Chronic Obstructive Lung Disease

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ACOI Board Review 2018

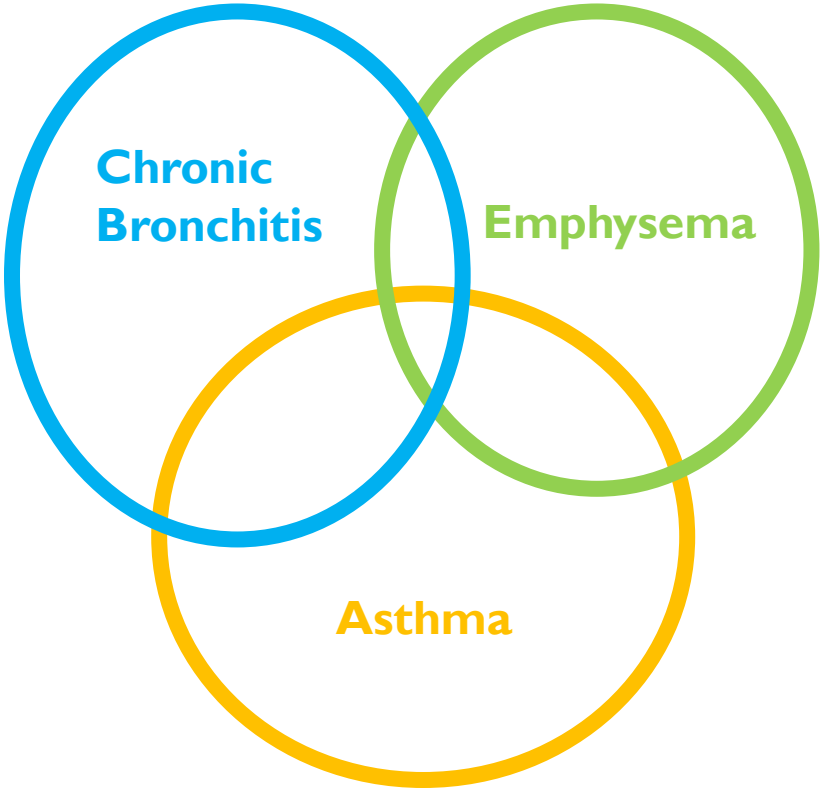
American College of Osteopathic Internists

Disclosures

- No Disclosures

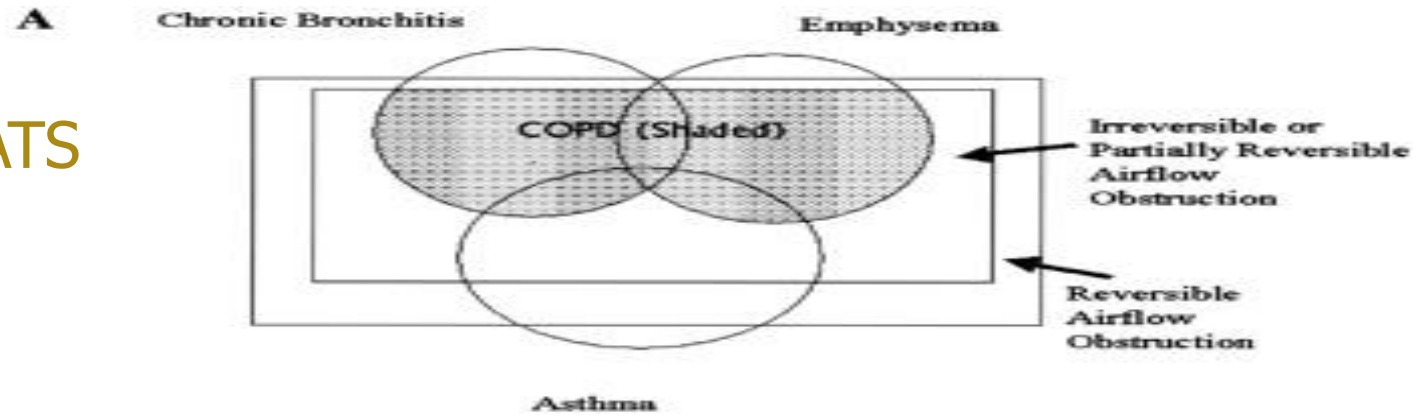
Obstructive Lung Diseases

- COPD
  - Chronic Bronchitis
  - Emphysema
- Asthma
- Other
  - Bronchiectasis
  - Bronchiolitis
  - Cystic Fibrosis
  - Alpha 1 anti-trypsin deficiency

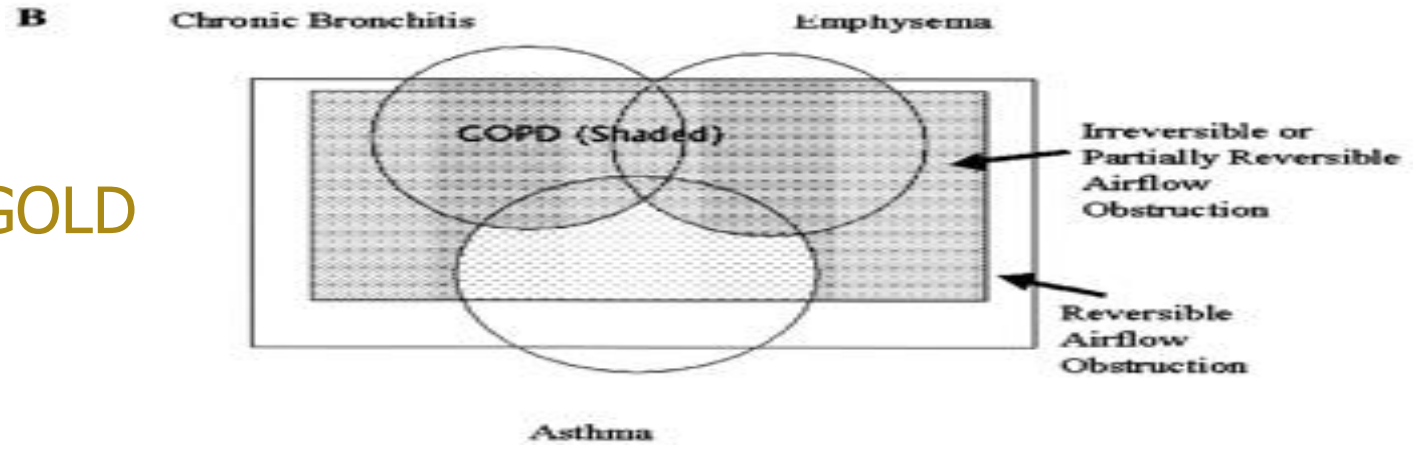


Inter-relationship: Inflammation and Bronchial Hyperreactivity

ATS



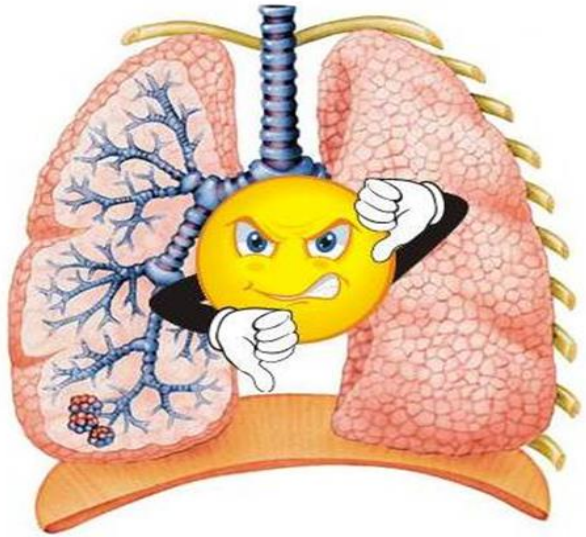
GOLD

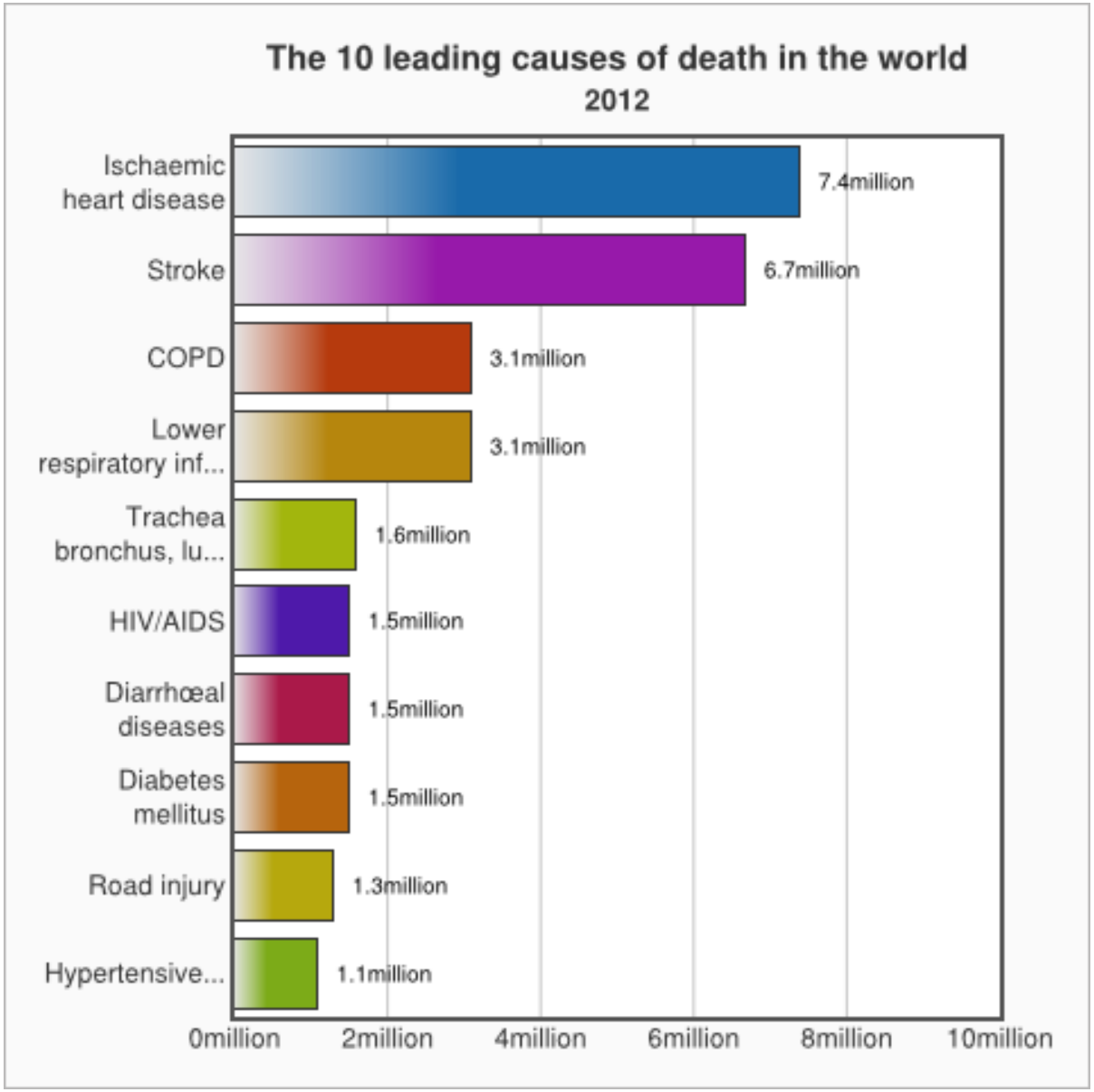


CHEST 2002; 121: 121S-126S

COPD

- THIRD leading cause of death worldwide
- It is the only leading cause of death whose prevalence is increasing!

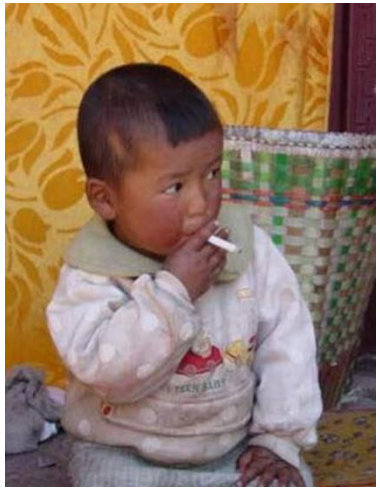




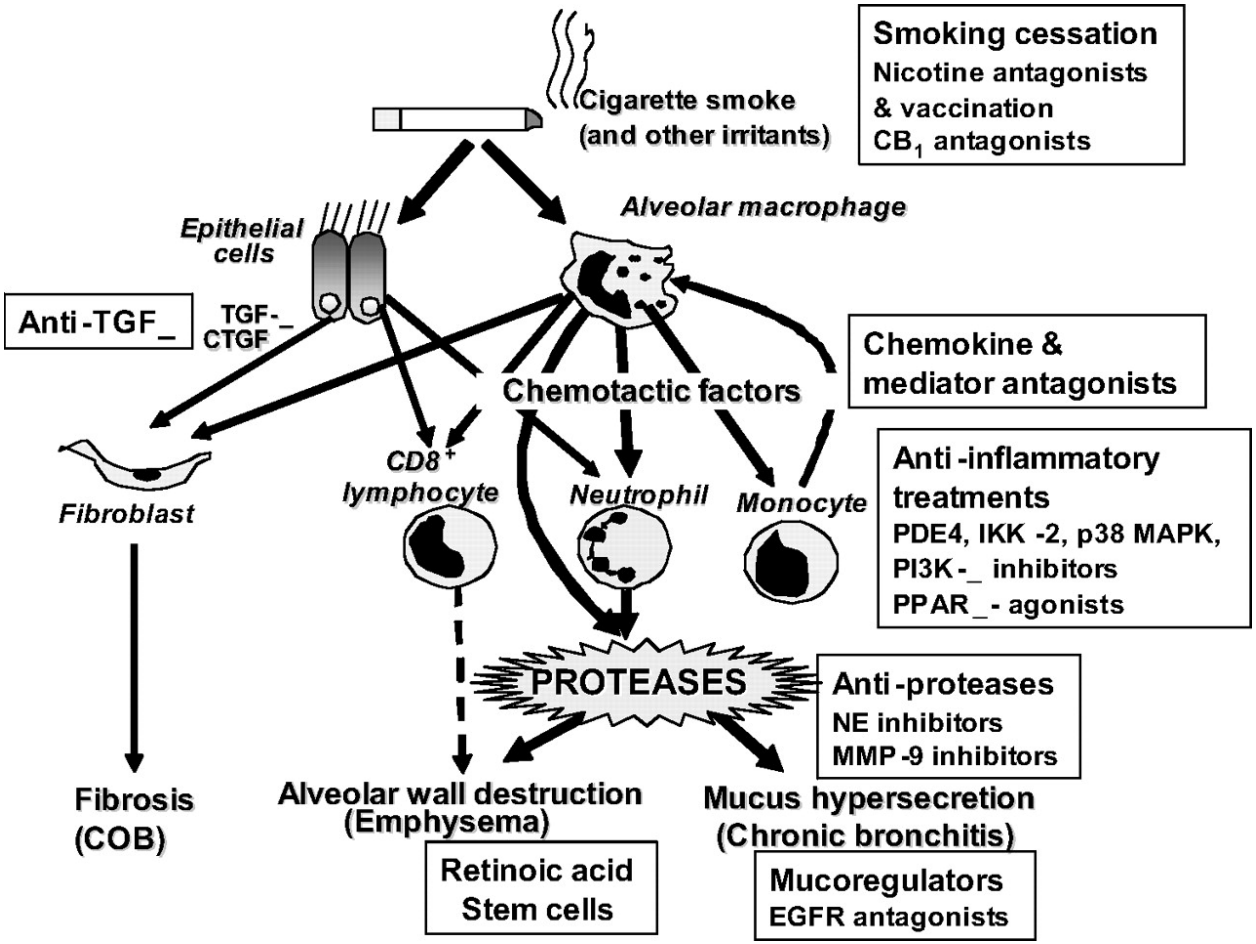
http://www.who.int/mediacentre/factsheets

COPD Risk Factors

- Cigarette smoking
- Occupational exposures
  - Silica, formaldehyde, toluene, nickel, cadmium etc
- Air pollution
- Biomass fuel
- Hyperresponsive airway
- Asthma
- Genetic factors



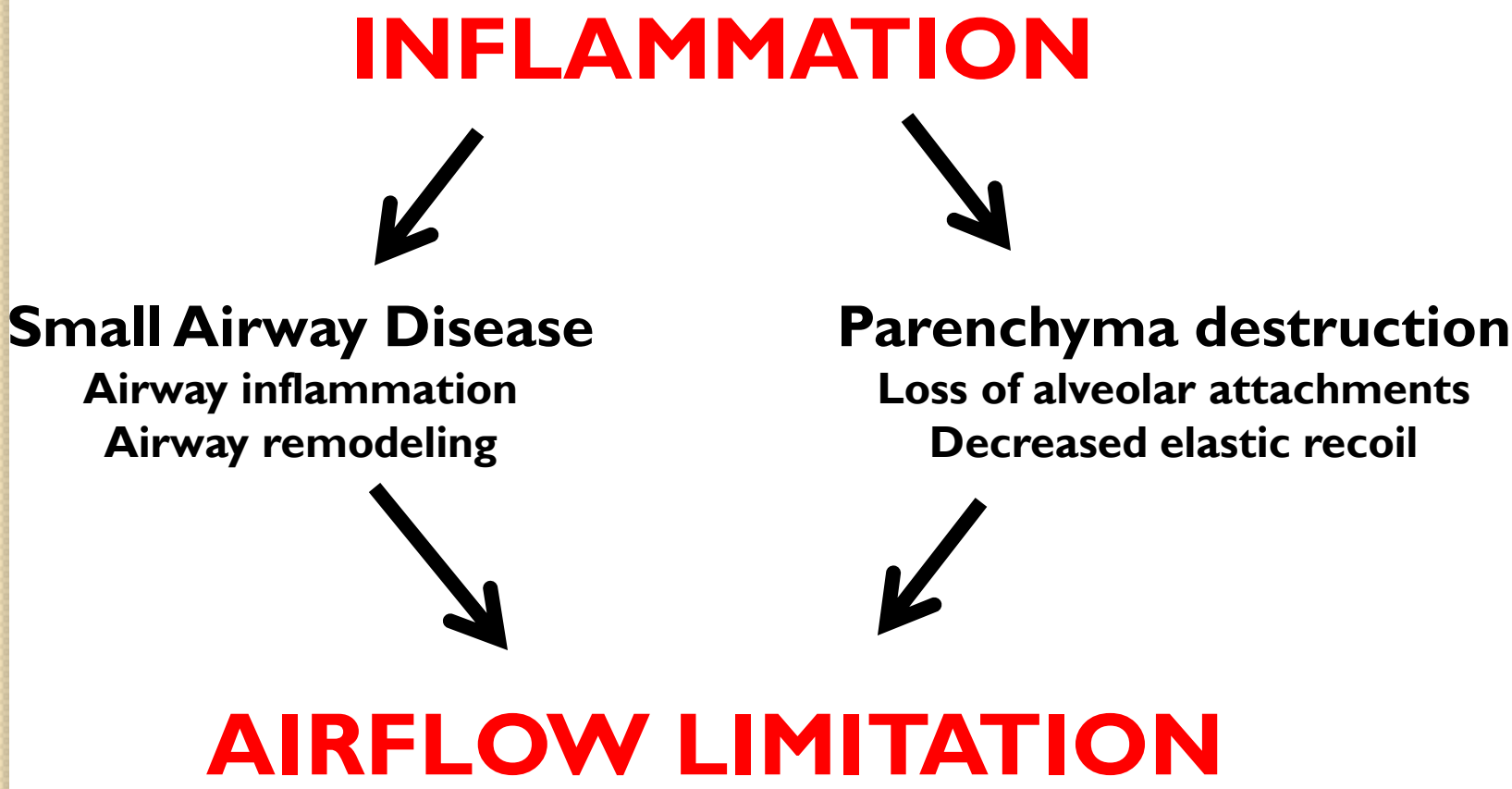
Pathogenesis of COPD



CHEST 2008; 134(8): 1278-1288

Inflammatory Mediators: COPD

	COPD
Cells	Neutrophils ++, Macrophages +++, CD8+ (Tc1)
Key Mediators	IL-8, TNF, IL-1b, IL-6, NO
Oxidative Stress	+++
Site of Disease	Peripheral airways, Lung parenchyma, Pulmonary vessels
Consequences	Squamous metaplasia Mucous metaplasia Small airway fibrosis Parenchymal destruction Vascular remodeling
Response to therapy	Small BD response Poor steroid response


INFLAMMATION
Small Airway Disease
Airway inflammation
Airway remodeling
Parenchyma destruction
Loss of alveolar attachments
Decreased elastic recoil
AIRFLOW LIMITATION

Inflammation and Exacerbations

- Exacerbations represent a further amplification of the inflammatory response in the airways of patients with COPD, and may be triggered by infection with bacteria or viruses or by environmental pollutants

COPD: Chronic Bronchitis

- Defined as excessive tracheobronchial mucus production associated with cough and sputum expectoration for at least 3 months a year for more than 2 consecutive years
- +/- reversible or fixed airway obstruction

COPD: Chronic Bronchitis Pathology

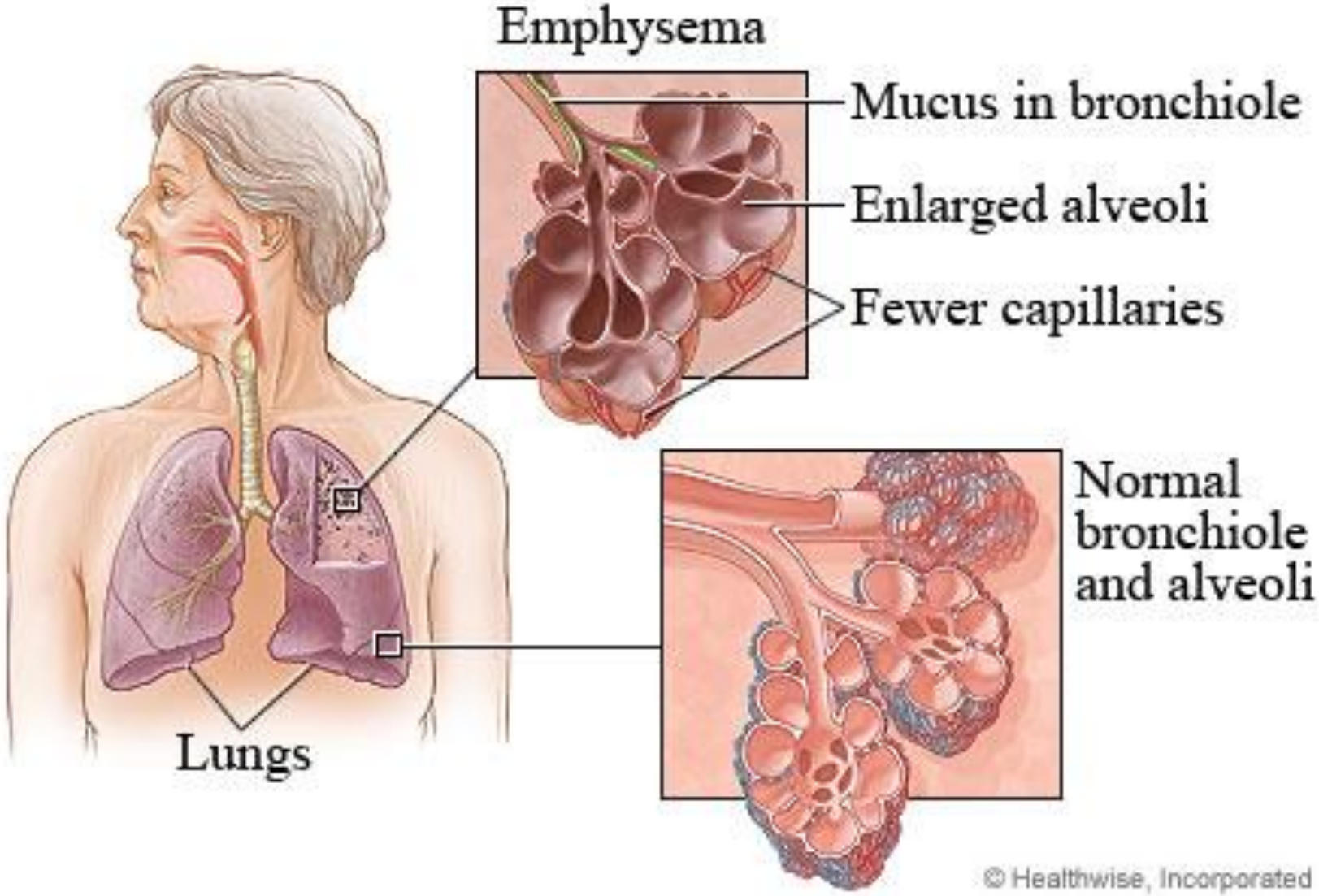
- Large (cartilaginous) airways
  - Hyperplasia and hypertrophy of the mucus producing glands in the submucosa
- Small (non-cartilaginous) airway
  - Goblet cell hyperplasia
  - Mucosal/submucosal inflammation
  - Edema
  - Peribronchial fibrosis
  - Plugs
  - Smooth muscle hypertrophy
- MOSTLY RESPONSIBLE FOR AIRWAY OBSTRUCTION

Normal bronchi

Bronchitis

Mucus membrane swelling
No muscle contraction
Copious mucus secretion
Narrowing of bronchial opening

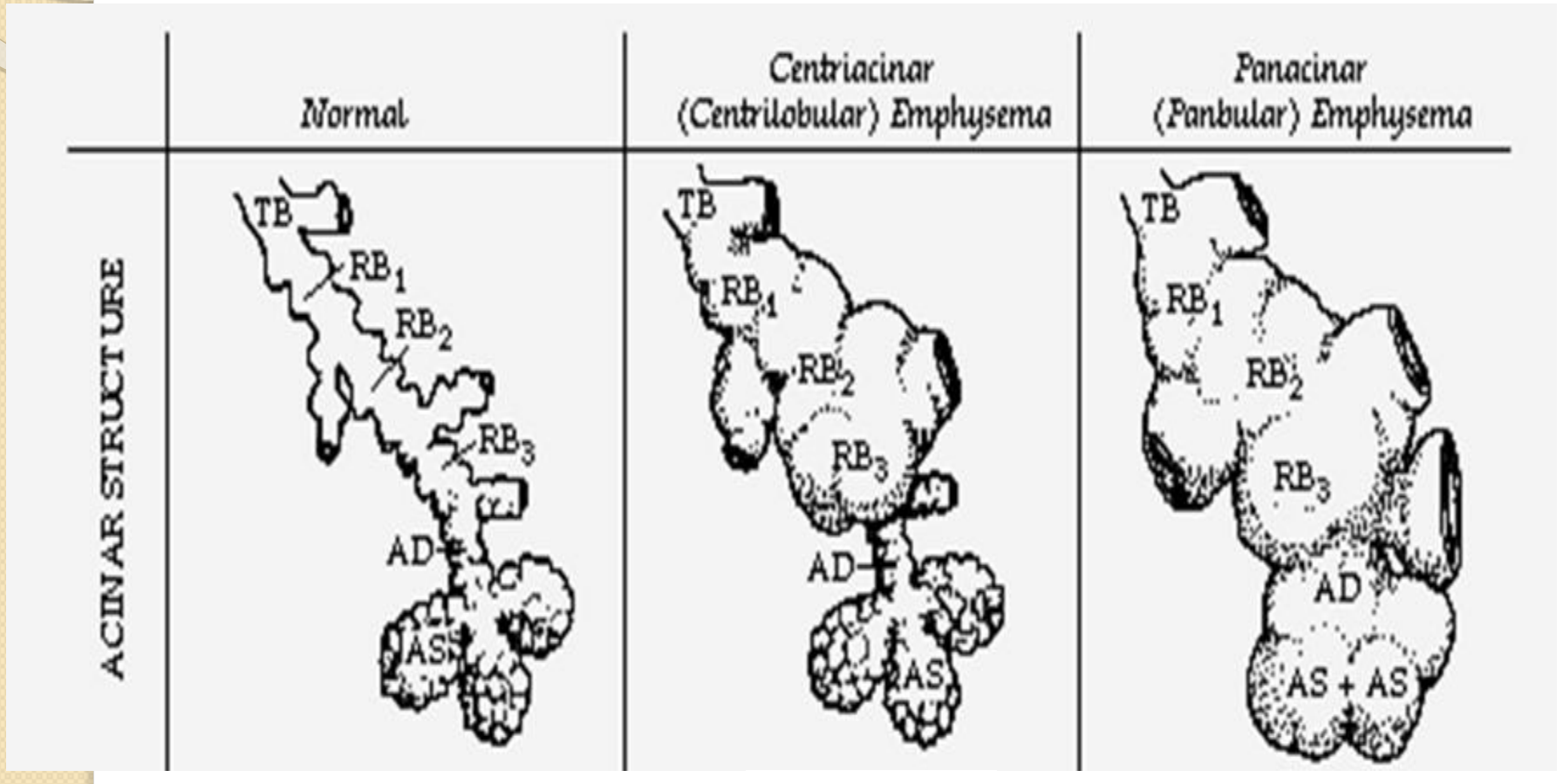
A.D.A.M.


Emphysema
Mucus in bronchiole
Enlarged alveoli
Fewer capillaries
Normal bronchiole and alveoli
Lungs
© Healthwise, Incorporated

Morphologic Types of Emphysema

Upper lobe

Lower lobe



Alpha 1 AT

COPD Definition: GOLD

- 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
- Airflow limitation that is NOT fully reversible
- Airflow limitation is usually persistent and progressive
- Associated with an abnormal inflammatory response to noxious particles and gases

COPD Definition: GOLD

- 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.

- Spirometric evaluation is necessary for the clinical diagnosis.

COPD Definition: GOLD

- A post bronchodilator FEV1/FVC <70%
- In combination with an FEV1 <80% predicted
- In an individual with cough, sputum production or dyspnea, and exposure to risk factors confirms the diagnosis

Severity of COPD: GOLD

Stage	Severity	FEV1/FVC	FEV1 (%PRED)
1	Mild	< 70%	80% or >
2	Moderate	< 70%	50 to 79%
3	Severe	< 70%	30 to 49%
4	Very Severe	< 70%	< 30% or < 50 with CRF

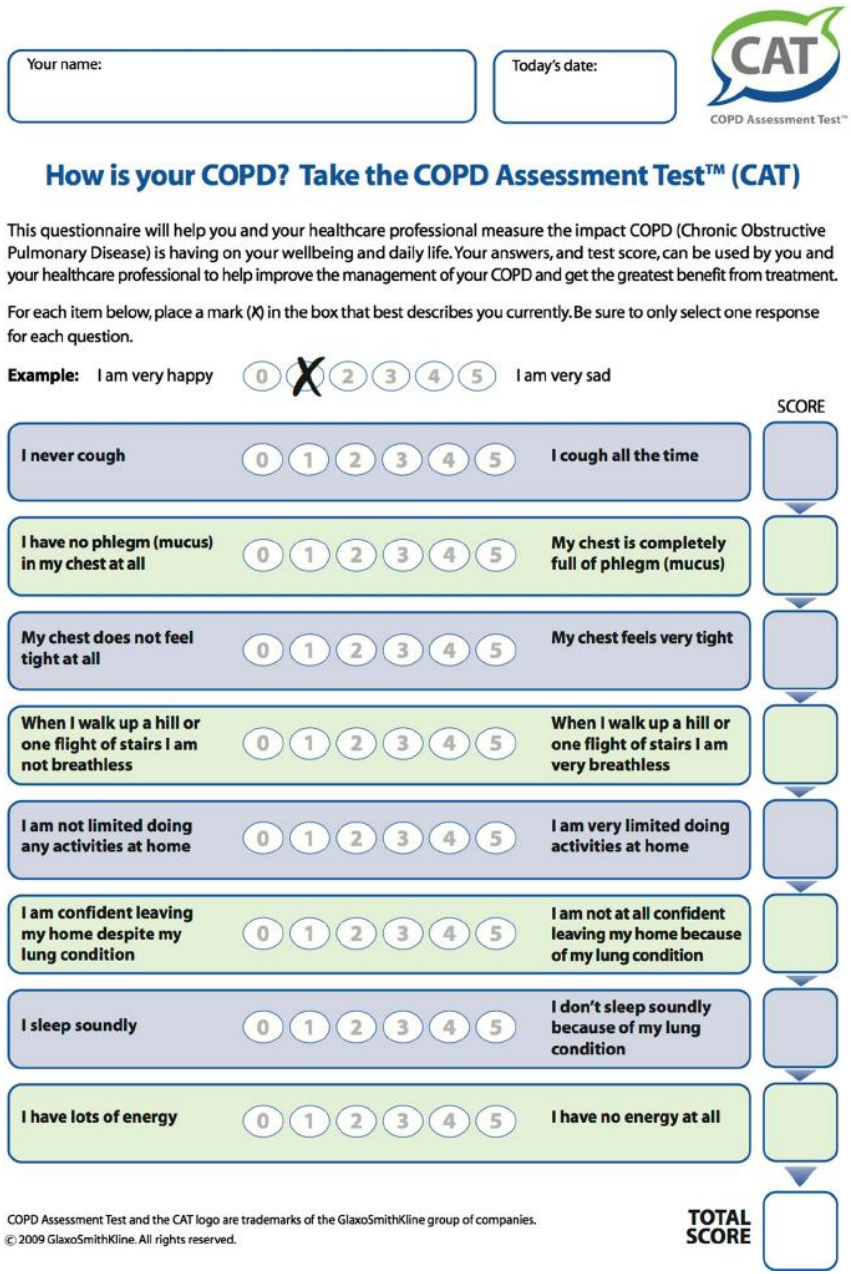
Definition of Reversibility

ATS	Increase in FEV1 of 200 cc and a 12% from baseline following BD
ERS	Greater than 10% improvement in FEV1 post BD
GOLD	Increase in FEV1 of 200 cc and a 12% improvement in FEV1 post Tx with either BD or ICS

Assessment

- CAT (COPD Assessment Test)
  - Numeric scale relating 8 functional parameters
    - Cough, sputum, walking, sleeping, energy, etc
  - Lower score=fewer symptoms
  - Higher score=more symptoms
- mMRC Questionnaire (Modified Medical Research Council)
  - Degree of breathlessness using 0-4 scale
  - Higher values indicating decreasing exercise tolerance

CAT



Your name:

Today's date:

CAT
COPD Assessment Test™

How is your COPD? Take the COPD Assessment Test™ (CAT)

This questionnaire will help you and your healthcare professional measure the impact COPD (Chronic Obstructive Pulmonary Disease) is having on your wellbeing and daily life. Your answers, and test score, can be used by you and your healthcare professional to help improve the management of your COPD and get the greatest benefit from treatment.

For each item below, place a mark (X) in the box that best describes you currently. Be sure to only select one response for each question.

Example: I am very happy 0 X 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	

TOTAL SCORE

mMRC Questionnaire

Modified Medical Research Council (mMRC) Questionnaire for Assessing Severity of Breathlessness

Score	Description of Dyspnea	Severity
0	I get breathless only with strenuous exercise	None
1	I get short of breath when hurrying on level ground or walking up a slight hill	Mild
2	On level ground, I walk slower than other people my age because of breathlessness, or I have to stop for breath when walking at my own pace	Moderate
3	I stop for breath after walking approximately 100 yards or after a few minutes on level ground	Severe
4	I am too breathless to leave the house, or breathless when dressing	Very severe

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GOLD: Severity of COPD

GOLD Model for Classifying Severity of Disease in COPD

Patient Category	Characteristics	Spirometric Classification[a]	Exacerbations Per Year	CAT Score	mMRC Score
A	Low risk, fewer symptoms	GOLD 1-2	≤1	<10	0-1
B	Low risk, more symptoms	GOLD 1-2	≤1	≥10	≥2
C	High risk, fewer symptoms	GOLD 3-4	≥2	<10	0-1
D	High risk, more symptoms	GOLD 3-4	≥2/≥1 with hospital admission	≥10	≥2

CAT = COPD Assessment Test; mMRC = Modified Medical Research Council.

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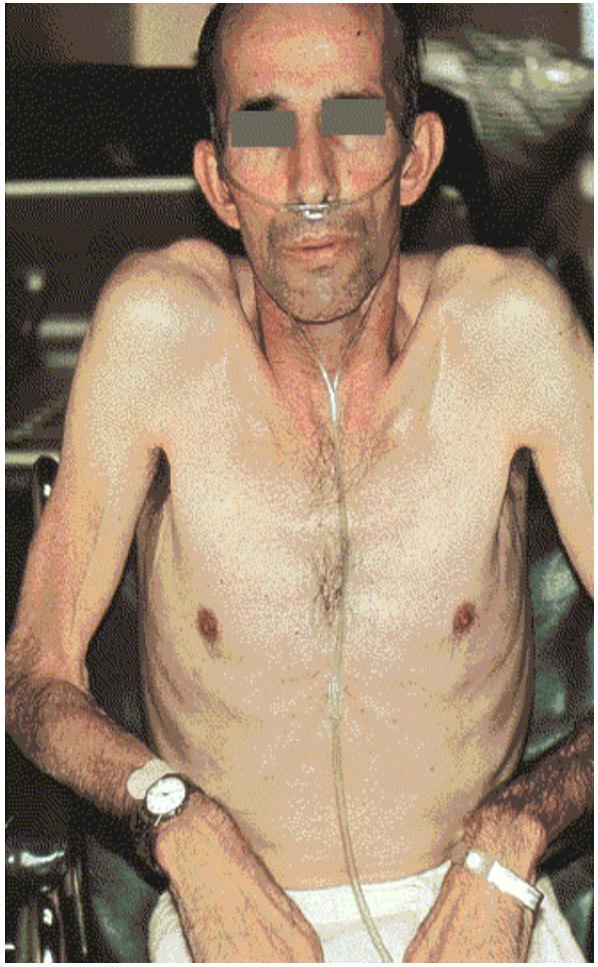
Reasons for delay in Diagnosis

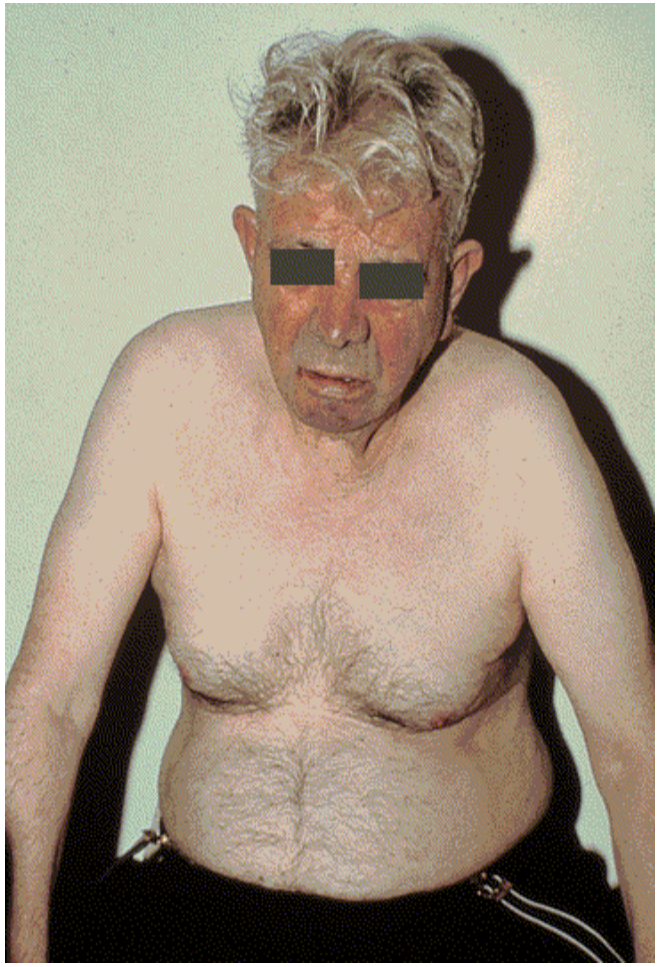
- Patient does not seek medical attention until late in disease process (ie emphysema)
- Physicians focus on treatment of symptoms rather than disease prevention
- We may be looking at the wrong thing (waiting too long until PFT, x-rays, spirometry, etc are abnormal).

Diagnostic Techniques

- History/Physical (symptoms – more sensitive)
- Pulmonary Function Testing
- Imaging: CXR, Chest CT, V/Q scan
- Pulse oximetry at rest and with activity
- ABG
- Alpha 1 Antitrypsin Deficiency Screen
  - COPD in caucasian under age 45 y or with strong family history of COPD

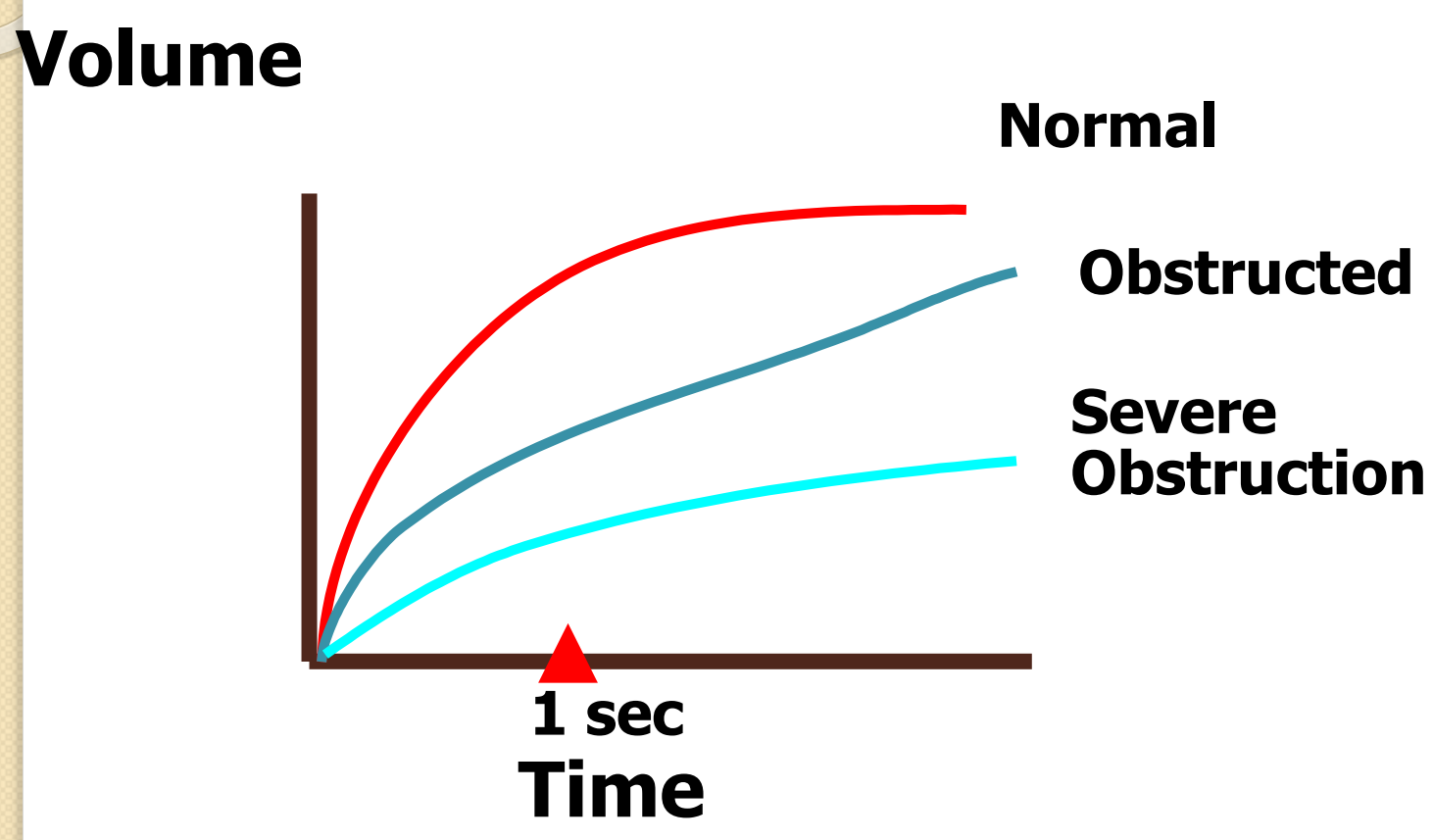
Physical Exam





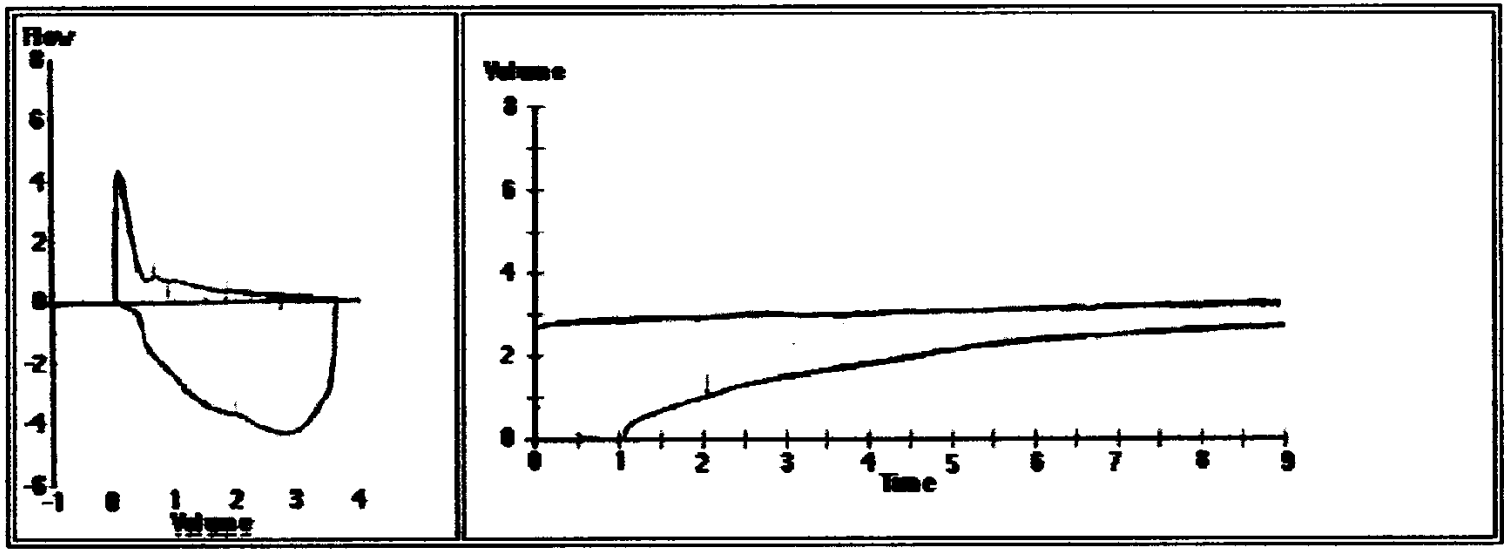
	Predominant Bronchitis	Predominant Emphysema
Age (yr)	40–45	50–75
Dyspnea	Mild; late	Severe; early
Cough	Early; copious sputum	Late; scanty sputum
Infections	Common	Occasional
Respiratory insufficiency	Repeated	Terminal
Cor pulmonale	Common	Rare; terminal
Airway resistance	Increased	Normal or slightly increased
Elastic recoil	Normal	Low
Chest radiograph	Prominent vessels; large heart	Hyperinflation; small heart
Appearance	*Blue bloater*	*Pink puffer*

Volume/Time Curves: Obstruction



[redacted]

	Meas	Ref	%Pred
FVC	3.66	4.39	83
FEV1	1.03	2.87	36
FEV1/FVC	28	65	
FEF25-75	0.33	2.48	13
PEF	4.29	8.33	52



http://www.vh.org/cgi/cmepractest/Spirometry/SpiroTest.html 11/2/01

Systemic Features of COPD

- Cachexia: loss of fat free mass
- Skeletal muscle wasting: apoptosis, disuse atrophy
- Osteoporosis
- Depression
- Normochromic normocytic anemia
- Increased risk of cardiovascular disease: associated with CRP

Exercise limitation

- Normal individuals never reach a respiratory limitation at peak exercise
- However COPD patients have a reduced maximum ventilation and this can limit there exercise capacity
- These patients can have airflow limitation to exercise
- They can also desaturate with exercise

COPD Treatment: Goals

- Slow disease progression
- Reduce the frequency and severity of disease exacerbations
- Improve quality of life

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CAT = COPD Assessment Test; mMRC = Modified Medical Research Council.

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Optimizing Treatment: A

Patient Category[b]	Recommended First Choice	Alternative Choice	Other Possible Treatments[c]
A	Short-acting anticholinergic PRN *or* Short-acting β_2-agonist PRN	Long-acting anticholinergic *or* Long-acting β_2-agonist *or* Short-acting β_2-agonist *and* Short-acting anticholinergic	Theophylline

Optimizing Treatment: B

Patient Category[b]	Recommended First Choice	Alternative Choice	Other Possible Treatments[c]
B	Long-acting anticholinergic *or* Long-acting β_2-agonist	Long-acting anticholinergic *and* Long-acting β_2-agonist	Short-acting β_2-agonist *and/or* Short-acting anticholinergic *or* Theophylline

Optimizing Treatment: C

Patient Category[b]	Recommended First Choice	Alternative Choice	Other Possible Treatments[c]
C	Inhaled glucocorticoid + Long-acting β_2-agonist *or* Long-acting anticholinergic	Long-acting anticholinergic ***and*** Long-acting β_2-agonist *or* Long-acting anticholinergic ***and*** Phosphodiesterase-4 inhibitor *or* Long-acting β_2-agonist ***and*** Phosphodiesterase-4 inhibitor	Short-acting β_2-agonist ***and/or*** Short-acting anticholinergic *or* Theophylline

Optimizing Treatment: D

Patient Category[b]	Recommended First Choice	Alternative Choice	Other Possible Treatments[c]
D	*Inhaled* glucocorticoid + Long-acting β_2-agonist *and/or* Long-acting anticholinergic	Inhaled glucocorticoid + Long-acting β_2-agonist *and* Long-acting anticholinergic *or* Inhaled glucocorticoid + Long-acting β_2-agonist *and* Phosphodiesterase-4 inhibitor *or* Long-acting anticholinergic *and* Long-acting β_2-agonist *or* Long-acting anticholinergic *and* Phosphodiesterase-4 inhibitor	*N*-acetylcysteine *or* Short-acting β_2-agonist *and/or* Short-acting anticholinergic *or* Theophylline

Medication side effects

Bronchodilators		
Inhaled short-acting β_2-agonists (albuterol, fenoterol, levalbuterol, metaproterenol, pirbuterol, terbutaline)	Tachycardia and hypokalemia (usually dose dependent), but generally well tolerated by most patients	Generally used as needed for mild disease with few symptoms
Inhaled short-acting anticholinergic agents (ipratropium)	Dry mouth, mydriasis on contact with eye, tachycardia, tremors, rarely acute narrow angle glaucoma; this drug class has been shown to be safe in a wide range of doses and clinical settings	Not to be used with tiotropium; generally used as needed for mild disease with few symptoms; avoid using both short- and long-acting anticholinergics

Medication side effects

Inhaled long-acting anticholinergic agents (tiotropium, aclidinium, umeclidinium, glycopyrronium)	Dry mouth, mydriasis on contact with eye, tachycardia, tremors, rarely acute narrow angle glaucoma	Not to be used with ipratropium; use when short-acting bronchodilators provide insufficient control of symptoms for patients with an FEV_1 <60% of predicted
Inhaled long-acting β_2-agonists (salmeterol, formoterol, arformoterol, indacaterol, olodaterol)	Sympathomimetic symptoms such as tremor and tachycardia; overdose can be fatal	Use as maintenance therapy when short-acting bronchodilators provide insufficient control of symptoms for patients with an FEV_1 <60% of predicted; not intended to be used for treatment of exacerbations of COPD or acute bronchospasm

Medication side effects

Methylxanthines (theophylline, aminophylline; sustained and short-acting)	Tachycardia, nausea, vomiting, disturbed pulmonary function, and disturbed sleep; narrow therapeutic index; overdose can be fatal with seizures and arrhythmias	Used as maintenance therapy; generally use only after long-acting bronchodilator treatment to provide additional symptomatic relief of exacerbations; may also improve respiratory muscle function
Oral β_2-agonists (albuterol, metaproterenol, terbutaline)	Sympathomimetic symptoms such as tremor and tachycardia	Used as maintenance therapy; rarely used because of side effects but may be beneficial for patients who cannot use inhalers

Medication side effects

Oral Phosophodiesterase-4 Inhibitor		
Roflumilast	Diarrhea, nausea, backache, decreased appetite, dizziness	Used to reduce risk for exacerbations in patients with severe COPD (blood levels not required) with chronic bronchitis and history of exacerbations; roflumilast should not be used with methylxanthines owing to potential toxicity; very expensive and should be used only in select patients

Medication side effects

Anti-Inflammatory Agents		
Inhaled glucocorticoids (fluticasone, budesonide, mometasone, ciclesonide, beclomethasone)	Dysphonia, skin bruising, oral candidiasis, rarely side effects of oral glucocorticoids (see below)	Most effective in patients with a history of frequent exacerbations and when used in conjunction with long-acting bronchodilators; not approved by the FDA for treatment for COPD
Oral glucocorticoids (prednisone, prednisolone)	Skin bruising, adrenal suppression, glaucoma, osteoporosis, diabetes mellitus, systemic hypertension, pneumonia, cataracts, opportunistic infection, insomnia, mood disturbance	Use for significant exacerbations of COPD with taper; avoid, if possible, in stable COPD to limit glucocorticoid toxicity; consider inhaled glucocorticoids to facilitate weaning of systemic glucocorticoids

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Therapy at Each Stage of COPD

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

http://www.goldcopd.com/

Additional Treatment for COPD

- Smoking cessation
- Pulmonary rehabilitation
- Oxygen therapy
  - PaO2<=55mmHg or pox <=88%
  - PaO2<=59 with polycythemia or clinical evidence of cor pulmonale
- Surgery (LVRS –upper lobe dz, Lung Transplant)

Pharmacological Interventions

- Nicotine replacement
- Buproprion HCL
- Varenicline
- Clonidine HCL
- Nortriptyline

Assess COPD Comorbidities

- Cardiovascular disease
- Osteoporosis
- Respiratory infections
- Anxiety and Depression
- Diabetes
- LUNG CANCER

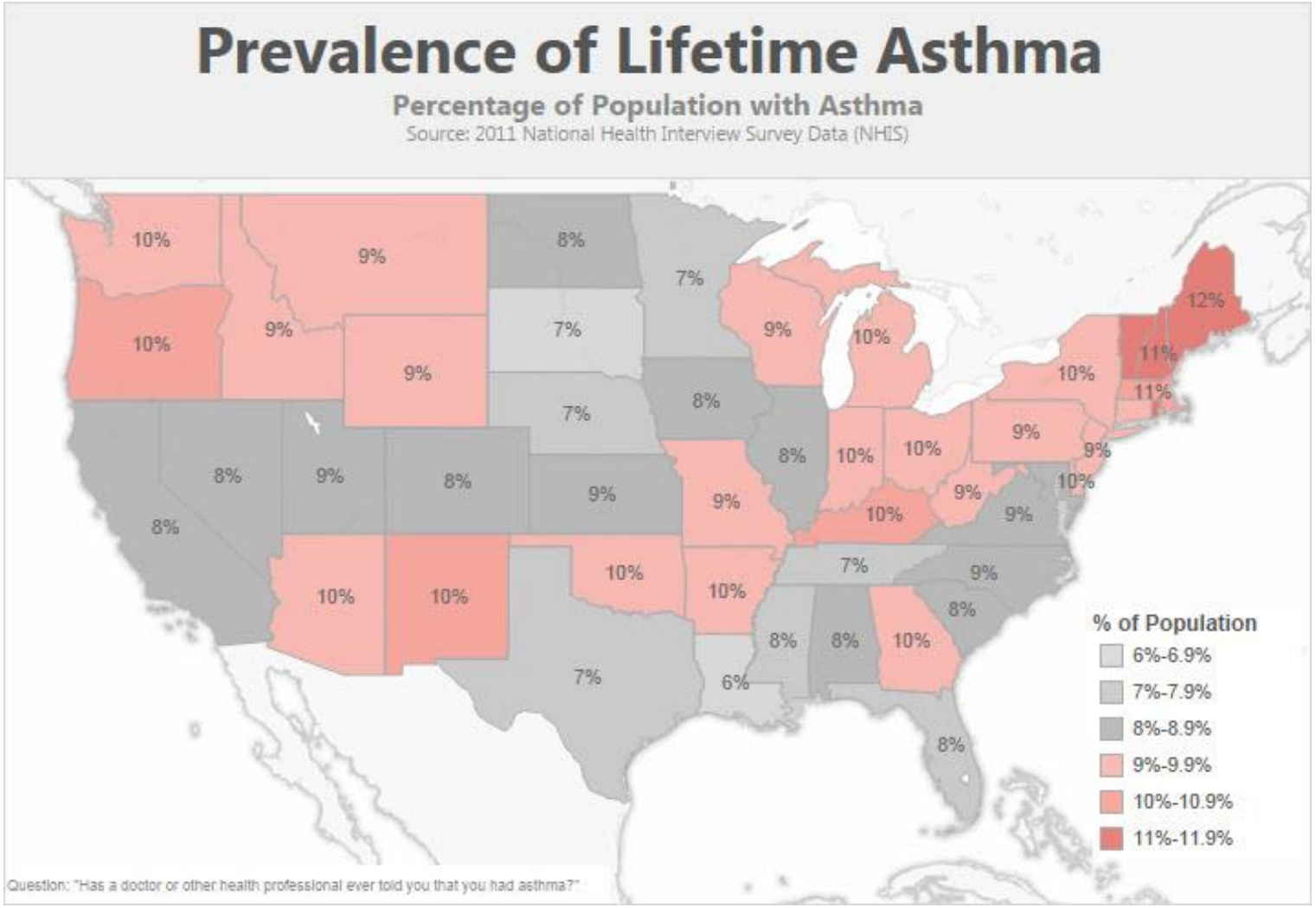
These comorbid conditions influence mortality and hospitalizations; and should be looked for routinely and treated appropriately

Vaccination: COPD

- Pneumococcal vaccination
  - All adults 65/+y and high risk <65y
  - PPSV23
  - PCV13
  - PCV13 is more effective in preventing invasive pneumococcal disease than PPSV23
- Flu vaccine
  - Given yearly

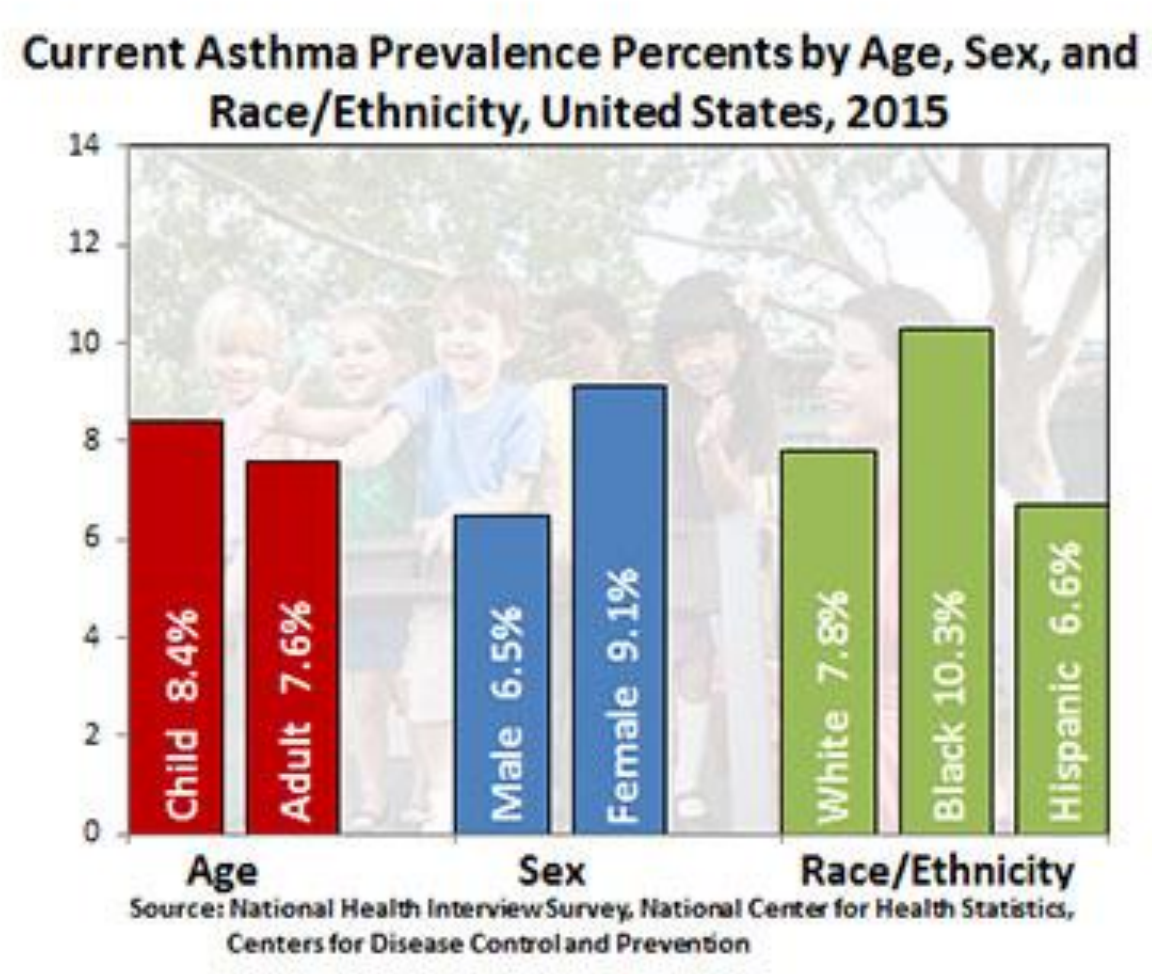
Asthma

Prevalence of Asthma: 2011



NHIS Data 2011

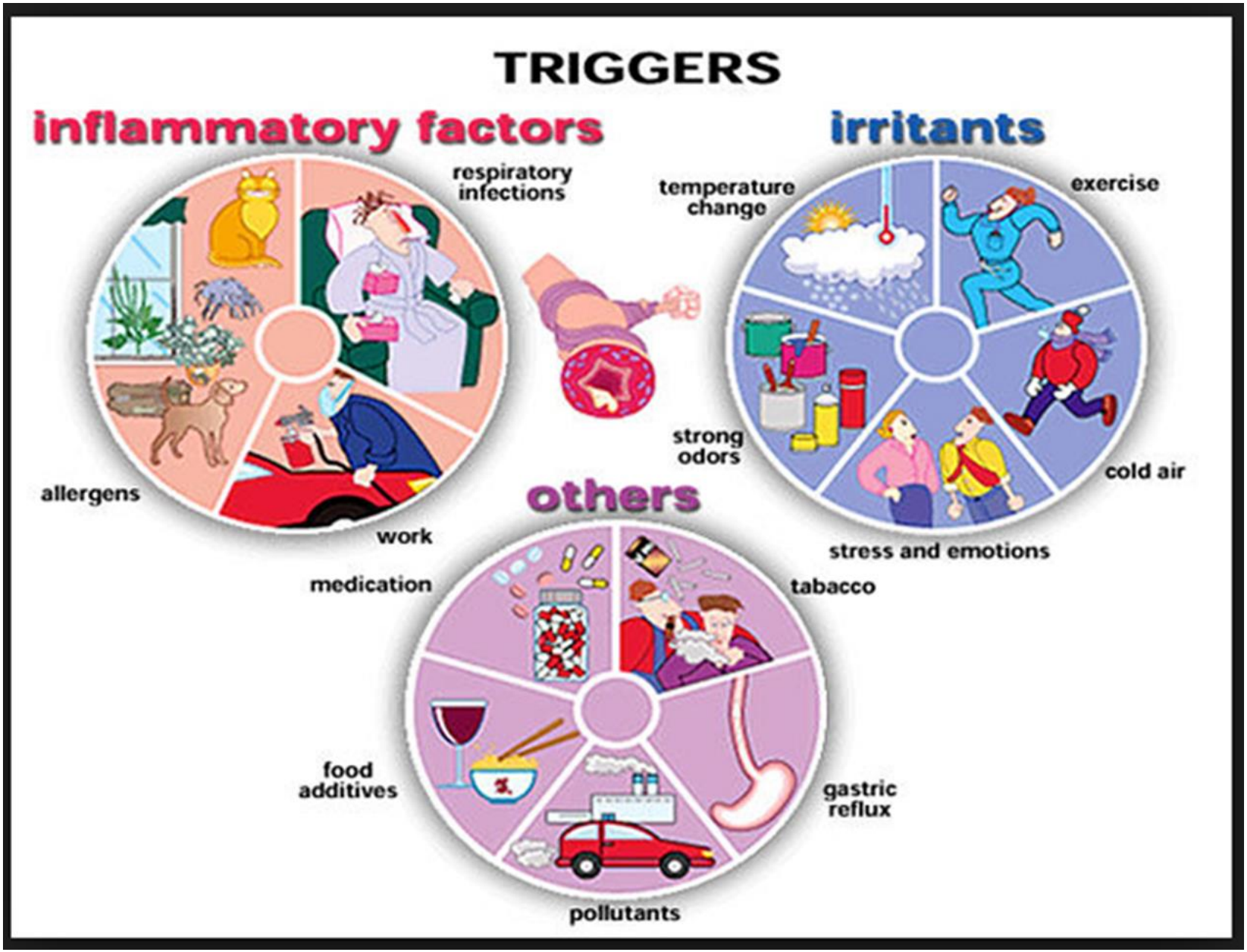
Prevalence of Asthma: 2015



National Center for Health Statistics/ CDC

Asthma

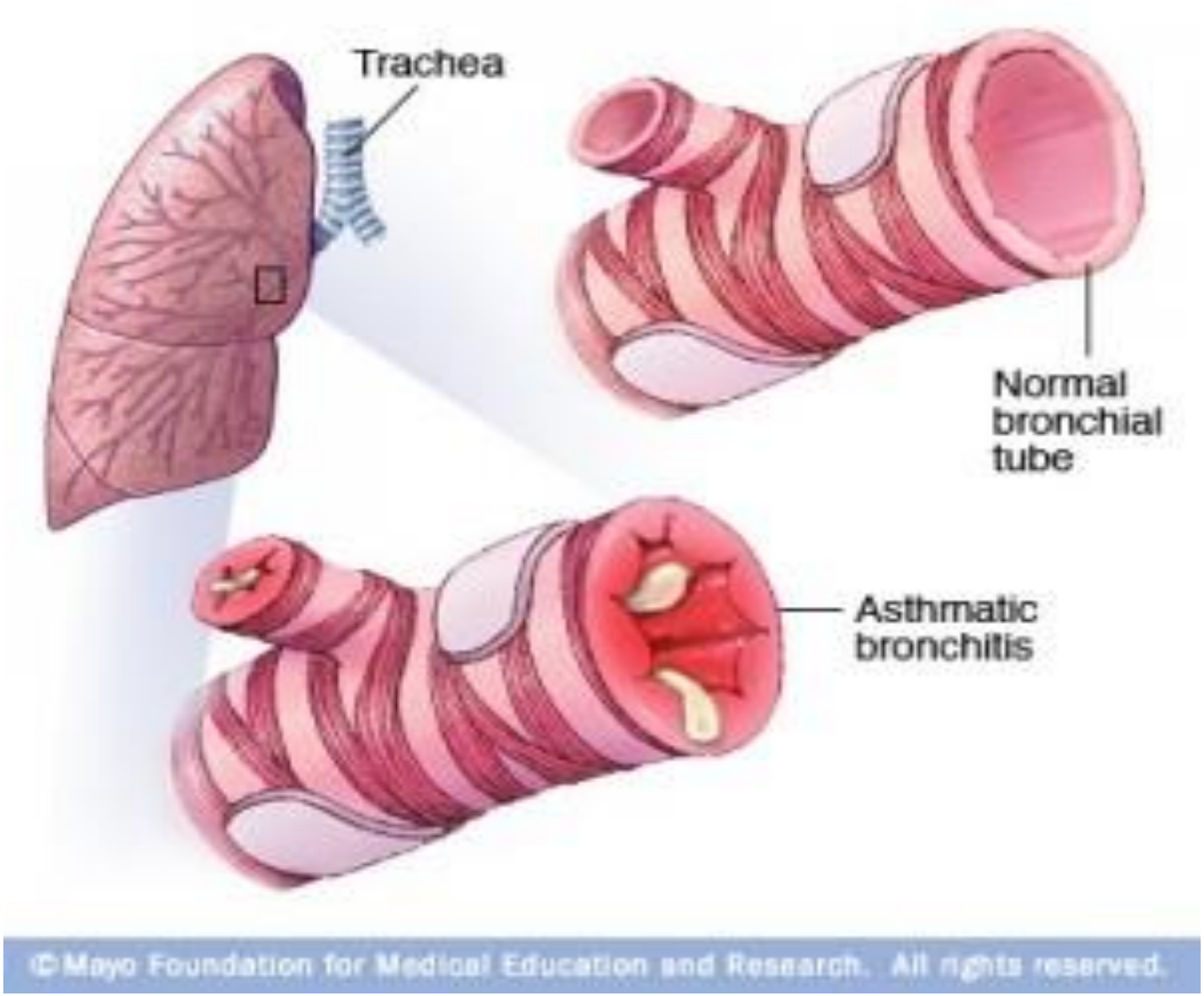
- Is an obstructive pulmonary disease with the following characteristics:
  - Airway obstruction that is reversible (in most patients)
  - Airway inflammation
  - Increased airway responsiveness
- Major Symptoms:
  - Cough
  - Wheeze
  - Dyspnea
  - Hypocapnea (usually)


TRIGGERS
inflammatory factors
respiratory infections
allergens
work
irritants
temperature change
exercise
strong odors
cold air
stress and emotions
others
medication
tabacco
food additives
gastric reflux
pollutants

Pathology of Advanced Chronic Asthma

- Hyperinflation♣
- Increased number of mucus glands
- Thick tenacious mucus♣
- Mucus plugs♣
- Muscular hypertrophy
- Thickened basement membrane
- Peribronchial Eosinophilic infiltration♣

♣All are significantly reversible



Differences in inflammatory cells between COPD and asthma
Ranked in relative order of importance

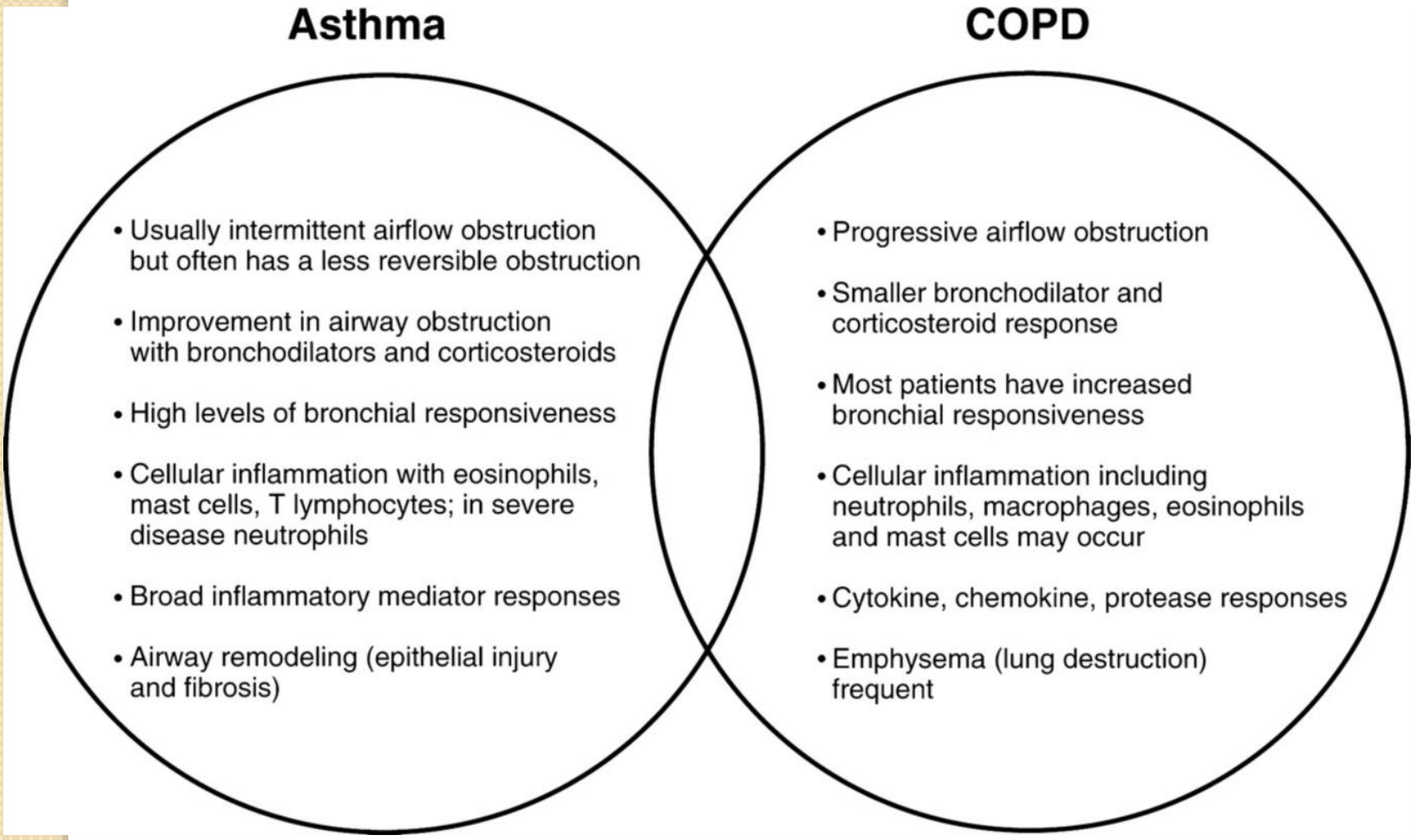
COPD	Asthma
Neutrophils	Eosinophils
Macrophages	Mast cells
CD8-T-lymphocytes	CD4-T-lymphocytes
Eosinophils (exacerbations)	Macrophages, Neutrophils

Groneberg and Chung *Respiratory Research* 2004 5:18 doi:10.1186/1465-9921-5-18

CHEST

Similarities and Differences in Asthma and COPD*: The Dutch Hypothesis

CHEST. 2004;126(2_suppl_1):93S-95S.



Two Phases of Asthma

- Early (immediate) response
  - Major problem - bronchospasm
- Late (delayed) response
  - Major problem - inflammation
  - Typically more severe than early response

Characteristics of Early Asthmatic Response

- Occurs in all patients with asthma
- Caused by release of mediators from mast cells (Histamine)
- Occurs 5-10 minutes after exposure
- Lasts 1.5-2 hours
- Responds to:
  - Bronchodilators (b-agonists preferred)
  - Cromolyn sodium (effective prophylactically)
  - Corticosteroids (no effect acutely, partial effect chronically)

Characteristics of Late Asthmatic Response

- Occurs in 50%-90% of patients
- Caused by chemotactic factors recruiting eosinophils, platelets, neutrophils
- Occurs 3-8 hours after exposure
- Lasts a widely varying amount of time
- Responds well to:
  - Cromolyn sodium
  - Corticosteroids

Asthma Syndromes

- **Allergic Asthma**
  - Most common form of asthma in adults
  - Atopy, positive FH
- **Cough Variant**
- **Exercise Induced Bronchospasm**
  - Triggered by drying of airways
- **Occupational Asthma**
  - Farmers, factory workers, hairdressers
- **Aspirin Sensitive Asthma (Samter triad)**
  - Asthma, asa sensitivity, sinusitis/nasal polyposis
- **Reactive Airways Dysfunction Syndrome**
  - Exposure to high concentration of irritant; short lived
- **Virus-Induced bronchospasm**
- **Allergic Bronchopulmonary Aspergillosis**
  - Colonization of aspergillus sp
  - Mucus plugging, bronchiectasis, asthma, fleeting infiltrates

Contributing Factors

- GERD
- Sinus disease
- OSA/Obesity
- Chronic aspiration
- Vocal Cord Dysfunction
  - Mid-chest tightness, dyspnea, dysphonia/stridor, partial response to asthma medication
  - Adduction of VC on laryngoscopy

Four Components of Asthma Management

- Objective measures
- Patient education
  - Trigger avoidance
  - Peak flow measurements
- Environmental control measures
- Pharmacotherapy
  - Medications
  - Secretion clearance

Table 2

Asthma Management Therapies

Class	Examples	Properties and Uses
SABAs	Albuterol, levalbuterol	Relax airway smooth muscle; treatment of choice for acute symptoms
LABAs	Salmeterol, formoterol	Bronchodilation lasting for ≥ 12 hours; usually used in combination with ICS after step 2
ICS	Beclomethasone, budesonide, flunisolide, fluticasone, triamcinolone	Reduce airway hyperresponsiveness, decrease inflammatory cell migration and activation, block late-phase reactions to allergens
OCS	Prednisone	Systemic anti-inflammatory effects; used for moderate to severe exacerbations to accelerate recovery and prevent late-phase response; may be used for long-term control
Mast cell stabilizers	Cromolyn sodium, nedocromil	Interfere with release of inflammatory mediators from mast cells; maintenance therapy for mild to moderate asthma or as prophylaxis for exercise-induced asthma
Leukotriene modifiers	Montelukast, zafirlukast, zileuton	Interfere with leukotriene mediators released from mast cells, eosinophils and basophils; prophylaxis of exercise-induced asthma and long-term treatment as alternative to low doses of ICS
Methylxanthines	Theophylline, aminophylline	Mild to moderate bronchodilation; toxic at higher doses
Anticholinergics	Ipratropium bromide	Enhance effects of SABAs in acute attacks by inhibiting muscarinic cholinergic receptors and reducing vagal tone of airway
Immunomodulators	Omalizumab	Binds to IgE, forming complexes that prevent initiation of allergic cascade by inhibiting mast cell and basophil degranulation; reserved as add-on therapy for patients ≥ 12 years with refractory asthma (steps 5 and 6)

Abbreviations: ICS, inhaled corticosteroids; LABAs, long-acting beta-agonists; OCS, oral corticosteroids; SABAs, short-acting beta-agonists

Adapted from: National Asthma Education and Prevention Program Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. *Bethesda, MD: National Heart, Lung, and Blood Institute, US Dept of Health and Human Services; 2007. NIH publication 08-5846.*

Corticosteroid Mechanism of Action

- Prevents the activation and directed migration of inflammatory cells
- Interferes with arachidonic acid metabolism and the synthesis of leukotrienes and prostaglandins
- Increase the responsiveness of the β-receptors of airway smooth muscle

Systemic vs. Inhaled Corticosteroids
Major Adverse Effects

- **High dose, short-term, oral therapy:**
  - Reversible abnormalities in glucose metabolism, increased appetite, fluid retention, weight gain, rounding of the face, mood alteration, hypertension, peptic ulcer, and aseptic necrosis of the femur
- **Lowest possible dose, long-term, oral therapy:**
  - Osteoporosis, hypertension, Cushing's syndrome, cataracts, myopathy, hypothalamic-pituitary-adrenal axis suppression, impaired immune mechanisms (rare)
- **Aerosolized therapy:**
  - Infrequent systemic adverse effects
  - Local adverse events include oropharyngeal candidiasis, dysphonia, occasional coughing resulting from upper airway irritation caused by aerosol inhalation

LT Antagonist: Clinical Utility

- Prophylaxis of mild to moderate asthma
- Aspirin induced asthma
- Prevention of antigen and exercise induced asthma
- Not effective in relieving acute asthma exacerbations

- Bronchodilation
- Anti-inflammatory action
- Less effective than inhaled corticosteroids
- Potentiate oral corticosteroid action

LT Antagonist Side Effects

- Elevation of liver enzymes
- Headache
- Dyspepsia
- Rare:
  - Eosinophilic granulomatosis with polyangiitis (formerly Churg-Straus syndrome)

Theophylline: Pharmacologic Properties

- Mechanism of action:
  - Inhibits action of phosphodiesterase which prevents breakdown cAMP, thereby increasing cAMP levels in tissue resulting in smooth muscle relaxation
- Bronchodilation
- Improved airflow
- Increased mucociliary clearance
- Improved respiratory muscle strength and endurance
- Increased cardiac output (in some)
- Moderate respiratory center stimulation

Theophylline - Clinical Utility

- Chronic asthma
- Manage reversible components of chronic bronchitis and emphysema
- Effective at low doses, minimizing potential for serious side effects
- Additive effects with oral and inhaled β_2-agonists
- Especially useful when given before bedtime for the patient with primarily nocturnal symptoms

Adverse Effects of Theophylline

- Cardiac
  - Tachycardia, arrhythmia
- CNS
  - Seizure, tremors
- GI
  - Nausea, vomiting
- GU
  - Prostatism, detrusor muscle relaxation
- Metabolic
  - Hyperglycemia, hypokalemia

Theophylline Clearance

- **Increased by:**
  - B-agonist
  - Carbamazepine
  - Phenytoin
  - Furosemide
  - Hyperthyroidism
  - Ketoconazole
  - Marijuana
  - Phenobarbital
  - Rifampin
  - Tobacco smoke
- **Decreased by:**
  - Allopurinol
  - Macrolides
  - Ciprofloxacin
  - Isoniazid
  - Propranolol
  - Caffeine
  - Cirrhosis
  - CHF
  - Cimetidine
  - Mexiletine
  - Oral contraceptives
  - Viral infections

Immunomodulators

- Omalizumab
- Monoclonal antibody directed against human IgE
- Prevents IgE binding with its receptors on mast cells and basophils
- Decrease release of allergic mediators
- Used to treat allergic asthma
- Subcutaneous injection
- Expensive
- Not first line therapy
- Anti IL 5: Mepolizumab

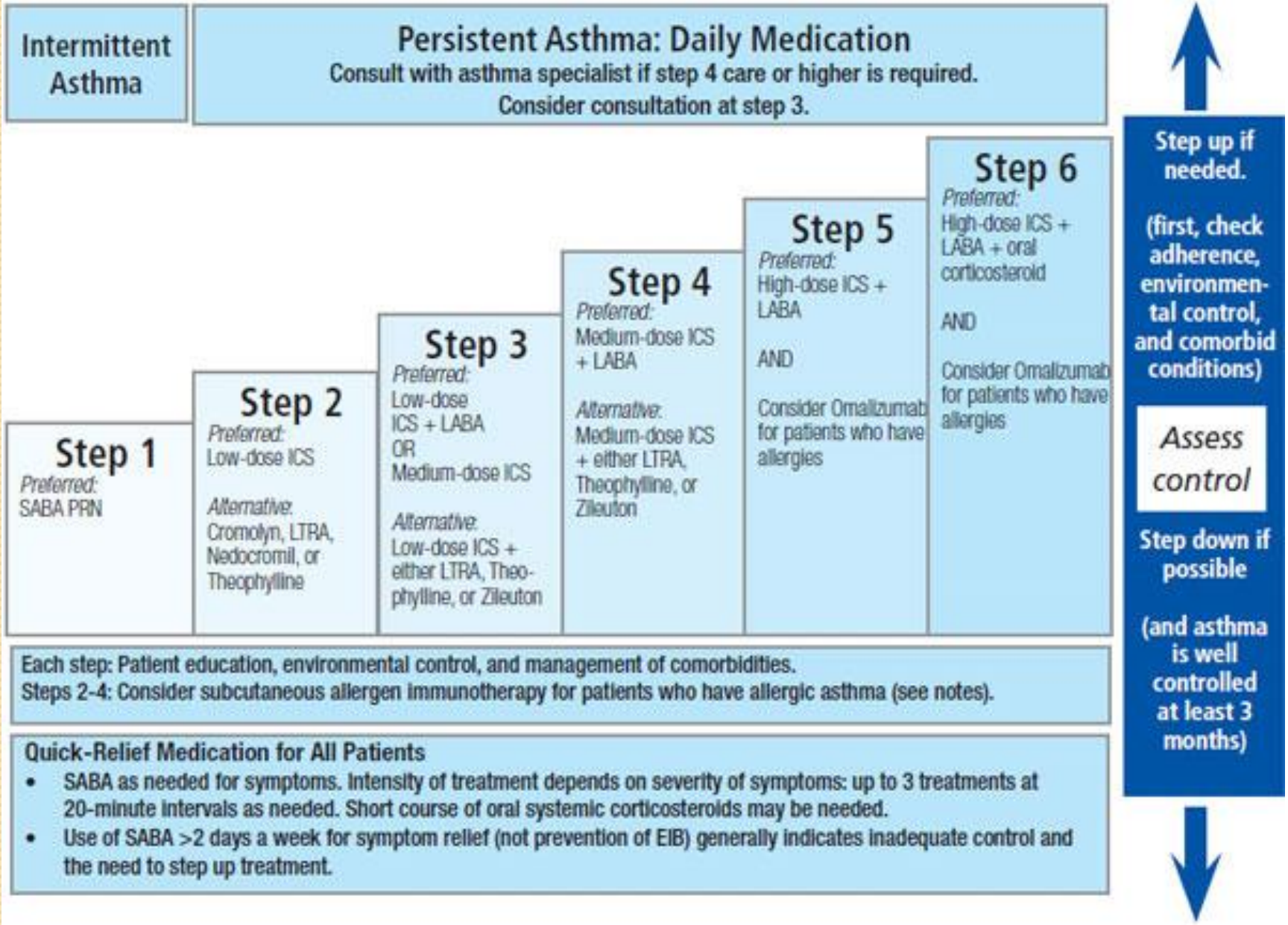
Classifying Asthma Severity and Initiating Treatment in Youths ≥ 12 Years of Age and Adults

Assessing severity and initiating treatment for patients who are not currently taking long-term control medications.

Components of Severity		Classification of Asthma Severity ≥ 12 years of age			
			Persistent		
		Intermittent	Mild	Moderate	Severe
Impairment Normal FEV_1/FVC: 8-19 yr 85% 20-39 yr 80% 40-59 yr 75% 60-80 yr 70%	Symptoms	≤2 days/week	>2 days/week but not daily	Daily	Throughout the day
	Nighttime awakenings	≤2 x/month	3-4 x/month	>1x/week but not nightly	Often 7x/week
	Short-acting beta agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week but not daily, and not more than 1x on any day	Daily	Several times per day
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
	Lung function	• Normal FEV_1 between exacerbations • FEV_1 > 80% predicted • FEV_1/FVC normal	• FEV_1 > 80% predicted • FEV_1/FVC normal	• FEV_1 > 60% but <80% predicted • FEV_1/FVC reduced 5%	• FEV_1 > 60% predicted • FEV_1/FVC reduced >5%
Risk	Exacerbations requiring oral systemic corticosteroids	0-1/year	>2/year		
		Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time for patients in any severity category. Relative annual risk of exacerbations may be related to FEV_1.			
Recommended Step for Initiating Treatment		Step 1	Step 2	Step 3	Step 4 or 5
				and consider short course of oral systemic corticosteriods	
		In 2-6 weeks, evaluate level of asthma control that is achieved and adjust therapy accordingly.			

FEV_1 - forced expiratory volume in one second; *FVC* - forced vital capacity

National Asthma Education and Prevention Program 2007 NHBLI



National Asthma Education and Prevention Program 2007 National Heart Lung Blood Institute

Bronchial thermoplasty

- FDA approved 2010
- Adjunctive therapy despite optimization of asthma treatment
- Bronchoscopically induced catheter applies thermal energy to conducting airways 3mm or greater with goal of reducing smooth muscle thickening
- 3 sessions, 3 weeks apart
- Lung function remains unchanged
- Notable improvement in symptoms
- Adverse effect: temporary bronchospasm after procedure

Also important to review…

- Alpha 1 Antitrypsin deficiency
- Cystic Fibrosis
- Bronchiectasis
  - Right Middle Lobe Syndrome
  - Ciliary Dyskinesia Syndrome
  - Allergic Bronchopulmonary Aspergillosis


COPD
CLINIC
POSTAL