Chronic Obstructive Pulmonary Disease (COPD)

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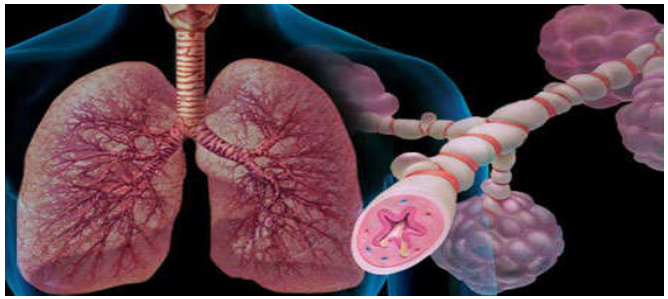
COPD Definition



- Chronic Obstructive Pulmonary Disease (COPD) is a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases.
- Chronic bronchitis: the presence of cough and sputum production for at least 3 months in each of two consecutive years, after exclusion of other causes of chronic cough.
- Emphysema: pathological term abnormal permanent enlargement of the airspaces distal to the terminal bronchioles with destruction of their wall without obvious fibrosis.

Prevalence of COPD

- Prevalence of COPD was higher in smokers and ex-smokers compared to non-smokers

- In each country, the prevalence of COPD increased steeply with age, with the highest prevalence among those > 60 years
- Higher in men than women
- COPD is a major cause of chronic morbidity and mortality throughout the world
- 3rd leading cause of death in the world
- Three million deaths annually.

- With increasing prevalence of smoking in developing countries, and aging populations in high-income countries, the prevalence of COPD is expected to rise over the next 30 years.

- By 2030 predicted 4.5 million COPD related deaths annually.

Risk factors(Etiology)

- **Enviromental risk factors:**
- **1-Smoking:**
- The main risk factor for COPD is tobacco smoking it accounts for 80 to 90% of the risk of developing COPD . a greater annual rate of decline in FEV1, and a greater COPD mortality rate than non-smokers caused by cigarette smoking.
- **2- OCCUPATIONAL EXPOSURE:** including organic and inorganic dusts, chemical agents and fumes carries a risk for COPD.

- **3- Air pollution**: indoor biomass exposure to modern and traditional fuels used during cooking may predispose women to develop COPD in many developing countries
- Almost three billion people worldwide use biomass and coal as their main source of energy for cooking, heating, and other household needs, so the population at risk worldwide is very large
- High levels of outdoor air pollution are harmful to individuals with existing lung disease.

- **4-Socioeconomic status:** lower socioeconomic status is associated with an increased risk of developing COPD. It may reflects
- exposures to indoor and outdoor air pollutants,
- crowding,
- poor nutrition,
- infections,
- or other factors related to low socioeconomic status.

Host factors

- **1-Genetic factors**
- The genetic risk factor that is best documented is a severe hereditary deficiency of alpha-1 antitrypsin (AATD), a major circulating inhibitor of serine proteases.
- **2-Age and sex**
- Age is often listed as a risk factor for COPD.
- In the past, most studies have reported that COPD prevalence and mortality are greater among men than women, but later data from developed countries has reported that the prevalence of COPD is now almost equal in men and women, probably reflecting the changing patterns of tobacco smoking

- **Lung growth and development**:Any factor that affects lung growth during gestation and childhood has the potential for increasing an individual's risk of developing COPD as early childhood lower respiratory tract infections.
- **Airway hyper-reactivity:** its presence in patients with mild COPD found to be responsible for decline in lung function.

PATHOLOGY &PATHOGENESIS

●COPD patients exhibit specific changes in the architecture of their central airways, peripheral airways, alveoli, and pulmonary vessels, secondary to inflammation caused by inhalation of noxious substances such as tobacco smoke.
●The inflammation persists for a long time even after smoking cessation.
●The increased inflammatory response leads to a protease/antiprotease imbalance and oxidant/antioxidant imbalance, and, in turn, damage to the airways and lungs
●Airflow obstruction occurs as a result of the complex effects of peripheral airway lesions and emphysematous lesions.
●The inflammation affects the whole body and leads to systemic comorbidities.

		COPD
Airways	Epithelial detachment	−
	Squamous metaplasia	+++
	Thickening of the basal membrane	+/−
	Angiogenesis	+/−
	Fibrosis	+++ (in peripheral airways)
	Smooth muscle hyperplasia	+ (in peripheral airways)
	Goblet cell and bronchial gland hyperplasia	+++
	Loss of alveolar attachments	+++
Alveolar region	Alveolar destruction/ enlargement	+++
Pulmonary vessels	Intimal/smooth muscle hyperplasia Fibrosis of the vessel wall	++

PATHOPHYSIOLOGY

- **1-Airflow limitation and gas trapping:** The basic pathologic conditions that lead to **exertional dyspnea** in COPD
- **2-Mucus Hypersecretion:** causes **chronic cough and sputum production**, but does not occur in all COPD patients.
- **3-Gas exchange abnormalities:**Uneven distribution of ventilation-perfusion ratios leads to **hypoxemia**. In severe cases, **hypercapnia** due to alveolar hypoventilation is also observed.
- **4-pulmonary hypertension**: in severe cases,The major cause is hypoxic pulmonary vasoconstriction may lead to right ventricular hypertrophy and eventually to right-side cardiac failure(cor-pulmonale).

●**5-Systemic features** :Systemic inflammation characterized by increased inflammatory cytokine and C-reactive protein levels.

●Nutritional disorders leading to decreased fat mass and lean-body mass

●Musculoskeletal disorders associated with decreased muscle mass and muscle strength

●Cardiovascular diseases, including myocardial infarction, angina pectoris, and cerebrovascular accidents

●Osteoporosis leading to vertebral compression fractures

●Diabetes mellitus

●Sleep disorders

●Anemia

ETIOLOGY, PATHOBIOLOGY AND PATHOLOGY OF COPD LEADING TO AIRFLOW LIMITATION AND CLINICAL MANIFESTATIONS

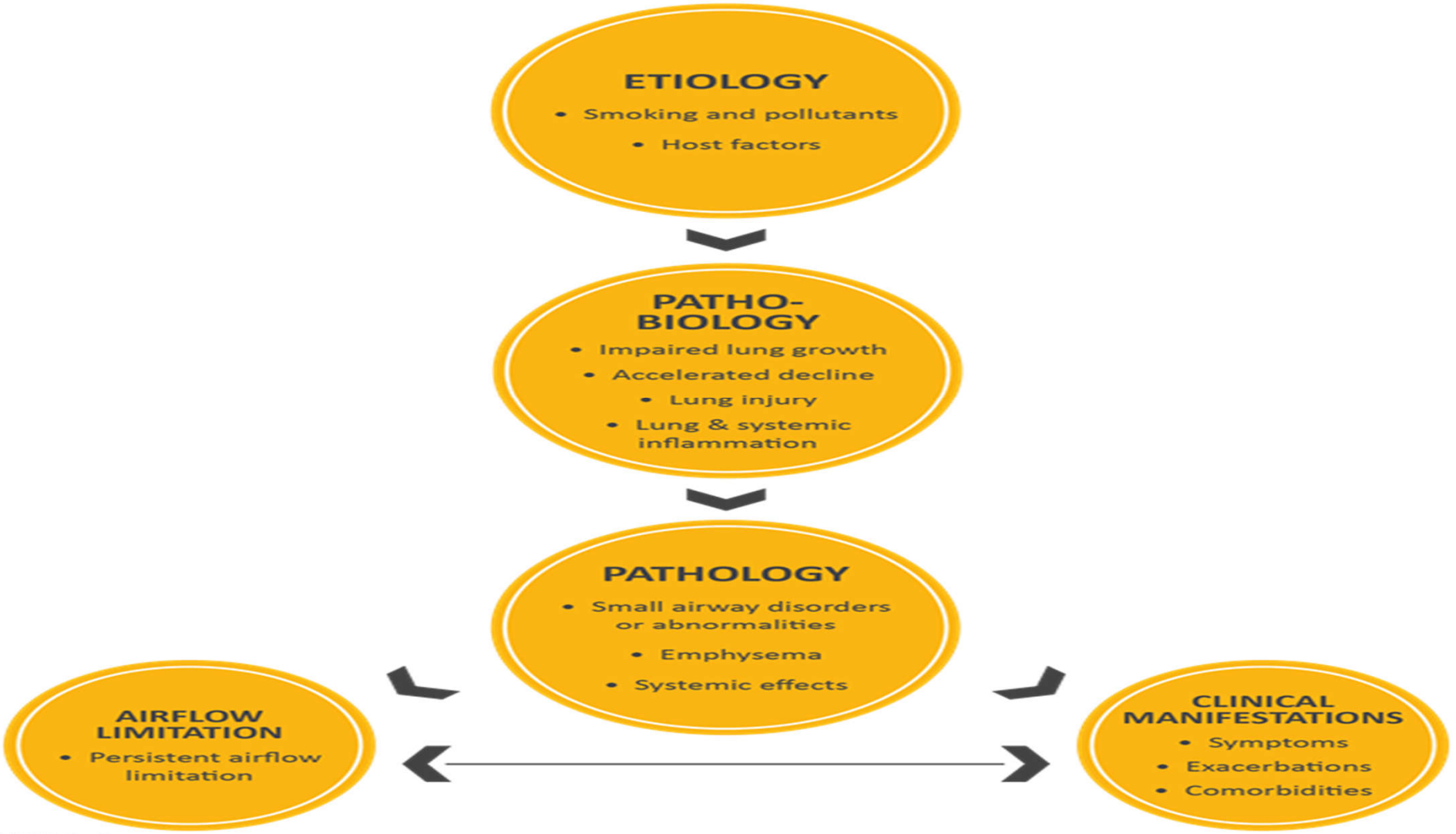
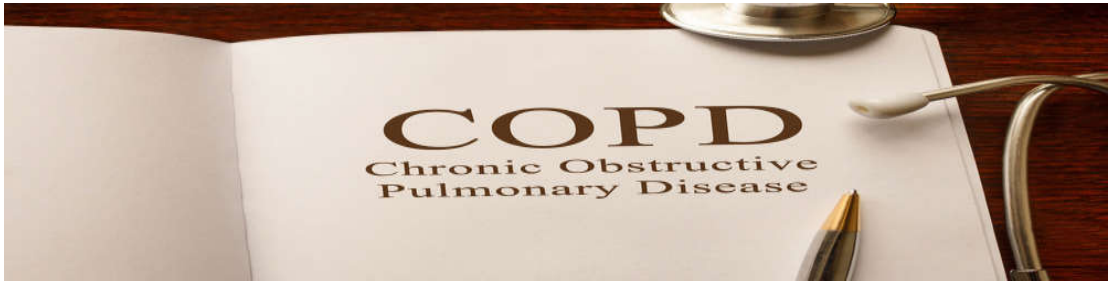


FIGURE 1.1

Diagnosis of COPD



- **<u>SYMPTOMS:</u> 1- Cough**.
- Chronic cough is often the first symptom of COPD and is frequently discounted by the patient as an expected consequence of smoking and/or environmental exposures.
- Initially, the cough may be intermittent, but subsequently may be present every day, often throughout the day.
- Chronic cough in COPD is productive.
- Other causes of chronic cough should be excluded.

SYMPTOMS:

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)

TABLE 2.2

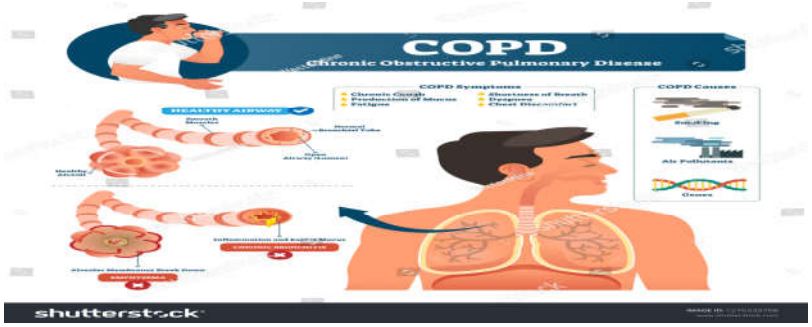
SYMPTOMS:

2-Sputum production: COPD patients commonly expectorate small quantities of tenacious sputum with coughing.

- Regular production of sputum for three or more months in two consecutive years (in the absence of any other conditions that may explain it) is the classical definition of **chronic bronchitis**.
- sputum production can be intermittent with periods of flare-up interspersed with periods of remission.
- The presence of purulent sputum reflects an increase in inflammatory mediators, and may identify the onset of a bacterial exacerbation.
- Patients producing large volumes of sputum may have underlying bronchiectatic changes.

SYMPTOMS:

- **3-Dyspnea**: a cardinal symptom of COPD, is a major cause of the disability and anxiety that is associated with the disease.
- Typical COPD patients describe their dyspnea as a sense of increased effort to breathe, chest heaviness, air hunger, or gasping.
- **4-Wheezing** :Audible wheeze may arise at the laryngeal level and need not be accompanied by abnormalities heard on auscultation. Alternatively, widespread inspiratory or expiratory wheezes can be present on auscultation.



Additional features in severe disease.

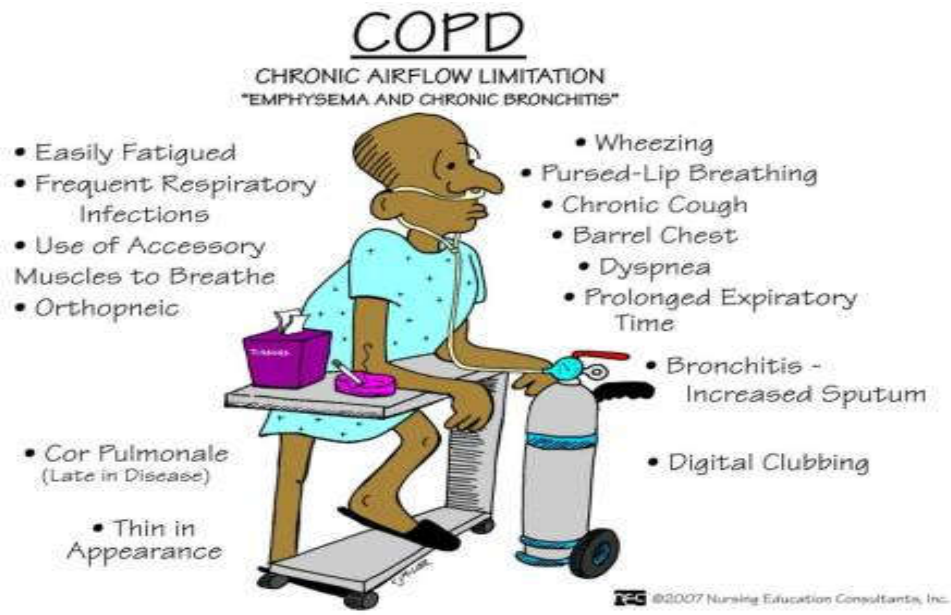
- common problems in patients with severe and very severe COPD
- Fatigue,
- weight loss,
- muscle loss,
- and anorexia

they can also be a sign of other diseases, such as tuberculosis or lung cancer, and therefore should always be investigated.

- Syncope during cough occurs due to rapid increases in intrathoracic pressure during prolonged attacks of coughing.
- Coughing spells may also cause rib fractures.
- Ankle swelling may be the only indicator of the presence of cor pulmonale.
- Symptoms of depression and/or anxiety they are common in COPD.

Physical examination

- Physical signs of airflow limitation are usually not present until significant impairment of lung function has occurred.
- A number of physical signs may be present in COPD, but absence does not exclude the diagnosis.



Physical examination

- Prolonged forced expiratory time >5 s, pursed lip breathing on expiration
- Tar stained fingers due to smoking habit
- Finger clubbing is not a manifestation of the disease and suggest the possibility of complicating lung cancer or bronchiectasis.
- Cyanosis in advanced disease indicating hypoxemia or secondary to polycythemia.
- An inspiratory tracheal tug :decrease distance between cricoid cartilage and suprasternal notch (3 fingers breadth normally)
- Flapping tremor associated with hypercapnia
- Use of accessory muscels of respiration specially sternomastoid muscle in advanced COPD.

Physical examination

- **On inspection** :Barrel shape chest as a sign of hyperinflation.
- Hoover's sign: the horizontal position of diaphragm pull in the lower ribs during inspiration.
- **On percussion** there is encroachment on hepatic and cardiac dullness due to overinflation.
- Hyperresonance note
- **On auscultation** : breath sounds have prolonged expiratory phase
- Adventitial sounds : ronchi and crepitations.
- **Clinical patterns of COPD** : Pink puffer (A) , BLUE Bloater (B).

CHRONIC BRONCHITIS

BLUE BLOATER

Dysphea on Exertion

Cough, DOE,
Hypercapnia,
Hypoxemia
Mild cyanosis

EMPHYSEMA

PINK PUFFER

Barrel-chested
Dyspneic
prolonged expiration,
Hunched-over position,
Breathes through pursed lips

Cardiovascular examination

- Difficulty in localizing the apex beat due to emphysema and decrease the cardiac dullness
- Signs of pulmonary arterial hypertension in advanced cases
- The heave of RT ventricular hypertrophy may be palpable at lower LT sternal edge
- Heart sounds are soft , there may be rt vent gallop rhythm with third sound audible in fourth intercostal space to the left of the sternum
- Peripheral vasodilatation accompanied hypercapnia cause warm peripheries with a high volume pulse ,collapsing pulse.
- Peripheral pitting oedema as a result of fluid retention.

Spirometry

- Measure the volume of air forcibly exhaled from the point of maximal inspiration (forced vital capacity, FVC) and the volume of air exhaled during the first second of this maneuver (forced expiratory volume in one second, FEV1), and the ratio of these two measurements (FEV1/FVC) should be calculated.
- Spirometry measurements are evaluated by comparison with reference values based on age, height, sex, and race.
- The spirometric criterion for airflow limitation remains a post-bronchodilator fixed ratio of **FEV1/FVC < 0.70**.
- Assessing the **degree of reversibility** of airflow limitation by measuring FEV1 before and after bronchodilator to differentiate the diagnosis from asthma.
- An improvement of 12% over baseline FEV1 or FVC and an increase at least 200 ml has been suggested as significant bronchodilator response .

SPIROMETRY - NORMAL TRACE

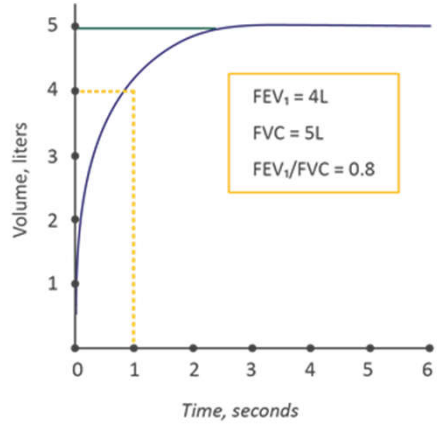


FIGURE 2.2A

SPIROMETRY - OBSTRUCTIVE DISEASE

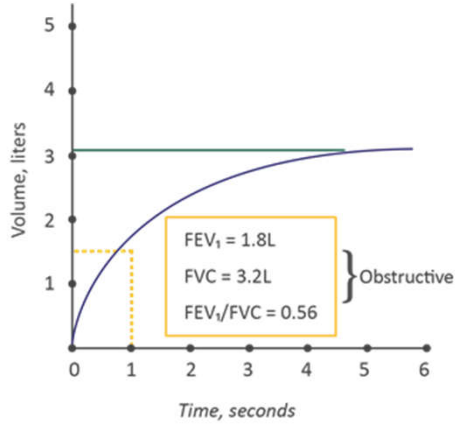


FIGURE 2.2B

FVC =

FEV1 =

Classification of severity of airflow limitation

GOLD Grades and Severity of Airflow Obstruction in COPD (based on post-bronchodilator FEV1) Table 2.6

In COPD patients (FEV1/FVC < 0.7):

GOLD 1:	Mild	FEV1 ≥ 80% predicted
GOLD 2:	Moderate	50% ≤ FEV1 < 80% predicted
GOLD 3:	Severe	30% ≤ FEV1 < 50% predicted
GOLD 4:	Very Severe	FEV1 < 30% predicted

Assessment of symptoms

- It should be noted that there is only a weak correlation between FEV1, symptoms and impairment of a patient's health status.
- For this reason, formal symptomatic assessment is required
- A simple measure of **breathlessness** such as the Modified British Medical Research Council (**mMRC)** Questionnaire.
- **COPD Assessment Test (CAT™):** is an 8-item uni-dimensional measure of health status impairment in COPD
- **Assessment of exacerbation risk**
- **COPD exacerbations** are defined as an acute worsening of respiratory symptoms that result in additional therapy. classified as mild, moderate (treated with SABDs plus antibiotics and/or oral corticosteroids) or severe (patient requires hospitalization or visits the emergency room).
- Frequent exacerbations (defined as two or more exacerbations per year)

MODIFIED MRC DYSPNEA SCALE[a]

PLEASE TICK IN THE BOX THAT APPLIES TO YOU | ONE BOX ONLY | Grades 0 - 4

mMRC Grade 0.	I only get breathless with strenuous exercise.	☐
mMRC Grade 1.	I get short of breath when hurrying on the level or walking up a slight hill.	☐
mMRC Grade 2.	I walk slower than people of the same age on the level because of breathlessness, or I have to stop for breath when walking on my own pace on the level.	☐
mMRC Grade 3.	I stop for breath after walking about 100 meters or after a few minutes on the level.	☐
mMRC Grade 4.	I am too breathless to leave the house or I am breathless when dressing or undressing.	☐

[a] Fletcher CM. BMJ 1960; 2: 1662.

TABLE 2.5

CAT™ ASSESSMENT

For each item below, place a mark (x) in the box that best describes you currently.
Be sure to only select one response for each question.

EXAMPLE: I am very happy	0 (X) 2 3 4 5	**I am very sad**	**SCORE**
I never cough	0 1 2 3 4 5	I cough all the time	
I have no phlegm (mucus) in my chest at all	0 1 2 3 4 5	My chest is completely full of phlegm (mucus)	
My chest does not feel tight at all	0 1 2 3 4 5	My chest feels very tight	
When I walk up a hill or one flight of stairs I am not breathless	0 1 2 3 4 5	When I walk up a hill or one flight of stairs I am very breathless	
I am not limited doing any activities at home	0 1 2 3 4 5	I am very limited doing activities at home	
I am confident leaving my home despite my lung condition	0 1 2 3 4 5	I am not at all confident leaving my home because of my lung condition	
I sleep soundly	0 1 2 3 4 5	I don't sleep soundly because of my lung condition	
I have lots of energy	0 1 2 3 4 5	I have no energy at all	

TOTAL SCORE: ( )

Reference: Jones et al. ERJ 2009; 34 (3); 648-54.

FIGURE 2.3

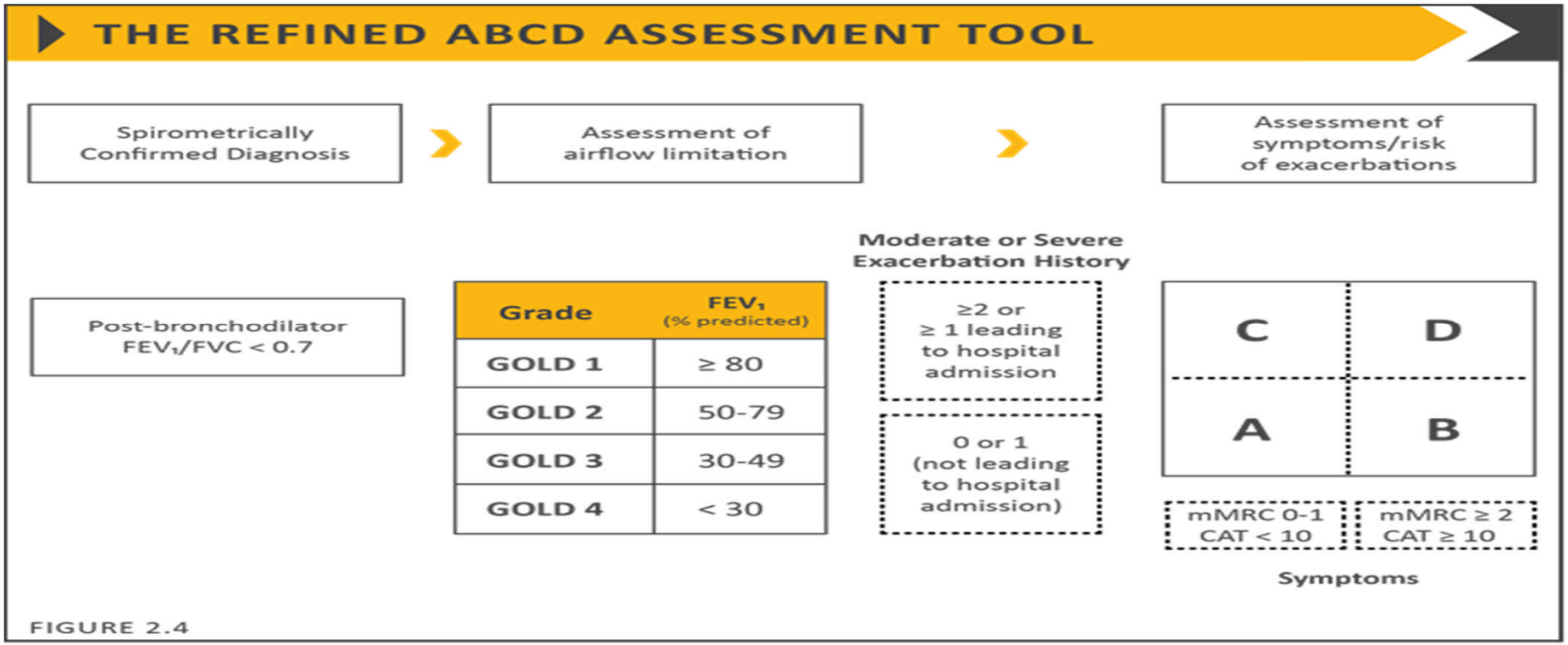
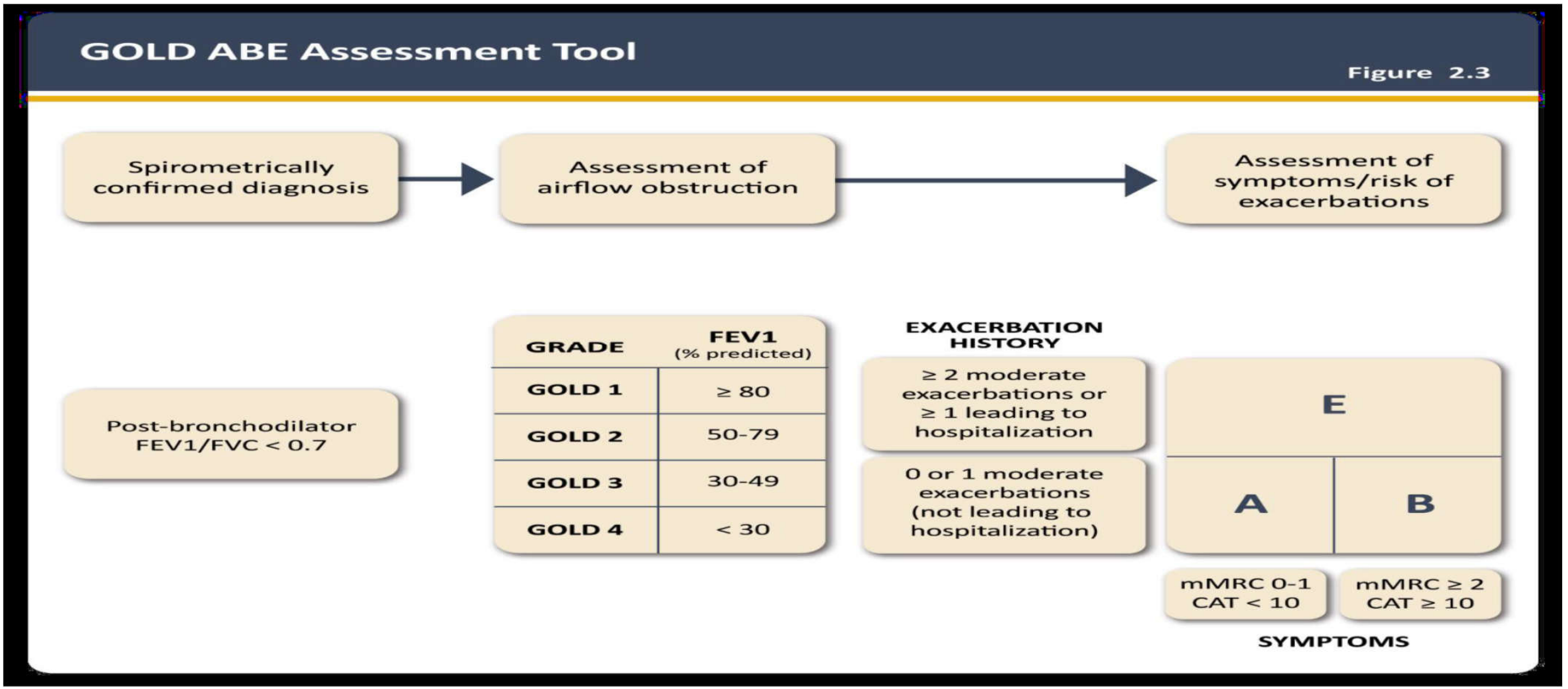

THE REFINED ABCD ASSESSMENT TOOL
Spirometrically Confirmed Diagnosis
Assessment of airflow limitation
Assessment of symptoms/risk of exacerbations
Post-bronchodilator FEV1/FVC < 0.7
Grade
FEV1 (% predicted)
GOLD 1
≥ 80
GOLD 2
50-79
GOLD 3
30-49
GOLD 4
< 30
Moderate or Severe Exacerbation History
≥2 or ≥ 1 leading to hospital admission
0 or 1 (not leading to hospital admission)
C
D
A
B
mMRC 0-1 CAT < 10
mMRC ≥ 2 CAT ≥ 10
Symptoms

FIGURE 2.4

GOLD ABE Assessment Tool

Figure 2.3



The “ABCD” assessment

- An understanding of the impact of COPD on an individual patient combines the symptomatic assessment with the patient’s spirometric classification and/or risk of exacerbations.
- The “ABCD” assessment was a major step forward from the simple spirometric grading system because it incorporated patient-reported outcomes and highlighted the importance of exacerbation prevention in the management of COPD.
- For some therapeutic recommendations, ABCD groups will be derived exclusively from patient symptoms and their history of exacerbation. Spirometry, in conjunction with patient symptoms and history of moderate and severe exacerbations, remains vital for the diagnosis, prognostication and consideration of other important therapeutic approaches.

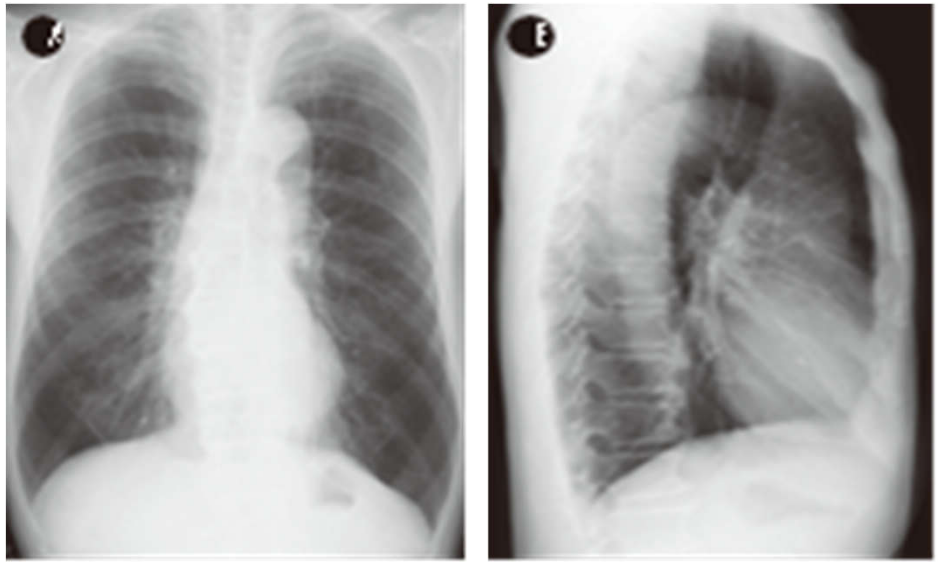
Investigations

1. Diagnostic imaging

- **A plain chest X-ray** is a useful means of excluding other diseases or diagnosing advanced emphysematous lesions and airway lesions, but it is not suitable for detecting early stage lesions.
- **High-resolution computed tomography (HRCT)** can be effective as a means of early detection of emphysematous lesions.
- Emphysematous lesions appear as ill-defined low attenuation areas (LAA) on HRCT images, and thus can be distinguished from normal lung.
- HRCT is capable of detecting airway wall thickening.
- Assessment of emphysematous lesions and airway lesions based on HRCT images is also useful in phenotype classification of COPD , panacinar , centrilobular, periseptal.

Chest X-ray

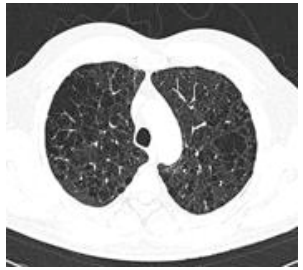
A : P-A view
Findings include increased radiolucency of the lung fields, diminished peripheral blood vessel shadows in the lung fields, flattening of the diaphragm, decrease in the cardiothoracic ratio and widening of the intercostal spaces.
B : Lateral view
Findings include flattening of the diaphragm, widening of the intercostal spaces, and increase in the retrocardiac space.



TYPES OF EMPHYSEMA

Depending upon the anatomic distribution within lobule emphysema is classified into

- Centriacinar (Centrilobular)
- Panacinar (Panlobular)
- Paraseptal (Distal acinar)
- Irregular (Para – Cicatrical)
- Mixed (Unclassified)



1-CENTRIACINAR EMPHYSEMA

- Involvement of central or proximal part of the acinus where as distal part is spared
- Usually co-exists with chronic bronchitis
- Predominant in smokers / coal-miners pneumoconiosis
- Common in upper lobes of lungs

2-PANACINAR EMPHYSEMA

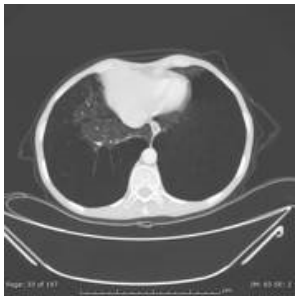
- All portions of the acinus are affected
- Often associated with α1-AT deficiency in smokers
- Common in lower zone of lungs
- Enlarged & over inflated lungs

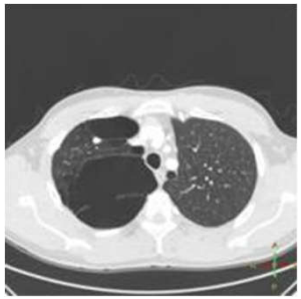
3-PARASEPTAL (DISTAL) EMPHYSEMA

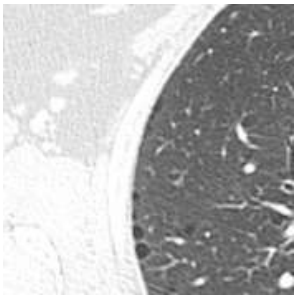
- Involves only distal part of acinus whereas proximal part is normal
- Localised along the pleura & perilobular septa
- More severe in the upper half of the lungs
- Common cause of spontaneous pneumothorax in young adults

4-IRREGULAR (PARA-CICATRICAL) EMPHYSEMA

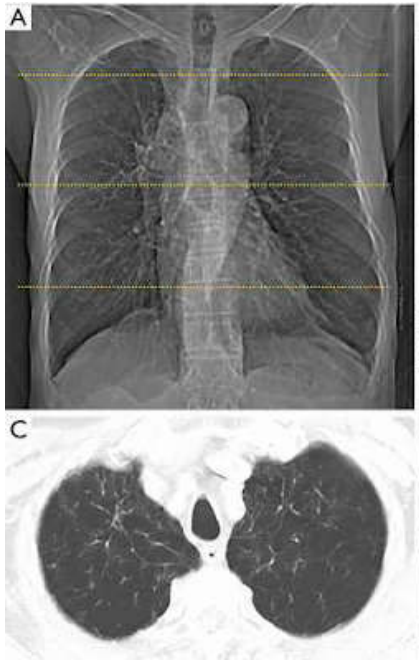
- Seen surrounding scars from any cause
- Irregular involvement
- Usually asymptomatic

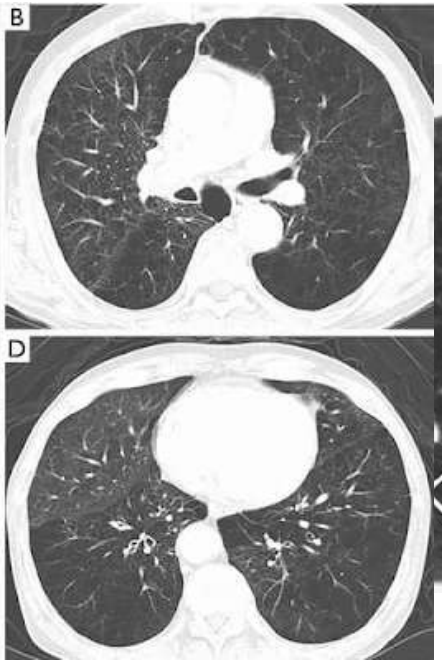


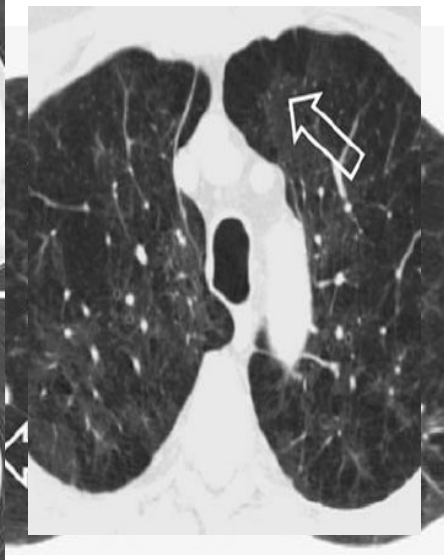


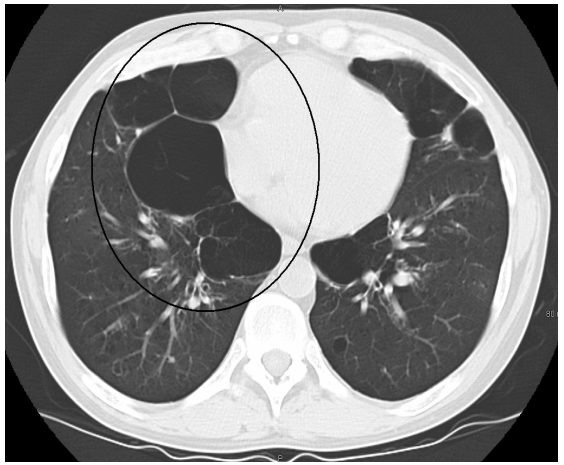


CT CHEST









2. Pulmonary function tests

- **Spirometry**: detection of an obstructive ventilation disorder
- A post-bronchodilator FEV1/FVC less than 70%
- **Lung volumes:** increase residual volume(RV), increase functional residual capacity (FRC)
- Increase total lung capacity (TLC).
- **pulmonary carbon monoxide diffusing capacity (DLCO):**
- Demonstrate the decreased gas exchange in COPD patients.

3. Arterial blood gas analysis :is a useful means of assessing ventilation status, oxygenation capacity, and acid-base balance in a patient.

- assessing the severity of the disease during exacerbations as well as during stable periods.
- A pulse oximeter allows continuous non-invasive measurement of oxygen saturation by pulse oximetry (SpO2).

4-Exercise testing and assessment of physical activity.

Walking tests can be useful for assessing disability and risk of mortality and are used to assess the effectiveness of pulmonary rehabilitation.

5-Biomarkers: Increases in markers of inflammation such as C-reactive protein (CRP) and procalcitonin are observed in the peripheral blood of COPD patients.

The assessment of eosinophils provides the best guidance to the use of corticosteroids, especially in the prevention of some exacerbations.

OTHER INVESTIGATIONS

- CBC
- ECG
- ECHO
- **Alpha-1 antitrypsin deficiency (AATD) screening**: A low concentration (< 20% normal) is highly suggestive of homozygous deficiency.
- It should be measured in all patients with early onset emphysema (age under 45years), or non smoker with emphysema
- With family history of with early onset emphysema or non smoking related emphysema
- Emphysema predominantly in lung bases (panaciner)

DIFFERENTIAL DIAGNOSIS OF COPD

DIAGNOSIS	SUGGESTIVE FEATURES
COPD	Onset in mid-life. Symptoms slowly progressive. History of tobacco smoking or exposure to other types of smoke.
Asthma	Onset early in life (often childhood). Symptoms vary widely from day to day. Symptoms worse at night/early morning. Allergy, rhinitis, and/or eczema also present. Family history of asthma. Obesity coexistence.
Congestive Heart Failure	Chest X-ray shows dilated heart, pulmonary edema. Pulmonary function tests indicate volume restriction, not airflow limitation.
Bronchiectasis	Large volumes of purulent sputum. Commonly associated with bacterial infection. Chest X-ray/CT shows bronchial dilation, bronchial wall thickening.
Tuberculosis	Onset all ages. Chest X-ray shows lung infiltrate. Microbiological confirmation. High local prevalence of tuberculosis.
Obliterative Bronchiolitis	Onset at younger age, nonsmokers. May have history of rheumatoid arthritis or acute fume exposure. Seen after lung or bone marrow transplantation. CT on expiration shows hypodense areas.
Diffuse Panbronchiolitis	Predominantly seen in patients of Asian descent. Most patients are male and nonsmokers. Almost all have chronic sinusitis. Chest X-ray & HRCT show diffuse small centrilobular nodular opacities & hyperinflation.

These features tend to be characteristic of the respective diseases, but are not mandatory. For example, a person who has never smoked may develop COPD (especially in the developing world where other risk factors may be more important than cigarette smoking); asthma may develop in adult and even in elderly patients.

TABLE 2.7

Prevention of COPD

- **1-SMOKING CESSATION:** is the single <u>most important step</u> in prevention the progression of the disease.
- **<u>Pharmacotherapies for smoking cessation</u>**
- Nicotine replacement therapy (nicotine gum, inhaler, nasal spray, transdermal patch, sublingual tablet, or lozenge) reliably increases long-term smoking abstinence rates and is significantly more effective.
- Electronic cigarettes (e-cigarettes, vaping) :E-cigarettes provide a vaporized and doseable nicotine inhalation and have increased in usage as an alternative to cigarettes for those wishing to quit.
- Pharmacological products: Varenicline, bupropion, and nortriptyline have been shown to increase long-term quit rates but should always be used as a component of a supportive intervention program rather than a sole intervention for smoking cessation.

A five-step program for intervention provides a helpful strategic framework to guide healthcare providers interested in helping their patients stop smoking

BRIEF STRATEGIES TO HELP THE PATIENT WILLING TO QUIT

• **ASK:**	Systematically identify all tobacco users at every visit. *Implement an office-wide system that ensures that, for EVERY patient at EVERY clinic visit, tobacco-use status is queried and documented.*
• **ADVISE:**	Strongly urge all tobacco users to quit. *In a clear, strong, and personalized manner, urge every tobacco user to quit.*
• **ASSESS:**	Determine willingness and rationale of patient's desire to make a quit attempt. *Ask every tobacco user if he or she is willing to make a quit attempt at this time (e.g., within the next 30 days).*
• **ASSIST:**	Aid the patient in quitting. *Help the patient with a quit plan; provide practical counseling; provide intra-treatment social support; help the patient obtain extra-treatment social support; recommend use of approved pharmacotherapy except in special circumstances; provide supplementary materials.*
• **ARRANGE:**	Schedule follow-up contact. *Schedule follow-up contact, either in person or via telephone.*

TABLE 3.1

Prevention of COPD

- **2-VACCINATIONS**
- **Influenza vaccine :**reduce serious illness such as lower respiratory tract infections requiring hospitalization and death in COPD patients
- **Pneumococcal vaccine:**reduce the incidence of community-acquired pneumonia in COPD patients.
- **Other vaccines:** In adults with COPD the Centers for Disease Control (CDC) recommends the Tdap vaccination (also called dTaP/dTPa) to protect against pertussis (whooping cough), tetanus and diphtheria, in those who were not vaccinated in adolescence.

- **3-Avoidance of atmospheric pollution:** stay indoors in episods of air pollution or wearing respiratory protective equipments in exposure to heavy dust concentration.

PHARMACOLOGICAL THERAPY FOR STABLE COPD

- **Pharmacological therapy for COPD** is used to:

❖ reduce symptoms,

❖ reduce the frequency and severity of exacerbations,

❖and improve exercise tolerance and health status.

- **Bronchodilators**
- **Anti-inflammatory agents**
- **Antibiotics**
- **Mucolytic**
- **Other pharmacological treatments**

Bronchodilators

- Bronchodilator medications in COPD are most often given on a regular basis to prevent or reduce symptoms
- They act by altering airway smooth muscle tone and the improvements in expiratory flow reflect widening of the airways
- **1-Beta2-agonists:**
- **action :**relax airway smooth muscle by stimulating beta2- adrenergic receptors, which increases cyclic AMP and produces functional antagonism to bronchoconstriction
- There are short-acting (SABA) and long-acting (LABA) beta2-agonists.
- **SABAs** show duration of action within 4 to 6 hours as salbutamol ,terbutaline, albuterol for regular and as-needed use .
- **LABAs** show duration of action of 12 or more hours as Formoterol and salmeterol,
- Indacaterol ,Oladaterol and vilanterol are once daily LABAs that improve lung function and symptoms .
- **Adverse effects: sinus tachycardia, somatic tremor , hypokalemia**

COMMONLY USED MAINTENANCE MEDICATIONS IN COPD*

Generic Drug Name	Inhaler Type	DELIVERY OPTIONS *Nebulizer*	*Oral*	*Injection*	Duration Of Action
BETA$_2$-AGONISTS					
SHORT-ACTING (SABA)					
Fenoterol	MDI	√	pill, syrup		4-6 hours
Levalbuterol	MDI	√			6-8 hours
Salbutamol (albuterol)	MDI & DPI	√	pill, syrup, extended release tablet	√	4-6 hours 12 hours (ext. release)
Terbutaline	DPI		pill	√	4-6 hours
LONG-ACTING (LABA)					
Arformoterol		√			12 hours
Formoterol	DPI	√			12 hours
Indacaterol	DPI				24 hours
Olodaterol	SMI				24 hours
Salmeterol	MDI & DPI				12 hours
ANTICHOLINERGICS					
SHORT-ACTING (SAMA)					
Ipratropium bromide	MDI	√			6-8 hours
Oxitropium bromide	MDI				7-9 hours
LONG-ACTING (LAMA)					
Aclidinium bromide	DPI, MDI				12 hours
Glycopyrronium bromide	DPI		solution	√	12-24 hours
Tiotropium	DPI, SMI, MDI				24 hours
Umeclidinium	DPI				24 hours
Glycopyrrolate		√			12 hours
Revefenacin		√			24 hours
COMBINATION SHORT-ACTING BETA$_2$-AGONIST PLUS ANTICHOLINERGIC IN ONE DEVICE (SABA/SAMA)					
Fenoterol/ipratropium	SMI	√			6-8 hours
Salbutamol/ipratropium	SMI, MDI	√			6-8 hours
COMBINATION LONG-ACTING BETA$_2$-AGONIST PLUS ANTICHOLINERGIC IN ONE DEVICE (LABA/LAMA)					
Formoterol/aclidinium	DPI				12 hours
Formoterol/glycopyrronium	MDI				12 hours
Indacaterol/glycopyrronium	DPI				12-24 hours
Vilanterol/umeclidinium	DPI				24 hours
Olodaterol/tiotropium	SMI				24 hours
METHYLXANTHINES					
Aminophylline			solution	√	Variable, up to 24 hours
Theophylline (SR)			pill	√	Variable, up to 24 hours
COMBINATION OF LONG-ACTING BETA$_2$-AGONIST PLUS CORTICOSTEROID IN ONE DEVICE (LABA/ICS)					
Formoterol/beclometasone	MDI, DPI				12 hours
Formoterol/budesonide	MDI, DPI				12 hours
Formoterol/mometasone	MDI				12 hours
Salmeterol/fluticasone propionate	MDI, DPI				12 hours
Vilanterol/fluticasone furoate	DPI				24 hours
TRIPLE COMBINATION IN ONE DEVICE (LABA/LAMA/ICS)					
Fluticasone/umeclidinium/vilanterol	DPI				24 hours
Beclometasone/formoterol/glycopyrronium	MDI				12 hours
Budesonide/formoterol/glycopyrrolate	MDI				12 hours
PHOSPHODIESTERASE-4 INHIBITORS					
Roflumilast			pill		24 hours
MUCOLYTIC AGENTS					
Erdosteine			pill		12 hours
Carbocysteine†			pill		
N-acetylcysteine†			pill		

TABLE 3.3

**Not all formulations are available in all countries. In some countries other formulations and dosages may be available. † Dosing regimens are under discussion. MDI = metered dose inhaler; DPI = dry powder inhaler; SMI = soft mist inhaler. Note that glycopyrrolate & glycopyrronium are the same compound.*

Bronchodilators

- **2-Antimuscarinic drugs(anticholinergic bronchodilators):**
- **Action:** block the bronchoconstrictor effects of acetylcholine on M3 muscarinic receptors expressed in airway smooth muscle
- **Short-acting antimuscarinics (SAMAs),** as ipratropium and oxitropium,
- **Long-acting muscarinic antagonists (LAMAs),** such as tiotropium, aclidinium, glycopyrronium bromide (also known as glycopyrrolate) and umeclidinium have prolonged binding to M3 muscarinic receptors, cause prolonging the duration of bronchodilator effect.
- **Adverse effects:**dryness of mouth, a bitter metallic taste, Use of solutions with a facemask can precipitate acute glaucoma.

Bronchodilators

- **3-Methylxanthines:**act as non-selective phosphodiesterase inhibitors,
- have a range of non-bronchodilator actions:
- **Theophylline,** the most commonly used methylxanthine
- Addition of theophylline to salmeterol produces a greater improvement in FEV1 and breathlessness than salmeterol alone
- **Adverse effects.** Toxicity is dose-related, which is a particular problem with xanthine derivatives because their therapeutic ratio is small and most of the benefit occurs only when near-toxic doses are given
- atrial and ventricular arrhythmias , grand mal convulsions
- headaches, insomnia, nausea, and heartburn
- These medications have significant interactions with commonly used medications such as erythromycin (but not azithromycin), certain quinolone antibiotics (ciprofloxacin)

- **4-Combination bronchodilator therapy:**
- Different mechanisms and durations of action increase the degree of bronchodilation with a lower risk of side-effects compared to increasing the dose of a single bronchodilator.
- combinations of a LABA and LAMA in a single inhaler available
- a combination of long-acting bronchodilators is more effective than long-acting bronchodilator monotherapy for preventing exacerbations.

Anti-inflammatory agents

- **Inhaled corticosteroids (ICS):**
- Inhaled corticosteroids can reduce the frequency of exacerbations and prevent deterioration of QOL in patients who experience repeated exacerbations and whose %FEV1 is less than 50%.
- The combined use of an inhaled glucocorticoid and a long-acting β2-agonist is more effective in improving respiratory function, preventing exacerbations, and improving QOL than treatment with a single drug.
- The use of long-acting anticholinergic agents or long-acting β2-agonists combined with inhaled glucocorticoids may slow the progression of airflow obstruction and reduce mortality.
- **Adverse effects.** oral candidiasis, hoarse voice, skin bruising and pneumonia.

Anti-inflammatory agents

- **Oral glucocorticoids:**oral glucocorticoids play a role in the acute management of exacerbations as improve lung function and breathlessness.
- they have no role in the chronic daily treatment in COPD.
- **Phosphodiesterase-4 (PDE4) inhibitors:** Roflumilast is a once daily oral medication reduces moderate and severe exacerbations.
- Adverse effects. PDE4 inhibitors have more adverse effects than inhaled medications for COPD. The most frequent are diarrhea, nausea, reduced appetite, weight loss, abdominal pain, sleep disturbance, and headache.

Other pharmacological treatments

- **Alpha-1 antitrypsin augmentation therapy:** Intravenous augmentation therapy has been recommended for individuals with alpha-1 antitrypsin deficiency (AATD), The main limitation for this therapy is very high cost and lack of availability in many countries.
- **Antitussives:** The role of antitussives in patients with COPD is inconclusive.

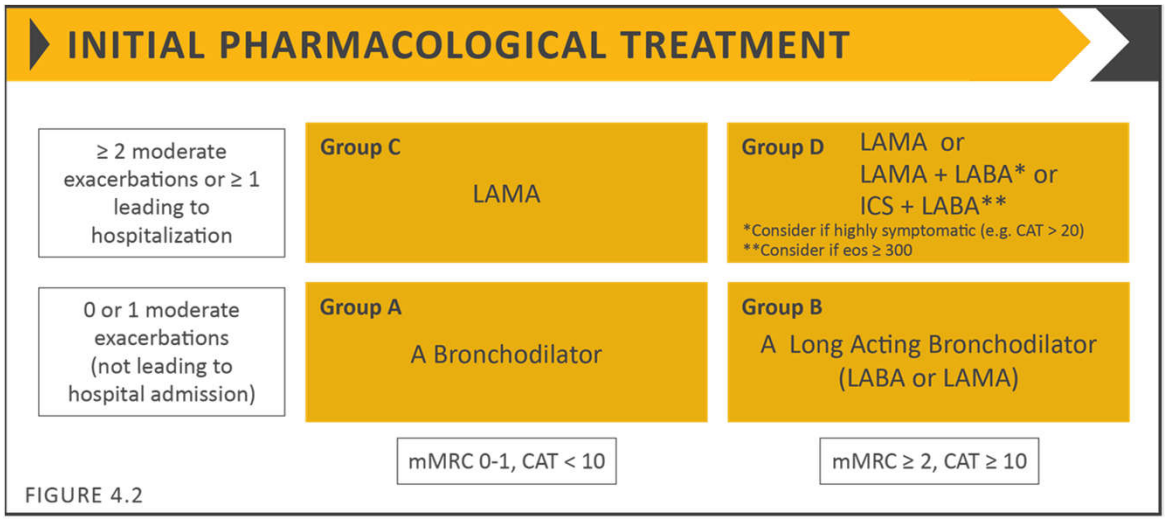

INITIAL PHARMACOLOGICAL TREATMENT
≥ 2 moderate exacerbations or ≥ 1 leading to hospitalization
Group C
LAMA
Group D
LAMA or
LAMA + LABA* or
ICS + LABA**
*Consider if highly symptomatic (e.g. CAT > 20)
**Consider if eos ≥ 300
0 or 1 moderate exacerbations (not leading to hospital admission)
Group A
A Bronchodilator
Group B
A Long Acting Bronchodilator (LABA or LAMA)
mMRC 0-1, CAT < 10
mMRC ≥ 2, CAT ≥ 10

FIGURE 4.2

Non-pharmacologic therapy of COPD

A-Pulmonary rehabilitation: that include,

1. Exercise training :is the core of pulmonary rehabilitation
2. Education: help patients deepen their understanding of the disease and gain the skills they will need for self-management during the stable period and exacerbations

AIM : improve the physical and psychological condition of people with chronic respiratory disease and improve quality of life.

B -Nutrition management: The incidence of progression to respiratory failure and the risk of death are high in patients with weight loss. nutritional supplementation therapy should be considered.

C-Oxygen therapy :receive long-term oxygen therapy (LTOT) or home oxygen therapy (HOT) for more than 15 h/day improves the survival prognosis of COPD patients with severe chronic respiratory failure.

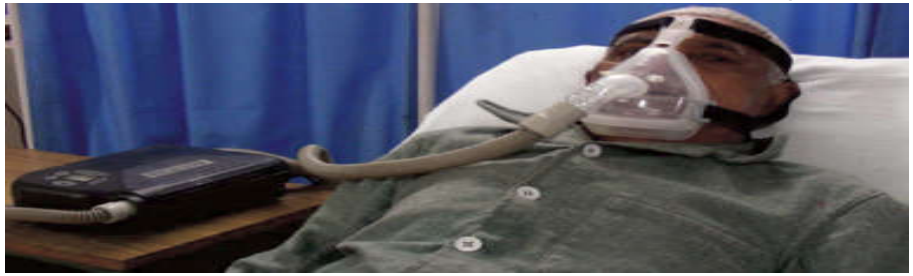
Indications of LTOT:1- Resting room air Pao2 <55 mmHg or oxygen saturation < 88%

2- Resting room air Pao2 56 to 60 mmHg or oxygen saturation < 88% to 89% with supporting evidence of chronic hypoxemia such as

- Polycythemia
- Pulmonary hypertention
- Cor-pulmonale or
- Psychological impairment

Oxygen administrated by nasal cannula with the flow rate adjusted to maintain a resting saturation greater than 90%

- **D-Ventilatory Support :**During exacerbations of COPD. Noninvasive ventilation (NIV) in the form of noninvasive positive pressure ventilation (NPPV) is the standard of care for decreasing morbidity and mortality in patients hospitalized with an exacerbation of COPD and acute respiratory failure.
- Stable patient: In patients with both COPD and obstructive sleep apnea there are clear benefits associated with the use of continuous positive airway pressure (CPAP) to improve both survival and the risk of hospital admissions



INTERVENTIONAL THERAPY

- **Surgical Interventions:**
- **Lung volume reduction surgery (LVRS).** LVRS is a surgical procedure in which parts of the lungs are resected to reduce hyperinflation
- LVRS increases the elastic recoil pressure of the lung and thus improves expiratory flow rates and reduces exacerbations
- **Bullectomy.** Bullectomy is an older surgical procedure for bullous emphysema. Removal of a large bulla that does not contribute to gas exchange and is, or has been, responsible for complications decompresses the adjacent lung parenchyma
- **Lung transplantation:In appropriately selected patients with very severe COPD** Bilateral lung transplantation has been reported to provide longer survival than single lung transplantation ,The complications most commonly seen in COPD patients after lung transplantation are acute rejection, bronchiolitis obliterans, opportunistic infections and lymphoproliferative disease.
- **Bronchoscopic interventions:** a less invasive procedure to reduce hyperinflation in severe emphysema

Complications of COPD

- 1- ACUTE EXACERBATION OF COPD
- 2-PNEUMOTHORAX
- 3-Cor-pulmonal
- 4-Supraventricular tachyarrhythmias
- 5- Hypercapnic Respiratory failure
- 6-LUNG CANCER
- 7-PNEUMONIA
- 8-PULMONARY EMBOLISM

Acute Exacerbation of COPD

- **Definition:** sudden worsening of symptoms such as dyspnea, cough, and sputum, that differs from ordinary physiological fluctuations and requires changes from the treatment during the stable period**.**
- “Exacerbation” does not refer to aggravations of symptoms that are attributable to concurrent diseases such as heart failure, pneumothorax, or pulmonary thromboembolism.
- **Causes :**The most common causes are respiratory infection and air pollution.
- However, in about 30% of the cases the cause is unknown.

Classification of the severity of exacerbations of COPD

- ► **Mild** :At least **one of the three** indices:
- aggravation of dyspnea,
- increase in sputum volume, purulent sputum is positive,
- and at least **one of the following is present**: upper respiratory tract infection within 5 days,
- pyrexia that cannot be attributed to other causes,
- increased wheezing, increased cough,
- more than 20% increase in respiration rate or heart rate.
- ► **Moderate: Two of the three indices are positive.**
- ► **Severe: All the three indices are positive**

POTENTIAL INDICATIONS FOR HOSPITALIZATION ASSESSMENT*

- Severe symptoms such as sudden worsening of resting dyspnea, high respiratory rate, decreased oxygen saturation, confusion, drowsiness.
- Acute respiratory failure.
- Onset of new physical signs (e.g., cyanosis, peripheral edema).
- Failure of an exacerbation to respond to initial medical management.
- Presence of serious comorbidities (e.g., heart failure, newly occurring arrhythmias, etc.).
- Insufficient home support.

*Local resources need to be considered.

TABLE 5.2

- **Indications for ICU admission :**
- Respiratory rate: > 30 breaths per minute; using accessory respiratory muscles;
- acute changes in mental status;
- hypoxemia not improved with supplemental oxygen via Venturi mask or requiring FiO_2 > 40%;
- hypercarbia i.e., $PaCO_2$ increased compared with baseline or elevated > 60 mmHg or the presence of respiratory acidosis (pH ≤ 7.25).

Management of Exacerbations

- **Pharmacological treatment**
- **Bronchodilators:**that short-acting inhaled beta2-agonists, with or without short-acting anticholinergics, are the initial bronchodilators for acute treatment of a COPD exacerbation
- Using metered dose inhalers (MDI) (with or without a spacer device) or nebulizers to deliver the agent
- If a nebulizer is chosen to deliver the bronchodilator agent, air-driven bronchodilator nebulization is preferable to oxygen-driven in acute exacerbations of COPD in order to avoid the potential risk of increasing the PaCO2 associated with oxygen-driven bronchodilator administration

- **Glucocorticoids:** A dose of 30-60 mg prednisone per day for 5 days is recommended
- **Antibiotics:** the infectious agents in COPD exacerbations can be viral or bacterial(Haemophilus influenza,Morraxella catarrhalis, Streptococus pneumoniae)
- antibiotics should be given to patients with exacerbations of COPD who have three cardinal symptoms: increase in dyspnea, sputum volume, and sputum purulence; have two of the cardinal symptoms, if increased purulence of sputum is one of the two symptoms; or require mechanical ventilation (invasive or noninvasive)
- Choice of antibiotic:Usually **initial empirical treatment** is an aminopenicillin with clavulanic acid, macrolide, or tetracycline.
- In patients with frequent exacerbations, severe airflow limitation and/or exacerbations requiring mechanical ventilation **cultures** from sputum or other materials from the lung should be performed, as gram-negative bacteria (e.g., Pseudomonas species) or resistant pathogens that are not sensitive to the above-mentioned antibiotics may be present.
- The route of administration (oral or intravenous) depends on the patient's ability to eat and the pharmacokinetics of the antibiotic,
- Improvements in dyspnea and sputum purulence suggest clinical success.

Adjunct therapies

- use of diuretics
- Anticoagulants
- Oxygen therapy
- Ventilatory support: Noninvasive mechanical ventilation

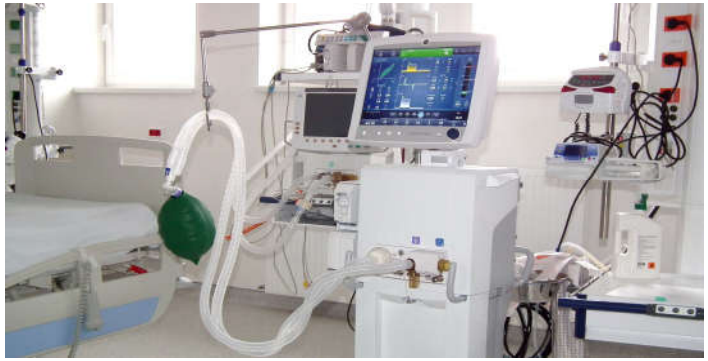
INDICATIONS FOR NONINVASIVE MECHANICAL VENTILATION (NIV)

At least one of the following:

- Respiratory acidosis ($PaCO_2 \geq 6.0$ kPa or 45 mmHg and arterial pH ≤ 7.35).
- Severe dyspnea with clinical signs suggestive of respiratory muscle fatigue, increased work of breathing, or both, such as use of respiratory accessory muscles, paradoxical motion of the abdomen, or retraction of the intercostal spaces.
- Persistent hypoxemia despite supplemental oxygen therapy.

TABLE 5.6

Invasive mechanical ventilation



INDICATIONS FOR INVASIVE MECHANICAL VENTILATION

- Unable to tolerate NIV or NIV failure.
- Status post - respiratory or cardiac arrest.
- Diminished consciousness, psychomotor agitation inadequately controlled by sedation.
- Massive aspiration or persistent vomiting.
- Persistent inability to remove respiratory secretions.
- Severe hemodynamic instability without response to fluids and vasoactive drugs.
- Severe ventricular or supraventricular arrhythmias.
- Life-threatening hypoxemia in patients unable to tolerate NIV.

TABLE 5.7

THANK YOU FOR WEARING A MASK.

Wearing a mask helps me protect you, and you protect me.

Kansas Department of Health and Environment

For more information on masks, visit
kdheks.gov/coronavirus