COPD

CHRONIC OBSTRUCTIVE PULMONARY DISEASE

DR.PARISA REZAEIFAR

Definition

- **persistent respiratory symptoms and airflow limitation that is not fully reversible**
- ***COPD includes:***
  - **emphysema, an anatomically defined condition characterized by destruction of the lung alveoli with air space enlargement**
  - **Chronic bronchitis, a clinically defined condition with chronic cough and phlegm;**
  - **small airway disease, a condition in which small bronchioles are narrowed and reduced in number.**

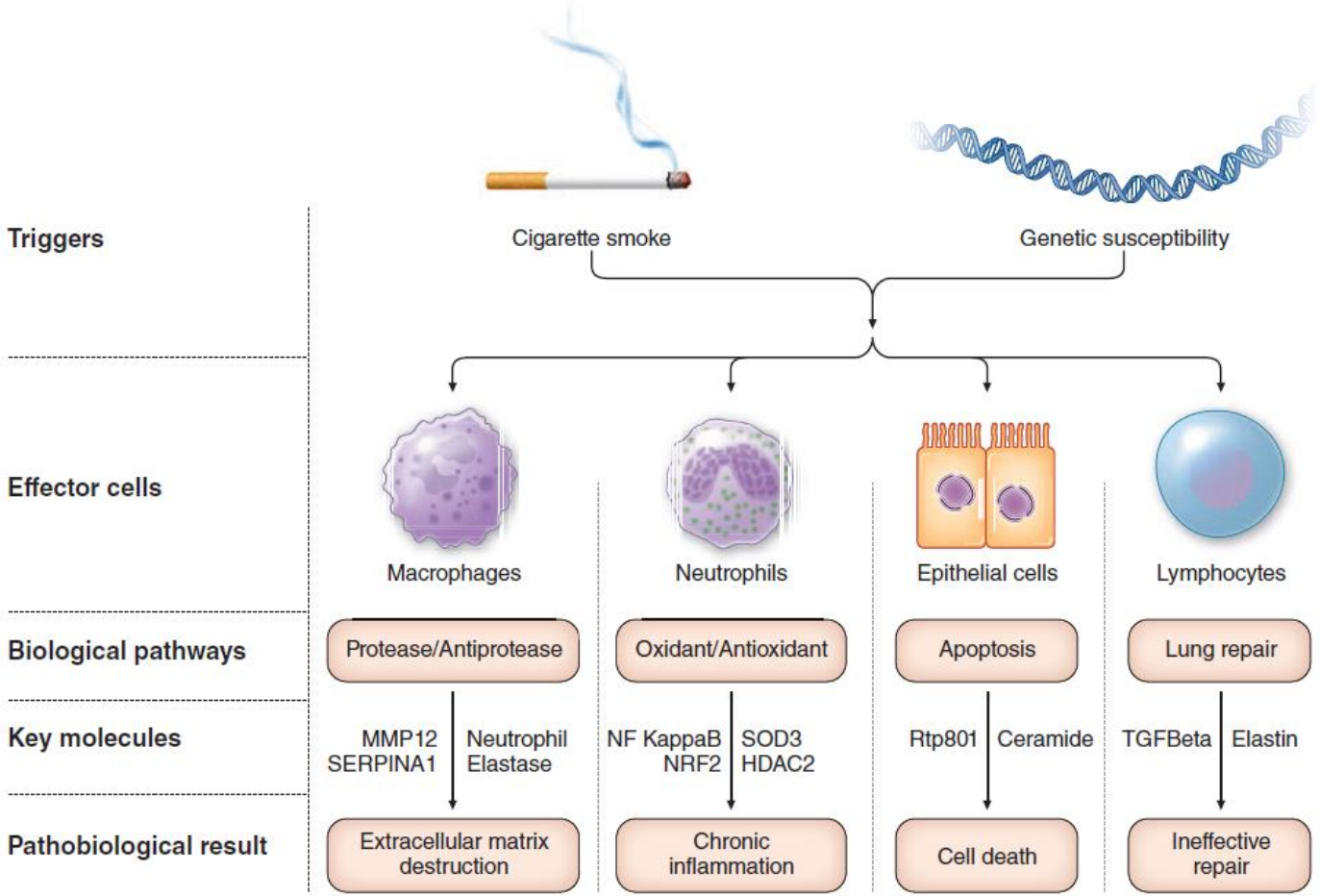
Epidemiology

- **COPD is the third leading cause of death and affects >10 million persons in the United States.**
- **Estimates suggest that COPD will rise to the third most common cause of death worldwide by 2020.**

Pathogenesis

- **The precise biological mechanisms leading to COPD have not been determined, a number of key cell types, molecules, and pathways have been identified from cell-based and animal model studies.**

1. **Chronic exposure to cigarette smoke in genetically susceptible individuals triggers inflammatory and immune cell recruitment within large and small airways and in the terminal air spaces of the lung**
2. **Inflammatory cells release proteinases that damage the extracellular matrix (Elastin) supporting airways, vasculature, and gas exchange surfaces of the lung**
3. **Structural cell death occurs through oxidant-induced damage, cellular senescence,and proteolytic loss of cellular-matrix attachments leading to extensive loss of smaller airways, vascular pruning, and alveolar destruction.**
4. **Disordered repair of elastin and other extracellular matrix components contributes to air space enlargement and emphysema.**


Triggers
Cigarette smoke
Genetic susceptibility
Effector cells
Macrophages
Neutrophils
Epithelial cells
Lymphocytes
Biological pathways
Protease/Antiprotease
Oxidant/Antioxidant
Apoptosis
Lung repair
Key molecules
MMP12
SERPINA1
Neutrophil Elastase
NF KappaB
NRF2
SOD3
HDAC2
Rtp801
Ceramide
TGFBeta
Elastin
Pathobiological result
Extracellular matrix destruction
Chronic inflammation
Cell death
Ineffective repair

PATHOLOGY

- **Cigarette smoke exposure may affect the large airways, small airways (≤2 mm diameter), and alveoli**
- **Changes in large airways because of mucus gland enlargement and goblet cell hyperplasia cause cough and sputum production (chronic Brochitis), while changes in small airways and alveoli are responsible for physiologic alterations.**
- **The early stages of COPD, based on the severity of airflow obstruction (GOLD1 & 2), appear to be primarily associated with medium and small airway disease. The major site of increased resistance in COPD is in airways ≤2 mm diameter.**
- **Advanced stages of COPD (GOLD 3 and 4) are typically characterized by extensive emphysema**

PATHOPHYSIOLOGY

- **AIRFLOW OBSTRUCTION: chronically reduced ratio of FEV1/FVC. In contrast to asthma**
- **HYPERINFLATION: "air trapping" (increased residual volume and increased ratio of residual volume to total lung capacity)**
- **GAS EXCHANGE:**
  - **Pao2 usually remains near normal until the FEV1 is decreased to ~50%**
  - **elevation of Paco2 is not expected until the FEV1 is <25%**
  - **Pulmonary hypertension severe enough to cause cor pulmonale and right ventricular failure due to COPD typically occurs in individuals who have marked decreases in FEV1 (<25% of predicted) and chronic hypoxemia (Pao2 <55 mmHg);**

TABLE 286-1 GOLD Criteria for Severity of Airflow Obstruction in COPD

GOLD STAGE	SEVERITY	SPIROMETRY
I	Mild	$FEV_1/FVC < 0.7$ and $FEV_1 \geq 80\%$ predicted
II	Moderate	$FEV_1/FVC < 0.7$ and $FEV_1 \geq 50\%$ but $< 80\%$ predicted
III	Severe	$FEV_1/FVC < 0.7$ and $FEV_1 \geq 30\%$ but $< 50\%$ predicted
IV	Very severe	$FEV_1/FVC < 0.7$ and $FEV_1 < 30\%$ predicted

RISK FACTORS

- **CIGARETTE SMOKING: expressed as pack-years which is the most highly significant predictor of FEV1**
- **AIRWAY RESPONSIVENESS: Both asthma and airway hyper responsiveness are risk factors for COPD.**
- **RESPIRATORY INFECTIONS :controversial**
- **OCCUPATIONAL EXPOSURES: coal mining, gold mining, and cotton textile dust**
- **AMBIENT AIR POLLUTION : biomass, air pollution(?)**
- **PASSIVE, OR SECOND-HAND, SMOKING EXPOSURE: maternal smoking, second hand smoking in severe reduction of PFT is uncertain**
- **GENETIC CONSIDERATIONS: α1 Antitrypsin Deficiency**

CLINICAL PRESENTATION & PHYSICAL EX.

- **cough, sputum production, and exertional dyspnea.**
- **prolonged expiratory phase and ,wheezing, barrel chest and enlarged lung volumes, use of accessory muscles, cyanosis, visible in the lips and nail beds.**
- **pink puffers & Blue bloaters**
- **cachexia, with significant weight loss, bitemporal wasting, and diffuse loss of subcutaneous adipose tissue.**
- **Signs of overt right heart failure**
- **Hoover’s sign**
- **Clubbing**

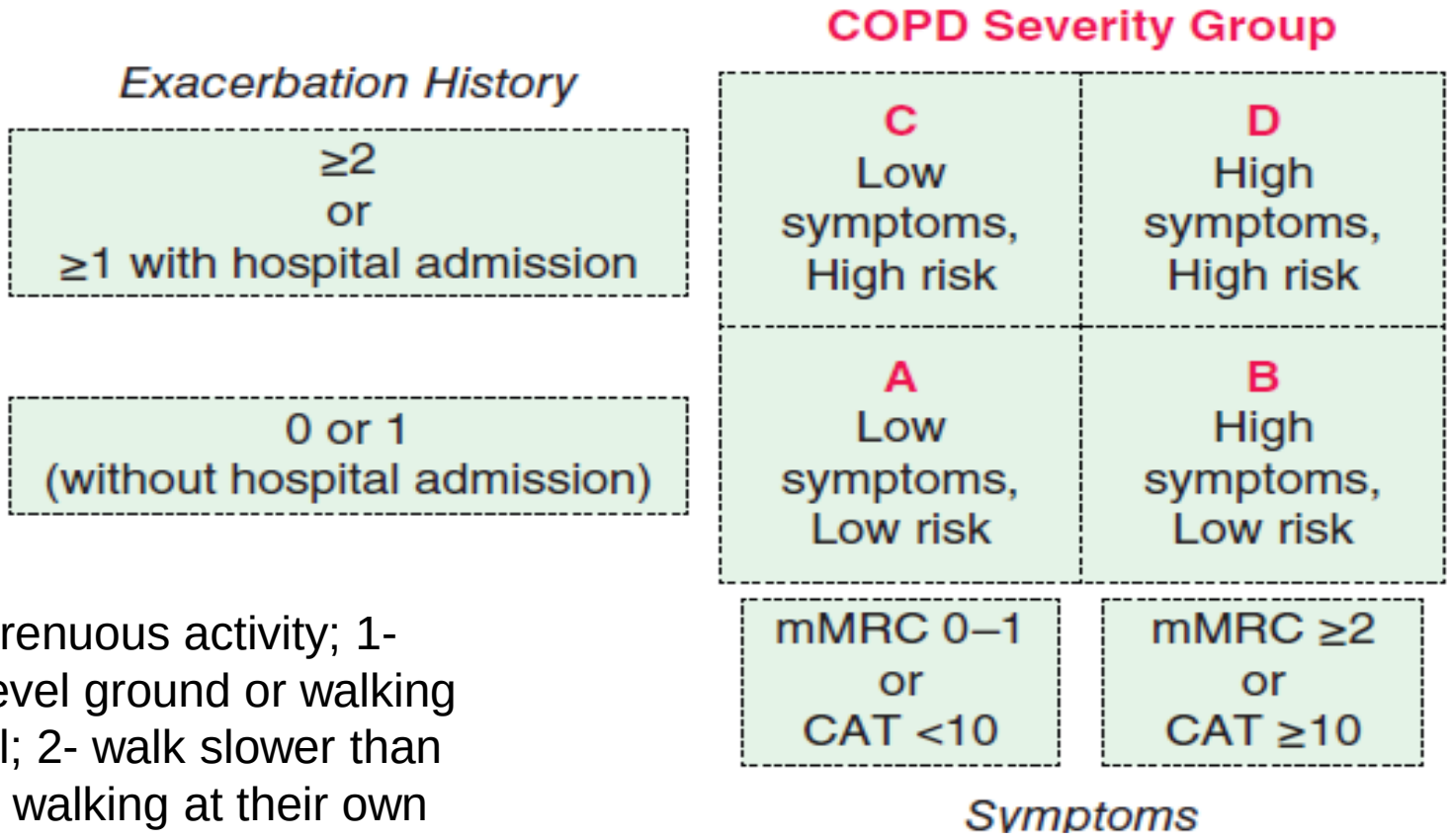
TREATMENT

- **The two main goals of therapy :**

1. **To provide symptomatic relief (reduce respiratory symptoms, improve exercise tolerance, improve health status)**

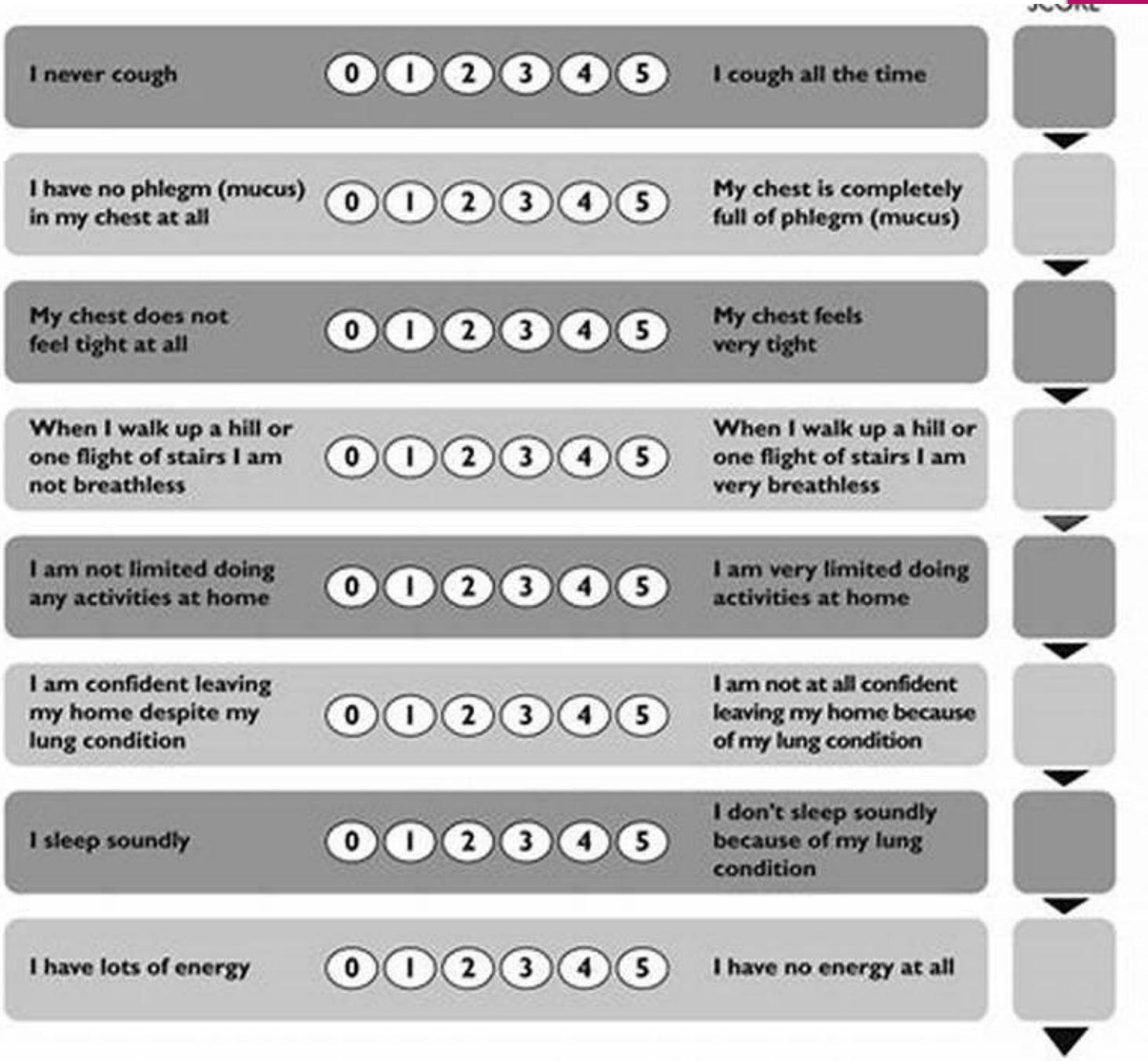
2. **To reduce future risk (prevent disease progression, prevent and treat exacerbations, and reduce mortality).**

COPD severity assessment



0-only with strenuous activity; 1-hurrying on level ground or walking up a slight hill; 2- walk slower than peers or stop walking at their own pace; 3-walking about 100 yards or after a few minutes on level ground; 4-too breathless to leave the house or when dressing.

CAT—COPD Assessment Test.

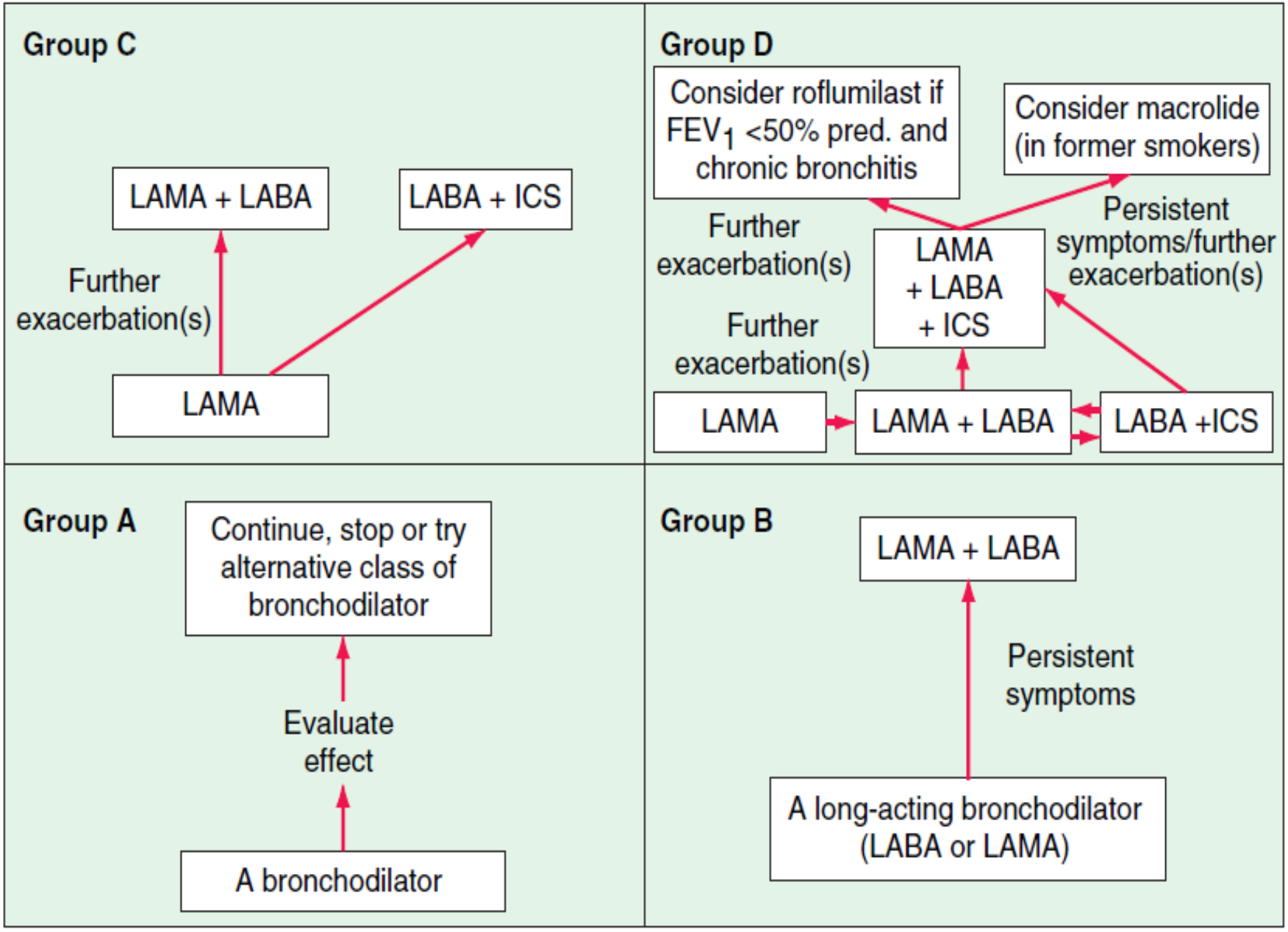


PHARMACOTHERAPY

- **Smoking Cessation: significant improvement in the rate of decline in pulmonary function, nicotine, bupropion; and varenicline**
- **Anticholinergic Muscarinic Antagonists**
- **SABA & LABA**
- **Inhaled Corticosteroids; it should be considered in patients with frequent exacerbations, defined as two or more per year, and inpatients with features of asthma, such as eosinophilia.**
- **Oral Glucocorticoids**
- **Theophylline**

- **PDE4 Inhibitors:roflumilast**
- **Antibiotics : macrolid**
- **Oxygen**
- **α1AT Augmentation Therapy**

- **smoking cessation, oxygen therapy in chronically hypoxemic patients, and lung volume reduction surgery (LVRS) in selected patients with emphysema—have been demonstrated to improve survival of patients with COPD**
- **(ICS) and muscarinic antagonists is indefinitive**


Group C
LAMA + LABA
LABA + ICS
Further exacerbation(s)
LAMA
Group D
Consider roflumilast if FEV1 <50% pred. and chronic bronchitis
Consider macrolide (in former smokers)
Further exacerbation(s)
LAMA + LABA + ICS
Persistent symptoms/further exacerbation(s)
Further exacerbation(s)
LAMA
LAMA + LABA
LABA +ICS
Group A
Continue, stop or try alternative class of bronchodilator
Evaluate effect
A bronchodilator
Group B
LAMA + LABA
Persistent symptoms
A long-acting bronchodilator (LABA or LAMA)

EXACERBATIONS OF COPD

- **Exacerbations are episodic acute worsening of respiratory symptoms, including increased dyspnea, cough, wheezing, and/ or change in the amount and character of sputum**
- **RF:**

1. **The strongest single predictor of exacerbations is a history of a previous exacerbation**
2. **patients with severe (FEV1 <50% predicted) or very severe airflow obstruction (FEV1 <30% predicted) on average have 1–3 episodes per year**
3. **Elevated ratio of the diameter of the pulmonary artery to aorta on chest CT**
4. **gastroesophageal reflux**

TREATMENT OF ACUTE EXACERBATIONS

- **Bronchodilators**
- **Antibiotics**
- **systemic glucocorticoids**
- **Oxygen**
- **Mechanical Ventilatory Support**

Contraindications to NIPPV include cardiovascular instability, impaired mental status, inability to cooperate, copious secretions or the inability to clear secretions, craniofacial abnormalities or trauma precluding effective fitting of mask, extreme obesity, or significant burns.