COPD
Common yet underdiagnosed

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Objectives

At the end of this lecture the student should known the following:

* The new GOLD definition of COPD
* The pathophysiology of COPD
* The risk factors for developing COPD
* clinical manifestation and how to mange a case with COPD
* The new GOLD classification of severity of COPD (2014)
* The new GOLD treatment guidelines for the treatment of COPD

Burden of COPD

- **The WHO estimates 1.1 billion smoker worldwide, increasing to 1.6 billion by 2025 in low&middle-income countries.**

- COPD is the 4th leading cause of death in the United States (behind heart disease, cancer, and cerebrovascular disease).
- In 2000, the WHO estimated 2.74 million deaths worldwide from COPD.
- In 1990, COPD was ranked 12th as a burden of disease; by 2020 it is projected to rank 5th.

67 Year old Male with shortness Of Breath with exertion

Your patient is a 67 year old male who complains of progressively worsening shortness of breath with exertion over the last year. He currently smokes half a pack of cigarettes daily and has accumulated 45 pack years. He uses a short acting beta agonist 3-4 times a day with limited relief. He is no longer able to ride a bike with his grandchildren.
His last hospitalization was 4 months ago secondary to right lower lobe pneumonia. He does not complain of weight loss or loss of appetite.
He has a past medical history of dietary controlled diabetes and mild osteoarthtitis.
Medications include Albuterol and Celecoxib.
On exam respiratory rate is 22 per minute; chest exam reveals mild end expiratory wheezing without use of accessory muscles of respiration and no retractions. No clubbing, cyanosis or lower extremity edema is noted. Spirometry reveals an FVC of 78% predicted, FEV1 of 62% predicted and FEV1/FVC of 68%, post bronchodilator.

Leading causes of death in the USA, 1998	Number
Heart disease	724,269
Cancer	538,947
Cerebrovascular disease (stroke)	158,060
Respiratory diseases (COPD)	**114,381**
Accidents	94,828
Pneumonia and influenza	93,207
Diabetes	64,574
Suicide	29,264
Nephritis	26,265
Chronic liver disease	24,936
All other causes of death	469,314


A TIP FROM A
FORMER
SMOKER
COPD MAKES
IT HARDER
AND HARDER
TO BREATHE.
You can quit. Call 1-800-QUIT-NOW.
CDC

Definition

Chronic Obstructive Pulmonary Disease (COPD) is a preventable and treatable disease with some significant extrapulmonary effects that may contribute to the severity in individual patients. Its pulmonary component is 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.

This definition *does not* use the terms chronic bronchitis and emphysema and excludes asthma (reversible airflow limitation).

- Airflow obstruction is defined as reduced FEV_1/FVC ratio (< 0.7)
- It is no longer necessary to have an FEV_1 < 80% predicted for definition of airflow obstruction
- If FEV_1 is ≥ 80% predicted, a diagnosis of COPD should only be made in the presence of respiratory symptoms, for example breathlessness or cough
- COPD produces symptoms, disability and impaired quality of life which may respond to pharmacological and other therapies that have limited or no impact on the airflow obstruction.

Mechanisms Underlying Airflow Limitation in COPD

Small Airways Disease

- Airway inflammation
- Airway fibrosis, luminal plugs
- Increased airway resistance

Parenchymal Destruction

- Loss of alveolar attachments
- Decrease of elastic recoil

AIRFLOW LIMITATION

Chronic bronchitis

Defined as the presence of cough and sputum production for at least 3 months in each of 2 consecutive years, is not necessarily associated with airflow limitation.

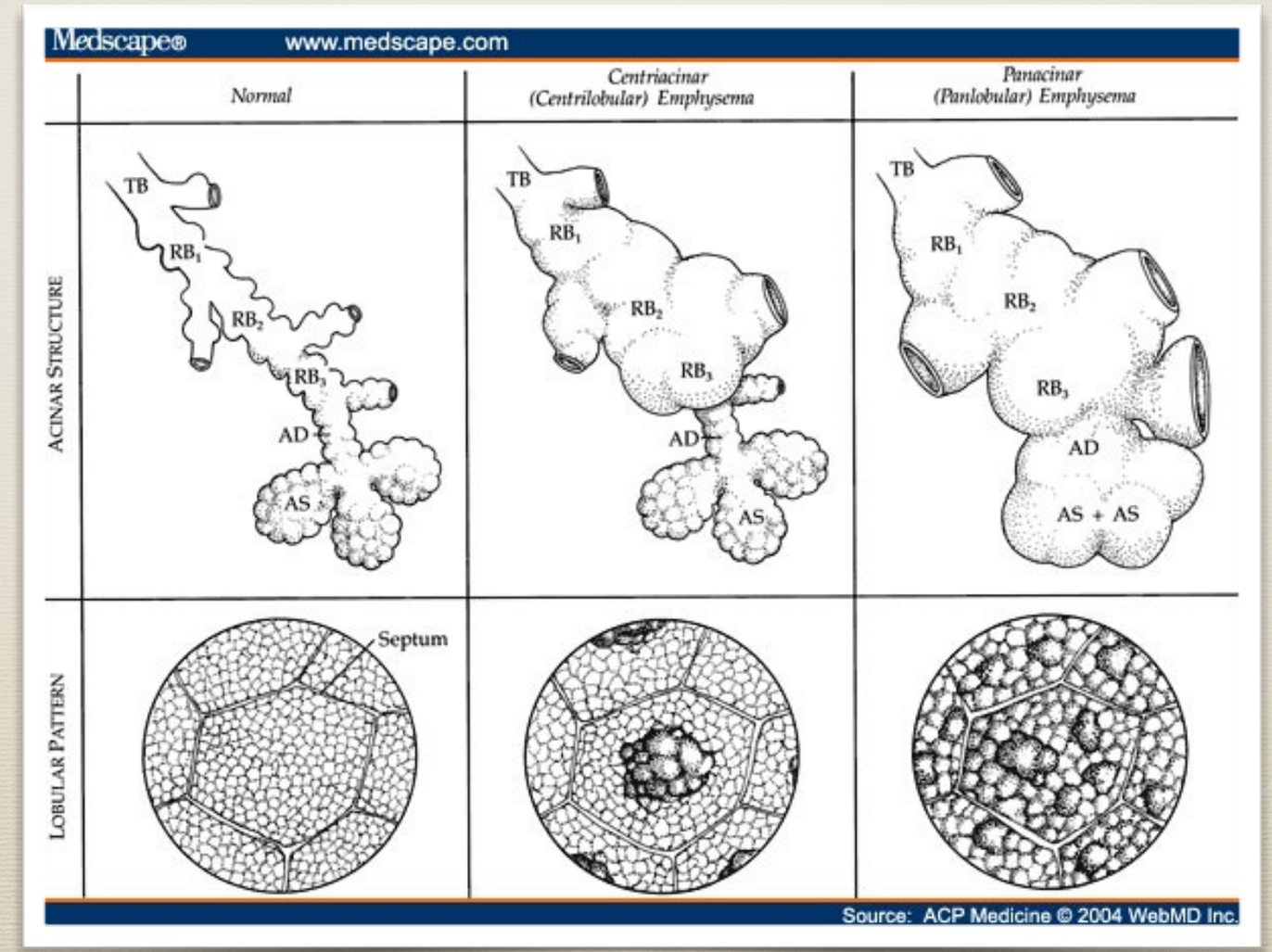
Emphysema

Defined as destruction of the alveoli, is a pathological term that is sometimes (incorrectly) used clinically.

Emphysema

- Abnormal permanent enlargement of the air space distal to the terminal bronchioles

- Accompanied by destruction of bronchioles



Diagnosis Of COPD

Indicators for considering the diagnosis of COPD	
Chronic cough	Present intermittently or every day, often present throughout the day
Chronic sputum production	Any pattern of sputum production may indicate COPD
Acute bronchitis	Repeated episodes
Dyspnea that is	Progressive, persistent, worse on exercise, worse during respiratory infections
History of exposure to risk factors	Smoke, biomass fuel, occupational dusts

The diagnosis should be confirmed by Spirometry

- COPD is predominantly caused by smoking and is characterised by airflow obstruction that:
  - is not fully reversible
  - does not change markedly over several months
  - is usually progressive in the long term
- Exacerbations often occur, where there is a rapid and sustained worsening of symptoms beyond normal day-to-day variations requiring a change in treatment

Risk Factors for COPD

* Genes
* 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

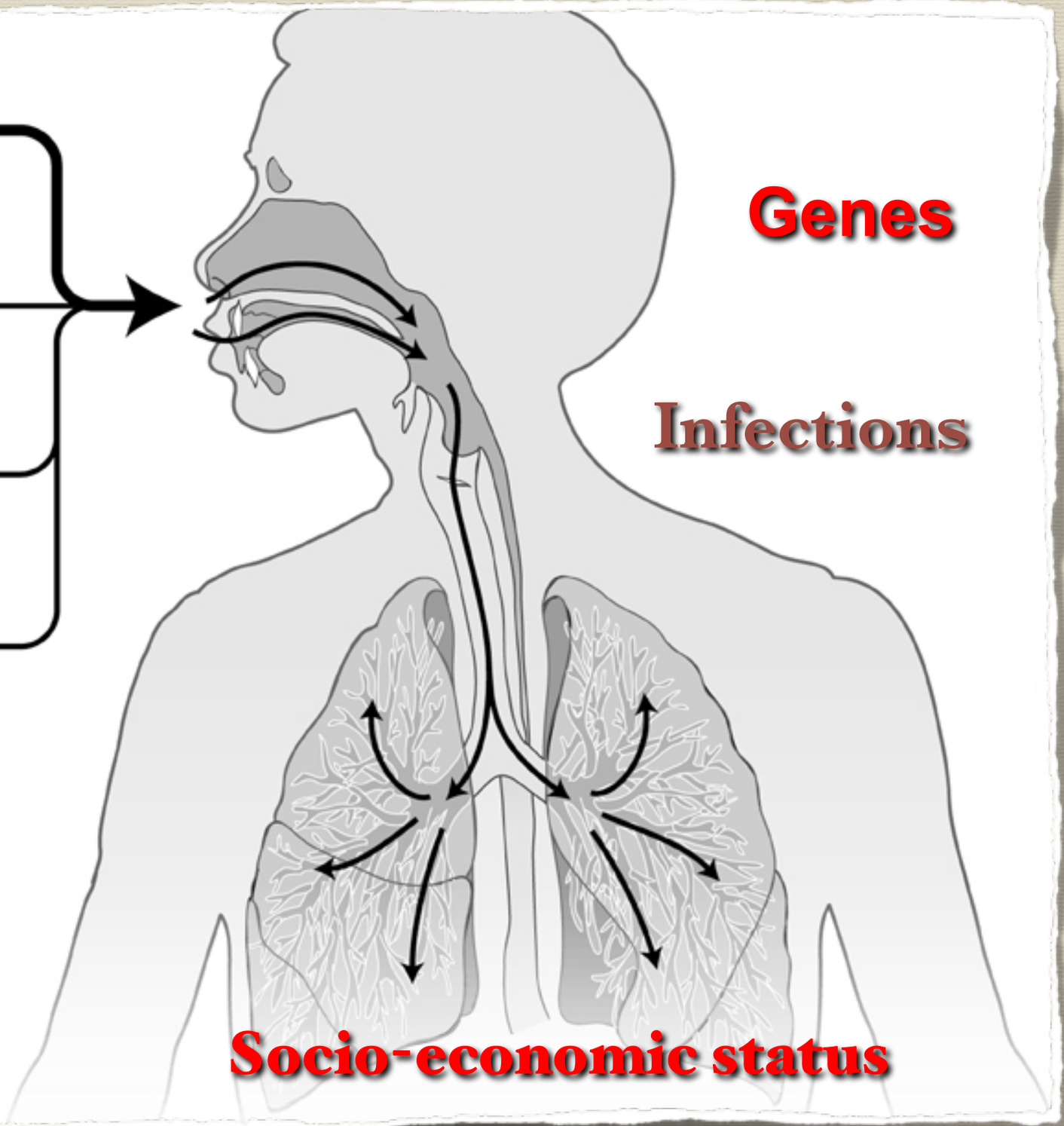
* Lung growth and development
* Gender
* Age
* Respiratory infections
* Socioeconomic status
* Asthma/Bronchial hyperreactivity
* Chronic Bronchitis

Cigarette smoke

Occupational dust and chemicals

Environmental tobacco smoke (ETS)

Indoor and outdoor air pollution



Genes

Infections

Aging Populations

Socio-economic status

Risk factors

- **Cigarette smoking**
  - **Primary cause of COPD*****
  - **Clinically significant airway obstruction develops in 15% of smokers**
  - **80% to 90% of COPD deaths are related to tobacco smoking**
  - **> 1 in 5 deaths is result of cigarette smoking**

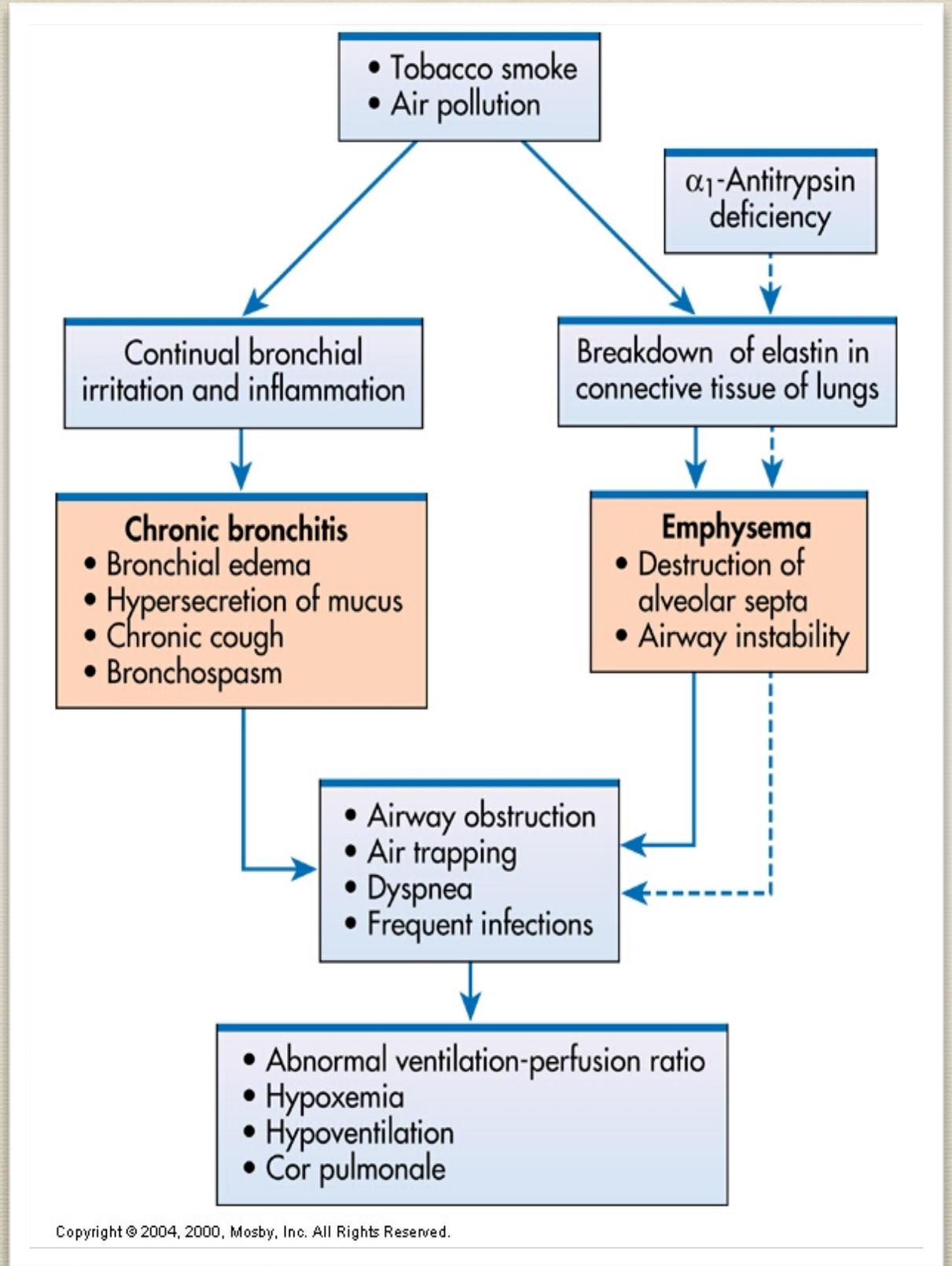
- **Cigarette smoking**
  - **Nicotine stimulates sympathetic nervous system resulting in:**
    - **↑ HR**
    - **Peripheral vasoconstriction**
    - **↑ BP and cardiac workload**

- Cigarette smoking
  - Compounds problems in a person with CAD
  - ↓ Ciliary activity
  - Possible loss of ciliated cells
  - Abnormal dilation of the distal air space
  - Alveolar wall destruction
  - Carbon monoxide
    - ↓ O_2 carrying capacity
    - Impairs psychomotor performance and judgment
  - Cellular hyperplasia
    - Production of mucus
    - Reduction in airway diameter
    - Increased difficulty in clearing secretions

Risk factor

- **Secondhand smoke exposure associated with:**
  - ↓ Pulmonary function
  - ↑ Risk of lung cancer
  - ↑ Mortality rates from ischemic heart disease
- **Infection**
  - Major contributing factor to the aggravation and progression of COPD
- **Heredity**
  - α-Antitrypsin (AAT) deficiency (produced by liver and found in lungs); accounts for < 1% of COPD cases
    - Emphysema results from lysis of lung tissues by proteolytic enzymes from neutrophils and macrophages

Pathophysiology of Chronic Bronchitis and Emphysema



Emphysema
Pathophysiology

- **Hyperinflation of alveoli**
- **Destruction of alveolar walls**
- **Destruction of alveolar capillary walls**
- **Narrowed airways**
- **Loss of lung elasticity**

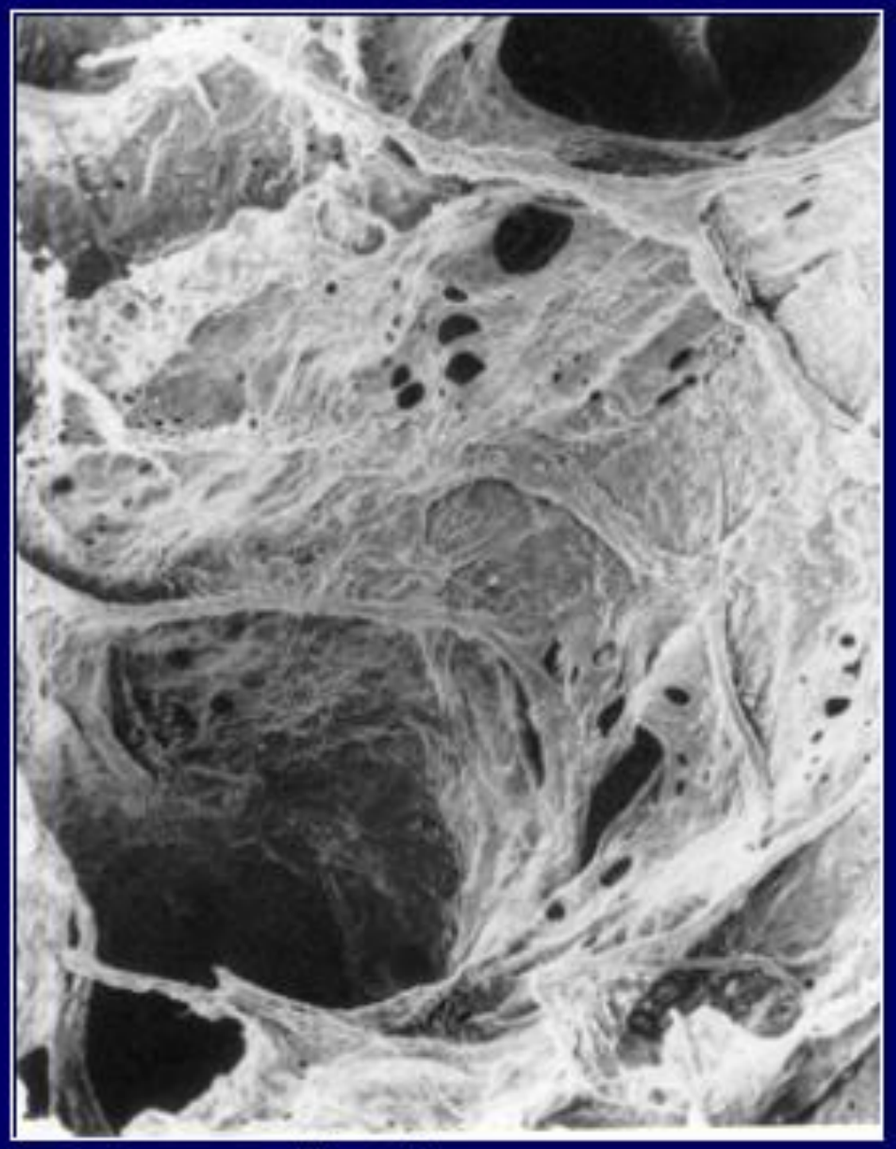
- **Two types:**
  - **Centrilobular (central part of lobule)**
    - Most common
  - **Panlobular (destruction of whole lobule)**
    - Usually associated with AAT deficiency

Emphysema
Pathophysiology

- **Small bronchioles become obstructed as a result of**
  - **Mucus**
  - **Smooth muscle spasm**
  - **Inflammatory process**
  - **Collapse of bronchiolar walls**
- **Recurrent infections → production/ stimulation of neutrophils and macrophages → release proteolytic enzymes → alveolar destruction → inflammation, exudate, and edema**

Alveolar Destruction With Emphysema

Normal



Emphysema

Nagai A, Thurlbeck WM. Scanning electron microscopic observations of emphysema in humans. A descriptive study. *Am Rev Respir Dis.* 1991;144:901-908. Official Journal Of The American Thoracic Society American Lung Association.
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Emphysema
Pathophysiology

- Elastin and collagen are destroyed
- Air goes into the lungs but is unable to come out on its own and remains in the lung
  - Causes bronchioles to collapse

- Trapped air → hyperinflation and overdistention
- As more alveoli coalesce, blebs and bullae may develop
- Destruction of alveolar walls and capillaries → reduced surface area for O_2 diffusion
- Compensation is done by increasing respiratory rate to increase alveolar ventilation
- Hypoxemia usually develops late in disease

Chronic bronchitis Pathophysiology

Pathologic lung changes are:

- **Hyperplasia of mucus-secreting glands in trachea and bronchi**
- **Increase in goblet cells**
- **Disappearance of cilia**
- **Chronic inflammatory changes and narrrowing of small airways**
- **Altered function of alveolar macrophages → infections**

- **Greater resistance to airflow increases work of breathing**

- **Hypoxemia and hypercapnia develop more frequently in chronic bronchitis than emphysema**

Chronic bronchitis Pathophysiology

Chronic inflammation

- **Primary pathologic mechanism causing changes**
- **Narrow airway lumen and reduced airflow d/t**
  - hyperplasia of mucus glands
  - Inflammatory swelling
  - Excess, thick mucus

- **Bronchioles are clogged with mucus and pose a physical barrier to ventilation**
- **Hypoxemia and hypercapnia d/t lack of ventilation and O_2 diffusion**
- **Tendency to hypoventilate and retain CO_2**
- **Frequently patients require O_2 both at rest and during exercise**

Damaging cycle of COPD

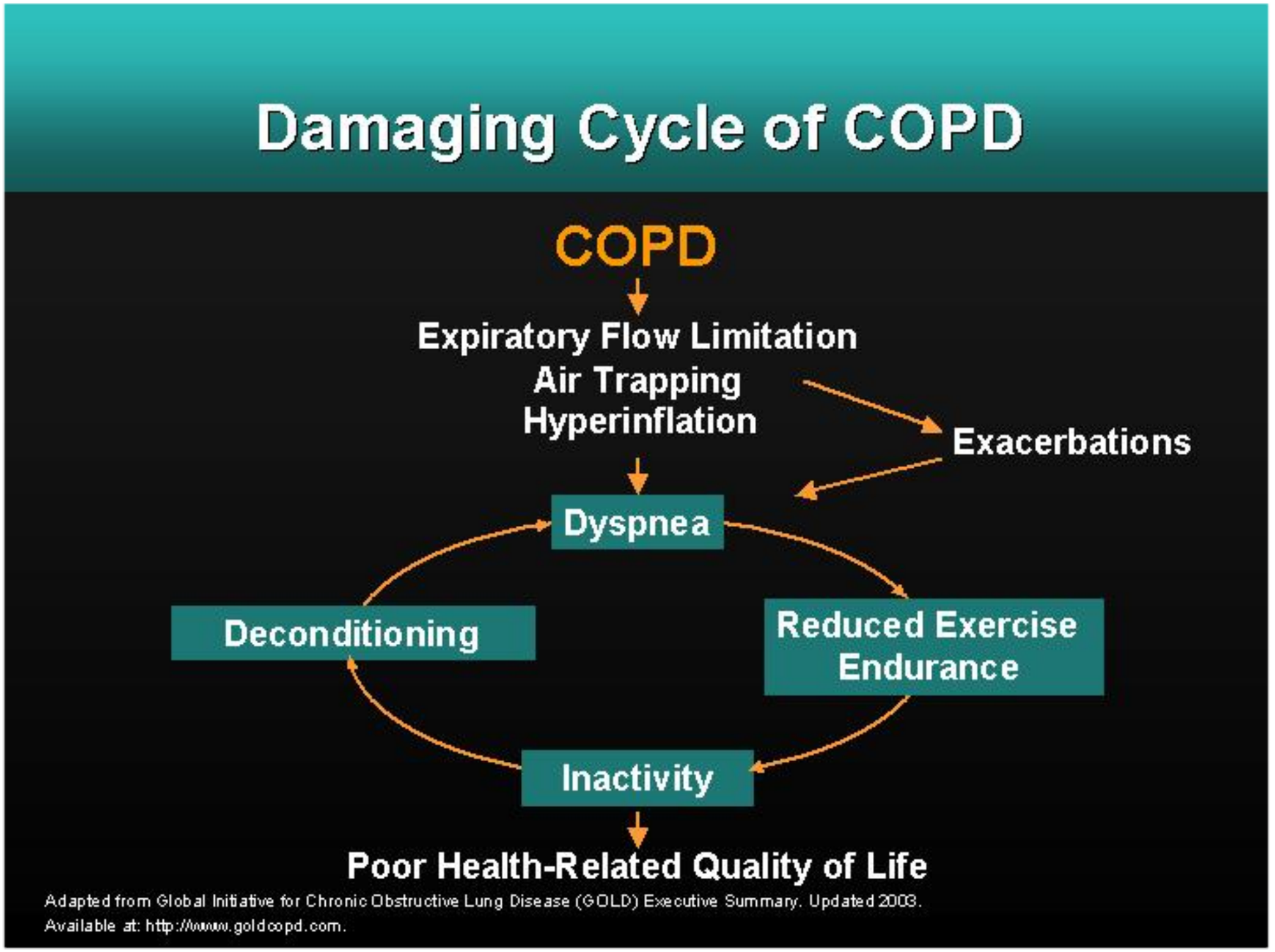
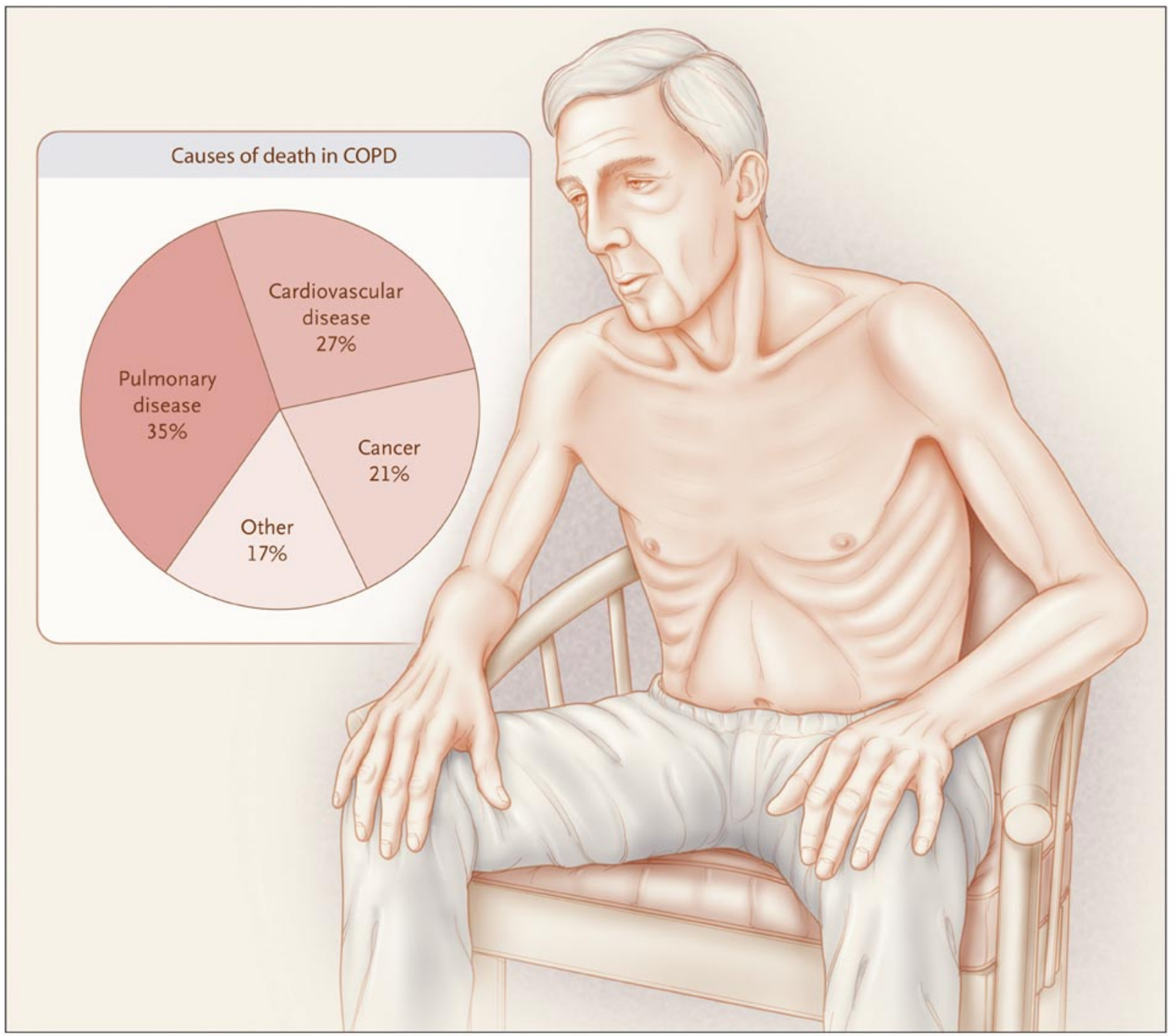


Figure 1: Key Indicators for Considering a COPD Diagnosis

Consider COPD, and perform spirometry, if any of these indicators are present in an individual over age 40. These indicators are not diagnostic themselves, but the presence of multiple key indicators increases the probability of a diagnosis of COPD.

- **Dyspnea** that is: Progressive (worsens over time).
  Usually worse with exercise.
  Persistent (present every day).
  Described by the patient as an "increased effort to breathe," "heaviness," "air hunger," or "gasping."
- **Chronic cough:** May be intermittent and may be unproductive.
- **Chronic sputum production:**
  Any pattern of chronic sputum production may indicate COPD.
- **History of exposure to risk factors:**
  Tobacco smoke (including popular local preparations).
  Occupational dusts and chemicals.
  Smoke from home cooking and heating fuel.

Causes of death in COPD patients

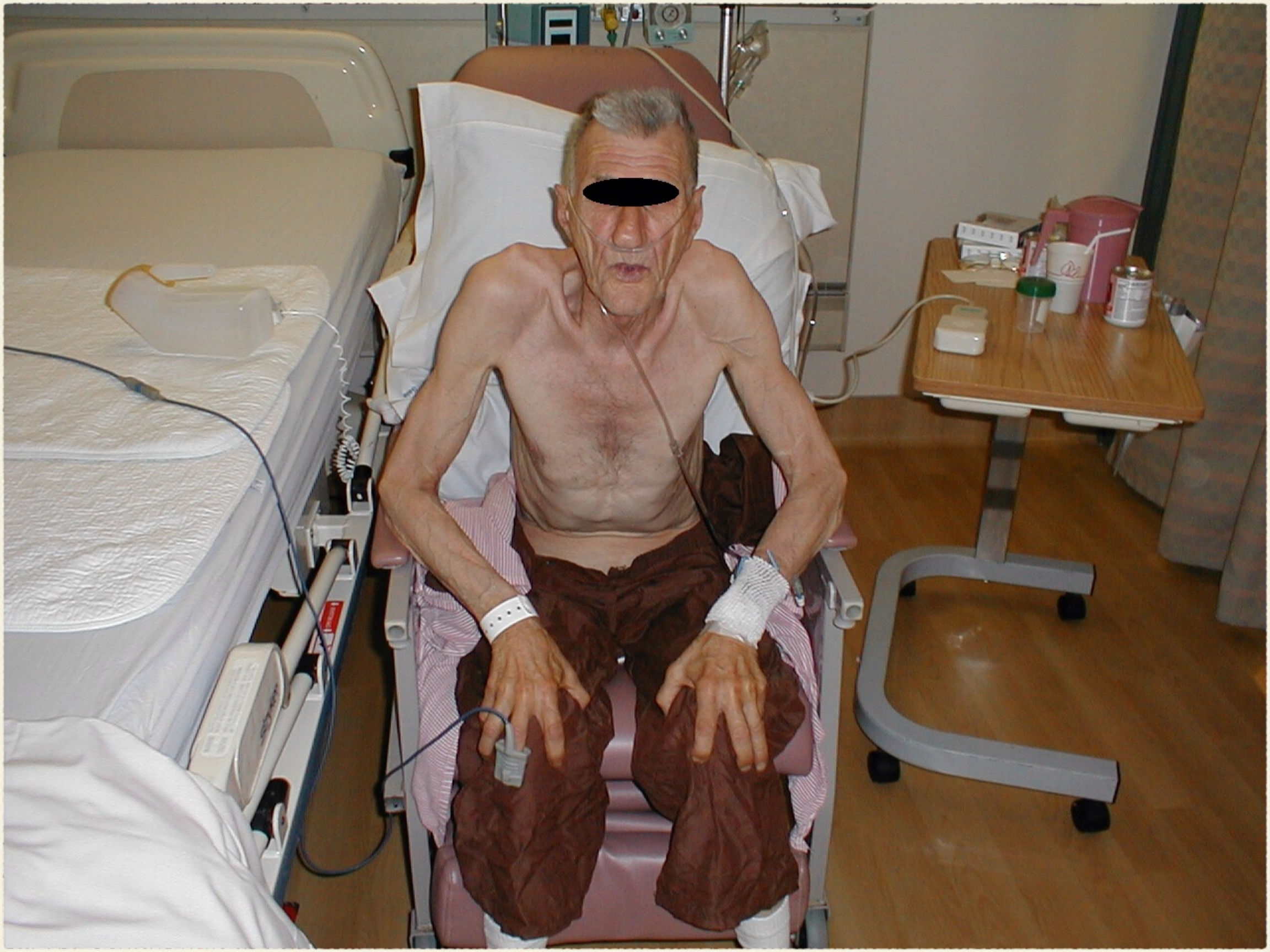


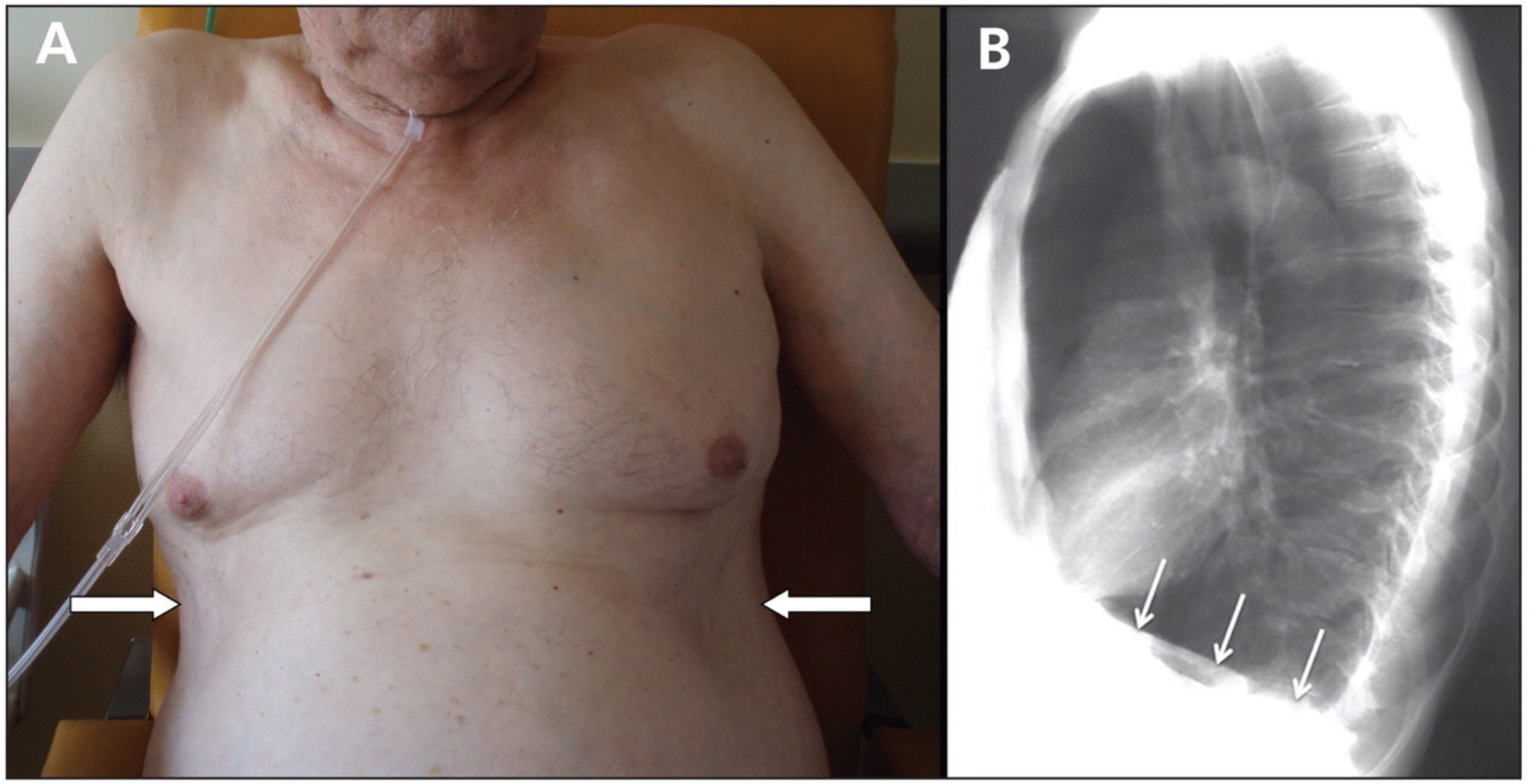
Emphysema
Clinical Manifestations

- **Dyspnea**
  - **Progresses in severity**
  - **Patient will first complain of dyspnea on exertion and progress to interfering with ADLs and rest**
- **Minimal coughing with no to small amounts of sputum**
- **Overdistention of alveoli causes diaphragm to flatten and AP diameter to increase**
- **Patient becomes chest breather, relying on accessory muscles**
  - **Ribs become fixed in inspiratory position**
- **Patient is underweight (despite adequate calorie intake)**

Chronic Bronchitis
Clinical Manifestations

- **Earliest symptoms:**
  - **Frequent, productive cough during winter**
  - **Frequent respiratory infections**
- **Bronchospasm at end of paroxysms of coughing**
- **Cough**
- **Dyspnea on exertion**
- **History of smoking**
- **Normal weight or overweight**
- **Ruddy (bluish-red) appearance d/t**
  - **polycythemia (increased Hgb d/t chronic hypoxemia)**
  - **cyanosis**
- **Hypoxemia and hypercapnia**
  - **Results from hypoventilation and ↑ airway resistance + problems with alveolar gas exchange**

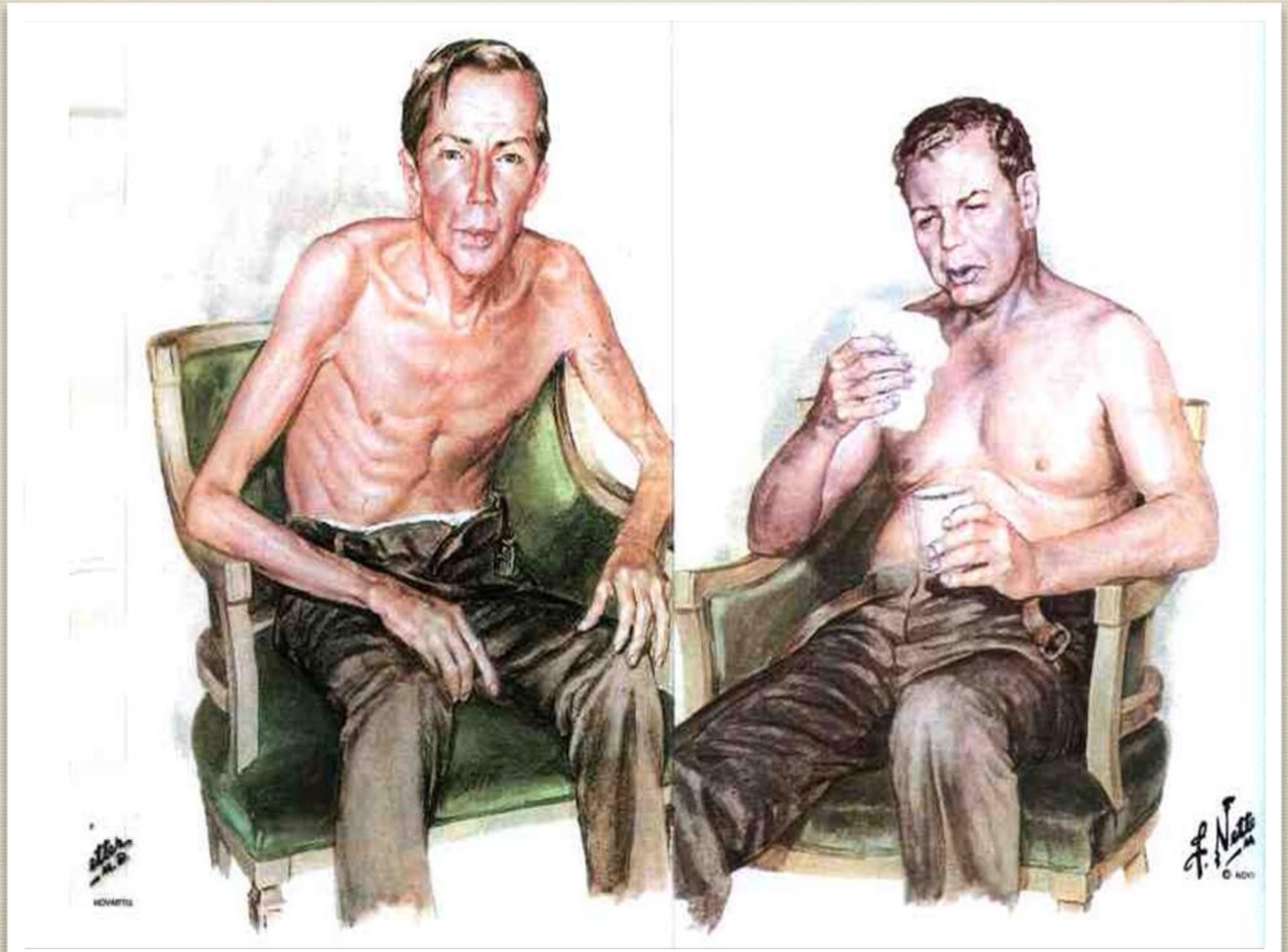




This case for A 70-year-old man with a 70 pack-year history of smoking was referred to the emergency department for an exacerbation of chronic obstructive pulmonary disease (COPD).

On examination, he breathed through pursed lips and had paradoxical indrawing of the lower rib cage margin with inspiration (**Hoover** sign),A chest radiograph showed distension of the lungs and flattening of the diaphragm.

Pink puffer vs Blue blotter



Cigarette advertising makes smoking look cool and cowboys look stupid!

Pathogenesis

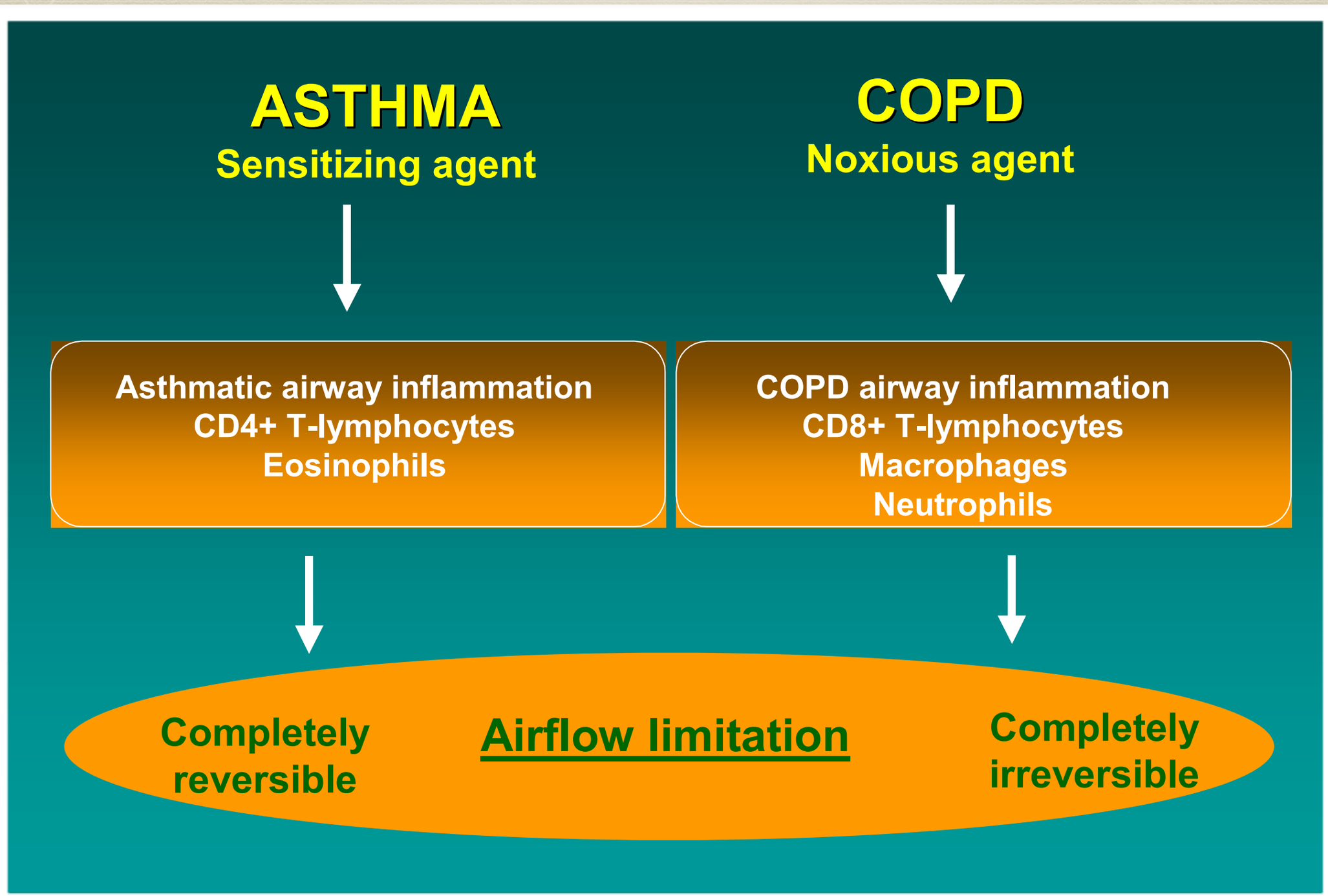
NOXIOUS AGENT
(tobacco smoke, pollutants, occupational agent)

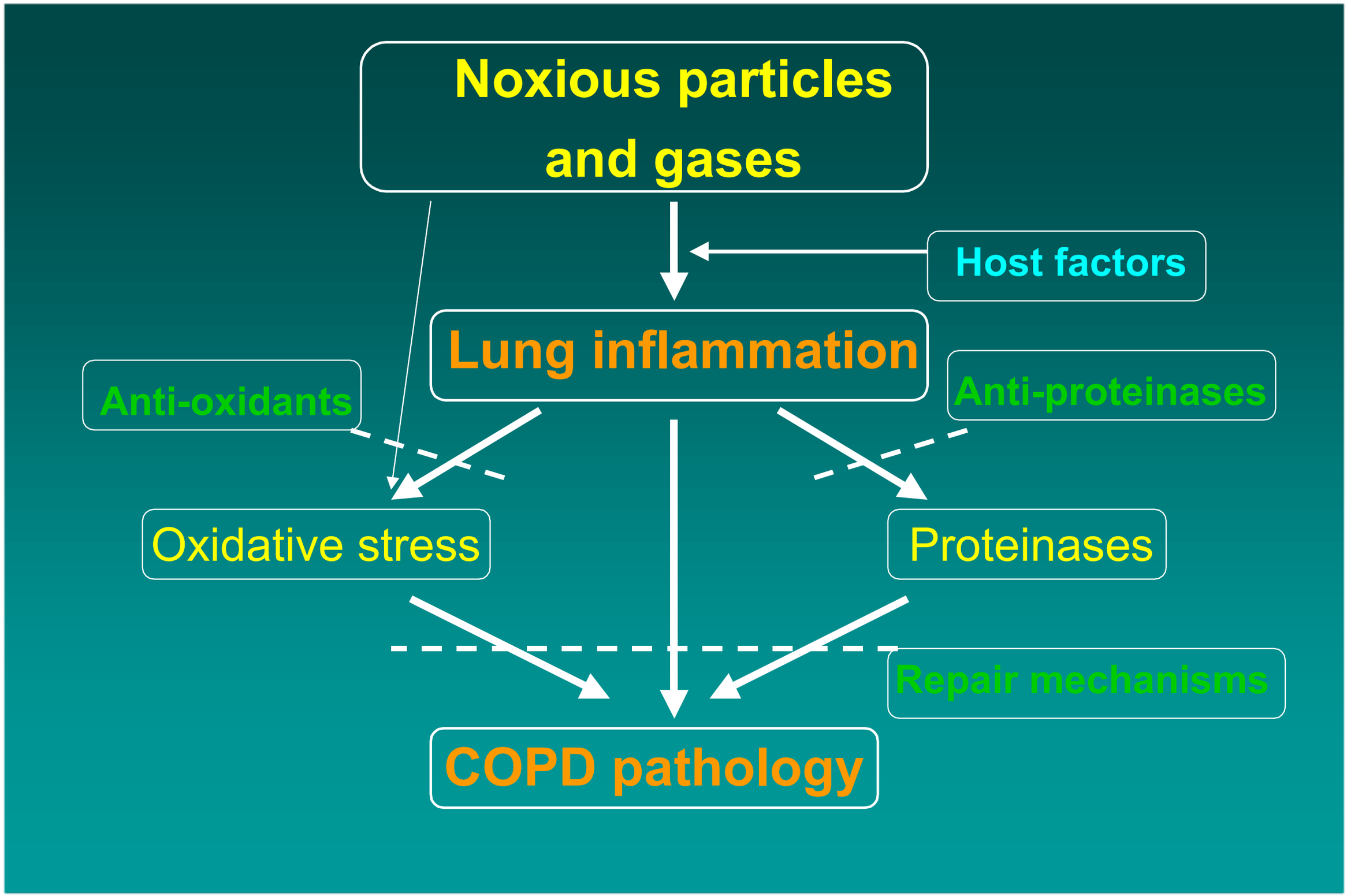
Genetic factors

Respiratory infection

Other

COPD


ASTHMA
Sensitizing agent
COPD
Noxious agent
Asthmatic airway inflammation
CD4+ T-lymphocytes
Eosinophils
COPD airway inflammation
CD8+ T-lymphocytes
Macrophages
Neutrophils
Completely reversible
Airflow limitation
Completely irreversible


Noxious particles and gases
Host factors
Lung inflammation
Anti-oxidants
Anti-proteinases
Oxidative stress
Proteinases
Repair mechanisms
COPD pathology

Diagnosis and Assessment: Key Points

- A clinical diagnosis of COPD should be considered in any patient who has dyspnea, chronic cough or sputum production, and a history of exposure to risk factors for the disease.
- Spirometry is required to make the diagnosis; the presence of a post-bronchodilator $FEV_1/FVC < 0.70$ confirms the presence of persistent airflow limitation and thus of COPD.

Diagnosis

- The goals of COPD assessment are to determine the severity of the disease, including the severity of airflow limitation, the impact on the patient's health status, and the risk of future events.
- Comorbidities occur frequently in COPD patients, and should be actively looked for and treated appropriately if present.

SYMPTOMS
shortness of breath
chronic cough
sputum

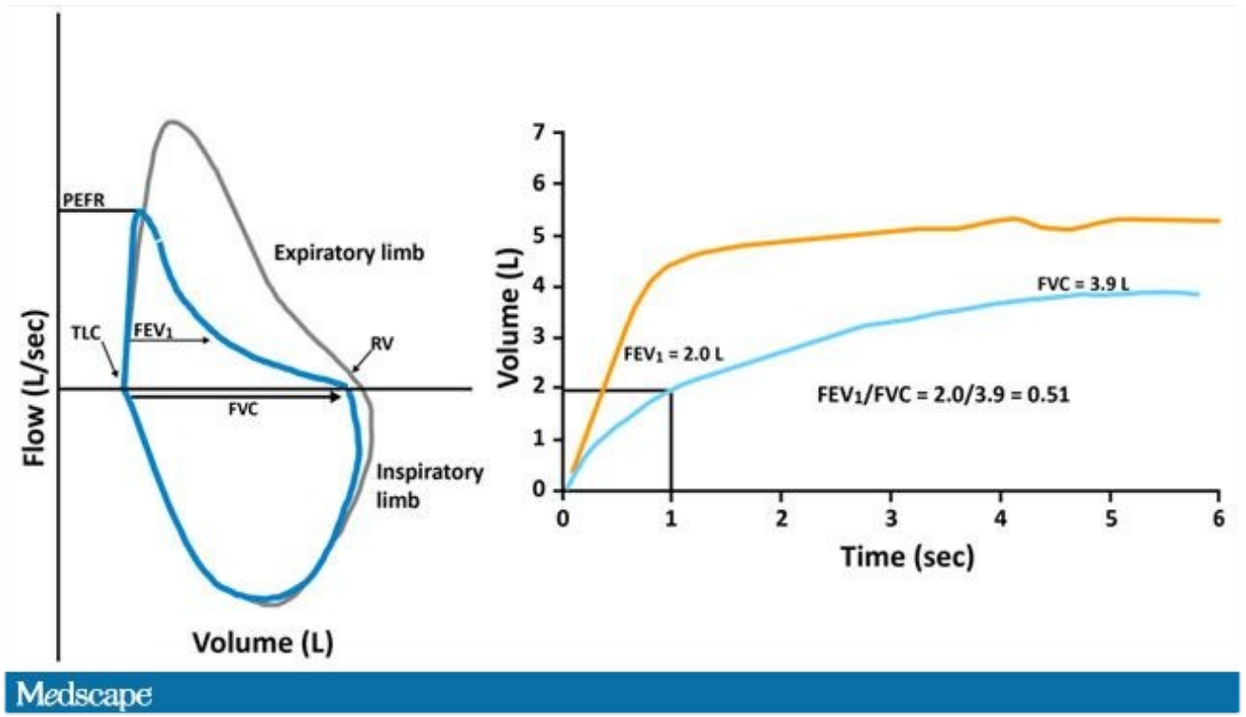
EXPOSURE TO RISK FACTORS
tobacco
occupation
indoor/outdoor pollution

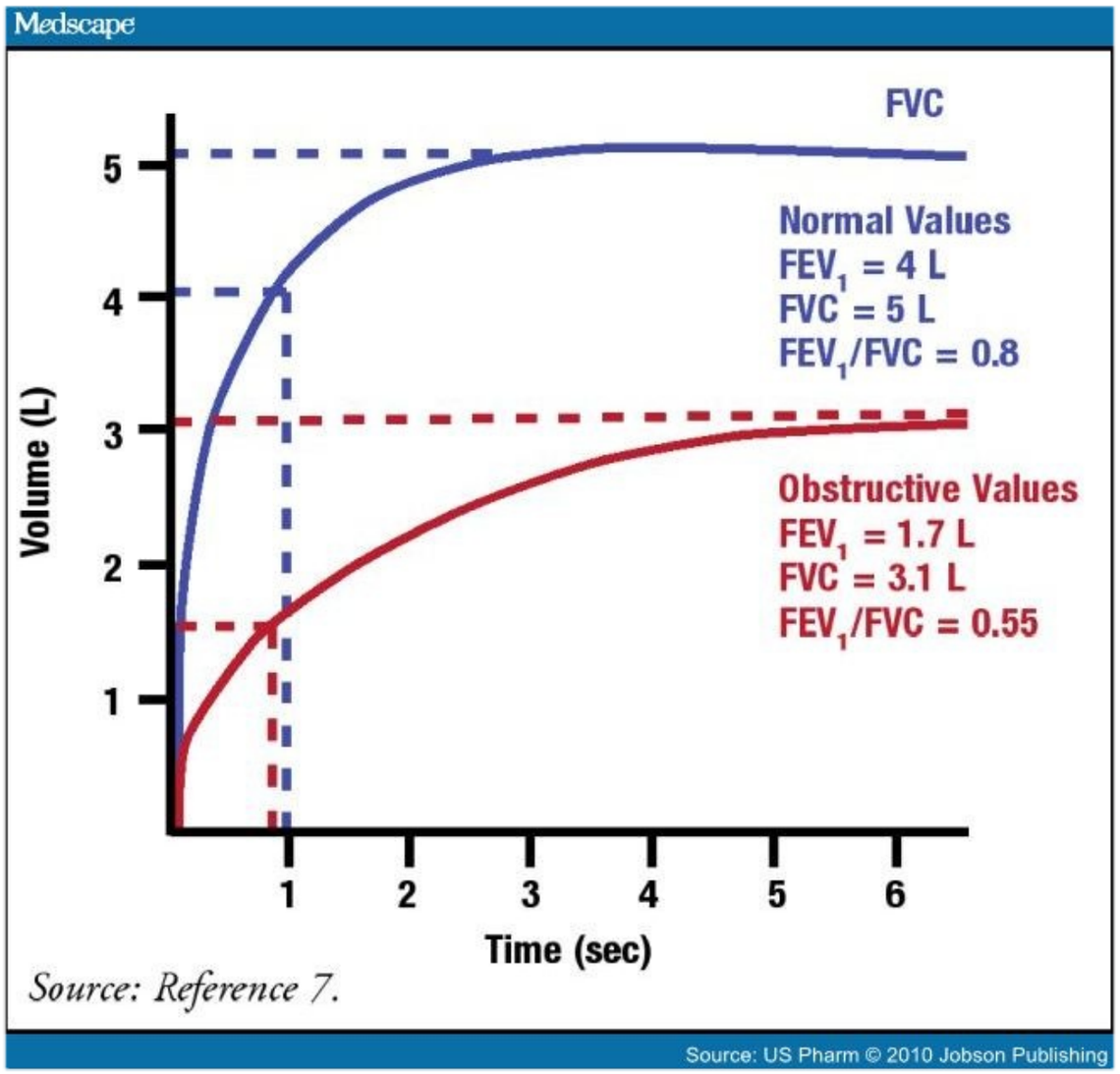
SPIROMETRY
Required to establish diagnosis

Assessment of Airflow Limitation: Spirometry

- Spirometry should be performed after the administration of an adequate dose of a short-acting inhaled bronchodilator to minimize variability.
- A post-bronchodilator $FEV_1/FVC < 0.70$ confirms the presence of airflow limitation.
- Where possible, values should be compared to age-related normal values to avoid overdiagnosis of COPD in the elderly.

Spirometry in COPD

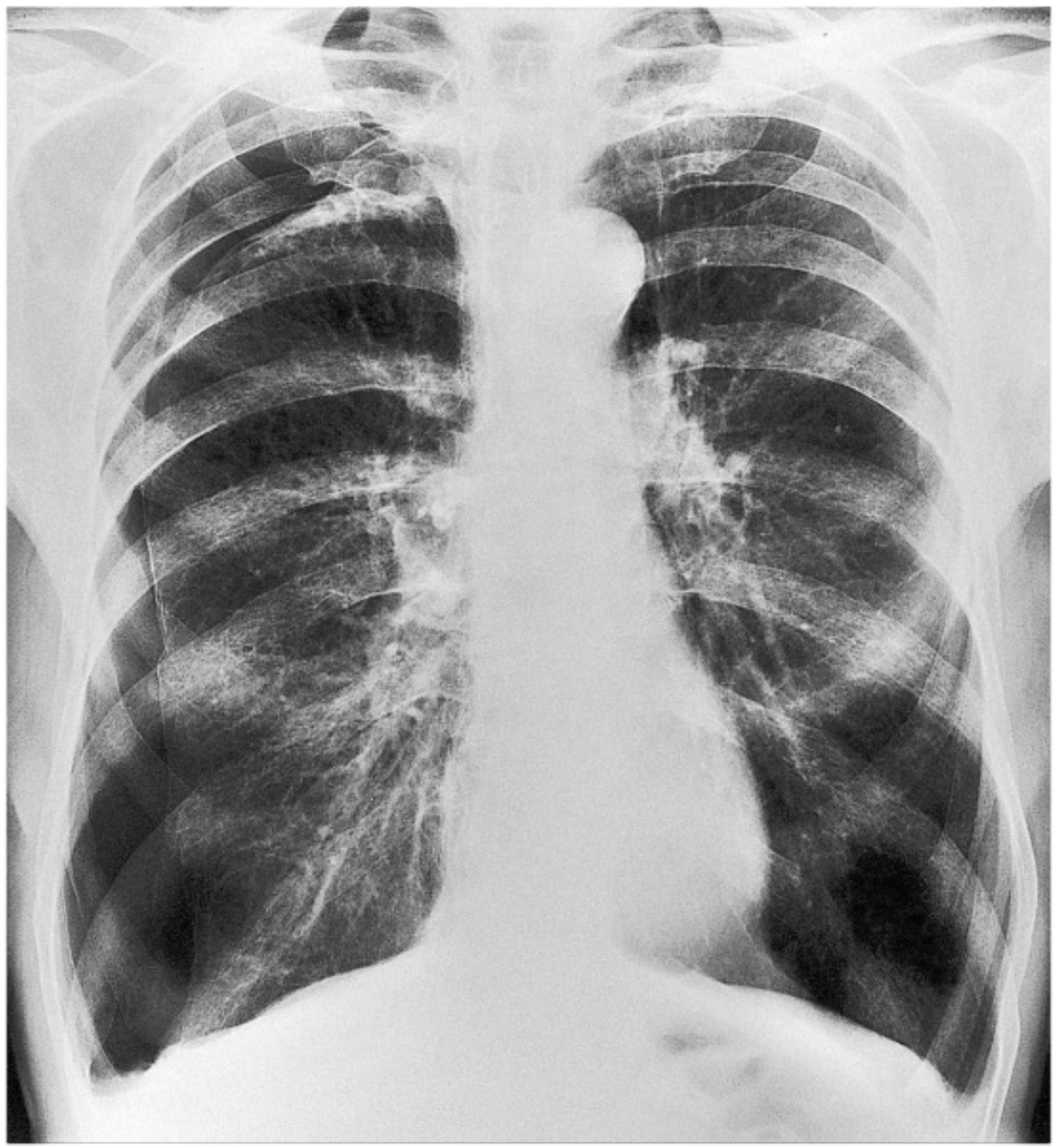


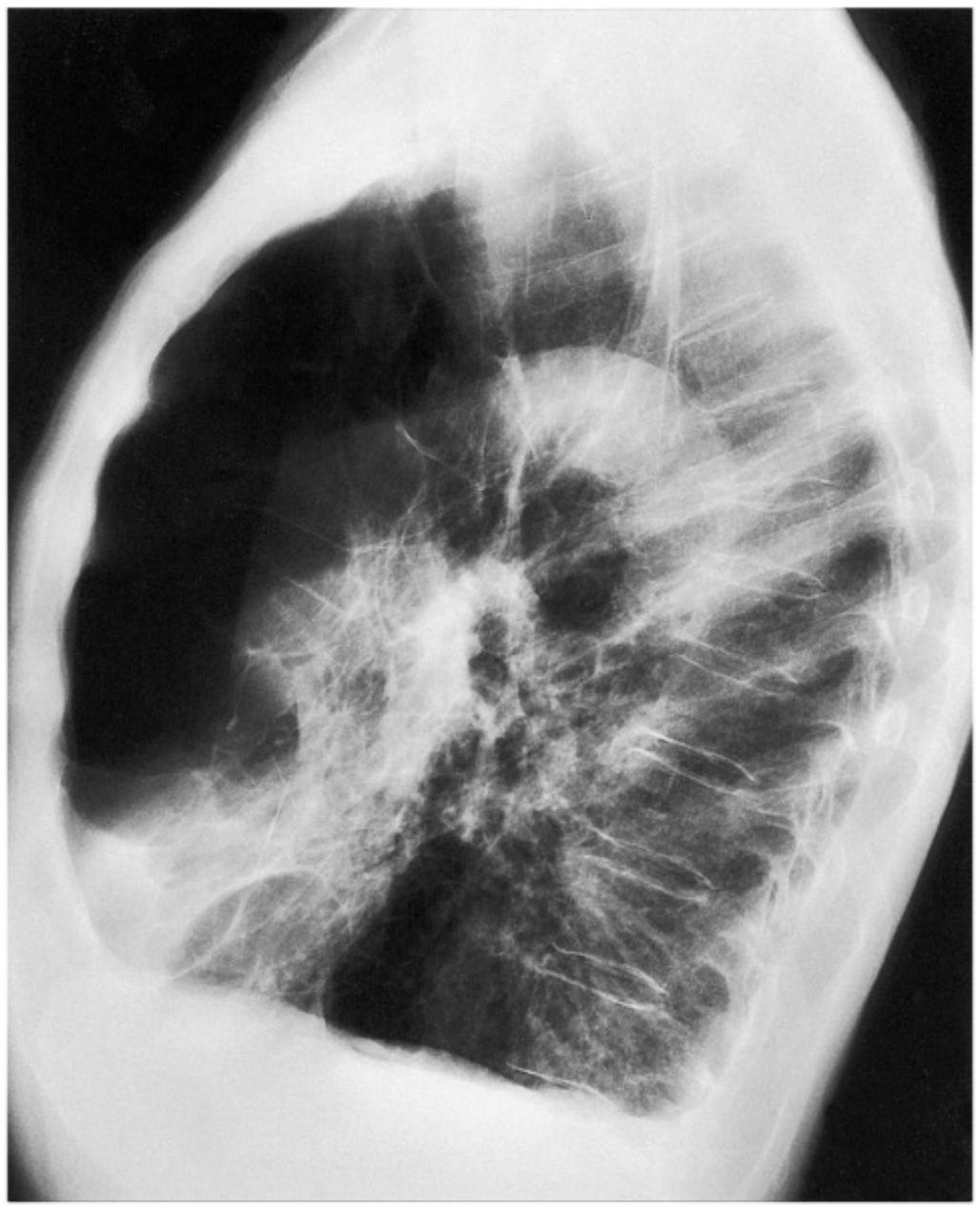


Category/Severity Stage	FEV_1/FEV	FEV_1 (% Predicted)
Normal (healthy patients)	0.80	~100
I: Mild	<0.70	≥80
II: Moderate	<0.70	50 to <80
III: Severe	<0.70	30 to <50
IV: Very Severe	<0.70	<30[a]

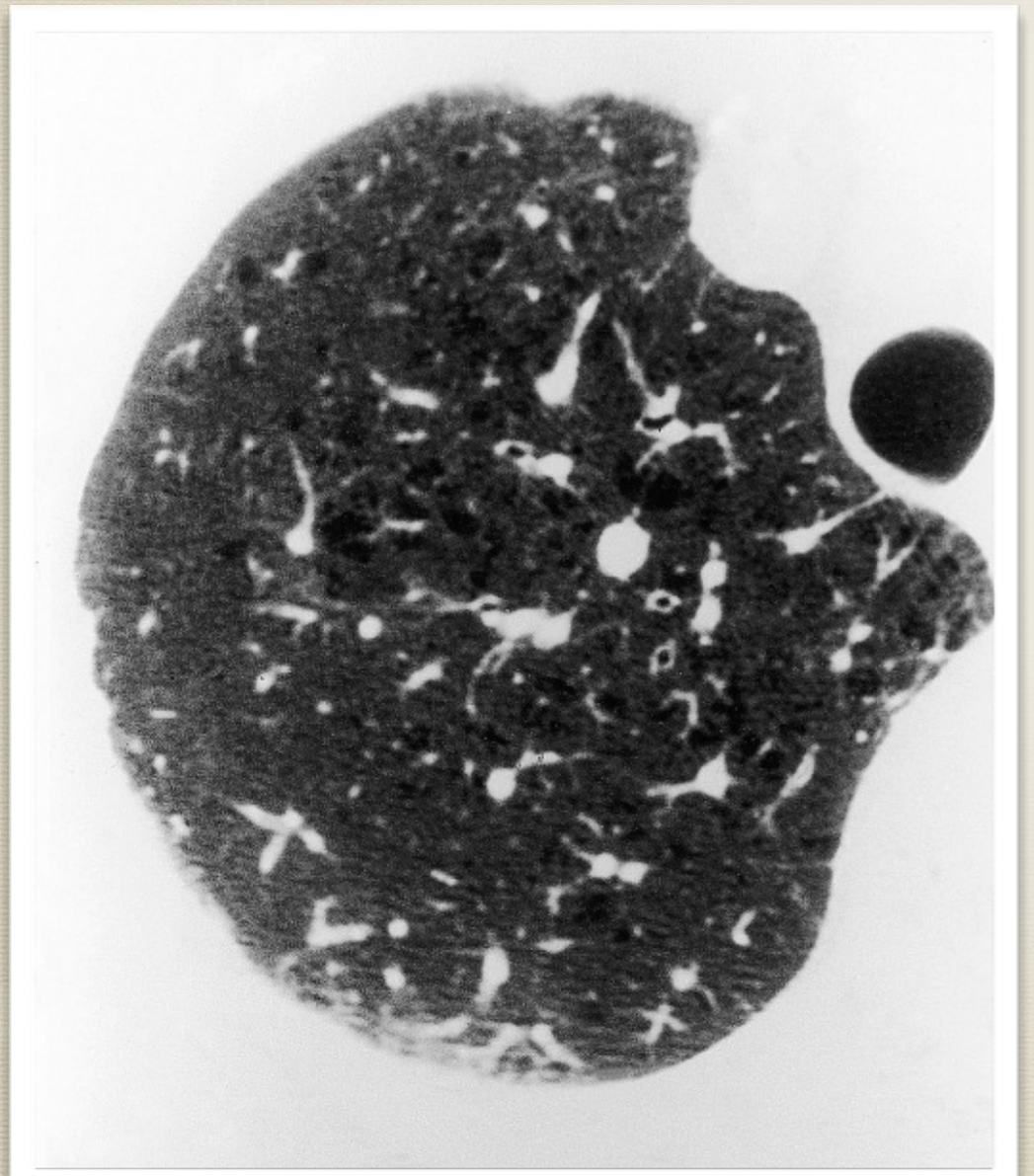
ANCILLARY INVESTIGATIONS IN COPD	
CBC	may show polycythemia, anemia of chronic disease
Oximetry & ABG	hypoxemia, hypercapnia (advanced COPD)
CXR	Hyper-inflation, low lying diaphragms, dirty chest
Chest HRCT	Centrilobular, para septal and pan lobular emphysema, bullae
Alpha-1 anti-trypsin level	In cases with early onset emphysema
Echo	In cases with suspected pulmonary hypertension
Lung volumes and diffusing capacities	Help to characterize severity, but not essential to patient management
Exercise testing	Objectively measured exercise impairment

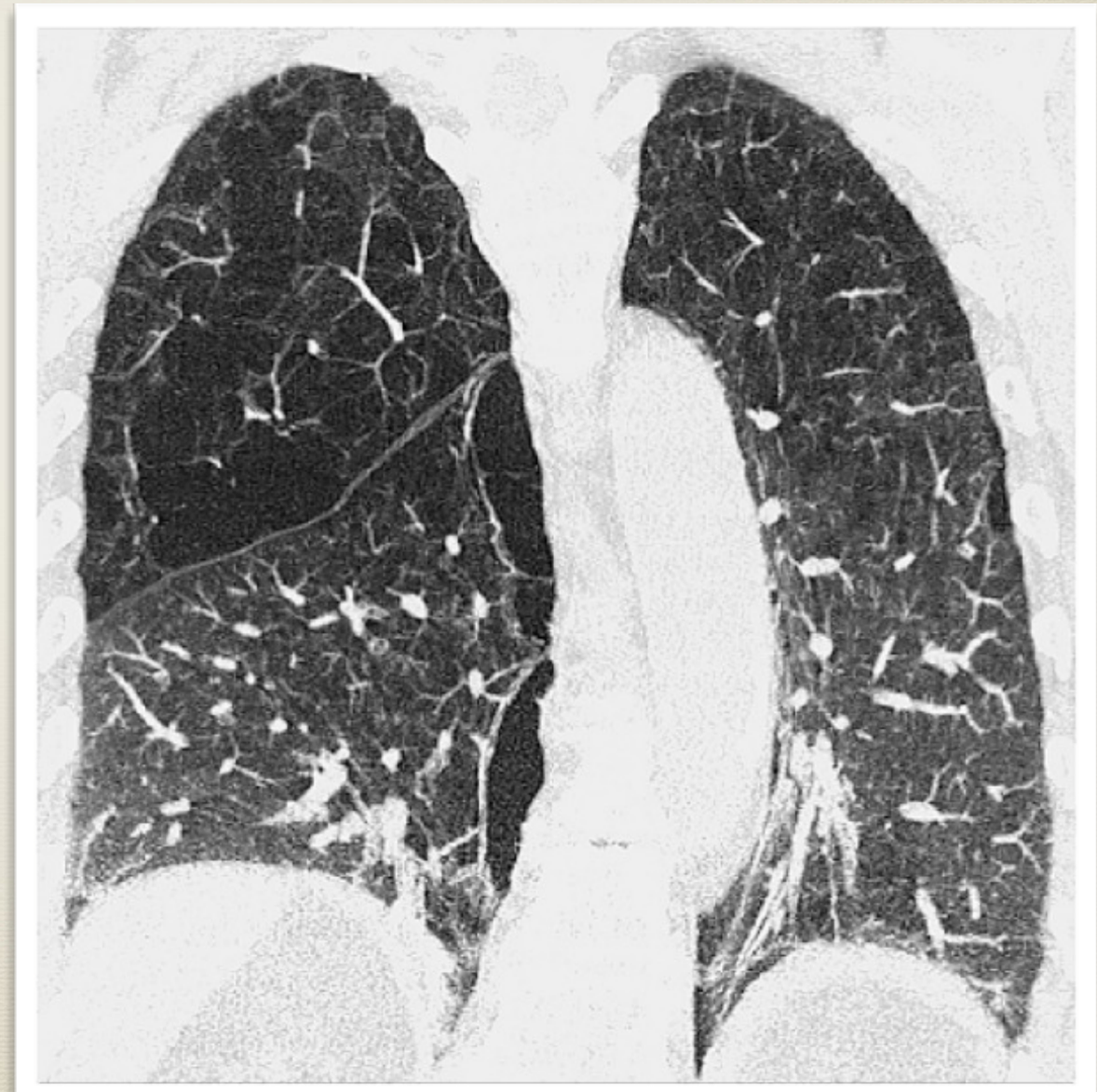
CXR in emphysema



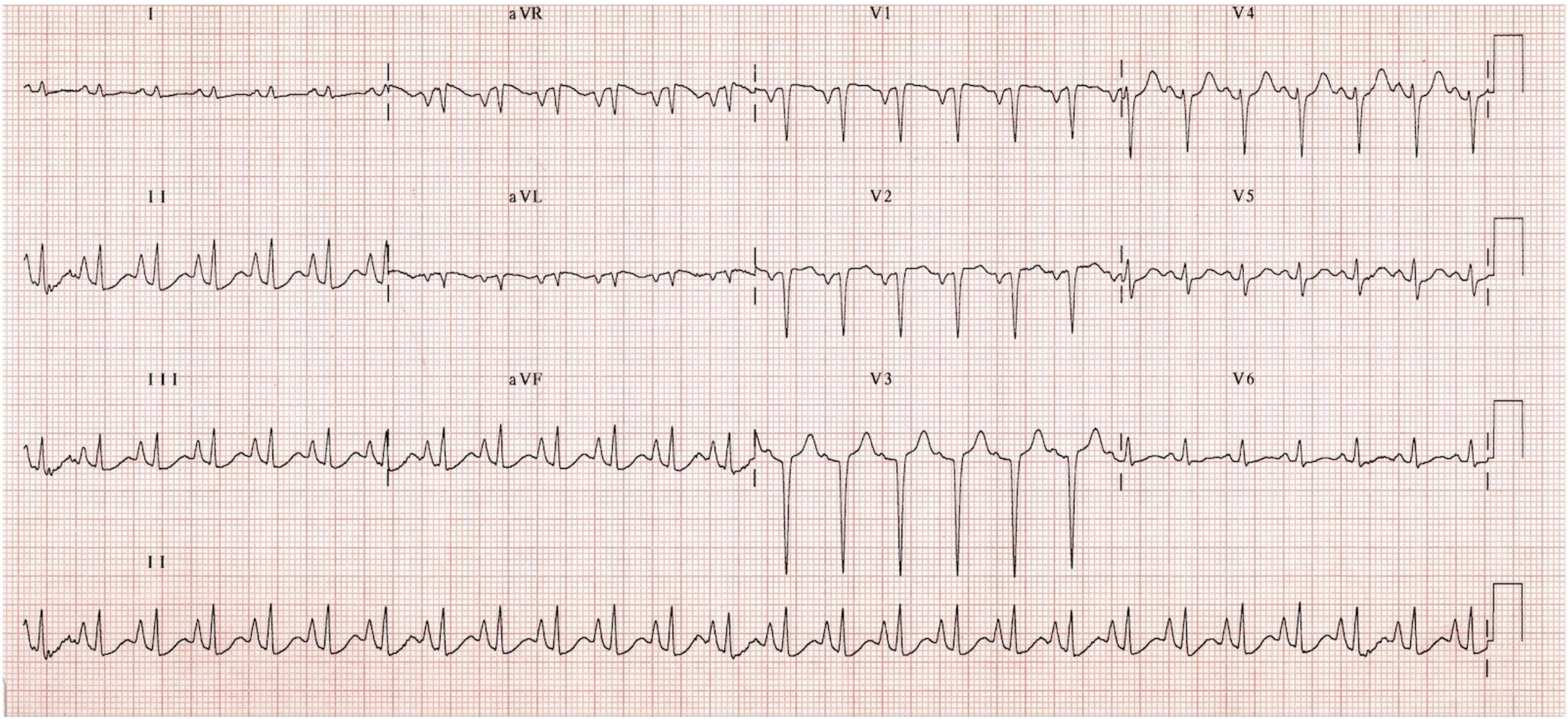


CT in emphysema

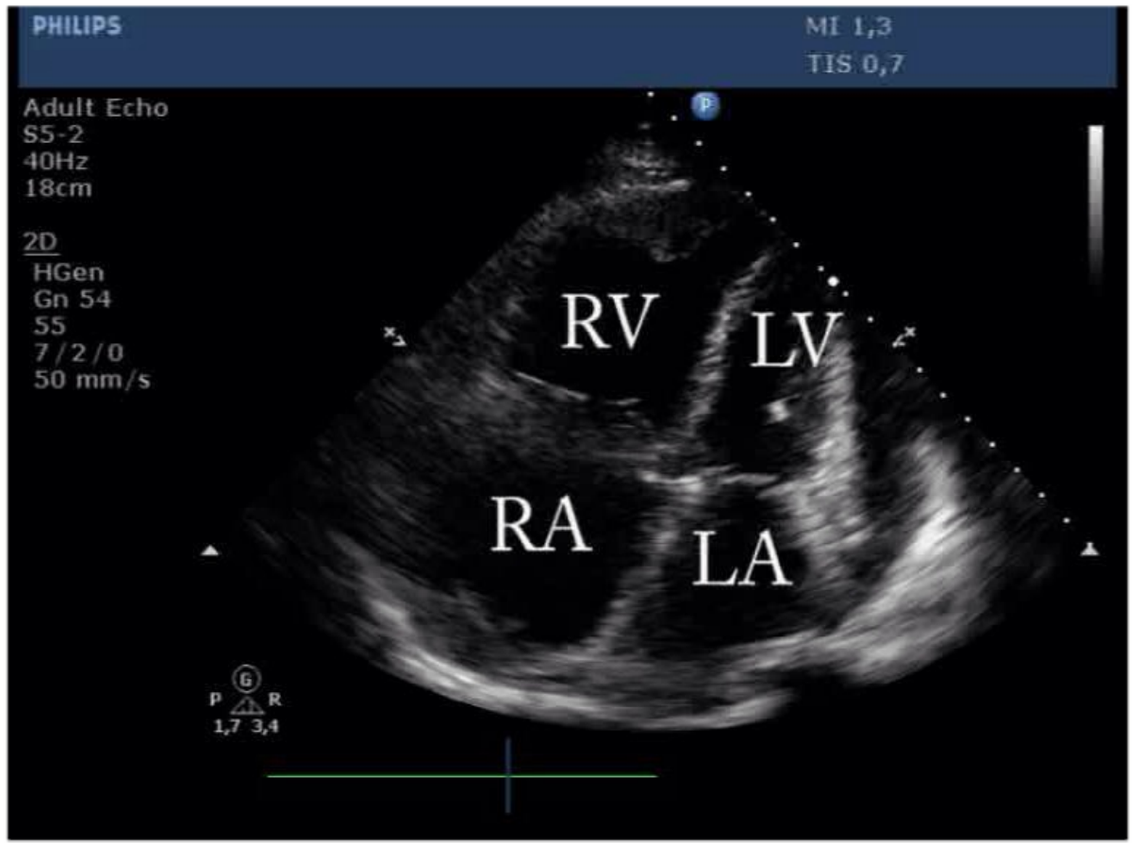


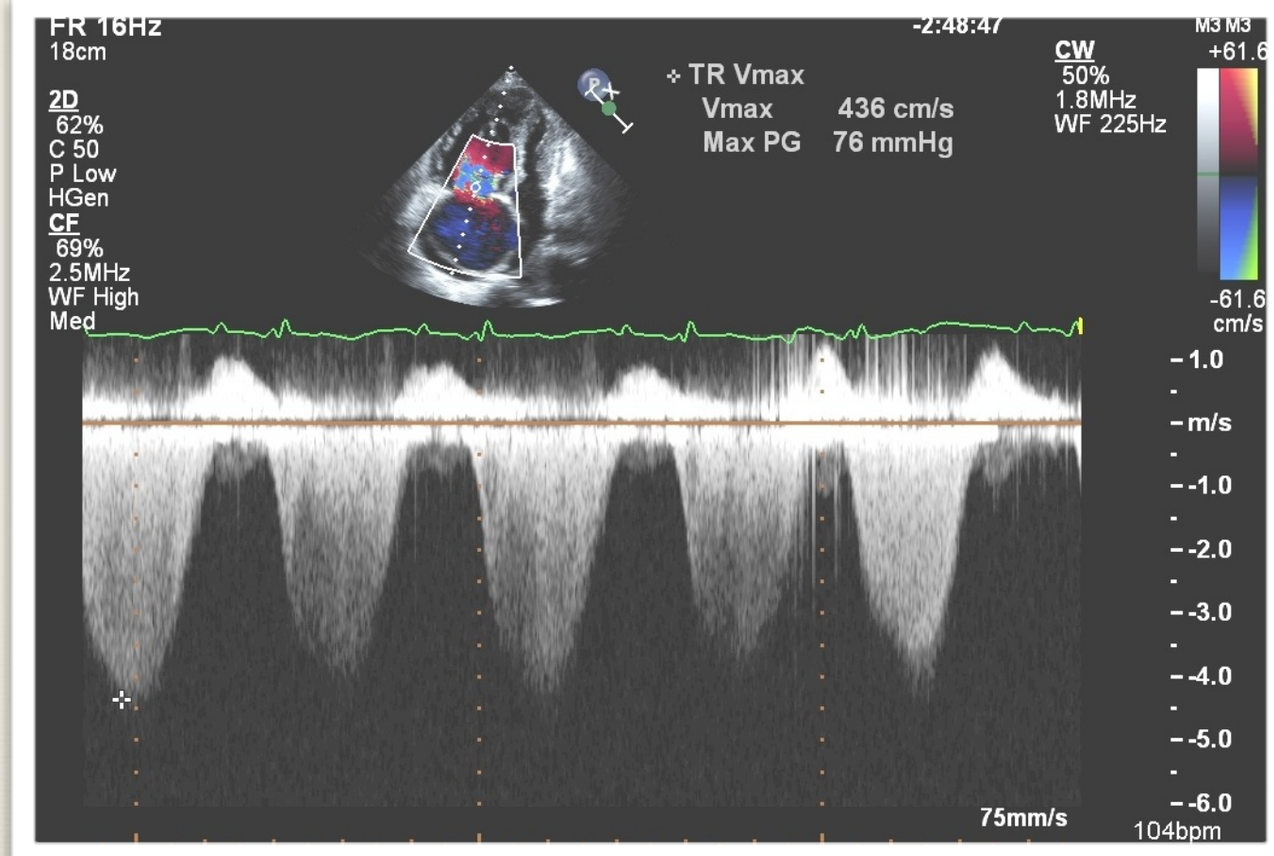


ECG in cor pulmonale
(p pulmonale)



Echo in cor pulmonale





Complications of COPD

* acute exacerbation of COPD
* cor pulmonale
* Pneumothorax
* Pulmonary hypertension
* Respiratory failure
* Polycythemia

Systemic Inflammation in COPD

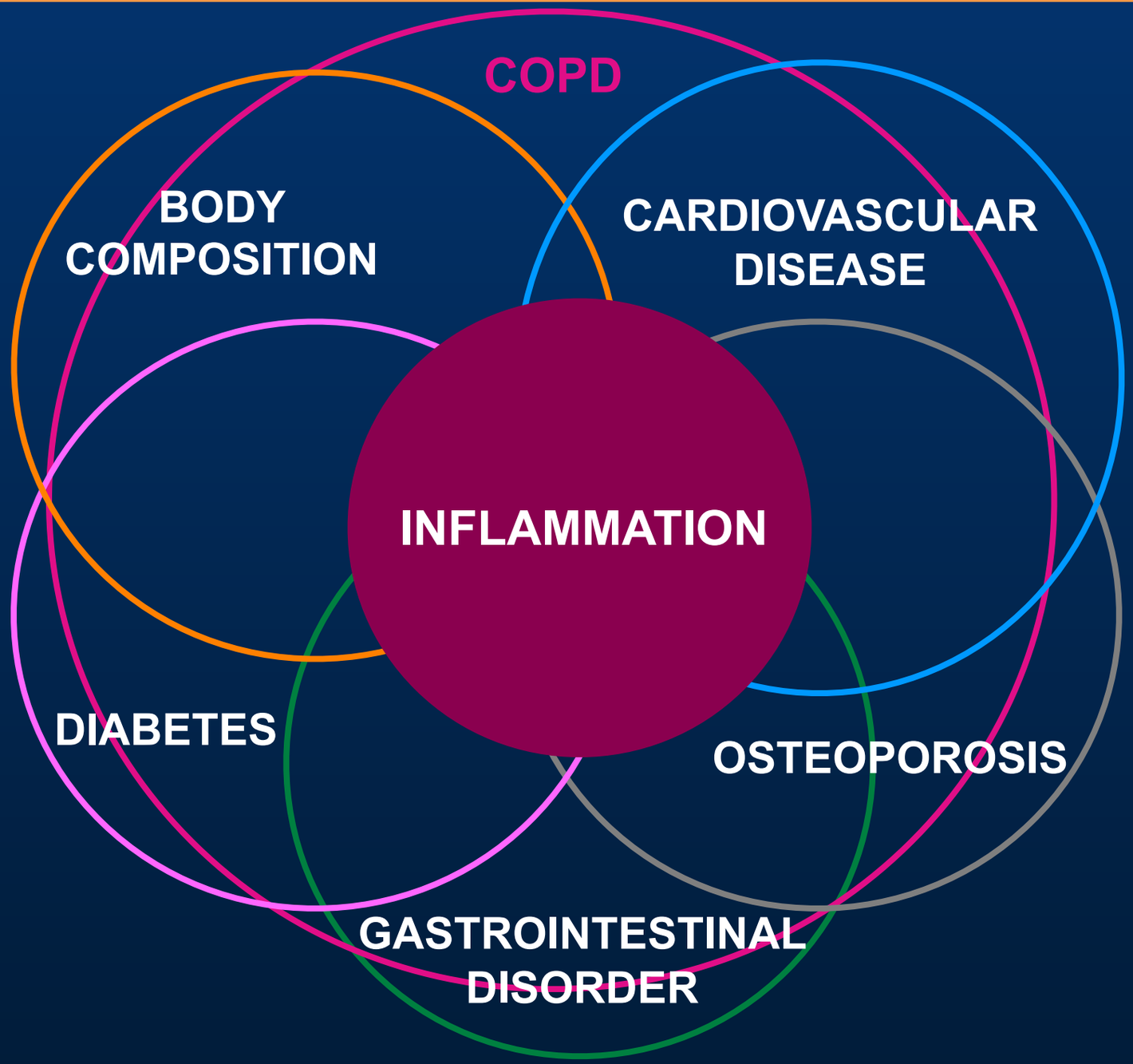
- COPD is an inflammatory condition
- Pro-inflammatory mediators may be the driving force behind the disease process
- Inflammation and actions of pro-inflammatory mediators may extend beyond the lungs and play a part in COPD comorbidities
- As effective anti-inflammatory therapy becomes available for COPD, it will be important to monitor the effects on lungs and associated comorbidities

Systemic Inflammation in COPD: Potential Clinical Consequences

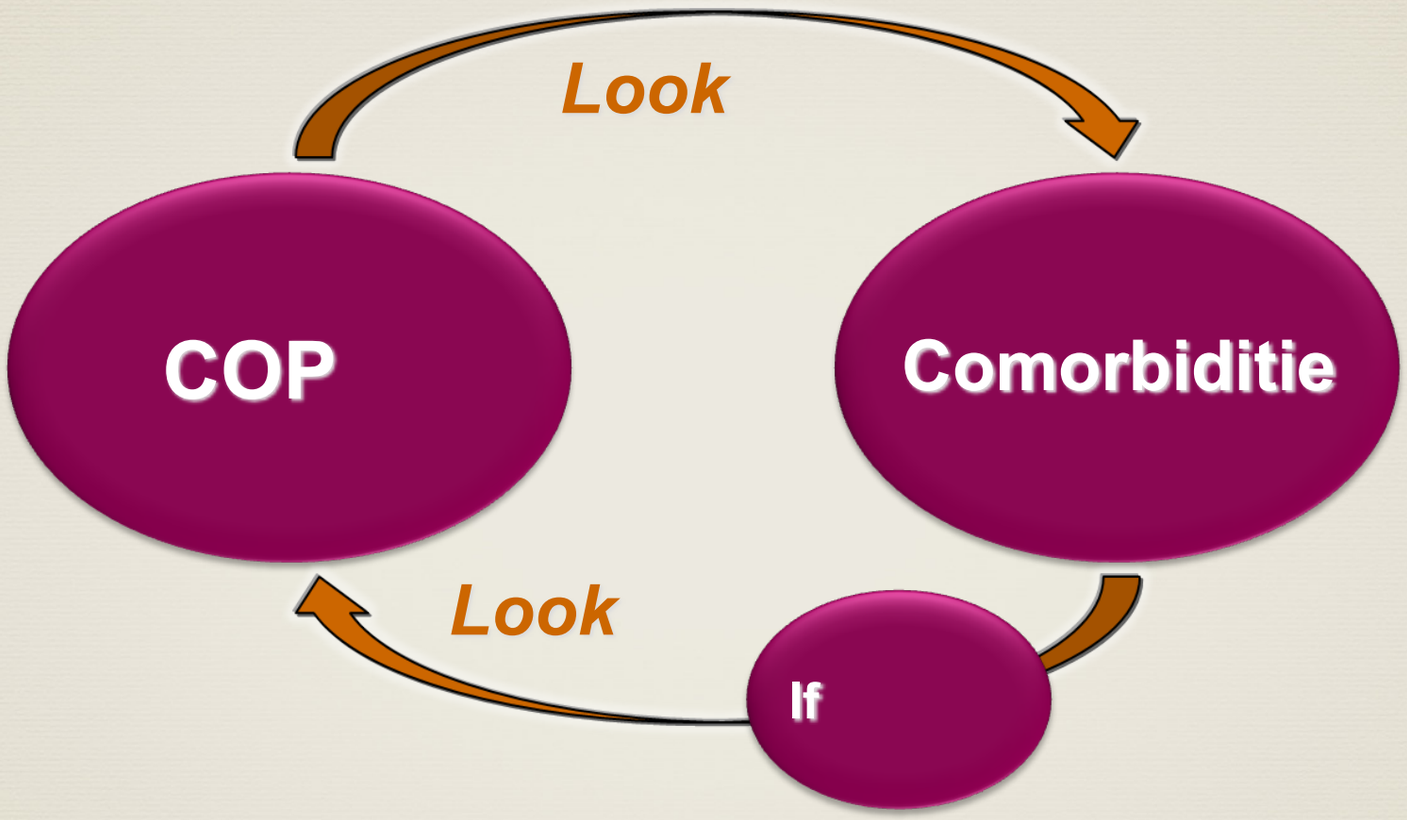
- Skeletal Muscle Dysfunction
- Cardiovascular
  - CHF
  - Arrhythmias
  - Hypertension (systemic pulmonary)
- Osteoporosis
- Anaemia of Chronic Disease
- Metabolic Disease
  - Diabetes
  - Metabolic Syndrome
- Depression
- Gastrointestinal
  - Ulcer Disease

COPD is a Systemic Disease

Systemic Inflammation and Comorbidities



Assessing Comorbidities in COPD



These comorbid conditions may influence mortality and hospitalizations and should be looked for routinely, and treated appropriately.

Objectives of COPD Management

- Prevent disease progression
- Relieve symptoms
- Improve exercise tolerance
- Improve health status
- Prevent and treat exacerbations
- Prevent and treat complications
- Reduce mortality
- Minimize side effects from treatment

Global Strategy for Diagnosis, Management and Prevention of COPD
Assessment of COPD: Goals

Determine the severity of the disease, its impact on the patient's health status and the risk of future events (for example exacerbations) to guide therapy. Consider the following aspects of the disease separately:

- current level of patient's symptoms
- severity of the spirometric abnormality
- frequency of exacerbations
- presence of comorbidities.

Assessment of COPD

- Assess symptoms
- Assess degree of airflow limitation using spirometry
- Assess risk of exacerbations
- Assess comorbidities

Assessment of symptoms

COPD Assessment Test (CAT)

or

Clinical COPD Questionnaire (CCQ)

or

mMRC Breathlessness scale

The Modified Medical Research Council (MMRC) Dyspnoea Scale

Grade of dyspnoea	Description
0	Not troubled by breathlessness except on strenuous exercise
1	Shortness of breath when hurrying on the level *or* walking up a slight hill
2	Walks slower than people of the same age on the level because of breathlessness *or* has to stop for breath when walking at own pace on the level
3	Stops for breath after walking about 100 m *or* after a few minutes on the level
4	Too breathless to leave the house *or* breathless when dressing or undressing

Assess degree of airflow limitation using spirometry

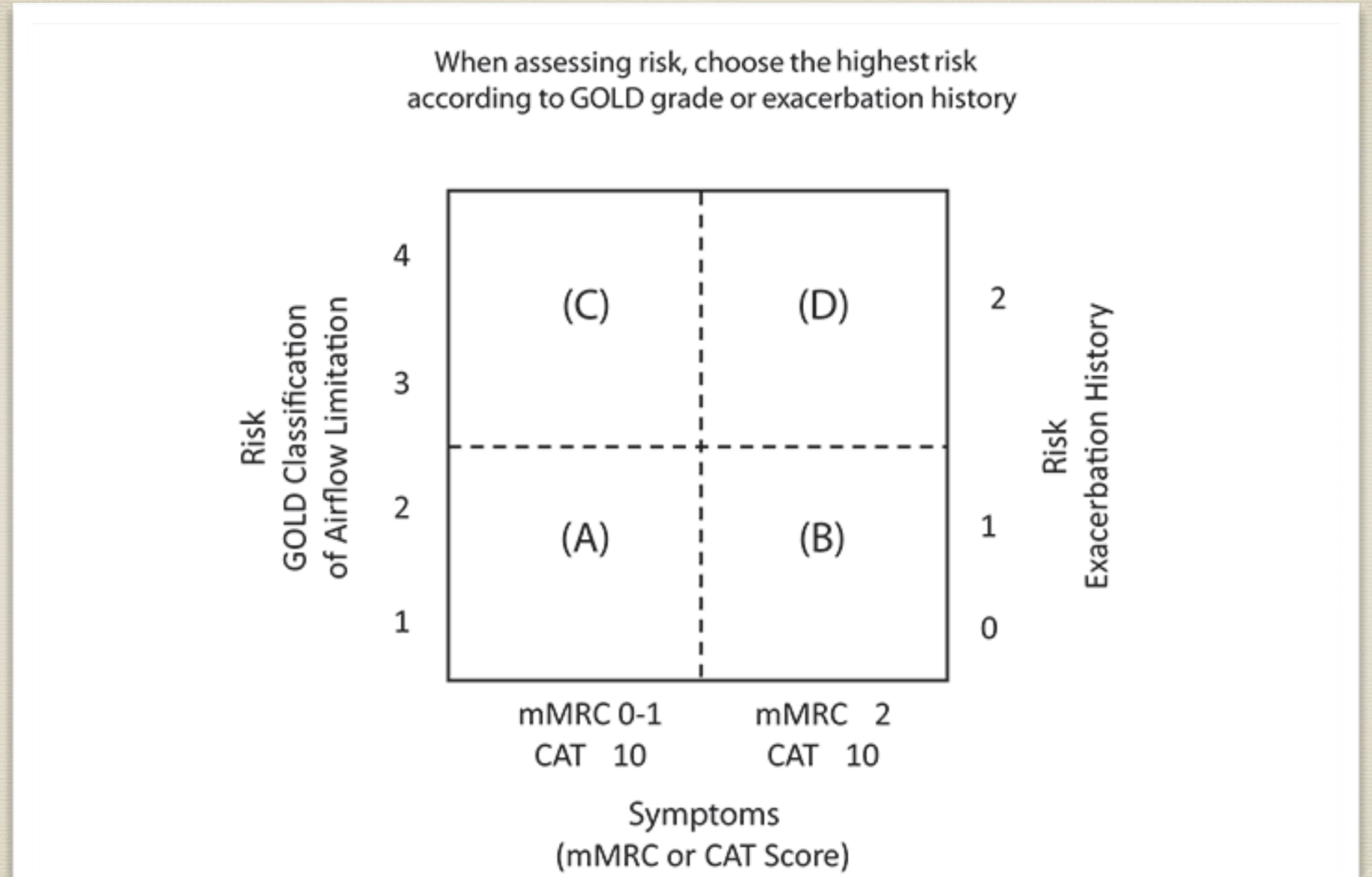
Category/Severity Stage	FEV_1/FEV	FEV_1 (% Predicted)
Normal (healthy patients)	0.80	~100
I: Mild	<0.70	≥80
II: Moderate	<0.70	50 to <80
III: Severe	<0.70	30 to <50
IV: Very Severe	<0.70	<30[a]

Assess risk of exacerbations

To assess risk of exacerbations use history of exacerbations and spirometry:

- **Two or more exacerbations within the last year or an FEV_1 < 50 % of predicted value are indicators of high risk.**
- **One or more hospitalizations for COPD exacerbation should be considered high risk.**

Combined Assessment of COPD



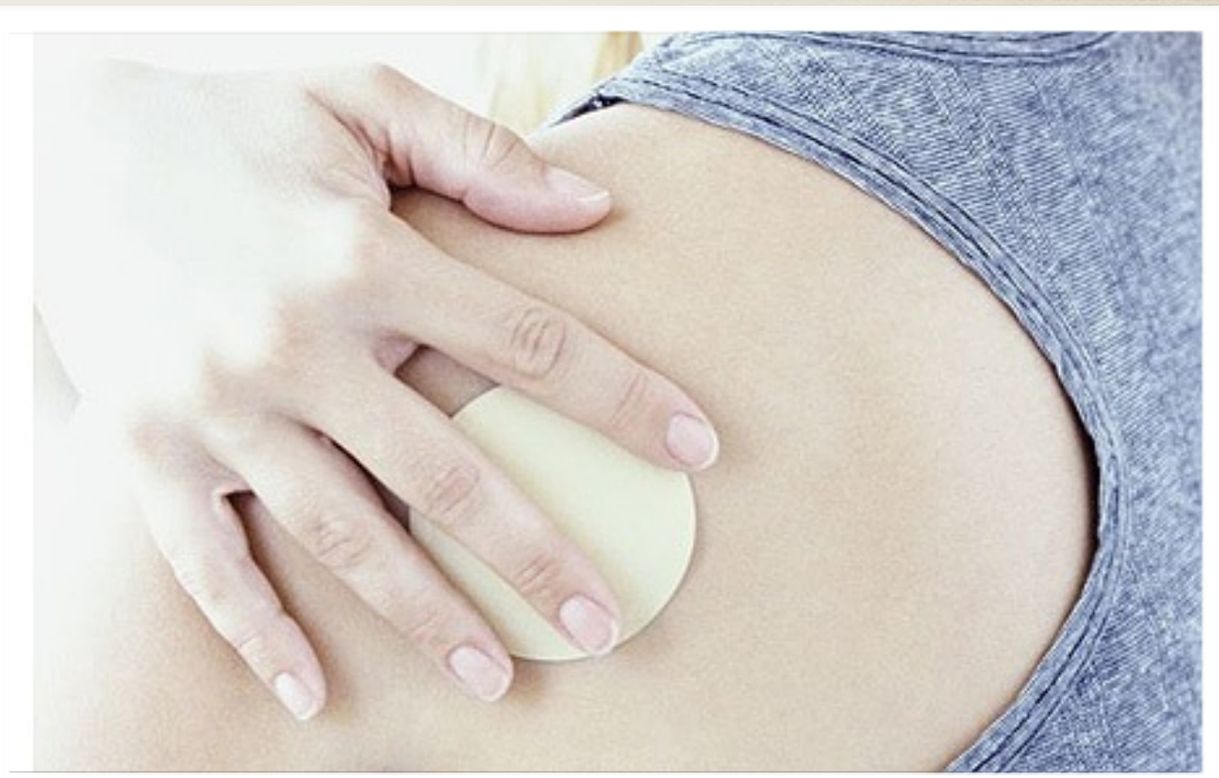
Patient Category	Characteristics	Spirometric Classification	Exacerbations Per Year	mMRC	CAT
A	Low Risk, Less Symptoms	GOLD 1-2	1	0-1	<10
B	Low Risk, More Symptoms	GOLD 1-2	1	2	10
C	High Risk, Less Symptoms	GOLD 3-4	2	0-1	<10
D	High Risk, More Symptoms	GOLD 3-4	2	2	10

Therapeutic Options

- Smoking cessation has the greatest capacity to influence the natural history of COPD. Health care providers should encourage all patients who smoke to quit.
- Pharmacotherapy and nicotine replacement reliably increase long-term smoking abstinence rates.
- All COPD patients benefit from regular physical activity and should repeatedly be encouraged to remain active.
- Influenza and pneumococcal vaccination should be offered depending on local guidelines.

Brief Strategies to Help the Patient Willing to Quit Smoking

- **ASK** Systematically identify all tobacco users at every visit
- **ADVISE** Strongly urge all tobacco users to quit
- **ASSESS** Determine willingness to make a quit attempt
- **ASSIST** Aid the patient in quitting
- **ARRANGE** Schedule follow-up contact.




CLEAR
with patented SmartControl® Technology
NICODERM CQ
NICOTINE TRANSDERMAL SYSTEM
21mg DELIVERED OVER 24 HOURS
STOP SMOKING AID
If You Smoke:
• more than 10 cigarettes per day: start with Step 1
• 10 or less cigarettes per day: start with Step 2
STEP 1
14 Clear Patches 2-Week Kit
BONUS PACK
9 EXTRA PIECES
Nicorette®
nicotine polacrilex lozenge, 2mg • stop smoking aid
Lozenge
Includes User's Guide
2 mg
FOR THOSE WHO SMOKE THEIR FIRST CIGARETTE MORE THAN 30 MINUTES AFTER WAKING UP.
If you smoke your first cigarette WITHIN 30 MINUTES of waking up, use Nicorette 4mg Lozenge
Cherry
81 LOZENGES, 2mg Each
(3 Poppoc® Containers of 27)
CLEAR
with patented SmartControl® Technology
NICODERM CQ
NICOTINE TRANSDERMAL SYSTEM
7mg DELIVERED OVER 24 HOURS
STOP SMOKING AID
For use after completing Step 2
STEP 3


60 tablets
Zyban™
150mg Tablets
Bupropion HCl
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CHAMPIX
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COMPRIMÉS DE TARTRATE DE VARÉNICLINE
0.5 mg
and / et
1 mg
Starter Pack
Trousse de départ
11 x 0.5 mg tablet / comprimé à 0,5 mg
14 x 1 mg tablet / comprimé à 1 mg
Week / Semaine 1
Week / Semaine 2
CHAMPIX 0.5 mg
CHAMPIX 1 mg

e-cigarettes

The latest study on e-cigarettes, published in the journal **Lancet**, supports that claim. In the first clinical trial comparing e-cigarettes and nicotine patches in helping people to quit smoking, both methods proved equally successful. After a 13-week smoking cessation program, similar numbers of smokers who used e-cigarettes remained smoke-free after six months as used nicotine patches.

Therapeutic Options: COPD Medications

Beta
Short-acting beta
Long-acting beta
Anticholinergics
Short-acting anticholinergics
Long-acting anticholinergics
Combination short-acting beta
Combination long-acting beta
Methylxanthines
Inhaled corticosteroids
Combination long-acting beta
Systemic corticosteroids
Phosphodiesterase-4 inhibitors

Medications used in the treatment of COPD

Table 2. Medications Used in the Treatment of COPD in the U.S.

Class	Drug (Brand)	Most Common Adverse Effects
Short-acting beta$_2$ agonists (SABAs)	Albuterol (ProAir, Proventil, Ventolin) Levalbuterol (Xopenex)	Palpitations, tachycardia, insomnia, irritability, tremors, hypokalemia
Long-acting beta$_2$ agonists (LABAs)	Formoterol (Foradil, Perforomist) Arformoterol (Brovana) Salmeterol (Serevent) Indacaterol (Arcapta)	Same as above
Short-acting anticholinergic (SAMA)	Ipratropium bromide (Atrovent)	Xerostomia, metallic taste
Long-acting anticholinergics (LAMAs)	Tiotropium (Spiriva) Alcidinium (Turdorza)	Xerostomia, metallic taste Headache, nasopharyngitis, cough
Combination: SABA + anticholinergic	Albuterol/ipratropium (Combivent)	Upper respiratory tract infections, headache
Methylxanthines	Aminophylline Theophylline (Theo-Dur, Theo-24)	Atrial and ventricular arrhythmias, grand mal convulsions, headache, nausea
Inhaled corticosteroids (ICS)	Beclomethasone (Qvar)[a] Budesonide (Pulmicort) Fluticasone (Flovent)	Oral candidiasis, skin bruising
Combination: LABA + ICS	Formoterol/budesonide (Symbicort) Salmeterol/fluticasone (Advair) Formoterol/mometasone (Dulera)[a]	Headache, nasopharyngitis, stomach discomfort
Phosphodiesterase-4 (PDE4) inhibitor	Roflumilast (Daliresp)	Nausea, weight loss, diarrhea, headache, abdominal pain

[a] Currently FDA approved only for asthma. COPD: chronic obstructive pulmonary disease.
Source: References 4, 10.

Therapeutic Options: Bronchodilators

- **Bronchodilator medications are central to the symptomatic management of COPD.**
- **Bronchodilators are prescribed on an as-needed or on a regular basis to prevent or reduce symptoms.**
- **The principal bronchodilator treatments are beta$_2$ agonists, anticholinergics, theophylline or combination therapy.**
- **The choice of treatment depends on the availability of medications and each patient's individual response in terms of symptom relief and side effects.**

Therapeutic Options: Bronchodilators

- Long-acting inhaled bronchodilators are convenient and more effective for symptom relief than short-acting bronchodilators.
- Long-acting inhaled bronchodilators reduce exacerbations and related hospitalizations and improve symptoms and health status.
- Combining bronchodilators of different pharmacological classes may improve efficacy and decrease the risk of side effects compared to increasing the dose of a single bronchodilator.

Therapeutic Options: Inhaled Corticosteroids

- Regular treatment with inhaled corticosteroids improves symptoms, lung function and quality of life and reduces frequency of exacerbations for COPD patients with an FEV_1 < 60% predicted.
- Inhaled corticosteroid therapy is associated with an increased risk of pneumonia.
- Withdrawal from treatment with inhaled corticosteroids may lead to exacerbations in some patients.

Therapeutic Options: Combination Therapy

- An inhaled corticosteroid combined with a long-acting beta$_2$-agonist is more effective than the individual components in improving lung function and health status and reducing exacerbations in moderate to very severe COPD.
- Combination therapy is associated with an increased risk of pneumonia.
- Addition of a long-acting beta$_2$-agonist/inhaled glucorticosteroid combination to an anticholinergic (tiotropium) appears to provide additional benefits.

Therapeutic Options: Systemic Corticosteroids

- Chronic treatment with systemic corticosteroids should be avoided because of an unfavorable benefit-to-risk ratio.

Therapeutic Options: Phosphodiesterase-4 Inhibitors

- In patients with severe and very severe COPD (GOLD 3 and 4) and a history of exacerbations and chronic bronchitis, the phospodiesterase-4 inhibitor, roflumilast, reduces exacerbations treated with oral glucocorticosteroids.

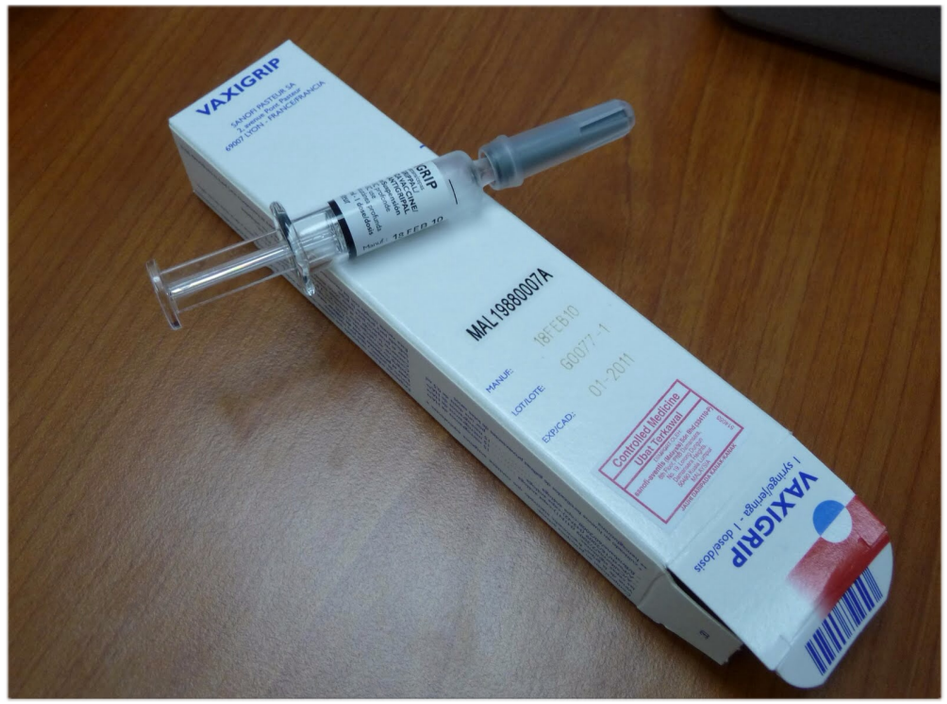
Therapeutic Options: Theophylline

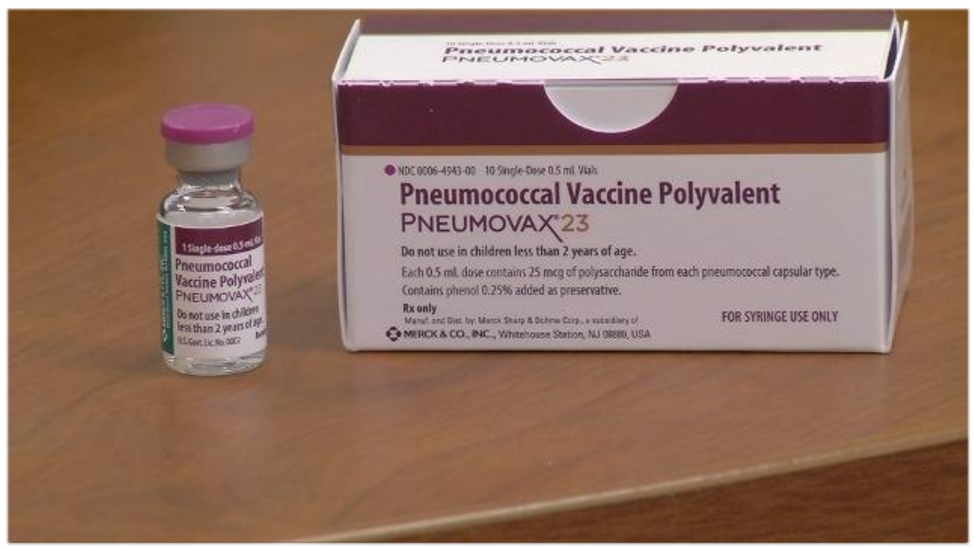
- Theophylline is less effective and less well tolerated than inhaled long-acting bronchodilators and is not recommended if those drugs are available and affordable.
- There is evidence for a modest bronchodilator effect and some symptomatic benefit compared with placebo in stable COPD. Addition of theophylline to salmeterol produces a greater increase in FEV_1 and breathlessness than salmeterol alone.
- Low dose theophylline reduces exacerbations but does not improve post-bronchodilator lung function.

Therapeutic Options: Other Pharmacologic Treatments

Influenza vaccines can reduce serious illness. Pneumococcal polysaccharide vaccine is recommended for COPD patients 65 years and older and for COPD patients younger than age 65 with an $FEV_1 < 40\%$ predicted.

The use of antibiotics, other than for treating infectious exacerbations of COPD and other bacterial infections, is currently not indicated.





Oxygen therapy (LTOT)

LTOT may be indicated for those clients with chronic lung disease who meet **EITHER** of the following criteria:

i. Documented hypoxaemia i.e. daytime $PaO_2 \leq 55mmHg$, measured at rest via ABG whilst breathing room air when clinically stable **OR**

ii. Daytime PaO_2 56 - 59mmHg, measured at rest via ABG whilst breathing room air when clinically stable, with evidence of end-organ damage due to hypoxia e.g. pulmonary hypertension, right heart failure, polycythaemia

Therapeutic Options: Rehabilitation

- All COPD patients benefit from exercise training programs with improvements in exercise tolerance and symptoms of dyspnea and fatigue.
- Although an effective pulmonary rehabilitation program is 6 weeks, the longer the program continues, the more effective the results.
- If exercise training is maintained at home, the patient's health status remains above pre-rehabilitation levels.

Therapeutic Options: Rehabilitation

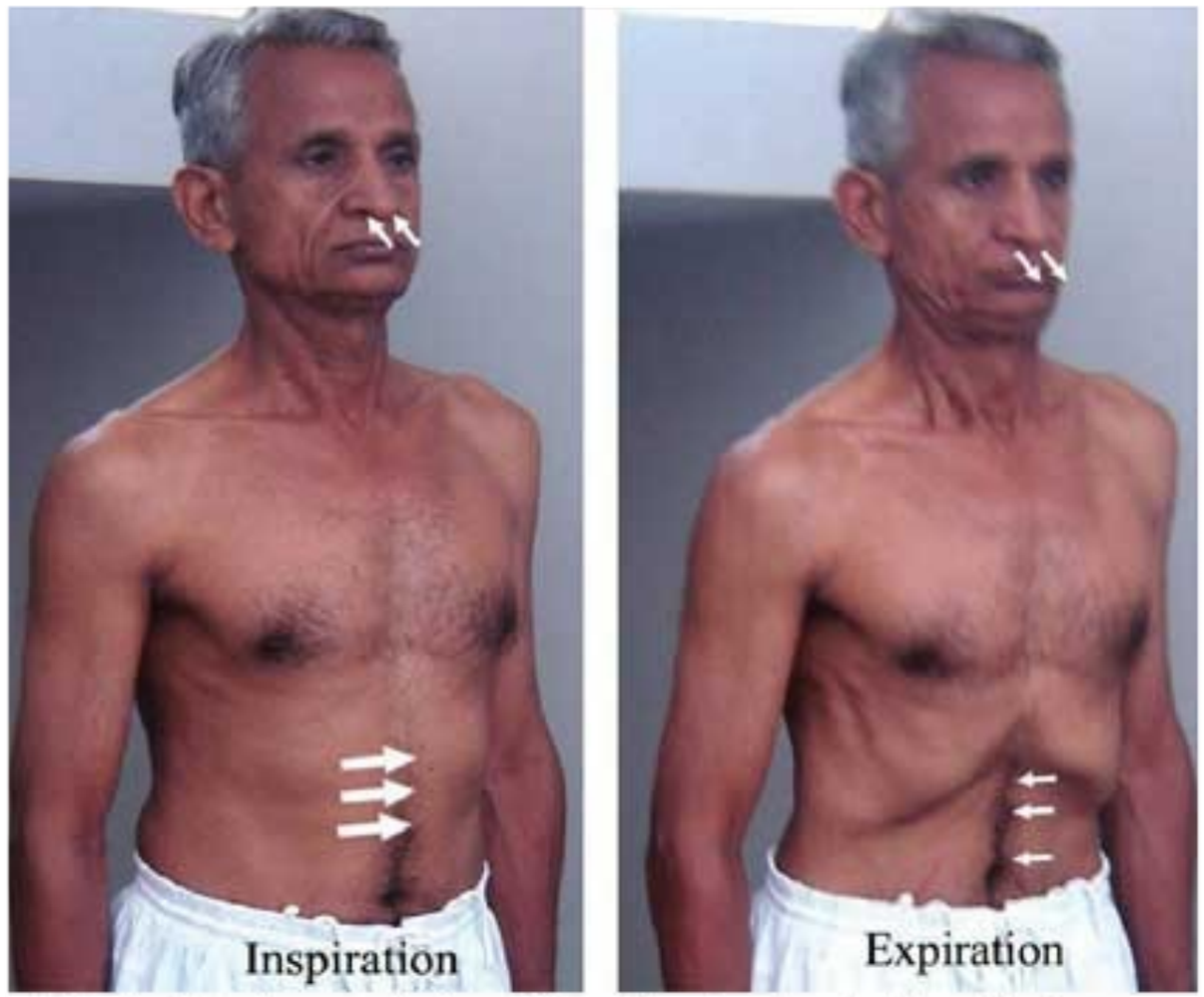


Fig. 2 : Diaphragmatic breathing: During inspiration diaphragm descends down and abdomen moves out. Patient exhales through nose with abdomen drawing in

Manage Stable COPD: Goals of Therapy

- Relieve symptoms
- Improve exercise tolerance
- Improve health status

Reduce symptom

- Prevent disease progression
- Prevent and treat exacerbations
- Reduce mortality

Reduce risk

Manage Stable COPD: Non-pharmacologic

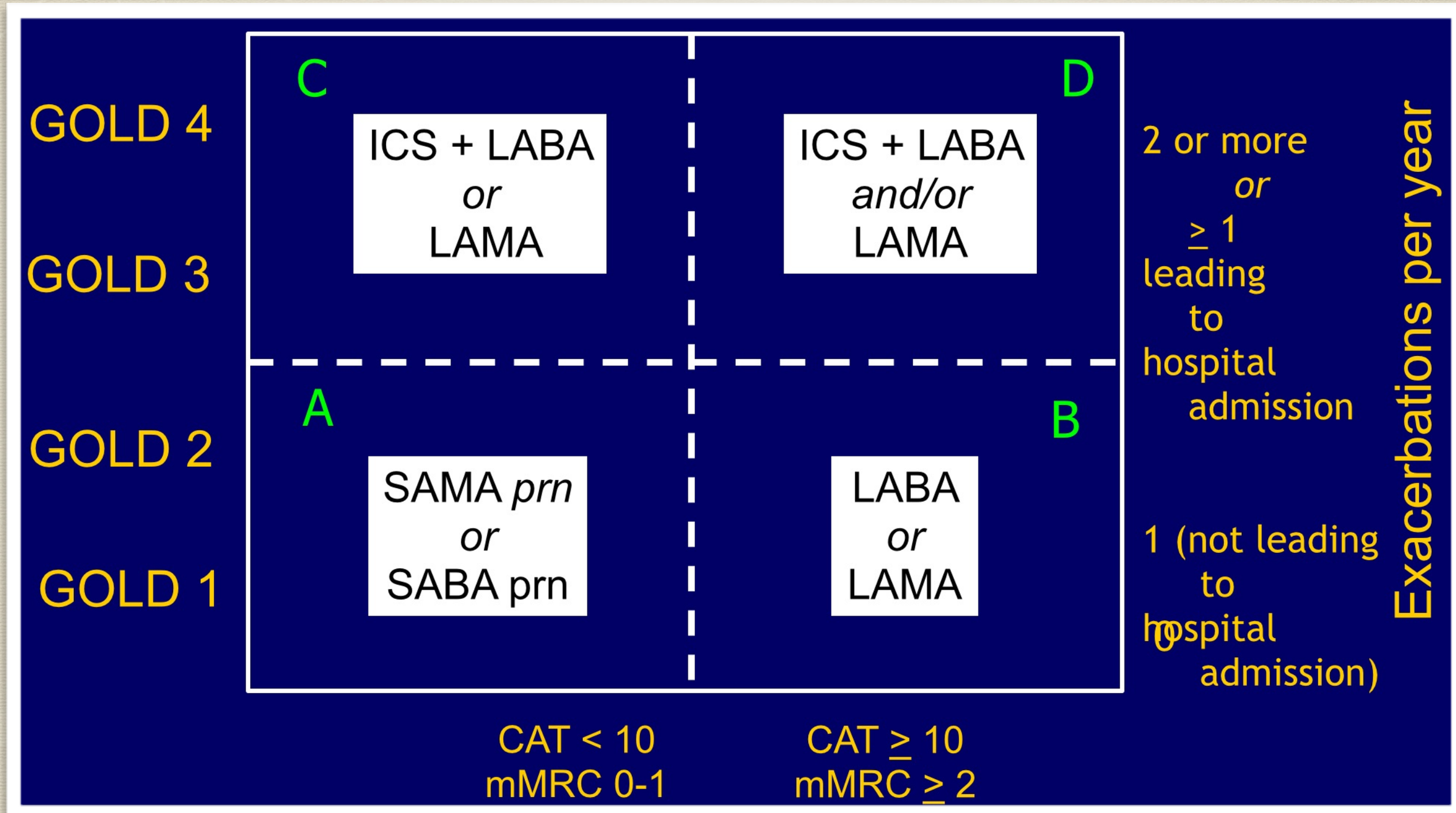
Patient Group	Essential	Recommended	Depending on local guidelines
A	Smoking cessation (can include pharmacologic treatment)	Physical activity	Flu vaccination Pneumococcal vaccination
B, C, D	Smoking cessation (can include pharmacologic treatment) Pulmonary rehabilitation	Physical activity	Flu vaccination Pneumococcal vaccination

Manage Stable COPD: Pharmacologic Therapy

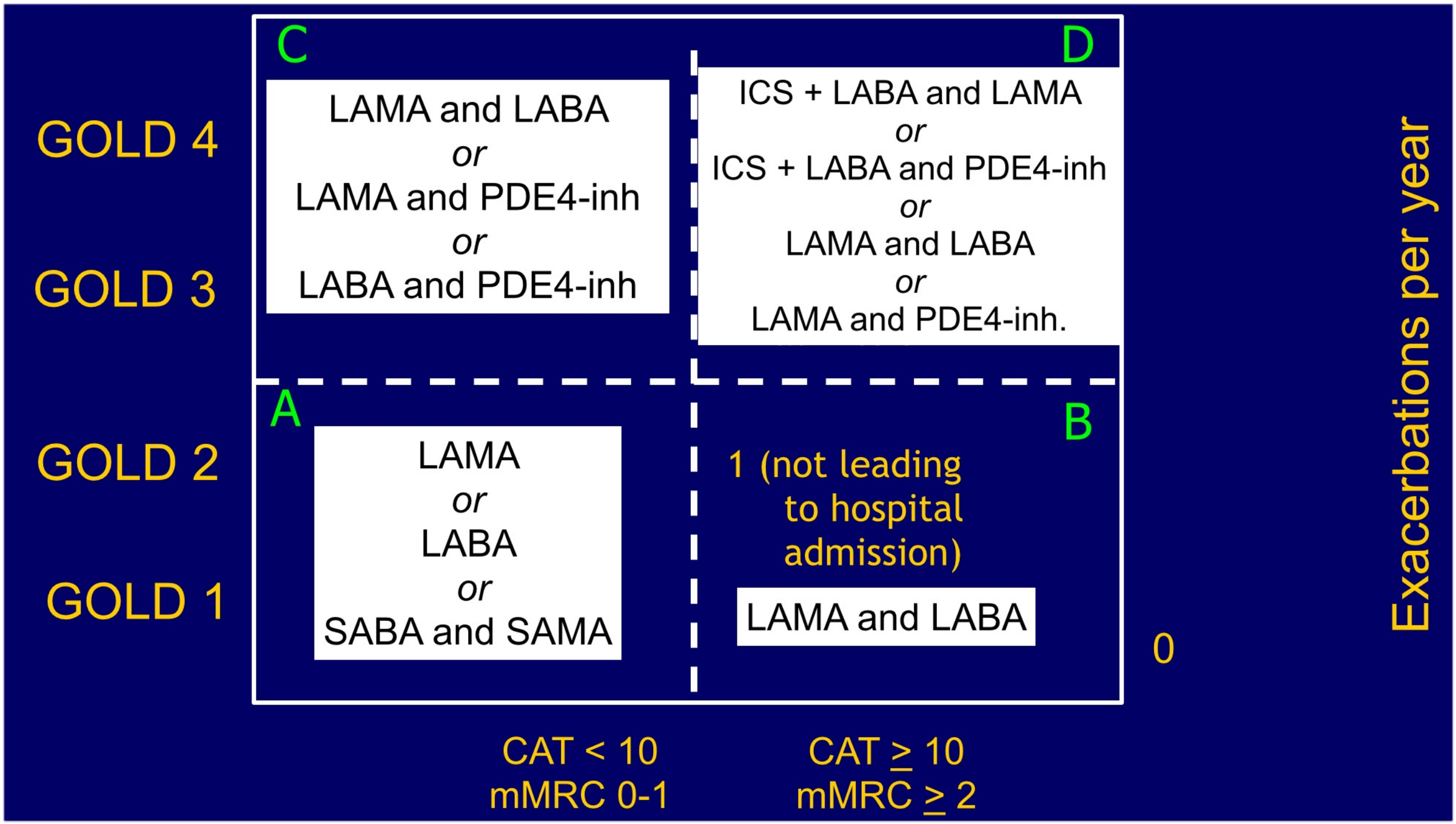
(Medications in each box are mentioned in alphabetical order, and therefore not necessarily in order of preference.)

Patient	Recommended First choice	Alternative choice	Other Possible Treatments
A	*SAMA prn* *or* *SABA prn*	*LAMA* *or* LABA *or* *SABA and SAMA*	*Theophylline*
B	***LAMA*** ***or*** ***LABA***	***LAMA and LABA***	***SABA and/or SAMA*** ***Theophylline***
C	*ICS + LABA* *or* *LAMA*	*LAMA and LABA or* *LAMA and PDE4-inh. or* *LABA and PDE4-inh.*	*SABA and/or SAMA* *Theophylline*
D	*ICS + LABA* *and/or* *LAMA*	*ICS + LABA and LAMA or* *ICS+LABA and PDE4-inh. or* LAMA and LABA *or* *LAMA and PDE4-inh.*	*Carbocysteine* *SABA and/or SAMA* *Theophylline*

Manage Stable COPD: Pharmacologic Therapy
RECOMMENDED FIRST CHOICE



Manage Stable COPD: Pharmacologic Therapy
ALTERNATIVE CHOICE



Manage Exacerbations

An exacerbation of COPD is:

"an acute event characterized by a worsening of the patient's respiratory symptoms that is beyond normal day-to-day variations and leads to a change in medication."

Severity Scale for Acute Exacerbations of Chronic Bronchitis	
Severe Exacerbation (Type 1)	3 of 3 clinical symptoms*
Moderate Exacerbation (Type 2)	2 of 3 clinical symptoms*
Mild Exacerbation (Type 3)	1 of 3 clinical symptoms* + ≥ 1 from: • Upper respiratory tract infection in last 5 days • Fever without other apparent cause • Increased wheezing • Increased cough • 20% increase in respiratory rate or heart rate over baseline

* *Clinical Symptoms: Worsening dyspnea, increase in sputum purulence, increase in sputum volume*

Manage Exacerbations: Key Points

- The most common causes of COPD exacerbations are viral upper respiratory tract infections and infection of the tracheobronchial tree.
- Diagnosis relies exclusively on the clinical presentation of the patient complaining of an acute change of symptoms that is beyond normal day-to-day variation.
- The goal of treatment is to minimize the impact of the current exacerbation and to prevent the development of subsequent exacerbations.

Assessment of acute exacerbation of COPD

ABG	PaO breathing room air indicates respiratory failure.
CXR	useful to exclude alternative diagnoses.
CBC	identify polycythemia, anemia or bleeding.
Biochemical tests	detect electrolyte disturbances, diabetes, and poor nutrition.
Sputum	Purulent sputum indicates the need for antibiotics
Biochemical tests	detect electrolyte disturbances, diabetes, and poor nutrition.
ECG	may aid in the diagnosis of coexisting cardiac problems.
Spirometry	not recommended during an exacerbation.
Serum troponin, serial CK-MB	Assess for myocardial injury or infarction Serum troponin, serial CK-MB measurement

Manage Exacerbations: Treatment Options

Oxygen	titrate to improve the patient's hypoxemia with a target saturation of 88-92%
Bronchodilators	Short-acting inhaled beta short-acting anticholinergics are preferred.
Systemic Corticosteroids	Shorten recovery time, improve lung function (FEV hypoxemia (PaO failure, and length of hospital stay. A dose of 40 mg prednisone per
Magnesium sulphate	Nebulized magnesium as an adjuvent to salbutamol treatment in the setting of acute exacerbations of COPD has no effect on FEV
Antibiotics	Should be given when indicated
NIV	for patients hospitalized with severe exacerbation of COPD

Table 1. Clinical guidelines for initiation of antibiotics in AECOPD

Global Initiative for Chronic Obstructive Lung Disease[3]	**Antibiotics should be given to:** 1. Patients with all three cardinal symptoms (increased dyspnea, increased sputum volume, increased sputum purulence) 2. Patients with two cardinal symptoms, if increased sputum purulence is present 3. Patients with severe exacerbations requiring noninvasive or invasive mechanical ventilation
American Thoracic Society/European Respiratory Society[4]	1. In hospitalized, non-ICU patients, antibiotics may be initiated in patients with changes in sputum characteristics 2. In patients requiring ICU admission, antibiotic therapy is recommended
National Institute for Health and Clinical Excellence[5] (United Kingdom)	1. Antibiotics should be used in exacerbations associated with a history of more purulent sputum 2. Patients with exacerbations who do NOT have increased sputum purulence do not need antibiotics unless there are signs of pneumonia
Canadian Thoracic Society[6]	1. Antibiotics may be beneficial in the treatment of more severe purulent AECOPD

Indications for Hospitalization

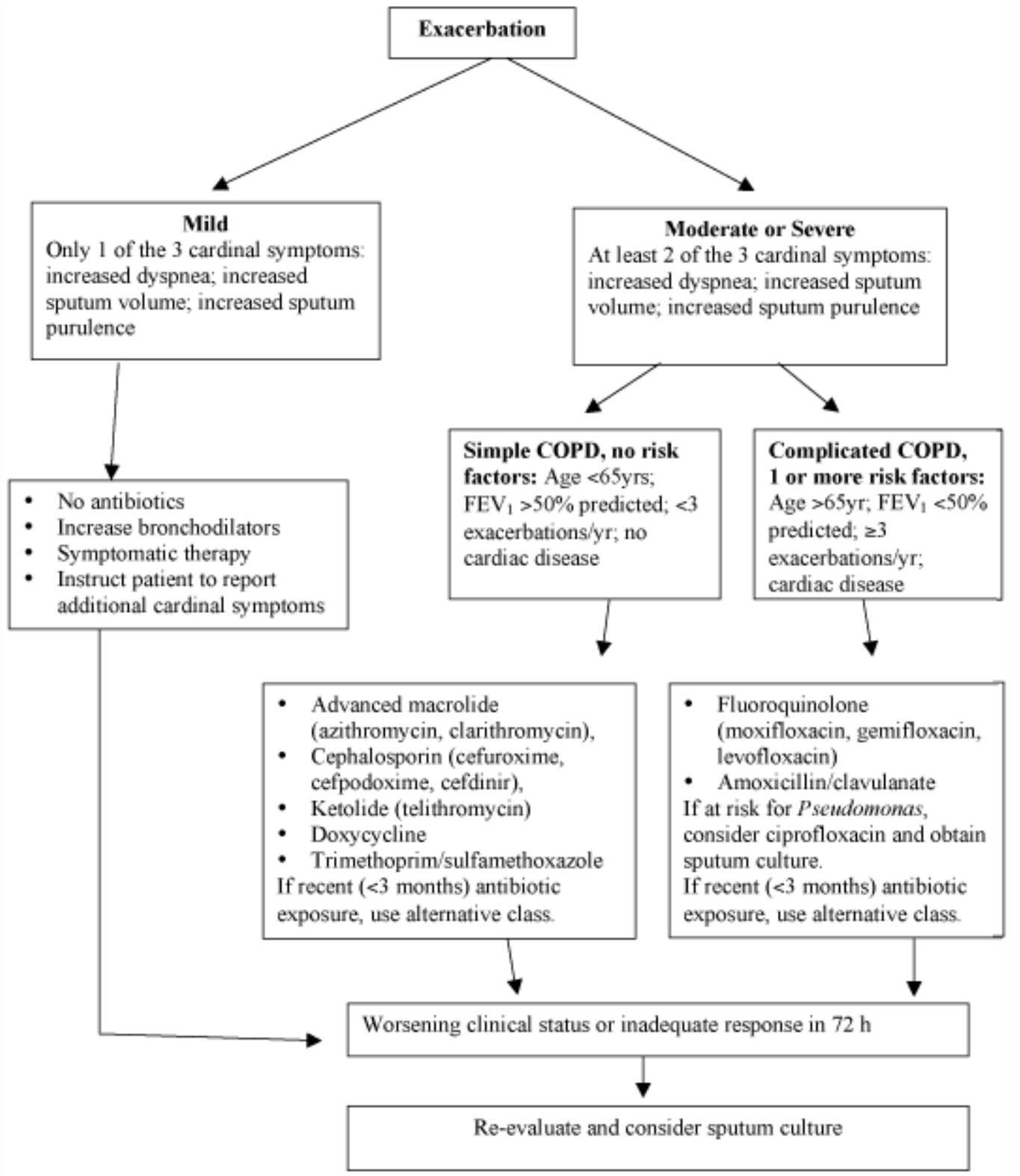
Hospital Room

Marked increase in symptom intensity[a]
Severe COPD
Onset of new physical signs
No response to outpatient management
Significant comorbidities[b]
Frequent exacerbations
Diagnostic uncertainty
Older age
Insufficient home support

Intensive Care Unit

Severe dyspnea not responsive to emergency therapy
Changes in mental status
Hypoxemia, hypercapnia, and/or acidosis despite supplemental oxygen and NIV
Need for invasive ventilation
Hemodynamic instability

[a] Sputum changes, dyspnea, chest tightness, malaise, fatigue, decreased exercise tolerance, fever, wheezing, decreased breath sounds, increased need for bronchodilators.
[b] Pneumonia, arrhythmia, congestive heart failure, diabetes, renal or hepatic failure.
COPD: chronic obstructive pulmonary disease; NIV: noninvasive ventilation.



Antibiotic Recommendations

Patient Characteristics	Pathogens	Therapy (no particular order)
Uncomplicated exacerbations <4 per year No comorbidities FEV_1 >50% predicted Resistance uncommon	*Streptococcus pneumoniae* *Haemophilus influenzae* *Moraxella catarrhalis* *Haemophilus parainfluenzae*	Azithromycin or clarithromycin 2nd- or 3rd-generation cephalosporin Doxycycline
Complicated exacerbations Age ≥65 years >4 per year FEV_1 36%-49% predicted	Above plus drug-resistant pneumococci, beta-lactamase-producing *H influenzae*, and *M catarrhalis*	Amoxicillin/clavulanate Fluoroquinolone with enhanced pneumococcal activity (levofloxacin, gemifloxacin, or moxifloxacin)
Complicated exacerbations with risk of Pseudomonas aeruginosa Chronic bronchial sepsis[b] Chronic corticosteroids Nursing home resident >4 per year FEV_1 >35% predicted	Enteric gram-negatives Above plus *P aeruginosa*	Levofloxacin[a] Possible IV therapy: beta-lactamase-resistant penicillin with antipseudomonal activity 3rd- or 4th-generation cephalosporin with antipseudomonal activity

[a] *Fluoroquinolone with enhanced pneumococcal/antipseudomonal activity.*
[b] *In sepsis, addition of aminoglycoside considered for double antipseudomonal coverage.*
FEV_1: forced expiratory volume in one second.

Indications for Invasive Mechanical Ventilation

Absolute indications	Relative indications
Cardiac or respiratory arrest	Severe dyspnea with use of accessory muscles
Failure of noninvasive ventilation or presence of exclusion criteria	Respiratory rate >35 breaths/min
Persistent hypoxemia (PaO_2<40 mm Hg) despite receiving optimal treatment	Vascular complications (hypotension, shock, heart failure)
Worsening of respiratory acidosis (pH<7.25) despite receiving optimal treatment	Other complications (severe pneumonia, pulmonary thromboembolism, etc)

HOSPITAL MANAGEMENT OF ACUTE EXACERBATIONS OF COPD

Definition
COPD is characterised by airflow obstruction, usually progressive, not fully reversible and not changing markedly over several months. It is predominantly caused by smoking

Severity of Airflow Obstruction
FEV1 50 – 80% predicted = **Mild** **FEV1** 30 – 49% predicted = **Moderate** **FEV1** < 30% predicted = **Severe**

Exacerbation characteristics include some or all of these:
- ↑ Dyspnoea
- ↑ Sputum volume & purulence
- ↑ Cough
- ↑ Wheeze / chest tightness
- ↑ Fatigue
- ↑ Fluid retention
- ↓ GCS
- ↓ Exercise Tolerance

Differential Diagnosis in COPD patients includes:
- Pneumonia
- Pneumothorax
- Pulmonary Oedema
- Lung Cancer
- Upper Airway Obstruction
- Pleural Effusion

Initial Assessment
- CXR
- ABG – note inspired FiO_2
- ECG
- FBC / U&Es
- Theophylline level if on it
- Sputum M C&S if purulent
- Blood cultures if pyrexial

Standard Therapy
- ↑ dose of bronchodilators
- Oral Prednisolone 30mg daily for 7-14 days
- Oxygen to maintain SaO_2 >90% but < 93%
- Antibiotics if sputum more purulent and / or pneumonia
- IV Theophylline if inadequate response to regular nebulised bronchodilators
- Physiotherapy using PEEP to help clear sputum when necessary
- No need for daily peak flow unless asthma suspected

Consider Hospital at Home or assisted early discharge if:
- Able to cope / good social circumstances / telephone
- Mild dyspnoea
- General condition and level of activity satisfactory
- Not on LTOT
- No confusion
- Onset not rapid
- No CXR consolidation
- pH > 7.35
- PO_2 > 7kPa

Indicators of a Severe Exacerbation
- Marked dyspnoea / tachypnoea
- Use of accessory respiratory muscles (sternomastoid and abdominal) at rest
- Pursed lip breathing
- New onset cyanosis
- New onset peripheral oedema
- Marked reduction in activities of daily living
- Acute confusion

In Severe Exacerbation
- NIV for persistent hypercapnic respiratory failure despite optimal medical therapy
- NIV should be delivered in dedicated setting with trained staff
- IV respiratory stimulants only where NIV not available
- Ceilings of treatment should be agreed
- Referral for consideration of intubation and ventilation in cases of progressive exhaustion and worsening ABGs
- Evidence of advanced directive should be sought

Maintenance management
- SaO_2 monitoring in non-hypercapnic, non acidotic respiratory failure
- Otherwise check ABGs intermittently and prior to discharge
- Re-establish optimal inhaled therapy pre discharge including checking inhaler technique
- Check BMI and spirometry pre discharge
- If still requiring O_2 arrange O_2 cylinder or interim LTOT on discharge, pending formal assessment when stable
- Consider pulmonary rehabilitation referral
- Provide written guided self-management plan to include advice on acute exacerbations
- Confirm 'flu' vaccine plans and home care support
- Consider follow up by respiratory nurse team in 4-6 weeks for those patients considered more vulnerable to early readmission

The BTS COPD CONSORTIUM

67 Year old Male with shortness Of Breath with exertion

Your patient is a 67 year old male who complains of progressively worsening shortness of breath with exertion over the last year. He currently smokes half a pack of cigarettes daily and has accumulated 45 pack years. He uses a short acting beta agonist 3-4 times a day with limited relief. He is no longer able to ride a bike with his grandchildren.
His last hospitalization was 4 months ago secondary to right lower lobe pneumonia. He does not complain of weight loss or loss of appetite.
He has a past medical history of dietary controlled diabetes and mild osteoarthtitis.
Medications include Albuterol and Celecoxib.
On exam respiratory rate is 22 per minute; chest exam reveals mild end expiratory wheezing without use of accessory muscles of respiration and no retractions. No clubbing, cyanosis or lower extremity edema is noted. Spirometry reveals an FVC of 78% predicted, FEV1 of 62% predicted and FEV1/FVC of 68%, post bronchodilator.