doubling the dose of the corticosteroid for improving asthma control and quality of life. The concerns about increased asthma-related deaths in patients using a long-acting β -agonist led the U.S. Food and Drug Administration to include a black box warning in the package insert for these drugs. The National Asthma Education and Prevention Program expert panel guidelines in 2007 affirmed the recommendation of adding a long-acting β -agonist in patients whose disease is not controlled with an inhaled corticosteroid but advised against using a long-acting β -agonist as a single controller therapy. Theophylline and leukotriene-modifying drugs are third-line agents that should be considered in patients who remain symptomatic despite the addition of a long-acting β -agonist to the corticosteroid therapy. Long-acting anticholinergic drugs are beneficial in patients with chronic obstructive pulmonary disease; however, their role in management of asthma is not defined.

Asthma

Q5: A 37-year-old man with asthma is evaluated for frequent episodes of wheezing and dyspnea unrelieved by short-acting β -agonist therapy. He uses his controller medications regularly, including an inhaled long-acting β -agonist and inhaled high-dose corticosteroids. He has symptoms daily and frequent nocturnal symptoms. On physical examination, the patient is in mild respiratory distress. The temperature is 37.0°C (98.6°F), blood pressure is 140/85 mm Hg, pulse rate is 90/min, and respiration rate is 18/min. He has bilateral wheezing. Spirometry shows an FEV1 of 65% of predicted. After the supervised use of a bronchodilator in the office, there was relief of symptoms, and repeat spirometry 10 minutes after the administration of the bronchodilator showed that the FEV1 increased to 85% of predicted. Which of the following is the most appropriate next step in this patient's management?

- A. Add a leukotriene-modifying drug
- B. Have the patient demonstrate his inhaler technique
- C. Have the patient keep a symptom and treatment log
- D. Start oral prednisone therapy

Explanation: The best initial management approach for this patient is to have him demonstrate his inhaler technique. Patient education is a key component in asthma care. Studies have shown that patient education by the physician decreases the number of visits to the emergency department and improves asthma control. Improper technique in the use of inhalers is a major reason that patients do not respond well to medications. A clue suggesting poor inhaler technique is the patient's rapid improvement in FEV1 after the supervised use of a bronchodilator. Although there used to be one type of inhalation device (the metered-dose inhaler) with one technique that could be taught to the patient, there are now several new and different devices with significant differences in the technique needed for their use. Physicians should learn the proper technique for use of these inhalers before prescribing them to patients in order to ensure proper technique to optimize drug delivery and effectiveness and to reduce side effects.

Adding a leukotriene-modifying agent would be appropriate if the patient is effectively using the current medications. Oral prednisone would be appropriate for an exacerbation of poorly controlled severe persistent asthma. It would improve asthma control, but without proper education in the use of the inhaler, symptoms would most likely return when the corticosteroid dosage is tapered. Furthermore, oral corticosteroids have increased adverse effects. Simply having the patient return with a symptom and treatment log would not be expected to identify poor inhaler technique, although it would be helpful to assess compliance and symptom pattern.

Q6: A 25-year-old woman is admitted to accident and emergency with a severe exacerbation of asthma. On examination, her respiratory rate is 30, oxygen saturations are 95 per cent on 15 L O2 and temperature is 37.2°C. As you feel the peripheral pulse, the volume falls as the patient inspires. Which of the following explains this clinical sign?

- A. Increased left atrial filling pressures on inspiration
- B. Decreased right ventricular filling pressures on inspiration
- C. Peripheral vasodilation
- D. Decreased right atrial filling pressures on inspiration
- E. Decreased left atrial filling pressures on inspiration

Explanation: As the patient inspires, at high respiratory rates, with air flow compromise due to the narrowing of airways that occurs in acute asthma exacerbations, this results in a sudden increase in negative intrathoracic pressure which causes dilatation of the pulmonary vasculature. This effect causes pooling of blood in the lungs which results in diminished pulmonary venous return to the left atrium (decreased left atrial filling (E)), hence reducing stroke volume, causing the blood pressure to drop and hence the volume of the pulse thus falls in response. In addition, an increase in negative intrathoracic pressure also causes increased venous return to the right atrium which leads to expansion of the right side of the heart resulting in compromised filling of the left side of the heart.

Q7: A 68-year-old woman with a prior diagnosis of asthma presents to your clinic for a routine clinic visit. She complains of occasional palpitations and tremor. Her dyspnea is well controlled. Her past medical history is remarkable for hospitalization for mild congestive heart failure 2 months ago; she notes occasional postprandial acid reflux. Her medications include lisinopril, digoxin, furosemide, an intermittent short-acting inhaled beta agonist, and theophylline. She uses an over-the-counter pill (whose name she cannot remember) for the reflux symptoms. On examination her heart rate is 112 beats/minute. S1 and S2 are normal; she has a mild tremor of the outstretched hands. What is the best next step in her management?

- A. Chest x-ray to rule out exacerbation of congestive heart failure
- B. Theophylline level
- C. Spirometry before and after bronchodilator
- D. Intermittent lorazepam 0.5 mg po tid
- E. Discontinue beta agonist and substitute inhaled ipratropium

Explanation: Theophylline has been used as a bronchodilator for a number of years. It has been less commonly used in recent years owing to its narrow therapeutic window. The drug is metabolized in the liver. A drug or process that interferes with the activity of the cytochrome P450 system will slow the metabolism of theophylline and may lead to the accumulation of toxic levels in the blood. The metabolism of theophylline is slowed by age, infection, CHF (resulting from decreased hepatic blood flow), and a number of drugs. Commonly used drugs that impair the metabolism of theophylline include cimetidine, erythromycin, ciprofloxacin, allopurinol, and zafirlukast. This patient has probably been using over-the-counter cimetidine to treat her reflux symptoms. Stopping theophylline until the drug level has returned will relieve her palpitations and tremor. In the absence of dyspnea, wheezing, or clinical signs of CHF, chest film and spirometry would not be helpful. Using a benzodiazepine to treat her tremor would leave a potentially serious theophylline toxicity undetected. Finally beta agonists are more effective bronchodilators in asthma than is ipratropium; the tremulousness associated with beta agonist use is usually short lived.

Asthma

Q8: A 67-year-old man is brought to the emergency department because of increasing shortness of breath that began while playing outdoors with his grandson. He has a history of asthma but does not take any medications for it. On arrival, he is alert and oriented. He is out of breath and unable to finish his sentences. His pulse is 130/min, respirations are 23/min and labored, and blood pressure is 110/70 mm Hg. Physical examination shows nasal flaring and sternocleidomastoid muscle use. Pulmonary examination shows poor air movement bilaterally but no wheezing. Cardiac examination shows no abnormalities. Oxygen is administered via a nonrebreather mask. He is given three albuterol nebulizer treatments, inhaled ipratropium, and intravenous methylprednisolone. The patient is confused and disoriented. Arterial blood gas analysis shows:

pH	7.34
Pco ₂	44 mm Hg
Po ₂	54 mm Hg
O ₂ saturation	87%

- A. Flexible bronchoscopy
- B. Intravenous magnesium sulfate therapy
- C. Continuous albuterol nebulizer therapy
- D. Intravenous theophylline therapy
- E. Endotracheal intubation

Explanation: This patient has a severe asthma exacerbation unresponsive to medications. His difficulties speaking, altered mental state, use of accessory respiratory muscles (indicating respiratory fatigue), and normal to high Pco₂ (≥ 42 mm Hg) are concerning for respiratory failure, for which endotracheal intubation is indicated. Patients with acute asthma exacerbation generally initially present with respiratory alkalosis (decreased Pco₂) due to tachypnea. With worsening airway obstruction and increasing respiratory fatigue, Pco₂ increases and pH decreases. The absence of wheezing also provides a clue to the severity of this patient's condition: wheezing is not heard because there is not enough air movement to generate it. He should be intubated urgently and moved to the intensive care unit.

Q9: A 20-year-old man comes to the physician because of recurrent episodes of shortness of breath and a nonproductive cough for the past 4 months. He has two episodes per week, which resolve spontaneously with rest. Twice a month, he wakes up at night with shortness of breath. His pulse is 73/min, respirations are 13/min, and blood pressure is 122/70 mm Hg. Pulse oximetry on room air shows an oxygen saturation of 98%. Physical examination shows no abnormalities. Spirometry shows an FVC of 95%, an FEV₁:FVC ratio of 0.85, and an FEV₁ of 81% of predicted. Which of the following is the most appropriate initial pharmacotherapy?

- A. Fluticasone inhaler
- B. Cromolyn sodium inhaler
- C. Mometasone inhaler and oral zafirlukast
- D. Salmeterol inhaler
- E. Albuterol inhaler

Explanation: Albuterol is an inhaled, short-acting β_2 -adrenergic agonist and is the drug of choice for acute treatment of asthma symptoms. Patients who have intermittent attacks, in which the trigger of asthmatic symptoms is known and can be predicted (e.g., exercise-induced bronchoconstriction), can also use a short-acting inhaled β_2 -agonist as a prophylactic measure ~ 10 minutes before the triggering event (e.g., exercise). According to the National Asthma Education and Prevention Program (NAEPP), the low frequency of symptom occurrence associated with intermittent asthma only requires symptomatic treatment for acute exacerbations, whereas more severe forms of asthma require a constant therapeutic regimen to prevent exacerbations. The Global Initiative for Asthma (GINA), however, differs in its recommendations for intermittent asthma: long-term management includes an inhaled corticosteroid-containing controller inhaler for every adult and adolescent with asthma, in addition to formoterol or a short-acting β_2 -agonist as needed.

Q10: A 15-year-old boy is brought to the physician because of recurrent episodes of shortness of breath, chest tightness, and nonproductive cough that first started about 4 months ago. He says these episodes usually occur during or shortly after his soccer practice and resolve spontaneously when he stops exercising. He has no shortness of breath at other times, including at night. His sister has allergic rhinitis. His pulse is 68/min, respirations are 14/min, and blood pressure is 120/75 mm Hg. Pulse oximetry on room air shows an oxygen saturation of 98%. Physical examination shows no abnormalities. Spirometry shows an FEV₁:FVC ratio of 88% and an FEV₁ of 91% of predicted. Which of the following is the most appropriate next step in diagnosis?

- A. Bronchodilator reversibility test
- B. Chest x-ray
- C. Eosinophils and total IgE concentration
- D. Methacholine challenge test
- E. Single-breath diffusing capacity

Explanation: Exercise is a trigger of bronchoconstriction, which typically occurs in individuals with underlying asthma. A methacholine challenge test is a type of bronchial provocation test used to diagnose asthma in patients with inconclusive spirometry findings. Although a methacholine challenge test is an effective way of determining both the hyperresponsiveness of airways and the reversibility of the obstruction, it should be carried out carefully because of its inherent but minimal risk of inducing a life-threatening asthma attack. An exercise challenge test is the method of choice for the definitive diagnosis of exercise-induced bronchoconstriction.

A bronchodilator reversibility test, which is performed when lung function tests show airflow obstruction (i.e., decreased FEV₁:FVC), can be a helpful step in the diagnosis of obstructive lung diseases (e.g., asthma). However, this patient's spirometry findings are normal (i.e., FEV₁:FVC 88%, FEV₁ 91% of predicted value).

Community acquired pneumonia

Q1: A 67-year-old woman is admitted to accident and emergency with pyrexia (38.1°C) and a cough productive of green sputum. The observations show a pulse rate of 101, BP 80/60 and respiratory rate of 32. She is alert and orientated in space and time. Blood results reveal a WCC of 21, urea of 8.5 and chest x-ray shows a patch of consolidation in the lower zone of the right lung. She is treated for severe community-acquired pneumonia. Which of the following is the correct calculated CURB-65 score?

- A. 6
- B. 8
- C. 4
- D. 0
- E. 1

Explanation: The CURB-65 (C – confusion, U – urea >7 mmol/L, R – respiratory rate >30, B – blood pressure of less than 90 systolic or less than 60 diastolic and 65 – age of 65 or above) criteria is a clinical prediction rule validated and recommended by the British Thoracic Society for assessing the severity of community-acquired pneumonia. The score ranges from 0 to 5 and a score of 1 or 0 can be given if each of the above risk factors are present or not, respectively. A score between 0 and 1 indicates that the patient may be treated as an outpatient. Patients with a score of 2 may be considered for a short stay in hospital with outpatient follow up. Scores between 3 and 5 indicate severe pneumonia and hospitalization with the possibility of escalation to intensive care being required. The CURB-65 criteria is regarded as a prognostic score and should not be used as a stand-alone tool for assessing the severity of pneumonia. For example, there are patients over the age of 65 who have a baseline urea of >7 mmol/L which puts the CURB-65 score at 2. Therefore the tool should be used in the context of the clinical situation, existing co-morbidities and social circumstances of the patient.

Q2: Which of the following organisms would typically be found in a patient with atypical community-acquired pneumonia?

- A. Staphylococcus aureus
- B. Pseudomonas spp.
- C. Streptococcus pneumoniae
- D. Legionella pneumophila
- E. Haemophilus influenzae

Explanation: From the list of answers above, H. influenzae (E) and S. pneumoniae (C) are organisms which are usually responsible for community-acquired pneumonia. S. aureus (A) and Pseudomonas spp. (B) are usually found in patients with hospital-acquired pneumonia. L. pneumophila (D), along with Chlamydia spp. and Mycoplasma pneumoniae, are the atypical pneumonia-causing organisms. A urinary antigen test is routinely used for the detection of Legionella spp. Serological tests can be used for the detection of Mycoplasma and Chlamydia spp. and also Legionella spp.

Q3: A 55-year-old man, who has never smoked and with no past medical history, has been diagnosed with right basal community-acquired pneumonia. There are minimal changes on his chest x-ray and bloods reveal a neutrophil count of 8.2 and a C-reactive protein (CRP) of 15. He has no drug allergies. Although he has a productive cough of green sputum, his respiratory rate is 16, oxygen saturations are 97 per cent on room air and his temperature is 37.4°C. You are asked to place him on treatment. Which of the following treatment options would be appropriate for this patient?

- A. Oral amoxicillin
- B. Oral erythromycin
- C. Intravenous ertapenem
- D. Intravenous ertapenem with a macrolide (e.g. clarithromycin)
- E. Intravenous tazocin

Explanation: From the history we can see that this patient has a CURB-65 score of 0 putting him into a good prognostic category. Second, he is normally fit and well and has no past medical history. Therefore, he is in the category of non-severe pneumonia and does not require hospitalization. Hence, oral antibiotic therapy is preferred. From the list, amoxicillin (A) would be preferred over erythromycin (B) as it covers the most common organism (S. pneumoniae) and has a broad spectrum of action while the macrolide will cover for atypical organisms (e.g. legionella, mycoplasma, etc.). In some centres, amoxicillin with a macrolide may be given if there is any reason to suspect atypical pneumonia (e.g. patient works with air conditioners, or has just come back from holiday and living in an air-conditioned room, plumber dealing with water tanks, etc.). Intravenous tazocin (E) and ertapenem (C + D) are not always used across all hospital trusts; antibiotic protocols vary and it is important to check the hospital trust policy for updated guidelines.

Community acquired pneumonia

Q4: You see a 76-year-old woman in accident and emergency who has been admitted with a 1-day history of shortness of breath and pyrexia (38.4°C). The patient's past medical history includes hypertension, stroke and insulin-dependent diabetes. She has no known drug allergies. The nursing staff report that the patient vomited after her lunchtime meal yesterday. On examination the patient's respiratory rate is 26, oxygen saturations 93 per cent on room air. On auscultation of the chest, you hear right basal crackles. You suspect that this patient is suffering from aspiration pneumonia. From the list below, which is the most appropriate antibiotic regimen for this patient?

- A. Intravenous cefuroxime and metronidazole
- B. Oral amoxicillin and metronidazole
- C. Intravenous clarithromycin
- D. Intravenous cefuroxime
- E. Oral co-amoxiclav

Explanation: It is very important to consider the use of a broad spectrum antibiotic coupled with another agent that will cover for anaerobic bacteria from the oral flora and gastric contents (e.g. *Bacteroides* spp., *Prevotella* spp., *Fusobacterium* spp., etc.). In addition, this patient is systemically unwell and the use of intravenous antibiotics would be more appropriate in the initial stages of treatment. From the list above, the use of intravenous cefuroxime and metronidazole (A) is therefore the most appropriate answer. Intravenous clarithromycin (C) treatment would be indicated if the patient had a penicillin allergy and, by itself, may not be enough to cover the range of aerobic and anaerobic bacteria. Refer to your local hospital trust for relevant antibiotic protocol prescribing, as these differ from one hospital to the next.

Q5: A 40-year-old alcoholic develops cough and fever. Chest x-ray, shown below, shows an air-fluid level in the superior segment of the right lower lobe. Which of the following is the most likely etiologic agent?

- A. *Streptococcus pneumoniae*
- B. *Haemophilus influenzae*
- C. *Legionella pneumophila*
- D. Anaerobes
- E. *Mycoplasma pneumoniae*



Explanation: The chest x-ray shows a pulmonary abscess in the right lower lobe with an air-fluid level. This is characteristic of an anaerobic infection. These are usually associated with a period of loss of consciousness and with poor oral hygiene. The location of the infiltrate suggests aspiration, also making anaerobic infection most likely. The superior segment of the right lower lobe is the segment most likely to develop aspiration pneumonia. Lung abscess indicates a necrotizing process, which is uncommon with the "typical" bacterial pathogens pneumococci and *H influenzae*, and very rare in the usually patchy "atypical" pneumonias caused by *Legionella* and *Mycoplasma*.

Q6: A 40-year-old man without a significant past medical history comes to the emergency room with a 3-day history of fever and shaking chills, and a 15-minute episode of rigor. He also reports a cough productive of yellow-green sputum, anorexia, and the development of right-sided pleuritic chest pain. Shortness of breath has been present for the past 12 hours. Chest x-ray reveals a consolidated right middle lobe infiltrate, and CBC shows an elevated neutrophil count with many band forms present. Which feature would most strongly support inpatient admission and IV antibiotic treatment for this patient?

- A. Recent exposure to a family member with influenza
- B. Respiratory rate of 36/minute
- C. Recent sexual exposure to an HIV-positive patient
- D. Purulent sputum with gram positive diplococci on Gram stain
- E. Signs of consolidation (bronchial breath sounds, egophony) on physical examination

Explanation: Because of the development of effective oral antibiotics (respiratory fluoroquinolones, extended spectrum macrolides), most patients with community-acquired pneumonia (CAP) can be managed as an outpatient as long as compliance and close followup are assured. The CURB-65 score is the most strongly validated instrument for determining if inpatient admission (either observation or full admission) is indicated. Factors predicting increased severity of infection include confusion, urea above 19mg/dL, respiratory rate above 30, BP below 90 systolic (or 60 diastolic), and age above 65. If more than one of these factors is present, hospitalization should be considered.

This patient's presentation (lobar pneumonia, pleuritic pain, purulent sputum) suggests pneumococcal pneumonia. Pneumococci are the commonest organisms isolated from patients with CAP. Fortunately, *S pneumoniae* is sensitive to oral antibiotics such as clarithromycin/azithromycin and the respiratory quinolones. A Gram stain suggestive of pneumococci would therefore only confirm the clinical diagnosis. Exposure to influenza is an important historical finding. However, without a prodrome of influenzalike illness (upper respiratory symptoms, myalgias, prostrating weakness), this is still garden variety CAP. In the setting of an influenza-like illness, *H influenzae* (easily treated with standard antibiotics) and *S aureus* pneumonia (more problematic to treat) must be considered. Acute lobar pneumonia, even in an HIV-positive patient, is due to the pneumococcus and can be treated as an outpatient. *Pneumocystis jirovecii* pneumonia is usually insidious in onset, causes diffuse parenchymal infiltrates, and does not cause pleurisy or pleural effusion. Physical examination signs of consolidation confirm the CXR finding of a lobar pneumonia (as opposed to a patchy bronchopneumonia) and would simply affirm the importance of coverage for classic bacterial pathogens (ie, pneumococci, *H flu*). Atypical pneumonias (still often pneumococcal, but sometimes due to *Mycoplasma* or *Chlamydia*) are usually patchy and also do not affect the pleura. Currently recommended treatment regimens cover both typical and atypical pathogens.

Community acquired pneumonia

Q7: An 80-year-old man is brought to the emergency department from a nursing home because of a 2-day history of increasing cough, fever, and dyspnea. He has type 2 diabetes mellitus and hypertension. Current medications include insulin and enalapril. On arrival, he has dyspnea and is disoriented to time, place, and person. His temperature is 38.1°C (100.6°F), pulse is 113/min, respirations are 35/min, and blood pressure is 78/60 mm Hg. Pulse oximetry on room air shows an oxygen saturation of 77%. Auscultation shows diffuse crackles over the right lung field. Cardiac examination shows an S4 gallop. Intravenous fluid resuscitation is begun. He is intubated, mechanically ventilated, and moved to the intensive care unit. An x-ray of the chest shows right upper and middle lobe infiltrates and an enlarged cardiac silhouette. A norepinephrine infusion is begun and the patient is administered intravenous antibiotics. Which of the following would most likely be found on Gram stain examination of this patient's sputum?

- A. Gram-negative rods
- B. Gram-positive cocci in clusters
- C. Gram-positive diplococci
- D. Gram-negative coccobacilli
- E. No findings

Explanation: Gram-positive diplococci are classic Gram stain findings for *Streptococcus pneumoniae*, which is the most common cause of pneumonia among residents of long-term care facilities. *S. pneumoniae* is also the most common cause of community-acquired pneumonia across all age groups.

Q8: A 52-year-old man is brought to the emergency department by a friend because of a 5-day history of fever and cough productive of purulent sputum. One week ago, he was woken up by an episode of heavy coughing while lying on his back. He drinks large amounts of alcohol daily and has spent most of his time in bed since his wife passed away 2 months ago. His temperature is 38°C (100.4°F), pulse is 96/min, respirations are 24/min, and blood pressure is 110/84 mm Hg. Pulse oximetry on room air shows an oxygen saturation of 87%. Physical examination shows poor dentition and swollen gums. A CT scan of the chest is most likely to show a pulmonary infiltrate in which of the following locations?

- A. Posterior basal segment of the right lower lobe
- B. Posterior basal segment of the left lower lobe
- C. Superior segment of the right lower lobe
- D. Apicoposterior segment of the left upper lobe
- E. Posterior segment of the right upper lobe

Explanation: The superior segment of the right lower lobe is the most common site of aspiration injury within the lungs. This lung segment is also most likely to be affected when aspiration occurs while in the supine position. The right main bronchus is wider and more vertical than the left and continues in a straight path after diverging from the trachea, making it more likely that aspiration injury will occur in the right lung. Injuries to the posterior segment of the right upper lobe are common when aspiration occurs in bedridden patients lying in the right lateral decubitus position. However, this patient was in the supine position when aspiration occurred.

Q9: A 68-year-old man comes to the emergency department because of a cough, dyspnea, and fever for 1 day. The cough is productive of small amounts of green phlegm. He has metastatic colon cancer and has received three cycles of chemotherapy with 5-fluorouracil, leucovorin, and oxaliplatin; his last chemotherapy session was 2.5 months ago. He has chronic obstructive pulmonary disease and has been treated with antibiotics and prednisolone for acute exacerbations three times in the past year. His medications include a fluticasone-salmeterol inhaler and a tiotropium bromide inhaler. He has smoked one pack of cigarettes daily for 48 years. His temperature is 39.1°C (103.1°F), pulse is 112/min, respirations are 32/min, and blood pressure is 88/69 mm Hg. Pulse oximetry on room air shows an oxygen saturation of 88%. Pulmonary examination shows diffuse crackles and rhonchi. An x-ray of the chest shows a left upper-lobe infiltrate of the lung. Two sets of blood cultures are obtained. Endotracheal aspirate Gram stain shows gram-negative rods. Two large bore cannulas are inserted and intravenous fluids are administered. Which of the following is the most appropriate pharmacotherapy?

- A. Ceftriaxone and azithromycin
- B. Cefepime and levofloxacin
- C. Clarithromycin and amoxicillin-clavulanate
- D. Ertapenem
- E. Vancomycin

Explanation: Cefepime and levofloxacin are the first-line treatment for patients with CAP in whom there is a high suspicion of *P. aeruginosa* infection. Other treatment options for CAP with *P. aeruginosa* include piperacillin/tazobactam, meropenem, or imipenem plus a fluoroquinolone. An aminoglycoside may be added as well.

Community acquired pneumonia

Q10: A 67-year-old woman is brought to the emergency department for the evaluation of fever, chest pain, and a cough productive of a moderate amount of greenish-yellow sputum for 2 days. During this period, she has had severe malaise, chills, and difficulty breathing. She has hypertension, hypercholesterolemia, and type 2 diabetes mellitus. She smoked one pack of cigarettes daily for 20 years, but quit 5 years ago. Current medications include simvastatin, captopril, and metformin. Temperature is 39°C (102.2°F), pulse is 110/min, respirations are 33/min, and blood pressure is 143/88 mm Hg. Pulse oximetry on room air shows an oxygen saturation of 94%. Crackles are heard on auscultation of the right upper lobe. Laboratory studies show a leukocyte count of 12,300/mm³, an erythrocyte sedimentation rate of 60 mm/h, and a urea nitrogen of 15 mg/dL. A chest x-ray is shown. Which of the following is the most appropriate next step in the management?

- A. ICU admission and administration of ceftriaxone and azithromycin
- B. ICU admission and administration of aztreonam and levofloxacin
- C. Inpatient treatment with azithromycin and cefotaxime
- D. Inpatient treatment with cefepime, azithromycin, and gentamicin
- E. Outpatient treatment with azithromycin

Explanation: Inpatient treatment with a combination of a macrolide and an anti-pneumococcal beta-lactam (e.g., azithromycin and cefotaxime) is indicated in patients with community-acquired pneumonia and a CURB-65 score ≥ 2 . Hospital admission and administration of a respiratory fluoroquinolone (e.g., levofloxacin) would also be an appropriate treatment in this case. Since this patient has no further complications or risk factors such as acute respiratory failure, septic shock, or decompensation of comorbidities, non-ICU management is possible

COPD and Bronchiectasis

Q1: You see a 46-year-old woman on your ward who has been diagnosed with bronchiectasis following a three-month history of a mucopurulent cough. Which of the following from the list below is not a cause of bronchiectasis?

- A. Kartagener's syndrome
- B. Cystic fibrosis
- C. Pneumonia
- D. Left ventricular failure
- E. Bronchogenic carcinoma

Explanation: Bronchiectasis is defined as chronic infection of the bronchi and bronchioles leading to permanent dilatation of these airways. The main organisms involved in this condition are *H. influenzae*, *S. pneumoniae*, *S. aureus* and *P. aeruginosa*. Answers A–C and E are all known causes of bronchiectasis. The causes can be divided into: (1) Congenital: cystic fibrosis, Young's syndrome, primary ciliary dyskinesia, Kartagener's syndrome; and (2) Acquired: Post-infection with measles, pertussis, bronchiolitis, pneumonia, TB and HIV. Other acquired causes include bronchial obstruction secondary to tumours or foreign bodies, allergic bronchopulmonary aspergillosis (ABPA), hypogammaglobulinaemia, rheumatoid arthritis, ulcerative colitis and idiopathic.

Q2: The severity of COPD is assessed using post bronchodilator spirometry analysis. From the list below, select the values that you would expect to see in a patient with moderate COPD.

- A. FEV1/FVC <0.7, FEV1 per cent predicted 30–49 per cent
- B. FEV1/FVC <0.7, FEV1 per cent predicted \geq 80 per cent
- C. FEV1/FVC <0.7, FEV1 per cent predicted <30 per cent
- D. FEV1/FVC <0.7, FEV1 per cent predicted 50–79 per cent
- E. FEV1/FVC <0.7, FEV1 per cent predicted 60–70 per cent

Explanation: With reference to the NICE guidelines 2010, COPD can be divided into mild, moderate, severe and very severe. The values are obtained with post bronchodilator spirometry and are as follow: Mild COPD: FEV1/FVC <0.7, FEV1 % predicted \geq 80 per cent (B) Moderate COPD: FEV1/FVC <0.7, FEV1 % predicted 50–79 per cent (D) Severe COPD: FEV1/FVC <0.7, FEV1 % predicted 30–49 per cent (A) Very severe COPD: FEV1/FVC <0.7, FEV1 % predicted <30 per cent (C) Very severe COPD can also be seen in patients with FEV1 % predicted <50 per cent with respiratory failure.

Q3: A 65-year-old man with chronic obstructive pulmonary disease is evaluated in the emergency department for a 4-day history of worsening dyspnea, cough, and increased production of purulent sputum. His albuterol inhaler has been ineffective in relieving his symptoms. On physical examination, the patient is in respiratory distress using pursed-lip breathing. Temperature is 36.7°C (98.0°F), blood pressure is 145/84 mm Hg, pulse rate is 102/min, and respiration rate is 20/min. He has audible polyphonic wheezes but no crackles. Heart sounds are distant but otherwise normal. The remainder of his physical examination is normal. Arterial blood gases performed on 2 L/min nasal cannula: pH, 7.31; PCO₂, 50 mm Hg (6.7 kPa); PO₂, 65 mm Hg (8.6 kPa). Chest radiograph displays hyperinflation but no infiltrates. Intravenous corticosteroids and inhaled albuterol are begun. Which of the following treatments should also be initiated?

- A. Amoxicillin
- B. Inhaled corticosteroids
- C. Levofloxacin
- D. Theophylline

Explanation: Levofloxacin should be initiated at this time. Oral or intravenous corticosteroids, short-acting bronchodilators (such as albuterol or ipratropium), and supplemental oxygen are the principle treatments for acute exacerbations of COPD; however, many patients will also benefit from the addition antibiotics. In select populations, antibiotics have improved several clinical outcomes, including resolution of symptoms, shorter hospital stay, and mortality. Antibiotics are recommended for patients with severe COPD exacerbations and those on mechanical ventilation. Patients with moderate to severe exacerbations characterized by increased dyspnea, increased sputum volume, increased sputum purulence, or need for hospitalization also benefit from antibiotics. The optimal antibiotic regimen for the treatment of exacerbations is based on the most commonly isolated bacterial pathogens, including *Haemophilus influenzae*, *Streptococcus pneumoniae*, and *Moraxella catarrhalis*. Generally, antibiotic regimens for community-acquired infection include coverage with a third-generation cephalosporin in combination with a macrolide or monotherapy with a fluoroquinolone. Because of the high incidence of *H. influenzae* and *M. catarrhalis* resistance, amoxicillin is no longer considered a first-line agent for patients with moderate to severe COPD exacerbations. The addition of inhaled corticosteroids would not likely add any benefit to a patient already receiving intravenous (or oral) corticosteroids. Theophylline is not recommended for the treatment of acute exacerbations of COPD because it provides no additional benefit beyond that of inhaled bronchodilators and oral or inhaled corticosteroids but is associated with significant side effects, including nausea, vomiting, palpitations, and arrhythmias.

Key Point : Recommended antibiotics for moderate to severe exacerbations of COPD include a third-generation cephalosporin combined with a macrolide or monotherapy with a fluoroquinolone.

COPD and Bronchiectasis

Q4: A 58-year-old man with chronic obstructive pulmonary disease (COPD) is evaluated for slowly progressive dyspnea beginning 6 months ago. He now has dyspnea with minimal exertion, such as walking two blocks, and he can no longer climb a flight of stairs. He has a 42-pack-year smoking history, quitting 2 years ago. His medications are albuterol and tiotropium inhalers. On physical examination, temperature is 36.6°C (97.8°F), blood pressure is 140/86 mm Hg, pulse rate is 90/min, and respiration rate is 16/min. Oxygen saturation by pulse oximetry is 87% on ambient air. Breath sounds are decreased, but no audible wheezes are present. Arterial blood gas analysis, on ambient air, reveals: pH, 7.38; PO₂, 54 mm Hg (7.2 kPa); PCO₂, 45 mm Hg (6.0 kPa). Chest radiograph shows hyperinflation. Spirometry shows an FEV₁ of 30% of predicted and an FEV₁/FVC ratio of 50%. Which of the following interventions is most likely to improve this patient's survival?

- A. Continuous oxygen therapy
- B. Inhaled corticosteroid
- C. Inhaled salmeterol
- D. Theophylline

Explanation: The use of long-term oxygen therapy in patients with chronic respiratory failure improves survival and has a beneficial effect on hemodynamics, exercise capacity, and mental status. Oxygen is usually prescribed for patients who have arterial PO₂ less than 55 mm Hg (7.3 kPa) or oxygen saturation less than 88% with or without hypercapnia or who exhibit arterial PO₂ of 56 to 59 mm Hg (7.4 to 7.8 kPa) or oxygen saturation less than 89% with one or more of the following: pulmonary hypertension, evidence of cor pulmonale or edema as a result of right heart failure, or hematocrit greater than 56%. The duration of treatment should be at least 15 hours a day. Oxygen as needed or oxygen with activity has no proven mortality benefit. Inhaled corticosteroids and a long-acting β -agonist, such as salmeterol, may be indicated in this patient and likely would reduce the frequency of exacerbations, reduce hospitalizations, and improve lung function, but these medications do not increase survival. Methylxanthines, such as theophylline, are usually used only after other long-acting bronchodilators have been tried. They have a narrow therapeutic window, and most patients are effectively treated with plasma levels of 5 to 12 μ g/mL (27.8 to 66.6 μ mol/L). Toxicity is dose-related, and common side effects include headache, insomnia, nausea, and heartburn, as well as a potential for development of arrhythmias and tremor. Methylxanthines are metabolized by cytochrome P450, and drug interactions are common. Methylxanthines decrease dyspnea and improve lung function, but do not impact survival.

Key Point : Continuous oxygen improves mortality in patients with hypoxic COPD

Q5: A 55-year-old man with a 7-year history of severe chronic obstructive pulmonary disease is evaluated after being discharged from the hospital following an acute exacerbation; he has had three exacerbations over the previous 18 months. He is a long-term smoker who stopped smoking 1 year ago. His medications are albuterol as needed and inhaled tiotropium and salmeterol. On physical examination, vital signs are normal. Breath sounds are decreased bilaterally; there is no edema or cyanosis. Oxygen saturation after exertion is 92% on ambient air. Spirometry shows an FEV₁ of 32% of predicted and an FEV₁/FVC ratio of 40%. Chest radiograph done in the hospital 3 weeks ago showed no active disease. Which of the following medications should now be initiated?

- A. An inhaled corticosteroid
- B. Ipratropium
- C. N-acetylcysteine
- D. Oral prednisone

Explanation: This patient should be started on an inhaled corticosteroid. Regular use of inhaled corticosteroids in patients with chronic obstructive pulmonary disease (COPD) is associated with a reduction in the rate of exacerbations, and patients who have frequent exacerbations benefit most. The Global Initiative for Chronic Obstructive Lung Disease guidelines recommend consideration of inhaled corticosteroids in patients whose lung function is less than 50% and those who have exacerbations. When inhaled corticosteroids are combined with a long-acting β 2-agonist, the rate of decline in quality of life and health status is significantly reduced; lung function is also improved and dyspnea is alleviated. The effects of combination therapy on mortality are uncertain. Anticholinergic agents in COPD are especially useful when combined with short-acting or long-acting β 2-agonists. Tiotropium is effective in patients with stable COPD for up to 24 hours and should not be combined with short-acting anticholinergic agents, such as ipratropium. Mucolytic agents have little effect on lung function. The antioxidant N-acetylcysteine, a drug with both mucolytic and antioxidant action, did not reduce the number of exacerbations of COPD in a large prospective 3-year trial. Oral corticosteroids are not recommended for regular use in a long-term maintenance program because their use is not associated with superior outcomes compared with standard therapy and is associated with increased side effects.

Key Point : Inhaled corticosteroids may offer significant benefit in patients with severe chronic obstructive pulmonary disease.

COPD and Bronchiectasis

Q6: A 72-year-old woman is evaluated for fatigue and decreased exercise capacity. She has severe chronic obstructive pulmonary disease, which was first diagnosed 10 years ago. She was hospitalized 1 month ago for her second exacerbation this year. She stopped smoking 5 years ago. She has no other significant medical problems. Her medications are albuterol as needed, an inhaled corticosteroid, a long-acting bronchodilator, and oxygen, 2 L/min by nasal cannula. On physical examination, vital signs are normal. Breath sounds are decreased. Spirometry done 1 month ago showed an FEV1 of 28% of predicted, and blood gases measured at that time (on supplemental oxygen) showed a pH of 7.41, PCO2 of 43 mm Hg (5.7 kPa), and PO2 of 64 mm Hg (8.4 kPa); DLCO is 30% of predicted. There is no nocturnal oxygen desaturation. Chest radiograph at this time shows hyperinflation. CT scan of the chest shows homogeneous distribution of emphysema. Which of the following is the most appropriate management for this patient?

- A. Lung transplantation
- B. Lung volume reduction surgery
- C. Nocturnal assisted ventilation
- D. Pulmonary rehabilitation

Explanation: This patient, who is on maximum medical treatment for chronic obstructive pulmonary disease (COPD) and is still symptomatic, would benefit from pulmonary rehabilitation. Comprehensive pulmonary rehabilitation includes patient education, exercise training, psychosocial support, and nutritional intervention as well as the evaluation for oxygen supplementation. Referral should be considered for any patient with chronic respiratory disease who remains symptomatic or has decreased functional status despite otherwise optimal medical therapy. Pulmonary rehabilitation increases exercise capacity, reduces dyspnea, improves quality of life, and decreases health care utilization. Lung transplantation should be considered in patients who are hospitalized with COPD exacerbation complicated by hypercapnia (PCO2 greater than 50 mm Hg [6.7 kPa]) and patients with FEV1 not exceeding 20% of predicted and either homogeneous disease on high-resolution CT scan or DLCO less than 20% of predicted who are at high risk of death after lung volume reduction surgery. Lung transplantation is, therefore, not an option for this patient. The effect of lung volume reduction surgery is larger in patients with predominantly upper-lobe disease and limited exercise performance after rehabilitation. The ideal candidate should have an FEV1 between 20% and 35% of predicted, a DLCO no lower than 20% of predicted, hyperinflation, and limited comorbidities. There is no indication for nocturnal assisted ventilation in this patient because she does not have daytime hypercapnia and worsening oxygen desaturation during sleep.

Key Point : Pulmonary rehabilitation in patients with advanced lung disease can increase exercise capacity, decrease dyspnea, improve quality of life, and decrease health care utilization

Q7: A 40-year-old man who is a new patient is evaluated for a 6-month history of mild shortness of breath, which occurs primarily with exertion, and also occasional wheezing. He has smoked a half pack of cigarettes daily since the age of 18 years. He is otherwise healthy and takes no medications. He works in an automobile repair shop. His father, a cigarette smoker, died of emphysema at the age of 55 years. On physical examination, vital signs are normal. Breath sounds are diminished bilaterally, and there is occasional wheezing posteriorly. Spirometry shows an FEV1 of 58% of predicted and an FEV1/FVC ratio of 65%. Chest radiograph shows bilateral basilar lucency (lung bullae). Which of the following is the most appropriate next step in management?

- A. Measure plasma α 1-antitrypsin
- B. Measure sweat chloride
- C. Obtain a flow-volume loop
- D. Obtain high-resolution CT scan of the chest

Explanation: This patient may have α 1-antitrypsin (AAT) deficiency, a clinically underdiagnosed disorder that primarily affects the lungs but also the liver and, rarely, the skin. AAT protects against proteolytic degradation of elastin, a protein that promotes elasticity of connective tissue. The normal plasma concentration of AAT is 150 to 350 mg/dL (1.5 to 3.5 g/L). Patients with plasma levels lower than 50 to 80 mg/dL (0.5 to 0.8 g/L) have severe deficiency. In the lungs, severe deficiency of AAT predisposes to early-onset chronic obstructive pulmonary disease, especially panacinar emphysema, which involves the lung bases. This patient is younger than 45 years and has bilateral basilar emphysema, and, therefore, AAT deficiency must be ruled out. The sweat chloride test is a screening test for cystic fibrosis. Nearly 10% of patients diagnosed with cystic fibrosis are older than 18 years. Of these patients, gastrointestinal symptoms and infertility are the most common presenting problems. In cystic fibrosis lung disease, chest radiography typically shows hyperinflation and accentuated bronchovascular markings, appearing first in the upper lobes, followed by bronchiectasis and cyst formation. This patient's age, presenting symptoms, and chest radiograph findings make cystic fibrosis unlikely. A flow-volume loop, which includes forced inspiratory and expiratory maneuvers, is indicated for patients with unexplained dyspnea and can detect upper airway obstruction that cannot be diagnosed with spirometry. However, this patient has no physical findings suggestive of upper airway obstruction (for example, stridor), and even if such findings were present, they would not explain the patient's findings on chest radiography.

Key Point : Patients with severe α 1-antitrypsin deficiency are predisposed to early-onset chronic obstructive pulmonary disease, especially panacinar emphysema, which involves the lung bases

COPD and Bronchiectasis

Q8: A 74-year-old man is evaluated for a 5-year history of gradually progressive dyspnea and dry cough without wheezing or hemoptysis. He has not had fever or lost weight. He smoked one pack of cigarettes per day between the ages of 18 and 60 years. He worked as an insulator for 40 years. Physical examination shows no digital clubbing or cyanosis. Auscultation of the lungs reveals bilateral end-inspiratory crackles. Pulmonary function testing and chest radiograph show the following:

Which of the following is the most likely diagnosis?

- A. Asbestosis
- B. Idiopathic pulmonary fibrosis
- C. Pulmonary sarcoidosis
- D. Rheumatoid interstitial lung disease



Total lung capacity	67% of predicted
Residual volume	72% of predicted
FVC	65% of predicted
FEV1	75% of predicted
Diffusing capacity of lung for carbon dioxide (DLCO)	52% of predicted
FEV1/FVC ratio	89% of predicted

Explanation: The diagnosis of asbestosis is based on a convincing history of asbestos exposure with an appropriately long latent period (10 to 15 years) and definite evidence of interstitial fibrosis without other likely causes. This patient worked as an insulator when asbestos exposure was still widespread and is at risk for asbestos-related lung disease. The most specific finding on chest radiograph is bilateral partially calcified pleural plaques. Pleural plaques are focal, often partially calcified, fibrous tissue collections on the parietal pleura and are considered a marker of asbestos exposure. Idiopathic pulmonary fibrosis presents with slowly progressive dyspnea and a chronic, nonproductive cough. The chest radiograph is almost always abnormal at the time of presentation, with decreased lung volumes and basal reticular opacities. Almost all patients have a physiologic restrictive process (decreased FVC, total lung capacity, functional residual capacity) as well as impaired gas exchange with a decreased DLCO. However, asbestosis is a much more likely diagnosis in a patient with a positive exposure history and radiographic evidence of pleural plaques. Sarcoidosis occurs most commonly in young and middle-aged adults, with a peak incidence in the third decade. More than 90% of patients with sarcoidosis have lung involvement. The chest radiograph may show hilar lymphadenopathy alone, hilar lymphadenopathy and reticular opacities predominantly in the upper lung zone, or reticular opacities without hilar lymphadenopathy. Pulmonary function tests may reveal a restrictive pattern and reduction in DLCO or may be normal. The patient's age, predominantly lower lobe involvement, occupational history, and pleural plaques argue against pulmonary sarcoidosis. Rheumatoid lung disease has many manifestations, including an interstitial lung disease, which is most common in patients with severe rheumatoid arthritis. This patient does not have evidence of rheumatoid arthritis.

Key Point : Pleural plaques are focal, often partially calcified, fibrous tissue collections on the parietal pleura and are a marker of asbestos exposure

Q9: A 60-year-old man has had a chronic cough with clear sputum production for over 5 years. He has smoked one pack of cigarettes per day for 40 years and continues to do so. X-ray of the chest shows hyperinflation without infiltrates. Arterial blood gases show pH of 7.38, PCO₂ of 40 mm Hg, PO₂ of 65 mm Hg, O₂ saturation of 93%. Spirometry shows an FEV₁/FVC of 45% without bronchodilator response. Which of the following is the most important treatment modality for this patient?

- A. Oral corticosteroids
- B. Home oxygen
- C. Broad-spectrum antibiotics
- D. Smoking cessation program
- E. Oral theophylline

Explanation: This patient's chronic cough, hyperinflated lungs, abnormal pulmonary function tests, and smoking history are all consistent with chronic bronchitis. A smoking cessation program can decrease the rate of lung deterioration and is successful in as many as 40% of patients, particularly when the physician gives a strong antismoking message and uses both counseling and nicotine replacement. Continuous low-flow oxygen becomes beneficial when resting arterial oxygen saturation falls below 88%. Inhaled beta agonists or anticholinergics such as ipratropium or tiotropium are the cornerstones of symptomatic therapy but do not prevent progression of airways obstruction if the patient continues to smoke. Antibiotics are indicated only for acute exacerbations of chronic lung disease, which present with fever, change in sputum color, and increasing shortness of breath. Oral corticosteroids are helpful in acute exacerbations, but their side-effect profile precludes chronic use. Theophylline is a fourth-line treatment in COPD.

COPD and Bronchiectasis

Q10: A 70-year-old patient with chronic obstructive lung disease requires 2 L/minute of nasal O₂ to treat his hypoxia, which is sometimes associated with angina. The patient develops pleuritic chest pain, fever, and purulent sputum. While using his oxygen at an increased flow of 5 L/minute, he becomes stuporous and develops a respiratory acidosis with CO₂ retention and worsening hypoxia. What would be the most appropriate next step in the management of this patient?

- A. Stop oxygen.
- B. Begin medroxyprogesterone.
- C. Intubate and begin mechanical ventilation.
- D. Treat with antibiotics and observe on the general medicine ward for 24 hours.
- E. Begin sodium bicarbonate

Explanation: This patient presents with severe COPD and hypoxemia. Chronic CO₂ retention has blunted his hypercarbic drive to breathe; he is dependent on mild hypoxia to stimulate respiration. An inappropriately high oxygen delivery has decreased even that drive, with resulting acute respiratory acidosis and CO₂ narcosis. However, stopping the oxygen will result in severe hypoxemia. Of the choices listed, the initiation of mechanical ventilation is the only acceptable choice. If the patient's mental status were better, noninvasive ventilation (BiPAP) might be considered. Medroxyprogesterone has only a mild stimulatory effect on the respiratory center, and is not appropriate therapy in this case. Antibiotics and inhaled bronchodilators are appropriate treatments for COPD exacerbation but would not manage this patient's acute hyper-carbic respiratory failure. The patient has declared a deteriorating course. Continuing to monitor his status on the general medicine ward would probably be fatal. This patient has respiratory (not metabolic) acidosis. Bicarbonate plays a minimal role in this acidosis. The correct therapy is to improve the patient's ventilation.

Q11: A 55-year-old woman with long-standing chronic lung disease and episodes of acute bronchitis complains of increasing sputum production, which now occurs on a daily basis. Sputum is thick, and daily sputum production has dramatically increased over several months. There are flecks of blood in the sputum. The patient has lost 8 lb. Fever and chills are absent, and sputum cultures have not revealed specific pathogens. Chest x-ray and CT chest are shown on the following page. Which of the following is the most likely cause of the patient's symptoms?

- A. Pulmonary tuberculosis
- B. Exacerbation of chronic bronchitis
- C. Bronchiectasis
- D. Anaerobic lung abscess
- E. Carcinoma of the lung

Explanation: While symptoms such as sputum production and cough are nonspecific, particularly in a patient with known chronic lung disease, the high volume of daily sputum production suggests bronchiectasis. In this process, an abnormal and permanent dilatation of bronchi occurs as the muscular and elastic components of the bronchi are damaged. Clearance of secretions becomes a major problem, contributing to a cycle of bronchial inflammation and further deterioration. High-resolution CT scan, the diagnostic test of choice for this disease, shows prominent dilated bronchi and the signet ring sign of a dilated bronchus adjacent to a pulmonary artery. This CT scan picture is pathognomonic for bronchiectasis. Tuberculosis usually causes upper lobe cavitory disease. COPD causes hyperexpansion, upper lobe bullae, and nonspecific bronchial wall thickening. CT scan in anaerobic lung abscess would show an air-fluid level, usually within a shaggy inflammatory infiltrate. This CT scan shows no nodule or mass to suggest lung cancer.

Q12: A 43-year-old woman complains of gradually worsening dyspnea over the past year. She smokes 1 pack of cigarettes a day. She is trying to "cut back," because her father, also a smoker, died at age 52 of emphysema. She works as an equestrian riding instructor, often with exposure to animals and hay, but has not noticed exacerbation of symptoms while at work. She has 3 healthy children, one of whom has childhood asthma. On examination, she is comfortable at rest. Her O₂ saturation is 93%. She has no basilar crackles or wheezing, but her breath sounds are distant. Chest x-ray shows hyperexpansion especially prominent in the lung bases. Spirometry reveals FEV₁ of 46% of predicted but near normal forced vital capacity (FVC). The ratio of FEV₁ to FVC is 52%. In addition to advice about smoking cessation, what study would be most important to obtain?

- A. Sweat chloride
- B. Diffusing capacity of carbon monoxide
- C. High-resolution CT scan of the chest
- D. Serum alpha-1 antitrypsin level
- E. Hypersensitivity pneumonitis serology panel

Explanation: This woman has COPD (chronic symptoms, obstructive defect on spirometry) at age younger than 45. Early-onset symptoms, even in a smoker, coupled with a positive family history, should raise the possibility of alpha-1 antitrypsin (AAT) deficiency, and a serum AAT level should be ordered. If it is low, a phenotype assay will confirm the abnormal gene product. AAT deficiency tends to cause more prominent alveolar destruction in the lower lung zones, as opposed to usual smoker's emphysema, which has an upper lobe predominance. Diagnosing AAT deficiency would be important for her family members. In addition, infusion of pooled human AAT, although quite expensive, can raise AAT levels and probably slows progression of the disease. Cystic fibrosis, which is diagnosed by the sweat chloride level, can present with lung disease in adulthood. However, this woman's lack of cough and sputum production, as well as her normal fertility, makes this a less likely diagnosis than AAT deficiency. Diffusing capacity will be low in any cause of emphysema, and CT scanning will confirm bullous changes, but neither is recommended in the routine management of COPD. High-resolution CT scanning is used in the diagnosis of interstitial, not obstructive, lung disease. This woman has a history of exposure to organic compounds known to cause hypersensitivity pneumonitis, but her lack of symptoms during or soon after exposure, as well as the absence of patchy infiltrates on CXR, makes this diagnosis less likely. Many agricultural workers have immunoprecipitins to thermophilic actinomycetes. In the absence of convincing history, these results are nonspecific.

COPD and Bronchiectasis

Q13: A 25-year-old man presents to the clinic for evaluation of infertility. He has a life-long history of a productive cough and recurrent pulmonary infections. On his review of symptoms he has indicated chronic problems with abdominal pain, diarrhea, and difficulty gaining weight. He also has diabetes mellitus. His chest x-ray suggests bronchiectasis. Which is the most likely diagnosis?

- a. COPD
- b. Immunoglobulin deficiency
- c. Cystic fibrosis
- d. Whipple disease
- e. Asthma

Explanation: Patients with cystic fibrosis are now surviving into adulthood. The median survival is approximately age 41. Most cases are diagnosed in childhood; however, because of variable penetration of the genetic defect, approximately 7% are not found until the patient is an adult. Most male patients (> 95%) are azoospermic. Chronic pulmonary infections occur, and bronchiectasis frequently develops. Diabetes mellitus and gastrointestinal problems indicate pancreatic insufficiency. This patient should have sweat chloride measurement; if abnormal (sweat Cl above 70 mEq/L), cystic fibrosis transmembrane conductance regulator (CFTR) mutation analysis should be ordered. COPD or emphysema at this age would be unusual unless the patient were deficient in alpha-1 antitrypsin. Immunoglobulin deficiencies can cause recurrent sinopulmonary infections but would not cause malabsorption or infertility. Whipple disease causes malabsorption but not the pulmonary manifestations or infertility; it would be vanishingly rare in a young patient. Asthma would not cause the abdominal symptoms, diabetes, or changes of bronchiectasis.

Q14: A 62-year-old man seeks your advice for management of his COPD. He is a former 60-pack-year smoker, but stopped smoking 3 years ago. He uses inhaled albuterol when he feels particularly short of breath. He has noticed mild peripheral edema. He has diabetes mellitus, hypertension, and peripheral vascular disease. For these conditions he takes metformin, HCTZ, lisinopril, and cilostazol. Physical examination reveals a thin man who appears older than his stated age. His BP is 136/78, HR is 88, and RR 18. Room air O₂ saturation is 85%. He has distant breath sounds, but no rales, rhonchi, or wheezes. What treatment is most important in his overall health status?

- A. Long acting bronchodilator such as tiotropium or salmeterol b
- B. Inhaled corticosteroids
- C. Oxygen to keep O₂ saturation 90% or above
- D. Pulmonary rehabilitation
- E. Antibiotics promptly at time of purulent exacerbation.

Explanation: Oxygen treatment (as close to 24 hours a day as possible) is the one active treatment modality that has been shown to decrease mortality in COPD. Interestingly, it decreases the incidence of sudden death. This effect is presumably due to the beneficial effect of oxygen on cor pulmonale and right heart strain. It is important to emphasize to the patient that they should use the oxygen continuously, not just at times of increased dyspnea. Several treatments (inhaled corticosteroids, long-acting bronchodilators) are symptomatically useful and may slow progression of functional loss but have not been shown to prolong life. Pulmonary rehabilitation can increase functional status but does not improve parameters such as FEV₁ or mortality. The number of exacerbations is an important determinant of functional decline in COPD, but preventing them is difficult. Prompt antibiotic treatment of purulent exacerbations decreases the rate of hospitalization but has not been proven to affect mortality. Methods to slow progression of COPD are important research topics, as COPD is approaching cerebrovascular disease as the third leading cause of death in the United States.

Q15: A 20-year-old man has a cough and history of bronchitis with thick greenish sputum. There is no history of cigarette smoking. The patient has also been treated for abdominal cramping and malabsorption. What is the most likely diagnosis?

- A. Eosinophilic pneumonia
- B. Asbestosis
- C. Cystic fibrosis
- D. Bronchoalveolar carcinoma of the lung
- E. Silicosis

Explanation: The 20-year-old man has evidence of chronic airway infection not associated with cigarette smoking. Cystic fibrosis is a multisystem disease with signs and symptoms usually beginning in childhood. However, 7% of patients are diagnosed as adults. This is an autosomal recessive disease with a gene mutation on chromosome 7. In addition to respiratory tract infection, there are intestinal complications and exocrine pancreatic insufficiency. This results in malabsorption with bulky stools.

Pulmonary embolism

Q1: You are discussing a patient with your registrar who has become acutely short of breath on the ward. After performing an arterial blood gas, you have high clinical suspicion that the patient has a pulmonary embolism. Which of the following is the investigation of choice for detecting pulmonary embolism?

- A. Magnetic resonance imaging (MRI) of the chest
- B. High-resolution CT chest (HRCT)
- C. Chest x-ray
- D. Ventilation/perfusion scan (V/Q scan)
- E. CT pulmonary angiogram (CT-Pa)

Explanation: CT-Pa (E) is regarded as the investigation/diagnostic tool of choice for the detection of pulmonary embolisms (being the most readily available, sensitive and specific test). CT-Pa is able to detect PEs down to the 5th order pulmonary arteries and is readily obtainable out of hospital hours. Although V/Q scans (D) have high sensitivity/specificity, they are unlikely to be available out of hours and results are reported as low, moderate or high probability. Low probability V/Q scan results may require follow up with CT-Pa for exclusion/diagnosing PEs. Chest x-rays (C) may be normal or may show decreased vascular markings, atelectasis or a small pleural effusion. An occasional late sign on chest x-ray may be a homogenous wedge-shaped area of pulmonary infarction in the lung periphery. High resolution CT-chest (B) may not accurately detail the pulmonary vasculature but will confirm atelectasis and pleural effusion. MRI chest (A) is not used for the exclusion/diagnosis of PEs due to inaccurate imaging of pulmonary vasculature, lengthy scan times and difficulty obtaining a scan out of hours.

Q2: You see a 46-year-old man who has presented to accident and emergency with an acute onset of shortness of breath. Your registrar has high clinical suspicion that the patient is suffering from a pulmonary embolism and tells you that the patient's ECG has changes pointing to the suspected diagnosis. From the list below, which of the following ECG changes are classically seen?

- A. Inverted T-waves in lead I, tall/tented T-waves in lead III and flattened T-waves in lead III
- B. Deep S-wave in lead I, pathological Q-wave in lead III and inverted T-waves in lead III
- C. Flattened T-wave in lead I, inverted T-wave in lead III, and deep S-wave in lead III
- D. No changes in lead I, deep S-wave in lead III
- E. Deep S-wave in lead I with no changes in lead III

Explanation: Although rare, the 'S1Q3T3' (B) (deep S-wave in lead I, pathological Q-wave in lead III, and inverted T-waves in lead III) pattern may be seen in patients with pulmonary embolism. More commonly, sinus tachycardia is usually observed. Right axis deviation, right bundle branch block, right ventricular strain patterns (inverted T-waves in V1-V4) or atrial fibrillation (new onset) have also been seen in patients with pulmonary embolism.

Q3: A 68-year-old woman has presented with acute onset shortness of breath 24 hours after a long haul flight. Her blood results show a raised D-dimer level and the arterial blood gas shows a PO₂ of 8.3 kPa and PCO₂ of 5.4 kPa. Your consultant suspects a pulmonary embolism and the patient needs to be started on treatment while a CT-PA is awaited. From the list below, please select the most appropriate treatment regime.

- A. Commence loading with warfarin and aim for an international normalized ratio (INR) between 2 and 3
- B. Thromboembolic deterrent stockings
- C. Aspirin 75 mg daily
- D. Prophylactic dose subcutaneous low molecular weight heparin + loading with warfarin and aim for INR between 2 and 3
- E. Treatment dose subcutaneous low molecular weight heparin + loading with warfarin and aim for INR between 2 and 3

Explanation: Once pulmonary embolism is suspected, anti-coagulation must be commenced. Low molecular weight heparin (LMWH) is preferred over unfractionated heparin (UFH) as it is easier to use and does not require monitoring. LMWH is usually given as a once daily subcutaneous injection. Once the INR has stabilized, usually between a therapeutic range of 2-3, the low molecular weight heparin may be stopped and the patient is to continue on warfarin for a minimum of three months. If this is a first presentation of pulmonary embolism, treatment usually ranges from three to six months. If there is a recurrent history of pulmonary embolism, the patient will usually stay on warfarin for life. Patients who have pulmonary emboli secondary to a malignant process (e.g. ovarian carcinoma, bronchogenic carcinoma) will usually be on life-long treatment dose low molecular weight heparin as studies have shown improved anti-coagulation when compared to warfarin. Therefore, answers A-D are incorrect here.

Pulmonary embolism

Q4: A 75-year-old woman is admitted to the hospital from her home for treatment of community-acquired pneumonia because of extreme weakness and nausea. She has a history of hypertension and compensated heart failure. Medications are metoprolol, lisinopril, and hydrochlorothiazide. On physical examination, temperature is 38.9°C (102.0° F), blood pressure is 110/74 mm Hg, pulse rate is 100/min, and respiration rate is 20/min. Oxygen saturation by pulse oximetry is 92% on ambient air. Crackles are heard at the left lower lung base. Cardiopulmonary examination is otherwise normal. Which of the following venous thrombosis prophylactic interventions is most appropriate for this patient?

- A. Aspirin
- B. Knee-high compression stockings
- C. Lepirudin
- D. Unfractionated heparin
- E. Prophylaxis not indicated

Hemoglobin	15 g/dL (150 g/L)
Leukocyte count	18,500/μL (18.5 × 10 ⁹ /L)
Platelet count	150,000/μL (150 × 10 ⁹ /L)
Creatinine	1.2 mg/dL (106.1 μmol/L)
Electrolytes	Normal

Explanation: The most appropriate venous thrombosis prophylactic intervention for this patient is unfractionated heparin. Preventing venous thromboembolism (VTE) was the highest ranked intervention for patient safety in a recent Agency for Healthcare Research and Quality report. Appropriate prophylaxis can reduce the rate of VTE by approximately two thirds; however, various studies have shown suboptimal use of prophylaxis in medical and surgical patients. The American College of Chest Physicians (ACCP) guidelines recommends the use of unfractionated heparin, low-molecular-weight heparin (LMWH), and fondaparinux for prevention of venous thromboembolism in hospitalized, medically ill patients. In patients with renal impairment (glomerular filtration rate <30 mL/min/1.73 m²), dosing of LMWH must be adjusted and fondaparinux is contraindicated. ACCP guidelines state that aspirin should not be used as the sole prophylaxis in any high-risk group because it is not as effective as equally safe alternatives. The evidence for graduated compression stockings in the prevention of venous thromboembolism is weak, and compression stockings are not recommended as primary prophylaxis in hospitalized patients. Three direct thrombin inhibitors are in clinical use: lepirudin, the recombinant form of the leech enzyme hirudin; bivalirudin, an engineered form of hirudin that alters its thrombin-binding capacity and half-life; and argatroban, a small molecule that binds irreversibly to the active site of thrombin. Each of these is a parenterally administered drug with limited Food and Drug Administration-approved indications, and all require therapeutic monitoring. Lepirudin should be considered when a patient has heparin-induced thrombocytopenia, which is not present in this patient. Additionally, lepirudin is very expensive. Lepirudin is not indicated for routine prevention of venous thromboembolism in the hospitalized, medically-ill patient.

Key Point: Unfractionated heparin, low-molecular-weight heparin (LMWH), and fondaparinux can be used for prevention of venous thromboembolism in hospitalized, medically ill patients.

Q5: A 54-year-old man is evaluated in the emergency department for a 1-hour history of chest pain and dyspnea. The patient had been hospitalized 1 week ago for a colectomy for colon cancer. His medical history also includes hypertension and nephrotic syndrome secondary to membranous glomerulonephritis. His medications are furosemide, ramipril, and pravastatin. On physical examination, the temperature is 37.5°C (99.5°F), the blood pressure is 110/60 mm Hg, the pulse rate is 120/min, the respiration rate is 24/min, and the BMI is 30. Oxygen saturation is 89% with the patient breathing ambient air and 97% on oxygen, 4 L/min. Cardiac examination shows tachycardia and an S4. Breath sounds are normal. Serum creatinine concentration is 2.1 mg/dL (185.6 μmol/L). Chest radiograph is normal. Empiric unfractionated heparin therapy is begun. Which of the following tests should be done next?

- A. Assay for plasma D-dimer
- B. CT pulmonary angiography
- C. Lower extremity ultrasonography
- D. Measurement of antithrombin III
- E. Ventilation/perfusion scan

Explanation: A ventilation/perfusion lung scan should be done next. This patient is at high risk for pulmonary embolism (PE) because of his recent hospitalization, cancer, and nephrotic syndrome. A positive ventilation/perfusion scan would confirm the diagnosis of PE in this patient with a high pretest probability for the condition, especially in the absence of parenchymal lung defects on chest radiograph. The probability of PE is very high based on this patient's presentation that included chest pain, dyspnea, recent hospitalization and surgery, active cancer, and protein-losing nephropathy. A negative D-dimer test would not be sufficient evidence to rule out a PE under these circumstances, and a high D-dimer level would add little to the diagnostic evaluation. CT angiography is an acceptable modality to diagnose acute PE but requires a significant amount of contrast infusion, which would be contraindicated in a patient with an elevated serum creatinine level. Lower extremity ultrasonography can disclose asymptomatic deep venous thrombosis in a small percentage of patients presenting with symptoms of PE. However, the yield is relatively low and ventilation/perfusion scanning would have a much higher degree of accuracy. Decreased antithrombin III levels may result from nephrotic syndrome, and levels are lowered during acute thrombosis, especially during treatment with heparin. Therefore, measuring antithrombin III would add little to the accuracy of the diagnosis of PE or have any implication for immediate management decisions.

Key Point: Ventilation/perfusion scanning is an appropriate noninvasive test to diagnose acute pulmonary embolism, especially in the presence of chronic kidney disease.

Pulmonary embolism

Q6: A 50-year-old woman is evaluated in the emergency department for a 4-day history of pain, swelling, and erythema of the left leg. There is no history of recent immobilization, cancer, surgery, or deep venous thrombosis. On physical examination, temperature is 37.7°C (100.0°F), blood pressure is 132/82 mm Hg, pulse rate is 65/min, and respiration rate is 16/min. Examination of the left leg discloses warmth and circumscribed erythema and tenderness limited to the posterior tibial portion of the leg. The circumference of the left leg is 1 cm greater than the right when measured 10 cm below the tibial tuberosity. Localized tenderness along the distribution of the deep venous system and pitting edema are absent, as are venous varicosities. Which of the following is the most appropriate next step in diagnosis?

- A. CT of the leg
- B. D-dimer assay
- C. MRI of the leg
- D. Venography

Explanation: The most appropriate next diagnostic test is a D-dimer assay. Several imaging procedures can exclude deep venous thrombosis (DVT), but the diagnostic goal is to use the most efficient, least invasive, and least expensive method with the fewest side effects. A D-dimer assay is a simple, relatively noninvasive test that has been shown to have a high negative predictive value, especially if the suspicion for DVT is low. The Wells criteria have been established to help the clinician assess the likelihood of DVT, and studies have shown that with a low clinical suspicion (as in this patient) and a negative D-dimer assay, the presence of DVT can be reliably excluded without the need for more invasive or complex imaging. In the Wells criteria, the following clinical variables each earn 1 point: active cancer; paralysis or recent plaster cast; recent immobilization or major surgery; tenderness along the deep veins; swelling of the entire leg; greater than a 3-cm difference in calf circumference compared with the other leg; pitting edema; and collateral superficial veins. The clinical suspicion that an alternative diagnosis is likely earns -2 points. Based on this system, the pretest probability of DVT is considered high in patients with scores of greater than or equal to 3, moderate in patients with scores of 1 to 2, and low in patients with scores less than or equal to 0. This patient's Wells score is -2, and the likelihood for DVT is therefore low. This patient's fever, circumscribed area of warmth, and tenderness localized to the posterior calf could represent cellulitis, a reasonable alternative to the diagnosis of venous thrombosis. Venography, the traditional gold standard for diagnosis of DVT, is rarely performed today because of its invasiveness, discomfort, costs, and complexity. Neither an MRI nor CT of the leg has been substantially validated as a reliable diagnostic test for DVT.

Key Point: Negative D-dimer assay results and a low Wells criteria probability score reliably exclude a diagnosis of deep venous thrombosis

Q7: A 57-year-old woman is evaluated in the emergency department for a 1-week history of swelling and pain in the left leg. She has had two normal pregnancies and no miscarriages. There is no family or personal history of thromboembolic disease. The patient is otherwise healthy. A proximal deep venous thrombosis is confirmed on ultrasound. Unfractionated heparin is given as an initial bolus followed by a continuous infusion at a dose to prolong the activated partial thromboplastin time to two times the control value. Warfarin, 5 mg/d, is also initiated. Which of the following is the most appropriate duration of heparin therapy for this patient?

- A. Minimum of 3 days
- B. Minimum of 3 days, with one INR measurement of >2
- C. Minimum of 5 days
- D. Minimum of 5 days, with two INR measurements of >2, 24 h apart

Explanation: The appropriate treatment for a patient with deep venous thrombosis that is either idiopathic or associated with a transient risk factor is an initial short course of an immediate-acting anticoagulant such as unfractionated heparin, low-molecular-weight heparin, or fondaparinux for at least 5 days. Warfarin should be started at approximately the same time that heparin is administered, and the two drugs should be overlapped until the INR reaches a therapeutic range (>2) measured on two occasions approximately 24 hours apart. This timing allows for further reduction of prothrombin, the vitamin K-dependent factor with the longest half-life (approximately 60 h), which is responsible for much of the antithrombotic effect of warfarin. Usually 5 to 7 days of therapy are required to achieve this therapeutic level. The initial recommended daily warfarin dose is 5 mg, but occasionally 7.5 to 10 mg may be used. Lower doses (2.5 mg) are recommended in the elderly, especially in the setting of malnourishment, liver disease, or recent major surgery.

Key Point: Treatment of deep venous thrombosis consists of an immediate-acting anticoagulant such as unfractionated heparin, low-molecular-weight heparin, or fondaparinux for at least 5 days.

Q8: A 60-year-old man develops acute shortness of breath, tachypnea, and tachycardia while hospitalized for congestive heart failure. On physical examination the patient is tachypneic and anxious; there is no jugular venous distention and the lungs are clear to auscultation and percussion. There is a loud P2 sound. Examination of the lower extremities shows no edema or tenderness. Which of the following is the most important diagnostic step?

- A. Catheter pulmonary angiogram
- B. Thin-cut chest CT pulmonary angiogram with contrast
- C. D-dimer assay
- D. Venous ultrasound
- E. High-resolution chest CT without contrast

Explanation: For suspected pulmonary embolism, CT with intravenous contrast has surpassed the ventilation-perfusion scan as the diagnostic method of choice. New multislice scanners can detect peripheral as well as central clots. Lung scanning may be useful in selected circumstances. PE is very unlikely in patients with normal or near-normal scans, and is highly likely in patients with high-probability scans. In patients with a high clinical index of suspicion for pulmonary embolism but low-probability scan, the diagnosis becomes more difficult. Catheter-based contrast pulmonary angiography (the "gold standard") may occasionally be necessary but is not the first step. About two-thirds of patients with pulmonary embolism have evidence of deep venous disease on venous ultrasound. Therefore, pulmonary embolism cannot be excluded by a normal study. The quantitative D-dimer enzyme-linked immunosorbent assay is positive in 90% of patients with pulmonary embolism. It has been used to rule out PE in patients with a low-probability scan. A contrast CT study is needed, however, in patients with intermediate or high pretest probability of pulmonary embolism. High-resolution CT scan of the chest is useful in the diagnosis of interstitial disease but does not adequately assess pulmonary vasculature; IV contrast is necessary to diagnose PE.

Pulmonary embolism

Q9: A 57-year-old man is admitted to the hospital because of acute shortness of breath shortly after a 12-hour automobile ride. Findings on physical examination are normal except for tachypnea and tachycardia. He does not have edema or popliteal tenderness. An electrocardiogram reveals sinus tachycardia but is otherwise normal. Which of the following statements is correct?

- A. A normal D-dimer level excludes pulmonary embolus.
- B. If there is no contraindication to anticoagulation, full-dose heparin or enoxaparin should be started pending further testing.
- C. Normal findings on examination of the lower extremities make pulmonary embolism unlikely.
- D. Early treatment of pulmonary embolism has little effect on overall mortality.
- E. A normal lower extremity venous Doppler study will rule out a pulmonary embolus.

Explanation: The clinical situation strongly suggests pulmonary embolism. In greater than 80% of cases, pulmonary emboli arise from thrombosis in the deep venous circulation (DVT) of the lower extremities, but a normal lower extremity Doppler does not exclude the diagnosis. DVTs often begin in the calf, where they rarely if ever cause clinically significant pulmonary embolic disease. However, thromboses that begin below the knee frequently “grow,” or propagate, above the knee; clots that dislodge from above the knee cause clinically significant pulmonary emboli. Untreated pulmonary embolism is associated with a 30% mortality rate. Interestingly, only about 50% of patients with DVT of the lower extremities have clinical findings of swelling, warmth, erythema, pain, or palpable “cord.” When a clot does dislodge from the deep venous system and travels into the pulmonary vasculature, the most common clinical findings are tachypnea and tachycardia; chest pain is less likely and usually indicates pulmonary infarction. The ABG is usually abnormal, and a high percentage of patients exhibit low PCO₂ with respiratory alkalosis, and a widening of the alveolar-arterial oxygen gradient. The ECG usually shows sinus tachycardia, but atrial fibrillation, pseudoinfarction in the inferior leads, and acute right heart strain are also seen. Initial treatment for suspected pulmonary embolic disease includes prompt hospitalization and institution of intravenous heparin or therapeutic dose subcutaneous low-molecular-weight heparin. It is particularly important to make an early diagnosis of pulmonary embolus, as intervention can decrease the mortality rate from 30% down to 5%. A normal D-dimer level helps exclude pulmonary embolus in the low-risk setting. This patient, however, has a high pretest probability of PE; further testing (CT pulmonary angiogram, V/Q lung scan) must be done to exclude this important diagnosis.

Q10: A 65-year-old man with mild congestive heart failure is scheduled to receive total hip replacement. He has no other underlying diseases and no history of hypertension, recent surgery, or bleeding disorder. Which of the following is the best approach to prevention of pulmonary embolus in this patient?

- A. Aspirin 75 mg/d
- B. Aspirin 325 mg/d
- C. Enoxaparin 30 mg subcutaneously bid
- D. Early ambulation
- E. Graded compression elastic stockings

Explanation: Effective prophylaxis against DVT in the high-risk setting (eg, after major orthopedic surgery of the hip or knee) requires pharmacologic treatment with unfractionated heparin, low-molecular-weight heparin, fondaparinux, or therapeutic doses of warfarin. These treatments, when given at approved dosages and time intervals, decrease the risk of radiographic DVT by over 50%; dosage guidelines should be carefully followed. Aspirin alone is not effective in prevention of pulmonary embolus. Early ambulation, sequential compression devices, and elastic stockings provide some additional benefit, but are not adequate in themselves in this high-risk situation.

Pleural effusion

Q1: A 45-year-old woman with unexpected weight loss, loss of appetite and shortness of breath presents to you in clinic. On examination, there is reduced air entry and dullness to percussion in the right lung. A pleural tap is performed and the aspirate samples sent for analysis. You are told that the results reveal a protein content of >30 g/L. From the list below, select the most likely diagnosis:

- A. Bronchogenic carcinoma
- B. Congestive cardiac failure
- C. Liver cirrhosis
- D. Nephrotic syndrome
- E. Meig's syndrome

Explanation: Pleural effusions can be categorized into transudates and exudates according to their protein content. Transudates (protein content <30 g/L) occur as a result of increased venous pressure (cardiac failure (B), restrictive pericarditis, fluid overload), hypoproteinaemia (cirrhosis (C), nephrotic syndrome (D), malabsorption) hypothyroidism and Meig's syndrome (E) (right pleural effusion coupled with ovarian fibroma). Exudates occur as a result of increased capillary permeability secondary to infection (pneumonia, tuberculosis), inflammation (pulmonary infarction, rheumatoid arthritis, SLE) or malignancy (bronchogenic carcinoma, secondary metastases, lymphoma, mesothelioma, lymphangitis carcinomatosa). From the history, the most likely answer is bronchogenic carcinoma (A).

Q2: A 40-year-old man is evaluated for shortness of breath and left-sided chest discomfort without cough, fever, or hemoptysis. The patient has a history of lymphoma that is now in remission. Examination of the chest shows dullness to percussion and decreased breath sounds on the left side. Chest radiograph shows a moderate-sized, left-sided pleural effusion without a pneumothorax. Serum protein is 5.8 g/dL (58 g/L), cholesterol is 200 mg/dL (5.2 mmol/L), and triglycerides are 100 mg/dL (1.1 mmol/L). Thoracentesis yields 500 mL of milky-appearing pleural fluid, and analysis shows the following: Cytology, Gram stain, acid-fast bacilli stain, and bacterial culture are negative. Which of the following is the most likely diagnosis?

- A. Chylothorax
- B. Heart failure
- C. Parapneumonic effusion
- D. Tuberculous pleural effusion

Cell count	Erythrocytes 300/ μ L (300 \times 10 ⁶ /L); leukocytes 890/ μ L (890 \times 10 ⁹ /L) with 65% lymphocytes, 22% neutrophils, 8% mesothelial cells, and 4% eosinophils	pH	7.50
		Amylase	25 U/L
Total protein	3.5 g/dL (35 g/L)	Triglycerides	145 mg/dL (1.6 mmol/L)
Lactate dehydrogenase	250 U/L	Cholesterol	38 mg/dL (1.0 mmol/L)

Explanation: The most likely diagnosis is chylothorax. Chylothorax is drainage of lymphatic fluid into the pleural space secondary to disruption or blockage of the thoracic duct or one of its lymphatic tributaries. Malignancy is the most common cause of chylothorax, but trauma is the second most common cause. Chylothorax can also occur in association with pulmonary tuberculosis and chronic mediastinal infections, sarcoidosis, lymphangiomyomatosis, and radiation fibrosis. The pleural fluid in chylothorax is usually milky but may also be serous or serosanguineous in malnourished patients with little fat intake. The pleural fluid triglyceride concentration in a chylothorax is typically greater than 110 mg/dL (1.24 mmol/L) and occurs in association with a low pleural fluid cholesterol concentration. If the pleural fluid triglyceride level is less than 50 mg/dL (0.6 mmol/L), chylothorax is unlikely. Heart failure is associated with a transudative pleural effusion. The pleural fluid protein to serum protein ratio is >0.5 and milky appearance of the effusion excludes heart failure as a possible diagnosis. Parapneumonic effusion is usually associated with a neutrophilic pleocytosis. Tuberculosis is the most common cause of lymphocyte-predominant exudate worldwide, typically as high as 90% to 95% lymphocytes. Patients with tuberculous pleural effusion usually present with a nonproductive cough, chest pain, and fever, and the effusion is usually pale yellow in color. This patient's presentation and history of lymphoma do not support tuberculosis as the cause of the effusion.

Q3: A 56-year-old woman who has recently been discharged from your ward, with oral antibiotics for right basal community-acquired pneumonia, is re-admitted with transient pyrexia and shortness of breath. She is found to have a right-sided pleural effusion which is drained and some pleural aspirate sent for analysis. The results reveal an empyema. Which of the following, from the pleural aspirate analysis, would typically be found in a patient with an empyema?

- A. pH >7.2 , Increased LDH , Increased glucose
- B. pH <7.2 , Increased LDH , Increased glucose
- C. pH >7.2 , Decreased LDH , Decreased glucose
- D. pH <7.2 , Increased LDH , Decreased glucose
- E. pH <7.2 , Normal LDH , Normal glucose

Explanation: Empyema can be defined as pus in the pleural space which can occur in patients with resolving pneumonia. Associated symptoms include transient fever, shortness of breath and pleural effusion on the side of the resolving pneumonia. Management includes ultrasound-guided chest drain insertion coupled with antibiotic therapy. The pleural aspirate obtained during the chest drain insertion may appear turbid and (yellow) straw in colour. Empyema falls into the category of exudates, hence protein content is >30 g/L. The pH of pleural fluid is used to ascertain pleural infection. The normal pH of pleural fluid is approximately 7.6. A pleural pH of <7.2 with a normal blood pH is usually found in:

- pleural infections
- empyema
- TB
- malignancy
- oesophageal rupture

Pleural effusion

Q4: A 76-year-old woman presents with worsening dyspnea for the past 4 weeks. She has noticed fatigue, 10-lb weight loss, and occasional night sweats. On examination, she is in mild respiratory distress. Her RR is 22, and her BP is 134/76. She has mild generalized lymphadenopathy, with the largest node measuring 1.5 cm. Lung examination reveals bibasilar dullness without rales or wheezes. Her neck veins are not distended. CXR shows moderate left-sided pleural effusion. A thoracentesis is performed, revealing milky fluid. Pleural fluid protein and LDH demonstrate an exudative effusion. The pleural fluid cell count is 4800/mm³ with 14% neutrophils, 12% mesothelial cells, and 74% lymphocytes. Pleural fluid triglyceride is 170 mg/dL. What is the likely cause of this patient's illness?

- A. Tuberculosis
- B. Lung cancer
- C. Lymphoma
- D. Congestive heart failure
- E. Pneumonia with parapneumonic effusion

Explanation: Milky pleural fluid associated with high pleural fluid triglyceride level (above 110) indicates chylothorax, usually caused by disruption or compression of the thoracic duct. Hence, most chylous effusions are left-sided. Trauma is the commonest cause, but in this patient, lymphoma should be strongly considered. The lymphocytes in the pleural fluid may be monoclonal in origin. Flow cytometry of these cells or biopsy of one of the accessible peripheral lymph nodes will reveal the diagnosis. Tuberculosis can cause a chylous effusion but would typically be associated with parenchymal lung disease. Generalized lymphadenopathy would be unusual unless the TB were associated with AIDS. Lung cancer would usually be accompanied by a parenchymal mass and would rarely cause chylothorax. Congestive heart failure usually causes bilateral effusions; if unilateral, the effusion in CHF is almost always right sided. In addition, unless the patient has had vigorous diuresis, CHF causes a transudate (not an exudate). A parapneumonic effusion is exudative, but is seen in the setting of an acute illness and parenchymal infiltrate. Parapneumonic effusions are not chylous.

Q5: A 64-year-old woman is found to have a right-sided pleural effusion on chest x-ray. Analysis of the pleural fluid reveals pleural fluid to serum protein ratio of 0.38, a lactate dehydrogenase (LDH) level of 110 IU (normal 100-190), and pleural fluid to serum LDH ratio of 0.46. Which of the following disorders is most likely in this patient?

- A. Bronchogenic carcinoma
- B. Congestive heart failure
- C. Pulmonary embolism
- D. Sarcoidosis
- E. Systemic lupus erythematosus

Explanation: Classifying a pleural effusion as either a transudate or an exudate is useful in identifying the underlying disorder. Pleural fluid is exudative if it has any one of the following three properties: a ratio of concentration of total protein in pleural fluid to serum greater than 0.5, an absolute LDH greater than 2/3 the upper normal in serum, or a ratio of LDH concentration in pleural fluid to serum greater than 0.6 (the "Light criteria"). Causes of exudative effusions include malignancy, pulmonary embolism, pneumonia, tuberculosis, abdominal disease, collagen vascular diseases, sarcoidosis, uremia, Dressler syndrome, and chylothorax. Exudative effusions may also be drug induced. If none of the aforementioned properties are met, the effusion is a transudate. Differential diagnosis for a transudative effusion includes congestive heart failure, nephrotic syndrome, cirrhosis, Meigs syndrome (benign ovarian neoplasm with effusion), and hydronephrosis. Exudative effusions are the result of an inflammatory process causing proteins to leak across the capillary membrane. Transudative effusions are caused by alterations in hydrostatic or oncotic pressures with normal capillary permeability.

Q6: A 38-year-old man comes to the physician because of fever, malaise, productive cough, and left-sided chest pain for 2 weeks. During this time, he has woken up to a wet pillow in the morning on multiple occasions and has not been as hungry as usual. He was diagnosed with HIV infection 1 year ago. He currently stays at a homeless shelter. He has smoked one pack of cigarettes daily for 22 years. He has a history of intravenous illicit drug use. He drinks 5-6 beers daily. He is receiving combined antiretroviral therapy but sometimes misses doses. His temperature is 38.6°C (101.5°F), pulse is 106/min, and blood pressure is 125/85 mm Hg. Pulse oximetry on room air shows an oxygen saturation of 94%. Auscultation shows decreased breath sounds over the left base of the lung. There is dullness to percussion on the left lower part of the chest. An x-ray of the chest shows a left-sided pleural effusion and hilar lymphadenopathy. Analysis of the pleural fluid shows an effusion with lymphocyte-predominant leukocytosis, high protein, an LDH of 500 U/L, and high adenosine deaminase. Which of the following is the most likely cause of this patient's condition?

- A. Congestive heart failure
- B. Pulmonary embolism
- C. Lung cancer
- D. Pulmonary tuberculosis
- E. Rheumatoid arthritis

Explanation: Productive coughing, fever, decreased appetite, night sweats, and hilar lymphadenopathy in this immunocompromised patient (HIV, alcoholism, IV drug abuse) with possible TB exposure (resident at a homeless shelter) are all suggestive of pulmonary tuberculosis. In addition, the pleuritic pain (sharp, stabbing) and unilateral lymphocyte-predominant exudative pleural effusion with high ADA levels are highly specific and sensitive markers for tuberculous pleurisy in HIV patients, which typically occurs concurrently with pulmonary tuberculosis. The analysis of sputum specimens via culture, microscopy, and PCR is the easiest and least invasive way to confirm suspected active pulmonary TB

Pleural effusion

Match questions 7, 8 & 9 with the options below

Q7: A 52-year-old alcoholic man develops left chest pain after repeated bouts of vomiting. On presentation he is diaphoretic with fever of 101.5, heart rate 126, and BP 84/52. There are crackles and moderate dullness at the left base. The right lung is clear. He has subcutaneous emphysema over the left supraclavicular area.

Q8: A 72-year-old woman is admitted from the nursing home with fever and cough. Physical examination shows right basilar crackles and moderate dullness. CXR shows RLL pneumonia with moderate pleural effusion. She is treated with vancomycin and levofloxacin but remains febrile. Her shortness of breath worsens, and a follow-up chest x-ray shows enlarging pleural effusion.

Q9: A 52-year-old woman is admitted with abdominal pain and hypertriglyceridemia. Amylase is elevated, and she is treated for pancreatitis with IV fluids and narcotics. Over the next several days she becomes more short of breath; left basilar dullness develops.

- A. Unilateral effusion, turbid, cell count 90,000 (95% polymorphonuclear cells), protein 4.5 g/dL (serum protein 5.2), LDH 255 U/L (serum LDH 290), pH 6.84, glucose 20 mg/dL. Culture and Gram stain pending.
- B. Bilateral effusions, straw colored, cell count 150 (20% polys, 35% lymphocytes, 45% mesothelial cells), protein 1.4 g/L (serum protein 5.4), LDH 66 U/L (serum LDH 175), pH 7.42, glucose 100 mg/dL.
- C. Bilateral effusions, slightly turbid, cell count 980 (10% polys, 30% lymphocytes, 60% mesothelial cells), protein 3.9 g/L (serum 3.8), LDH 225 U/L (serum 240), pH 7.52, glucose 5 mg/dL.
- D. Bilateral effusions, straw colored, cell count 4200 (100% lymphocytes), protein 3 g/dL (serum 5.0), LDH 560 U/L (serum 450), pH 7.27, glucose 77 mg/dL.
- E. Right-sided effusion, bloody, white cell count 1200 (15% polys, 5% lymphocytes, 80% "reactive" mesothelial cells), RBC 130,000, protein 4.2 g/L (serum 4.6), LDH 560 U/L (serum 226), pH 6.90, glucose 120 mg/dL.
- F. Left-sided effusion, turbid, cell count 54,000 (92% polys, 8% lymphocytes), protein 5.2 g/L (serum 5.2), LDH 400 U/L (serum 200), pH 3.02, glucose 40 mg/dL.
- G. Left-sided effusion, straw colored, cell count 2000 (80% polys, 10% lymphocytes, 10% mesothelial cells) protein 2.0 (serum 4.8), LDH 158 (serum 220), pH 7.52, Gram stain negative, amylase 32,000.

Explanation: The first step in determining the cause of a pleural effusion is to categorize it as either a transudate or exudate. Transudative effusions are caused by alteration in Starling forces (usually elevated hydrostatic pressure as in CHF or low plasma oncotic pressure as in hypoalbuminemia). The relatively low pleural fluid protein value means that capillary permeability is normal and that only small molecules (ie, salt and water) can leak out. Exudative effusions occur when an inflammatory (or neoplastic) process allows large molecules to enter the pleural space. According to the Light criteria, exudative effusions have one of the following characteristics: pleural fluid protein to serum protein ratio greater than 0.5, pleural fluid LDH to serum LDH ratio greater than 0.6, or pleural fluid LDH more than two-thirds the normal upper limit for serum.

The alcoholic patient with repetitive nausea and vomiting has ruptured his esophagus (Boerhaave syndrome). Gastric contents enter the left pleural space and cause an inflammatory (ie, exudative) effusion. The very low pH is a tip-off that gastric acid is present and will distinguish Boerhaave. The elderly woman with pneumonia has developed empyema, a bacterial infection of the pleural space. Empyema is characterized by a very high white cell count, turbid fluid, and pH less than 7.2. Antibiotics alone will not cure empyema. Pleural fluid drainage, either with a chest tube (if the effusion is free flowing) or surgical drainage (if the fluid is loculated), is necessary to fully eradicate the infection.

The patient with abdominal pain has developed a pleural effusion resulting from pancreatitis. Many peripancreatic effusions simply occur in response to nearby inflammation of the pancreas (so-called sympathetic effusion). Occasionally, as in this case, a pancreaticopleural fistula will form, leading to an exudate with very high amylase level. Such effusions often require chest tube drainage. Almost all effusions resulting from pancreatitis are left-sided exudates.

The pleural fluid in answer b (bilateral transudative fluid) suggests congestive heart failure. Answer c is characteristic of rheumatoid arthritis, with a chronic exudate, very low glucose, and high LDH in the absence of infection. Choice d suggests tuberculosis (exudative effusion with high lymphocyte count). A unilateral bloody effusion with atypical mesothelial cells (choice e) raises concern for mesothelioma.

Q10: A 61-year-old man comes to the emergency department because of shortness of breath and right-sided chest pain for 3 days. The pain is sharp and worsens with deep inspiration. He has also had a fever and a cough productive of yellow sputum for 5 days. His temperature is 38.1°C (100.5°F), pulse is 85/min, respirations are 22/min, and blood pressure is 132/85 mm Hg. Physical examination shows dullness to percussion at the bases of the right lung; breath sounds are diminished over the right middle and lower lobes. An x-ray of the chest shows blunting of the right costophrenic angle. Pleural fluid obtained via diagnostic thoracentesis shows a pH of 7.1 and glucose concentration of 55 mg/dL. In addition to broad-spectrum antibiotics, which of the following is the most appropriate next step in management?

- a. Thoracoscopic debridement
- b. Thoracoscopic debridement
- c. Chest tube placement
- d. Pleural decortication

Explanation: This patient meets criteria for chest tube placement. A pleural fluid pH < 7.20 or glucose < 60 mg/dL indicates that effusion very likely requires drainage because these are signs of empyema formation, and empyemas are unlikely to resolve spontaneously. Chest tube placement (tube thoracostomy) is the least invasive treatment modality for drainage of the pleural space.

Investigation of lung diseases

Q1: You are asked to request imaging for a patient with a suspected pneumothorax who you have just examined in accident and emergency. Which of the following would be the most appropriate first step imaging modality?

- A. CT-chest
- B. Ultrasound chest
- C. Chest x-ray
- D. V/Q scan
- E. CT-PA

Explanation: Although CT-chest (A) would give an accurate confirmation of pneumothorax, it would not be the most appropriate first step in imaging modality. A simple chest x-ray (C) would suffice in identifying a pneumothorax. V/Q scanning (D) and CT-PA are usually requested for the assessment of pulmonary emboli. An ultrasound of the chest (B) is better at assessing pleural effusions and are increasingly used in guiding chest drain insertions.

Small pneumothoraces (small rim of air around the lung) do not usually require treatment with a chest drain if the patient is not short of breath, has good oxygen saturations, does not have a history of previous pneumothoraces and no existing lung disease. A repeat chest x-ray will be required in 7–10 days to assess whether the pneumothorax is resolving.

Large pneumothoraces (lung collapsed half-way towards heart border) require aspiration with a chest drain. Chest x-rays post chest drain insertion and after 24 hours are usually taken to assess correct chest drain placement and resolution of pneumothorax, respectively.

Complete pneumothoraces (airless lung, separate from diaphragm) will warrant the same treatment as moderate pneumothoraces (see above).

Q2: A 50-year-old Afro-Caribbean man, with no past medical history, presents with a four-month history of dry cough and shortness of breath on exertion. The patient's GP referred him to the chest clinic after performing blood tests which revealed a raised erythrocyte sedimentation rate (ESR) and serum angiotensin-converting enzyme (ACE) level. You review the patient's chest x-ray which reveals bilateral hilar lymphadenopathy. From the list below, select the most likely diagnosis:

- A. Rheumatoid arthritis
- B. Systemic lupus erythematosus (SLE)
- C. Sarcoidosis
- D. Idiopathic pulmonary fibrosis
- E. Bronchogenic carcinoma

Explanation: Sarcoidosis (C) is a multisystemic granulomatous disorder of unknown aetiology which commonly affects adults, with an increased prevalence in the Afro-Caribbean population compared to Caucasians. Usually discovered during incidental findings on chest x-ray, patients with sarcoidosis (20–40 per cent) are usually asymptomatic. Acute presentations include erythema nodosum (painful, erythematous, raised lesions on shin fronts with/ without arm/thigh involvement) with/without polyarthralgia. Ninety per cent of patients with pulmonary disease will have abnormal chest x-rays with bilateral hilar lymphadenopathy. Other signs on chest x-ray include pulmonary infiltrates or fibrosis. Patients may present with dry cough, progressive dyspnoea, reduced exercise tolerance and chest pain. In some patients with pulmonary sarcoidosis (10–20 per cent), symptoms progress leading to a decline in lung function. Some of the non-pulmonary manifestations of sarcoidosis include lymphadenopathy, hepatomegaly, splenomegaly, uveitis, conjunctivitis, lacrimal and parotid gland enlargement. Blood tests may reveal a raised ESR, lymphopenia, deranged LFTs, elevated serum ACE and raised immunoglobulins. Twenty-four hour urine collections may reveal hypercalciuria. Tissue biopsy (of lung, liver, lymph nodes, skin nodules or lacrimal glands) is usually diagnostic, with histology revealing non-caseating granulomata. Patients with bilateral hilar lymphadenopathy without systemic manifestations do not require corticosteroid treatment. Acute presentations usually require bed rest, NSAIDs and possibly corticosteroid therapy. Corticosteroid treatment is usually indicated in patients with parenchymal lung disease, uveitis, hypercalcaemia, neurological/cardiac involvement. In severe disease, intravenous corticosteroid therapy or immune suppressants may be required.

Q3: You are told by your registrar that a 69-year-old man has been admitted to the chest ward with dyspnoea, cyanosis and finger clubbing. His chest x-ray shows bilateral lower zone reticulo-nodular shadowing. From the list below, which is the most likely diagnosis?

- A. Bronchiectasis
- B. Pulmonary fibrosis
- C. Bronchogenic carcinoma
- D. Bronchitis
- E. COPD

Explanation: Classically, answers A and C–E do not produce bilateral reticulo-nodular shadowing on a chest x-ray. In addition, only the diseases mentioned in answers A–C produce clubbing as one of the clinical signs. This pattern of opacification occurs in the spectrum of fibrosing lung disease (B). In advanced fibrotic lung disease, honeycombing of the lung may be seen. Fibrosis of the lung usually starts at the bases and spreads superiorly to the upper zones of the lung as disease progresses.

Investigation of lung diseases

Q4: A 60-year-old man is evaluated for progressive exertional dyspnea. For the past year, he has been unable to walk three blocks without stopping twice because of shortness of breath. He has a daily cough productive of a small amount of white sputum. He has smoked 1 pack per day since the age of 20 years. On physical examination, he is comfortable at rest. Vital signs are normal. Oxygen saturation by pulse oximetry is 90% on ambient air. Estimated central venous pressure is normal and no murmurs or extra cardiac sounds are heard. His lung examination reveals decreased air movement without wheezes or crackles. The remainder of the examination is normal.

Chest x-ray shows increased radiolucency and low-lying diaphragms.

Which of the following is the most likely diagnosis?

Pulmonary function studies following administration of a bronchodilator:

- A. Asthma
- B. Chronic obstructive pulmonary disease (COPD)
- C. Heart failure
- D. Interstitial lung disease

FEV1	65% of predicted
FVC	75% of predicted
FEV1/FVC ratio	0.60
Total lung capacity (TLC)	105% of predicted
Diffusing capacity of lung for carbon dioxide (DLCO)	44% of predicted

Explanation: The most likely diagnosis is chronic obstructive pulmonary disease (COPD). A clinical diagnosis of COPD should be considered in any patient who has dyspnea, chronic cough or sputum production, or a history of risk factors for the disease. The diagnosis of COPD is confirmed and staged by spirometry. Spirometry should be performed after the administration of an adequate dose of an inhaled bronchodilator (for example, salbutamol 400 µg) to minimize variability. Although measurements of postbronchodilator FEV1/FVC ratio and FEV1 are recommended for the diagnosis and assessment of severity of COPD, respectively, determining the degree of reversibility of airflow limitation (change in FEV1 after administration of bronchodilators or corticosteroids) is no longer recommended for diagnosis, for distinguishing COPD from asthma, or for predicting the response to long-term treatment with bronchodilators or corticosteroids. A postbronchodilator FEV1 less than 80% of predicted and FEV1/FVC ratio less than 0.70 confirm the presence of airflow limitation that is not fully reversible, establishes the diagnosis of COPD, and excludes the diagnosis of asthma. Finally, this patient has a low DLCO, which is not compatible with asthma. DLCO measures the ability of the lungs to transfer gas from alveoli to the red blood cells in pulmonary capillaries. It is low in conditions characterized by barriers to diffusion (interstitial edema, interstitial infiltrates, tissue fibrosis) or loss of lung tissue (for example, emphysema). Heart failure is usually associated with increased central venous pressure, an S3 on cardiac examination, and crackles on lung auscultation. Patients with heart failure typically have normal pulmonary function testing, except for the possibility of decreased DLCO due to interstitial edema. In interstitial lung disease, the patient may have dry crackles on examination. Additionally, pulmonary function testing typically shows a proportionate decrease in FEV1 and FVC resulting in a normal FEV1/FVC ratio, a decreased TLC, and decreased DLCO.

Q5: A 25-year-old woman is evaluated for a 3-month history of progressive breathlessness and decreased exercise capacity. She reports no recent illness, fever, cough, or previous history of breathing problems. She has a 1-year history of pain and stiffness in the joints of her hands and wrists. On physical examination, her vital signs are normal. She has a normal cardiopulmonary examination. She has active synovitis involving her wrists and second and third metacarpophalangeal joints bilaterally. The chest x-ray is normal.

Pulmonary function studies following administration of a bronchodilator:

- A. Chronic obstructive lung disease
- B. Asthma
- C. Pulmonary embolism
- D. Interstitial lung disease

FEV1	60% of predicted
FVC	63% of predicted
FEV1/FVC ratio	0.85
Total lung capacity (TLC)	65% of predicted
Diffusing capacity of lung for carbon dioxide (DLCO)	45% of predicted

Explanation: The most likely diagnosis is rheumatoid arthritis-interstitial lung disease. The diagnosis of rheumatoid arthritis is suggested by the symmetrical synovitis of the wrists and metacarpophalangeal joints. The chest x-ray is often normal in patients with rheumatoid arthritis-interstitial lung disease, particularly in the early course of the disease. However, the pulmonary function tests show proportionate reduction in FEV1 and FVC resulting in a normal FEV1/FVC ratio. This finding is consistent with a restrictive pattern, which is supported by the finding of reduced TLC. Additionally, the decreased DLCO is compatible with interstitial lung disease. DLCO measures the ability of the lungs to transfer gas from alveoli to the red blood cells in pulmonary capillaries. It is low in conditions characterized by loss of lung tissue or barriers to gas diffusion (for example, interstitial edema, interstitial infiltrates, tissue fibrosis) or loss of lung tissue (emphysema). Chronic obstructive lung disease and asthma would have shown an obstructive pattern, with reduced FEV1/FVC ratio; the TLC may be normal or increased. In COPD, the DLCO is often low but it is normal in patients with asthma. A pulmonary embolism would not affect the spirometry or lung volumes, but may show a decrease in DLCO.

Investigation of lung diseases

Q6: A 55-year-old man is found to have a pleural effusion after a 2-week history of cough, sputum production, dyspnea, chills, and pleuritic chest pain. Upright and lateral decubitus chest x-rays confirm that the effusion is free flowing (without evidence of loculation). He has otherwise been in good health and takes no medications. A thoracentesis is performed and 1.2 L of fluid is removed. Analysis of the pleural fluid is performed. Gram stain and culture are pending. Blood cultures are obtained. Empiric broad-spectrum antibiotics are begun. Which of the following is the most appropriate next step in the management of this patient?

- A. Chest CT
- B. Chest tube drainage of the effusion
- C. Video-assisted thorascopic surgery (VATS)
- D. No additional treatment

Leukocytes	3000/ μ L (3×10^9 /L) with 82% neutrophils
Glucose	25 mg/dL (1.4 mmol/L)
Lactate dehydrogenase	2500 U/L
pH	6.95

Explanation: The next step in the management of this patient is chest tube drainage of the pleural effusion. In pleural effusions associated with pneumonia, the presence of loculated pleural fluid, pleural fluid with a pH less than 7.20, pleural fluid with a glucose level less than 60 mg/dL (3.3 mmol/L), lactate dehydrogenase level greater than 1000 U/L, positive pleural fluid Gram stain or culture, or the presence of gross pus in the pleural space predicts a poor response to antibiotics alone; such effusions are treated with drainage of the fluid through a catheter or chest tube. This patient's history is compatible with community-acquired pneumonia (cough, sputum, fever, chills), and the radiographic findings are consistent with a free-flowing pleural effusion. Because this patient's pleural fluid findings predict a poor response to antibiotics alone, his effusion is called a complicated parapneumonic effusion. A CT scan may be helpful to detect very small effusions, to determine thickness of the pleural lining, to distinguish empyema (pus in the pleural space) from a lung abscess, or to detect an underlying malignancy obscured by the pleural fluid; however, none of these indications apply to this patient and a CT scan is not needed. Most pleural effusions resolve with treatment of the underlying disease. The only effusions that usually require invasive treatment are complicated parapneumonic effusions (such as this one), empyema, and malignancy. In patients with pneumonia, thoracic empyema develops when antibiotics are not given (or delayed) and the pleural space is not drained in a timely manner. In this case, video-assisted thorascopic surgery (VATS) is indicated to break down loculations and drain pus from the pleural cavity. Therefore, not intervening with chest tube placement is inappropriate for this patient, and VATS surgery is overly aggressive therapy at this point in time.

Q7: A 38-year-old woman with a 4-year history of systemic sclerosis is evaluated for a 6-month history of dry cough and shortness of breath. She has no fever, sputum production, or orthopnea. The clinical manifestations of her systemic sclerosis include arthralgia, gastroesophageal reflux disease, and Raynaud phenomenon. On physical examination, temperature is 36.9°C (98.5°F), blood pressure is 120/76 mm Hg, pulse rate is 88/min, and respiration rate is 18/min. Oxygen saturation by pulse oximetry is 90% on ambient air. Fine bibasilar late inspiratory crackles are heard. Cardiac examination is normal without murmurs or extra sounds. Complete blood count, serum electrolytes, and metabolic panel are normal. Chest x-ray is normal. Results of pulmonary function testing: FEV1, 75% of predicted; FVC, 71% of predicted; FEV1/FVC ratio, 100% of predicted; and diffusing capacity of lung for carbon monoxide (DLCO), 64% of predicted. Antitopoisomerase I antibody testing is positive. Which of the following is the most appropriate next diagnostic test?

- A. Bronchoalveolar lavage
- B. High resolution chest CT
- C. Lung biopsy
- D. Pulmonary artery angiogram

Explanation: The most appropriate next diagnostic test is high resolution chest CT. Connective tissue diseases, along with drugs and environmental causes, are the most common known causes of diffuse parenchymal lung disease (DPLD). DPLD is most likely in patients with systemic sclerosis who develop antitopoisomerase I (anti-Scl-70) antibody positivity. DPLD associated with systemic sclerosis usually manifests as dyspnea, dry cough, and decreased exercise tolerance. Fine bibasilar crackles that extend into late inspiration are heard on physical examination. On pulmonary function testing, these patients have a restrictive pattern with a decreased FVC and DLCO (and normal FEV1/FVC ratio). High-resolution CT (HRCT) is more sensitive than chest x-ray for DPLD and reveals ground-glass and reticular linear opacities, subpleural cysts, and honeycombing in patients with advanced disease. Together, the clinical findings and HRCT can establish the diagnosis in this patient. If the clinical context, temporal pattern of disease, and HRCT findings do not yield a diagnosis, it may be reasonable to obtain a bronchoscopic or surgical lung biopsy. The diagnostic yield of surgical lung biopsy is approximately 90%. However, a limited number of histopathologic patterns are recognized for a large number of DPLDs, and the specificity of lung biopsy depends on the pattern. Bronchoalveolar lavage can provide additional diagnostic information, including culture, cytology, and cell differential. Bronchoalveolar lavage is safe and simple to perform and may be helpful to diagnose infections and carcinoma, as well as eosinophilic pneumonia. Neither test is recommended before an HRCT. In patients with systemic sclerosis, pulmonary vascular disease may manifest as isolated pulmonary arterial hypertension (PAH) or as a complication of vascular obliteration in patients with DPLD. Patients with PAH may present with fatigue, decreased exercise tolerance, dyspnea, or syncope. Physical examination findings include an increased P2 and a persistently split S2. Chest radiographs are usually normal. A decrease in DLCO in the setting of normal lung volumes is consistent with PAH. This patient has a restrictive physiology on pulmonary function testing and no physical examination findings to support PAH.

.Key Point : Connective tissue diseases, along with drugs and environmental causes, are the most common known causes of diffuse parenchymal lung disease

Investigation of lung diseases

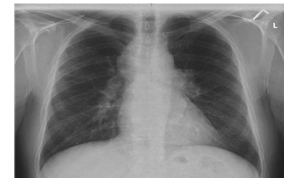
Q8: A 42-year-old woman presents with gradually worsening dyspnea over the preceding 6 months. She has a mild nonproductive cough. She previously had been diagnosed with systemic sclerosis (scleroderma) but her skin thickening has been stable. She controls her Raynaud syndrome with amlodipine and her esophageal reflux with daily omeprazole. She has no renal disease or hypertension. On physical examination, her RR is 22/minute and resting O₂ saturation is 92%. She has thickened, hide-bound skin on the face, torso, and abdomen. Lung examination shows mild “Velcro” rales in the bases bilaterally. Neck veins are flat. Cardiac examination is normal with normal P₂ and no lift or heave. Chest x-ray shows increased interstitial lung markings and a normal heart size. What is the most important next step in evaluating this patient’s dyspnea?

- A. Arterial blood gas
- B. 2D echocardiogram
- C. Measurement of autoantibodies including anti-topoisomerase (anti-Scl) antibodies
- D. Barium swallow to detect microaspiration
- E. Noncontrast high-resolution CT scan (HRCT) of chest

Explanation: This patient has interstitial lung disease (ILD) due to her systemic sclerosis. Over 75% of patients will have CT evidence of ILD. Now that scleroderma renal crisis can be managed with ACE inhibitors, ILD is the most common disease related cause of death in scleroderma. The two most important studies for the diagnosis of ILD are spirometry with measurement of diffusion capacity of carbon monoxide (DLCO) and high-resolution CT scan. The latter will show reticular interstitial thickening and subpleural microblebs. Advanced cases will show thickened fibrotic bands with parenchymal destruction known as honeycombing. Treatment of connective tissue disease associated ILD is unsatisfactory, but cyclophosphamide will slow progression in some patients. In addition to systemic sclerosis, ILD is an important potential complication of polymyositis/dermatomyositis, rheumatoid arthritis, and occasionally systemic lupus. An arterial blood gas study would probably show alveolar hyperventilation (ie, low PCO₂) with a widened alveolar-arterial oxygen gradient but would not give specific information as to cause and prognosis. In most cases, finger oxygen saturation measurements provide sufficient information. Pulmonary hypertension can be detected with 2D echocardiogram according to the degree of tricuspid regurgitation. Pulmonary hypertension can be an important complication of connective tissue disease (especially limited scleroderma but sometimes diffuse scleroderma as well). You would expect, however, a loud P₂ and evidence of central pulmonary artery enlargement on CXR. In addition, Velcro rales and increased interstitial markings are not seen in uncomplicated pulmonary hypertension. Autoantibodies are usually found in systemic sclerosis, but the diagnosis is already established. The titer of anti-Scl antibodies does not correlate with disease activity; so once the diagnosis is established, serial measurement of autoantibodies is not necessary. Aspiration due to esophageal dysmotility can complicate scleroderma, but usually causes intermittent exacerbations associated with sputum production, fever, and alveolar infiltrates, none of which has characterized this patient’s course.

Q9: A 34-year-old black woman presents to your office with symptoms of cough, dyspnea, and fatigue. Physical examination shows cervical adenopathy and hepatomegaly. Spleen tip is palpable. Her chest radiograph is shown below. Which of the following is the best approach in establishing a diagnosis?

- A. Open lung biopsy
- B. Liver biopsy
- C. Bronchoscopy and transbronchial lung biopsy
- D. Mediastinoscopic lymph node biopsy
- E. Serum angiotensin-converting enzyme (ACE) level



Explanation: Sarcoidosis is a systemic illness of unknown etiology. There is a higher prevalence in female patients and in the African American population. Most patients have respiratory symptoms, including cough and dyspnea. Hilar and peripheral lymphadenopathy is common, and 20% to 30% of patients have hepatosplenomegaly. The chest x-ray shows symmetrical hilar lymphadenopathy. The diagnostic method of choice is fiberoptic bronchoscopy with transbronchial biopsy, which will show a mononuclear cell granulomatous inflammatory process. While liver and mediastinal lymph node biopsies are often positive, bronchoscopy is a safer and less invasive procedure. ACE levels are elevated in two-thirds of patients; since an elevated ACE value is common in other granulomatous diseases, it is not specific enough to exclude alternative diagnoses. Open-lung biopsy is more invasive and would only be considered if fiberoptic bronchoscopy failed to yield a diagnosis.

Q10: A previously healthy 60-year-old man comes to his physician because of progressively worsening shortness of breath for the past 2 months. He does not experience shortness of breath at rest. He also occasionally has a dry cough. He has not had fever, chills, or night sweats. He has smoked a pack of cigarettes daily for the past 40 years. He drinks a beer daily and occasionally more on weekends. He does not use illicit drugs. He is 183 cm (6 ft 0 in) tall and weighs 66 kg (145 lbs); BMI is 19.7 kg/m². His temperature is 37°C (98.6°F), pulse is 94/min, respirations are 21/min, and blood pressure is 136/88 mm Hg. Lung auscultation reveals a prolonged expiratory phase and end-expiratory wheezing. Spirometry shows an FEV₁:FVC ratio of 62%, an FEV₁ of 60% of predicted, and a total lung capacity of 125% of predicted. The diffusion capacity of the lung (DLCO) is decreased. Which of the following is the most likely diagnosis?

- A. Bronchiectasis
- B. Bronchial asthma
- C. Bronchoscopy and transbronchial lung biopsy
- D. Chronic obstructive pulmonary disease
- E. Interstitial lung disease

Explanation: Smoking is responsible for over 90% of cases of COPD, which would result in decreased FEV₁/FVC, decreased FEV₁, and increased TLC (due to increased lung compliance). This patient is almost cachectic, with progressively worsening dyspnea, an end-expiratory wheeze, and an occasional dry cough, which most likely indicates emphysema-predominant COPD. In emphysema, destruction of the alveoli results in a decreased surface area for air exchange; DLCO levels are therefore decreased.

General pulmonary

Q1: You see a 68-year-old man in clinic, with a 40 (cigarette) pack year history, who has been experiencing breathlessness on exertion and a productive cough of white sputum over the last four months. You assess his spirometry results which reveal an FEV1/FVC of 51 per cent with minimal reversibility after a 2-week trial of oral steroids. Cardiological investigations are normal. Which of the following is the most likely diagnosis?

- A. Asthma
- B. Chronic obstructive pulmonary disease (COPD)
- C. Left ventricular failure
- D. Chronic bronchitis
- E. Lung fibrosis

Explanation: The patient's symptom history coupled with the spirometry results indicate that he has an obstructive defect. Spirometry is typically used to measure functional lung volumes. The ratio of the forced expiratory volume in one second (FEV1) to the forced vital capacity (FVC), provides a reliable approximation of severity of airflow obstruction; the normal being 80 per cent. An FEV1/FVC ratio of less than 80 per cent indicates an obstructive defect seen in COPD and asthma while a ratio of greater than 80 per cent is representative of a restrictive defect seen in lung fibrosis (E). The spirometry results coupled with minimal reversibility points the diagnosis to COPD (B) rather than asthma (A), where reversibility of the FEV1/FVC ratio is usually seen. Chronic bronchitis (D) can be defined as cough productive of sputum for three months of two successive years which does not corroborate with the onset of symptoms. Left ventricular failure (C) is obviously incorrect due to the fact that cardiological tests have been mentioned as normal.

Q2: A 54-year-old woman is seen in clinic with a history of weight loss, loss of appetite and shortness of breath. Her respiratory rate is 19 and oxygen saturations (on room air) range between 93 and 95 per cent. On examination, there is reduced air entry and dullness to percussion on the lower to midzones of the right lung. There is also reduced chest expansion on the right. From the list below, select the most likely diagnosis:

- A. Right middle lobe pneumonia
- B. Pulmonary embolism
- C. Right-sided pleural effusion
- D. Right-sided bronchial carcinoma
- E. Right lower lobe pneumonia

Explanation: The fact that there is reduced air entry, dullness to percussion in the lower and midzones of the right lung and reduced chest expansion, indicates that there is most likely to be a pleural effusion (C) from the list of answers above. 'Stony dullness' is usually used to describe the presence of a pleural effusion but, in clinical practice, distinguishing between dullness and stony dullness can be quite challenging for even the most experienced clinicians. Pulmonary embolism (B) does not usually present with any chest signs. Pneumonia (A and E) and bronchial carcinoma (D) can lead to a secondary pleural effusion, but during the initial stages will present with bronchial breathing over the affected area of the lung.

Q3: A 30-year-old man presents to your clinic with a cough and finger clubbing. From the list below, which of these answers is not a respiratory cause of finger clubbing?

- A. Empyema
- B. Mesothelioma
- C. Bronchogenic carcinoma
- D. Cystic fibrosis
- E. COPD

Explanation: The respiratory causes of clubbing include bronchogenic carcinoma (C), empyema (A), mesothelioma (B), cystic fibrosis (D), lung abscess, fibrosing alveolitis and bronchiectasis. In patients with COPD, the signs that may be seen in the hands are carbon dioxide retention tremor, peripheral cyanosis and tar staining in the fingertips.

Q4: You see a 28-year-old man, with no past medical history, in accident and emergency who developed an acute onset of pleuritic chest pain and shortness of breath while playing football. On examination, oxygen saturations are 93 per cent on room air, respiratory rate 20 and temperature is 37.1°C. There is decreased expansion of the chest on the left side, hyper-resonant to percussion and reduced air entry on the left. The most likely diagnosis is:

- A. Left-sided pneumothorax
- B. Left-sided pneumonia
- C. Left-sided pleural effusion
- D. Lung fibrosis
- E. Traumatic chest injury

Explanation: Hyper-resonance coupled with pleuritic chest pain and an acute onset from the history strongly points to a diagnosis of pneumothorax. Pneumothoraces are usually spontaneous in young thin men and tend to occur due to subpleural bulla rupture. Some other causes include asthma, COPD, TB, pneumonia, connective tissue disorders (e.g. Marfan's syndrome, Ehlers-Danlos syndrome), trauma, iatrogenic (e.g. pleural aspiration/biopsy, percutaneous liver biopsy, etc.) There is no history of cough and, in addition, the patient is afebrile with no bronchial breathing over the chest wall to suggest pneumonia (B). With pleural effusion (C) there would be dullness to percussion and reduced air entry on the affected side; there would also be a more chronic onset of symptoms from the history. Lung fibrosis (D) would not typically present with signs of hyper-resonance and furthermore, disease is usually bilateral with air entry. Fine inspiratory crackles are heard on auscultation. Although pneumothoraces can develop from chest trauma, there is no history of this from the question stem, making a traumatic chest injury (E) unlikely.

General pulmonary

Q5: A 56-year-old woman is evaluated for a 2-year history of episodic cough and chest tightness. Her symptoms began after a severe respiratory tract infection. Since then, she has had cough and chest discomfort after similar infections, typically lasting several weeks before resolving. She feels well between episodes. She is otherwise healthy and takes no medications. Physical examination reveals no abnormalities. Chest radiograph and spirometry are normal. Which of the following is the most appropriate next diagnostic test?

- A. Bronchoscopy
- B. CT scan of the sinuses
- C. Exercise echocardiography
- D. Methacholine challenge test

Explanation: The most appropriate next diagnostic test is a methacholine challenge. This patient's history is consistent with, but not typical of, asthma. This presentation is sometimes referred to as cough-variant asthma. Asthma is often an episodic disease, with normal examination findings and spirometry between episodes. In such cases, a bronchial challenge test, such as with methacholine, can induce bronchoconstriction even when the patient is asymptomatic and spirometry is normal. Methacholine challenge testing is done by giving the patient increasing concentrations of methacholine by nebulization and performing spirometry after each dose until there is a greater than 20% decrease in FEV1 from baseline. The methacholine dose that leads to a 20% decrease in the FEV1 is known as the provocative concentration 20 (PC20) and is calculated from a dose-response curve. In general, a PC20 of less than 4 mg/mL is consistent with asthma. A PC20 between 4 and 16 mg/mL suggests some bronchial hyperreactivity and is less specific for asthma. A PC20 above 16 mg/mL is considered normal. The sensitivity of a positive methacholine challenge test in asthma is in the range of 85% to 95%. False-positive results can occur in patients with allergic rhinitis, chronic obstructive pulmonary disease, heart failure, cystic fibrosis, or bronchitis. Bronchoscopy to evaluate the trachea could be helpful if an anatomic lesion is suspected. However, the symptoms in patients with such lesions are persistent or progressive rather than intermittent. Since this patient has intermittent symptoms, bronchoscopy is not indicated. Exercise echocardiography could help determine the presence of cardiac ischemia or myocardial dysfunction, the typical symptoms of which are dyspnea on exertion, chest tightness, or pain. Cough and wheezing can occur in coronary artery disease, particularly when associated with acute decompensation of the left ventricle, but this patient's intermittent episodes of cough and wheezing are provoked by an upper respiratory tract infection, making the diagnosis of coronary artery disease unlikely. Patients with rhinosinusitis have symptoms consisting of nasal congestion, purulent nasal secretions, sinus tenderness, and facial pain. Radiography, including sinus CT scan, is not indicated in the initial evaluation of acute sinusitis.

Q6: A 60-year-old man is hospitalized because of progressive dyspnea during the past month. He has a 45-pack-year smoking history, but he has no other medical problems. On physical examination, he is cyanotic and has paradoxical respiratory movements of his rib cage and abdomen. Blood pressure is 140/78 mm Hg, pulse rate is 105/min, and respiration rate is 28/min. Jugular venous distention is present. The lungs are clear. The remainder of the examination is normal. Pulmonary function studies: Arterial blood gases studies show a pH of 7.3, a PO₂ of 42 mm Hg (5.6 kPa), a PCO₂ of 55 mm Hg (7.3 kPa), and a bicarbonate level of 27 meq/L (27 mmol/L).

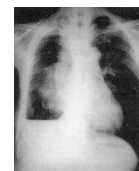
- A. Chronic obstructive pulmonary disease
- B. Idiopathic pulmonary fibrosis
- C. Neuromuscular weakness
- D. Pulmonary arterial hypertension

Total lung capacity	85% of predicted	Residual volume/total lung capacity	163%
Residual volume	72% of predicted	Maximum inspiratory pressure	36% of predicted
FVC	60% of predicted	Maximum expiratory pressure	45% of predicted
FEV1	63% of predicted	DLCO	82% of predicted
FEV1/FVC ratio	105%		

Explanation: This patient most likely has severe muscle weakness due to a subacute or chronic neuromuscular disorder such as amyotrophic lateral sclerosis or myasthenia gravis. Either condition can present with respiratory failure. An increased residual volume/total lung capacity (RV/TLC) ratio is commonly seen in obstructive disorders, but it may also be caused by a neuromuscular restrictive disorder. In such cases, the normal FEV1/FVC ratio and the low maximum respiratory pressures indicate neuromuscular weakness rather than an obstructive lung disease. Interstitial lung diseases, such as idiopathic pulmonary fibrosis (IPF), cause restriction but would not explain the increased RV/TLC ratio, normal DLCO, and reduced maximum respiratory pressures. When respiratory failure develops with IPF, it is usually characterized by hypoxemia. Hypercapnic respiratory failure is rare in IPF. Similarly, pulmonary hypertension presents with hypoxia and hypercapnia; hypercapnia would be unusual. In some patients, pulmonary arterial hypertension may be associated with a mild decrease FEV1 or FVC but the RV/TLC and maximal inspiratory pressure are normal. Finally, the DLCO is usually decreased in pulmonary arterial hypertension, and this is not compatible with this patient's findings.

Q7: A previously healthy 30-year-old man who is a lifelong nonsmoker is evaluated in the emergency department for sudden onset of right-sided chest pain and shortness of breath. On physical examination, vital signs are normal. There are decreased breath sounds over the posterior right thorax. The cardiac examination is normal. A chest radiograph is obtained and is shown. Which of the following is the most likely diagnosis?

- A. Heart failure
- B. Hydropneumothorax
- C. Pneumonia
- D. Pulmonary embolism



Explanation: This patient has a hydropneumothorax. Spontaneous pneumothorax is a relatively common event in healthy young persons. The radiographic abnormality is characterized by the loss of normal lung markings in the periphery of the hemithorax and the presence of a well-defined, visceral pleural line at some point between the chest wall and the hilum. Spontaneous pneumothorax occurs when a subpleural bleb ruptures into the pleural space, an event that commonly occurs during exertion. The presence of air within the pleural space allows the lung to collapse toward the hilum. Frequently, a small amount of bleeding accompanies rupture of the bleb and produces the characteristic appearance of a flat-line junction between the air and the fluid that collects at the base of the hemithorax; this is known as a hydropneumothorax. Large pneumothoraces require insertion of a chest tube to drain the pleural space and reexpand the lung. An initial chest radiograph showing shift of the mediastinum away from the side of the pneumothorax indicates the development of a tension pneumothorax and requires immediate chest tube insertion.

Typical radiographic findings of heart failure include cardiomegaly, pulmonary vascular congestion, Kerley B-lines, and pleural effusions; pulmonary edema may be recognized as perihilar interstitial infiltrates. Pneumonia may have various radiographic presentations, including lobar consolidation, interstitial infiltrates, and cavitation. Radiographic abnormalities are commonly associated with pulmonary embolism but are not specific. Findings such as atelectasis, infiltrates, and pleural effusions are found as frequently in patients with pulmonary embolism as in patients without pulmonary embolism. Slightly over 10% of patients with pulmonary embolism will have a normal chest radiograph.

General pulmonary

Q8: A 20-year-old woman is evaluated in the emergency department for an acute episode of wheezing and dyspnea without cough or sputum production. She has had frequent evaluations in emergency departments for similar episodes. In between these episodes, findings on physical examination and pulmonary function testing, including methacholine challenge, have been normal. She is otherwise healthy and takes no medications. On physical examination, the patient has inspiratory and expiratory wheezing and is in moderate discomfort. The temperature is 37.1°C (98.8°F), pulse rate is 100/min, and respiration rate is 24/min; oxygen saturation on ambient air is 96%. After receiving albuterol and intravenous corticosteroids, she continues to wheeze and is in moderate respiratory distress. Oxygen saturation on ambient air remains at 96%. Chest radiograph shows decreased lung volumes. Which of the following is the most appropriate management for this patient?

- A. Chest CT scan
- B. Intravenous aminophylline
- C. Intravenous azithromycin
- D. Laryngoscopy

Explanation: The most appropriate management for this patient is laryngoscopy. She likely has vocal cord dysfunction (VCD). Patients with VCD can have throat or neck discomfort, wheezing, stridor, and anxiety. The disorder can be difficult to differentiate from asthma; however, affected patients do not respond to the usual asthma therapy. Diagnosing VCD is made more difficult by the fact that many of these patients also have asthma. The chest radiograph in this patient showed decreased lung volumes, which is in contrast to hyperinflation that would be expected in acute asthma. Oxygen saturation is typically normal in patients with VCD. Laryngoscopy, especially when done while the patient is symptomatic, can reveal characteristic adduction of the vocal cords during inspiration. Another test that helps make the diagnosis is flow volume loops, in which the inspiratory and expiratory flow rates are recorded while a patient is asked to take a deep breath and then to exhale. In patients with VCD, the inspiratory limb of the flow volume loop is "flattened" owing to narrowing of the extrathoracic airway (at the level of the vocal cords) during inspiration. Recognition of VCD is essential to prevent lengthy courses of corticosteroids and to initiate therapies targeted at VCD, which include speech therapy, relaxation techniques, and treating underlying causes such as anxiety. The chest CT scan can be used to exclude parenchymal lung disease or evaluate the possibility of a pulmonary embolism; however, these disorders are unlikely in this patient with previous normal pulmonary examinations and radiographs and excellent oxygenation. Intravenous aminophylline is not recommended for treating either acute asthma or VCD. Azithromycin is a reasonable choice for acute bronchitis in patients with underlying lung disease, but there is little evidence that this patient has acute bronchitis, which would manifest with cough, sputum production, and fever.

Q9: A 24-year-old man is evaluated in the emergency department for a 10-day history of increasing shortness of breath and dry cough. Before this time, the patient was healthy and took no medications. On physical examination, temperature is 37.9°C (100.3°F), blood pressure is 105/70 mm Hg, pulse is 106/min, and respirations are 32/min. A lung examination reveals dullness to percussion, decreased tactile fremitus, and decreased breath sounds at the right base. The remainder of his physical examination is unremarkable. Which of the following is the most likely diagnosis?

- A. Heart failure
- B. Lobar consolidation
- C. Pleural effusion
- D. Pneumothorax

Explanation: The most likely diagnosis is parapneumonic pleural effusion. Large fluid accumulation in the pleural space blocks transmission of sound between the lung and the chest wall; percussion over an effusion is dull, and tactile (vocal) fremitus is diminished or absent. On auscultation, the most common findings are decreased to absent breath sounds over the effusion. Fever and pleural effusion suggests an underlying infection, malignancy, or associated collagen vascular disease. The patient's history of recent onset of fever and cough makes a pneumonia-related parapneumonic effusion most likely. Heart failure can be associated with a pleural effusion, but other symptoms and signs of heart failure such as orthopnea, elevated central venous pressure, S3, and peripheral edema are likely to be present. Furthermore, heart failure in a 24-year-old person who was previously well is very unusual. Patients with lobar pneumonia typically have tachypnea, fever, crackles, bronchial breath sounds, and dullness to percussion with reduced breath sounds. Because consolidated lung tissue is an excellent transmitter of sound and vibration, tactile fremitus is increased, not decreased as in pleural effusion. Pneumothorax should be considered in any patient with sudden onset of pleuritic chest pain and dyspnea. The physical examination may show decreased breath sounds and hyperresonance to percussion on the affected side rather than dullness to percussion.

General pulmonary

Q10: A 30-year-old medical resident is evaluated for cough, right-sided chest pain, and fever of 3 weeks' duration. He has no significant medical history, and he takes no medications. Hemoglobin is 14 g/dL (140 g/L), and the leukocyte count is 8000/ μ L (8.0×10^9 /L). Chest radiograph shows a right pleural effusion occupying approximately 50% of the hemithorax without other abnormalities. Thoracentesis yields turbid, yellow fluid, and analysis shows the following: Serum total protein is 7.0 g/dL (70 g/L) and serum lactate dehydrogenase is 100 U/L. Gram stain shows no organisms and culture is pending. Which of the following is the most appropriate next step in management?

- A. Azithromycin for 5 days
- B. Chest CT scan
- C. Flexible bronchoscopy
- D. Pleural biopsy
- E. Chest X-ray

Erythrocyte count	500/ μ L (500×10^6 /L)
Nucleated cell count	3500/ μ L (3.5×10^9 /L) with 20% neutrophils, 60% lymphocytes, 10% macrophages, 4% mesothelial cells, and 6% eosinophils
Total protein	4.2 g/dL (42 g/L)
Lactate dehydrogenase	240 U/L
pH	7.35
Glucose	68 mg/dL (3.8 mmol/L)

Explanation: The most appropriate next step is a pleural biopsy. He likely has a tuberculous pleural effusion based on the subacute (3-week) duration of symptoms and the characteristics of the pleural effusion. Because of the patient's age and the presentation with an isolated pleural effusion, primary tuberculosis is most likely. A tuberculous effusion is typically exudative by both protein (pleural fluid to serum protein ratio greater than 0.5) and lactate dehydrogenase (LDH) criteria (pleural fluid to serum LDH ratio greater than 0.6 and pleural fluid to serum upper limits of normal LDH ratio greater than 0.6). The cellular response in the pleural fluid is classically lymphocytic (greater than 80% mature lymphocytes). However, it can be neutrophilic within the first 2 weeks, after which it typically evolves into the classic lymphocyte-predominant exudate. Whereas pleural fluid cultures for *Mycobacterium* are positive in less than one third of cases, the combination of pleural biopsy for histologic evaluation and culture is typically positive in more than two thirds of cases. The 3-week history of symptoms is too long for a typical bacterial pneumonia, no definite infiltrate was present on the chest radiograph, and the cellular response in the pleural fluid was primarily lymphocytic rather than neutrophilic. Therefore, a bacterial pneumonia with a parapneumonic effusion is unlikely, and an empiric course of azithromycin would not be appropriate. Chest CT scan might be helpful to assess whether there is an underlying parenchymal infiltrate that was not visible on plain chest radiograph, but it would not help in determining the underlying cause of the pleural effusion. Flexible bronchoscopy, with collection of samples for histology and culture, is useful for diagnosing pulmonary tuberculosis in the setting of pulmonary parenchymal disease. However, the yield from culture of bronchopulmonary secretions (obtained either as sputum or bronchoscopic samples) is low, especially in the absence of pulmonary parenchymal abnormalities on chest radiograph.

Q11: A 56-year-old man attends your clinic with a three-month history of a productive cough with blood-tinged sputum, following his return from India. Associated symptoms include lethargy, night sweats and decreased appetite. He is normally fit and healthy with no past medical history. On examination, the patient's chest has good air entry bilaterally with no added sounds and his temperature is 37.3°C. A sputum sample sent from the patient's GP reveals a growth of acid fast bacilli. From the list below, which is the most likely diagnosis?

- A. Pulmonary embolism
- B. Tuberculosis
- C. Bronchitis
- D. Pneumonia
- E. Bronchogenic carcinoma

Explanation: Although answers A–E can all cause haemoptysis, the clue in this question points towards the sputum analysis report which shows a growth of acid fast bacilli seen in tuberculosis (TB) (B) which can be categorized into pulmonary (75 per cent of cases) and extrapulmonary (25 per cent of cases). The gram-positive aerobic bacterium (*Mycobacterium tuberculosis*) is usually airborne, transmitted by people suffering from active pulmonary TB (e.g. via coughing, sneezing, speaking, spitting, etc.), sharing of needles among intravenous drug users, within high-risk racial or ethnic minority populations and people suffering from immunocompromised conditions. Most people (90 per cent) infected with the bacterium are asymptomatic (latent TB) with an approximately 10–15 per cent lifetime chance that the latent infection will progress to full blown TB. Once the mycobacteria reach the alveoli (primary TB), replication of the bacteria occur with formation of a Ghon focus (granuloma formation), which is usually located in the upper or lower lobes of the lung. Granuloma formation occurs (aggregation of macrophages, T- and B-lymphocytes and fibroblasts) in an attempt to kill the mycobacteria but this is not always efficient, especially with dormant bacteria. The bacteria can spread via the lymphatic system or bloodstream to other organs causing secondary TB (refer to Section 11, Infectious diseases, for further reading). Symptoms of primary pulmonary TB include chronic cough, haemoptysis, pyrexia, night sweats, loss of appetite, weight loss and lethargy. Chest x-ray may show a 'coin lesion' in the upper or lower lobes of the lung, sputum analysis may show growths of mycobacterium but can sometimes be difficult to culture in vitro and may take from 4 to 12 weeks. Interferon gamma release assays (IGRAs) can also be performed where the detection of interferon gamma release, from the blood, is tested against certain mycobacterial proteins. Tuberculin skin tests, although widely performed, produce false negatives and therefore making the IGRAs more favourable in diagnostic capability due to the reduced number of false negatives. Bronchoscopy can also be performed with BAL specimens sent to the laboratory for culture and sensitivity.

General pulmonary

Q12: A 60-year-old woman is evaluated for a 2-month history of progressive exertional dyspnea, low-grade fever, and cough. She has never smoked and has worked all her life as a homemaker. Medical history includes 10-year history of hypertension and a 3-month history of atrial fibrillation. Her medications are hydrochlorothiazide, atenolol, amiodarone, and warfarin. On physical examination, temperature is 37.8°C (100.0°F), blood pressure is 138/78 mm Hg, pulse rate is 92/min, respiration rate is 24/min. Oxygen saturation on pulse oximetry is 94% on ambient air. No evidence of jugular venous distention is seen. Heart sounds are normal without extra cardiac sounds or murmur. Bilateral crackles at the lung bases are noted. No clubbing is noted. Hemoglobin is 11 mg/dL (110 g/L), leukocyte count is 12,800/μL (12.8 × 10⁹/L) with 9% eosinophils. Chest x-ray shows diffuse interstitial infiltrates with basilar predominance.

Which of the following is the most likely diagnosis?

- A. Acute eosinophilic pneumonitis
- B. Asbestosis
- C. Drug-induced lung toxicity
- D. Heart failure

Explanation: The most likely diagnosis is drug-induced lung toxicity. A high index of suspicion for drug-induced lung disease is essential, because early identification and drug withdrawal can prevent morbidity and mortality. Establishment of a definitive diagnosis of drug-induced lung disease requires exclusion of other known causes and symptom improvement with drug withdrawal. Most offending drugs cause a hypersensitivity-type reaction, with presenting symptoms of fatigue, low-grade fever, and cough. Peripheral blood eosinophilia may be present. Amiodarone is a well-known cause of drug-induced lung toxicity, and this diagnosis is supported by the temporal relationship between starting amiodarone for atrial fibrillation and onset of symptoms. The diagnosis of heart failure is unlikely in the absence of orthopnea, jugular venous distention, or an S3. Additionally, heart failure cannot account for the patient's low-grade fever and eosinophilia. Acute eosinophilic pneumonitis is a rapidly progressive illness occurring over days to 3 weeks associated with fever, sputum production, eosinophilia, and a peripherally distributed infiltrate. The patient's subacute illness that began 2 months ago is not consistent with this diagnosis nor is the pattern of infiltrates on her chest x-ray. The term asbestosis refers to bilateral interstitial fibrosis of the lung parenchyma caused by inhalation of asbestos fibers. An exposure history of appropriate duration, latency (typically 20-30 years), and intensity and radiographic evidence of interstitial fibrosis on chest radiograph or chest CT scan are usually sufficient for diagnosis. Symptoms include breathlessness, bibasilar inspiratory crackles, and digital clubbing and pulmonary function testing showing a restrictive pattern. This patient has a subacute process and no history of asbestos exposure, making asbestosis an unlikely diagnosis.

Key Point : Drug-induced lung toxicity typically presents as a hypersensitivity-type reaction, with symptoms of fatigue, low-grade fever, cough, and peripheral eosinophilia.

Q13: A 30-year-old man is admitted to the hospital after a motorcycle accident that resulted in a fracture of the right femur. The fracture is managed with traction. Three days later the patient becomes confused and tachypneic. A petechial rash is noted over the chest. Lungs are clear to auscultation. Arterial blood gases show PO₂ of 50, PCO₂ of 28, and pH of 7.49. Which of the following is the most likely diagnosis?

- A. Unilateral pulmonary edema
- B. Hematoma of the chest
- C. Fat embolism
- D. Pulmonary embolism
- E. Staphylococcus aureus pneumonia

Explanation: Because clinical signs of neurologic deterioration and a petechial rash have occurred in the setting of fracture and hypoxia, fat embolism is the most likely diagnosis. This process occurs when neutral fat is introduced into the venous circulation after bone trauma or fracture. The latent period is 12 to 36 hours. A pulmonary embolus usually has a longer latent period. In addition, pulmonary embolus would not cause the petechial rash. Confusion out of proportion to the degree of hypoxemia is also seen with fat emboli. Unilateral pulmonary edema can be seen with aspiration and after rapid expansion of a pneumothorax, but not with fat embolism. Hematoma of the chest wall can occur after trauma, but does not cause hypoxemia and confusion. An early pneumonia would not be associated with a petechial rash.

General pulmonary

Q14: A 34-year-old man comes to the physician for a follow-up examination. He has a 3-month history of a nonproductive cough. He has been treated with diphenhydramine since his last visit 2 weeks ago, but his symptoms have persisted. He does not smoke. He drinks 3 beers on the weekends. He is 177 cm (5 ft 10 in) tall and weighs 100 kg (220 lb); BMI is 32 kg/m². His temperature is 37.1°C (98.8°F), pulse is 78/min, respirations are 14/min, and blood pressure is 130/80 mm Hg. Pulse oximetry on room air shows an oxygen saturation of 97%. Physical examination and an x-ray of the chest show no abnormalities. Which of the following is the most appropriate next step in management?

- A. Azithromycin therapy
- B. CT scan of the chest
- C. Pulmonary function testing
- D. Oral corticosteroid therapy

Explanation: Patients presenting with a chronic cough (duration > 3 months) are treated empirically for the most common underlying conditions, including upper airway cough syndrome, GERD, and asthma. Since this patient's cough persisted despite treatment with diphenhydramine and he has no symptoms suggestive of GERD, cough-variant asthma is the most likely diagnosis. PFT is the preferred first step in management to detect obstructive lung disease

Q15: A 59-year-old woman comes to the physician because of a 1-month history of episodic cough and shortness of breath. The cough is nonproductive and worsens when she climbs stairs and during the night. She has not had chest pain or palpitations. Eight weeks ago, she had fever, sore throat, and nasal congestion. She has a 10-year history of hypertension. She has smoked half a pack of cigarettes daily for 16 years. Her only medication is enalapril. Her pulse is 78/min, respirations are 18/min, and blood pressure is 145/95 mm Hg. Pulse oximetry on room air shows an oxygen saturation of 96%. Diffuse end-expiratory wheezes are heard on pulmonary auscultation. An x-ray of the chest shows no abnormalities. Spirometry shows an FEV₁:FVC ratio of 65% and an FEV₁ of 60%. Which of the following is the most likely diagnosis?

- A. Pneumonia
- B. Chronic bronchitis
- C. Asthma
- D. α 1-Antitrypsin deficiency

Explanation: This patient likely has new-onset asthma, given her 1-month history of episodic dyspnea, coughing, and wheezing that is worst during exertion and at night. Spirometry showing an obstructive lung pattern (\downarrow FEV₁, \downarrow FEV₁/FVC ratio) also supports this diagnosis. A post-bronchodilator test would confirm the diagnosis of asthma. Although asthma most commonly presents in childhood, it can present at any age, and nonallergic asthma in particular tends to manifest in patients > 40 years. It can be triggered by viral respiratory infections and is exacerbated by exercise, as is the case in this patient