Chronic Obstructive Pulmonary Disease

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Introduction

Chronic Obstructive Pulmonary Disease (COPD)

- the 4th leading cause of death globally

- is projected to be the 3rd leading cause of death by 2020

Definition(2020)

- 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 and influenced by host factors including abnormal lung development. Significant comorbidities may have an impact on morbidity and mortality.

Definition

- COPD is a preventable and treatable disease with some significant extrapulmonary effects.

- Characterized by airflow limitation that is not fully reversible.

Definition

- The airflow limitation is usually progressive and associated with the chronic inflammatory response of the lung to noxious particles or gases.
- Acute exacerbations and other complications influence the severity of the disease.

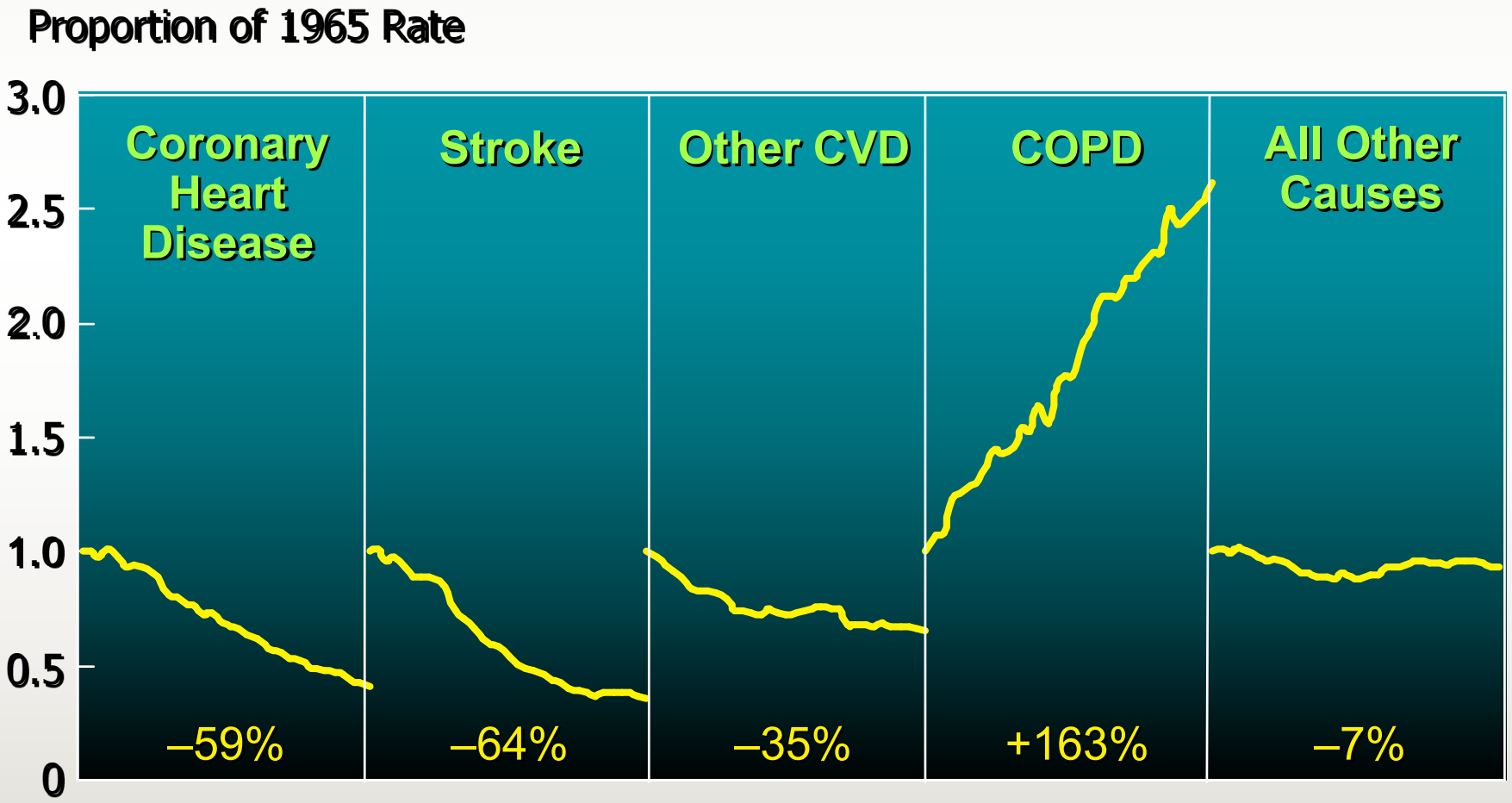
Burden of COPD

- a leading cause of morbidity and mortality worldwide and results in an economic and social burden that is both substantial and increasing.
- COPD prevalence, morbidity, and mortality vary across countries and across different groups within countries.

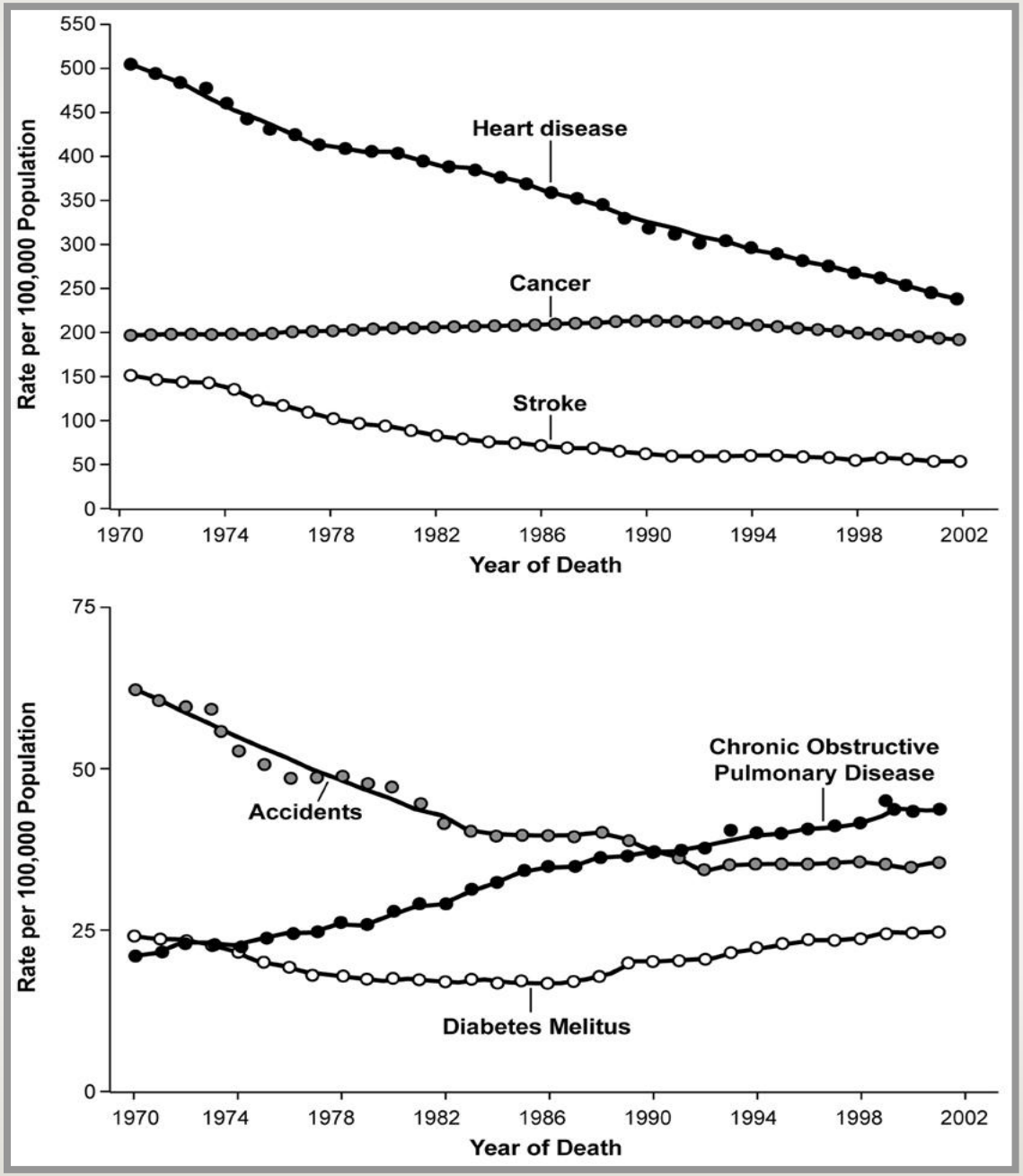
Burden of COPD

- The burden of COPD is projected to increase in the coming decades due to continued exposure to COPD risk factors and the changing age structure of the world's population.

Percent Change in Age-Adjusted Death Rates, U.S., 1965-1998

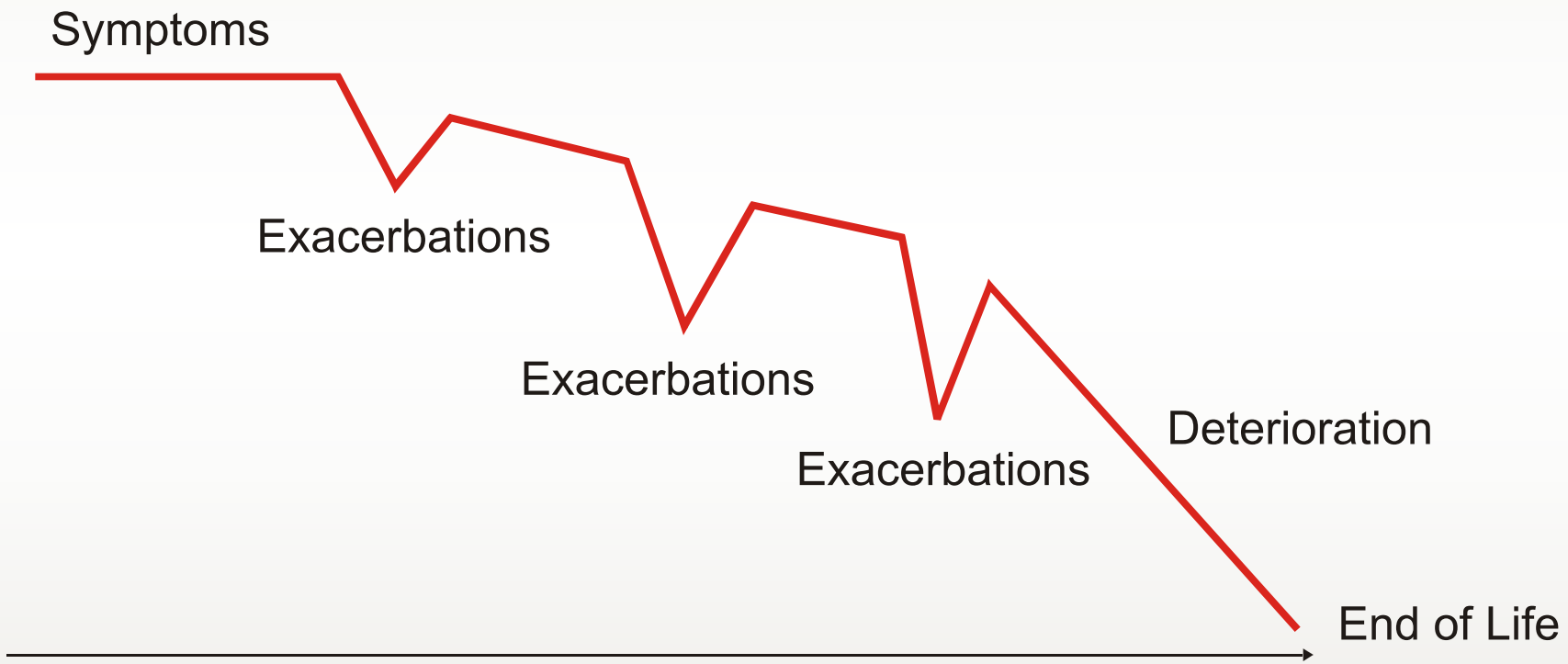


Of the six leading causes of death in the United States, only COPD has been increasing steadily since 1970



Source: Jemal A. et al. *JAMA* 2005

Disease Trajectory of a Patients with COPD



Risk Factors

Exposure to particles

- Tobacco smoke
- Occupational dusts, organic and inorganic
- Indoor air pollution from heating and cooking with biomass in poorly ventilated dwellings
- Outdoor air pollution

Lung growth and development

Oxidative stress

Gender

Age

Genes

Respiratory infections

Socioeconomic status

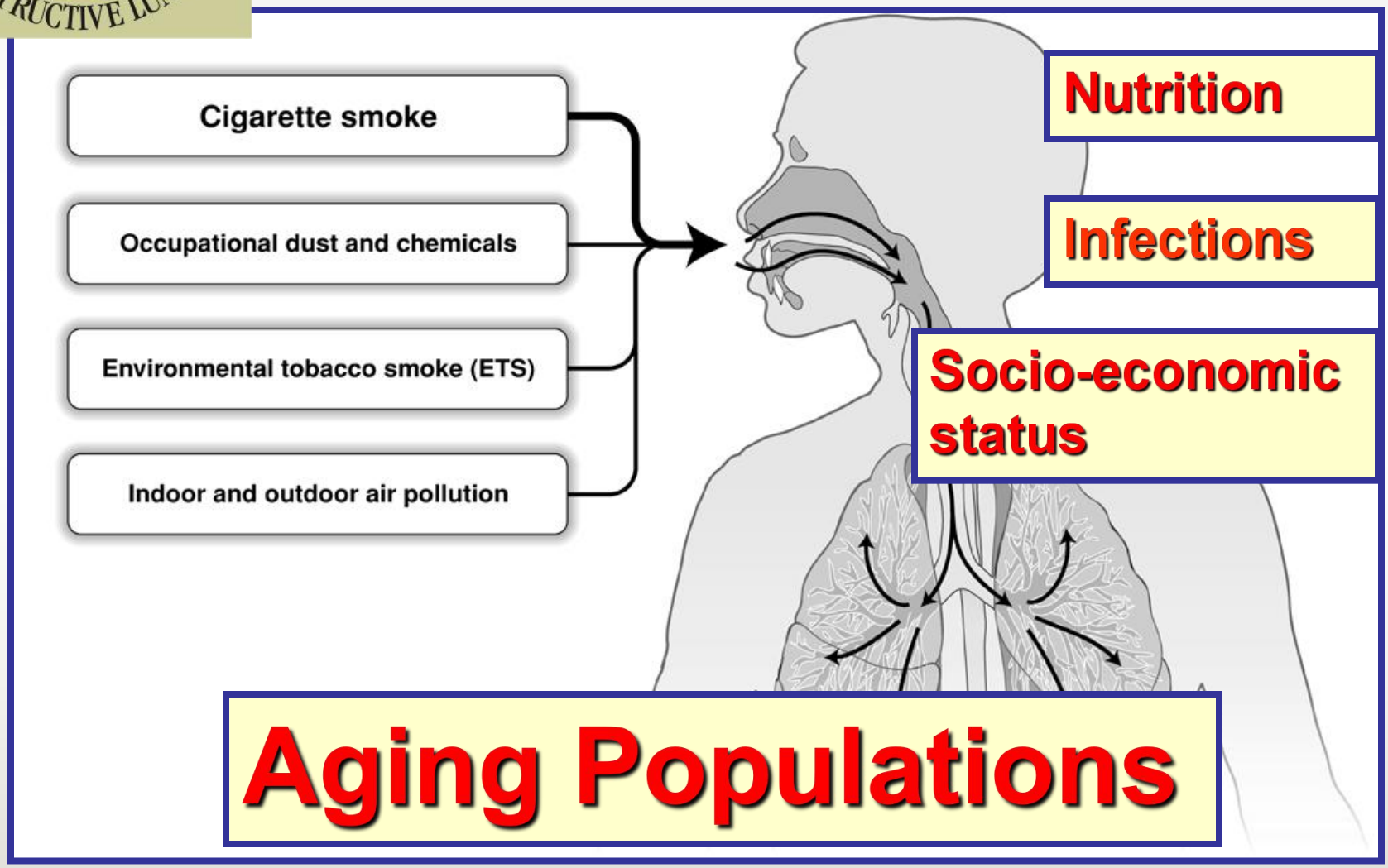
Nutrition

Comorbidities

Jobs

HIV

Risk Factors

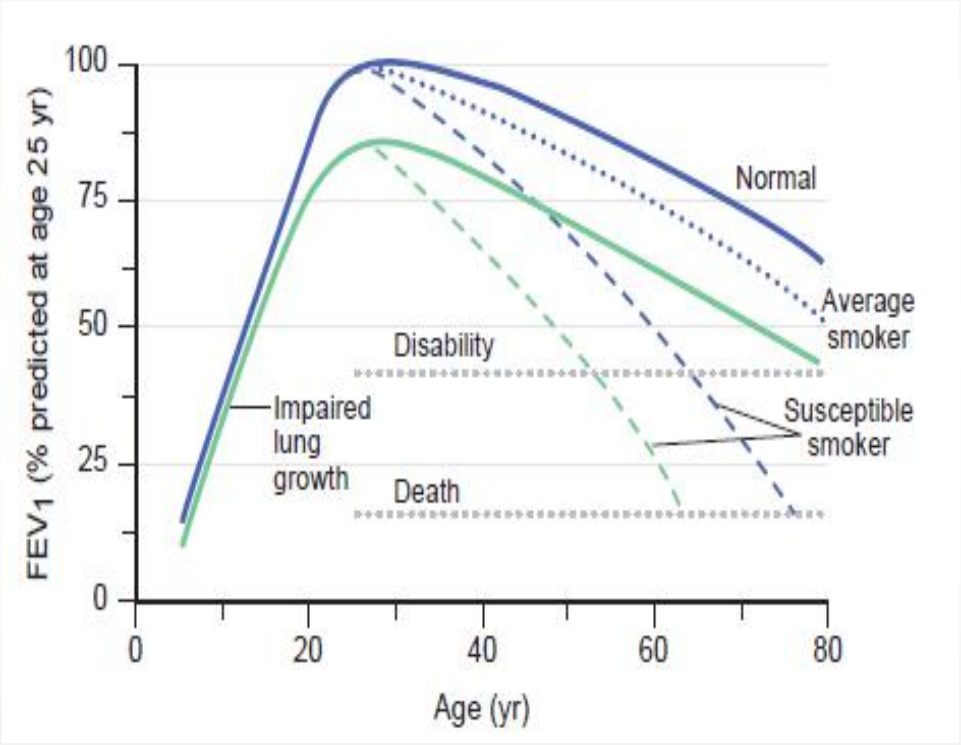


Cigarette smoking and aging

FEV1 reaches a maximum at 25 years of age and steadily declines owing to aging.

Lung function declines more rapidly in smokers.

A proportion of "susceptible smokers" lose lung function much faster than the average smokers.



Pathology

Pathological changes of COPD are found in:

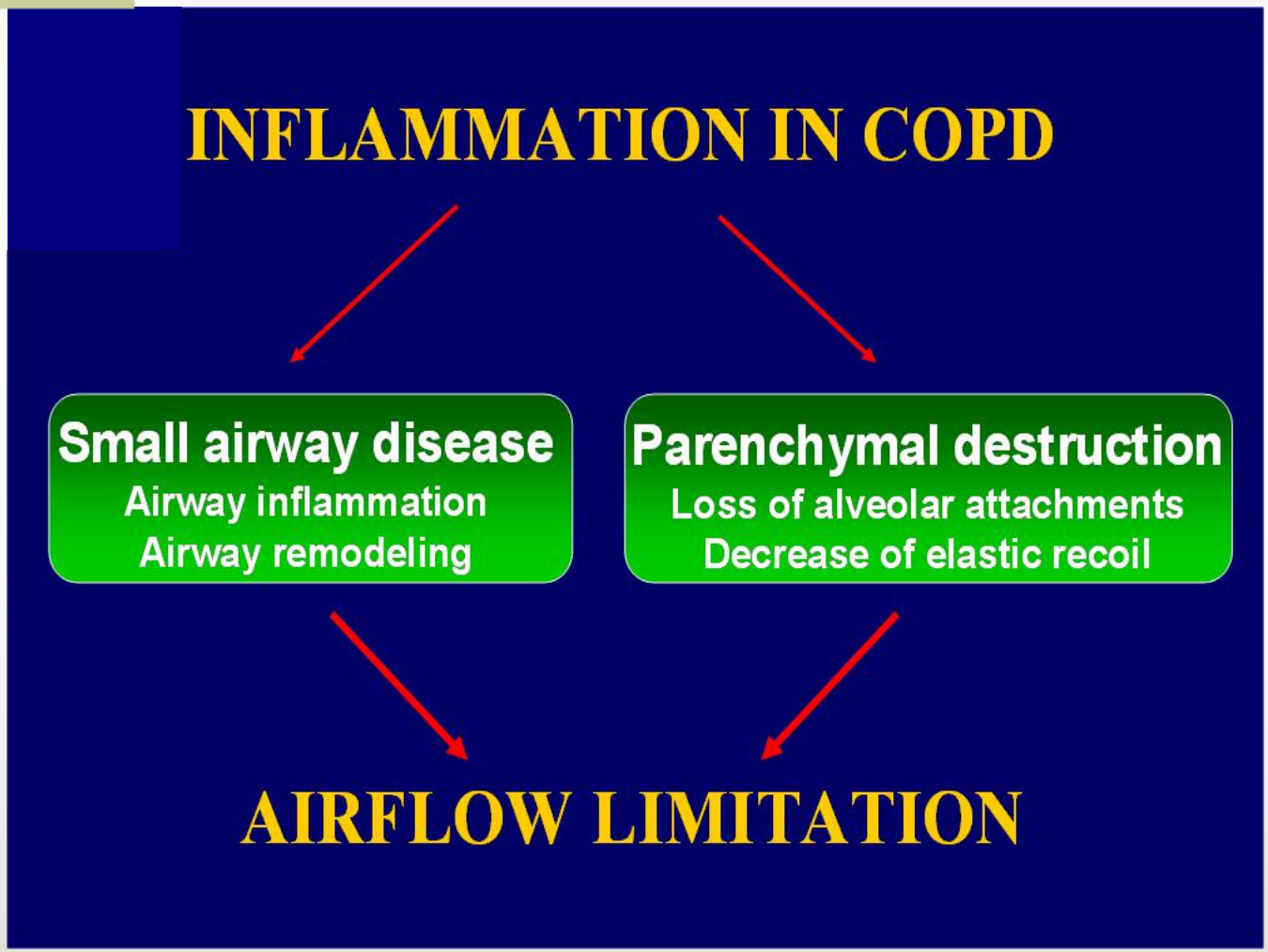
- proximal airways
- peripheral airways
- lung parenchyma
- pulmonary vasculature.

These changes include chronic inflammation and structural changes resulting from repeated injury and repair.

Pathology

- Inhaled cigarette smoke and other noxious particles cause lung inflammation, a normal response which appears to be amplified in patients who develop COPD.

- Lung inflammation is further amplified by oxidative stress and an excess of proteases in the lung.



Pathogenesis of COPD

Cigarette smoke

Biomass particles
Particulates
indoor air polution

Host factors
Amplifying mechanisms

LUNG INFLAMMATION

Anti-oxidants

Anti-proteinases

Oxidative stress

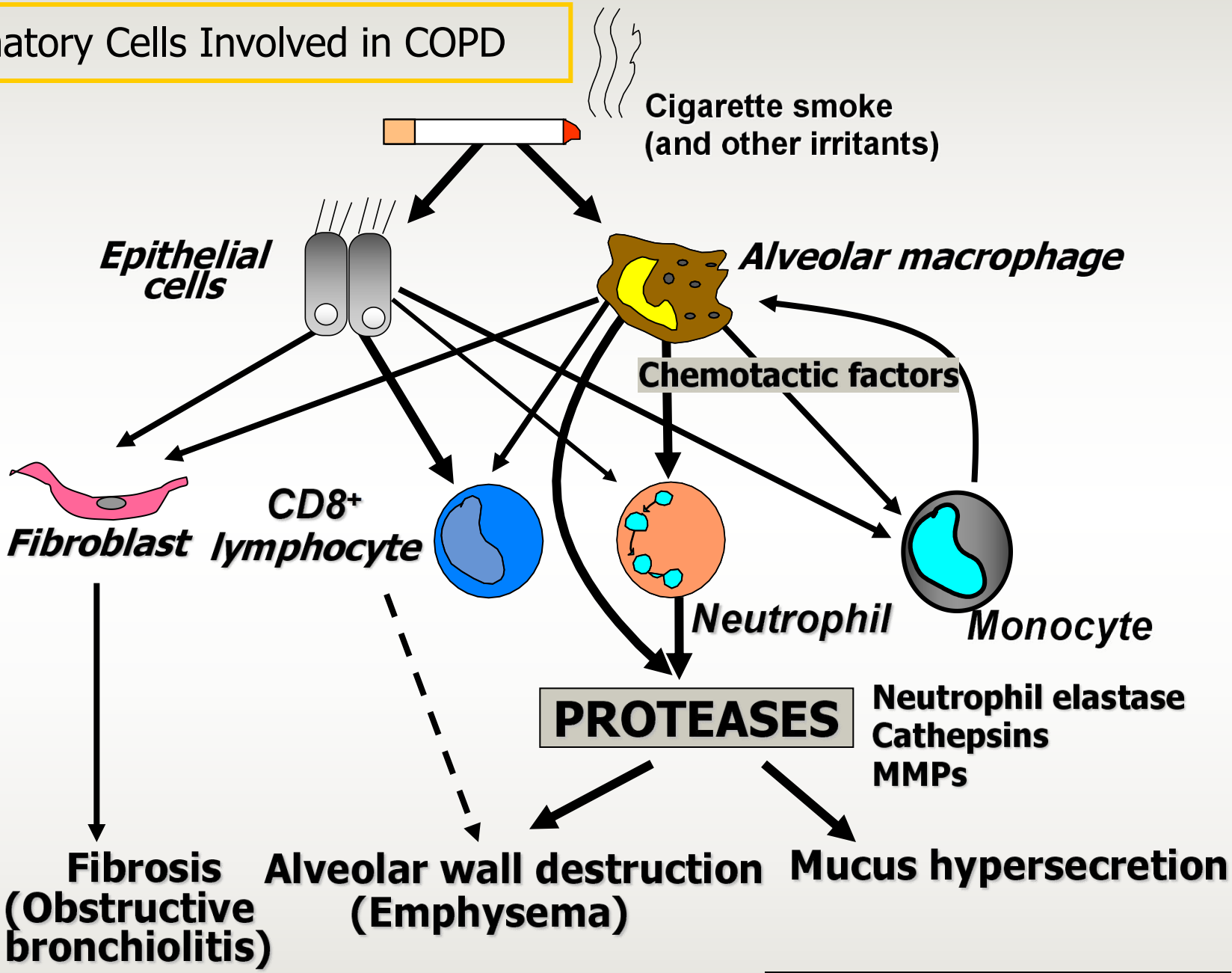
Proteinases

Repair mechanisms

COPD PATHOLOGY

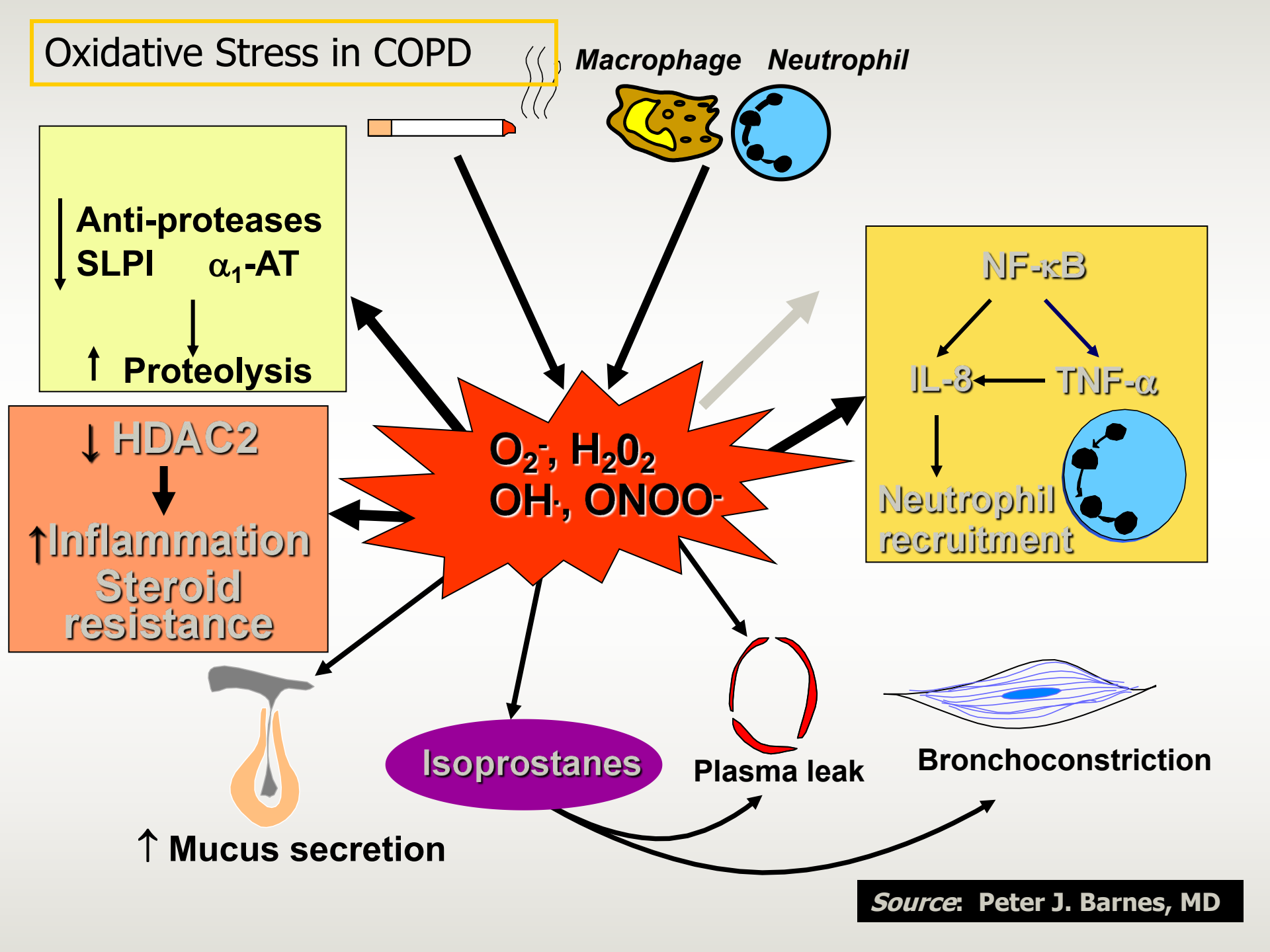
***Source*: Peter J. Barnes, MD**

Inflammatory Cells Involved in COPD



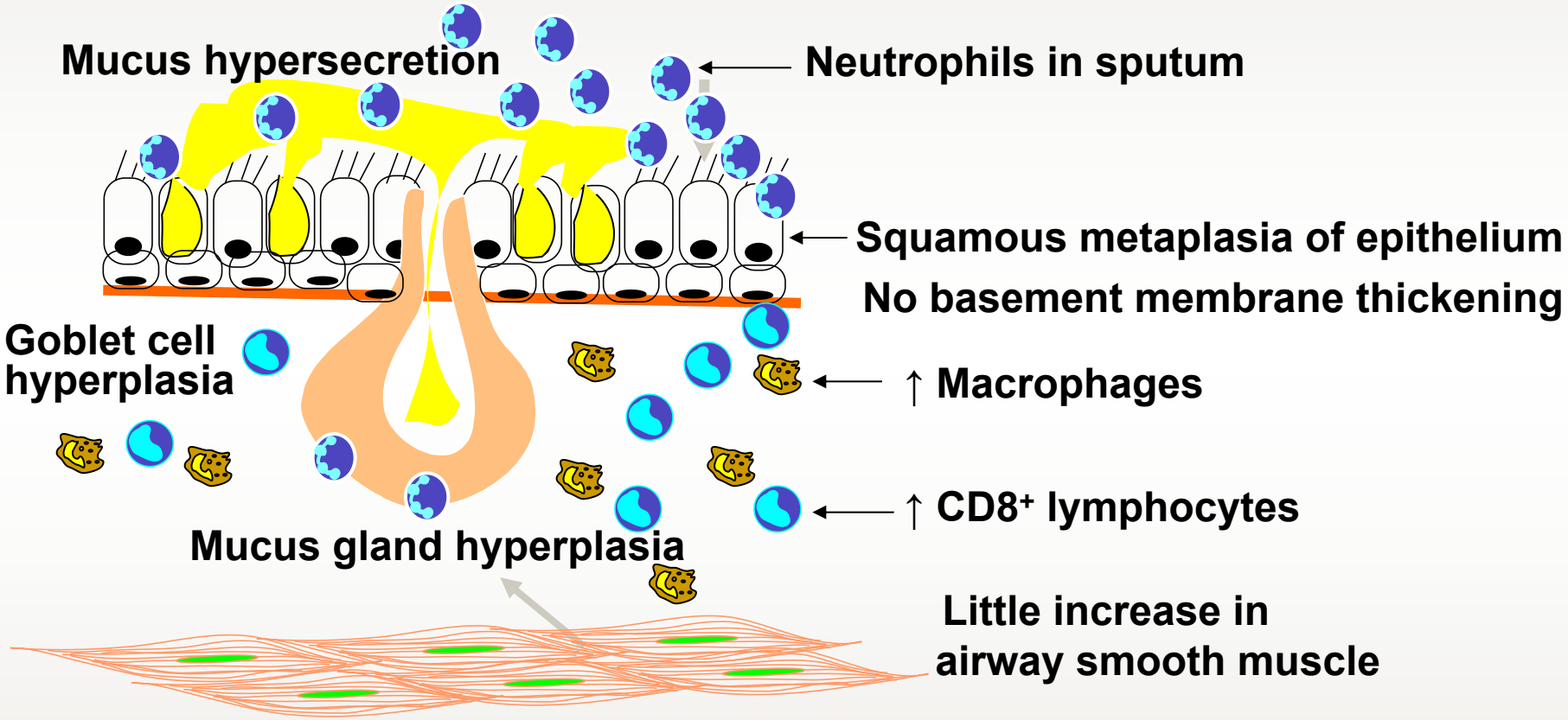
Source: Peter J. Barnes, MD

Oxidative Stress in COPD



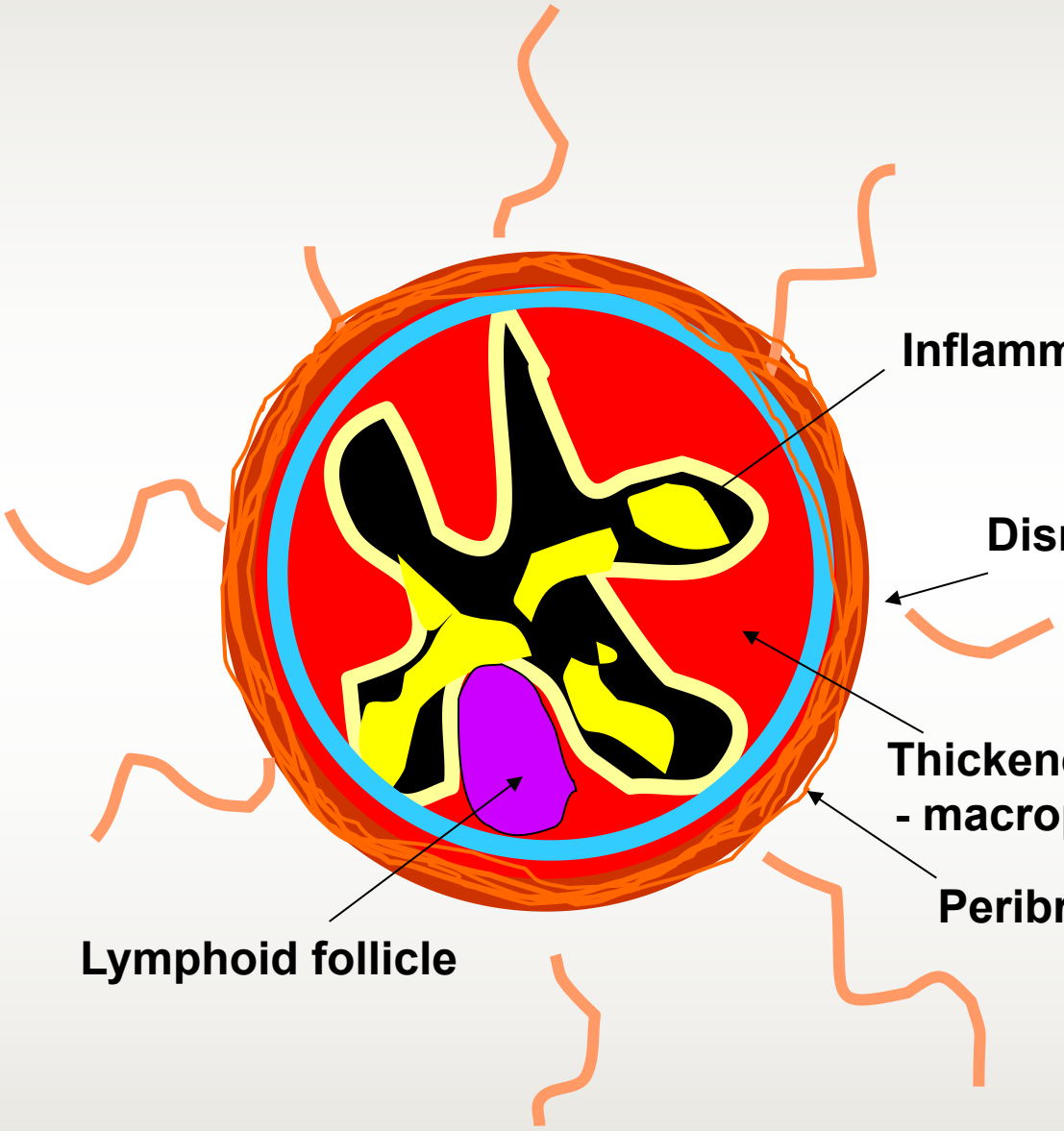
Source: Peter J. Barnes, MD

Changes in Large Airways of COPD Patients



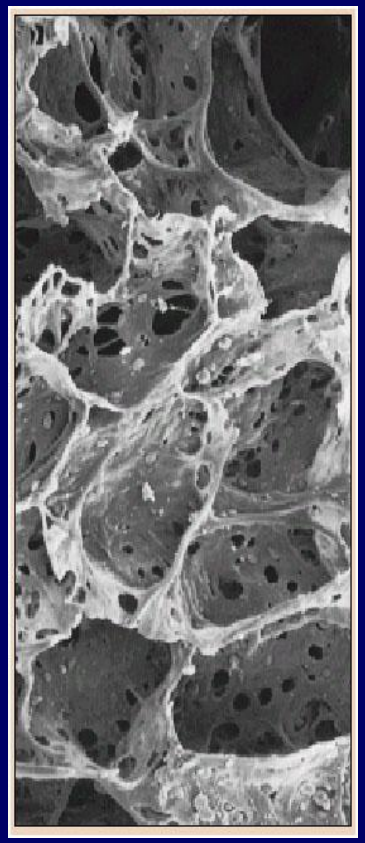
Source: Peter J. Barnes, MD

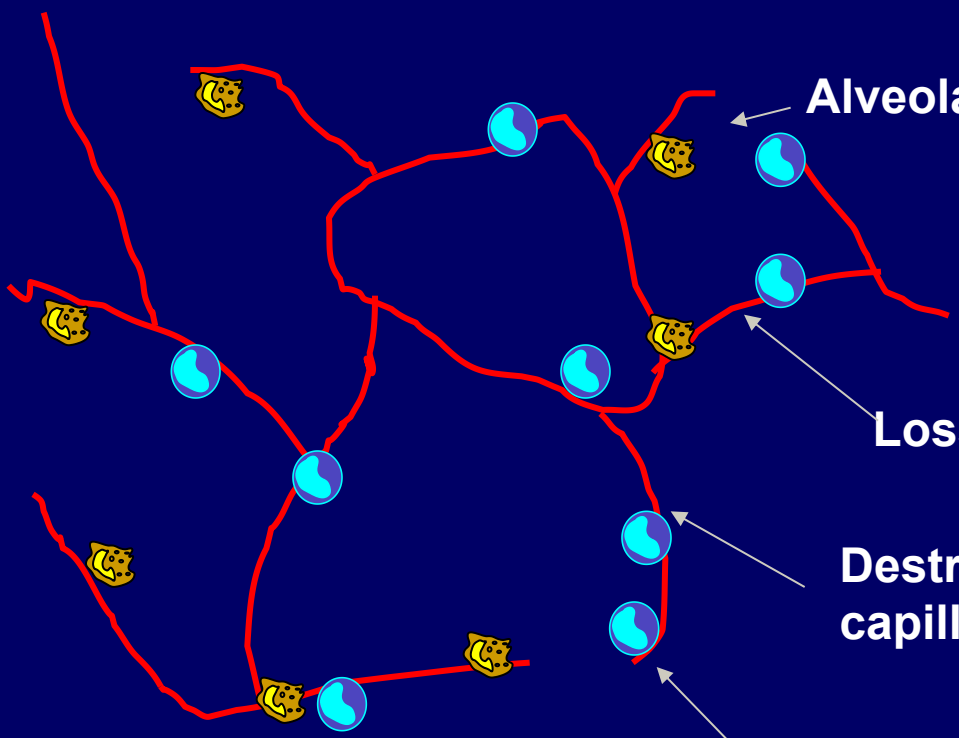
Changes in Small Airways in COPD Patients



Source: Peter J. Barnes, MD

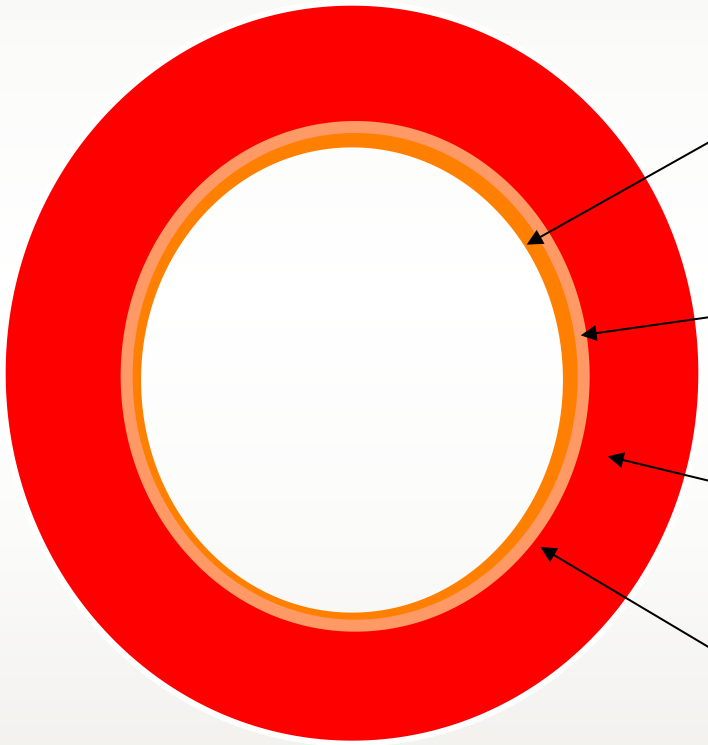
Changes in Lung Parenchyma in COPD





Source: Peter J. Barnes, MD

Changes in Pulmonary Arteries in COPD Patients



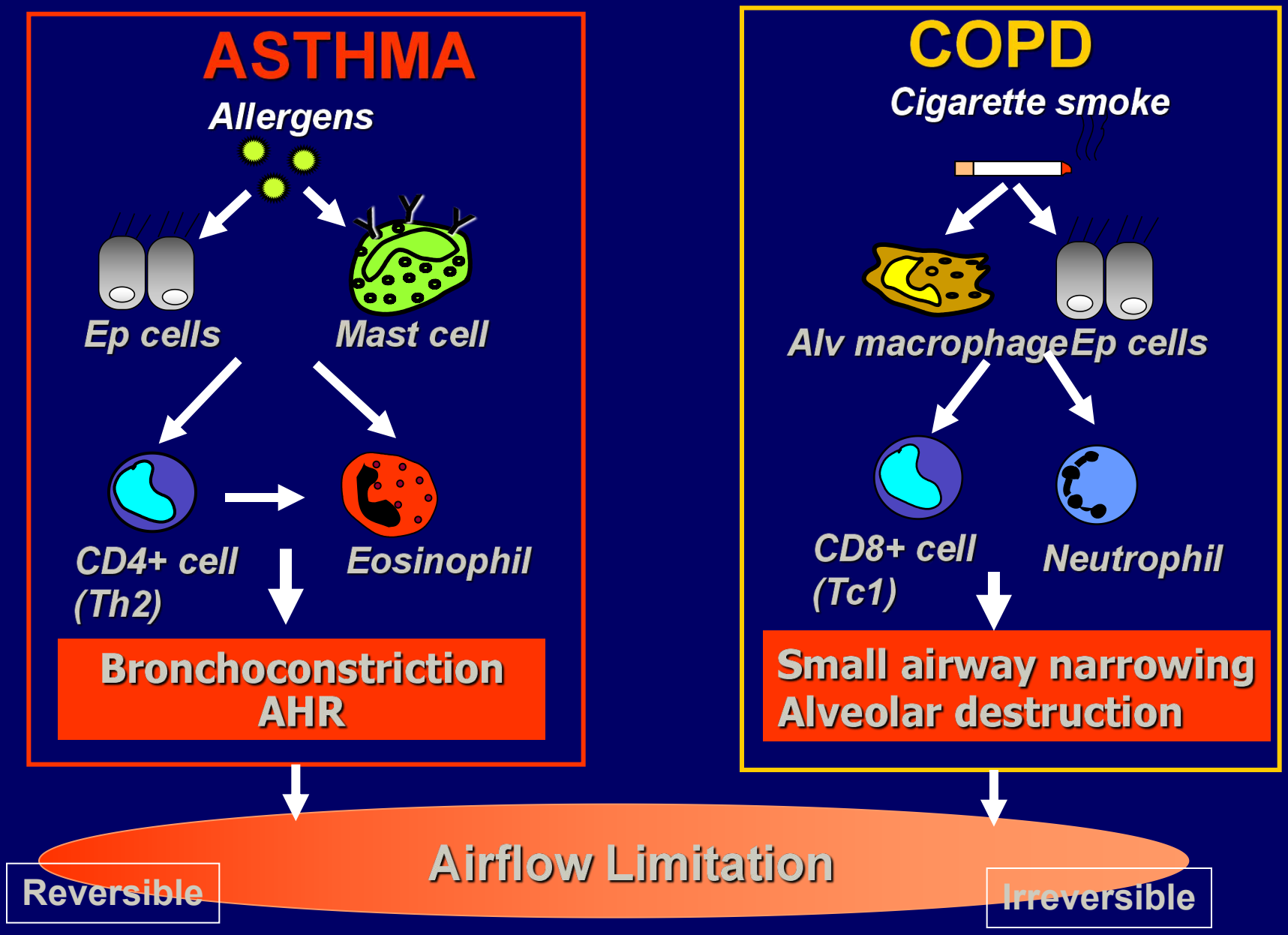
Endothelial dysfunction

Intimal hyperplasia

Smooth muscle hyperplasia

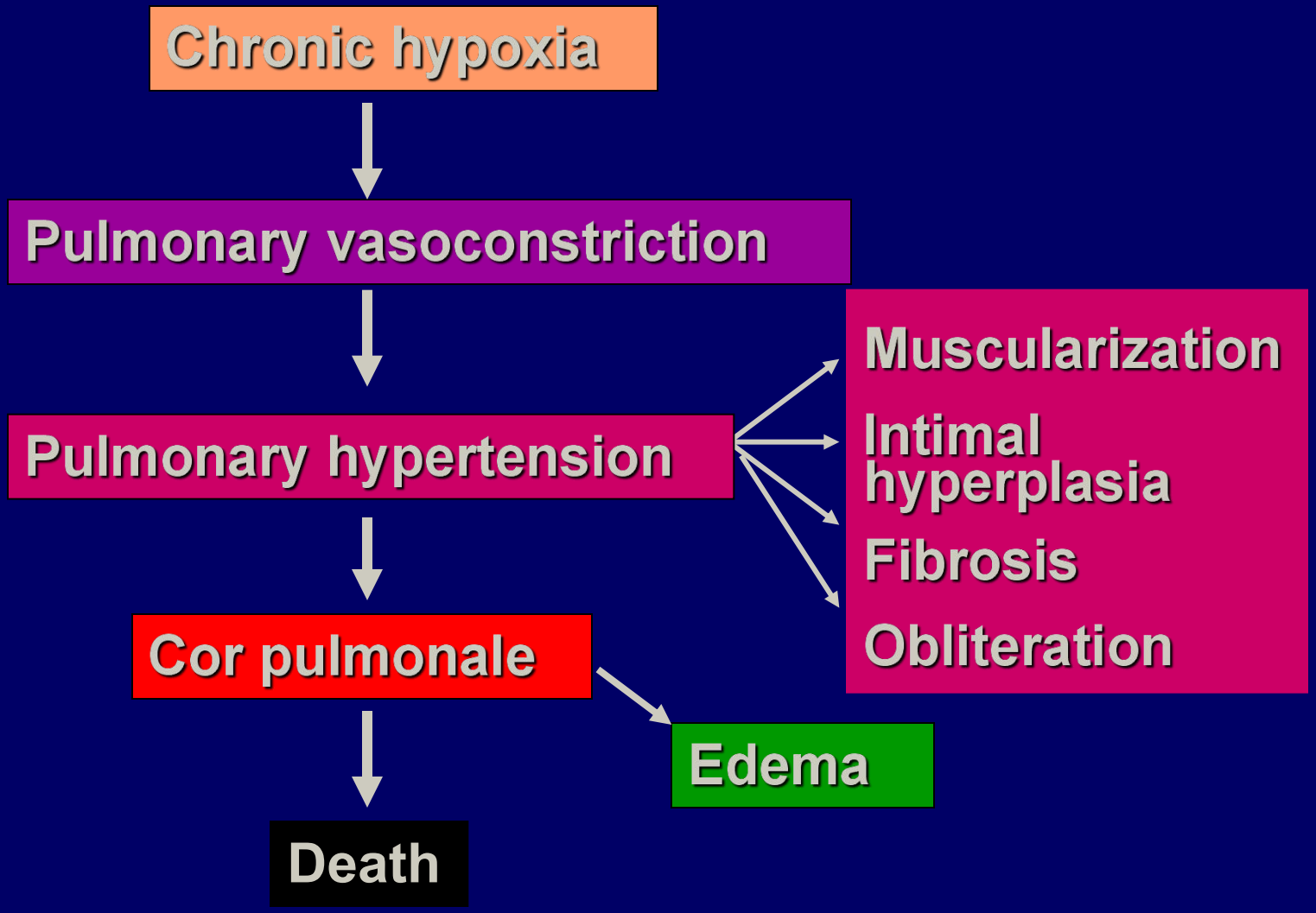
↑ Inflammatory cells (macrophages, $CD8^+$ lymphocytes)

***Source*: Peter J. Barnes, MD**



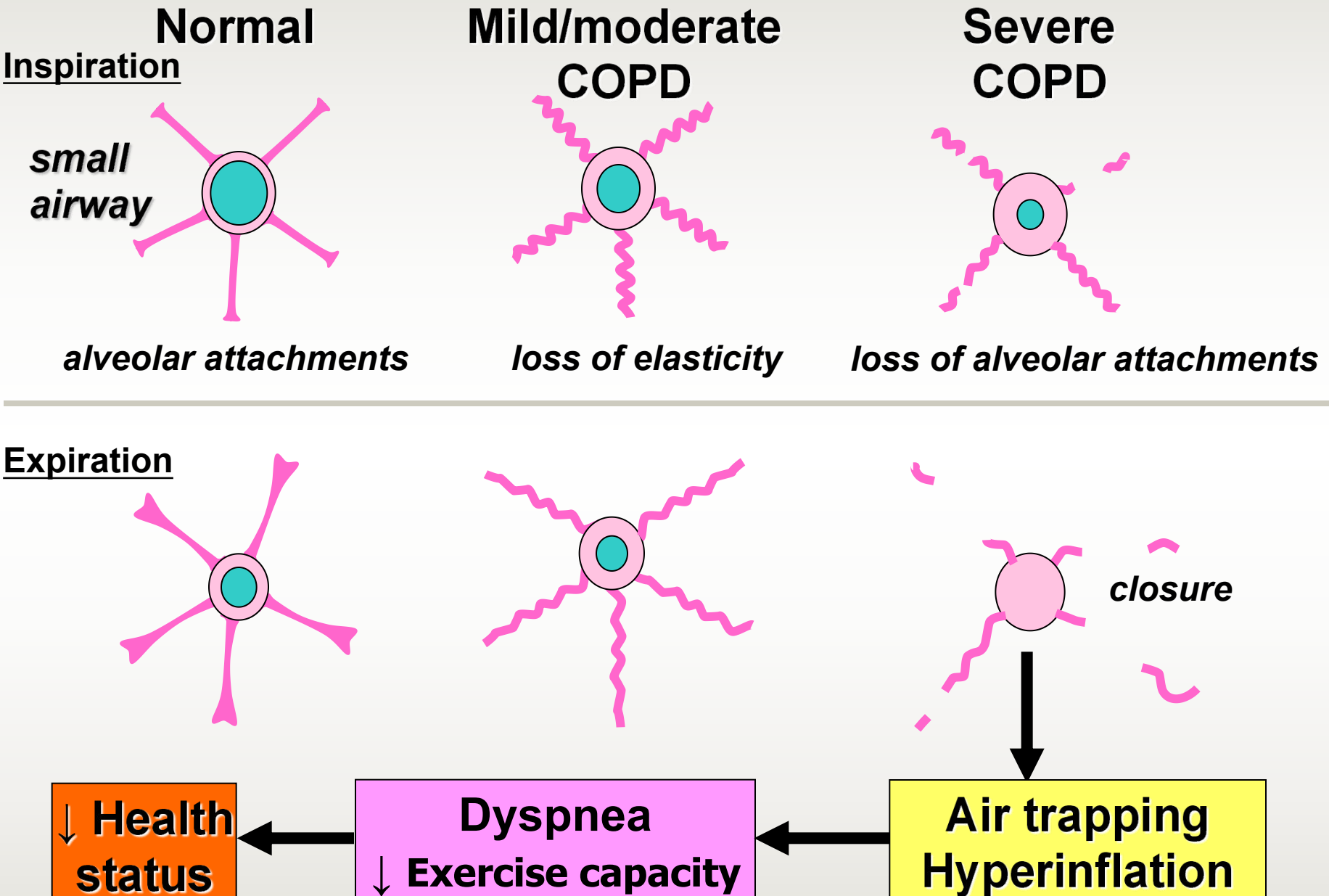
Source: Peter J. Barnes, MD

Pulmonary Hypertension in COPD



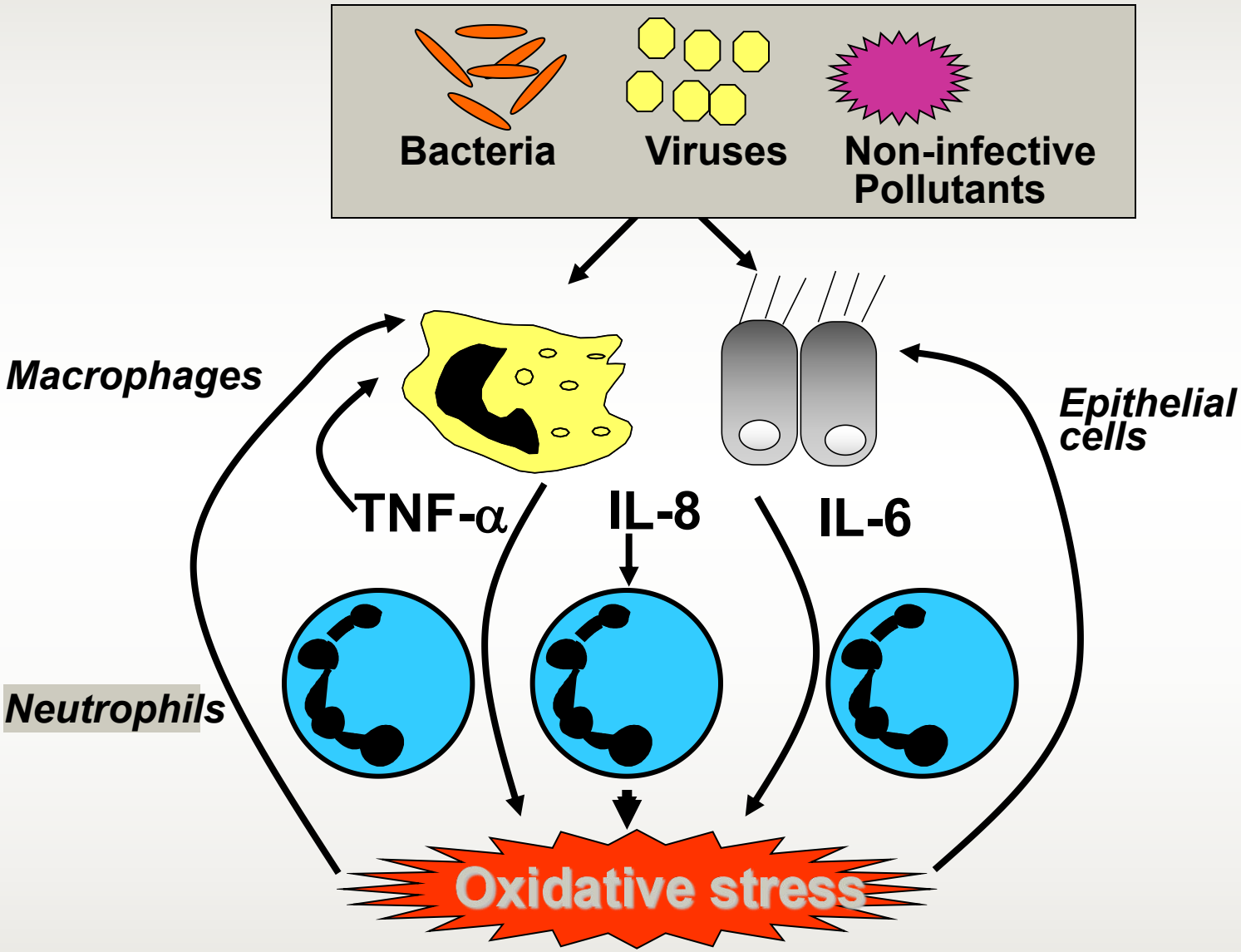
Source: Peter J. Barnes, MD

Air Trapping in COPD



Source: Peter J. Barnes, MD

Inflammation in COPD Exacerbations



Source: Peter J. Barnes, MD

Chronic bronchitis

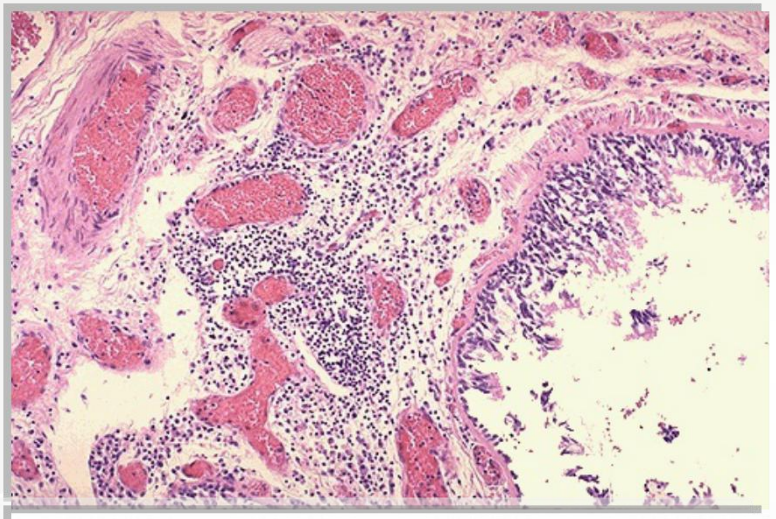
- Chronic bronchitis is an inflammation and eventual scarring of the lining of the bronchial tubes.
- Symptoms of chronic bronchitis include:

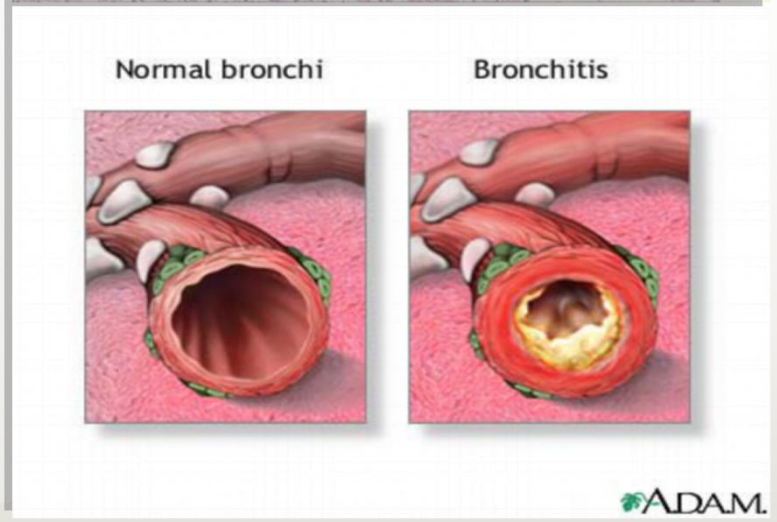
  chronic cough

  increased mucus

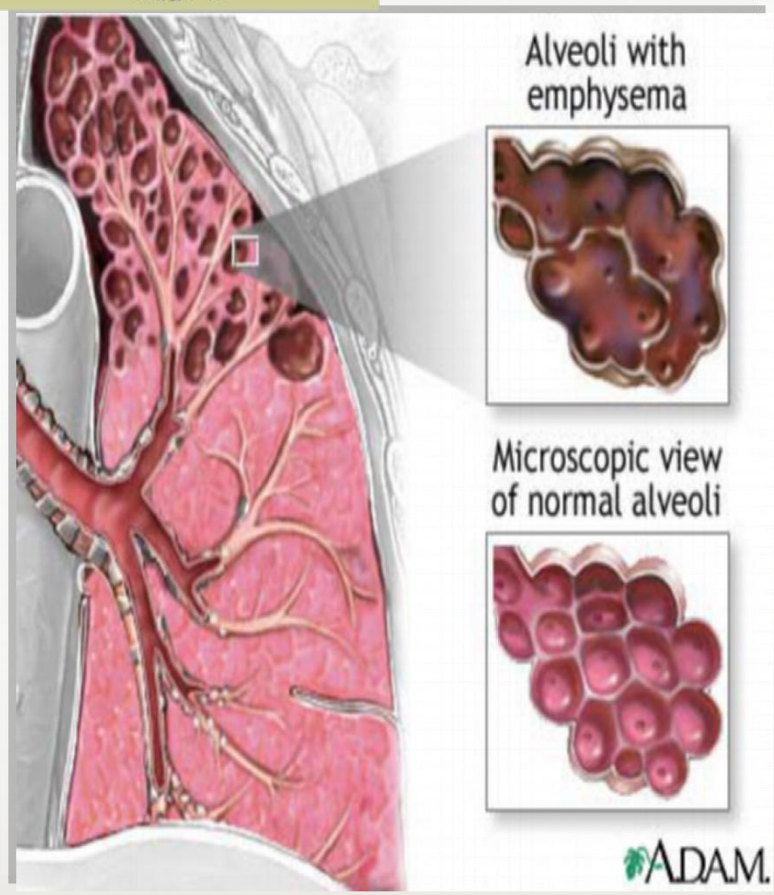
  frequent clearing of the throat

  shortness of breath





Emphysema



Emphysema indueces irreversible lung damage:

The walls between the air sacs within the lungs lose their ability to stretch and recoil.

Elasticity of the lung tissue is lost, causing air to be trapped in the air sacs and impairing the exchange of oxygen and carbon dioxide.

The Support of the airways is lost, allowing for obstruction of airflow.

Emphysema

- Symptoms of emphysema include:

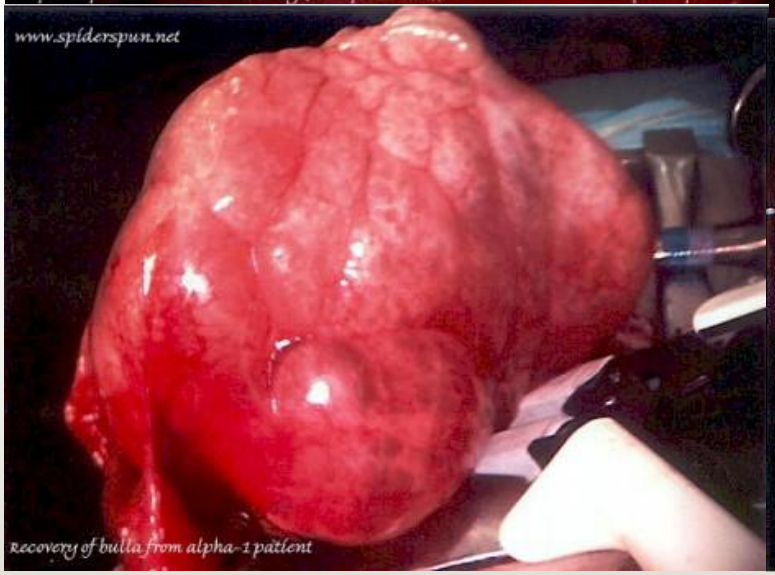
  cough

  shortness of breath

  a limited excercise tolerance

- Diagnosis is made by pulmonary function tests, along with the patient's history, examination and other tests.

Pathology of Emphysema



Pathology of Emphysema

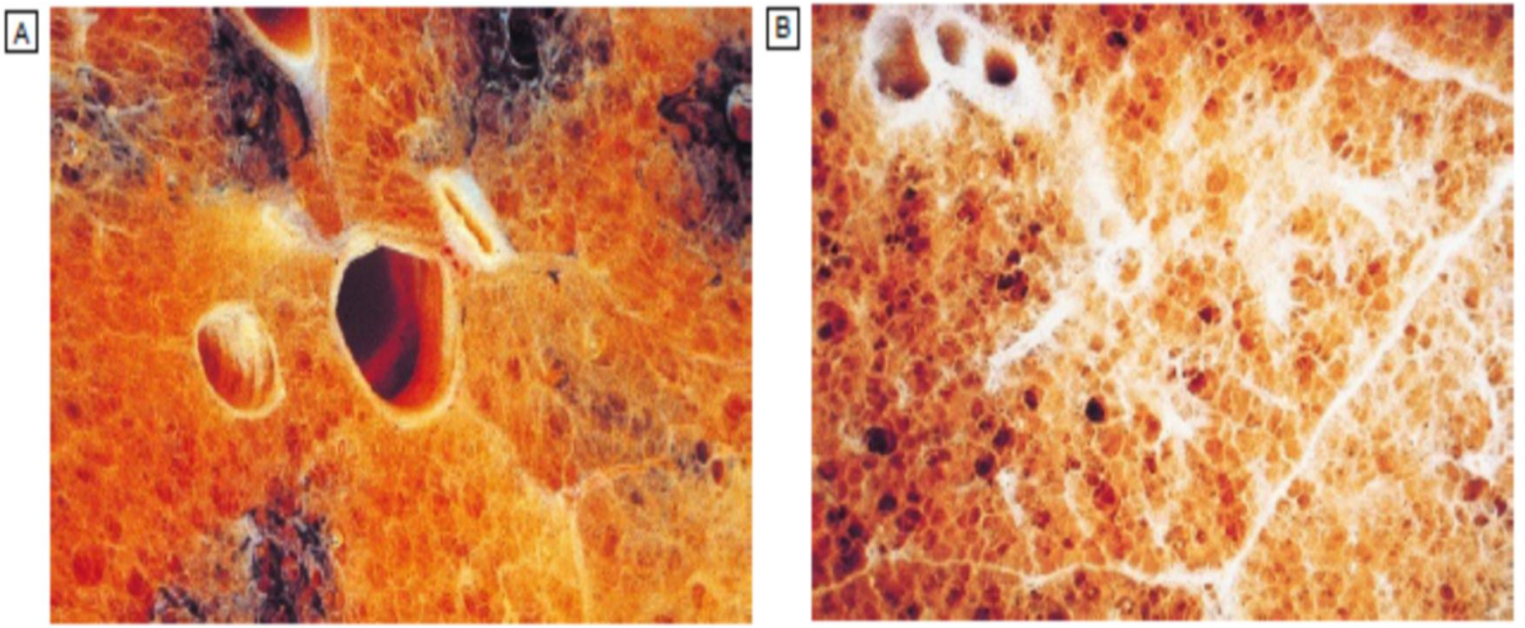


Fig. 19.24 The pathology of emphysema. A Normal lung. B Emphysematous lung showing gross loss of the normal surface area available for gas exchange.

——Davidson's Principles and Practice of Medicine 21st Ed

Pathophysiology

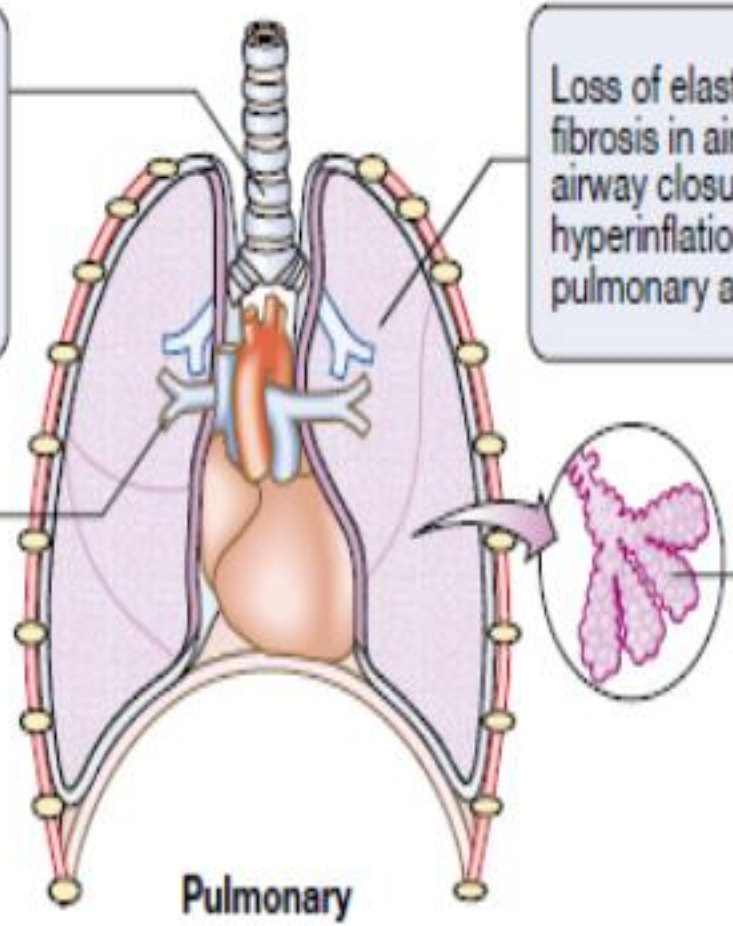
- Increased mucus production and reduced mucociliary clearance - cough and sputum production
- Loss of elastic recoil - airway collapse
- Increase smooth muscle tone
- Pulmonary hyperinflation
- Gas exchange abnormalities - hypoxemia and/or hypercapnia

Pathophysiology

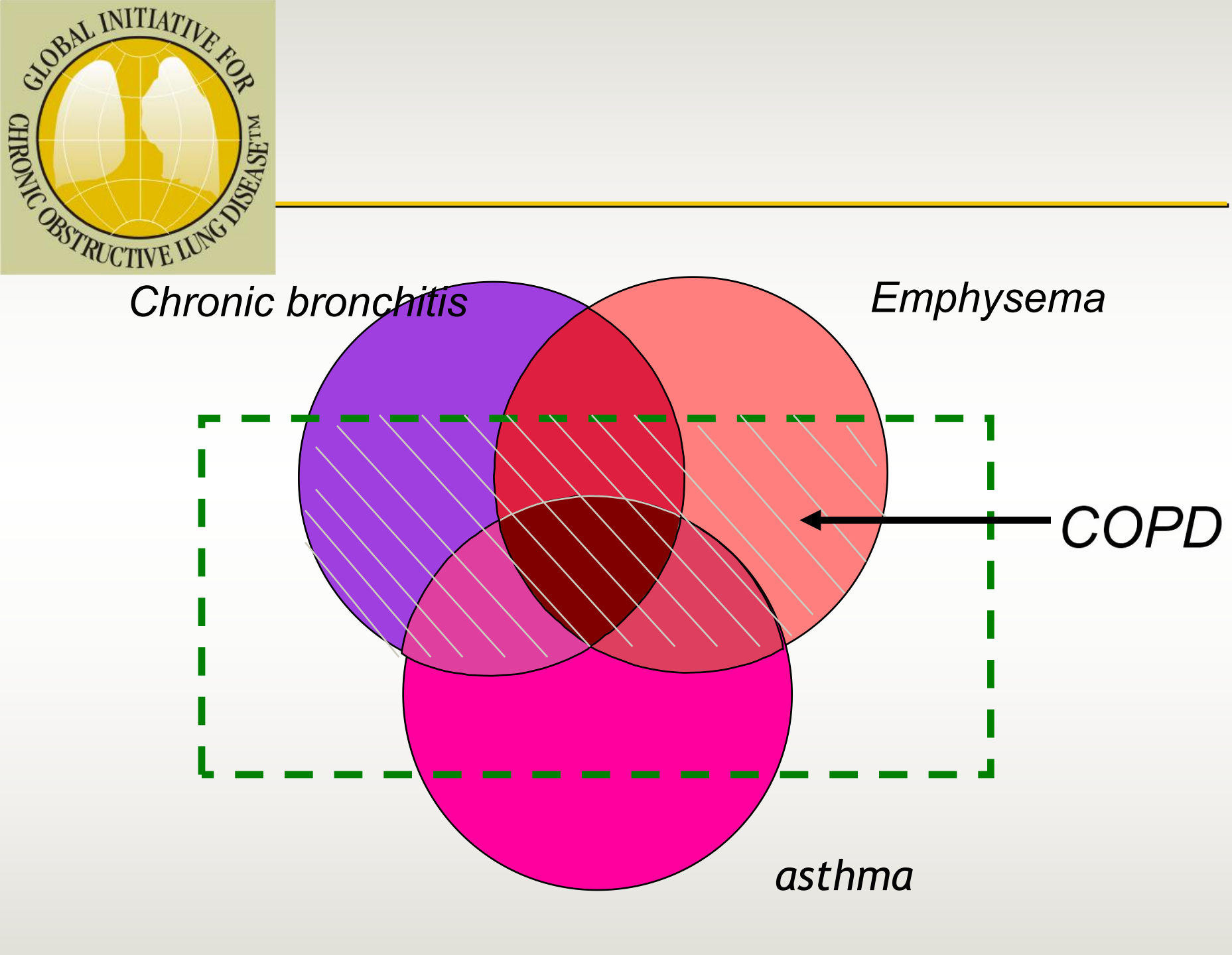
Enlargement of mucus-secreting glands and increase in number of goblet cells, accompanied by an inflammatory cell infiltrate, result in increased sputum production leading to chronic bronchitis

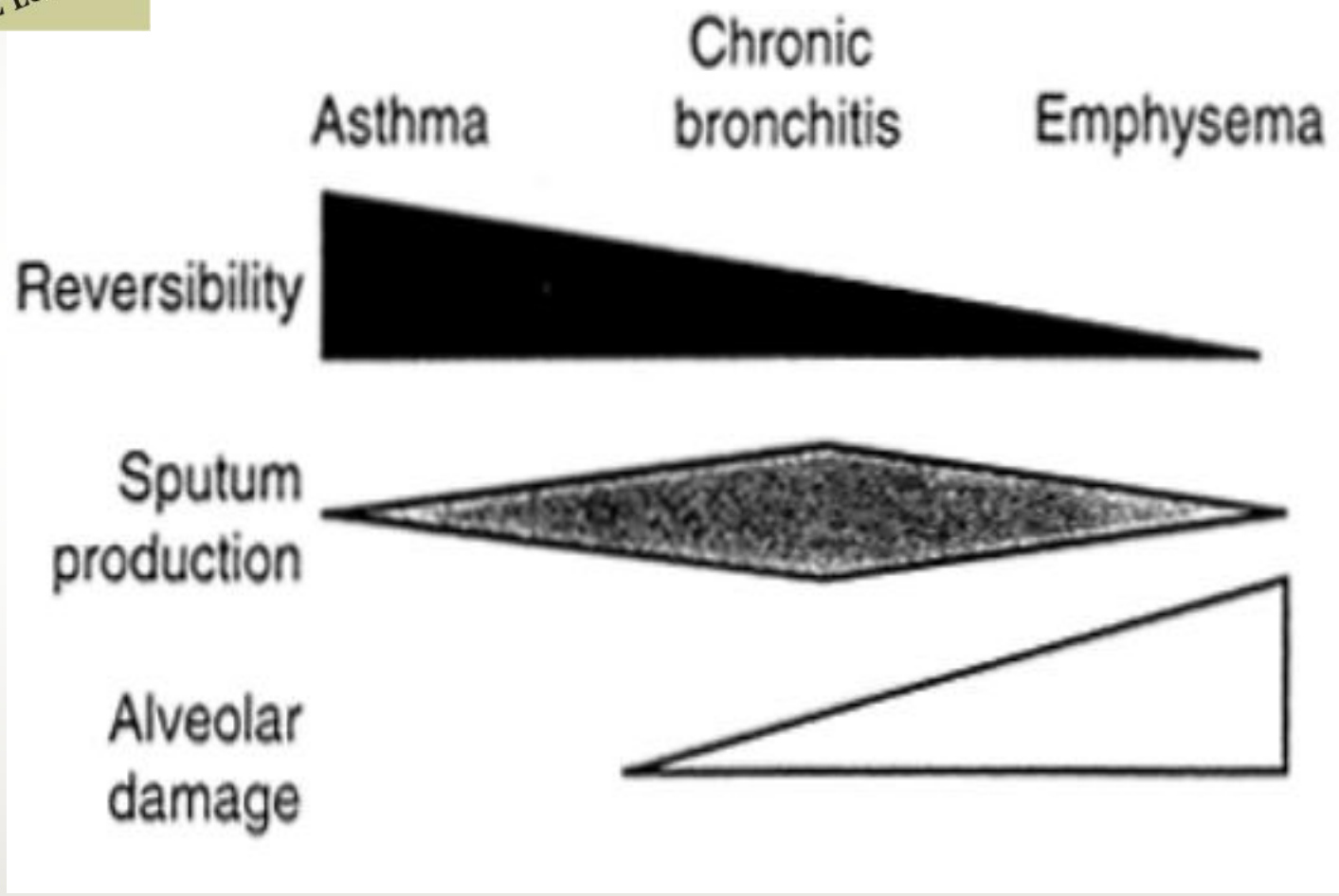
Loss of elastic tissue, inflammation and fibrosis in airway wall result in premature airway closure, gas trapping and dynamic hyperinflation leading to changes in pulmonary and chest wall compliance

Pulmonary vascular remodelling and impaired cardiac perfomance



Unopposed action of proteases and oxidants leading to destruction of alveoli and appearance of emphysema


GLOBAL INITIATIVE FOR
CHRONIC OBSTRUCTIVE LUNG DISEASE™
Chronic bronchitis
Emphysema
COPD
asthma


Asthma
Chronic bronchitis
Emphysema
Reversibility
Sputum production
Alveolar damage

Assess and Monitor COPD: Key Points

- A clinical diagnosis of COPD should be considered in any patient who has
  - dyspnea
  - chronic cough or sputum production
  - and/or a history of exposure to risk factors

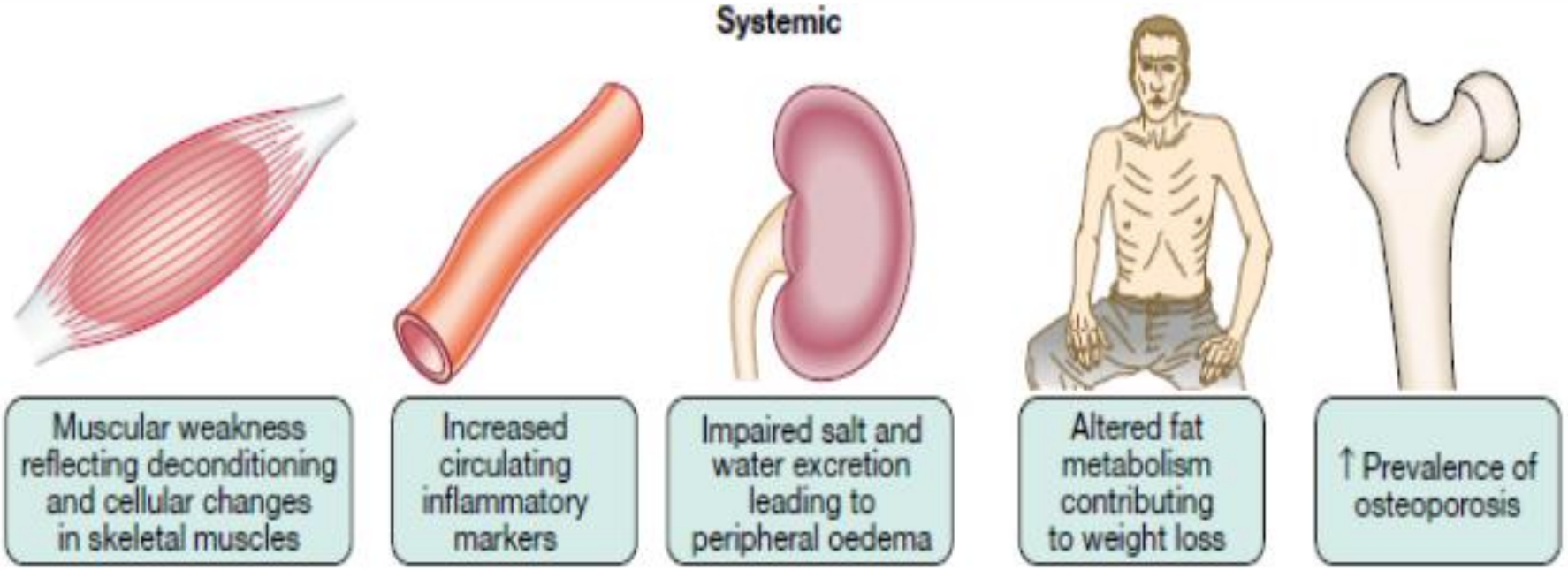
Assess and Monitor COPD: Key Points

- The diagnosis should be confirmed by spirometry.

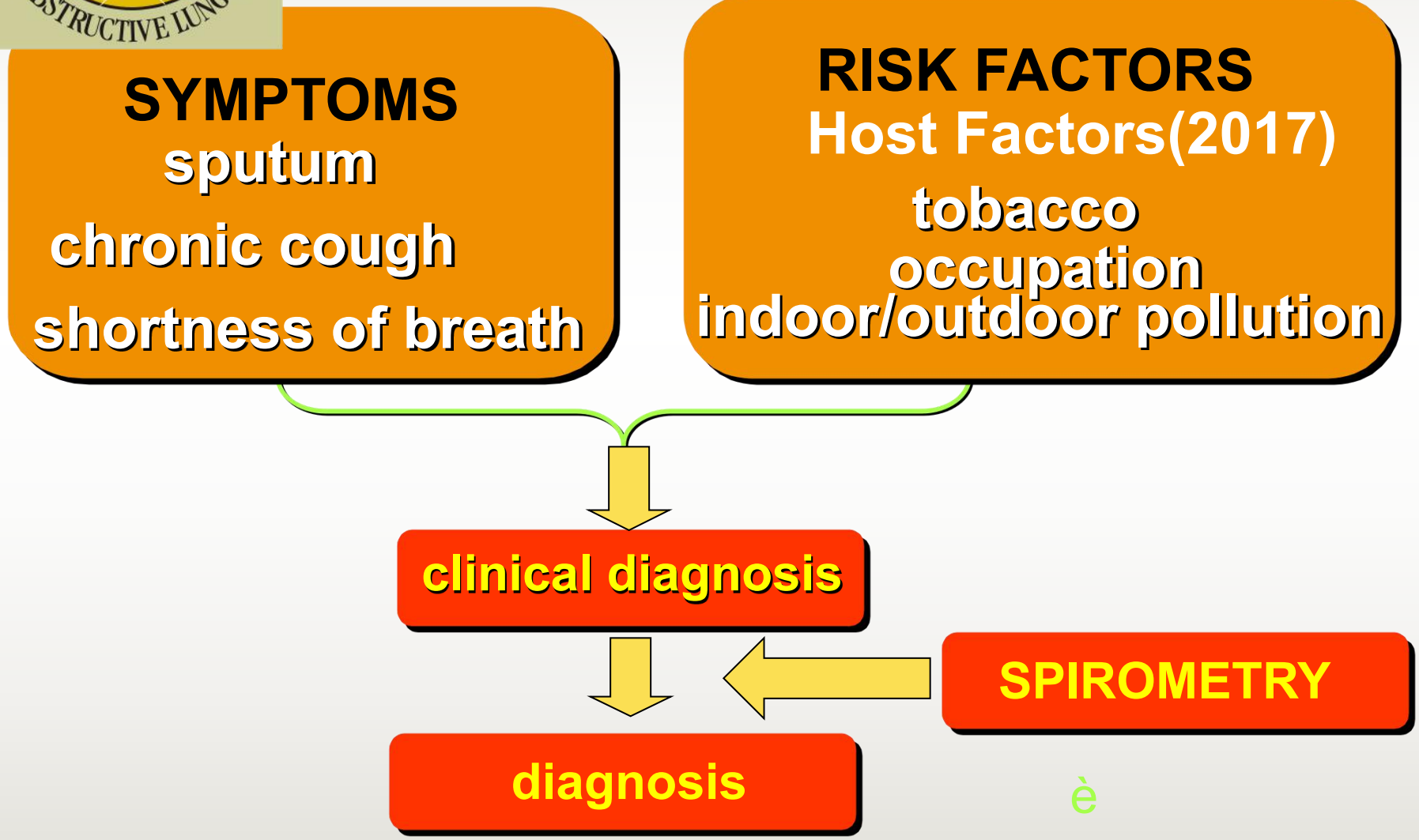
A post-bronchodilator FEV1/FVC < 0.70 confirms the presence of airflow limitation that is not fully reversible.

Assess and Monitor COPD: Key Points

Extrapulmonary (systemic) effects are common in COPD and should be actively identified.



Pathways to the diagnosis of COPD

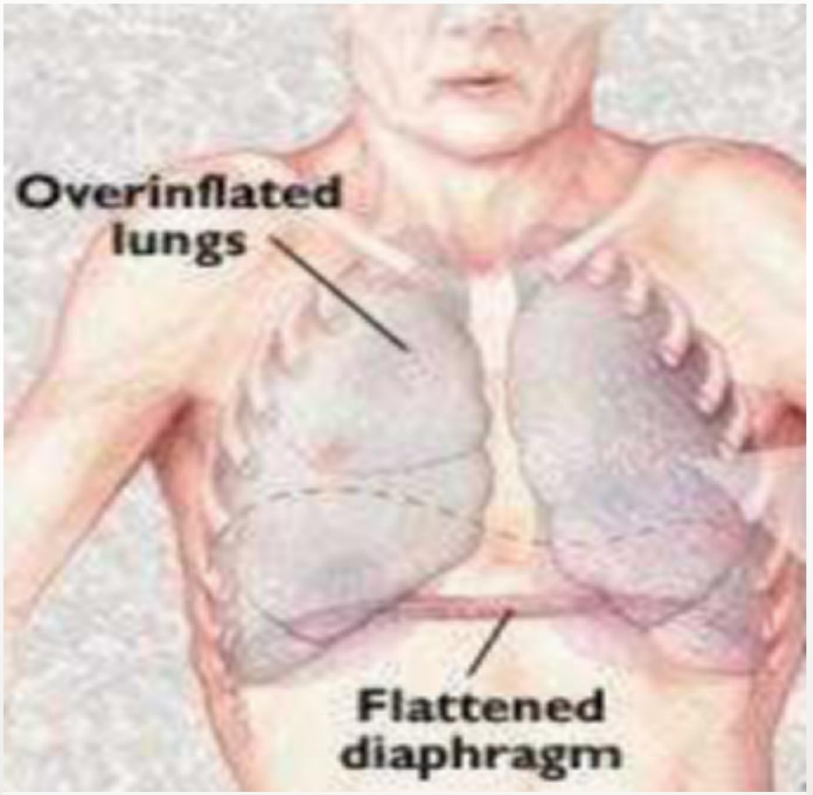


Key Indicators for COPD Diagnosis(2020)

Chronic cough	May be intermittent and may be unproductive. Recurrent wheeze.
Chronic sputum production	Any pattern of chronic sputum production may indicate COPD.
Dyspnea that is	Progressive (worsen over time) Persistent (present every day) Characteristically worse with exercise.
Recurrent lower respiratory tract infections.	
History of exposure to risk factors	Host factors(such as genetic factors,congenital/developmental abnormalities). Tobacco smoke (including popular local preparation) . somoke from home cooking and heat fuels. Occupational dusts ,vapors,fumes,gases and other chemicals.
Family history of COPD and/or childhood factors	For example low birthweight,childhood respiratory infectios.

Physical signs

- Large barrel shaped chest (hyperinflation)
- Prominent use of accessory muscle in respiration
- Low, flat diaphragm
- Diminished breath sound



Spirometry(肺功能)

- Diagnosis
- Assessing severity
- Assessing prognosis
- Monitoring progression

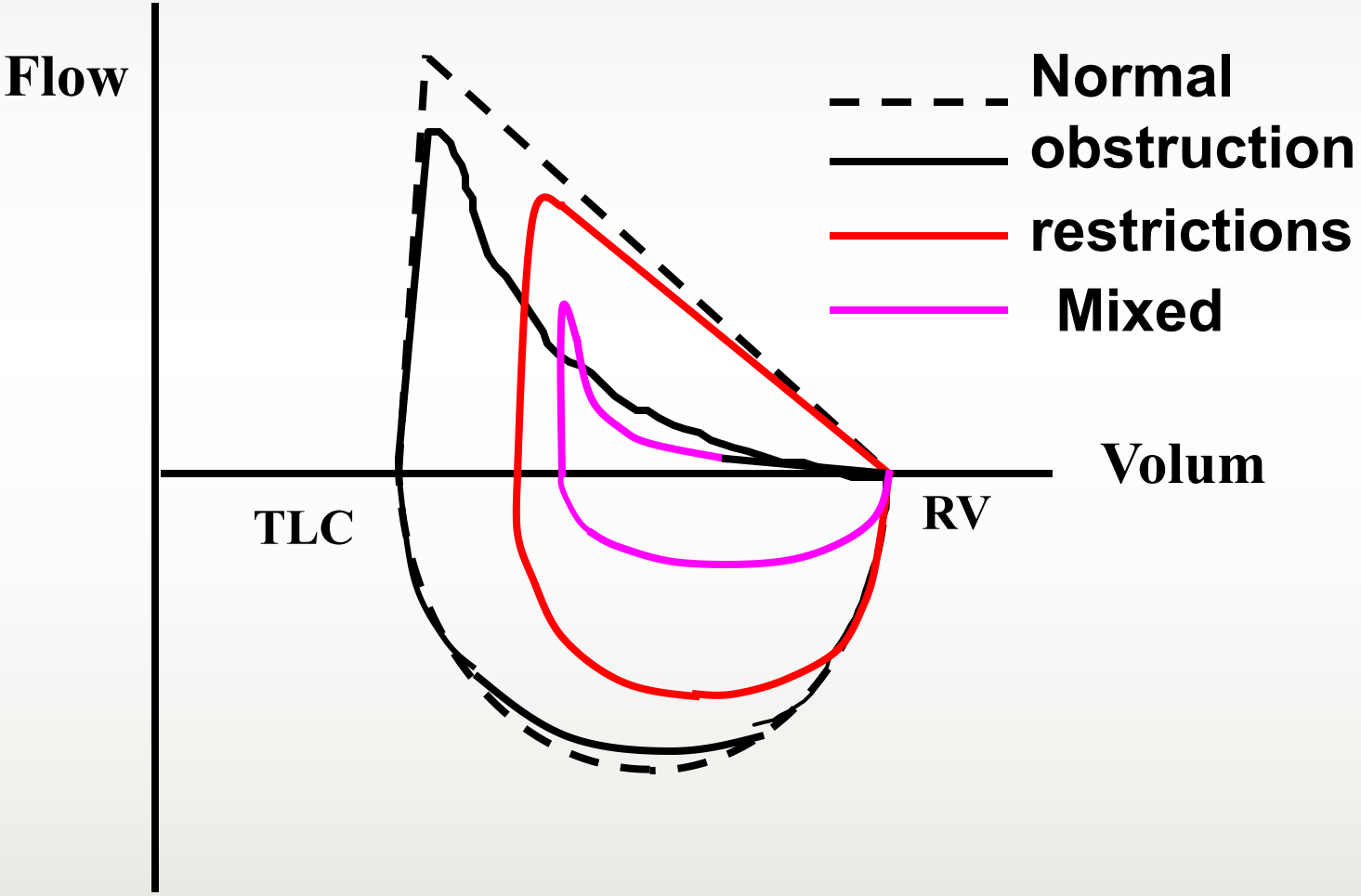
Spirometry

- **FEV_1** – Forced expired volume in the first second
- **FVC** – Total volume of air that can be exhaled from maximal inhalation to maximal exhalation
- **FEV_1/FVC%** - The ratio of FEV_1 to FVC, expressed as a percentage.

Spirometry

- Spirometry should be performed after the administration of an adequate dose of a short-acting inhaled bronchodilator to minimize variability.
- A post-bronchodilator FEV1/FVC < 0.70 confirms the presence of airflow limitation that is not fully reversible.
- When possible, values should be compared to age-related normal values to avoid overdiagnosis of COPD in the elderly.

Flow-volume curve



Grading of severity of airflow limitation in COPD

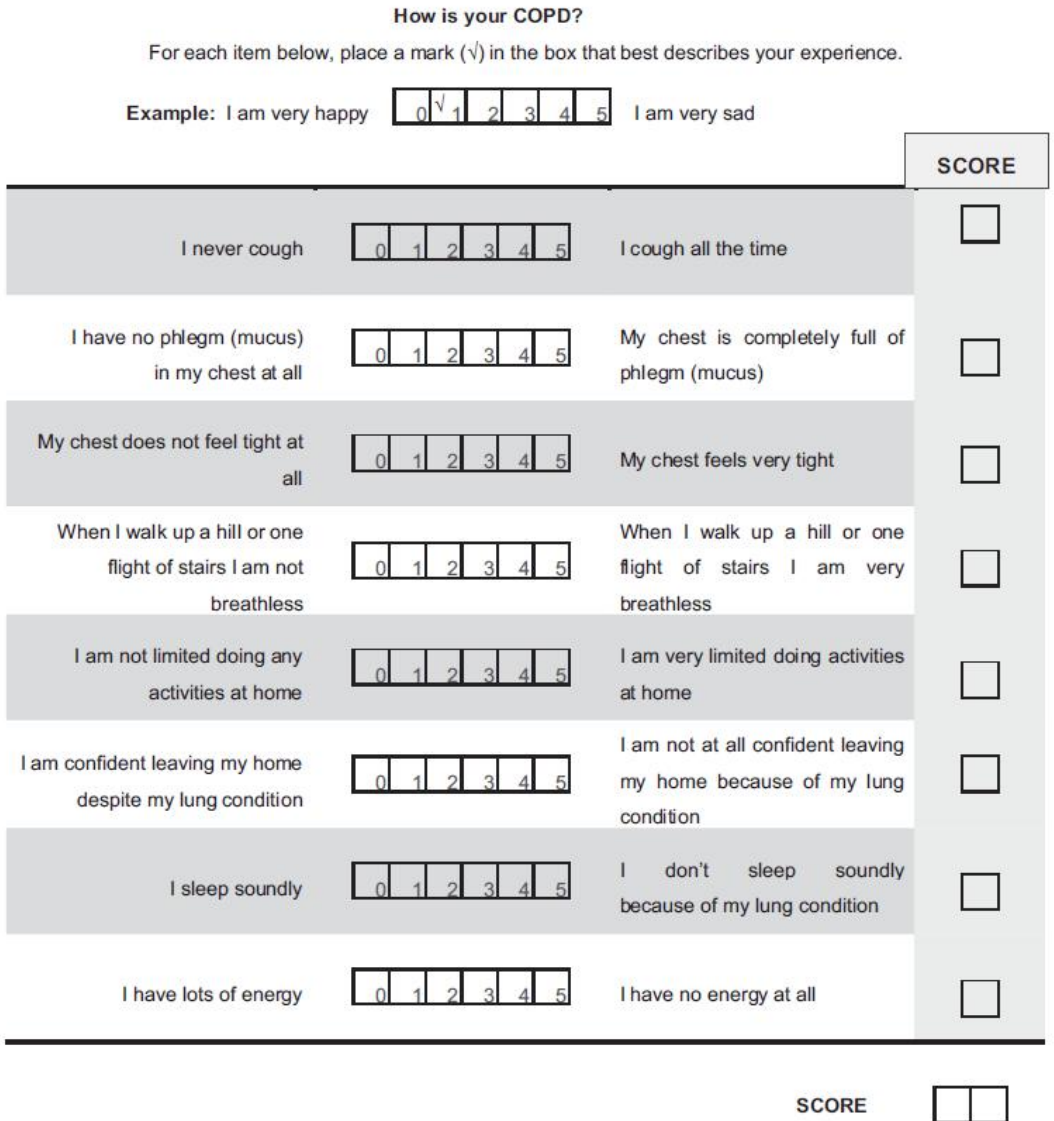
Severity	Postbronchodilator FEV_1/FVC	Postbronchodilator FEV_1% predicted
GOLD 1	<0.7	≥80
GOLD 2	<0.7	50-80
GOLD 3	<0.7	30-50
GOLD 4	<0.7	<30

SPIROMETRY is not to substitute for clinical judgment in the evaluation of the severity of disease in individual patients.

Assessment of symptoms

- COPD assessment test (**CAT**)

including eight common clinical problem, to evaluate the health damage of patients with COPD.



How is your COPD?

For each item below, place a mark (√) in the box that best describes your experience.

Example: I am very happy | 0 | √ | 1 | 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	

SCORE | |

Assessment of symptoms

- Modified british medical research council (**mMRC**)

Having a good correlation with health condition and can predict the future risk of death

Table 2.5. 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.

Assessment of exacerbation risk

The best predictor of frequent exacerbations (defined as ≥ 2 exacerbations per year) is a history of earlier treated events.

Hospitalization for a COPD exacerbation has a poor prognosis and an increased risk of death.

Assessment of comorbities

COPD patients are at increased risk for:

- Myocardial infarction, angina
- Osteoporosis
- Respiratory infection
- Depression
- Diabetes
- Lung cancer

Assessment of comorbities

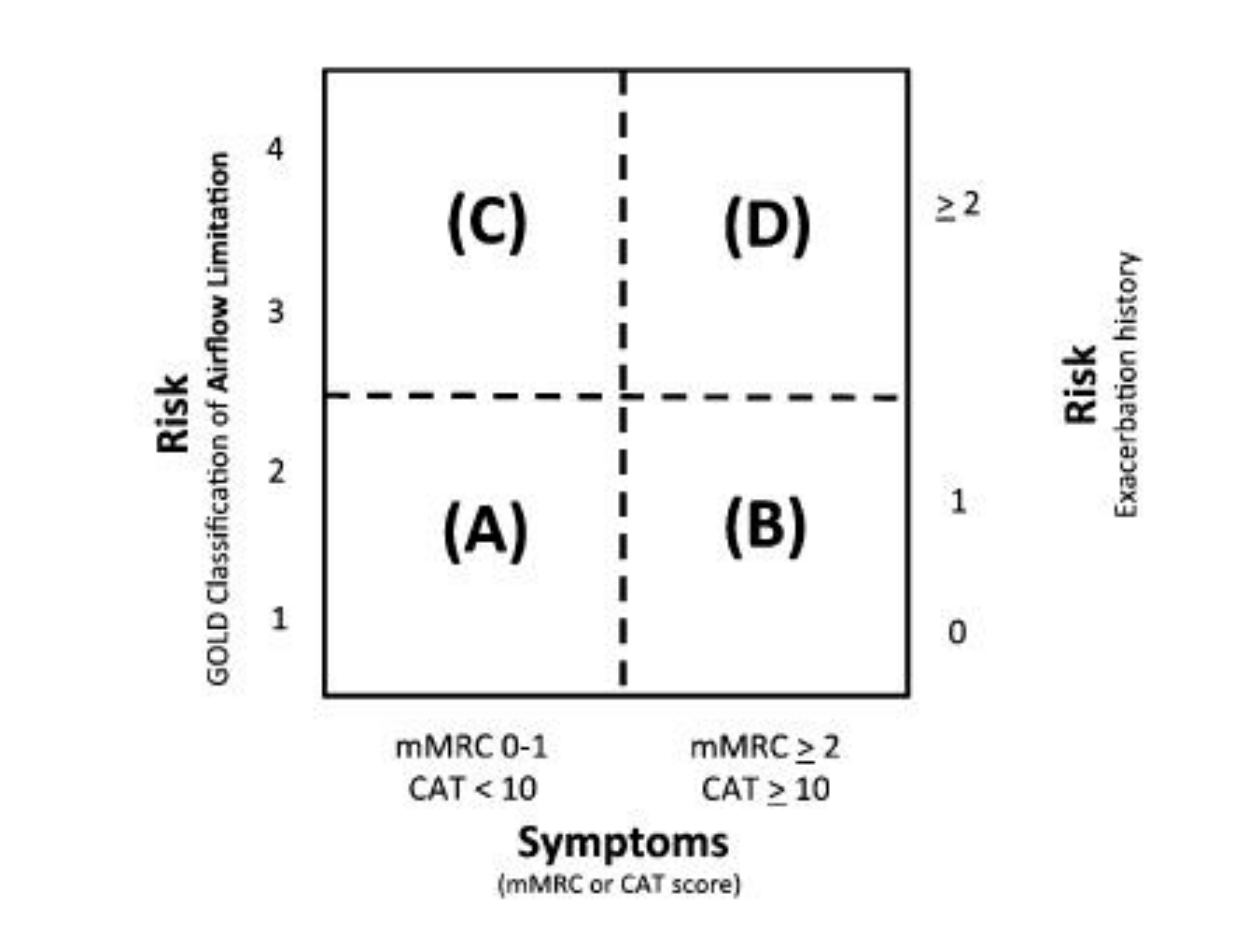
COPD has significant extrapulmonary

(systemic) effects including:

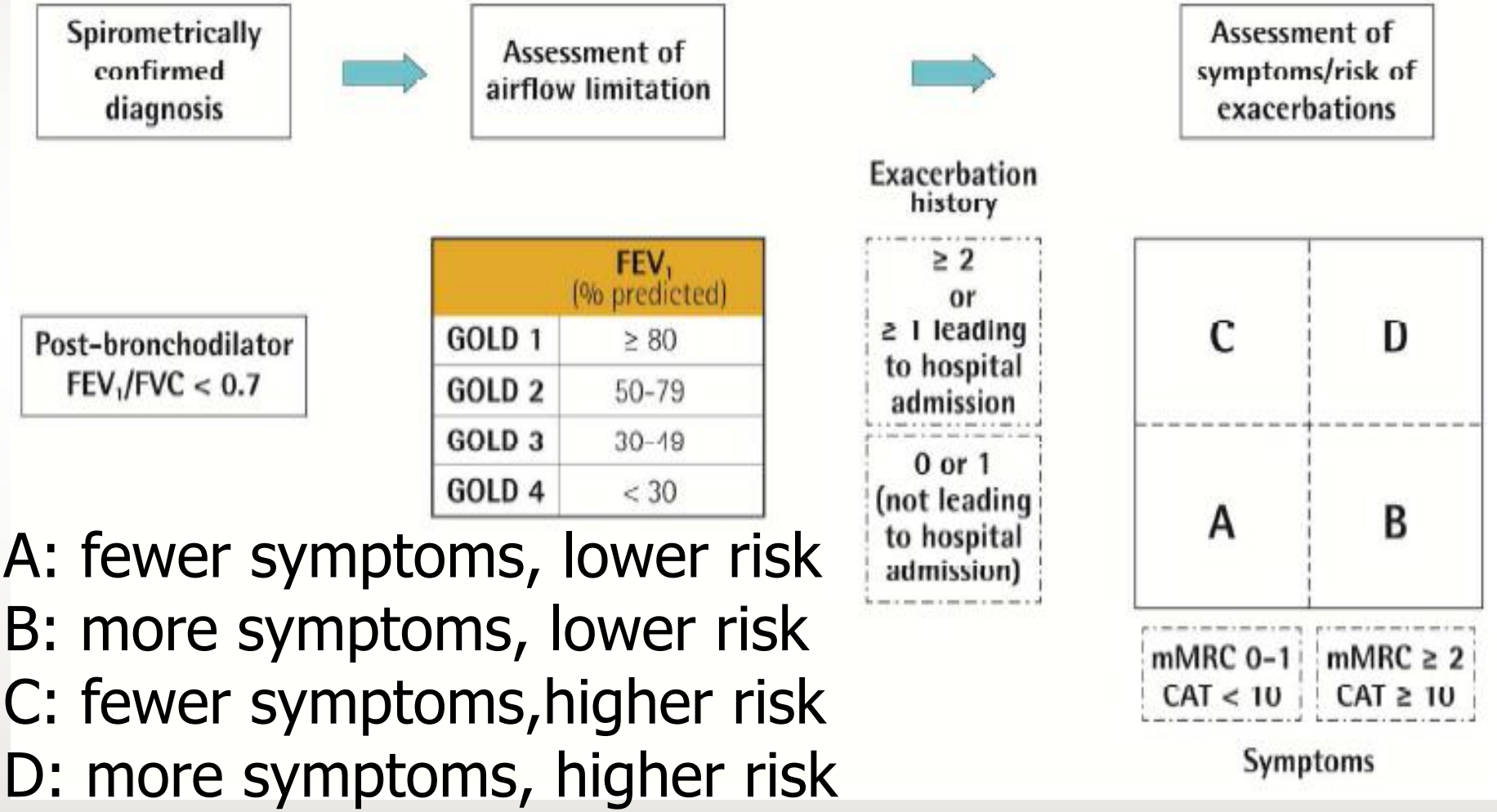
- Weight loss
- Nutritional abnormalities
- Skeletal muscle dysfunction

Revised combined COPD assessment (2011)

A: fewer symptoms, lower risk
B: more symptoms, lower risk
C: fewer symptoms, higher risk
D: more symptoms, higher risk



Refined ABCD assessment tool (2017)



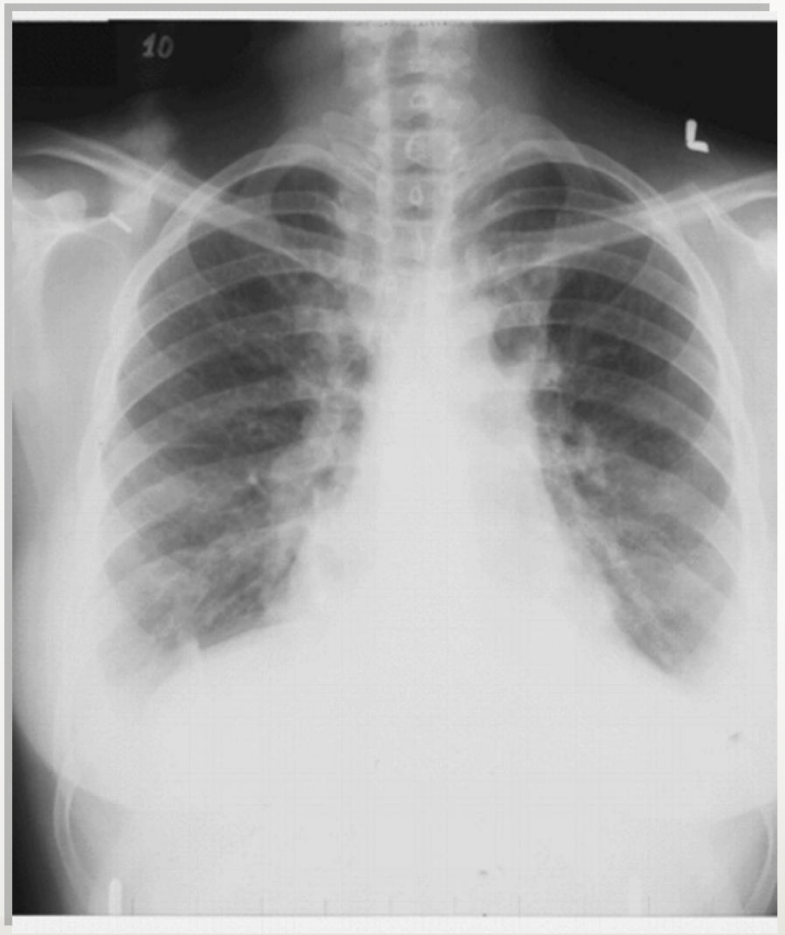
A: fewer symptoms, lower risk
B: more symptoms, lower risk
C: fewer symptoms,higher risk
D: more symptoms, higher risk

Additional investigations

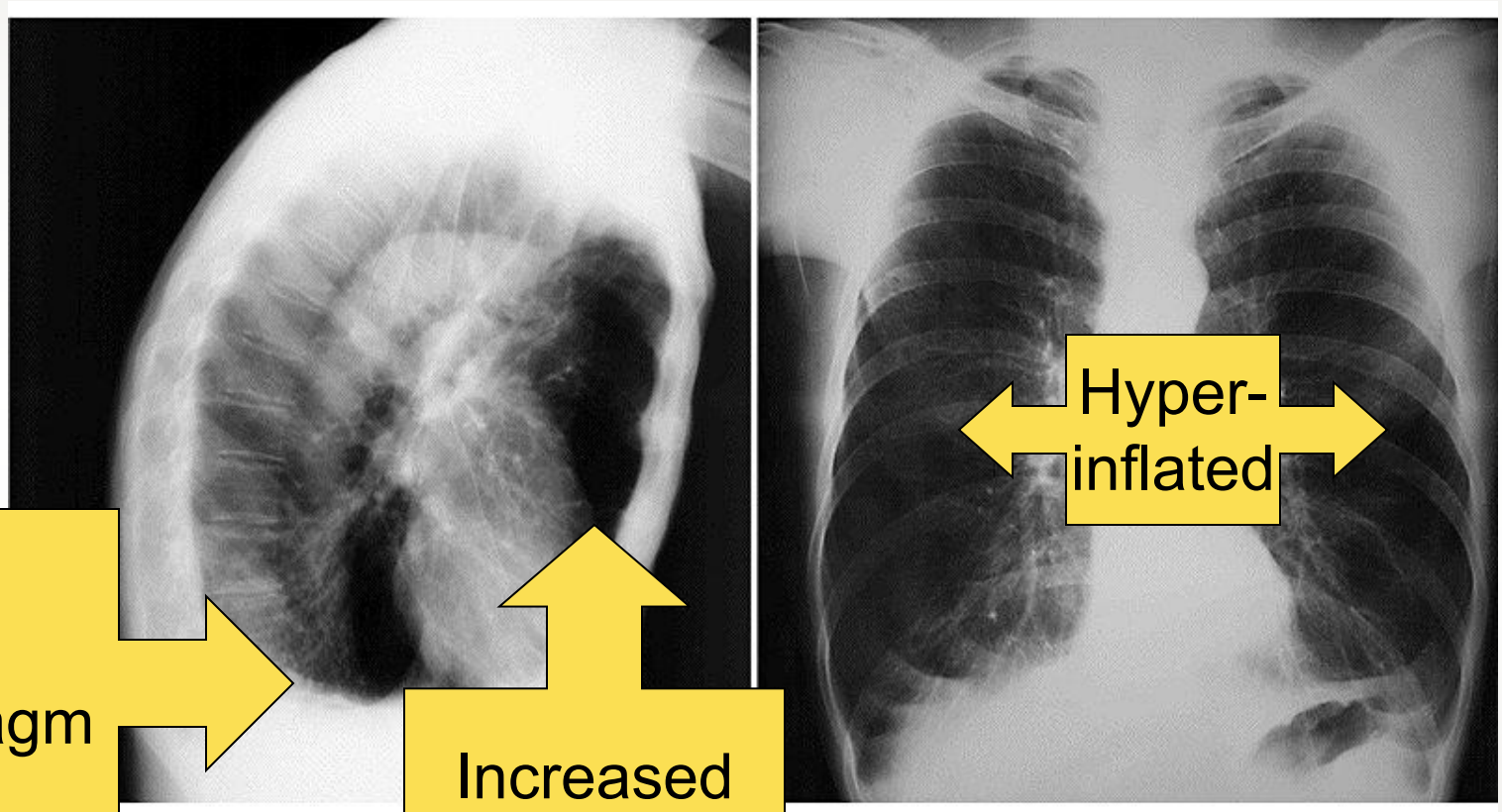
- Imaging
- Composite scores(BODE)
- Oximetry and arterial blood gas measurement
- Lung volumes and diffusing capacity
- Exercise testing and assessment of physical activity

Chest X-rays

- Emphysema
  - Hyperinflation
  - Flattened diaphragms
  - Decreased vascular markings
- Chronic Bronchitis
  - Usually normal

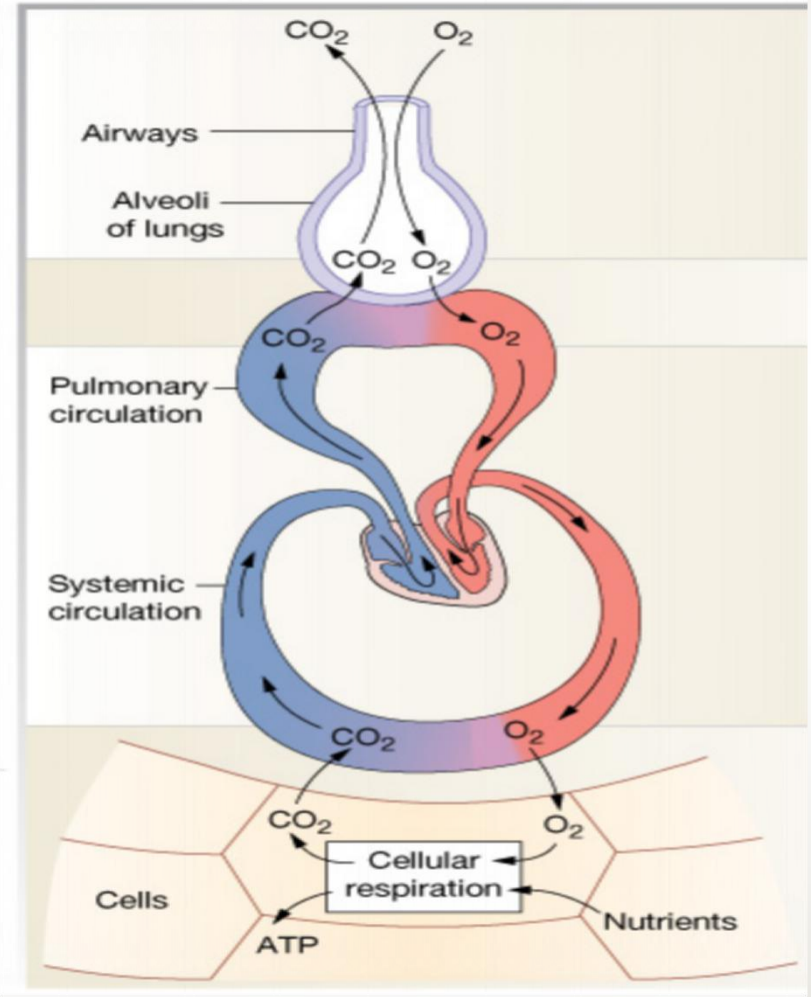


Chest X-rays


Hyper-inflated
Flat diaphragm
Increased Retrosternal air

Oximetry and Arterial Blood Gas (ABGs)

- If pulse oximetry shows peripheral arterial oxygen saturation is <92%,arterial blood gases(ABGs) should be assessed to determine whether you need any extra oxygen.



Parameters and Predictions

Parameter	Normal Values	Predictions
Arterial PO2	95 mmHg	decrease
Arterial PCO2	40 mmHg	increases
Aterial pH	approx. 7.4	decreases
Arterial HCO3- content	22-26 mEq/L	increases
Total Arterial O2 content	20 ml/dL	decrease

Differential Diagnosis of COPD

- Asthma☆
- Congestive Heart Failure

- Bronchiectasis
- Tuberculosis

- Obliterative Bronchiolitis
- Diffuse Panbronchiolitis

Differential Diagnosis: COPD and Asthma

COPD

- Onset in mid-life
- Symptoms slowly progressive
- Long smoking history
- Dyspnea during exercise
- Largely irreversible airflow limitation

ASTHMA

- Onset early in life (often childhood)
- Symptoms vary from day to day
- Symptoms at night/early morning
- Allergy, rhinitis, and/or eczema also present
- Family history of asthma
- Largely reversible airflow limitation

Management of Stable COPD

Goals

Reduce symptoms

- Relieve symptoms
- Improve exercise tolerance
- Improve health status

Reduce risk

- Prevent disease progression
- Prevent exacerbations
- Reduce motality

Management of Stable COPD

Reduce Risk Factors: Key Points

- Reduction of total personal exposure to tobacco smoke, occupational dusts and chemicals, and indoor and outdoor air pollutants are important goals to prevent the onset and progression of COPD.
- Smoking cessation : Smoking cessation is a key intervention for all COPD patients who continue to smoke.

Management of Stable COPD

Reduce Risk Factors: Key Points

- Indoor and outdoor air pollution: Reducing the risk from indoor and outdoor air pollution is feasible and requires a combination of public policy, local and national resources, cultural changes, and protective steps taken by individual patients.

Management of Stable COPD

Reduce Risk Factors: Key Points

- Ocupational exposures :no studies demonstrate whether interventions that reduce occupational exposures also reduce the burden of COPD, but it seems logical to advise patients to avoid ongoing exposures to potential irritants if possible.

Treatment of Stable COPD
Pharmacotherapy

Bronchodilators

- Short-acting β_2-agonist – *Salbutamol*
- Long-acting β2-agonist - *Salmeterol and Formoterol*
- Anticholinergics – *Ipratropium, Tiiotropium*
- Methylxanthines - *Theophylline*

corticosteoids

- Inhaled corticosteoids

(*Fluticasone,Budesonide*)

- Oral glucocorticoid

(*Prednisolone*)


信必可都保
60 吸
布地奈德福莫特罗粉吸入剂
160微克/4.5微克/吸
布地奈德福莫特罗粉吸入剂
160微克/4.5微克/吸
60 吸/支
AstraZeneca, Södertälje, Sweden
160
4.5
AstraZeneca


沙美特罗替卡松粉
吸入剂
50微克/500微克
准纳器®
0063993
28吸(揿)/盒


RX
PFIZER INC.
TI 01
18 mcg
Spiriva
HandiHaler
Spiriva® HandiHaler®
(tiotropium bromide inhalation powder)


A.D.A.M.

Bronchodilators

- central to the symptomatic management of COPD
- given on an as-needed basis or on a regular basis to prevent or reduce symptoms and exacerbations
- Long-acting bronchodilators is more effective and convenient than treatment with short-acting bronchodilators

Glucocorticosteroids

Inhaled corticosteroids:

- ICS combined with LABA/LAMA is more effective in improving lung function and health status and reducing risk of exacerbations.

Oral glucocorticoids:

- Long-term use has numerous side effects with no evidence of benefits.

Therapy at Each Stage of COPD (*GOLD2006*)

I: Mild	II: Moderate	III: Severe	IV: Very Severe
▪ $FEV_1/FVC < 70\%$ ▪ $FEV_1 \geq 80\%$ predicted	▪ $FEV_1/FVC < 70\%$ ▪ $50\% \leq FEV_1 < 80\%$ predicted	▪ $FEV_1/FVC < 70\%$ ▪ $30\% \leq FEV_1 < 50\%$ predicted	▪ $FEV_1/FVC < 70\%$ ▪ $FEV_1 < 30\%$ predicted *or* $FEV_1 < 50\%$ predicted plus chronic respiratory failure

Active reduction of risk factor(s); influenza vaccination →

Add short-acting bronchodilator (when needed) →

Add regular treatment with one or more long-acting bronchodilators (when needed); ***Add*** rehabilitation

Add inhaled glucocorticosteroids if repeated exacerbations

Add long term oxygen if chronic respiratory failure. ***Consider*** surgical treatments

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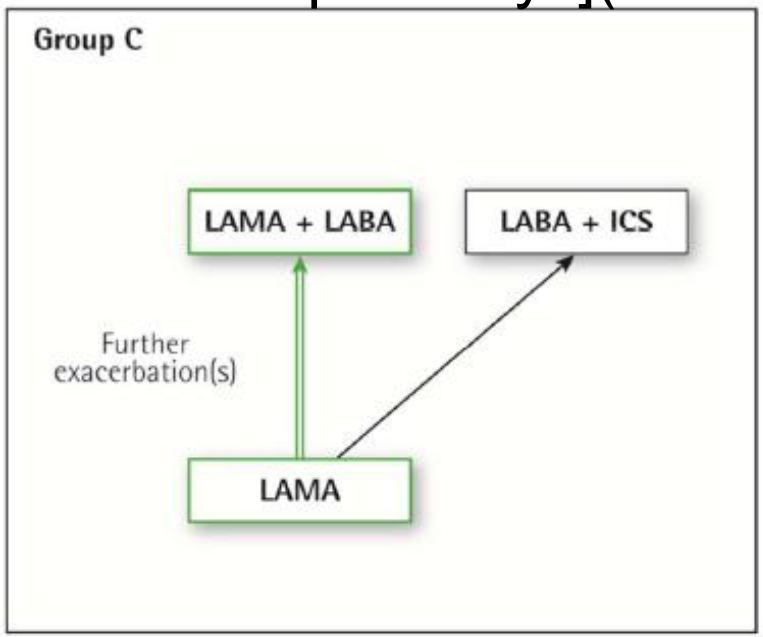
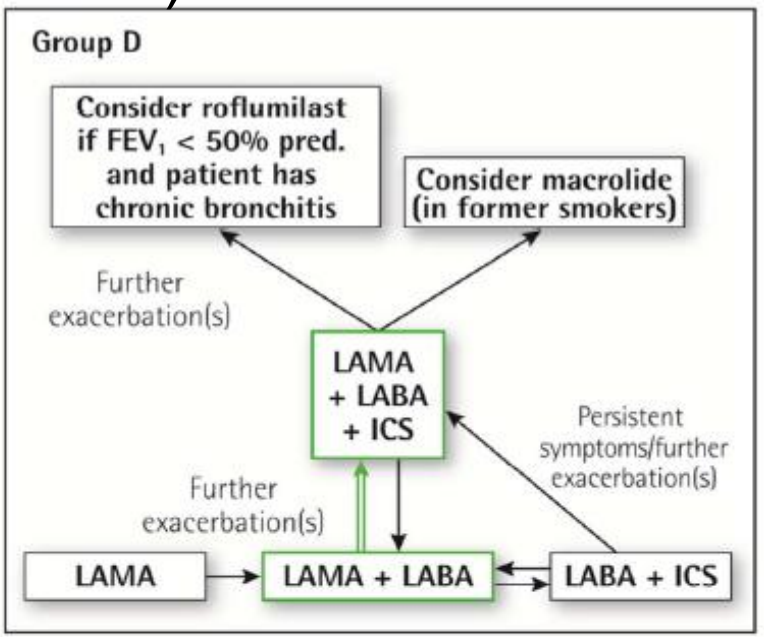
Therapy at Each Stage of COPD
(*GOLD2011*)

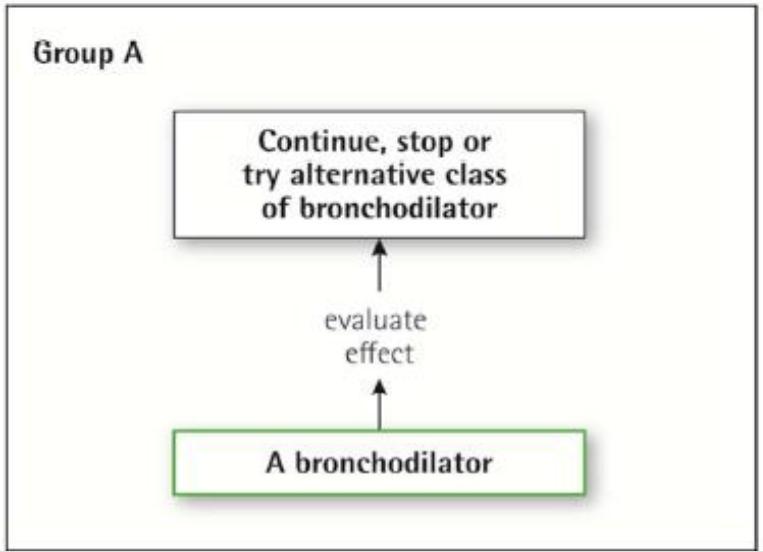
P	First choice	Second choice	Alternative choice
A	SABA /SAMA prn	LAMA/LABA or SAMA & SABA	Theophylline
B	LABA / LAMA	LAMA & LABA	SABA & /orSAMA ; Theophylline
C	ICS/LABA or LAMA	LAMA & LABA	PDE-4 inhibitors ; SABA & /orSAMA ; Theophylline
D	ICS/LABA or LAMA	ICS & LAMA ICS/LABA & LAMA ; ICS/LABA & PDE-4 inhibitors LAMA & LABA ; LAMA & PDE-4 inhibitors	Carbocisteine ; SABA & /orSAMA ; Theophylline

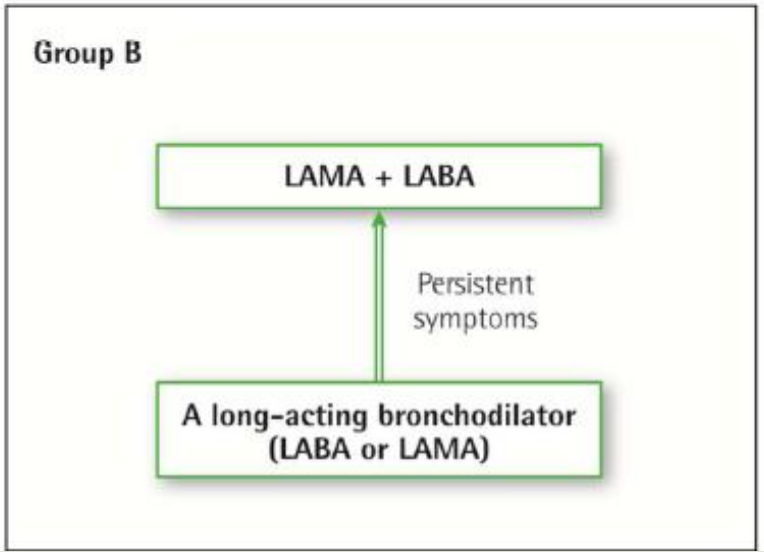
Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease Revised 2011

Pharmacologic treatment algorithms by GOLD Grade [highlighted boxes and arrows indicate preferred treatment pathways](*GOLD 2017*)

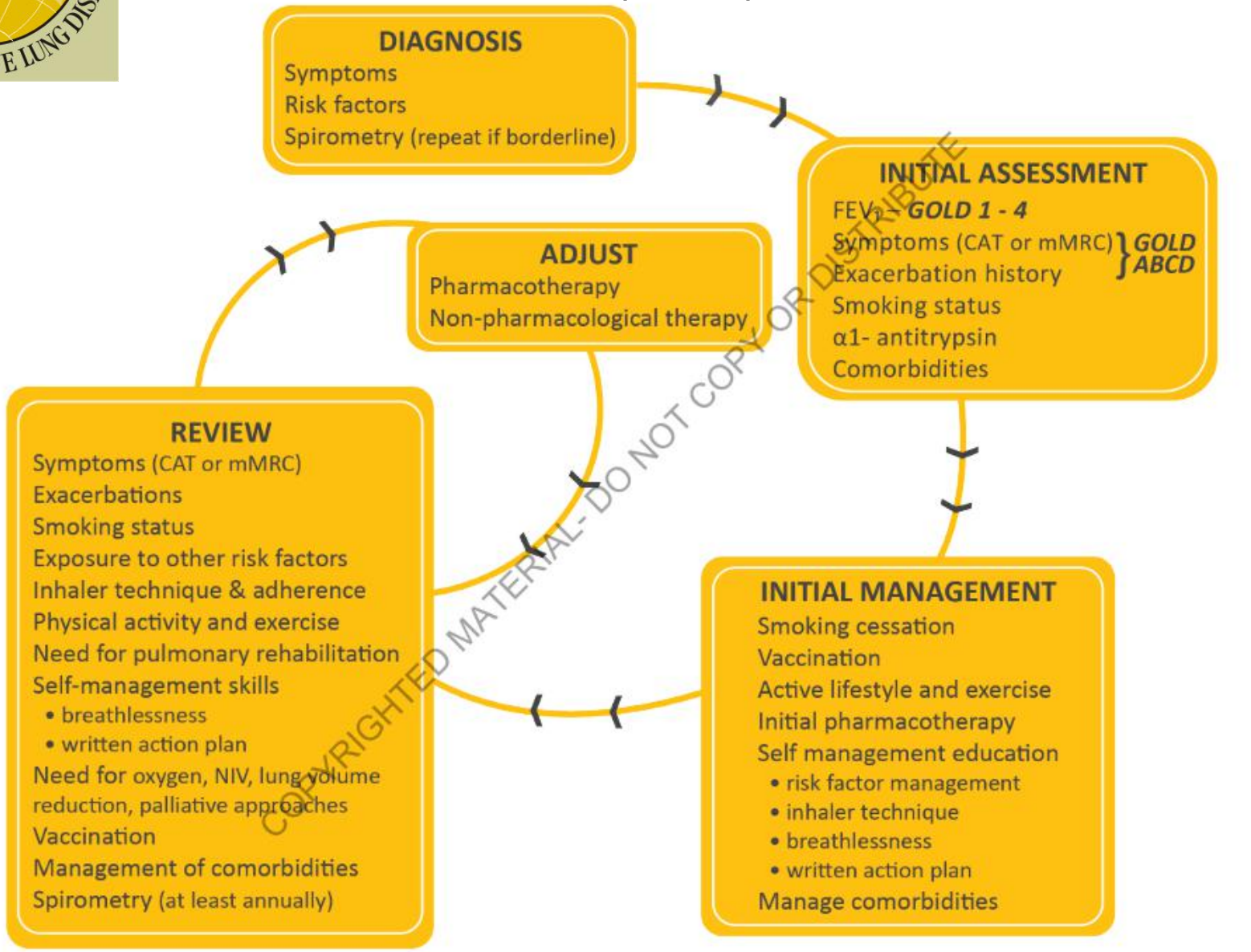








Pharmacological and non-pharmacological therapy should be adjusted as **necessary** and **further reviews** undertaken (2019)



Inhale pharmacological treatment (2020)

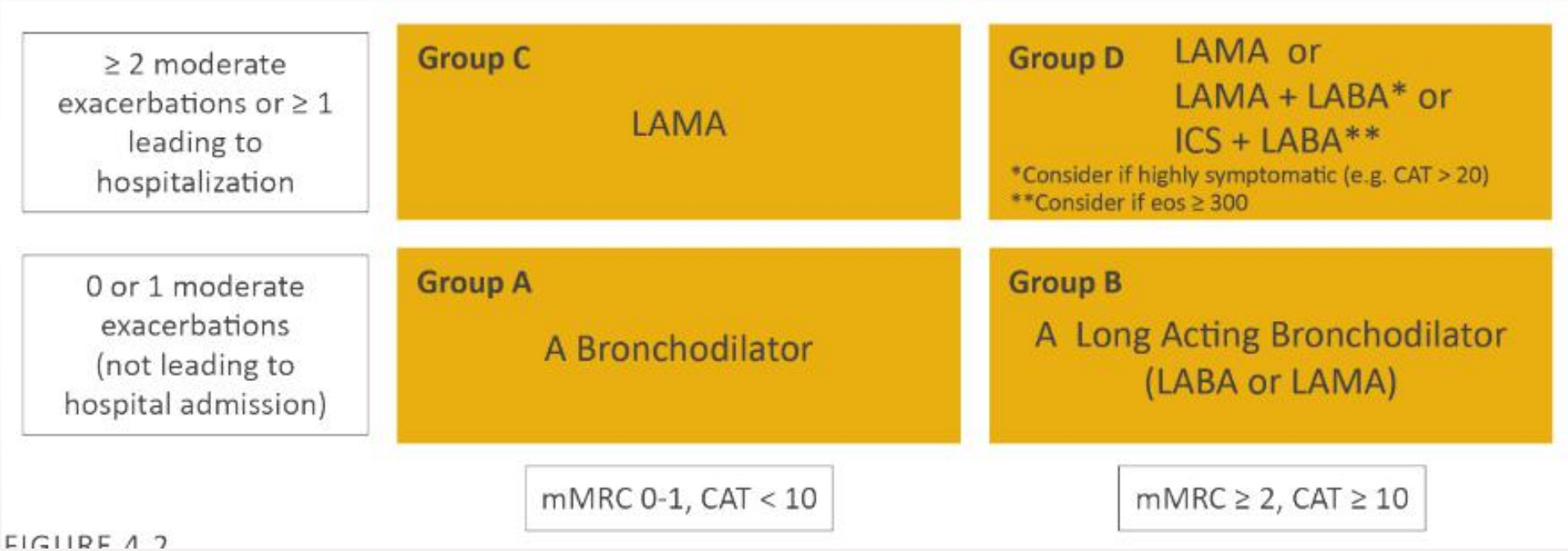


FIGURE 4.2

Treatment 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

Non-Pharmacologic Treatments

- Rehabilitation: All COPD patients benefit from exercise training programs, improving with respect to both exercise tolerance and symptoms of dyspnea and fatigue.

Non-Pharmacologic Treatments

- Education and self-management : improves health status and decreases hospitalizations and emergency department visits.

- integrative care program:integrated care and telehealth have no demonstrated benefits.

Non-Pharmacologic Treatments

- Oxygen Therapy: The long-term administration of oxygen (> 15 hours per day) to patients with chronic respiratory failure has been shown to increase survival.

Non-Pharmacologic Treatments

- Ventilatory support:NPPV may improve hospitalization-free survival in selected patients after recent hospitalization,particularly in those with pronounced daytime persistent hypercapnia ($PaCO_2 \geqq 52mmhg$).

Non-Pharmacologic Treatments

- Physical activity
- Exercise training
- Nutritional support
- Vaccination
- Ventilatory support
- Interventional bronchoscopy and surgery

Management cycle

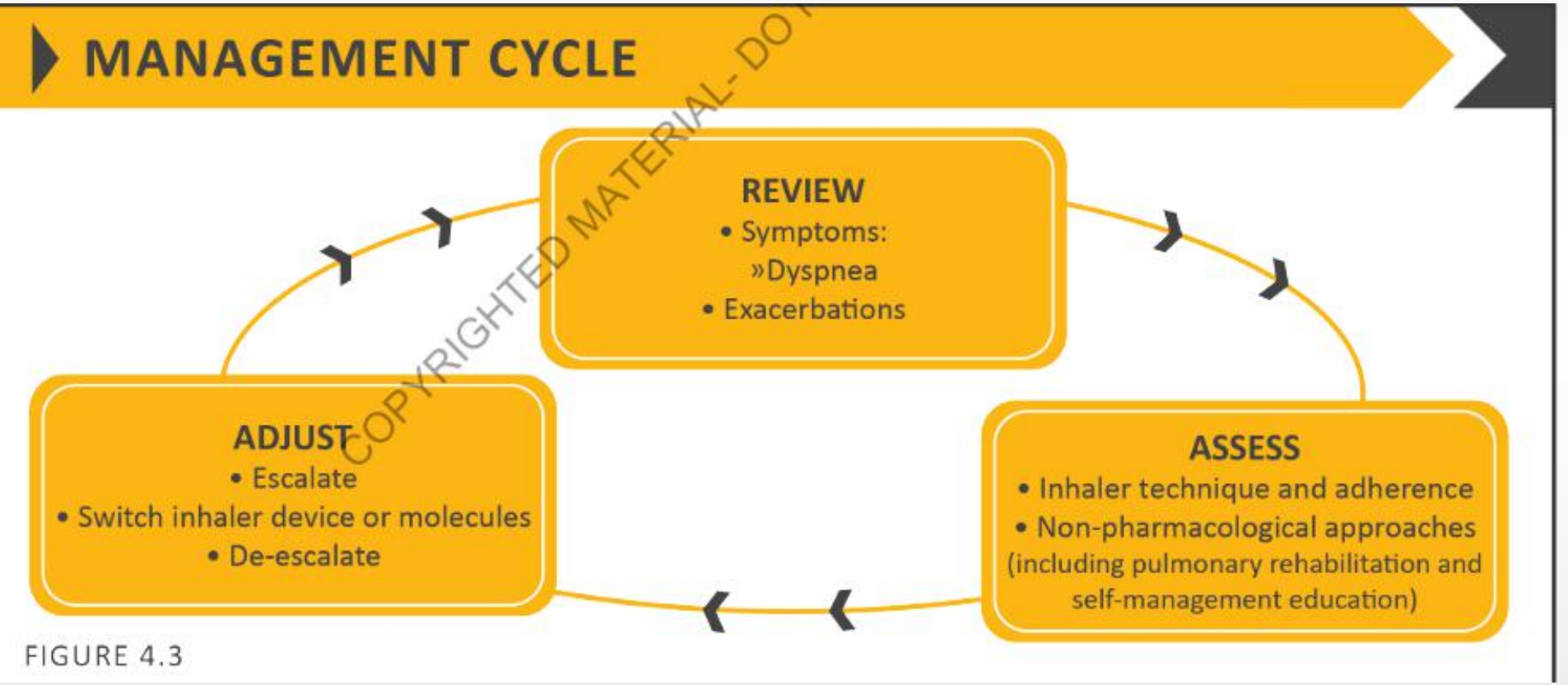
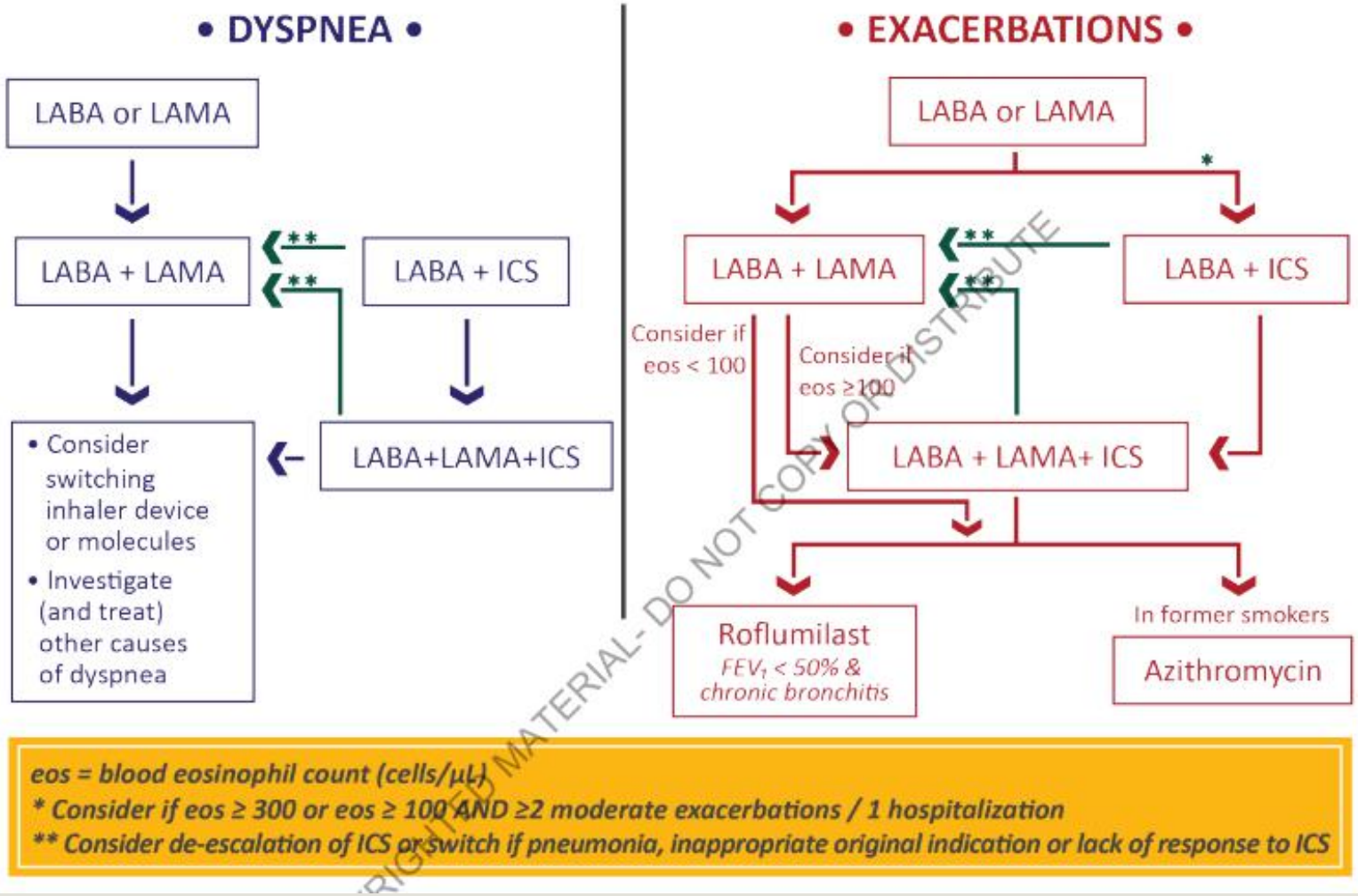


FIGURE 4.3

Follow-up pharmacological treatment (2019)

1. **IF RESPONSE TO INITIAL TREATMENT IS APPROPRIATE, MAINTAIN IT.**
2. **IF NOT:**
   - ✓ Consider the predominant treatable trait to target (dyspnea or exacerbations)
     - Use exacerbation pathway if both exacerbations and dyspnea need to be targeted
   - ✓ Place patient in box corresponding to current treatment & follow indications
   - ✓ Assess response, adjust and review
   - ✓ These recommendations do not depend on the ABCD assessment at diagnosis



eos = blood eosinophil count (cells/μL)

** Consider if eos ≥ 300 or eos ≥ 100 AND ≥2 moderate exacerbations / 1 hospitalization*

*** Consider de-escalation of ICS or switch if pneumonia, inappropriate original indication or lack of response to ICS*

Management of COPD Exacerbations

Key Points

An exacerbation of COPD is defined as:

"A change in the patient's baseline dyspnea, cough, and/or sputum that is beyond normal day-to-day variations, is acute in onset, and may warrant a change in regular medication."

Key Points

- The most common causes of an exacerbation are infection of the tracheobronchial tree and air pollution, but the cause of about one-third of severe exacerbations cannot be identified.

Key Points

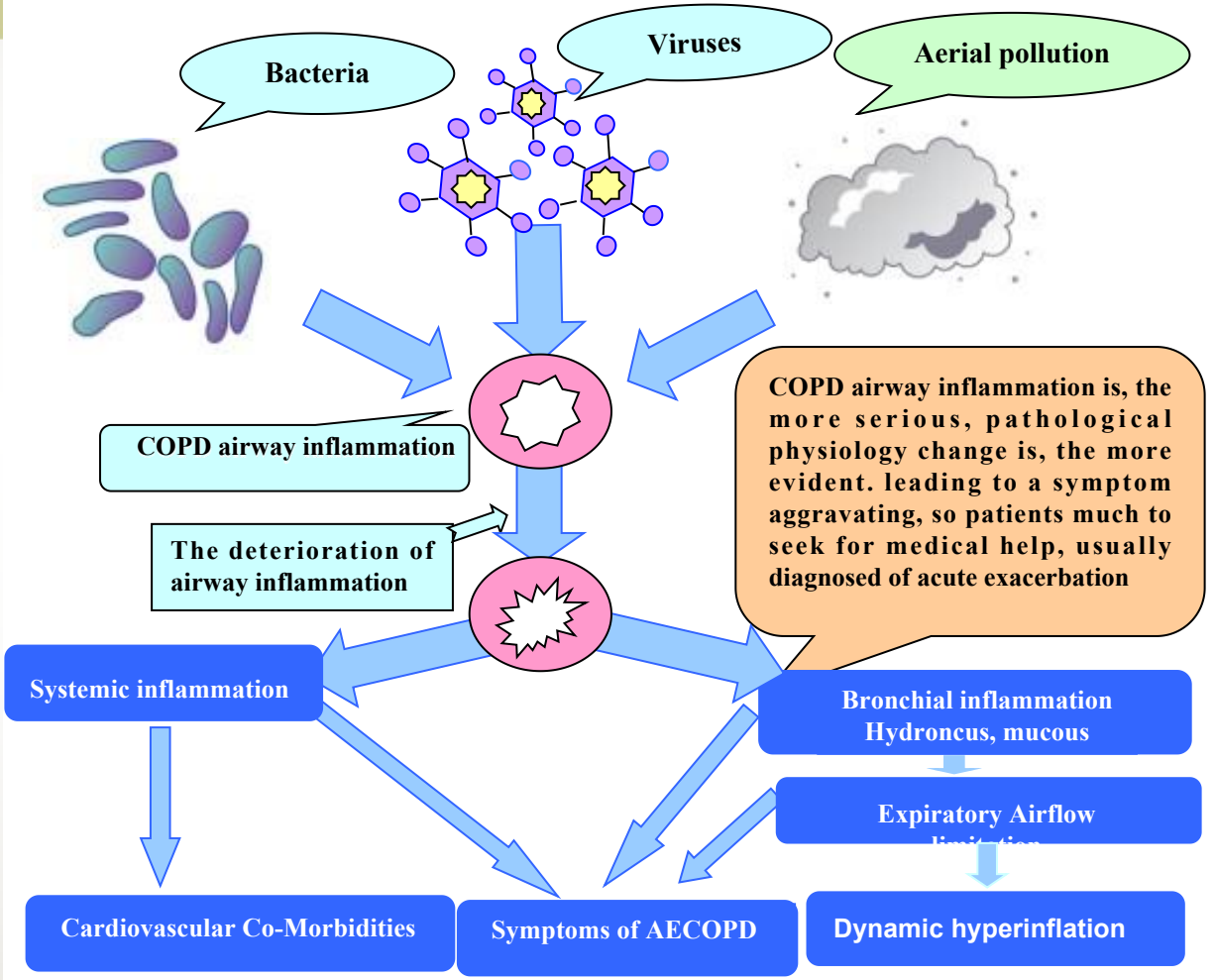
- Patients experiencing COPD exacerbations with clinical signs of airway infection (e.g. increased sputum purulence) may benefit from **antibiotic treatment**.

Key Points

- Inhaled bronchodilators (particularly inhaled $ß_2$-agonists with or without anticholinergics) and oral glucocorticosteroids are effective treatments for exacerbations of COPD.

Manage COPD Exacerbation

cause and mechanism



Wedzicha JA. Lancet 2007 ; 370 : 786-796
Antonio Anzueto. Proc Am Thorac Soc 2007 ; 4 : 554-564

Key Points

Noninvasive mechanical ventilation in exacerbations

- improves respiratory acidosis
- increases pH
- decreases the need for endotracheal intubation
- reduces $PaCO_2$, respiratory rate, severity of breathlessness, the length of hospital stay, and mortality

Key Points

- Medications and education to help prevent future exacerbations should be considered as part of follow-up, as exacerbations affect the quality of life and prognosis of patients with COPD.

Global Strategy for Diagnosis, Management and Prevention of COPD: Summary

- COPD is increasing in prevalence in many countries of the world.
- COPD is treatable and preventable.
- COPD can be prevented by avoidance of risk factors, the most notable being tobacco smoke.

Global Strategy for Diagnosis, Management and Prevention of COPD: Summary

- Patients with COPD have multiple other conditions (comorbidities) that must be taken into consideration.
- GOLD has developed a global network to raise awareness of COPD and disseminate information on diagnosis and treatment.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The End


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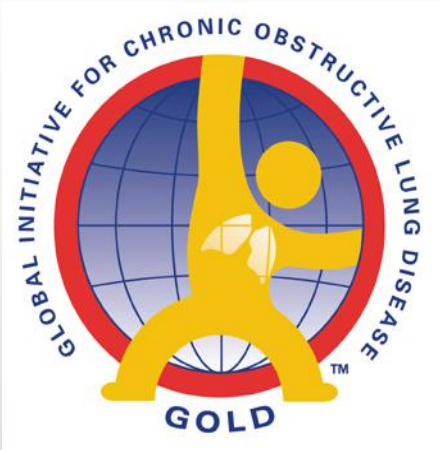
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