Pulmonary

- In addition, the A-a gradient ($P_AO_2 - P_aO_2$) can help determine the specific cause of hypoxemia. The A-a gradient is a measure of oxygen transfer from the alveoli to the blood. The alveolar oxygen tension can be calculated using the following equation:

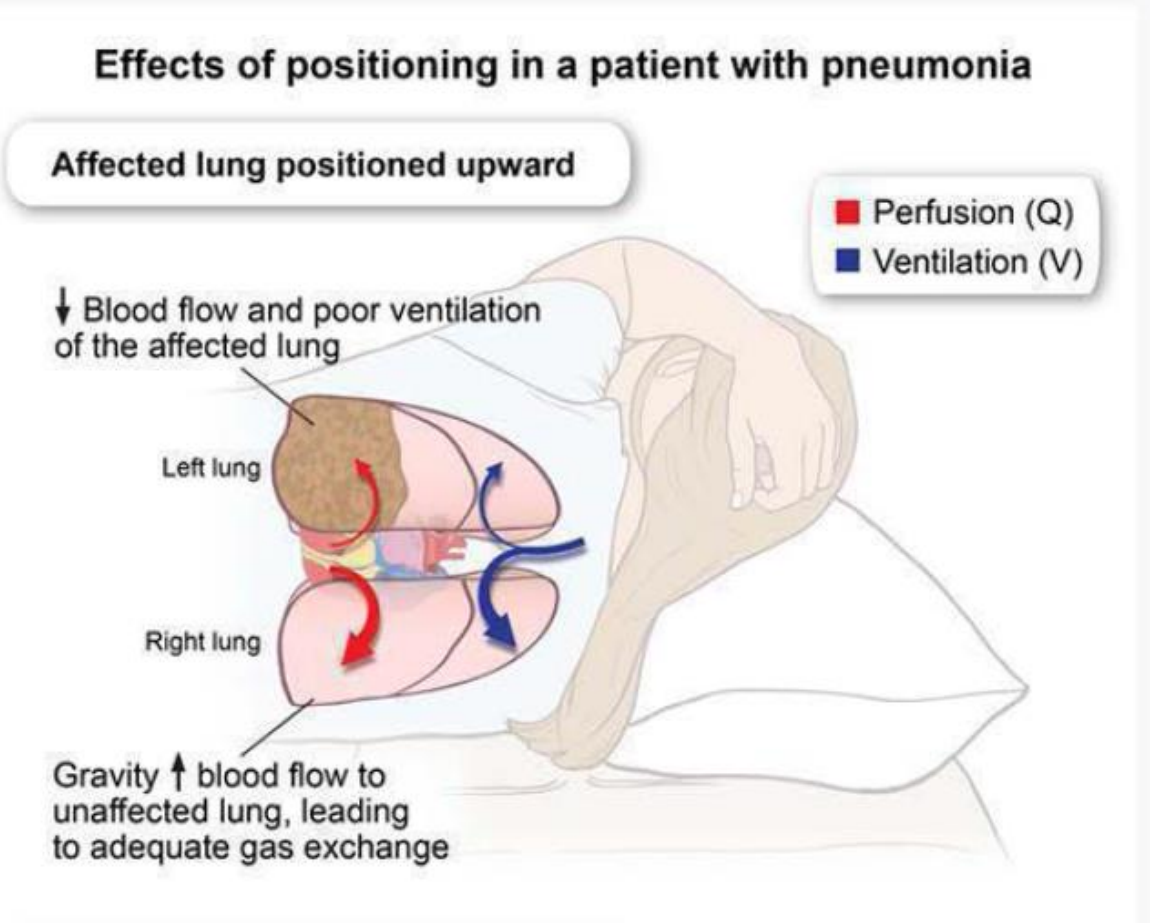
  $$PAO_2 = (FiO_2 \times [Patm - PH_2O]) - (PaCO_2/R) = (0.21 \times [760-47]) - (59/0.8) = 76$$

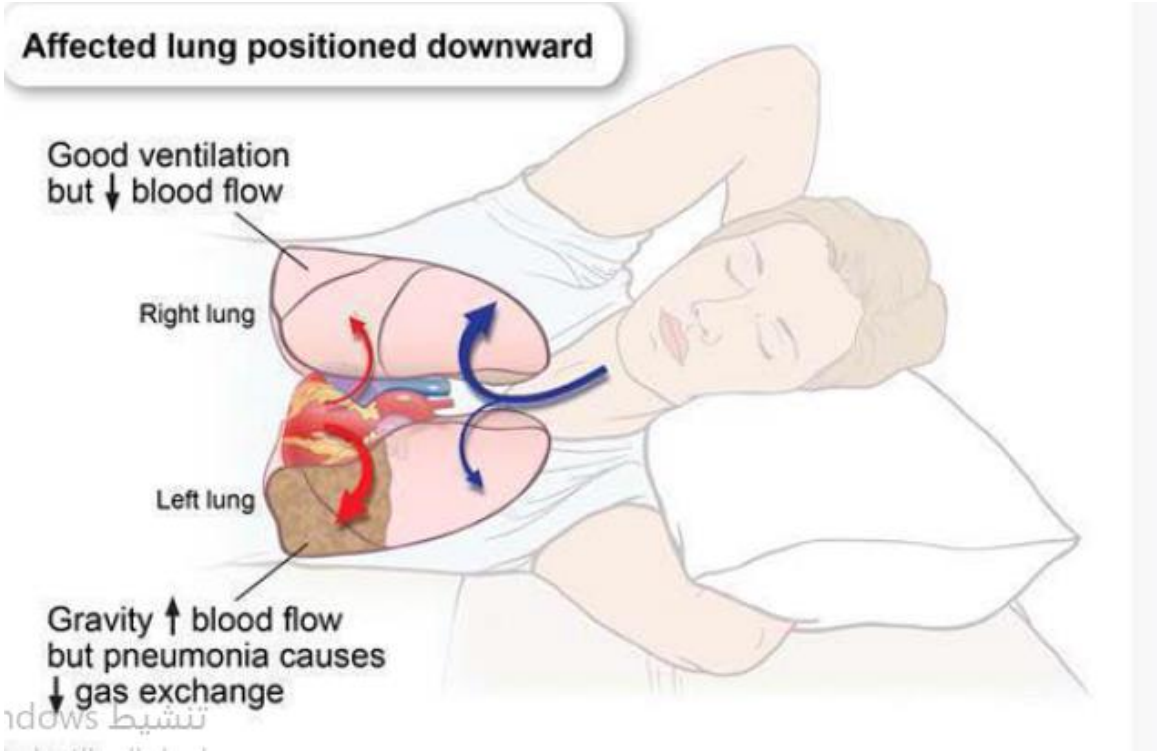
  Then, calculate the A-a gradient:

  $$\text{A-a gradient} = P_AO_2 - P_aO_2 = 76 - 62 = 14$$

  A normal A-a gradient is <15. Values increase with age, but an A-a gradient >30 is considered elevated regardless of age.

  The A-a gradient is normal in patients with reduced inspired oxygen tension and hypoventilation.

- 



- In the normal lung of an upright patient, **V and Q are highest in the bases of the lung** as gravity creates hydrostatic pressure acting on both air and blood. When this patient is lying on his left side, gravity induces an increase in blood flow to the left lung, where there is markedly reduced V due to alveolar consolidation. The result is a more profound **V/Q mismatch** (V remains approximately zero, but Q increases), **increased right-to-left intrapulmonary shunting**, and worsening hypoxemia. The opposite occurs when this patient is lying on his right side (decrease in Q to the area of alveolar consolidation), leading to a more favorable V/Q mismatch and improvement in hypoxemia.
- Measurement of airway pressures can be useful in mechanically ventilated patients. The peak airway pressure (the maximum pressure measured as the tidal volume is being delivered) equals the sum of the resistive pressure (flow x resistance) and the plateau pressure.

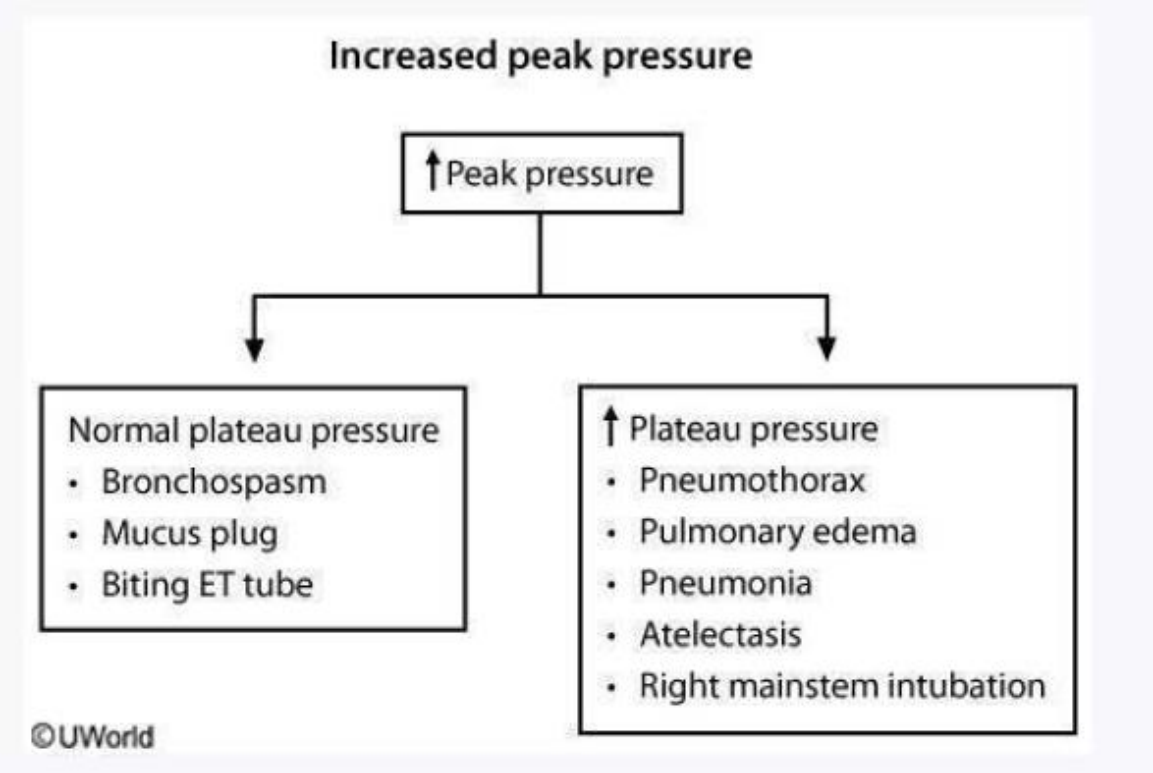
  Peak airway pressure = resistive pressure + plateau pressure

  The plateau pressure is the pressure measured during an inspiratory hold maneuver, when pulmonary airflow and thus resistive pressure are both 0. It represents the sum of the elastic pressure and positive end-expiratory pressure (PEEP).

  Plateau pressure = elastic pressure + PEEP

  Elastic pressure is the product of the lung's elastance and the volume of gas delivered. Because elastic recoil is inversely related to lung compliance, the elastic pressure can be calculated as tidal volume/compliance. Decreased compliance (eg, pulmonary fibrosis) causes stiffer lungs and higher elastic pressure.

  Increased peak pressure associated with an unchanged plateau pressure suggests a pathological process causing increased airway resistance, such as bronchospasm, mucus plug, or endotracheal tube obstruction **(Choice B)**. Elevation of both peak and plateau pressures indicates a process causing decreased pulmonary compliance, such as pulmonary edema, atelectasis, pneumonia, or right mainstem intubation.

- 

Acute respiratory distress syndrome	
Risk factors	• Infection, trauma, massive transfusion, acute pancreatitis
Pathophysiology	• Lung injury → fluid/cytokine leakage into alveoli • Impaired gas exchange, decreased lung compliance, PHTN
Diagnosis	• New/worsening respiratory distress within 1 week of insult • **Bilateral lung opacities** (pulmonary edema) *not* due to CHF/fluid overload • Hypoxemia with **PaO_2/FiO_2 ratio ≤300 mm Hg**
Management	• Mechanical ventilation (eg, low TV, high PEEP, permissive hypercapnia) Low Plateau P <30

Clinical features of acute bronchitis	
Etiology	• Preceding respiratory illness (90% viral)

Clinical presentation	• Cough
	  ◦ >5 days to 3 weeks
	  ◦ Can be productive (yellow, green, or purulent sputum)
	• Absent systemic findings (eg, fever, chills)
	• Wheezing or rhonchi, chest wall tenderness

Diagnosis & treatment	• Diagnosis is clinical
	  ◦ Chest x-ray only in patients with suspected pneumonia
	• Symptomatic treatment
	  ◦ NSAIDs/acetaminophen &/or bronchodilators
	• Antibiotics **not** recommended

- AAT deficiency can also affect the liver (eg, neonatal hepatitis, hepatocellular carcinoma) and skin (panniculitis)
- Smoking-induced centriacinar (centrilobular) emphysema most commonly causes disease in the **upper lobes** of the lungs, whereas the panacinar emphysema of AA T deficiency classically results in greater destruction of the **lower lobes**.
- AAT deficiency should be considered in a number of situations, including in patients with (1COPD at a young age ($45 years); 2) COPD with minimal or no smoking history; 3 basilar-predominant COPD; or 4) a history of unexplained liver disease.

Anaphylaxis	
Triggers	• Food (eg, nuts, shellfish) • Medications (eg, β-lactam antibiotics) • Insect stings

Clinical manifestations	• Cardiovascular
	  ◦ Vasodilation → hypotension & tissue edema
	  ◦ Tachycardia
	• Respiratory
	  ◦ Upper airway edema → stridor & hoarseness
	  ◦ Bronchospasm → wheezing
	• Cutaneous
	  ◦ Urticarial rash, pruritus, flushing
	• Gastrointestinal
	  ◦ Nausea, vomiting, abdominal pain

Treatment	• Intramuscular epinephrine • Airway management & volume resuscitation • Adjunctive therapy (eg, antihistamines, glucocorticoids)

- Intravenous epinephrine is indicated for patients with anaphylaxis who have not responded to initial intramuscular epinephrine. It is not administered initially due to higher risk of adverse effects (eg, cardiac arrhythmia).

	Obstructive lung disease	Restrictive lung disease including obesity
FEV_1	<80%	<80%
FEV_1/FVC	<70%	>70%
FVC	Normal to decreased	<80%

FEV_1= forced expiratory volume in 1 second; FVC= forced vital capacity.

-

Clinical features of asbestosis	
Clinical presentation	• Prolonged asbestos exposure (shipyard, mining & construction workers, pipe fitters) • Symptoms develop ≥20 years after initial exposure • Progressive dyspnea (over months), bibasilar end-inspiratory fine crackles & clubbing • Increased risk for malignancies (lung cancer, malignant mesothelioma)
Diagnostic evaluation	• History & clinical findings of exposure (eg, **pleural plaques** on chest imaging virtually pathognomonic) • Interstitial fibrosis on imaging or histology &/or pulmonary function tests with restrictive pattern • Exclusion of other diseases

	Invasive aspergillosis	Chronic pulmonary aspergillosis*
Risk factors	• Immunocompromise (**neutropenia**, glucocorticoids, HIV)	• Lung disease/damage (**cavitary tuberculosis**)
Findings	• **Triad** of fever, chest pain, hemoptysis • Pulmonary nodules with **halo sign** • Positive cultures • Positive cell wall biomarkers (galactomannan, beta-D-glucan)	• **>3 months:** Weight loss (>90%), cough, hemoptysis, fatigue • Cavitary lesion +/- **fungus ball** • Positive ***Aspergillus* IgG** serology
Management	• Voriconazole +/- caspofungin	• Resect aspergilloma (if possible) • **Azole** medication (voriconazole) • Embolization (if severe hemoptysis)

*Simple aspergilloma (fungus ball in preexisting lung cavity) is a form of chronic pulmonary aspergillosis but is usually quiescent with occasional hemoptysis.

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Predisposing conditions for aspiration pneumonia

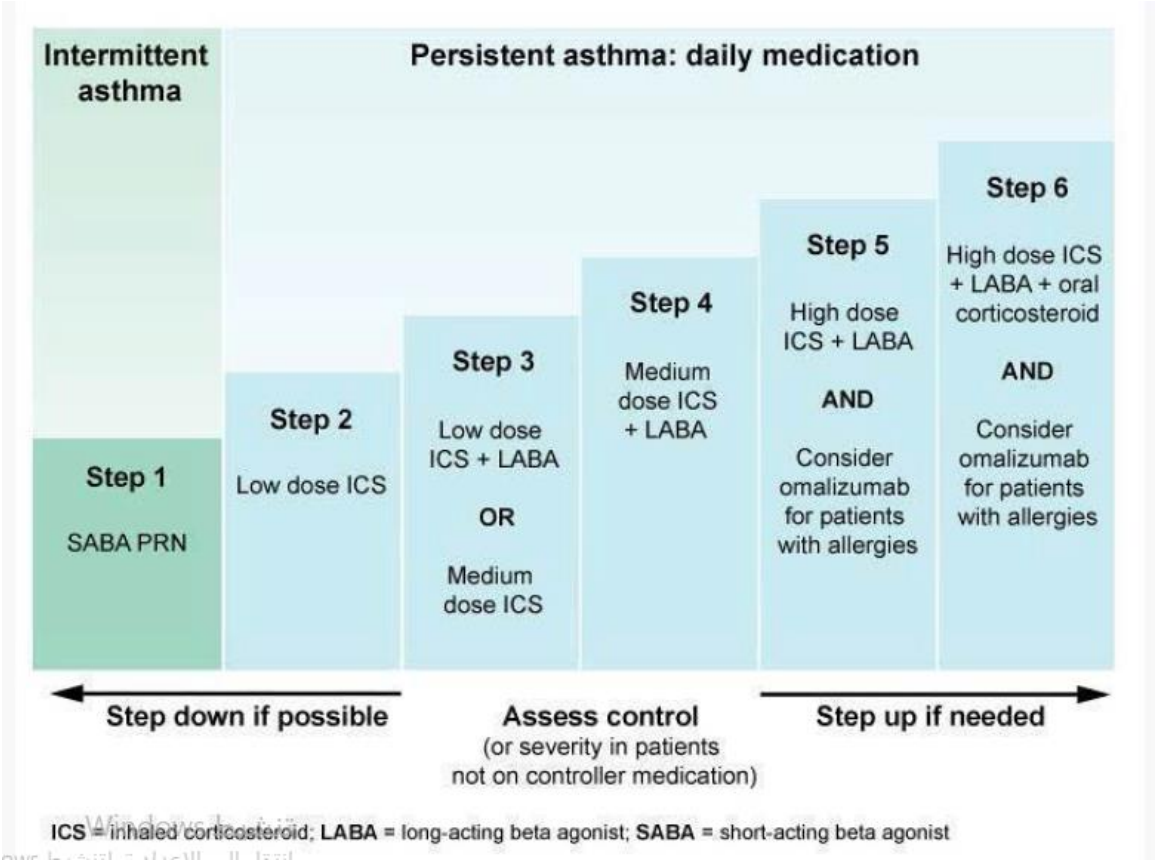
- Altered consciousness impairing cough reflex/glottic closure (eg, dementia, drug intoxication)
- Dysphagia due to neurologic deficits (eg, stroke, neurodegenerative disease)
- Upper gastrointestinal tract disorders (eg, GERD)
- Mechanical compromise of aspiration defenses (eg, nasogastric & endotracheal tubes)
- Protracted vomiting
- Large-volume tube feedings in recumbent position

GERD = gastroesophageal reflux disease.

- Imaging reveals infiltrate in the lower lobes or right middle lobe (aspiration while upright) or the posterior segment of the upper lobes (aspiration while recumbent).

Aspiration syndromes		
	Pneumonia	**Pneumonitis**
Pathophysiology	• Lung parenchyma **infection** • Aspiration of upper airway or stomach **microbes** (anaerobes)	• Lung parenchyma **inflammation** • Aspiration of **gastric acid** with direct tissue injury
Clinical features	• Present **days** after aspiration event • **Fever**, cough, ↑ sputum • CXR infiltrate in dependent lung segment (classically **RLL**) • Can progress to **abscess**	• Present **hours** after aspiration event • Range from no symptoms to nonproductive cough, ↓ O_2, respiratory distress • CXR infiltrates (one or both lower lobes) resolve without antibiotics
Management	**Antibiotics**: Clindamycin or β-lactam & β-lactamase inhibitor	Supportive (no antibiotics)

- **CXR** = chest x-ray; O_2 = oxygen; **RLL** = right lower lobe.



- **ICS** = inhaled corticosteroid; **LABA** = long-acting beta agonist; **SABA** = short-acting beta agonist

Asthma severity for patients not on controller medication			
sthma severity	Symptom frequency/SABA use	Nighttime awakenings	Indicated therapy initiation
Intermittent	≤2 days per week	≤2 times per month	Step 1
Mild persistent	>2 days per week but not daily	3-4 times per month	Step 2
oderate persistent	Daily	>1 time per week but not nightly	Step 3
evere persistent	Throughout the day	4-7 times per week	Step 4 or 5

1. Pulmonary hypertension associated with disorders of the respiratory system, hypoxemia, or both.
2. Pulmonary hypertension due to pulmonary venous hypertension (left ventricular heart disease, mitral valve disease, or pulmonary veno-occlusive disease).
3. Pulmonary hypertension following chronic thromboembolic disease.
4. Pulmonary arterial hypertension (primary pulmonary hypertension, pulmonary hypertension associated with vasculopathy).
5. Pulmonary hypertension due to disorders directly affecting the pulmonary vasculature (pulmonary capillary hemangiomatosis).

- The most common adverse effect associated with the use of any inhaled corticosteroid is oropharyngeal candidiasis (oral thrush).

Educational objective:
Aspirin-exacerbated respiratory disease (AERD) is a non-IgE-mediated reaction that results from aspirin-induced prostaglandin/leukotriene misbalance. It is most often seen in patients with a history of **asthma or chronic rhinosinusitis with nasal polyposis**. AERD is characterized by bronchospasm and nasal congestion following aspirin ingestion. Treatment includes avoidance of nonsteroidal anti-inflammatory drugs (NSAIDs), desensitization if NSAIDs are required, and the use of leukotriene receptor antagonists (eg, montelukast).

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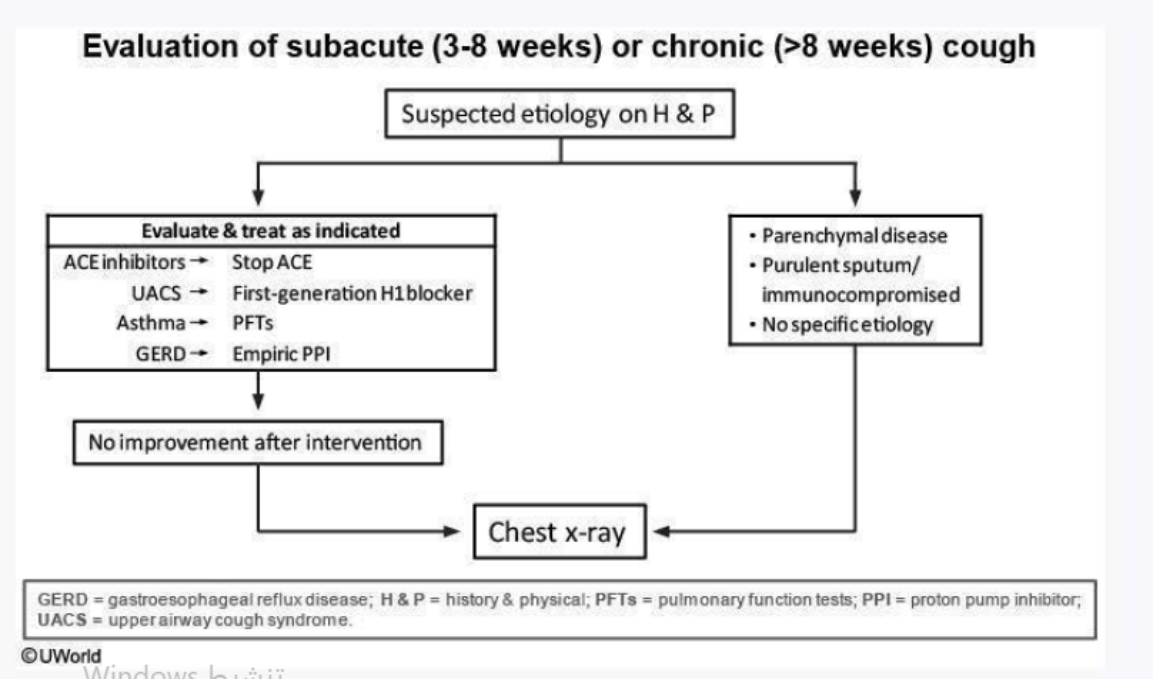
(Choice A) Severe hypoxemia (eg, PaO_2 <60 mm Hg on room air) is relatively rare in an acute asthma exacerbation and suggests a very severe exacerbation or the presence of comorbid pathology (eg, pneumonia). This patient's PaO_2 of 65 mm Hg indicates an expected level of hypoxemia and is not as concerning as the normal $PaCO_2$.

- Bronchiectasis

Signs & symptoms	• Cough with daily mucopurulent sputum production • Rhinosinusitis • Dyspnea, hemoptysis • Wheezing, crackles
Pathophysiology	• Infection PLUS • Impaired bacterial clearance (eg, obstruction of airway, impairment of drainage, defect in immune response)
Etiologies	• Airway obstruction (eg, cancer) • Congenital (eg, cystic fibrosis, alpha-1-antitrypsin deficiency) • Chronic infection (eg, aspergillosis, non-TB mycobacteria) • Immunodeficiency (eg, hypogammaglobulinemia) • Postinfection (eg, TB, necrotizing pneumonia) • Rheumatic disease (eg, RA, Sjögren syndrome) • Toxic inhalation/aspiration
Evaluation	• HRCT scan of the chest (needed for initial diagnosis) • Immunoglobulin quantification • Sweat chloride &/or genetic testing for CF • Sputum culture for bacteria, fungi & mycobacteria • Pulmonary function testing

- Typical symptoms of bronchiectasis include chronic cough with daily production of large amounts of mucopurulent sputum (>100 mUday), dyspnea, sinus congestion, fatigue, weight loss, and hemoptysis.
- In this young patient, the underlying etiology of bronchiectasis is most likely undiagnosed cystic fibrosis (CF).
- **Pseudomonas aeruginosa** is a characteristic finding in the sputum. In addition, upper lung lobe involvement (evidenced by upper lung field crackles and right **upper lobe** infiltrate in this patient) is characteristic of bronchiectasis due to CF and helps differentiate it from bronchiectasis due to other causes.
- 

- Women and individuals of Chinese descent have a higher chance of developing cough due to ACE inhibitor therapy, and a tickling or scratching sensation in the throat (as reported by this patient) is a common feature.
- The 3 most common causes of chronic cough (lasting >8 weeks) are upper-airway cough syndrome (postnasal drip), asthma, and gastroesophageal reflux disease (GERD). Upper-airway cough syndrome is caused by rhinosinus conditions including allergic, perennial nonallergic, and vasomotor rhinitis; acute nasopharyngitis; and sinusitis. Cough is caused by mechanical stimulation of the afferent limb of the cough reflex in the upper airway in these conditions.
- This patient's cough started after a recent upper respiratory infection, occurs primarily at night, and is without expectoration. This history is most consistent with upper-airway cough syndrome (postnasal drip). In some patients, postnasal drip can be "silent" without the classic presentation (eg, liquid dripping into the back of the throat, frequent throat clearing).
- The best diagnostic approach is to treat empirically with an oral first-generation antihistamine (eg, chlorpheniramine) or combined antihistamine-decongestant (eg, brompheniramine and pseudoephedrine). Patients who do not respond after **2-3 weeks** may require further investigation (eg, sinus imaging, pulmonary function tests, high-resolution computed tomography scan of the chest) or empiric sequential therapy for GERD, cough-variant asthma, chronic sinusitis, and non-asthmatic eosinophilic bronchitis **(Choices B, D, and E)**.

Causes of recurrent pneumonia	
Involving same region of lung	**Local airway obstruction** • Extrinsic bronchial compression (eg, neoplasm, adenopathy) • Intrinsic bronchial obstruction (eg, bronchiectasis, foreign body) **Recurrent aspiration** (region may vary depending on body position) • Seizures • Alcohol or drug use • GERD, dysphagia
Involving different regions of lung	• Immunodeficiency (eg, HIV, leukemia, CVID) • Sinopulmonary disease (eg, cystic fibrosis, immotile cilia) • Noninfectious (eg, vasculitis, BOOP)

-

Pulmonary auscultation examination findings				
Condition	**Breath sounds**	**Tactile fremitus**	**Percussion**	**Mediastinal shift**
Normal lung	Bronchovesicular (hilar), vesicular (peripheral)	Normal	Resonance	None
Consolidation (eg, lobar pneumonia)	Increased (crackles & egophony present)	Increased	Dullness	None
Pleural effusion	Decreased or absent	Decreased	Dullness	Away from effusion (if large)
Pneumothorax	Decreased or absent	Decreased	Hyperresonant	Away from tension pneumothorax
Emphysema	Decreased	Decreased	Hyperresonant	None
Atelectasis (eg, mucus plugging)	Decreased or absent	Decreased	Dullness	Toward atelectasis (if large)

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Obstructive sleep apnea	
Pathophysiology	• Relaxation of pharyngeal muscles leads to closure of airway • Loud snoring with periods of apnea
Symptoms	• Daytime somnolence • Non-restorative sleep with frequent awakenings • Morning headaches • Affective & cognitive symptoms
Sequelae	• Systemic hypertension • Pulmonary hypertension & right heart failure

-

Causes of hypoxemia			
	Example	**A-a gradient**	**Corrects with supplemental O_2?**
Reduced PiO_2	High altitude	Normal	Yes
Hypoventilation	CNS depression, neuromuscular weakness	Normal	Yes
V/Q mismatch	Emphysema, ILD, pulmonary embolism	Increased	Yes
Diffusion limitation	Emphysema, ILD	Increased	Yes
Intrapulmonary shunt	Pneumonia, pulmonary edema, atelectasis	Increased	No
Intracardiac shunt (right to left)	Tetralogy of Fallot, Eisenmenger syndrome	Increased	No

- **A-a gradient** = alveolar to arterial oxygen gradient; **CNS** = central nervous system; **ILD** = interstitial

- The A-a gradient is elevated if it is higher than the expected A-a gradient on room air, estimated by (2.5 + [0.21 × patient age]) or (patient age/4 + 4). A-a gradient elevation occurs in processes that cause impaired gas exchange.

Long-term supplemental oxygen therapy (LTOT) has demonstrated **prolonged survival** and improved quality of life in patients with COPD with significant chronic hypoxemia. The criteria for initiating LTOT in such patients include:

1. Resting arterial oxygen tension (PaO_2) ≤55 mm Hg or pulse oxygen saturation (SaO_2) ≤88% on room air
2. PaO_2 ≤59 mm Hg or SaO_2 ≤89% in patients with cor pulmonale, evidence of right heart failure, or **hematocrit >55%** (as in this patient)

- Atrial fibrillation (eg, irregular RR intervals, absent P waves, narrow QRS complexes) is associated with **PE** and may be caused by atrial strain from increased right atrial pressure. **Low oxygen saturation and atrial fibrillation are associated with poor prognosis in PE.**

Acute exacerbation of chronic obstructive pulmonary disease	
Cardinal symptoms	• Increased dyspnea • Increased cough (more frequent or severe) • Sputum production (change in color or volume)
Diagnostic testing	• Chest x-ray: Hyperinflation • ABG: Hypoxia, CO_2 retention (chronic &/or acute)
Management	• Oxygen (target SpO_2 of 88%-92%) • Inhaled bronchodilators • Systemic glucocorticoids • Antibiotics if ≥2 cardinal symptoms • Oseltamivir if evidence of influenza • NPPV if ventilatory failure • Tracheal intubation if NPPV failed or contraindicated

ABG = arterial blood gas; **NPPV** = noninvasive positive-pressure ventilation; **SpO_2** = peripheral oxygen saturation.

Noninvasive positive-pressure ventilation	

Indications (strongest evidence)	• COPD (severe exacerbation, prevent extubation failure)
	• Cardiogenic pulmonary edema
	• Acute respiratory failure
	  ○ Postoperative hypoxemic respiratory failure
	  ○ Immunosuppressed patients
	• Facilitate early extubation

Contraindications	**Medical instability**
	• Cardiac or respiratory arrest (or impending arrest)
	• Severe acidosis (pH <7.10)
	• Acute respiratory distress syndrome
	• Non-respiratory organ failure
	  ○ Unstable cardiac arrhythmia/hemodynamic instability
	  ○ Encephalopathy (Glasgow Coma Score <10)
	  ○ Gastrointestinal bleed
	Inability to protect airway
	• Uncooperative or agitated
	• Inability to clear secretions/high aspiration risk
	Mechanical issues
	• Recent esophageal anastomosis
	• Facial or neurological surgery, deformity, or trauma
	• Upper airway obstruction

- **Noninvasive positive-pressure ventilation (NPPV)** is ventilatory support delivered by facemask rather than endotracheal tube; it can be delivered in several different modes, including continuous positive airway pressure and bilevel positive airway pressure. NPPV decreases work of breathing, improves alveolar ventilation, and is the preferred method of respiratory support in patients with AECOPD. Physiologic benefits include a decrease in respiratory rate and arterial carbon dioxide tension ($PaCO_2$), with an increase in tidal volume, minute ventilation, and arterial oxygen tension (PaO_2). NPPV in patients with AECOPD is associated with a decrease in mortality, intubation rate, treatment failure, length of hospital stay, and incidence of nosocomial infection.
- If this patient fails a 2-hour trial of NPPV (eg, hypoxemia, severe respiratory distress, and/or acidosis), intubation would be considered.

- The patient's symptoms are consistent with theophylline toxicity. Theophylline has a narrow therapeutic index, and toxicity can occur from accumulation by reduced clearance or decreased metabolism due to saturation of metabolic pathways. Theophylline is metabolized predominantly by the cytochrome oxidase system in the liver. Inhibition of these enzymes by concurrent illness (eg, cirrhosis, cholestasis, respiratory infections with fever) or drugs (eg, cimetidine, ciprofloxacin, erythromycin, clarithromycin, verapamil) can raise serum concentration and cause toxicity.

  Symptoms of toxicity usually manifest as **central nervous system stimulation** (eg, headache, insomnia, seizures), gastrointestinal disturbances (eg, nausea, vomiting), and **cardiac toxicity** (arrhythmia). This patient recently began taking ciprofloxacin, a drug known to decrease clearance of theophylline. Therefore, the best next step is to measure serum theophylline levels to assess for toxicity.
- The dose of supplemental oxygen should be titrated so that SaO_2 is maintained at >90% during sleep, normal waking, and at rest. Survival benefits of home oxygen therapy are significant when it is used for ≥15 hours a day.
- Upper respiratory infection (URI) is the most common trigger of COPD exacerbation; in this patient, URI is suggested by the 1-week history of low grade *fever,* runny nose, and productive cough
Pulmonary contusion	
Clinical features	• Present **<24 hours** after blunt thoracic trauma • Tachypnea, tachycardia, **hypoxia**
Diagnosis	• Rales or decreased breath sounds • CT scan (most sensitive) or CXR with patchy, alveolar infiltrate **not restricted by anatomical borders**
Management	• Pain control • Pulmonary hygiene (eg, nebulizer treatment, chest PT) • Supplemental oxygen & ventilatory support

- In Pulmonary contusion , Administration of large volumes of intravenous fluid may worsen the underlying pulmonary edema.

Hyperinflation in COPD occurs through both static and dynamic mechanisms. The negative pressure created by the chest wall (expanding pressure) and the positive pressure created by the lungs (collapsing pressure) are in equilibrium at the functional residual capacity (FRC). In COPD, **decreased elasticity** of the alveoli results in decreased positive pressure created by the lungs to expel air. Consequently, the alveoli retain more air volume. At the increased lung volume, the chest wall generates more recoil pressure (less negative expanding pressure), which compensates for the lung's decrease in positive collapsing pressure. New pressure equilibrium is reached at a **higher lung volume** (higher FRC).

The dynamic mechanism is comparatively more responsible for hyperinflation in COPD. It occurs through a phenomenon of "**air stacking**." The expiratory phase is prolonged in patients with COPD due to an increase in airway resistance. When exertional demands trigger an increase in minute ventilation (breaths per minute × tidal volume), the patient is forced to begin inhalation prior to completion of exhalation. The result is additional air trapping and hyperinflation.

The diaphragm is the most important muscle for enlarging the thoracic cavity and creating negative pressure during inhalation. In COPD, the **diaphragmatic flattening** and muscular shortening caused by hyperinflation result in more difficulty in decreasing intrathoracic pressure during inspiration and therefore **increase the work of breathing**.

-

Glucocorticoid use causes a leukocytosis due to the following:

- **Mobilization of marginated neutrophils** into the bloodstream (predominant mechanism): Marginated neutrophils are attached to the endothelium of blood vessels; glucocorticoid-induced mobilization of these neutrophils leads to a higher number of circulating neutrophils
- Stimulation of release of immature neutrophils from the bone marrow (as evidenced by the 3% band forms in this patient)
- Inhibition of neutrophil apoptosis

In contrast, glucocorticoids decrease the number of circulating lymphocytes and eosinophils through a combination of increased apoptosis, increased emigration into the tissues, and decreased production.

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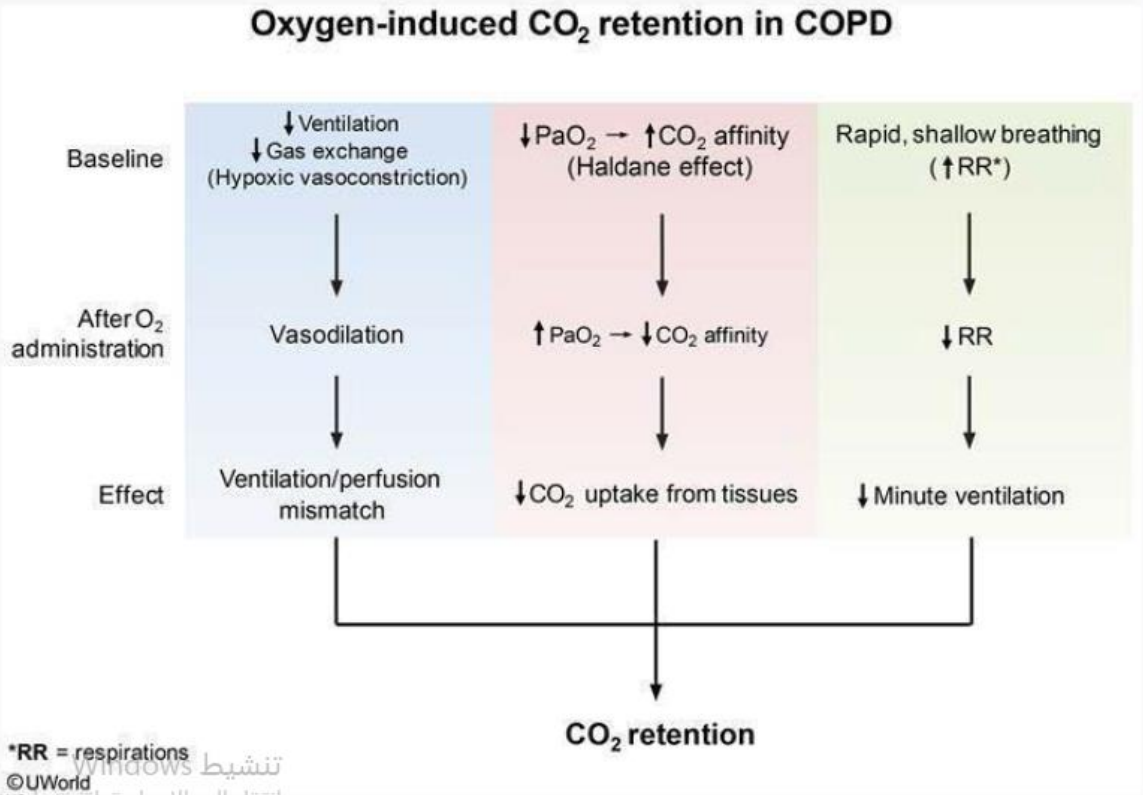

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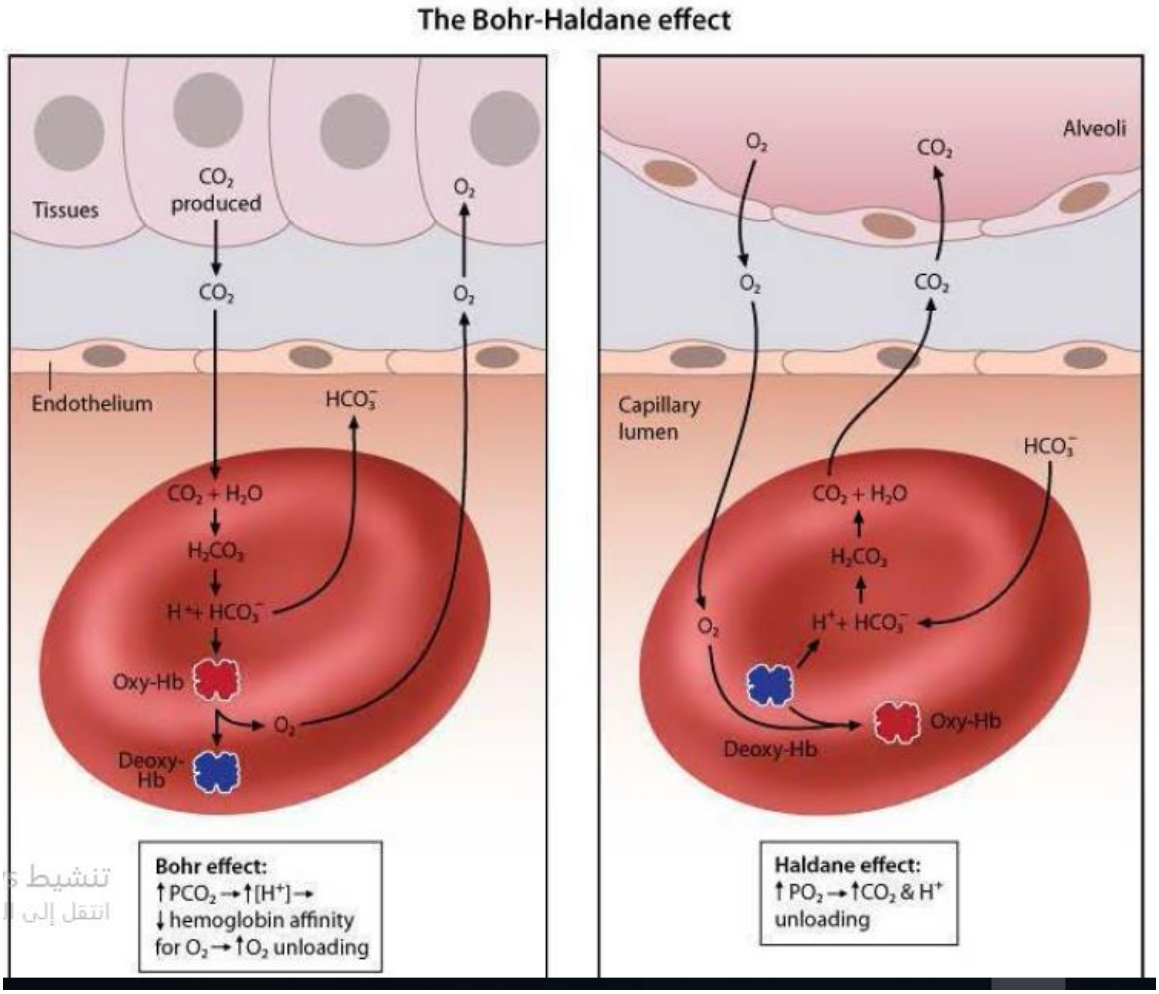
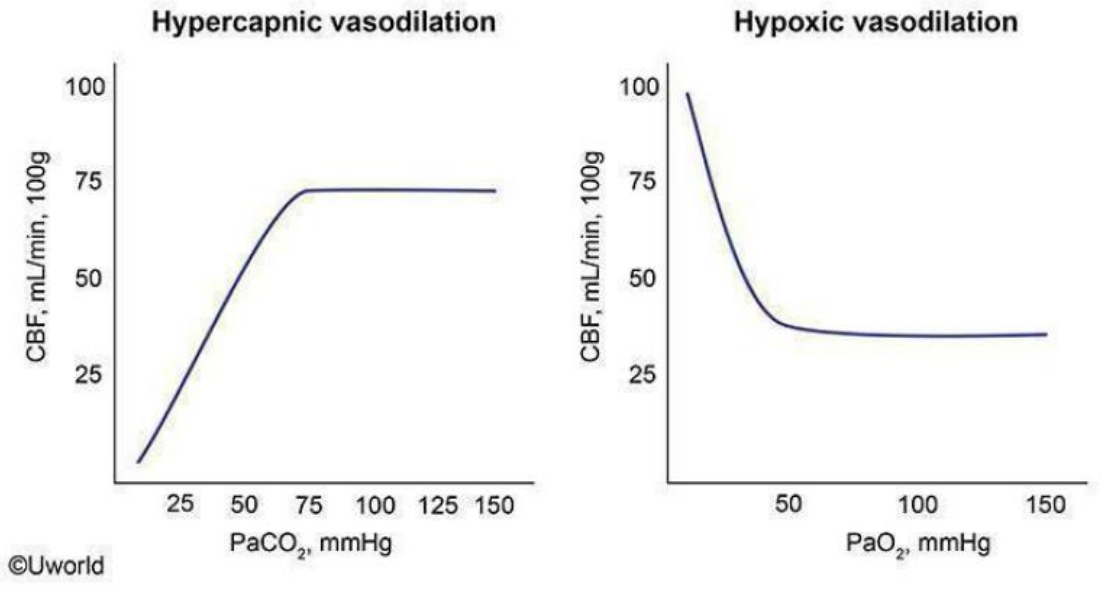
- The acidosis caused by an acute increase in CO_2 increases brain gamma-amino butyric acid and glutamine and decreases brain glutamate and aspartate, causing a change in level of consciousness. Hypercapnia also causes reflex cerebral vasodilation and may induce seizures, as seen in this patient **(Choice B)**. Oxygen should be used cautiously with a goal SaO_2 of 90%-93% or PaO_2 60-70 mm Hg. Patients who develop significant acidosis or have severely reduced level of consciousness require mechanical ventilation.

- 

- 

Characteristic findings of cor pulmonale	
Common etiologies	• COPD (most common) • Interstitial lung disease • Pulmonary vascular disease (eg, thromboembolic) • Obstructive sleep apnea
Symptoms	• Dyspnea on exertion, fatigue, lethargy • Exertional syncope (due to ↓ cardiac output) • Exertional angina (due to ↑ myocardial demand)
Examination	• Peripheral edema • ↑ Jugular venous pressure with prominent *a* wave • Loud S2 • Right-sided heave • Pulsatile liver from congestion • Tricuspid regurgitation murmur
Imaging	• **Electrocardiogram (ECG)**: Partial or complete right bundle branch block, right axis deviation, right ventricular hypertrophy, right atrial enlargement • **Echocardiogram**: Pulmonary hypertension, dilated right ventricle, tricuspid regurgitation • **Right heart catheterization**: Gold standard for diagnosis showing right ventricular dysfunction, pulmonary hypertension & no left heart disease

	Uncomplicated parapneumonic effusion	Empyema
Etiology	Movement of fluid from pneumonia into visceral pleura	Bacterial colonization, purulent fluid
Pleural fluid analysis	• pH >7.2 • ↓ to normal glucose • WBC <50,000/mm^3	• pH <7.2 • ↓ glucose • WBC >50, 000/mm^3
Pleural fluid Gram stain/culture	Negative	Positive
Treatment	Antibiotics	Antibiotics + drainage
WBC = white blood cell count.		

- Pleural effusions occur in about 40% of patients with pneumonia.

Granulomatosis with polyangiitis	
Clinical manifestations	• Upper respiratory: Sinusitis/otitis, saddle-nose deformity • Lower respiratory: Lung nodules/cavitation • Renal: Rapidly progressive GN • Skin: Livedo reticularis, nonhealing ulcers
Diagnosis	• ANCA: PR3 (~70%), MPO (~20%) • Biopsy: o Skin (leukocytoclastic vasculitis) o Kidney (pauci-immune GN) o Lung (granulomatous vasculitis)
Management	• Corticosteroids & immunomodulators (eg, MTX, cyclophosphamide)

ANCA = antineutrophil cytoplasmic antibody; **GN** = glomerulonephritis; **MPO** = myeloperoxidase; **MTX** = methotrexate; **PR3** = proteinase-3.

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Causes of hemoptysis	
Pulmonary	• Bronchitis • Lung cancer • Bronchiectasis
Cardiac	• Mitral stenosis/acute pulmonary edema
Infectious	• Tuberculosis • Lung abscess • Bacterial pneumonia • Aspergillosis
Hematologic	• Coagulopathy
Vascular	• Pulmonary embolism • Arteriovenous malformation
Systemic disease	• Granulomatosis with polyangiitis • Goodpasture syndrome
Other	• Trauma • Cocaine use (inhalation)

-
- Burn victims are at high risk for respiratory compromise because the **supraglottic** airway, which efficiently exchanges heat with inhaled air, is very susceptible to direct thermal injury and acute obstruction by edema

and blistering. (In contrast, the **subglottic** airway is protected from injury by reflexive closure of the vocal cords upon exposure to extremely hot air.)

- Adult-onset asthma tends to be more severe and less likely to go into remission.
- The DLCO in asthma is usually normal or increased (severe asthma). It is never increased in patients with COPD (though it may be normal in early chronic bronchitis).

Asthma versus COPD			
	Asthma	**COPD**	**Late-stage COPD**
FVC	Normal/↓	Normal/↓	↓/↓↓
FEV_1	↓	↓	↓↓
FEV_1/FVC	↓	↓	↓↓
Bronchodilator response	Reversible	Partially/ nonreversible	Usually nonreversible
Chest x-ray	Normal	Normal	Hyperinflation, loss of lung markings
DLCO	Normal/↑	Normal/↓	↓

- Hypertrophic osteoarthropathy (HOA) is a condition where digital clubbing is accompanied by sudden-onset arthropathy, commonly affecting the wrist and hand joints. Hypertrophic pulmonary osteoarthropathy (HPOA) is a subset of HOA where the clubbing and arthropathy are attributable to underlying lung disease like lung cancer, tuberculosis, bronchiectasis, or emphysema.

Clinical features of hypothermia	
Classification	**Mild:** 32-35 C (90-95 F) • Tachycardia, tachypnea • Ataxia, dysarthria, **increased shivering** **Moderate:** 28-32 C (82-90 F) • Bradycardia, lethargy, hypoventilation, **decreased shivering**, atrial arrhythmias **Severe:** <28 C (82 F) • Coma, cardiovascular collapse, ventricular arrhythmias
Treatment	**General** • Warmed (42 C [107 F]) crystalloid for hypotension • Endotracheal intubation in comatose patients **Rewarming techniques** • **Mild hypothermia**: Passive external warming (remove wet clothing, cover with blankets) • **Moderate hypothermia**: Active external warming (warm blankets, heating pads, warm baths) • **Severe hypothermia**: Active internal rewarming (warmed pleural or peritoneal irrigation, warmed humidified oxygen)

Clinical features of interstitial lung disease	
Common etiologies	• Sarcoidosis, amyloidosis, alveolar proteinosis • Vasculitis (eg, granulomatosis with polyangiitis) • Infections (eg, fungal, tuberculosis, viral pneumonia) • Occupational & environmental agents (eg, silicosis, hypersensitivity pneumonitis) • Connective tissue disease (eg, systemic lupus erythematous, scleroderma) • Idiopathic pulmonary fibrosis, interstitial pneumonia • Cryptogenic organizing pneumonia
Clinical presentation	• Progressive exertional dyspnea or persistent dry cough • Pulmonary findings due to other underlying conditions (eg, silicosis, connective tissue disease) • >50% of patients with significant smoking history • Lung examination with fine crackles during mid-late inspiration, possible digital clubbing

Laboratory/ Imaging	• Chest x-ray can show reticular or nodular opacities • High-resolution chest computed tomography usually shows fibrosis, honeycombing, or traction bronchiectasis • **Pulmonary function tests:** Normal or ↑FEV1/FVC ratio, ↓DLCO, ↓TLC, ↓RV* • Resting arterial blood gas can be normal or show mild hypoxemia • Exertion usually causes significant hypoxemia due to V/Q mismatch
***FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; DLCO, diffusion lung capacity of carbon monoxide; TLC, total lung capacity; RV, residual volume.**	

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Clinical presentation of Pancoast tumors

• Shoulder pain (most common)
• Horner syndrome (ipsilateral ptosis, miosis, enophthalmos & anhidrosis) from involvement of paravertebral sympathetic chain & inferior cervical ganglion
• C8-T2 neurological involvement
  ○ Weakness &/or atrophy of intrinsic hand muscles
  ○ Pain & paresthesias of 4th & 5th digits, medial arm & forearm
• Supraclavicular lymph node enlargement
• Weight loss

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- Patients with a clinical presentation and ANCA studies consistent with GPA may be initiated on therapy (high-dose corticosteroids and immunomodulators/cytotoxic agents) prior to confirmatory tissue biopsy

Type of tumor	Incidence	Location	Clinical associations
Adenocarcinoma	40%-50%	• Peripheral	• Clubbing • Hypertrophic osteoarthropathy
Squamous cell carcinoma	20%-25%	• Central • Necrosis & cavitation	• Hypercalcemia
Small cell carcinoma	10%-15%	• Central	• Cushing syndrome • SIADH • Lambert-Eaton syndrome
Large cell carcinoma	5%-10%	• Peripheral	• Gynecomastia • Galactorrhea

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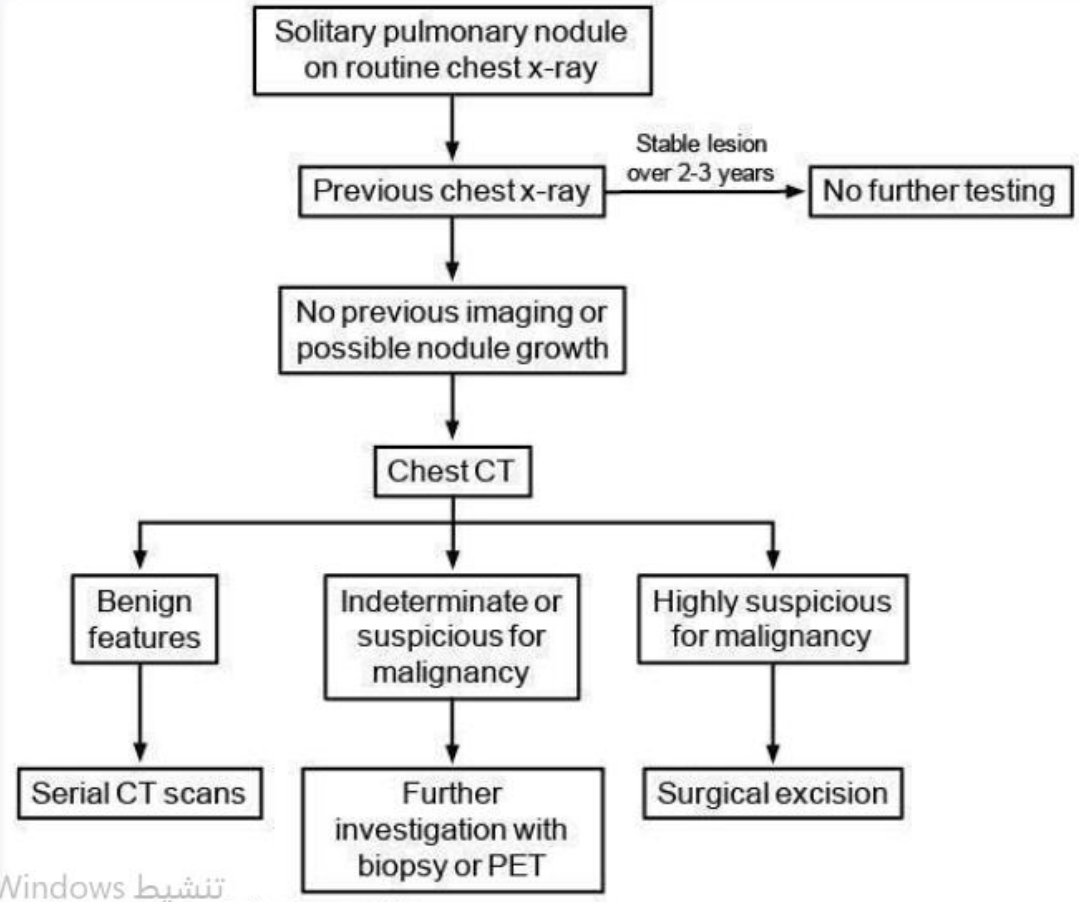
- Squamous cell lung carcinoma and lung adenocarcinoma are the most common SPS tumors, and smoking is the strongest risk factor.

Conditions commonly associated with digital clubbing	
Intrathoracic neoplasms	• Bronchogenic carcinoma • Metastatic cancers • Malignant mesothelioma • Lymphoma
Intrathoracic suppurative diseases	• Lung abscess • Empyema • Bronchiectasis • Cystic fibrosis • Chronic cavitary infections (eg, fungal, mycobacterial)
Lung disease	• Idiopathic pulmonary fibrosis • Asbestosis • Pulmonary arterio-venous malformations
Cardiovascular disease	• Cyanotic congenital heart disease

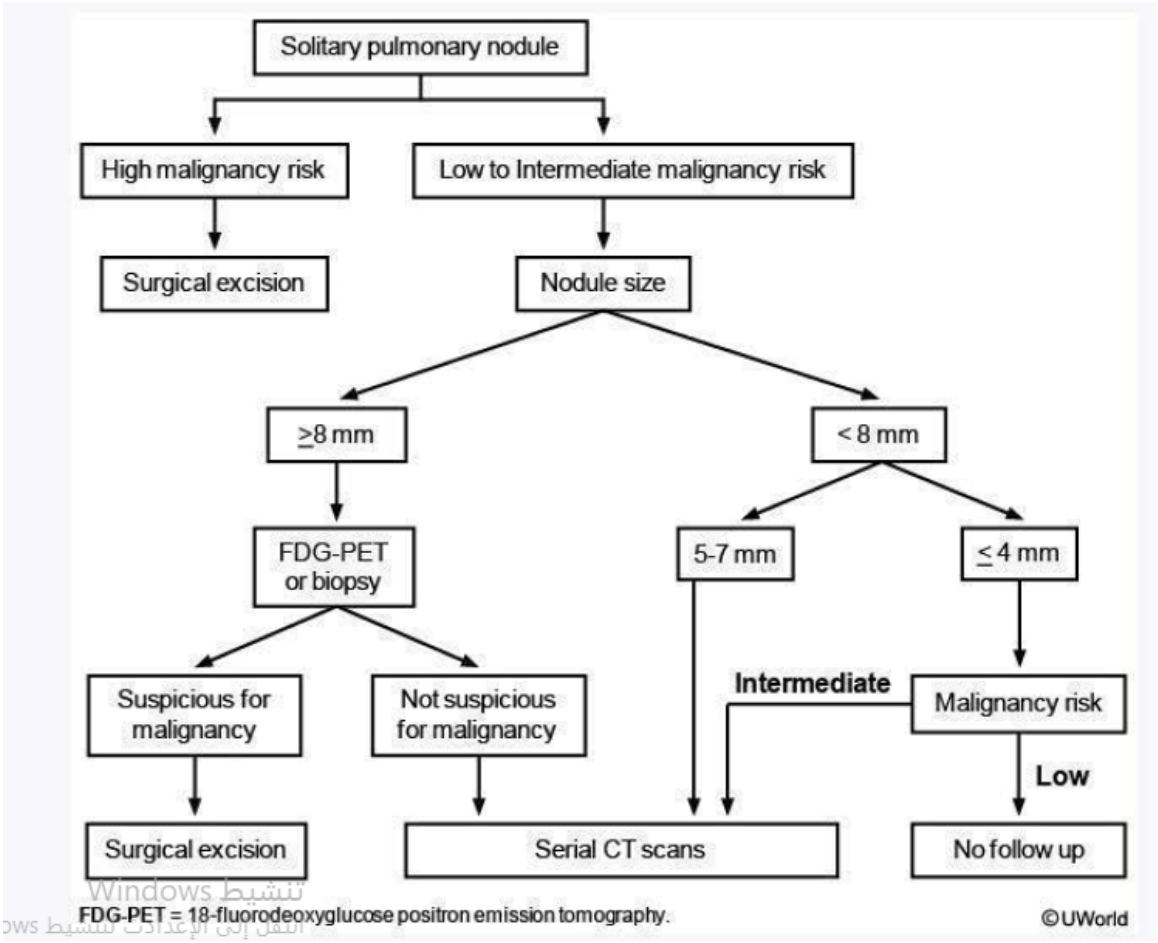
- **Digital clubbing** describes bulbous enlargement and broadening of the fingertips due to connective tissue proliferation at the nail bed and distal phalanx. It is diagnosed when the angle between the nail fold and the nail plate is >180° (**Lovibond angle**). Clubbing can occur by itself or associated with hypertrophic osteoarthropathy, which presents with painful joint enlargement, periostosis of long bones, and synovial effusions. Clubbing may be hereditary, but is most often due to pulmonary or cardiovascular diseases. The most common causes of secondary clubbing are **lung malignancies**, **cystic fibrosis**, and right-to-left cardiac shunts.

  Pathophysiology involves megakaryocytes that skip the normal route of fragmentation within pulmonary circulation (due to circulatory disruption from tumors, chronic lung inflammation) to enter systemic circulation. Megakaryocytes become entrapped in the distal fingertips due to their large size and release platelet-derived growth factor (PDGF) and vascular endothelial growth factor (VEGF). PDGF and VEGF have growth-promoting properties that increase connective tissue hypertrophy and capillary permeability and vascularity, ultimately leading to clubbing.



PET = positron emission tomography.

Assessment of malignancy risk for solitary pulmonary nodule			
Variable	**Low risk**	**Intermediate risk**	**High risk**
Nodule size (cm)	<0.8	0.8-2.0	≥2.0
Age (yr)	<40	40-60	>60
Smoking status	Never smoked	Current	Current
Smoking cessation (yr)	>15	5-15	<5
Nodule margin characteristics	Smooth	Scalloped	Corona radiata or spiculated

- 

Differential diagnosis based on carbon monoxide diffusing capacity of the lung			
	Obstructive pattern (FEV1/FVC <70% predicted)	**Restrictive pattern (FEV1/FVC >70% predicted, FVC <80% predicted)**	**Normal spirometry**
Low DLCO	• Emphysema	• Interstitial lung diseases • Sarcoidosis • Asbestosis • Heart failure	• Anemia • Pulmonary embolism • Pulmonary hypertension
Normal DLCO	• Chronic bronchitis • Asthma	• Musculoskeletal deformity • Neuromuscular disease	
Increased DLCO	• Asthma	• Morbid obesity	• Pulmonary hemorrhage • Polycythemia

- The DLCO, which measures gas exchange between the alveoli and pulmonary capillary blood, remains normal in chronic bronchitis (intact alveolar and capillary structures), but the alveolar destruction that occurs in emphysema results in decreased DLCO.

Obesity hypoventilation syndrome	
Diagnostic criteria	• Obesity with BMI ≥30 kg/m^2 • Awake daytime hypercapnia ($PaCO_2$ >45 mm Hg) • No alternate cause of hypoventilation
Workup	• ABG on room air (hypercapnia, normal A-a gradient) • No intrinsic pulmonary disease on chest x-ray • Restrictive pattern on PFTs • Normal TSH • Polysomnography
Treatment	• Nocturnal positive-pressure ventilation as first-line therapy • Weight loss (bariatric surgery in select cases) • Avoidance of sedative medications • Respiratory stimulants (eg, acetazolamide) as last resort

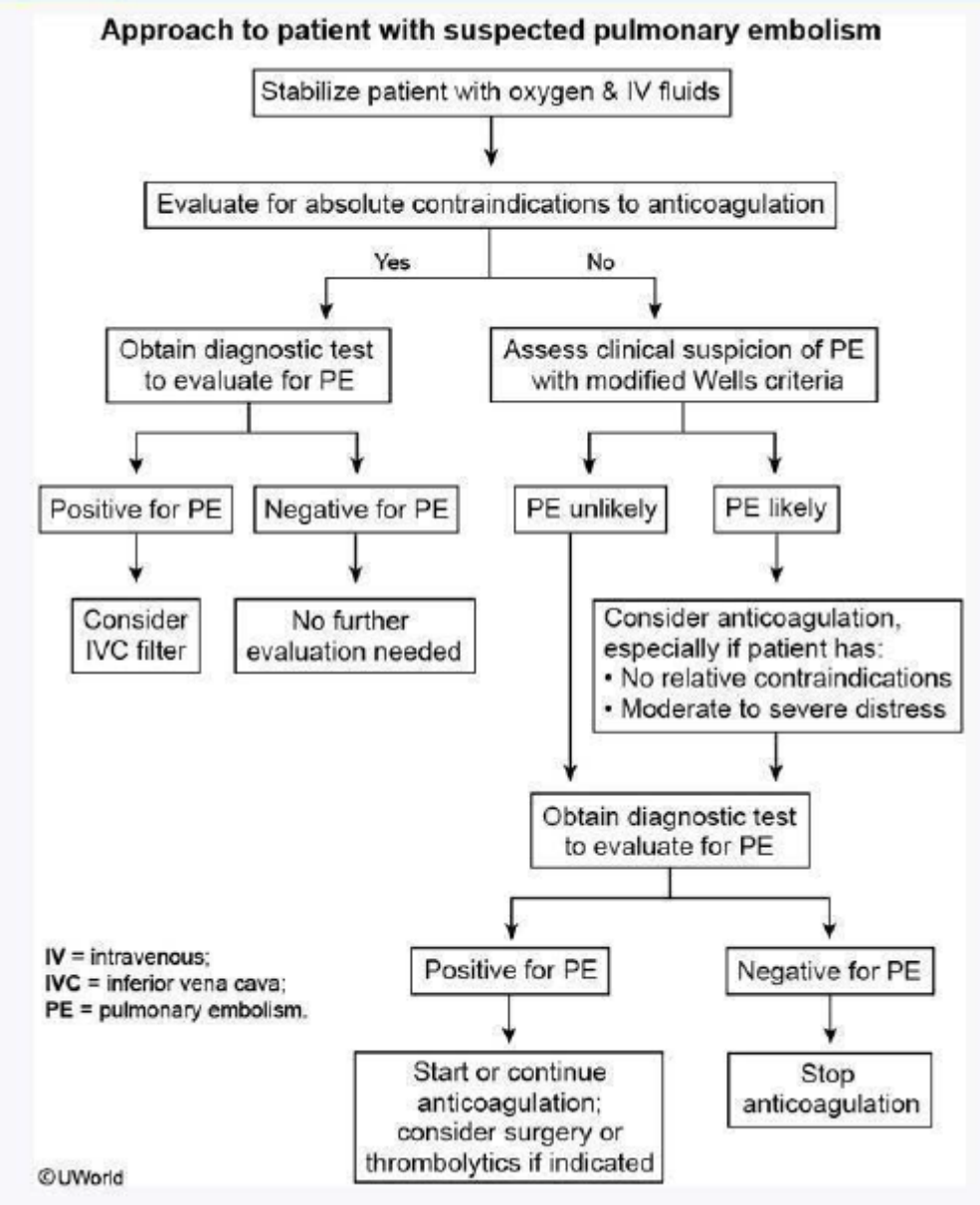
ABG = arterial blood gas; PFT = pulmonary function test

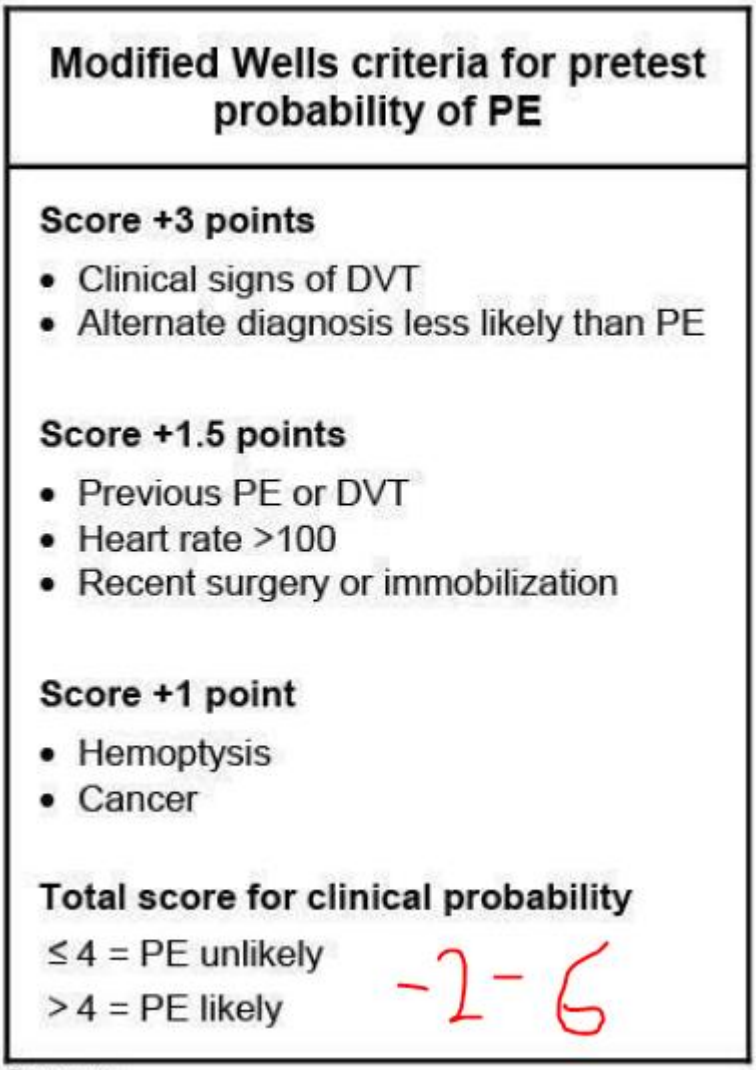
- Therefore, in this patient, the Fi0 2 should be slowly decreased to <60% to prevent oxygen toxicity to the lungs.

Obstructive sleep apnea	
Pathophysiology	• Relaxation of pharyngeal muscles leads to closure of airway • Loud snoring with periods of apnea
Symptoms	• Daytime somnolence • Non-restorative sleep with frequent awakenings • Morning headaches • Affective & cognitive symptoms
Sequelae	• Systemic hypertension • Pulmonary hypertension & right heart failure

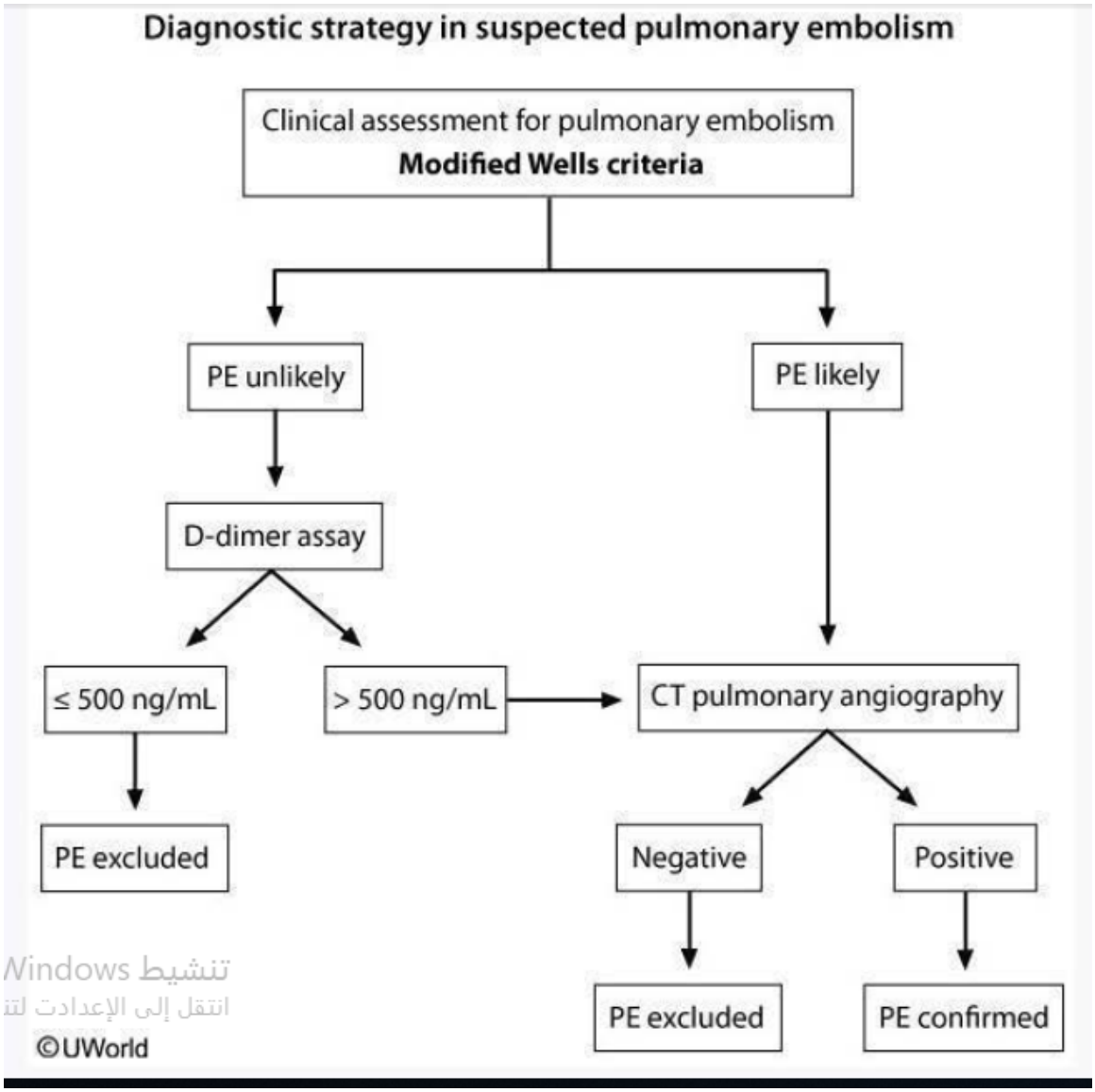
When OSA is suspected, **nocturnal polysomnography** is the gold standard for diagnosis. Polysomnography determines the frequency of abnormal ventilation events that occur during sleep. There are 2 types of abnormal ventilation during sleep: apnea (cessation of breathing for ≥10 seconds) and hypopnea (reduced airflow causing SaO_2 to decrease by ≥4%). Experiencing ≥15 obstructive respiratory events (apneas or hypopneas) per hour is diagnostic of OSA. 5 - 15 - 30

- Pleural fluid analysis provides decision-making information in 90% of cases. If a diagnostic thoracentesis shows exudative pleural fluid, further diagnostic investigations are indicated.
- Lung carcinoma, breast carcinoma, and lymphoma are the three tumors that cause approximately 75% of all malignant pleural effusions.
- Massive PE is defined as PE complicated by hypotension and/or acute right heart strain.
- Jugular venous distension on physical examination and right bundle branch block (RBBB) on electrocardiogram (ECG) are signs of acute right heart strain.

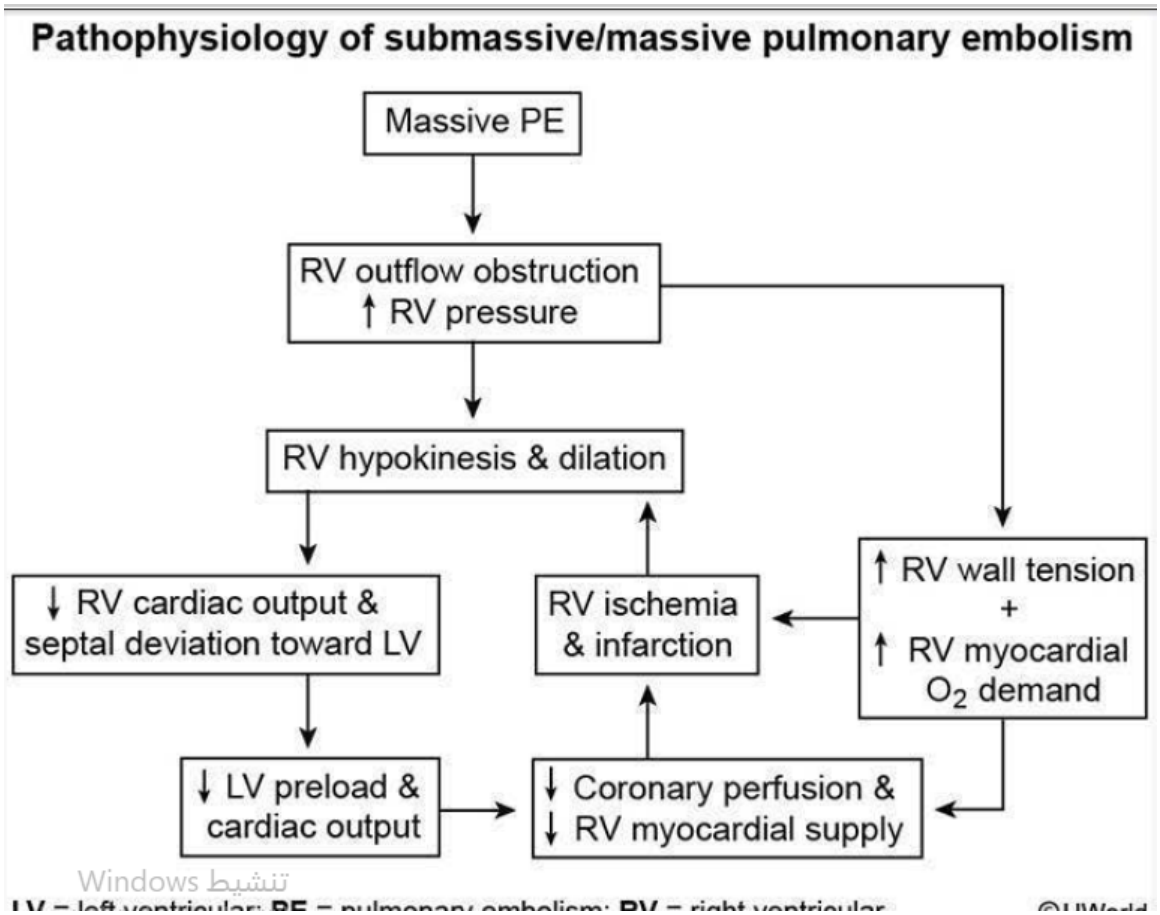
- Although echocardiography has poor sensitivity for segmental PE massive PE often has visible echocardiographic abnormalities that allow for rapid bedside diagnosis.
- 



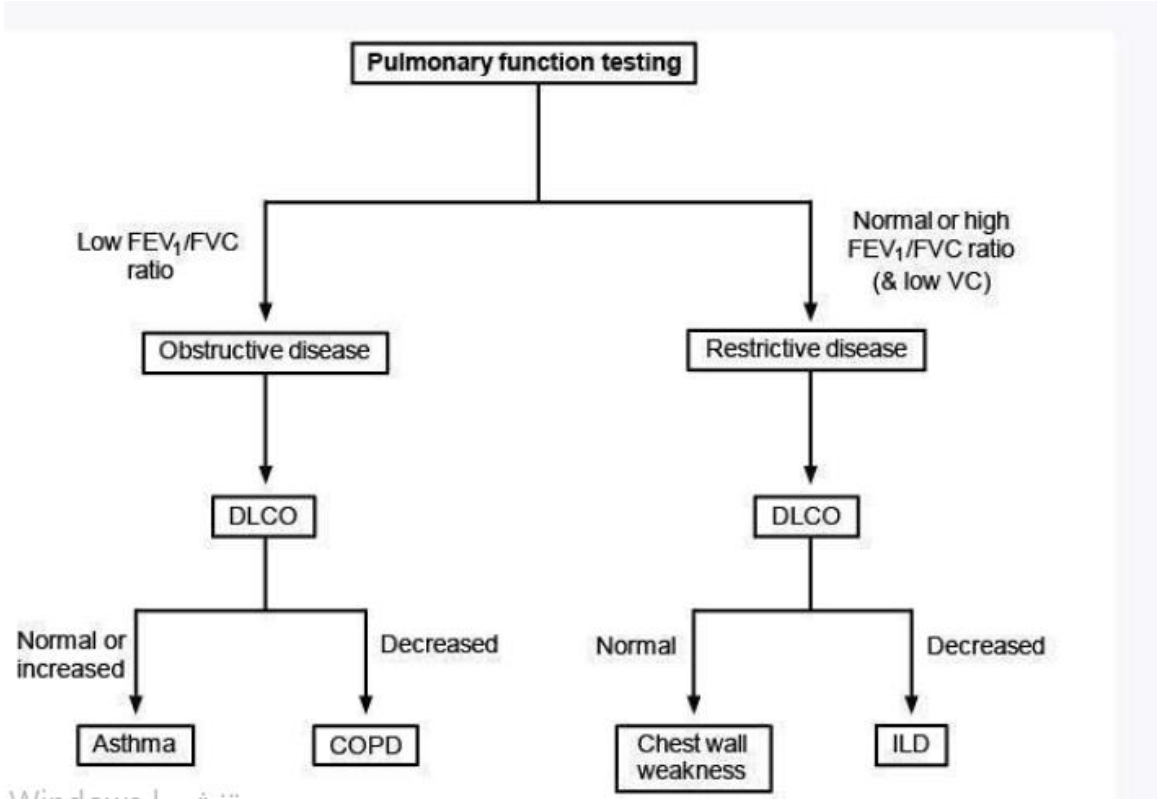
- Approximately 10% of patients with PE have occlusion of a peripheral pulmonary artery by thrombus, causing pulmonary infarction. These small peripheral thrombi are more likely to cause pleuritic chest pain and hemoptysis, due to inflammation and irritation of the lung parenchyma and adjacent visceral and parietal pleura.



- Long-distance flights, although a risk factor for venous thromboembolism (VTE), do not qualify as immobilization for 3 days



- (It may be difficult to differentiate PE from RV myocardial infarction [MI]. which can also cause RV dysfunction; however. RVMI is less likely to cause dyspnea or syncope and more likely to cause bradycardia or arrhythmias).
- Unfractionated heparin is recommended in patients with decreased estimated glomerular filtration rate as it is more convenient to monitor its therapeutic level via activated partial thromboplastin time (aPTT).



muscle fatigue) and impending respiratory failure. Other clinical signs or symptoms of impending respiratory failure include:

- Markedly decreased breath sounds
- Absent wheezing
- Decreased mental status
- Marked hypoxia with cyanosis

Patients with impending or actual respiratory arrest require admission to the intensive care unit with **endotracheal intubation** to maintain adequate oxygenation and ventilation.

This patient with a recent history of uveitis has mild dyspnea and a 2-week history of presyncope episodes likely due to conduction abnormalities, given her marked bradycardia with atrioventricular (AV) block and left bundle branch block. She most likely has **sarcoidosis** with cardiac involvement. Autopsy studies have suggested evidence of **cardiac noncaseating granulomas** in at least 25% of patients with sarcoidosis. However, only 5% of patients demonstrate signs or symptoms of cardiac involvement, suggesting that cardiac sarcoidosis is underdiagnosed or often remains subclinical. Infiltration of noncaseating granulomas leads to surrounding inflammation and can result in conduction defects (**complete AV block** is most common), **restrictive cardiomyopathy** (early manifestation), **dilated cardiomyopathy** (late manifestation), valvular dysfunction, and **heart failure**. Sudden cardiac death can occur due to complete AV block or ventricular arrhythmia.

Manifestations of sarcoidosis	
Pulmonary	• Bilateral hilar adenopathy • Interstitial infiltrates
Ophthalmologic	• Anterior uveitis (iridocyclitis or iritis) • Posterior uveitis
Reticuloendothelial	• Peripheral lymphadenopathy • Hepatomegaly • Splenomegaly
Musculoskeletal	• Acute polyarthritis (especially the ankle joints) • Chronic arthritis with periosteal bone resorption
Central nervous system/endocrine	• Central diabetes insipidus • Hypercalcemia
Lofgren syndrome	• Erythema nodosum • Hilar adenopathy • Migratory polyarthralgias • Fever

Syndrome of inappropriate antidiuretic hormone	
Etiologies	• CNS disturbance (eg, stroke, hemorrhage, trauma) • Medications (eg, carbamazepine, SSRIs, NSAIDs) • Lung disease (eg, pneumonia) • Ectopic ADH secretion (eg, small cell lung cancer) • Pain &/or nausea
Clinical features	• Mild/moderate hyponatremia - nausea, forgetfulness • Severe hyponatremia - seizures, coma • Euvolemia (eg, moist mucous membranes, no edema, no JVD)
Laboratory findings	• Hyponatremia • Serum osmolality <275 mOsm/kg H_2O (hypotonic) • Urine osmolality >100 mOsm/kg H_2O • Urine sodium >40 mEq/L
Management	• Fluid restriction +/- salt tablets • Hypertonic (3%) saline for severe hyponatremia

Hyponatremia			
Serum osmolality	**ECV**	**Urine findings**	**Cause**
Low (<275 mOsm/kg)	Hypovolemic	U_{Na} <40 mEq/L	• Nonrenal salt loss (eg, vomiting, diarrhea, dehydration)
		U_{Na} >40 mEq/L	• Renal salt loss (eg, diuretics, primary adrenal insufficiency)
	Euvolemic	U_{Osm} <100 mOsm/kg	• Psychogenic polydipsia • Beer potomania
		U_{Osm} >100 mOsm/kg & U_{Na} >40 mEq/L	• SIADH (rule out hypothyroidism, secondary adrenal insufficiency)
	Hypervolemic	Variable	• CHF, hepatic failure, nephrotic syndrome
Normal	Variable		• Pseudohyponatremia (eg, paraproteinemia, hyperlipidemia)
High (>295 mOsm/kg)			• Hyperglycemia • Exogenous solutes (eg, mannitol)

Clinical features of pulmonary hypertension	
Classification	• PAH (WHO group 1) • Due to left heart disease (WHO group 2) • Due to chronic lung disease (eg, COPD, ILD) (WHO group 3) • Due to chronic thromboembolic disease (WHO group 4) • Due to other causes* (WHO group 5)
Symptoms	• Dyspnea, fatigue/weakness • Exertional angina, syncope • Abdominal distension/pain
Signs	• Left parasternal lift, prominent **right ventricular heave** • **Loud P2**, right-sided S3 • Pansystolic murmur of tricuspid regurgitation • JVD, ascites, peripheral edema, hepatomegaly

*Other causes include hematologic (eg, myelodysplastic syndromes), systemic (eg, sarcoidosis), and metabolic (eg, glycogen storage) disorders.

COPD = chronic obstructive pulmonary disease; **ILD** = interstitial lung disease; **JVD** = jugular venous distension; **PAH** = pulmonary arterial hypertension; **WHO** = World Health Organization.

Systemic sclerosis subtype characteristics	
Limited cutaneous	**Diffuse cutaneous**

• Scleroderma on head & distal UE
• Prominent vascular manifestations
  ○ Raynaud phenomenon
  ○ Cutaneous telangiectasia
  ○ Pulmonary arterial hypertension
• CREST syndrome
• Anticentromere antibodies
• Better prognosis
	• Scleroderma on trunk & UE
	• Prominent internal organ involvement
	  ○ Scleroderma renal crisis
	  ○ Myocardial ischemia & fibrosis
	  ○ Interstitial lung disease
	• Anti-Scl-70 (topoisomerase-1) antibodies
	• Anti-RNA polymerase III antibodies
	• Worse prognosis

E = upper extremities.

	Nonallergic rhinitis	Allergic rhinitis
Clinical features	• Nasal congestion, rhinorrhea, sneezing, postnasal drainage • Later onset common (age >20) • No obvious allergic trigger • Perennial symptoms (may worsen with season changes) • Erythematous nasal mucosa	• Watery rhinorrhea, sneezing, eye symptoms • Earlier age of onset • Identifiable allergen or seasonal pattern • Pale/bluish nasal mucosa • Associated with other allergic disorders (eg, eczema, asthma, eustachian dysfunction)
Treatment	• **Mild**: Intranasal antihistamine or glucocorticoids • **Moderate to severe**: Combination therapy	• Intranasal glucocorticoids • Antihistamines