Chronic Obstructive Pulmonary Disease

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Timetable

- 1. Definition
- 2. Burden of COPD
- 3. Factors influencing disease development and progression
- 4. Pathology, pathogenesis and pathophysiology
- 5. Diagnosis
- 6. Prevention
- 7. Management of COPD
- 8. COPD and comorbidities

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Table 2.1. Key indicators for considering a diagnosis of COPD	
Consider COPD, and perform spirometry, if any of these indicators are present in an individual over age 40. These indicators are not diagnostic themselves, but the presence of multiple key indicators increases the probability of a diagnosis of COPD. Spirometry is required to establish a diagnosis of COPD.	
Dyspnea that is:	Progressive over time. Characteristically worse with exercise. Persistent.
Chronic cough:	May be intermittent and may be unproductive. Recurrent wheeze.
Chronic sputum production:	Any pattern of chronic sputum production may indicate COPD.
Recurrent lower respiratory tract infections	
History of risk factors:	
	Host factors (such as genetic factors, congenital/developmental abnormalities etc.). Tobacco smoke (including popular local preparations). Smoke from home cooking and heating fuels. Occupational dusts, vapors, fumes, gases and other chemicals.
Family history of COPD and/or childhood factors:	
	For example low birthweight, childhood respiratory infections etc.

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Table 2.2. Other causes of chronic cough
Intrathoracic
• Asthma
• Lung cancer
• Tuberculosis
• Bronchiectasis
• Left heart failure
• Interstitial lung disease
• Cystic fibrosis
• Idiopathic cough
Extrathoracic
• Chronic allergic rhinitis
• Post nasal drip syndrome (PNDS)
• Upper Airway Cough Syndrome (UACS)
• Gastroesophageal reflux
• Medication (e.g. ACE inhibitors)

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Table 2.4. Classification of airflow limitation severity in COPD (Based on post-bronchodilator FEV_1)		
In patients with $FEV_1/FVC < 0.70$:		
GOLD 1:	Mild	$FEV_1 \geq 80\%$ predicted
GOLD 2:	Moderate	$50\% \leq FEV_1 < 80\%$ predicted
GOLD 3:	Severe	$30\% \leq FEV_1 < 50\%$ predicted
GOLD 4:	Very Severe	$FEV_1 < 30\%$ predicted

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COPD Assessment

- COPD Assessment Test
- The COPD Control Questionnaire
- Modified British Medical Research Council Questionnaire

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Spirometry

- Diagnosis
- Assessment of severity of airflow obstruction (for prognosis)
- Follow-up assessment
- Therapeutic decisions
- Identification of rapid decline

TABLE 55.6 Pharmacotherapy of Chronic Obstructive Pulmonary Disease

Generic Name (Trade Name)	Usual Dosing Range (Maximum Dose)	Main Adverse Drug Effects	Comments
Ipratropium bromide 0.03% MDI (Atrovent)	2–4 puffs TID-QID	Occasional dry mouth, cough, nausea; rare palpitations	If accidentally sprayed in eyes, acute narrow-angle glaucoma
Ipratropium bromide 0.02% solution (Atrovent)	0.5 mg in nebulizer every 4–8 hours	Occasional dry mouth, cough, nausea; rare palpitations	If accidentally sprayed in eyes, acute narrow-angle glaucoma
Albuterol MDI (outside United States: salbutamol) (Proventil, Ventolin)	2–4 puffs TID-QID (maximum 12 puffs/day)	Palpitations, tremors, nervousness	Can be used either for acute symptoms or as scheduled medication
	(6–8 puffs every 1/2–2 hours acutely)		
Albuterol nebulizer solution	2.5–5 mg in nebulizer every 1/2–2 hours acutely	Palpitations, tremors, nervousness	
Combination ipratropium and albuterol MDI (Atrovent or Combivent)	2 puffs QID	Palpitations, tremors, nervousness	Some studies show increased effectiveness compared with separate MDIs
Salmeterol Diskus (Serevent)	1 puff BID	Palpitations	Should not be used for acute symptoms Expensive
Formoterol (Foradil)	1 puff BID	Palpitations	Should not be used for acute symptoms Expensive
Tiotropium (Spiriva Handihaler)	1 inhalation QD	Dry mouth	Expensive
Theophylline, sustained release (Theo-Dur)	200–400 mg BID	Nausea, GERD, tremor, palpitations	In toxic doses, causes seizures; desirable serum level 5–12 μg/L
Albuterol, sustained-release tablets	4–8 mg every night or BID	Palpitations, tremors, nervousness	
Inhaled corticosteroids inhaler (e.g., beclomethasone)	For most, 2–4 puffs BID	Irritation of throat, thrush, increased risk of pneumonia	If used in high doses, can increase risk of cataracts and adrenal suppression
Prednisone, short-term	40–60 mg daily for 5–10 days	Increased BP, hyperglycemia, hypokalemia, irritability or euphoria	If used for less than 14 days, can be stopped without taper

BP = blood pressure; GERD = gastroesophageal reflux disease; MDI = metered-dose inhaler; QID = four times daily; TID = three times daily.
Based on prices at *www.drugstore.com*.

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Table 3.4. Bronchodilators in stable COPD

- Inhaled bronchodilators in COPD are central to symptom management and commonly given on a regular basis to prevent or reduce symptoms **(Evidence A)**.
- Regular and as-needed use of SABA or SAMA improves FEV_1 and symptoms **(Evidence A)**.
- Combinations of SABA and SAMA are superior compared to either medication alone in improving FEV_1 and symptoms **(Evidence A)**.
- LABAs and LAMAs significantly improve lung function, dyspnea, health status, and reduce exacerbation rates **(Evidence A)**.
- LAMAs have a greater effect on exacerbation reduction compared with LABAs **(Evidence A)** and decrease hospitalizations **(Evidence B)**.
- Combination treatment with a LABA and LAMA increases FEV_1 and reduces symptoms compared to monotherapy **(Evidence A)**.
- Combination treatment with a LABA and LAMA reduces exacerbations compared to monotherapy **(Evidence B)** or ICS/LABA **(Evidence B)**.
- Tiotropium improves the effectiveness of pulmonary rehabilitation in increasing exercise performance **(Evidence B)**.
- Theophylline exerts a small bronchodilator effect in stable COPD **(Evidence A)** and that is associated with modest symptomatic benefits **(Evidence B)**.

Table 3.5. Anti-inflammatory therapy in stable COPD

Inhaled corticosteroids

- An ICS combined with a LABA is more effective than the individual components in improving lung function and health status and reducing exacerbations in patients with exacerbations and moderate to very severe COPD **(Evidence A)**.
- Regular treatment with ICS increases the risk of pneumonia especially in those with severe disease **(Evidence A)**.
- Triple inhaled therapy of ICS/LAMA/LABA improves lung function, symptoms and health status **(Evidence A)** and reduces exacerbations **(Evidence B)** compared to ICS/LABA or LAMA monotherapy.

Oral glucocorticoids

- Long-term use of oral glucocorticoids has numerous side effects **(Evidence A)** with no evidence of benefits **(Evidence C)**.

PDE4 inhibitors

- In patients with chronic bronchitis, severe to very severe COPD and a history of exacerbations:
  - A PDE4 inhibitor improves lung function and reduces moderate and severe exacerbations **(Evidence A)**.
  - A PDE4 inhibitor improves lung function and decreases exacerbations in patients who are on fixed-dose LABA/ICS combinations **(Evidence A)**.

Antibiotics

- Long-term azithromycin and erythromycin therapy reduces exacerbations over one year **(Evidence A)**.
- Treatment with azithromycin is associated with an increased incidence of bacterial resistance **(Evidence A)** and hearing test impairments **(Evidence B)**.

Mucolytics/antioxidants

- Regular use of NAC and carbocysteine reduces the risk of exacerbations in select populations **(Evidence B)**.

Other anti-inflammatory agents

- Simvastatin does not prevent exacerbations in COPD patients at increased risk of exacerbations and without indications for statin therapy **(Evidence A)**. However, observational studies suggest that statins may have positive effects on some outcomes in patients with COPD who receive them for cardiovascular and metabolic indications **(Evidence C)**.
- Leukotriene modifiers have not been tested adequately in COPD patients.

TABLE 55.1 Differential Diagnosis of Chronic Respiratory Symptoms

COPD	• Mid-life onset • Slowly progressive symptoms • Smoking history • Dyspnea with exertion • Largely irreversible airway obstruction
Asthma	• Early onset • Symptoms vary day to day • Atopic conditions often present • Family history of asthma • Airflow obstruction is largely reversible
Congestive heart failure	• Fine basilar crackles on exam • Dilated heart, pulmonary edema on chest radiograph • Volume restriction on pulmonary function tests • Brain natriuretic peptide elevated
Bronchiectasis	• Large volume of purulent sputum • Commonly associated with bacterial infection • Coarse crackles and clubbing on exam • Bronchial dilatation and bronchial wall thickening on imaging
Tuberculosis	• Onset at all ages • Lung infiltrate or granulomata (nodular lesions) on chest film • Acid fast bacilli–positive
Sarcoidosis	• Dry cough • Fever present • Symptoms and signs of systemic inflammation present
Obliterative bronchiolitis	• Onset at younger age and in nonsmokers • History of rheumatoid arthritis or fume exposure • Computed tomography on expiration shows hypodense areas

Table 3.7. Other pharmacological treatments
Alpha-1 antitrypsin augmentation therapy
• Intravenous augmentation therapy may slow down the progression of emphysema **(Evidence B)**.
Antitussives
• There is no conclusive evidence of a beneficial role of antitussives in patients with COPD **(Evidence C)**.
Vasodilators
• Vasodilators do not improve outcomes and may worsen oxygenation **(Evidence B)**.

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TABLE 55.2 Common Comorbidities in Patients with COPD

Anemia
Anxiety
Cachexia
Congestive heart failure
Depression
Diabetes
Ischemic heart disease
Lung cancer
Metabolic syndrome
Obstructive sleep apnea
Osteoporosis
Pulmonary hypertension
Skeletal muscle wasting

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References:

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