Chronic Obstructive Pulmonary Disease (COPD)

Pathogenesis of COPD : (IHLL)

1- **I**nflammation & fibrosis of the bronchial wall,
2- **H**ypertrophy of the submucosal glands and hypersecretion of mucus

} Both lead to obstruction of airflow & cause : **mismatching of ventilation & perfusion.**

3- **L**oss of alveolar tissue → decreases the surface area for gas exchange.
4- **L**oss of elastic fibers → leads to airway collapse.

Normally *the elastic fibers have 2 functions:*

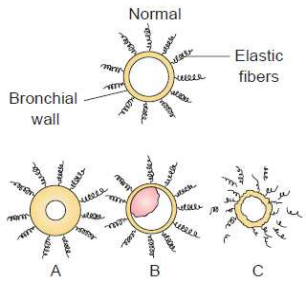
1- Recoil of elastic fibers that were stretched during inspiration provides the force needed to move air out of the lung during expiration.
2- Elastic fibers are attached to the airways,providing radial traction to hold airways open during expiration

In persons with COPD : the loss of elastic fibers causes:

1- Predisposes to airway collapse.
2- Increases air trapping.
3- Impairs the expiratory flow rate.

The term *COPD* encompasses **two** types of obstructive airway disease:

- **Emphysema,** with enlargement of air spaces and destruction of lung tissue.
- **Chronic obstructive bronchitis,** with obstruction of airways.



(Top) Normal bronchial airway with elastic fibers that provide traction and hold the airway open.

(Bottom) Obstruction of the airway caused by :
(**A**) hypertrophy of the bronchial wall,
(**B**) inflammation and hypersecretion of mucus
(**C**) loss of elastic fibers that hold the airway open

Chronic Bronchitis

Definition :

Chronic productive cough of more than 3 months' duration for more than 2 consecutive years .

➔ *Typically,the cough has been present for many years, with a gradual increase in acute exacerbations that produce frankly purulent sputum.*

Types :

1- **Simple bronchitis** → Chronic bronchitis without airflow obstruction.
2- **Chronic obstructive bronchitis**→ chronic bronchitis with airflow obstruction.

Causes :

- It's associated with chronic irritation from **smoking & recurrent infections.**

In chronic bronchitis, **airway obstruction** is caused by :

1- Inflammation of the major and small airways.
2- There is edema and hyperplasia of submucosal glands and excess mucus excretion into the bronchial tree.

Emphysema

Normally, the lung is protected by antiprotease enzymes as : **α1-antitrypsin**

Two recognized causes of emphysema : →

In smokers in whom COPD develops :
- Inadequate antiprotease production and release to neutralize
- Excess protease production

1- Increased elastase production:

- Cigarette smoke stimulate **movement of inflammatory cells into the lungs**, → resulting in **increased release of proteinases as: elastase** (serine elastase from neutrophils / metalloelastase from alveolar macrophages) → that digests elastin resulting in breakdown of elastin and other alveolar wall components.

2- Inherited deficiency of α1-proteinase inhibitor (α1 – antitrypsin):

- Accounts for 1% of all cases of COPD.
- More common in young persons before age of 40 years .
- Smoking & repeated respiratory tract infections, → decrease **α1**-antitrypsin levels→ risk for emphysema .
- Human **α1**-antitrypsin is available for replacement therapy.

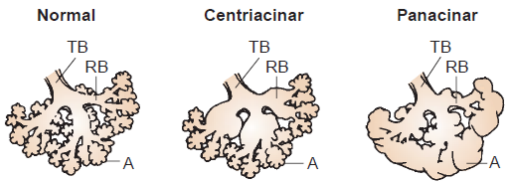
Emphysema is characterized by :

1- **Loss of lung elasticity**
2- **Destruction of the alveolar walls and capillary beds.**
3- **Abnormal enlargement of the air spaces distal to the terminal bronchioles,**
Enlargement of the air spaces leads to → **hyperinflation of the lungs** → produces an increase in (TLC).

There are two commonly recognized types of emphysema:

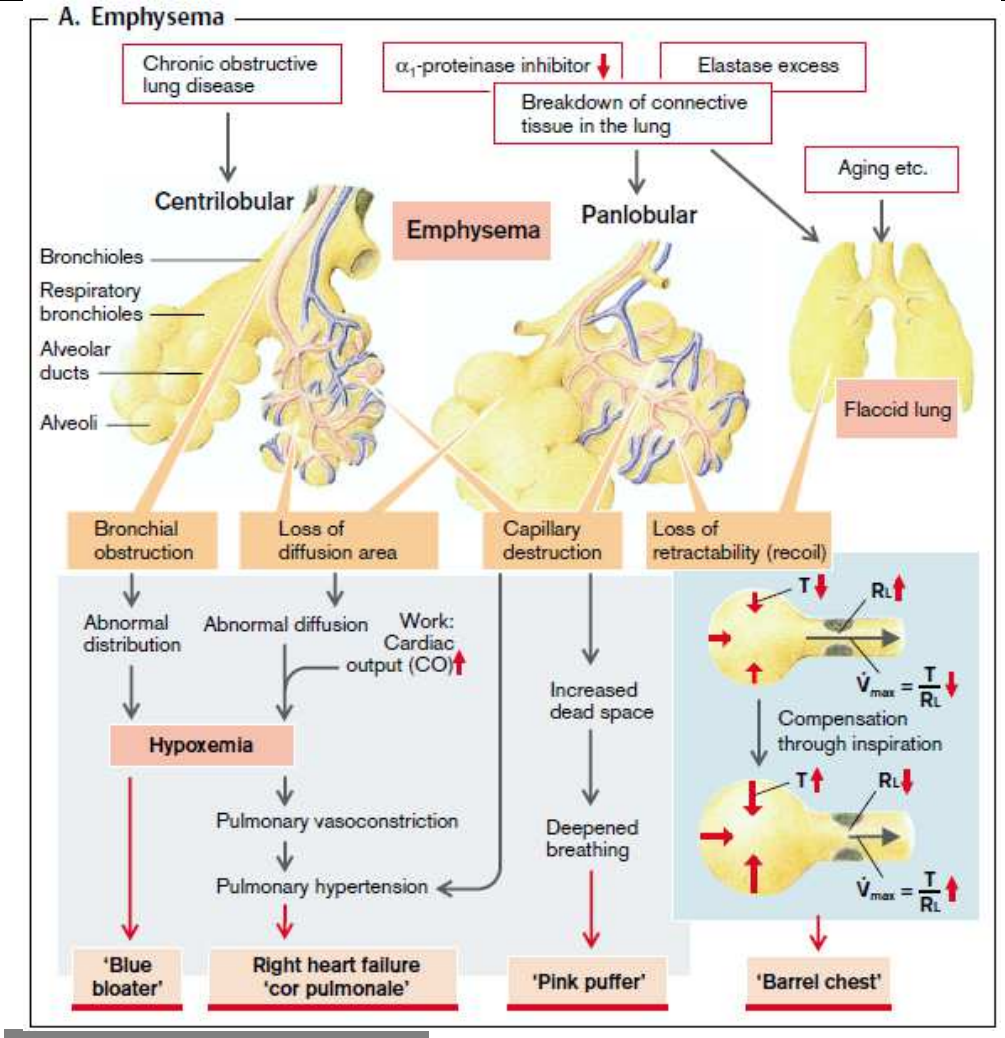
1- Centriacinar :

- Affects the bronchioles in the central part of the respiratory lobule (terminal bronchioles (TB) & respiratory bronchioles (RB)), with initial preservation of the alveolar ducts and sacs.
- Most common type of emphysema.
Seen predominantly in male smokers.
- Centriacinar changes in upper parts of the lung.



2- Panacinar

- Produces initial involvement of the peripheral alveoli → Later extends to involve the more central bronchioles.
- More common in persons with **α1**-antitrypsin deficiency.
Also found in smokers in association with centrilobular emphysema.
- Panacinar changes are seen in lower parts of the lung



Clinical Manifestations

1. Dyspnea : In Emphysema & chronic bronchitis

- Persons with emphysema have **marked dyspnea and struggle to maintain normal blood gas levels** with increased ventilatory effort (overventilate) , including prominent use of the accessory muscles.
- The seated position,which stabilizes chest structures and allows for maximum chest expansion and use of accessory muscles, is preferred

2. Productive chough : In Chronic Bronchitis

- **Cough is productive** of thick, purulent sputum owing to→ ongoing local inflammation & infection.
- **Sputum viscosity is increased** largely as a result of presence of free DNA (of high molecular weight and highly viscous) from lysed cells.
- **Hemoptysis** → with increased inflammation and mucosal injury.
- **Cough is much less effective** owing to → 1- narrow airway caliber & 2- greater volume and viscosity of secretions.

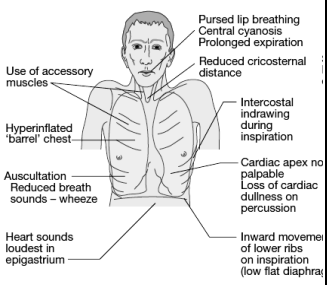
3. Breath sounds :

In Emphysema :
- Decreased in intensity of breathing sound → reflecting decreased airflow.
- Wheezes, when present , are of diminished intensity - Crackles & rhonchi, in superimposed processes as infection

In Chronic Bronchitis : Persistent airway narrowing & mucus obstruction :
- Produce localized or diffuse wheezing (responsive to bronchodilators).
- Prolonged expiratory time .
- Inspiratory & expiratory coarse crackles : ↑ mucus production + defective mucociliary clearance → excessive secretions in the airways.

4. Cardiac examination :

- Tachycardia → as in chronic bronchitis, especially with exacerbations of bronchitis or hypoxemia.
- Pulmonary hypertension → If hypoxemia is significant and chronic,,, Cardiac examination may reveal :
  - Prominent pulmonary valve closure (increased P_2, pulmonary component of the 2nd heart sound) or
  - Elevated jugular venous pressure AND peripheral edema resulting from Rt heart failure.



5. Imaging :

- Hyperinflation with → 1- flattened hemidiaphragms 2- ↑ anteroposterior chest diameter.
- Parenchymal destruction produces : attenuated peripheral vascular markings.
- Pulmonary hypertension produces : proximal pulmonary artery dilation .
- Cardiac size may be increased, suggesting right heart volume overload.
- Cystic or bullous changes.

6. Pulmonary function tests :

In Emphysema :
- The loss of elastic recoil in lung tissue supporting the airways results in increased dynamic compression of airways, (especially during forced expiration)→ all flow rates are reduced:**With premature airway collapse, FEV_1, FVC, FEV_1/FVC (FEV_1% ratio) ↓.**
- **"Expiratory flow-volume curve" shows substantial limitation in flow**.

In Chronic Bronchitis :
- Diffuse airway obstruction is demonstrated as a global reduction in expiratory flows & volumes. **FEV_1, FVC, FEV_1/FVC (FEV_1%) ↓.**
- **expiratory flow-volume curve" shows substantial limitation in flow**.
- **Increased RV and FRC**, reflecting *air trapped in the lung* as a result of :
  a- Diffuse airway obstruction (chronic bronchitis)
  b- Early airway closure caused by loss of elastic recoil (emphysema)
- **TLC is increased** → substantial amount of this increase comes from gas trapped in poorly lung units, including bullae.

7. Arterial blood gases :

In Emphysema : (Emphysema is a disease of alveolar wall destruction)
- The loss of the alveolar capillaries creates: **areas of high ventilation relative to perfusion.**
- They may ***able to maintain nearly normal PO_2 and PCO_2 levels*** despite advanced disease
- **Hypercapnia, respiratory acidosis, and a compensatory metabolic alkalosis** are *common in severe disease.*

In Chronic Bronchitis :
- In contrast to persons with emphysema, those with chronic obstructive bronchitis are ***unable to maintain normal blood gases by increasing their breathing effort*** → **" Ventilation-perfusion mismatching "** is common in chronic bronchitis.
- **Hypoxemia** (arterial PO2 levels fall below 55 mm Hg) at rest tends to be more profound than in emphysema → causes reflex vasoconstriction of the pulmonary vessels → persons with chronic obstructive bronchitis develop **pulmonary hypertension** and, eventually, **right-sided heart failure with peripheral edema (*i.e.,* cor pulmonale).**
- **Hypercapnia, Cyanosis, respiratory acidosis, and a compensatory metabolic alkalosis**.

8. **Polycythemia :** Chronic hypoxemia (especially in chronic bronchitis) is associated with erythropoietin-mediated increase in **hematocrit**.

The mnemonics **"pink puffer" and "blue bloater"** used to differentiate the clinical manifestations of **:**
Emphysema & Chronic obstructive bronchitis (In practice, differentiation between the two types is often difficult)
A major difference between the pink puffers & the blue bloaters is the respiratory responsiveness to the hypoxic stimuli.

- **Chronic obstructive bronchitis** is characterized by **excessive bronchial secretions and airway obstruction that causes mismatching of ventilation & perfusion** → Thus, persons with chronic bronchitis are unable to compensate by increasing their ventilation; → instead, **hypoxemia & cyanosis** develop. (These are **blue bloaters, or nonfighters**).
  - In centrilobular emphysema a ***distribution abnormality*** also develops, because of differing resistances in different bronchioles → resulting in ***hypoxemia***.
  - Patients with centrilobular emphysema are called **"blue bloaters"** .

Centrilobular emphysema :

- **Pulmonary emphysema :** there is a **proportionate loss of ventilation & perfusion area** in the lung.
  - These persons are **pink puffers, or fighters** able to overventilate and thus maintain relatively normal blood gas levels ***until late in the disease.***
  - In panlobular emphysema , an ***enlargement of the functional dead space*** forces them to ***breathe more deeply***.
  - Patients with panlobular emphysema are called are called **"pink puffers".**

Panlobular emphysema :

1- Reduced elastic recoil: leads to

The lung's reduced ability to retract (*flaccid lung*) can lead to **obstructive lung disease**, because :

reduced elastic recoil (increased compliance) of the lung requires an increase in intrathoracic pressure for expiration, resulting in compression of the intrathoracic airways → massive **increase in flow resistance.**

- **Positive pressure in alveoli :**
  1- **Reduced lung's elastic recoil** generates the positive pressure in the alveoli :
  - With loss of lung elasticity and hyperinflation of the lungs → greater intrathoracic pressure is necessary for expiration because compliance and resistance are increased → This causes **compression of the bronchioles** →so, **airway pressure increases further**.
  - The airways often collapse during expiration because pressure in surrounding lung tissues exceeds airway pressure → Air becomes trapped in lungs, producing an increase in the anteroposterior dimensions of the chest, the so-called *barrel chest*.
  - Elastic recoil can be raised by increasing the inspiratory volume → leading to a *shift in the resting position* toward inspiration (*barrel chest*).
  - Pursed-lip breathing, → increases the resistance to the outflow of air, → preventing airway collapse by increasing airway pressure.

  2- **External compression** produces positive pressure in the alveoli by contraction of expiratory muscles, BUT this will **also compress the bronchioles** → thus bring a massive **increase in flow resistance.**

THUS :

Maximal expiratory flow rate (V max) is a function of the ratio between *elastic recoil (K)* and resistance (RL) .

- **Respiratory function :**
  - If tidal volume(TV) remains constant :
    1- ↑ functional residual capacity (FRC) 2- ↑ residual volume (RV) 3- ↑ dead space.
  - Vital capacity (VC) is ↓ because of the reduced expiratory volume.

2- Bronchial obstruction : leads to

1- ↓ maximum breathing capacity ($\dot{V}$ max)
2- ↓ FEV1 .
3- differing ventilation of various alveoli results in ***abnormal distribution*** → resulting in : **Hypoxemia.**

3- Loss of alveolar wall : leads to

1- **diminished diffusion area** → ***abnormal diffusion*** of gases → resulting in : **Hypoxemia .**

The hypoxia of underventilated alveoli leads to →vasoconstriction, → increased pulmonary vascular resistance, → **pulmonary hypertension**, → an **increased right ventricular load (cor pulmonale)**.

4- Loss of pulmonary capillaries : leads to

1- ***increase in functional dead space***
2- ***increased pulmonary artery pressure and vascular resistance*** → **with development of " *cor pulmonale*"**

- *The fluid retention and peripheral oedema is due to failure of excretion of sodium and water by the hypoxic kidney rather than Rt. heart failure.*
- *With severe fluid overload,* → ***tricuspid incompetence*** *may develop with :*
elevated jugular venous pressure (JVP) / ascites / upper abdominal discomfort due to liver swelling.

Investigations

1- Lung function tests:
- **Show evidence of airflow limitation** : FEV_1: FVC ratio is reduced /and PEFR is low.
  In many patients the airflow limitation is partly reversible (usually a change in FEV_1 of <15%), and it can be difficult to distinguish between COPD and asthma.
- **Lung volumes :** be normal or increased;
- **Carbon monoxide gas transfer factor:** is low when significant emphysema is present.

2- Chest X-ray : see above in clinical manifestations

3- High-resolution CT scans : when the plain chest X-ray is normal.

4- Haemoglobin level and PCV : can be elevated as a result of persistent hypoxaemia (2ry polycythaemia).

5- Blood gases :
- **At rest** → normal - **On exercise** → patients desaturate .
- **In more advanced cases** → 1- resting hypoxaemia and 2- hypercapnia.

6- Sputum examination :
- Strep. pneumoniae and H. influenzae are the only common organisms to produce acute exacerbations.
- Occasionally, Moraxella catarrhalis may cause infective exacerbations.

7- Electrocardiogram: is often normal, BUT In advanced pulmonary hypertension :
- P wave is tall (P pulmonale) . - Right bundle branch block (RBBB) - Rt. ventricular hypertrophy.

8- Echocardiogram : is useful to assess cardiac function where there is disproportionate dyspnoea.

9- α_1-Antitrypsin : levels & genotype are worth measuring in: 1- premature disease or 2- lifelong non-smokers.

Acute exacerbations of COPD → Presence of hypercarbia (P_{CO_2} >45 mmHg) has important implications for treatment (discussed below).

- Exacerbations are **episodes of increased dyspnea and cough and change in the amount and character of sputum.**
- They may or may not be accompanied by other signs of illness, including **fever, myalgias, and sore throat**.
- Presence of **cyanosis, peripheral oedema or alteration in consciousness** → indicates the need for referral to hospital.

1- Oxygen : (In patients with an exacerbation of severe COPD, high concentrations of oxygen may cause respiratory depression & worsening acidosis)
- The aim is maintaining : **PaO2** > 60 mmHg or **SaO2** between 88% & 92% without worsening acidosis.

2- Bronchodilator s :
- Nebulised short-acting β2-agonists (salbutamol) **combined with** anticholinergic agent (ipratropium).
- These may be administered separately or together.

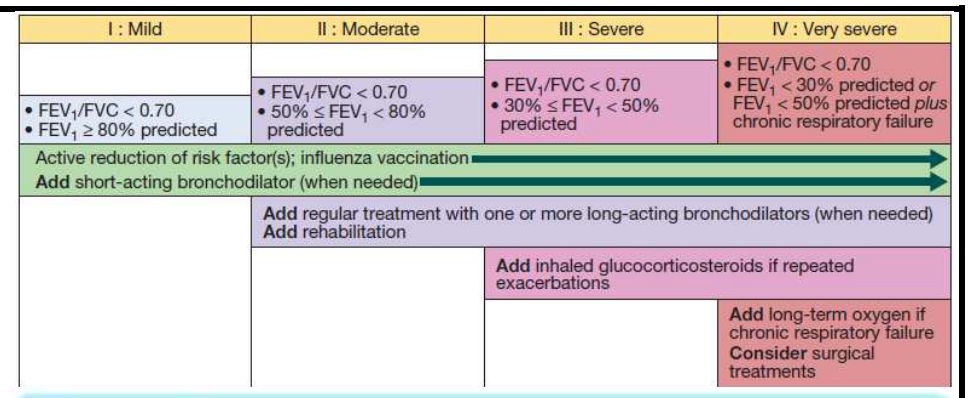
3- Glucocorticoids :
- 1- Reduce length of stay 2- hasten recovery 3- reduce chance of subsequent exacerbation or relapse for a period of up to 6 m.
- The GOLD guidelines recommend : **oral prednisolone (30 mg) for a period of 2 weeks.**

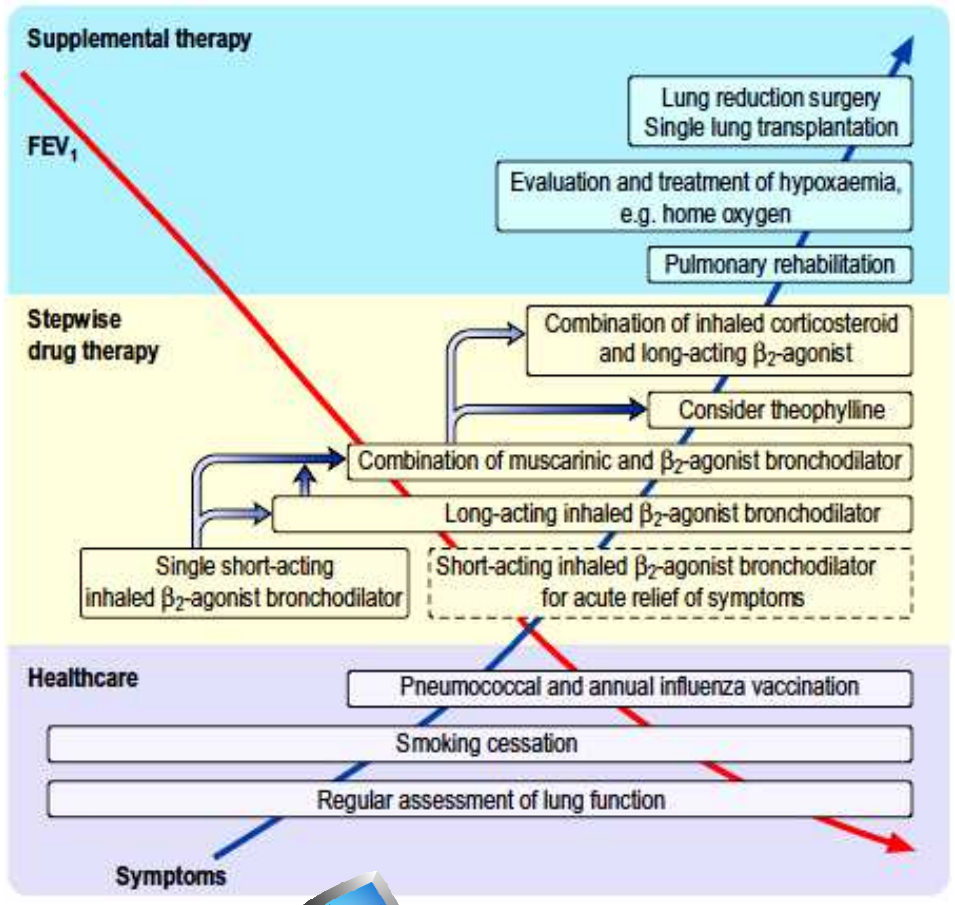
4- Antibiotics :
- Patients with COPD are frequently colonized with potential respiratory pathogens (*s. pneumoniae*, *H. influenzae*, *M. catarrhalis)*.
- Indications: **Currently recommended for patients reporting increase in sputum purulence, sputum volume or breathlessness.**
- Regimens : **Aminopenicillin or a macrolide**. / **Co-amoxiclav** if β-lactamase-producing organisms susceptible.

5- Mechanical Ventilatory Support :

A) **Noninvasive positive-pressure ventilation (NIPPV)** :
- Indications: If, despite above measures, patient remains **tachypnoeic, hypercapnic ,acidotic (PaCO2 > 45 mmHg / pH < 7.35)**
- Its use is associated with reduced requirements for mechanical ventilation and reduced mortality

B) **Invasive Mechanical Ventilation** :
- Indications:
  1- Severe respiratory distress despite initial therapy, 2- life-threatening hypoxemia, 3- severe hypercarbia and/or acidosis, 4- markedly impaired mental status 5- respiratory arrest 6- hemodynamic instability





MedicoNotes www.mediconotes.com

Pharmacotherapy

Reducing exposure to noxious particles & gases	• Complete cessation of smoking is accompanied by → 1- improvement in lung function 2- deceleration in the rate of FEV1 decline . • Pharmacologic approaches: **1- Bupropion** **2- Nicotine replacement therapy** as: gum, transdermal patch, inhaler **3- varenicline**, nicotinic acid receptor agonist/antagonist.
Bronchodilators	- Bronchodilator therapy is central to the **management of breathlessness.** - Compound bronchodilators, a selective β2 agonist and an antimuscarinic agent, are used. - Oral bronchodilator therapy may be used in patients who cannot use inhaled devices efficiently. - Significant improvements in breathlessness may be reported, despite minimal changes in FEV1 → reflecting improvements in lung emptying that reduce dynamic hyperinflation .
β-Adrenergic agonists	• **In mild COPD :** Short-acting β2-agonists → **Salbutamol or Terbutaline** . • **In moderate & severe COPD :** long-acting β2 agonists → **Formoterol or salmeterol** .
Antimuscarinic drugs	• **In mild COPD :** Short-acting → **Ipratropium bromide** (improves symptoms and produces acute improvement in FEV_1). • **In moderate & severe COPD :** long-acting → **Tiotropium bromide** (improve symptoms and reduce exacerbations BUT does not affect the decline in FEV1).
Theophyllines	• **Theophylline preparations**: improve breathlessness and quality of life, BUT their use is limited by : 1- side-effects 2- unpredictable metabolism 3- drug interactions.
Phosphodiesterase inhibitors	• **Roflumilast** is an inhibitor with anti-inflammatory properties. → It is used as an adjunct to bronchodilators for the maintenance treatment of COPD patients.
Corticosteroids **Combination of :** - Corticosteroid with - Long-acting β_2 agonist may protect against lung function decline BUT does not improve overall mortality.	**Inhaled Corticosteroids (ICS)** • **Indications :** - Recommended in patients with **severe disease (FEV1 < 50%) who report two or more exacerbations requiring antibiotics or oral steroids per year .** • **Effects :** - Reduce the frequency and severity of exacerbations. - Regular use is associated with a small improvement in FEV1 (but ICS do not alter the natural history of the FEV1 decline). **Oral Corticosteroids** **Prednisolone** 30 mg daily should be given for 2 weeks • **Indications :** - Useful **during exacerbations** (BUT maintenance therapy contributes to osteoporosis "other side effects" should be avoided) . • **effects :** - If there is objective evidence of a substantial **degree of improvement in airflow limitation (FEV1 increase >15%),** → prednisolone should be discontinued and replaced by : inhaled corticosteroids (beclometasone 40 µg twice daily adjusted according to response)
Oxygen therapy **Long-term oxygen therapy (LTOT)**	• **long-term domiciliary oxygen therapy (LTOT) will benefit patients who have:** Arterial blood gases measured in clinically stable patients on optimal medical therapy *on at least two occasions 3 weeks apart* : **1- PaO2 < 55 mmHg** irrespective of PaCO2 and **FEV1 < 1.5 L** **2- PaO2 55–60 mmHg** plus **secondary polycythaemia**, **pulmonary hypertension, peripheral oedema or nocturnal hypoxaemia** **3- Carboxyhaemoglobin of <3% (i.e. patients who have stopped smoking).** → **Use : at least 15 hrs/day at 2–4 L/min** → **Aim : to achieve → *Pa*O2 > 60 mmHg *or* SaO2 > 90 %** • **A fall in pulmonary artery pressure** : was achieved if oxygen was given for 15 hours daily, • **Substantial improvement in mortality:** was only achieve if oxygen was given for 19 hours daily.
Other measures	**1- Vaccination:** → **1- Influenza vaccine (annually) 2- Polyvalent pneumococcal vaccine (single dose)** **2- Mucolytic therapy :** →**4-week trial of Carbocysteine** (Reduce sputum viscosity + can reduce the number of acute exacerbations) . **3- Diuretic therapy:** → This is necessary for all oedematous patients. **4- α1-Antitrypsin replacement**:→Weekly or monthly infusions of **α1-antitrypsin** have been recommended for : **1-patients with serum levels below 310 mg/L & 2-abnormal lung function.** **5- Heart failure** : → should be treated. **6- Secondary polycythaemia** :→ requires **venesection** if the PCV is >55% **7- Sensation of breathlessness:** → an be reduced by either **promethazine** or **dihydrocodeine** Although opiates are the most effective treatment for intractable breathlessness they depress ventilation and carry the risk of respiratory failure.

Nonpharmacologic Therapies

Pulmonary rehabilitation	• **Exercise** should be encouraged at all stages • **Multidisciplinary programmes** that incorporate: **1-** Physical training **2-** Disease education and nutritional counselling reduce symptoms **3-** Improve health status and enhance confidence.
Surgical intervention	**1- Bullectomy :** - Patients in whom large bullae compress surrounding normal lung tissue, who otherwise have minimal airflow limitation and a lack of generalised emphysema, → considered for bullectomy. **2- Lung volume reduction surgery (LVRS) :** Patients with : - **Predominantly upper lobe emphysema - with preserved gas transfer - No evidence of pulmonary hypertension,** → benefit from **lung volume reduction surgery (LVRS),** in which: *peripheral emphysematous lung tissue is resected → with the aim of reducing hyperinflation and decreasing the work of breathing.*
Lung Transplantation	• Candidates for lung transplantation: **1- <65 years 2- have severe disability despite maximal medical therapy 3- free of comorbid conditions** (liver, renal diseases). • In contrast to LVRS, the anatomic distribution of emphysema *AND* presence of pulmonary hypertension are not *contraindications to lung transplantation.*

Gestational Diabetes Mellitus

White's Classification of diabetes during pregnancy

Women can be separated into :
- Those who were known to have diabetes before pregnancy—***pregestational*** or ***overt***,
- Those diagnosed during pregnancy—***gestational***.

Class	Onset	Plasma Glucose Level: Fasting	Plasma Glucose Level: 2-hour Postprandial	Therapy
A_1	**Gestational Diabetes** glucose intolerance developing during pregnancy	<105 mg/dL (Normal)	<120 mg/dL (normal)	Diet alone
A_2	**Gestational Diabetes**	>105 mg/dL	>120 mg/dL	Insulin

Class	Onset	Age of Onset (yr)	Duration (yr)	Vascular Disease	Therapy
B	Overt Diabetes , developing :	Over 20	<10	None	Insulin
C		10 to 19	10 to 19	None	Insulin
D		Before 10	>20	Benign retinopathy	Insulin
F		Any	Any	Nephropathy[a]	Insulin
R		Any	Any	Proliferative retinopathy	Insulin
H		Any	Any	Heart	Insulin

- **Class A : Gestational diabetes** , subdivided into → those with fasting hyperglycemia of 105 mg/dL **(A1)** or greater **(A2).**
- **Classes B to H :** have overt diabetes antedating pregnancy.
  The White system emphasized that end-organ derangements, especially involving the eyes, kidneys, and heart, have significant effects on pregnancy outcome.

Definition & Incidence

Overt Diabetes , Diagnosis during pregnancy :
- Women with **high plasma glucose levels** + **glucosuria** + **ketoacidosis** present no problem in diagnosis.
- Women with a **random plasma glucose level > 200 mg/dL**
  plus
  Classic signs & symptoms such as polydipsia, polyuria,
- **Fasting plasma glucose level exceeding 125 mg/dL (>= 126 mg/dl)**
  - *The diagnostic cutoff value for overt diabetes is a fasting plasma glucose of **126 mg/dL or higher**.*

The likelihood of impaired carbohydrate metabolism is increased in women who:
1- have a strong familial history of diabetes,
2- have given birth to large infants,
3- demonstrate persistent glucosuria, or have unexplained fetal losses.

Gestational Diabetes : (diagnosis will be explained later)

It's defined as glucose intolerance with onset or first recognition during pregnancy.
- Pregnancy is associated with progressive insulin resistance.
- Human placental lactogen, progesterone, prolactin, cortisol, and tumor necrosis factor are associated with increased insulin resistance during pregnancy**.**
- Some women with gestational diabetes have previously unrecognized overt diabetes. It was found that women with fasting hyperglycemia diagnosed before 24 weeks had pregnancy outcomes similar to those for women with overt diabetes. Thus, fasting hyperglycemia early in pregnancy almost invariably represents overt diabetes.

- Reports show a rate of 3% to 8% of gestational diabetes mellitus (GDM).
- Pregestational diabetes is present in about 1% of pregnancies.
- 90% of diabetes in pregnant women is gestational - 10% is pregestational.
- Studies suggest that women who develop GDM have chronic insulin resistance and that GDM is a "stress test" for the development of diabetes in later life.

Screening

- **Instead of *universal screening*,** recommendations are now for *selective screening* using the guidelines shown in Table →.
- This evaluation is usually done in two steps (the two-step procedure)L
  1- **Screening :** 50-g oral glucose challenge test (GCT) is followed by →
  2- **Diagnostic:** 100-g oral glucose tolerance test (OGTT)*if initial results exceed a predetermined plasma glucose concentration.*

1- Screening test → 1h 50-g Oral Glucose Challenge Test (OGCT)

- Screening should be performed between **24 to 28 weeks.**
- Screening is advised **at the first prenatal visit** in pregnant women with risk factors **(see table →)**

→ Without regard to time of day or time of last meal (no fasting state is needed):
Plasma glucose level is measured 1 hour after a 50-g glucose load
- **Normal Value :** < 140 mg/dl
- **Abnormal Value:** >= 140 mg/dL identifies 80 % of all women with gestational diabetes.

- **If the first-trimester screen is negative, it should be repeated at → 24 to 28 weeks.**
- **Glucose values above 130 to 140 mg/dL on a GCT are considered abnormal** and have an 80% to 90% sensitivity in detecting GDM
- if 130 mg/d used as cutoff value results in 20% to 25% false positive results, compared to 14% to 18% false positive results with 140mg/dl .
- **If the 1-hour screening (50-g oral glucose) plasma glucose exceeds 200 mg/dL, a glucose tolerance test is not required and may dangerously elevate blood glucose values.**

2- Diagnostic test → 3h 100-g oral glucose tolerance test (OGTT)

- **An abnormal screening GCT is followed with a diagnostic** : 3-hour 100-g oral glucose tolerance test.

→ After an overnight fast , a fasting blood sugar (FBS) is drawn :
- **If FBS > 125 mg/dl** , indicates overt diabetes mellitus→ No further testing is performed
- **If FBS < 126 mg/dl** → Administer a 100-g glucose load, and check glucose levels hourly for 3 hours.

Time	100-g Glucose (Used in USA)	
Fasting	**95 mg/dL**	5.3 mmol/L
1-h	**180 mg/dL**	10.0 mmol/L
2-h	**155 mg/dL**	8.6 mmol/L
3-h	**140 mg/dL**	**mmol/L**

- If two or more abnormal values :
Patient is diagnosed with GDM

- If only one value is abnormal :
Impaired glucose tolerance

Table: Recommended Screening Strategy Based on Risk Assessment for Detecting GDM

GDM risk assessment: Should be ascertained at the first prenatal visit

Low Risk: Blood glucose testing **not routinely required** if all the following are present:
- Member of an ethnic group with a low prevalence of GDM
- No known diabetes in first-degree relatives
- Age < 25 years
- Weight normal before pregnancy
- Weight normal at birth
- No history of abnormal glucose metabolism
- No history of poor obstetrical outcome

Average Risk: Perform blood glucose testing at **24 to 28 weeks using either**:
- Two-step procedure:
  - Screening test :50-g oral glucose challenge test (GCT), followed by →
  - Diagnostic test : 100-g oral glucose tolerance test ,for those meeting the threshold value in the GCT.
- One–step procedure:
  - Diagnostic 100-g oral glucose tolerance test performed on all subjects.

High Risk: Perform blood glucose testing, using the procedures described above if one or more of these present :
- **P**ositive glucosuria (not necessary in GDM , but if found need further investigation) .
- Severe o**b**esity > 90 kg .
- **P**ositive family history of type 2 diabetes .
- **P**revious history of :
  - Gestational diabetes mellitus
  - Impaired glucose metabolism, or glucosuria.
  - Repeated unexplained abortions
  - Unxplained IUFD
  - Major congenital anomalies
  - Macrosomic infant > 4 kg
  - Neonatal death
- History of :
  - **P**olyhydramnios
  - Recurrent moniliasis or UTI.

If GDM is not diagnosed, blood glucose testing should be repeated at 24 to 28 weeks or at any time there are symptoms or signs suggestive of hyperglycemia.

Fetal & Neonatal complications

Entity	Monitoring
1- Macrosomia with traumatic delivery (shoulder dystocia, Erb's palsy)	Ultrasonography for estimated fetal weight before delivery; consider cesarean delivery if estimated fetal weight > 4250-4500 g
DELAYED ORGAN MATURITY	
2- Pulmonary, hepatic, neurologic, pituitary-thyroid axis; with respiratory distress syndrome, hypocalcemia	Avoid delivery before 39 weeks in the absence of maternal or fetal indications unless amniocentesis indicates lung maturity. Maintain euglycemia intrapartum.
CONGENITAL DEFECTS	
1- Cardiovascular anomalies (Most common)	- Preconception counseling and glucose control, - HbA_{Ic} in the first trimester
2- Neural tube defects	- Maternal serum alpha-fetoprotein screening; - fetal ultrasonography and fetal echocardiogram; - amniocentesis and genetic counseling
3- Caudal regression syndrome(most specific	- If U/S showns sacral agenesis (most specific) → HbA_{Ic}
4- Other defects, e.g., renal	
FETAL COMPROMISE	
1- Intrauterine growth restriction	Serial ultrasonography for fetal growth and estimated fetal weight, serial fetal surveillance with nonstress test, amniotic fluid index, and fetal Doppler. Avoid postdates pregnancy.
2- Intrauterine fetal death	
3- Abnormal fetal heart rate patterns	

Metabolic Assessments Recommended after Pregnancy with Gestational Diabetes

Time	Test	Purpose
Postdelivery (1–3 d)	Fasting or random plasma glucose	Detect persistent, overt diabetes
Early postpartum (6–12 wks)	75-g 2-h OGTT	Postpartum classification of glucose metabolism
1 yr postpartum	75-g 2-h OGTT	Assess glucose metabolism
Annually	Fasting plasma glucose	Assess glucose metabolism
Tri-annually	75-g 2-h OGTT	Assess glucose metabolism
Prepregnancy	75-g 2-h OGTT	Classify glucose metabolism
Classification of the American Diabetes Association (2003)		
Normal	**IFG or IGT**	**Diabetes Mellitus**
Fasting < 110 mg/dL	110–125 mg/dL	>= 126 mg/dL
2 hr < 140 mg/dL	2 hr >= 140–199 mg/dL	2 hr >= 200 mg/dL

Maternal Complications of Diabetes Mellitus

Entity	Monitoring
OBSTETRIC COMPLICATIONS	
1-Polyhydramnios	- Close prenatal surveillance; - blood glucose monitoring, - ultrasonography
2- Preeclampsia	Evaluation for signs and symptoms
3- Infections,	**e.g., UTI & candidiasis**: Urine culture, wet mount, appropriate therapy
4- C.S delivery	- Blood glucose monitoring, - insulin and dietary adjustment to prevent fetal overgrowth
5- Genital trauma	U/S to detect macrosomia, cesarean delivery for macrosomia
DIABETICE MERGENCIES	
1- Hypoglycemia	Teach signs and symptoms; blood glucose monitoring; insulin and dietary adjustment; check for ketones, blood gases, and electrolytes if glucose > 300 mg/dL
2- Diabetic coma	
3- Ketoacidosis	
VASCULARAND END-ORGAN INVOLVEMENT OR DETERIORATION (IN PATIENTS WITH PREGESTATIONAL DIABETES MELLITUS)	
1- Cardiac	Electrocardiogram first visit and as needed
2- Renal	Renal function studies, first visit and as needed
3- Ophthalmic	Funduscopic evaluation, first visit and as needed
4-Periph.vascular	Check for ulcers, foot sores; noninvasive Doppler studies
5- NEUROLOGIC	
-Peri.neuropathy	Neurologic and gastrointestinal consultations as needed
-GIT disturbance	
6- LONG-TERM OUTCOME	
- Type 2 diabetes	Postpartum glucose testing, lifestyle changes (diet & exercise)
- Metabolic syndrome	Lifestyle changes (diet and exercise)
- Obesity	Lifestyle changes (diet and exercise)
- CVS disease	Annual checkup by physician, lifestyle changes (diet and exercise)