Chronic Obstructive Pulmonary Disease (COPD)

THE Guideline

- Global Initiative for Chronic Obstructive Lung Disease (GOLD), World Health Organization (WHO), National Heart, Lung and Blood Institute (NHLBI)

Definition of COPD

- COPD is a preventable and treatable chronic lung disease characterized by airflow limitation that is not fully reversible
- The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lung to noxious particles or gases, primarily caused by cigarette smoking
- Although COPD affect the lungs, it also produces significant systemic consequences

Adapted from the Global Initiative for Chronic Obstructive Lung Disease 2007

- ATS/ERS Guidelines 2004

Epidemiology of COPD

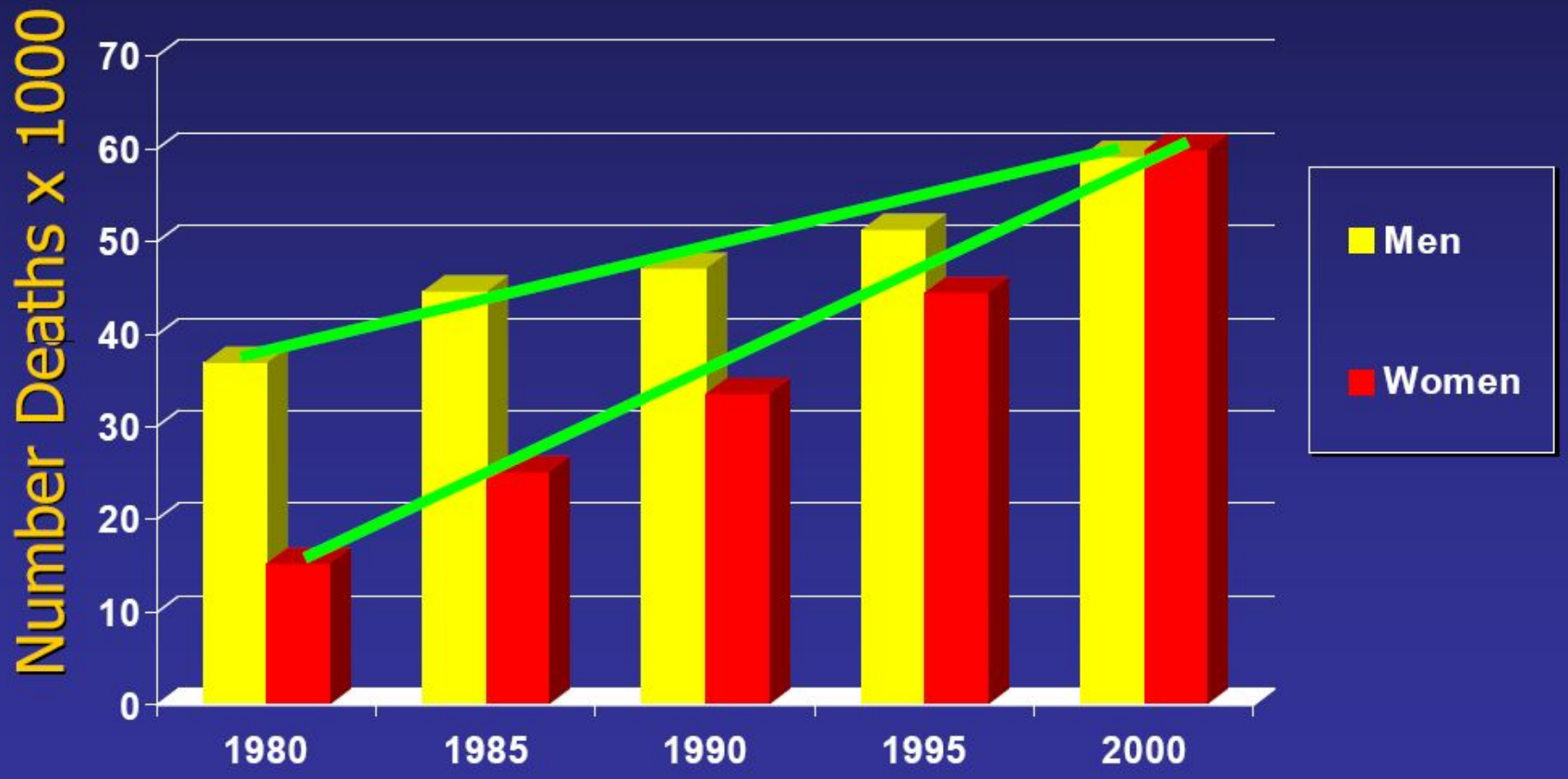
- **4th leading cause of death in world**
- **4th leading cause of death in U.S.A.**
- **3rd most common reason for hospitalization.**
- **Rare under 40, common in elderly**
- **greater in men than in women.**

Prevalence of 9.34/1,000 in men and 7.33/1,000 in women (Global Burden of Disease Study, 2007).

COPD includes:

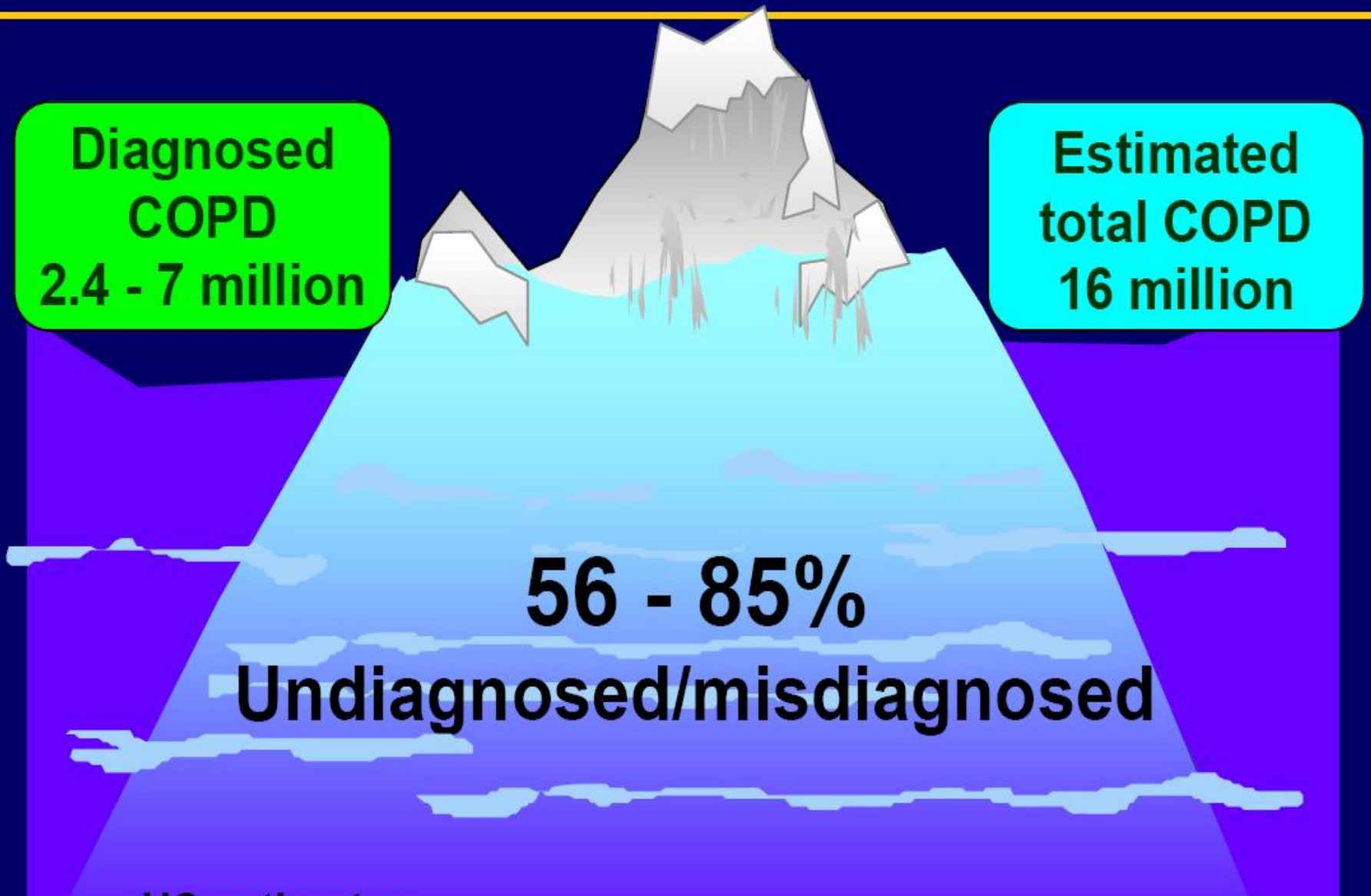
- chronic bronchitis
- chronic bronchiolitis (small air way disease)
- Emphysema

COPD Mortality by Gender, U.S., 1980-2000



Source: US Centers for Disease Control and Prevention, 2002

COPD Prevalence



Risk Factors for COPD

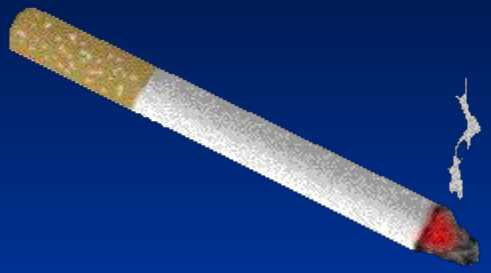
Host factors

- Alpha-1-antitrypsin deficiency
- airway hyperrespon-siveness
- Disordered lung development

Environmental factors

- *Tobacco smoke*
- Occupational dusts/chemicals
- Air pollution
- Childhood infections

Risk factors



- cigarette smoking remains the most important.
- Susceptibility to cigarette smoke varies but both the dose and duration of smoking appear to be important and it is unusual to develop COPD with less than 10 pack years.
- (1 pack year = 20 cigarettes / day /year).

Alpha-1-antitrypsin deficiency

- α1-Antitrypsin is a proteinase inhibitor which is produced in the liver, secreted into the blood and diffuses into the lungs.
- Mechanism of action: an inhibition of proteolytic enzymes such as neutrophil elastase, which are capable of destroying alveolar wall connective tissue.

Pathophysiology

COPD has both

- Pulmonary components
- Systemic components

Pulmonary components:

- **Mucus secretion** An enlargement of mucous secreting glands and an increasing number of goblet cells in the large airways → increase mucous that causes chronic bronchitis
- **Loss of elastic tissue** surrounding the smaller airways combined by **inflammation** and fibrosis in the airway wall → **airflow limitation.**

Pulmonary components:

- Premature airway closure leads to gas trapping and hyperinflation → ↓ pulmonary and chest wall compliance. (during exercise the time available for expiration shortens resulting in progressive hyperinflation)

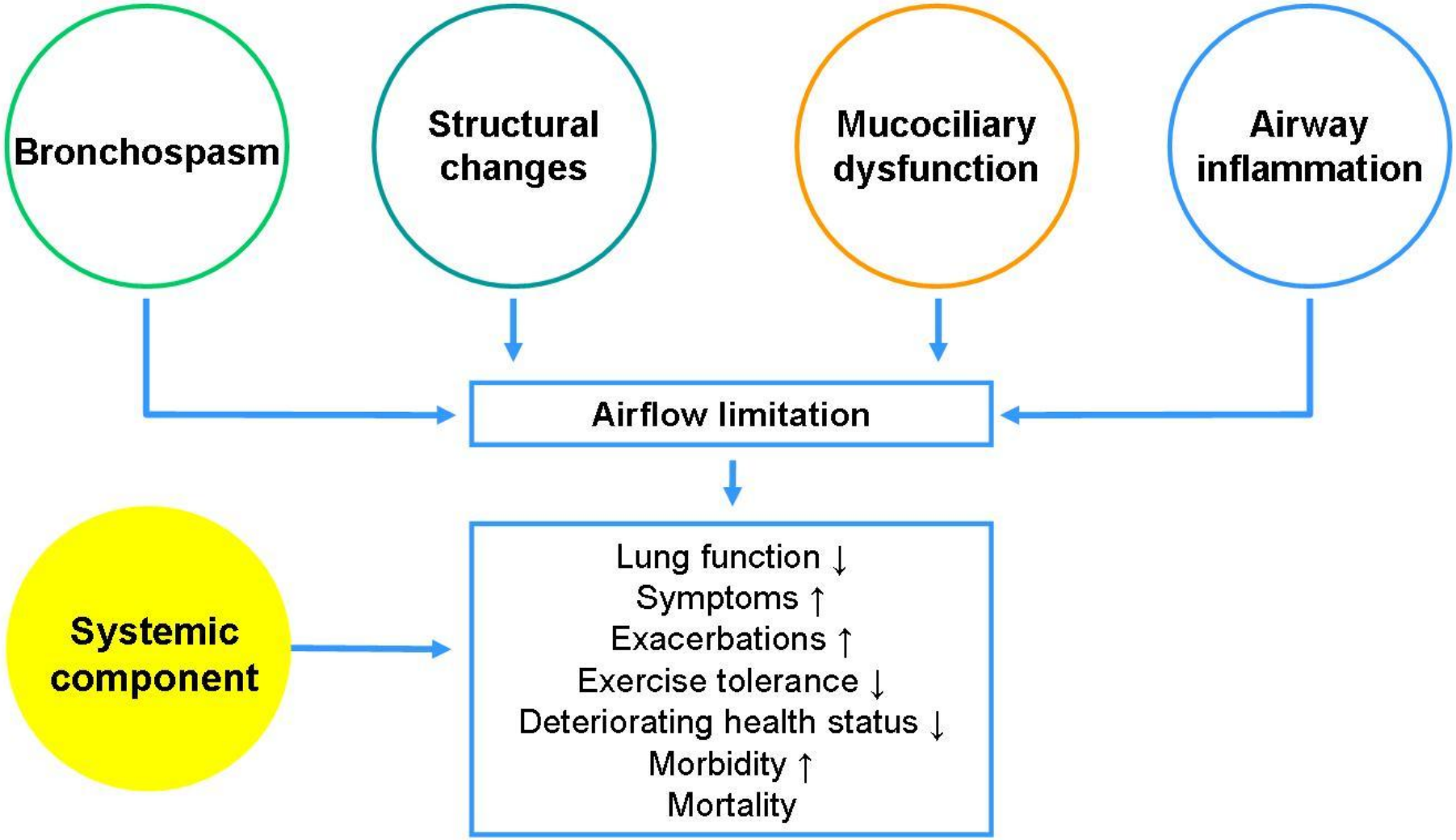
Pulmonary components:

- Flattening of the diaphragmatic muscles and increase horizontal alignment of the intercostals muscles → mechanical disadvantage of respiratory muscles → increase work of breathing first on exercise but then at rest.

Pulmonary components:

- In the alveolar capillary units the unopposed action of proteases and oxidants → destruction of the alveoli → bullae formation in some individuals which → impaired gas exchange and respiratory failure.

Pathophysiological features of COPD



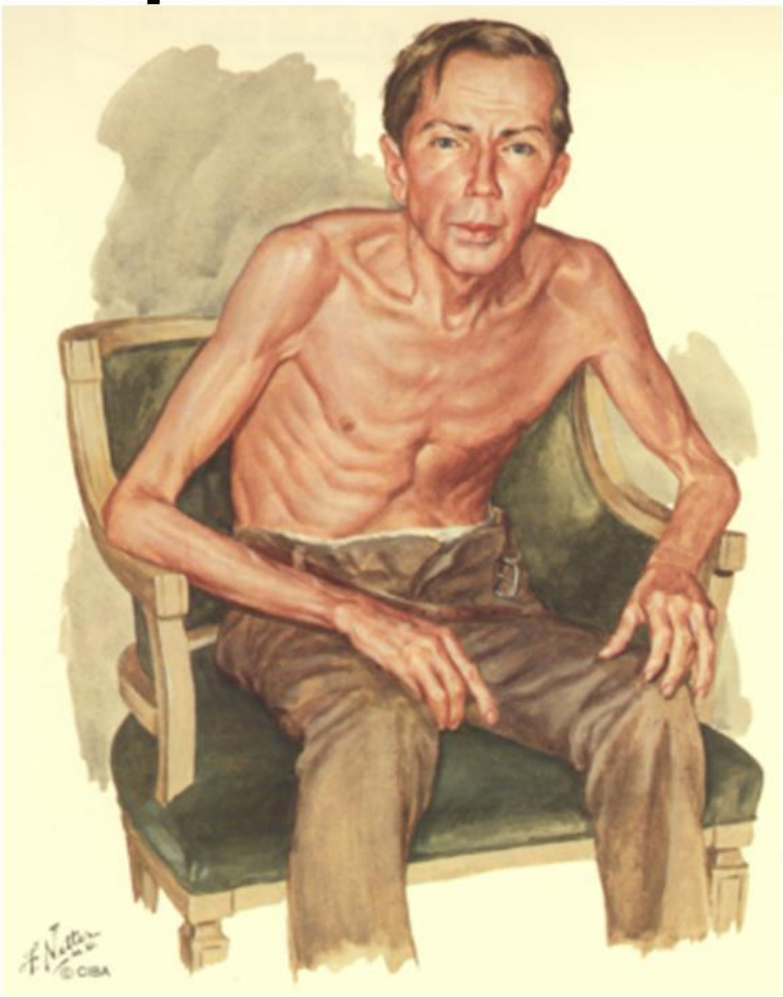
Systemic components:

1. Skeletal muscle weakness.
2. Increase circulating inflammatory markers.
3. Impaired salt and water excretion leading to peripheral edema.
4. Altered fat metabolism contributing to weight loss.
5. Increase prevalence of osteoporosis.

Pathophysiology of COPD: systemic component

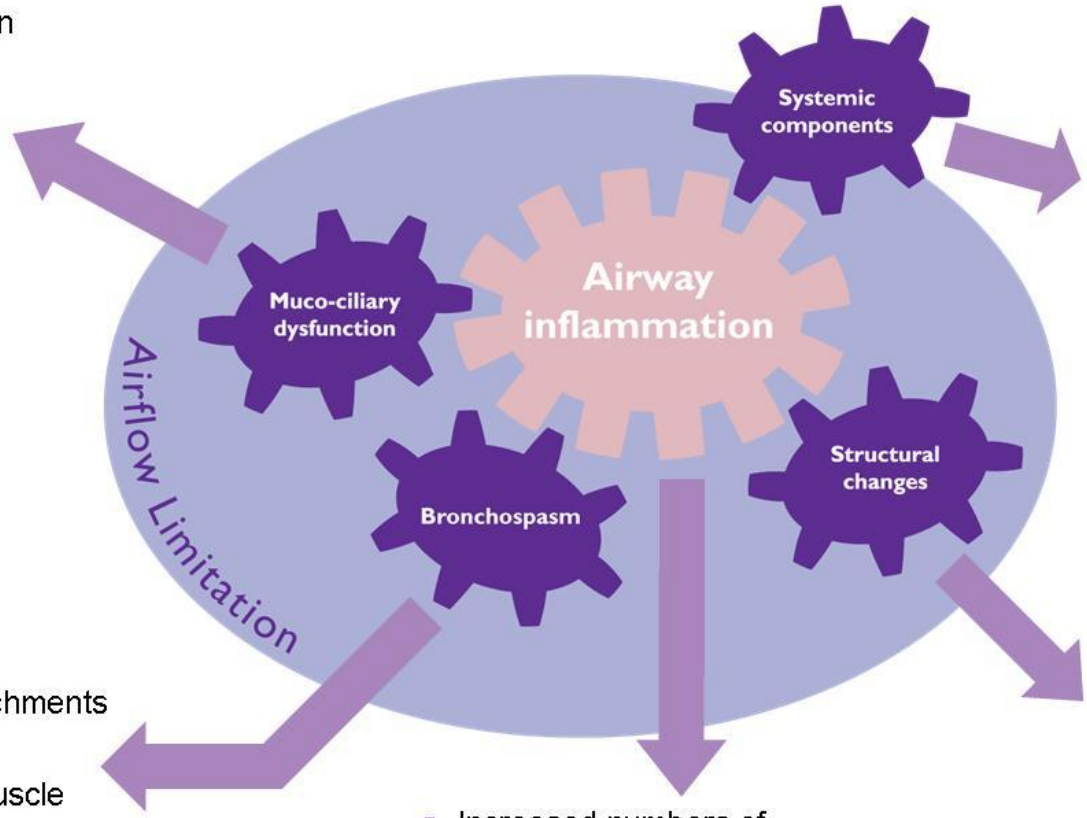
Systemic component

- Systemic inflammation
- Poor nutritional status
- Reduced BMI
- Impaired skeletal muscle
  - weakness
  - wasting
- Impact on other organs e.g. cardiovascular disease



Pathophysiological features of COPD

- Mucus hypersecretion
- Reduced mucociliary transport
- Mucosal damage



- Poor nutritional status
- Reduced BMI
- Impaired skeletal muscle
  - weakness
  - wasting

- Loss of alveolar attachments
- Loss of elastic recoil
- Increased smooth muscle contraction

- Increased numbers of inflammatory cells/activation
- Elevated inflammatory mediators: IL-8, TNF-α, LTB-4 and oxidants
- Protease/anti-protease imbalance

- Goblet cell hyperplasia/ metaplasia
- Mucous gland hypertrophy
- Increased smooth muscle mass
- Airway fibrosis
- Alveolar destruction

IL = interleukin
LTB-4 = leukotriene B4
TNF-α = tumour necrosis factor- α

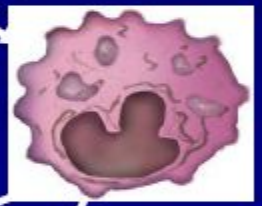
COPD Pathogenesis

Environmental and occupational exposure

Childhood respiratory infections

Genetic susceptibility

CD8 + lymphocyte



Alveolar macrophage (IL-8)

Neutrophil

Protease inhibitors

X

Proteases

Airway inflammation and remodeling

Tissue destruction

Airflow limitation

Pathophysiology (conclusion)

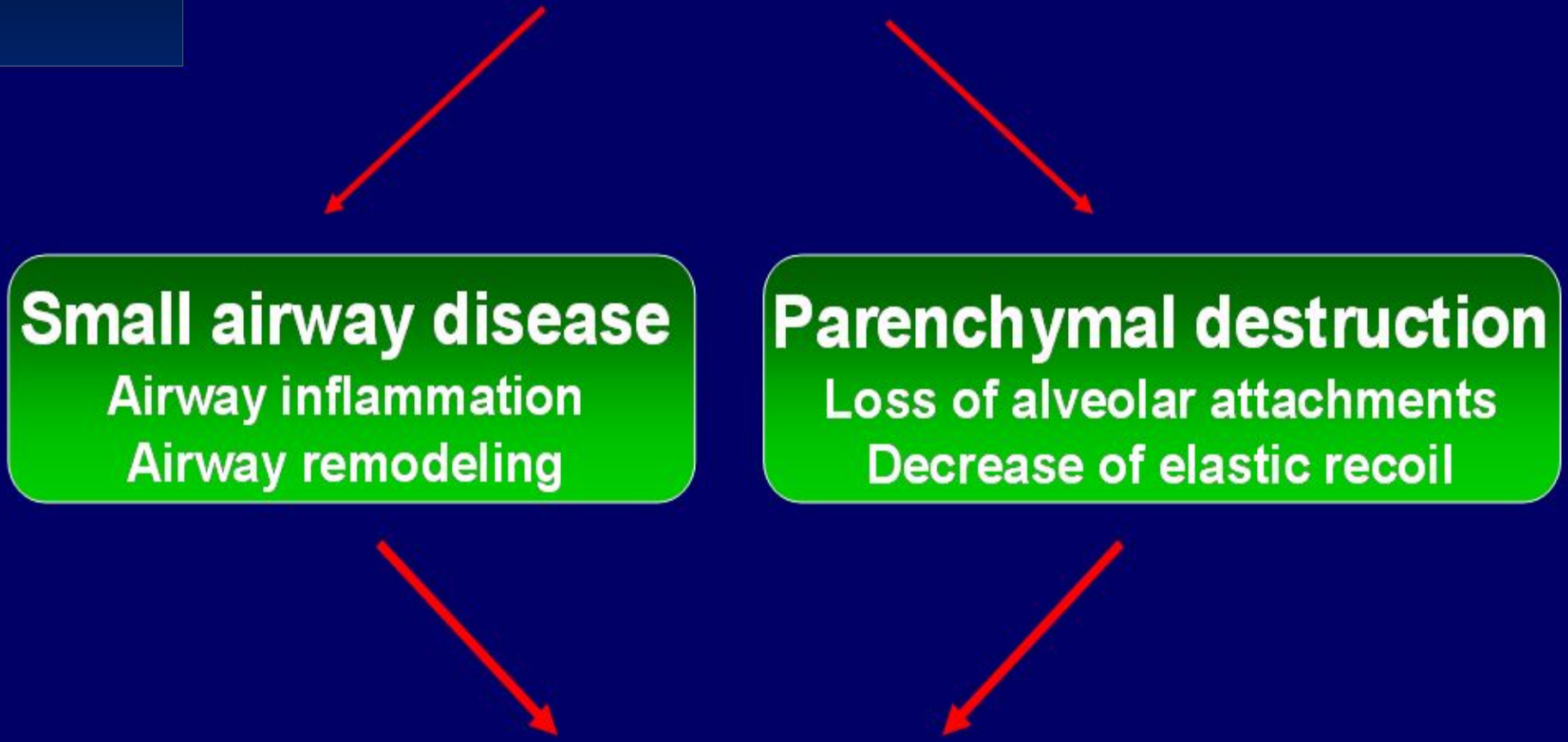
inflammation, bronchial wall edema, mucous secretion, hyperinflation and air trapping

Increase in proteinases & free radicals lead to parenchymal destruction

Changes in pulmonary vasculature lead to ventilation-perfusion mismatching, pulmonary hypertension

cor pulmonale

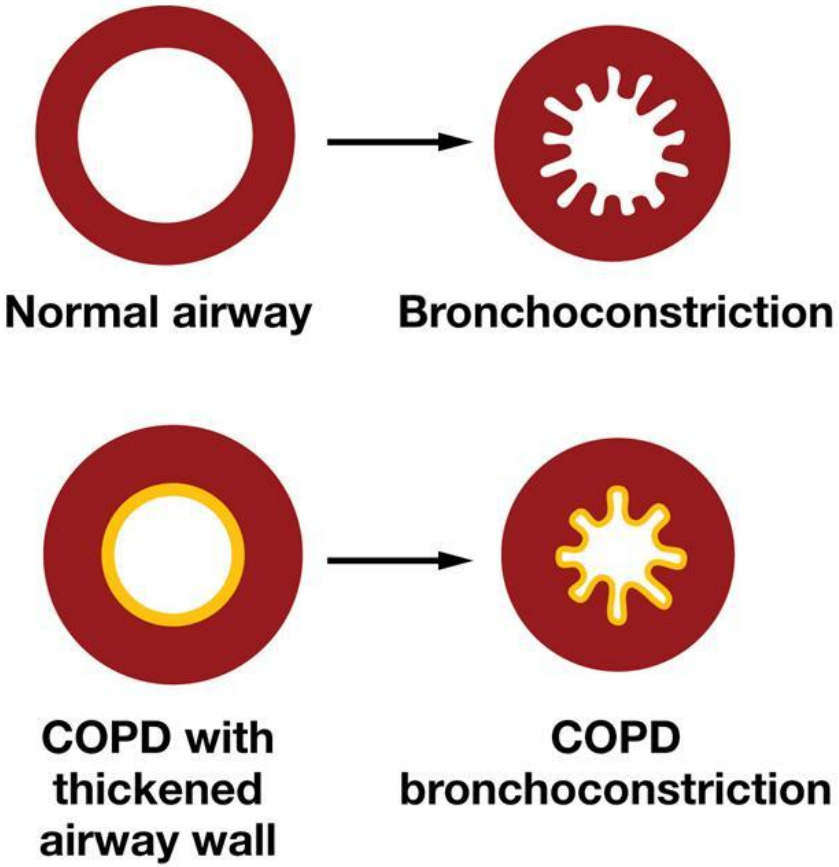
INFLAMMATION IN COPD



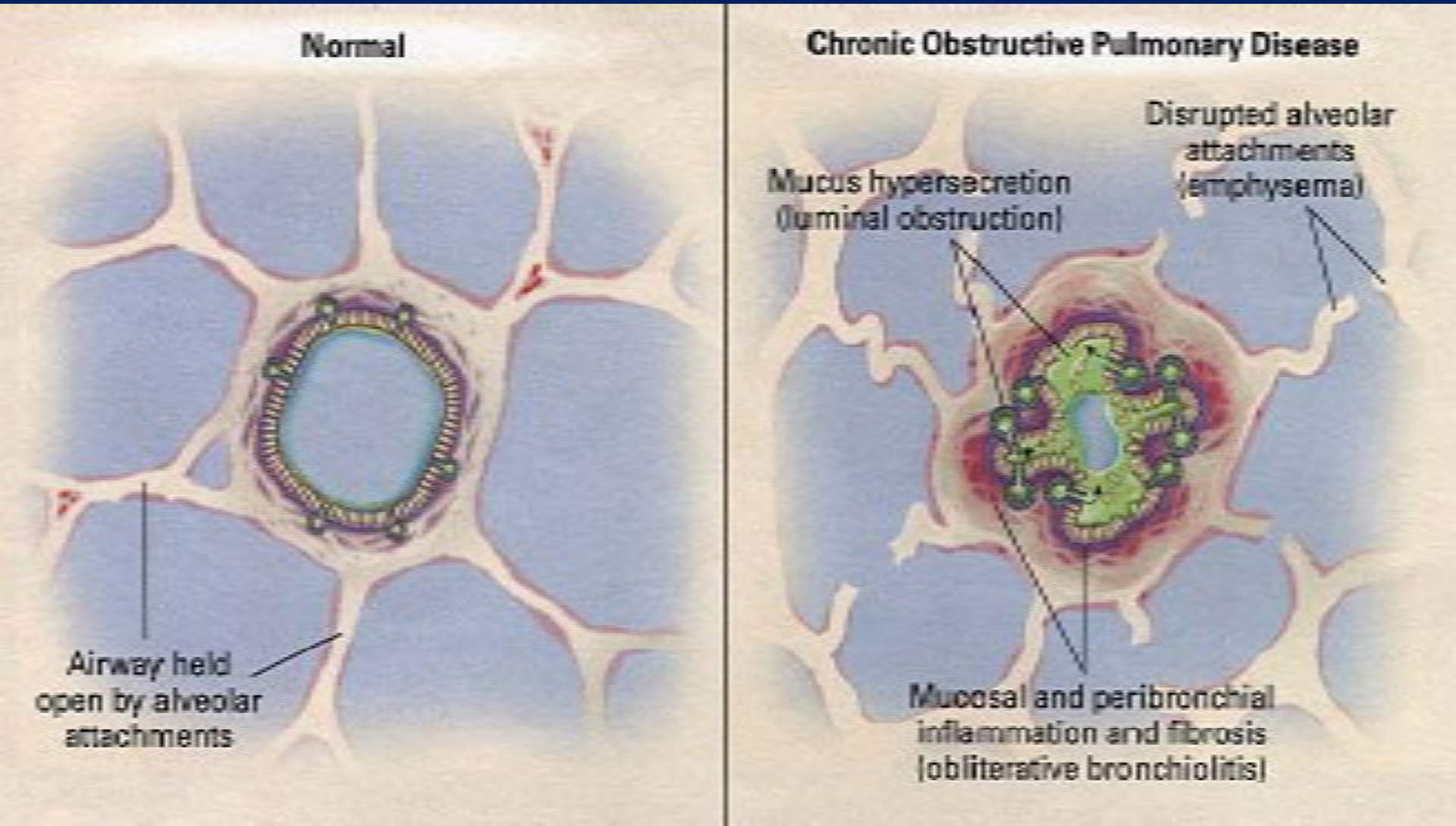
Pathophysiology of COPD: bronchospasm

Bronchospasm

- Smooth muscle contraction
- Increased cholinergic tone
- Bronchial hyper-reactivity
- Loss of elastic recoil
- Inflammation
- Structural changes



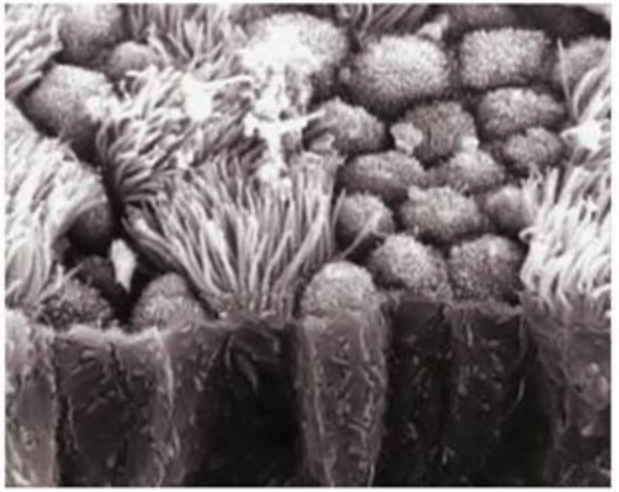
COPD: Pathology

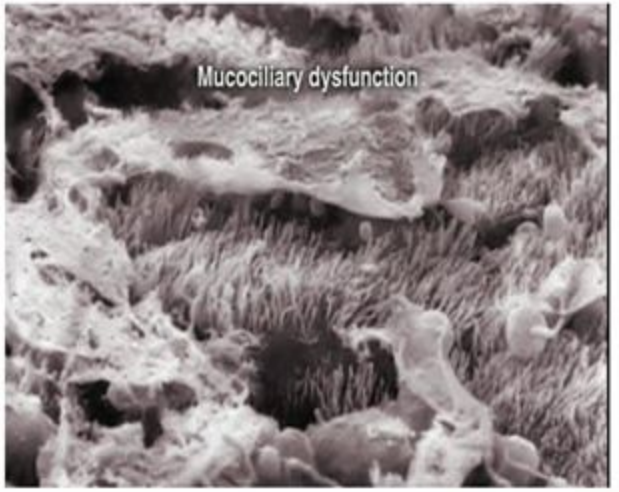


Pathophysiology of COPD: mucociliary dysfunction

Mucociliary dysfunction

- Mucus hypersecretion
- Increased mucus viscosity
- Reduced mucociliary transport
- Mucosal damage



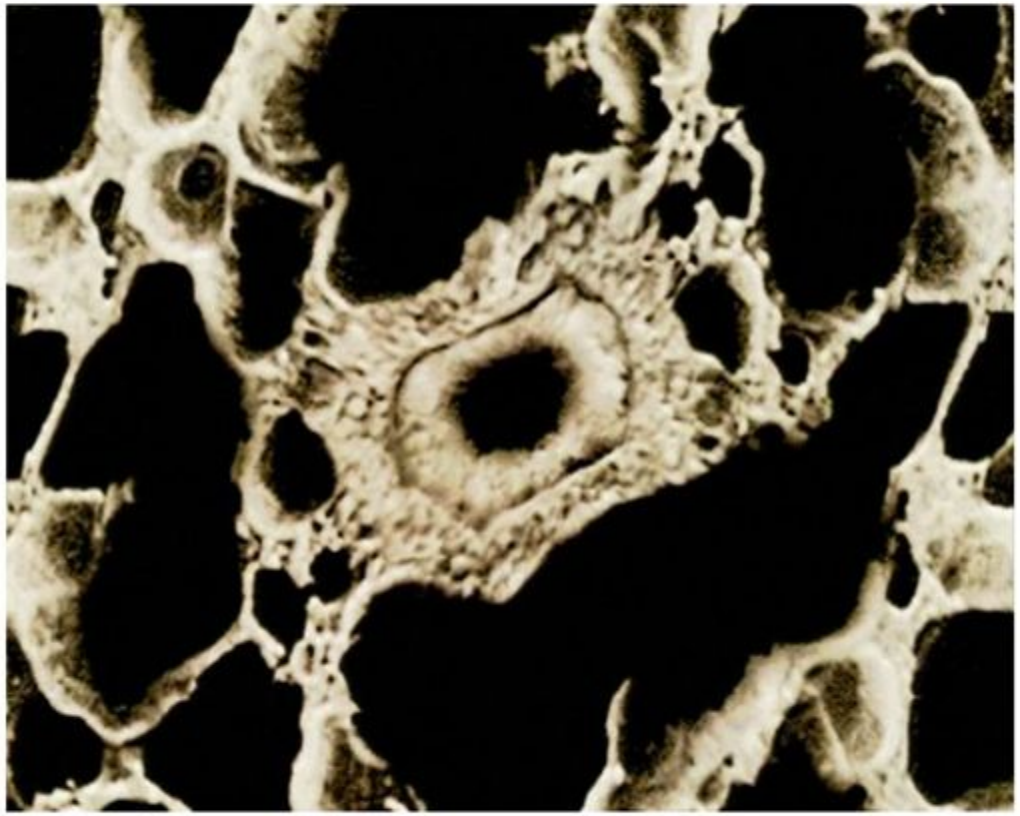


Agusti Respir Med 2005

Pathophysiology of COPD: structural changes

Structural changes

- Alveolar destruction
- Epithelial hyperplasia
- Glandular hypertrophy
- Goblet cell metaplasia
- Airway fibrosis



Jeffery. Thorax 1998

Causes of Airflow Limitation

Irreversible

- Fibrosis and narrowing of the airways
- Loss of elastic recoil due to alveolar destruction
- Destruction of alveolar support that maintains patency of small airways

Reversible

- Accumulation of inflammatory cells, mucus and plasma exudate in bronchi
- Smooth muscle contraction in peripheral and central airways
- Dynamic hyperinflation during exercise

Assess for COPD:

- Cough
  - intermittent or daily
  - present throughout day, seldom only nocturnal
- Sputum
  - Any pattern of chronic sputum production
- Dyspnea
  - *Progressive and Persistent*

"increased effort to breathe" "heaviness" "air hunger" or "gasping"

  - Worse on exercise
  - Worse during respiratory infections

COPD: Symptoms and Findings

- Chronic cough
- Sputum production
- Dyspnea (shortness of breath)
- Exercise Intolerance
- Fatigue
- Decreased quality of life
- Hypoxemia
- Hypercapnia
- Pulmonary hypertension
- Cor pulmonale
- Weight loss
- Effort intolerance
- Waking at night
- Ankle swelling
- Fatigue

Diagnosis of COPD

- Considered in patients with cough, sputum production, or dyspnoea +/- risk factors.
- Confirmed by ***spirometry.***
- FEV1/FVC <70% + postbronchodilator FEV1 <80% of predicted value.
- A low peak expiratory flow has poor specificity for the diagnosis of COPD.

Classification of COPD

- *Stage 0* *At Risk*
- *Stage I* *Mild*
- *Stage II* *Moderate*
- *Stage III* *Severe*
- *Stage IV* *Very Severe*

Figure 1-2. Spirometric Classification of COPD Severity Based on Post-Bronchodilator FEV_1

Stage I: Mild	$FEV_1/FVC < 0.70$ $FEV_1 \geq 80\%$ predicted
Stage II: Moderate	$FEV_1/FVC < 0.70$ $50\% \leq FEV_1 < 80\%$ predicted
Stage III: Severe	$FEV_1/FVC < 0.70$ $30\% \leq FEV_1 < 50\%$ predicted
Stage IV: Very Severe	$FEV_1/FVC < 0.70$ $FEV_1 < 30\%$ predicted or $FEV_1 < 50\%$ predicted plus chronic respiratory failure

FEV_1: forced expiratory volume in one second; FVC: forced vital capacity; respiratory failure: arterial partial pressure of oxygen (PaO_2) less than 8.0 kPa (60 mm Hg) with or without arterial partial pressure of CO_2 ($PaCO_2$) greater than 6.7 kPa (50 mm Hg) while breathing air at sea level.

Stage 0 At Risk

- Normal spirometry
- +/- Chronic symptoms (cough, sputum, production)

Stage I Mild COPD

- FEV1/FVC <70%
- FEV1 ≥80% predicted
- With or without chronic symptoms (cough, sputum production)

Stage II Moderate COPD

- FEV1/FVC <70%
- 50% ≤FEV1 <80% predicted
- With or without chronic symptoms (cough, sputum production)

Stage III Severe COPD

- FEV1/FVC <70%
- 30% ≤FEV1 <50% predicted
- With or without chronic symptoms (cough, sputum production)

Stage IV Very Severe COPD

- **FEV1/FVC <70%**
- **FEV1 <30% predicted *or* FEV1 <50% predicted plus**
- **chronic respiratory failure**

Spirometric Classification of COPD Severity Based on Post-Bronchodilator FEV_1

Stage I : Mild	$FEV_1/FVC < 0.70$ $FEV_1 \geq 80\%$ predicted
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Diagnosis of COPD

SYMPTOMS

cough

sputum

shortness of breath

EXPOSURE TO RISK FACTORS

tobacco

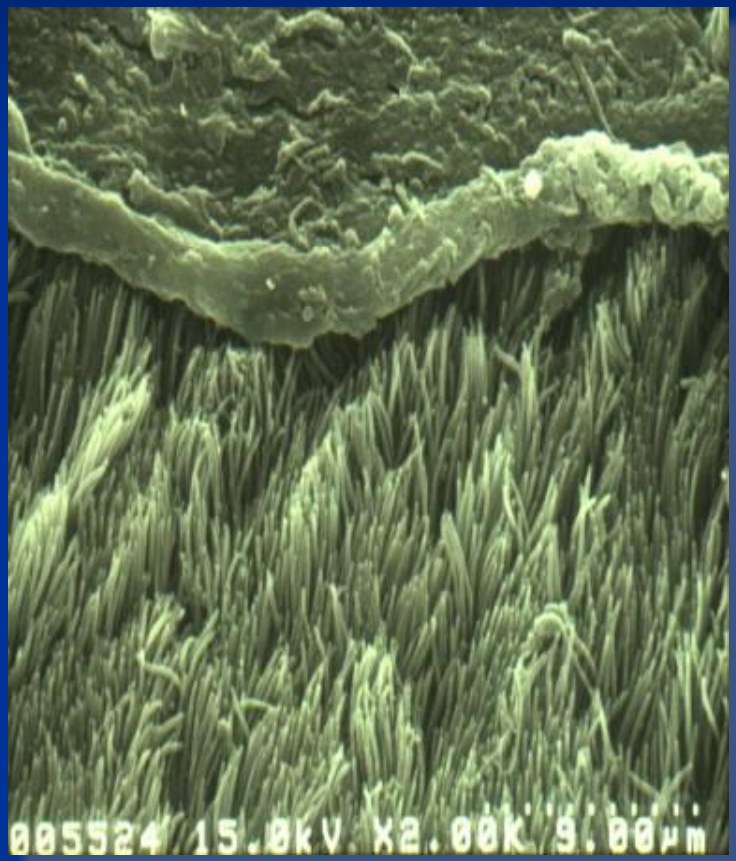
occupation

indoor/outdoor pollution

SPIROMETRY

Diagnosis of COPD

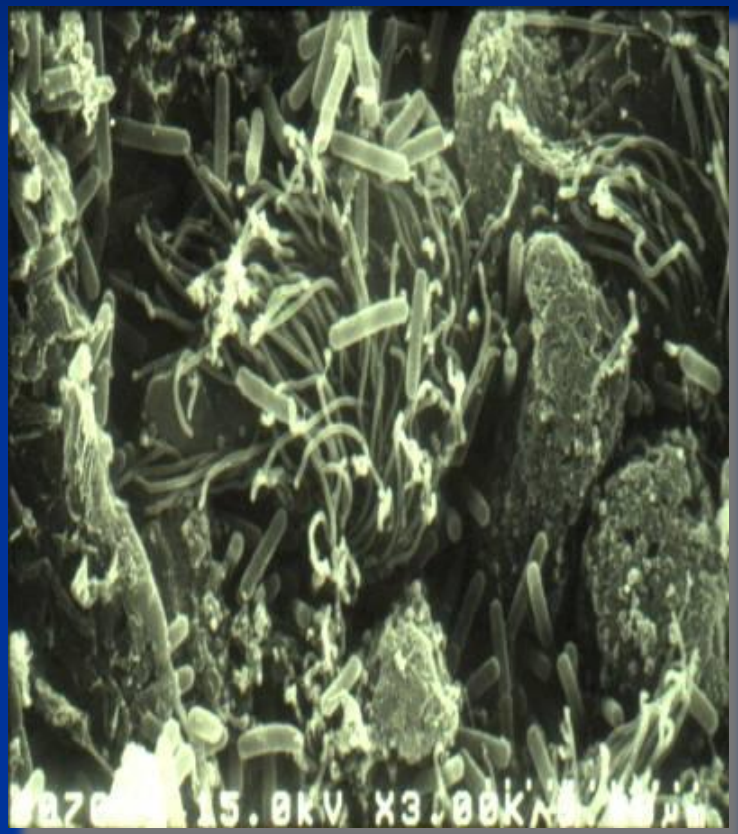
Healthy Respiratory Mucosa



- This electron micrograph shows the respiratory mucosa in a healthy state
- The cells are fully ciliated
- The cilia beat in a co-ordinated fashion to move mucus out of the airways (mucociliary transport)

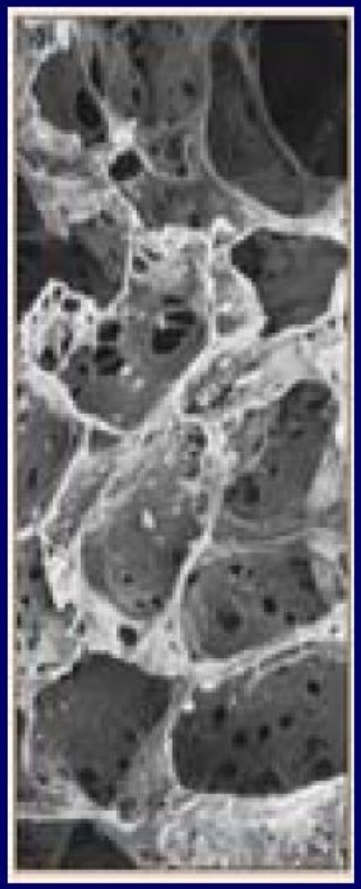
Scanning electron micrograph showing a sheet of mucus being moved along by the cilia

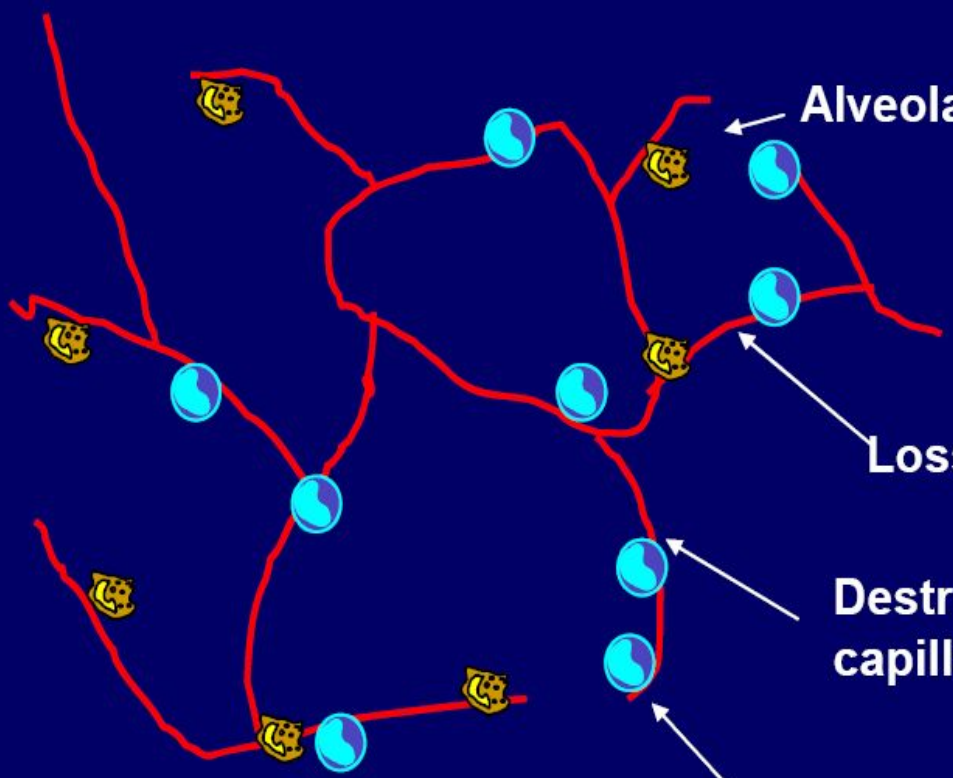
Damaged Respiratory Mucosa



- Damage to the cilia and epithelium occur as a result of disease processes in COPD. This can also occur as a result of bacterial damage
- This slide shows the result of bacterial infection stripping away the cilia from the mucosa
- The damage to the cilia means they are less effective in removing mucus from the airways

Changes in Lung Parenchyma





Source: Peter J. Barnes, MD

smokers lung – Emphysema

Emphysema

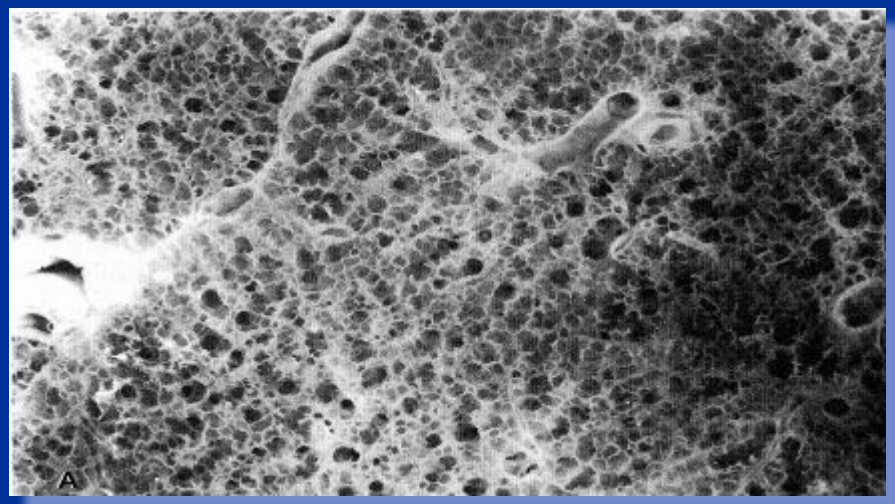
Dilation of alveolar wall

↓ alveolar capillary network, loss of guy rope effect

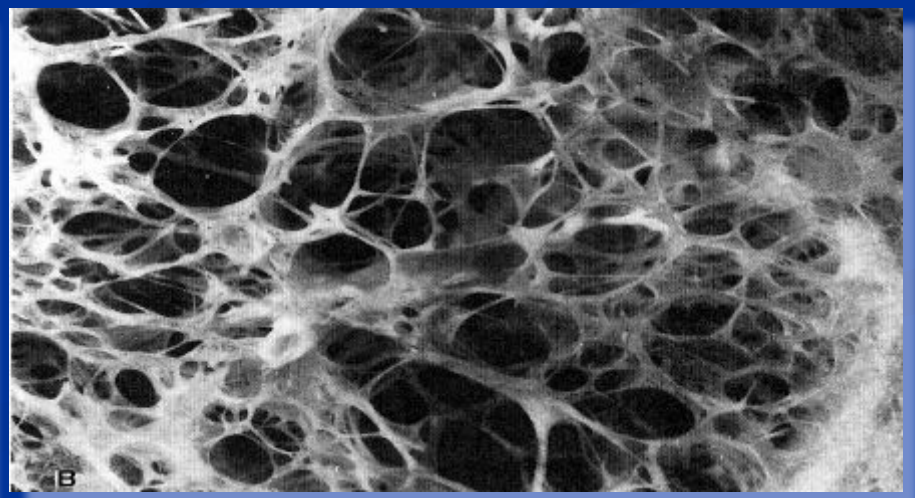
↓ lung tissue elasticity

Caused by smoking » irritation » inflammation » neutrophils and macrophages » release neutrophil elastase (type of proteases)

Normal Lung



Emphysema



Emphysema

- is defined pathologically as dilatation and destruction of the lung tissue distal to the terminal bronchiole.

classification

- Centri-acinar emphysema.
- Pan-acinar emphysema.
- Irregular emphysema.

Centri-acinar emphysema

- Distension and damage of lung tissue is concentrated around the respiratory bronchioles, whilst the more distal alveolar ducts and alveoli tend to be well preserved
- is associated with substantial airflow limitation

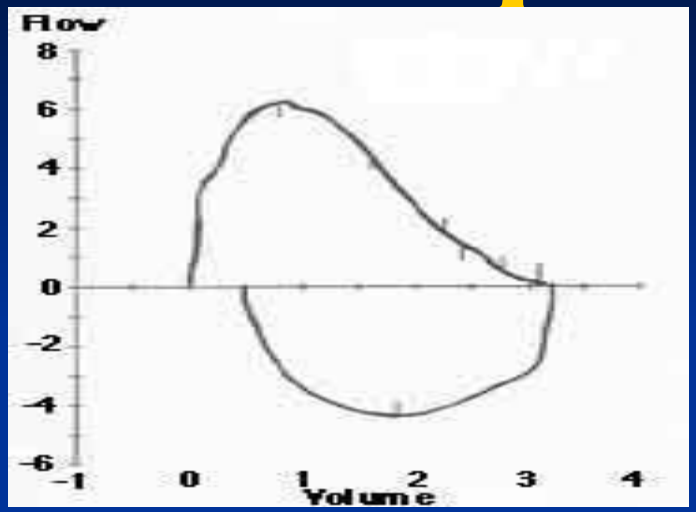
Pan-acinar emphysema

- Distension and destruction appear to involve the whole of the acinus, and in the extreme form the lung becomes a mass of bullae.
- Occurs in α1-antitrypsin deficiency

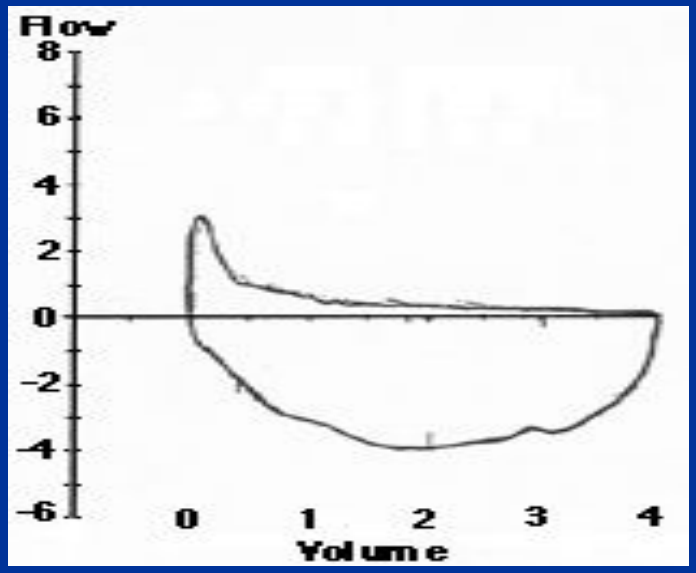
Irregular emphysema

- scarring and damage affect the lung parenchyma patchily without particular regard for acinar structure

Spirometry

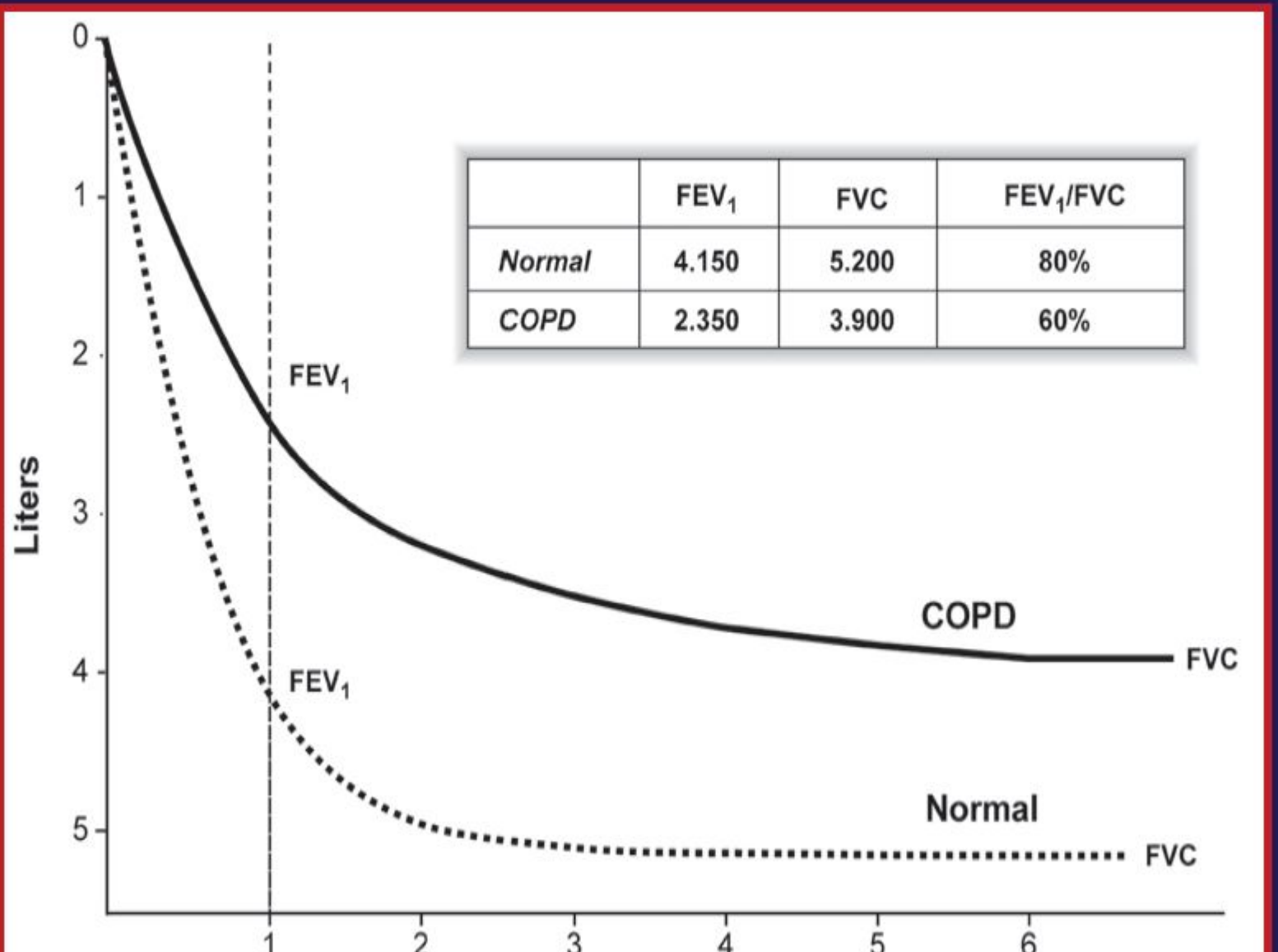


- Normal flow-volume loop



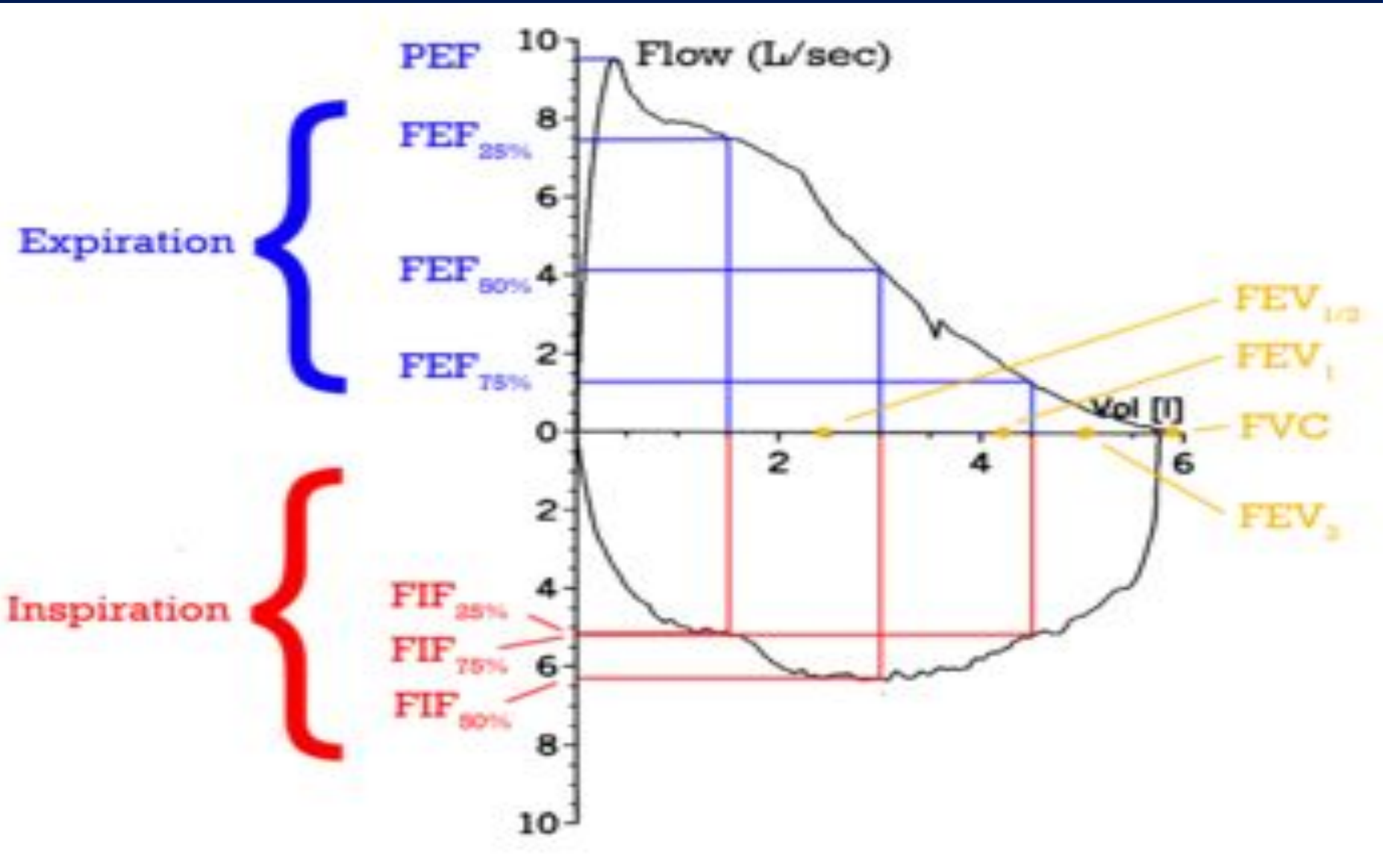
- Flow-volume loop in severe COPD

Spirometry: Normal and Patients with COPD



	FEV_1	FVC	FEV_1/FVC
Normal	4.150	5.200	80%
COPD	2.350	3.900	60%

Pulmonary Function Tests

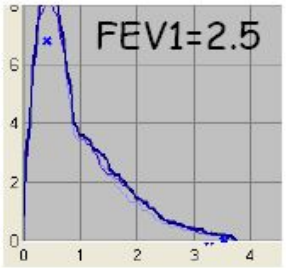


Differential Diagnosis: Spirometry

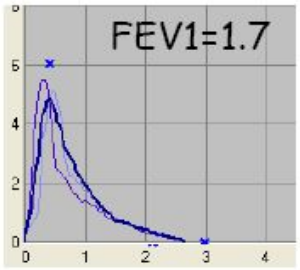
- FVC: the forced vital capacity, the volume delivered during an expiration
- FEV_1: the forced expiratory volume in 1 second
- FEV_1/FVC: the ratio of forced vital capacity to forced expiratory volume in 1 second

The best outcome measure depends on COPD severity

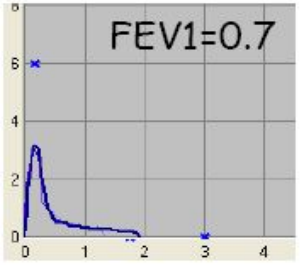
(recruiting/inclusion/exclusion criteria)



mild



moderate

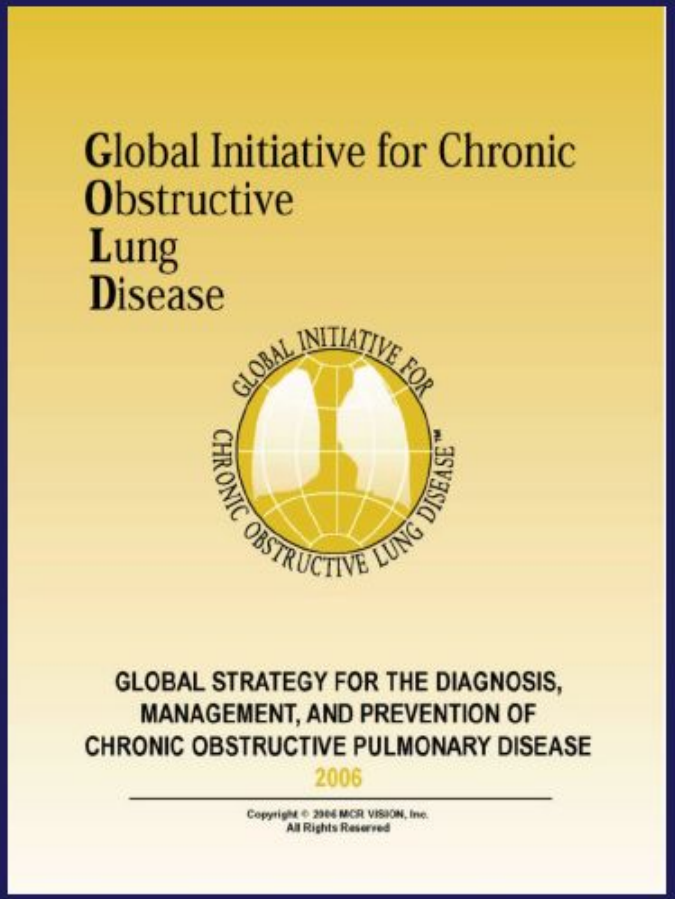


severe

Assess:
Measure Airflow Limitation

- **Patients with COPD typically show a *decrease in both FEV1 and FVC***
- **Postbronchodilator FEV1 < 80% predicted + FEV1/FVC < 70% confirms the presence of airflow limitation that is not fully reversible**
- **FEV1/FVC < 70% is an early sign of airflow limitation in patients whose FEV1 remains normal (≥80% predicted).**

Four Components of COPD Management



1. Assess and monitor disease
2. Reduce risk factors
3. Manage stable COPD
   - Education
   - Pharmacologic
   - Non-pharmacologic
4. Manage exacerbations

COPD Therapy Based on Symptoms and Staging

Symptoms	Asymptomatic	Mild	Moderate	Severe	Very Severe
Staging	0 At Risk	I Mild	II Moderate	III Severe	IV Very Severe
	Avoidance of risk factor(s); influenza vaccination				
		Add short-acting bronchodilators when needed – either LABAs or anticholinergics			
			Add regular Rx c ≥ 1 long-acting bronchodilator. **Add** rehabilitation		
				Add inhaled corticosteroids if repeated exacerbations	
					Add oxygen **Consider** surgery

ted by the author from the Global Initiative for Chronic Obstructive Lung Disease. Global strategies for the diagnosis, management, and prevention of chronic obstructive pulmonary disease.

GOALS of COPD MANAGEMENT

- Relieve symptoms
- Prevent disease progression
- Improve exercise tolerance
- Improve health status
- Prevent and treat complications
- Prevent and treat exacerbations
- Reduce mortality

Avoidance/reduction of risk factors

- **Reduction of total personal exposure to:**
  - tobacco smoke
  - occupational dusts
  - Chemicals
  - indoor and outdoor air pollutants

- **Smoking cessation is the single most cost-effective intervention for reducing the risk of developing COPD and stop its progression**

Adapted from the GOLD Workshop Report 2001

General Points

- Only smoking cessation and O2 therapy have been shown to prolong survival
- Other therapies aimed at relieving symptoms, improving quality of life, reducing exacerbations and need for hospitalizations

- Exacerbation management
- Chronic stable management
- Adjuvant therapy

Therapy at Each Stage of COPD: Stages I and II

<table>
<tr><th>Staging</th><th>0
At Risk</th><th>I
Mild</th><th>II
Moderate</th><th>III
Severe</th><th>IV
Very Severe</th></tr>
<tr><td rowspan="2"></td><td rowspan="2"></td><td colspan="4">Add short-acting bronchodilators when needed – either LABAs or anticholinergics</td></tr>
<tr><td></td><td colspan="3">Add regular Rx c ≥ 1 long-acting bronchodilator. Add rehabilitation</td></tr>
</table>

Recommendations:

1. Inhaled bronchodilators relieve, prevent, and reduce symptoms (A) Beta$_2$-agonists, anticholinergics, theophylline*: alone or combination

2. Long-acting bronchodilators: more effective, more convenient, more expensive (A)

3. Combining bronchodilators: may improve efficacy and decrease risk of side effects compared with increasing dose of single agent (A)

* Not FDA-approved for treating COPD.

Adapted by the author from the Global Initiative for Chronic Obstructive Lung Disease. Global strategies for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. 2005. Retrieved August 16, 2006, from the World Wide Web: http://www.goldcopd.com/Guidelineitem.asp?l1=2&l2=1&intId=989.

Management of Stable COPD

Pharmacotherapy: Bronchodilators

- Bronchodilator medications are central to the symptomatic management of COPD (Evidence A). They are given on an as-needed basis or on a regular basis to prevent or reduce symptoms and exacerbations.
- The principal bronchodilator treatments are β_2- agonists anticholinergics, and methylxanthines used singly or in combination (Evidence A).
- Regular treatment with long-acting bronchodilators is more effective and convenient than treatment with short-acting bronchodilators (Evidence A).

Beta2-Agonists

Short acting B2-Agonists:

- Salbutamol (albuterol)(4-6hrs)
- fenoterol (4-6hrs)
- levalbuterol (6-8hrs)
- terbutaline(4-6hrs)

Long acting B2-Agonists (LABA) -

Therapy for Stage 2 , 3 and stages 4 of COPD.

- salmeterol (12+ hrs)
- formoterol (12+hrs)

Beta2-Agonists

- Excellent bronchodilator and quick effect. Therapy for all stages, mostly rescue and as needed dosing every 4 to 6 hours for shortness of breath.
- Relax airway smooth muscles by stimulation of B2- adrenergic receptors which increases cyclic AMP and produce antagonist effect to bronchoconstriction.
- Excess doses cause tremors, anxiety, tachycardia, arrhythmias, hypokalemia

Anticholinergics

Short acting Anticholinergics

- **ipratropium bromide** (6-8 hrs) now nebulised and inhaler
- **oxitropium bromide** (7-9hrs) in solution and inhaler

Research brought quaternary compound of atropine

Long acting

- **Tiotropium inhaled** (24+hrs) aerolised powder.

ipratropium bromide/salbutamol (Combivent)
fenoterol/ipratropium bromide (Berodual)

Anticholinergics (Tiotropium)

- Block muscarinic receptors and prevent smooth muscle contraction while ↓ release of secretion from submucosal glands.
- Ipratropium bromide, devoid of systemic effects, the nebulization dosage is 0.5mg every 4 hours

- **Drug therapy for COPD begins with *long acting anticholinergics and beta-2 agonist bronchodilators.* These provide symptom relief but do not stop progression of the disease**

Therapy at Each Stage of COPD
Stage II-IV

Staging	0 At Risk	I Mild	II Moderate	III Severe	IV Very Severe
			Add regular Rx c ≥ 1 long-acting bronchodilator. **Add** rehabilitation		

Recommendation: Add pulmonary rehabilitation (

- Improves exercise capacity, quality of life
- Reduces breathlessness, hospitalization, anxiety, depression
- Include exercise training, nutrition counseling, education
- Patients at all stages may benefit from exercise training
- Minimum length is two months; longer programs are best

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Stages III and IV

Staging	0 At Risk	I Mild	II Moderate	III Severe	IV Very Severe
				Add ICS if repeated exacerbations	

Recommendations:

1. Add ICS if frequent exacerbations. (A)

Reduces exacerbations, improves health status (beclomethasone*, budesonide*, fluticasone*, triamcinolone* or combination LABA + glucocorticosteroids: formoterol/budesonide*, salmeterol/fluticasone

2. Oral glucocorticosteroids are <u>not</u> recommended in COPD (A)

DA-approved for treating COPD.

y the author from the Global Initiative for Chronic Obstructive Lung Disease. Global strategies for the diagnosis, management, and prevention of chronic obstructive pulmonary d
ieved August 16, 2006, from the World Wide Web: http://www.goldcopd.com/Guidelineitem.asp?l1=2&l2=1&intId=989.

Inhaled Glucocorticoids in COPD

- Improve lung function, dyspnea and health status
- Reduce exacerbations for patients with more advanced COPD and repeated exacerbations
- Combined with LABA, reduce exacerbation rates versus monotherapy with either agent
- COPD natural history not substantially modified (e.g., little or no change in rate of FEV_1 decline)
- As in asthma, side effects depend on dose and type

Pharmacotherapy: Glucocorticosteroids

- The addition of regular treatment with inhaled glucocorticosteroids to bronchodilator treatment is appropriate for symptomatic COPD patients with an FEV1 < 50% predicted (*Stage III: Severe COPD and Stage IV: Very Severe COPD*) and repeated exacerbations (Evidence A).

- An inhaled glucocorticosteroid combined with a long-acting $ß_2$-agonist is more effective than the individual components (Evidence A).

Pharmacotherapy: Glucocorticosteroids

- The dose-response relationships and long-term safety of inhaled glucocorticosteroids in COPD are not known.
- Chronic treatment with systemic glucocorticosteroids should be avoided because of an unfavorable benefit-to-risk ratio (Evidence A).

Inhaled Steroids

- Front line therapy for COPD stages 3 and 4
- Budenoside Nebulizer
- Inhaled fluticasone
- Inhaled triamcinolone
- Inhaled beclomethasone
- Inhaled budenoside
- LABA and budenoside mixed in inhaler

Management of Stable COPD

Other Pharmacologic Treatments

- Antibiotics: Only used to treat infectious exacerbations of COPD
- Antioxidant agents: No effect of n-acetylcysteine on frequency of exacerbations, except in patients *not* treated with inhaled glucocorticosteroids
- Mucolytic agents, Antitussives, Vasodilators: Not recommended in stable COPD

Therapy at Each Stage of COPD: Stage IV

Staging	0 At Risk	I Mild	II Moderate	III Severe	IV Very Severe
					Add long-term O_2 if chronic respiratory failure

Recommendation: Add oxygen therapy (A)

- Increases survival in COPD
- Improves hemodynamics, hematologic characteristics, exercise capacity, lung mechanics, mental state

Goal: PaO_2 at rest to 60 mm Hg at sea level and rest or SaO_2 at $\geq$90%

Prescribed based on oxygen desaturation (eg, PaO_2 below 55 mm Hg)

Given continuous, nocturnal, or with exercise

Treatment of Stable COPD
Other Medications

- **Chronic oral Prednisone**
- Use in chronic COPD is controversial. No effect on survival. May improve symptoms and reduce hospitalizations in some patients already at maximum treatment
- **Mucolytics & Expectorants**
- Relives symptoms from copious, viscous secretions
- **Oral Theophylline** (If inhalers not sufficient) Side effects are common

Methylxanthines

- Multiple modes of action : bronchodilatation, ↑ dia-phragmatic contractility, stimulation of respiratory drive, inotropism, ↑ mucociliary clearance, and synergy with ß2-Agonists and Anticholinergics
- 5mg/kg IV over 10 to 15 min then 0.5mg/kg/hr if normal liver function
- 1mg/kg IV elevate a 2µg/ml in blood level (await blood level results before IV dose when patient on oral aminophylline)
- Lower dosing : Alcoholism, old age, chronic liver disease, CHF, fever, erythromycin. ciprofloxacin or H2-blocker

Mucokinetic Medications

- Nebulized water and saline and oral expectorants **guaifenesin** and saturated iodide ***are of no benefit***
- Acetylcysteine cause reflex bronchoconstriction
- Clinical improvement with oral iodinated glycerol but can cause thyroid dysfunction
- Simple oral hydration is the easiest and safest agent

Treatment of Stable COPD: Home Oxygen Therapy

- ≥ 15 hours/day *reduces mortality*
- Criteria for O2 therapy
  - Pa O2 ≤ 55 mm Hg (O2 saturation ≤ 88%) at rest or during exercise or sleep or
  - Pa O2 < 60 mm Hg and hematocrit >52%

COPD Medications Typically Used in the US

β_2-agonists (short-acting) ■ Albuterol ■ Levalbuterol ■ Metaproterenol	Combination short-acting β_2-agonist plus inhaled anticholinergic: ■ Albuterol/Ipratropium
β_2-agonists (long-acting) ■ Salmeterol ■ Formoterol	Inhaled Corticosteroids ■ Flunisolide ■ Triamcinolone ■ Fluticasone ■ Budesonide ■ Mometasone
Anticholinergic (short-acting) ■ Ipratropium bromide	Combination inhaled corticosteroid plus long-acting β_2-agonist ■ Fluticasone 250 mcg/ salmeterol 50 mcg
Anticholinergic (long-acting) ■ Tiotropium	

Exacerbations in COPD

Etiology

- **Primary**

– viral and bacterial infections

– air pollution

– discontinuation of medications

– unknown reasons

- **Secondary**

– pneumonia, pulmonary embolism, heart failure pneumothorax,

COPD Exacerbations

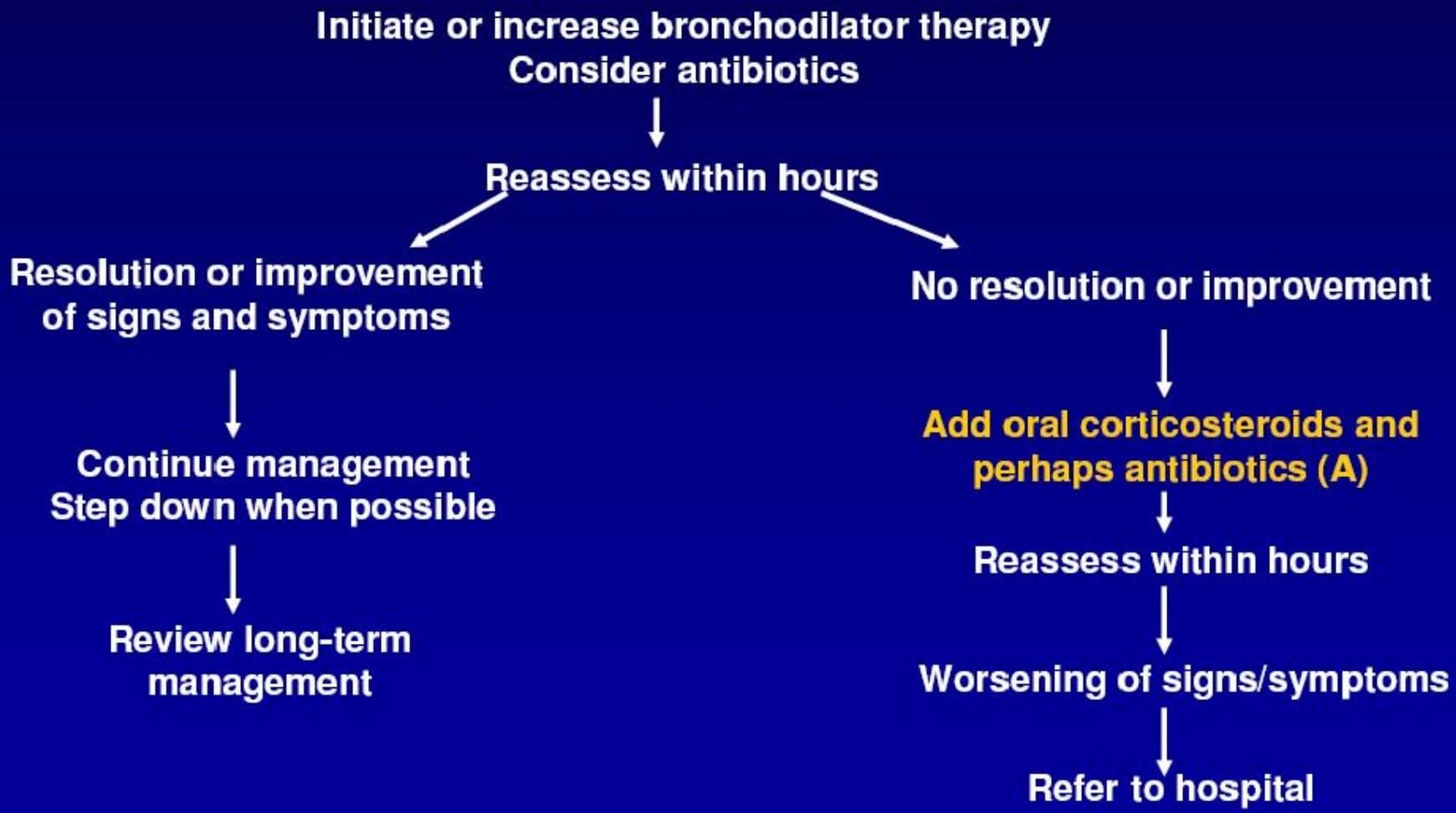
- **Primary symptom— increased dyspnea** —may be accompanied by wheezing and tightening of chest, increased cough and volume of sputum, a change in the color of sputum
- Possible malaise, insomnia, sleepiness, fatigue, fever, depression, confusion
- Most commonly caused by infection of the airways and air pollution
- Diagnosed through a targeted history and physical, spirometry, arterial blood gases or pulse oximetry

COPD Exacerbations: Indications for Hospital Assessment or Admission

- Impaired level of consciousness
- Acute confusion
- Sudden onset of resting dyspnea
- Severe COPD history
- Failure to respond to initial medical management of exacerbation
- Cyanosis or peripheral edema
- Significant co-morbiditi
- Newly occurring arrhythmias
- Uncertain diagnosis
- Older age
- Bed confinement
- Insufficient home support

COPD Exacerbations*

Requires reassessment within hours



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Managing COPD Exacerbations

- Bronchodilators
  - Short-acting, inhaled β_2-agonists are the preferred treatment
  - If no response, an anticholinergic is recommended
  - The role of long-acting inhaled bronchodilators in conjunction with short-acting agents has not been assessed
  - Use of aminophylline is controversial
  - In the case of a severe exacerbation or inadequate response, methylxanthine may be considered, but requires careful monitoring

Managing COPD Exacerbations

- Corticosteroids
  - Used in addition to bronchodilator therapy, for the COPD patient with an exacerbation who is admitted to the hospital or who is an outpatient with significant increase in breathlessness
  - Safe and efficacious dose: 30 to 40 mg oral prednisone daily for 10 to 14 days
  - Long-term use not advised

Management Options for Acute Exacerbations of COPD

- Inhaled bronchodilators (beta$_2$-agonists and/or anticholinergics)
- In patients with signs of infection, antibiotics
- Theophylline* or aminophylline* (?)
- Systemic, preferably oral, glucocorticoids
- Oxygen
- Hospitalization
- Noninvasive positive pressure ventilation

* Not FDA-approved for treating COPD.

Bronchodilators in Acute Exacerbations of COPD

- Initiate or increase dose of short-acting inhaled beta$_2$-agonists (e.g., albuterol*)
- Add anticholinergic (e.g., ipratropium) if no prompt response
- Role of methylxanthines (aminophylline*, theophylline*) is controversial: some benefits as third-line drug, but side effects and drug interactions
- Delivery method (nebulization or metered dose) can be individualized

* Not FDA-approved for treating COPD.

Information taken from: Global Initiative for Chronic Obstructive Lung Disease. Global strategies for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. 2005. Retrieved August 16, 2006, from the World Wide Web: http://www.goldcopd.com/Guidelineitem.asp?l1=2&l2=1&intId=989.

Antibiotics

– Have proven beneficial in treating acute infective exacerbations of COPD

– Should be used in patient with 2 or more symptoms :

- worsening dyspnea
- increased sputum volume
- increased sputum purulence

Antibiotics in Acute Exacerbations of COPD

- Traditional regimen: three to 14 days of tetracycline, amoxicillin or fluorquinolone
- Choice of agent should reflect local patterns of antibiotic sensitivity among S. pneumoniae, H. influenzae and M. catarrhalis
- Exacerbations have been linked to new strains of these organisms
- Treatment may include amoxicilin, macrolide, quinilone or tetracycline

Inpatient Treatment of Acute Exacerbations

- Oxygen to keep O2 sat >90%
- Nebulizer treatments with bronchodilators
- Steroids (40 to 60 mg daily for 7 to 14 days, IV or PO)
- Antibiotics Fluids

Mucolytic Therapy

- Mucus is a nearly universal complaint in COPD patients
- Mucolytics increase expectorations of sputum by reducing viscosity or hypersecretion
- Mucokinetic or mucoregulator agents include ambroxol, erdosteine, carbocysteine, iodinated glycerol, uridine 5'-triphosphate
- Use in COPD is controversial, not recommended in GOLD 2006 update of guidelines

Information taken from: Poole PJ, Black PN. Oral mucolytic drugs for exacerbations of chronic obstructive pulmonary disease: systematic review. BMJ 2001;322:1271-4.

Oxygen therapy

- Generally only considered in severe (stage III) COPD patients with PaO2 <55 mmHg
- Goal: to increase PaO2 to 60 mmHg or an SaO2 of >90%
- Administration: long-term continuous therapy, during exercise, or to relieve dyspnoea
- Benefits: long-term administration (>15 h/day) increases survival, improves haemodynamics, exercise capacity, lung mechanics and mental state
- Limitations: cost of supplemental home delivery is high

Future Treatments for COPD

Phosphodiesterase-4 Inhibition (Roflumilast)

- Inhibition raises intracellular levels of cAMP resulting in downregulation of signaling pathways in inflammatory cells
- Major isoenzyme in inflammatory cells implicated in inflammatory airway disease

Roflumilast

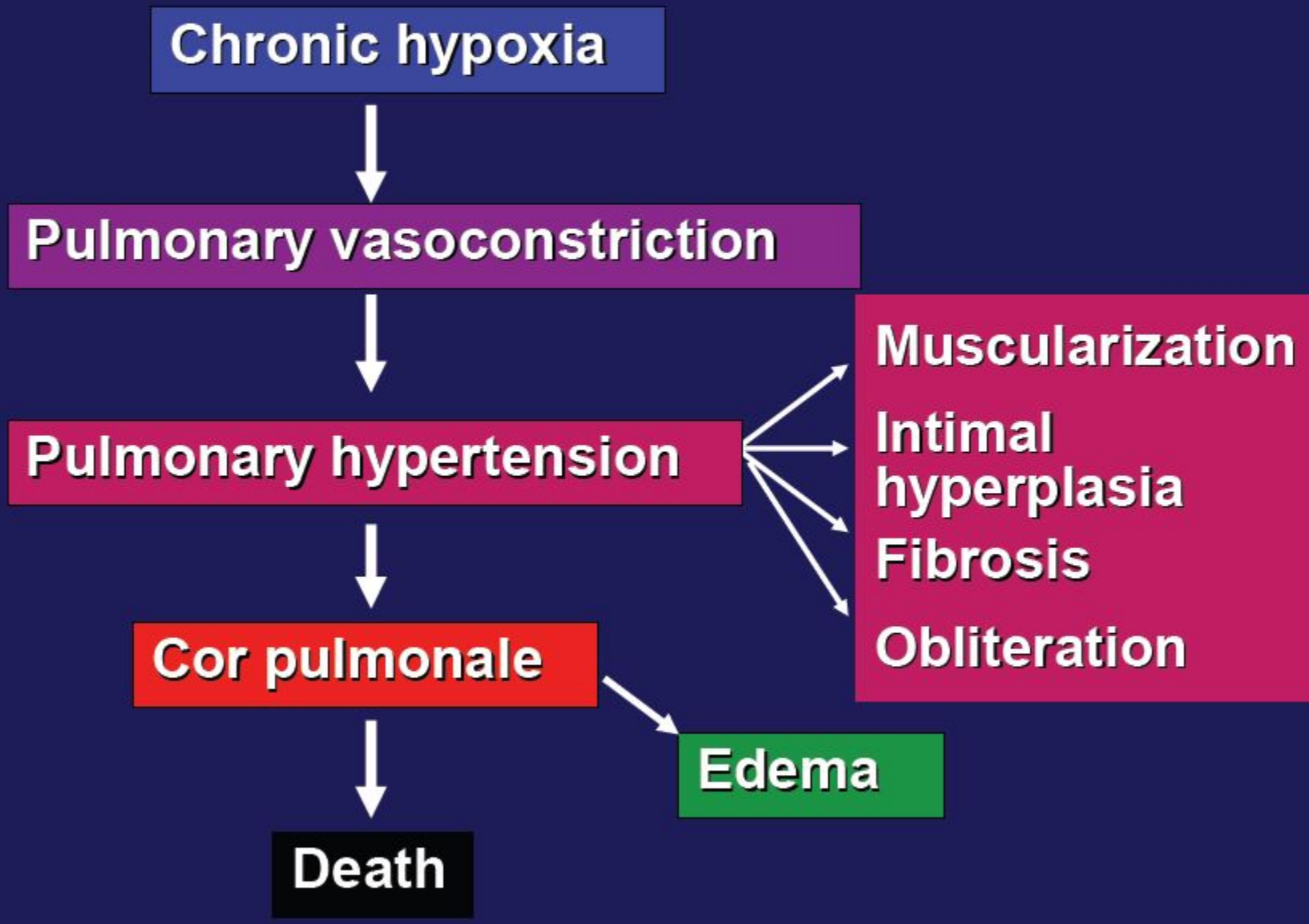
Dosing	500µg PO once daily
Pharmacokinetics	Oral bioavailability = 79% Peak plasma concentration in 1hr Mean half-life = 17hrs
Metabolism	Metabolized by cytochrome P450 3A4 and CYP 1A2 isozymes Active metabolite roflumilast N-oxide, accounts for 90% of pharmacologic effect
Adverse Effects	Diarrhea, nausea, headache

PDE-4 Inhibitors

Effects on Fibroblast Activity and Tissue Remodeling

- PDE-4 inhibitors may alter fibroblast activity in damaged lungs
- Fibroblasts produce scarring and distortion associated with fixed airway obstruction
- Specific PDE-4 inhibitors cilomilast and rolipram suppress fibroblast chemotaxis
- Thus, PDE-4 inhibitors may combine bronchodilator, anti-inflammatory and tissue remodeling actions

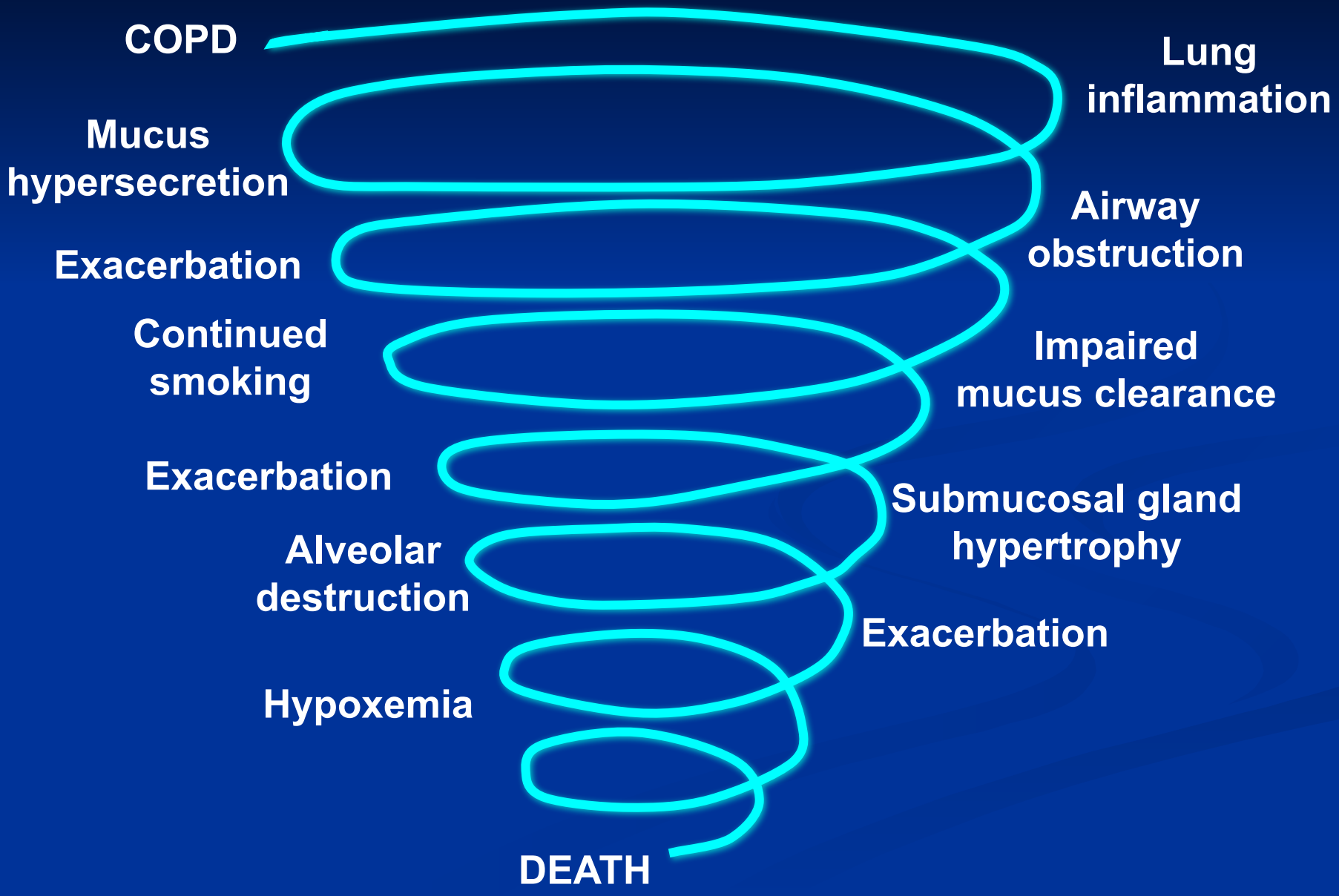
Pulmonary Hypertension in COPD



Source: Peter J. Barnes, MD

Smoke and Mirrors

"The Downward Spiral"



SMOKERS

"Hope and expect for the best. Prepare for the worst."

Back AL, Arnold RM, Quill TE. Hope for the best, and prepare for the worst. Ann Intern Med 2003;138:439-43.

NEXT STAGE…

PREVENT COPD

PREVENT COPD


Thanks for your kind attention