

# Asthma

Asma. S. Albtoosh,MD

Department of respiratory and sleep medicine

**JUH**

- Asthma: Asthma is a chronic disease characterized by recurrent attacks of shortness of breath and wheezing.
  - Vary in severity and frequency from person to person.
  - May become worse during physical activity or at night.

## Factors contributing to the rise of bronchial asthma in the region

- Increasing air pollution
- Fast modernization
- Widespread construction work
- Western diet
- Improved standard of living with reduced exercise rates
- Smoking

# Asthma in Jordan

- Asthma is moderately common in Jordan.
- No difference in prevalence of asthma diagnosed by a physician between an urbanized region and Bedouins having low socioeconomic status
- Common in male children (similar to other reports)
- **Twofold increase in the prevalence of asthma in Jordan in the last 10 years**

*(Allergy Asthma Proc 30:181–185, 2009; doi: 10.2500/aap.2009.30.3208)*

# Pathophysiology

- Anatomy of the airways:
  - Cartilaginous bronchi and membranous bronchi (anatomic dead space) contribute to airway resistance
  - The smallest **non-gas-exchanging airways**, the terminal bronchioles, are approximately 0.5 mm in diameter (small if airways are less than 2 mm in diameter)
  - **Gas-exchanging** bronchi (respiratory bronchioles and alveolar ducts)

# Pathophysiology

- Structure:
  - Mucosa: epithelial cells: capable of specialized mucous production and transport
  - Basement membrane
  - A smooth-muscle matrix extending to the alveolar entrances
  - Supporting connective tissue: fibrocartilaginous or fibroelastic

# Pathophysiology

- Cellular elements
  - mast cells
  - Basophils
  - Eosinophils
  - Neutrophils
  - Macrophages
  - Stretch and irritant receptors in the airways
  - Cholinergic motor nerves: which innervate the smooth muscle and glandular units

# Pathophysiology

- Airway inflammation
- Intermittent airflow obstruction
- Bronchial hyperresponsiveness
  - Asthma begins early in life
  - Risk factors: atopic disease, recurrent wheezing, parental history of asthma and smoking

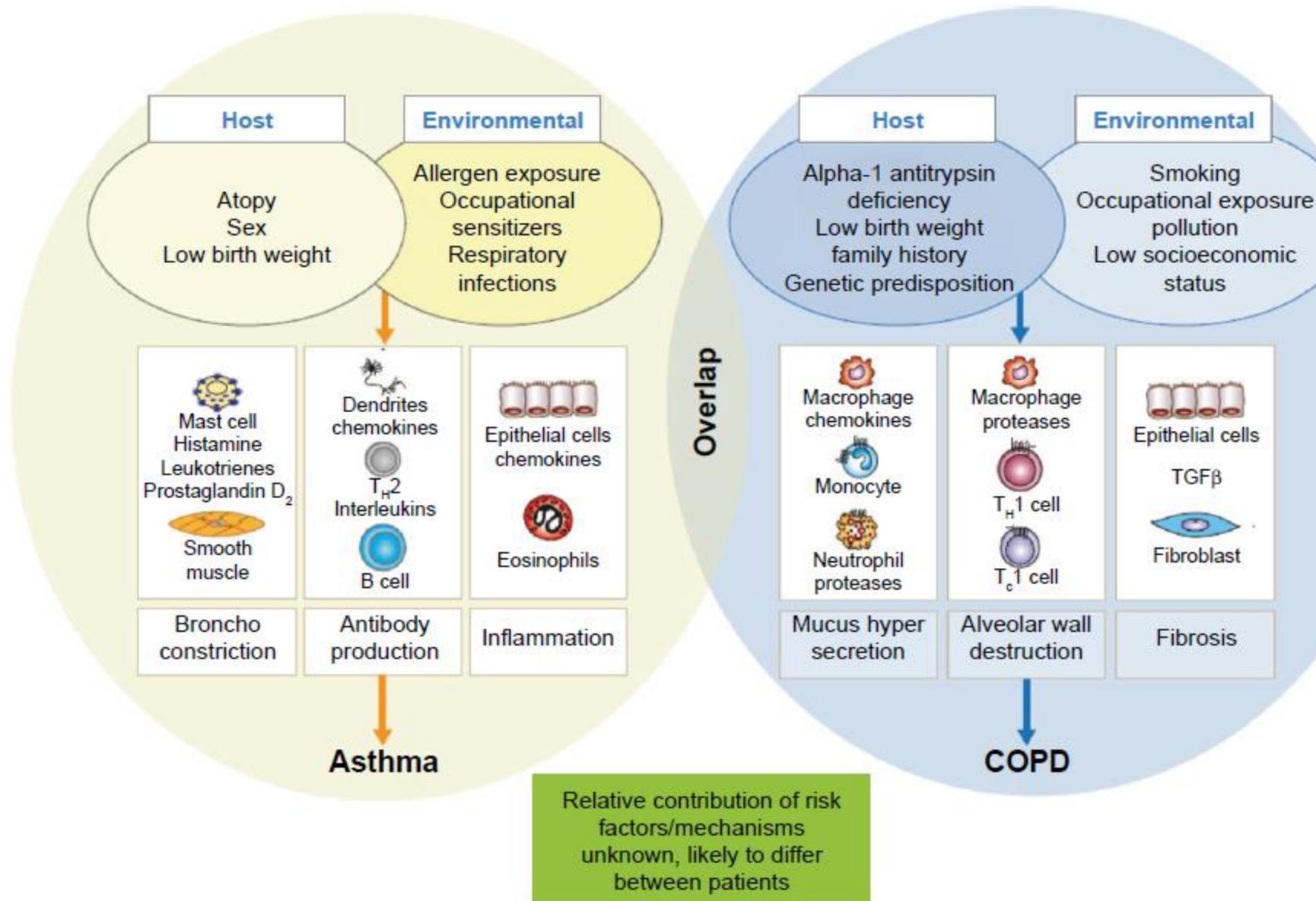
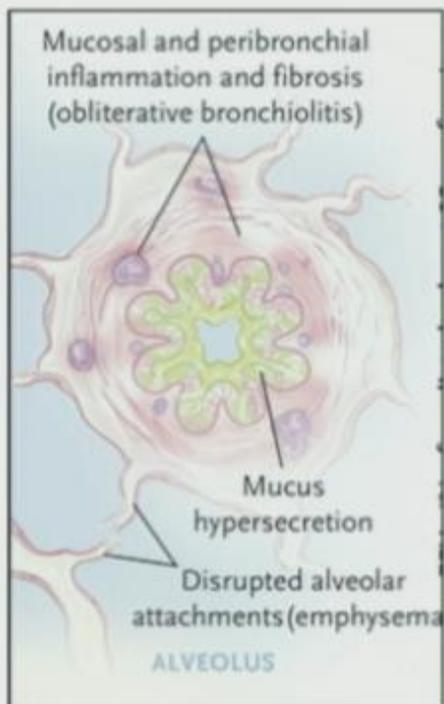


Figure 2 Pathophysiology of asthma, COPD, and overlap.

Notes: Data taken from Postma et al<sup>25</sup> and Barnes et al.<sup>27</sup>

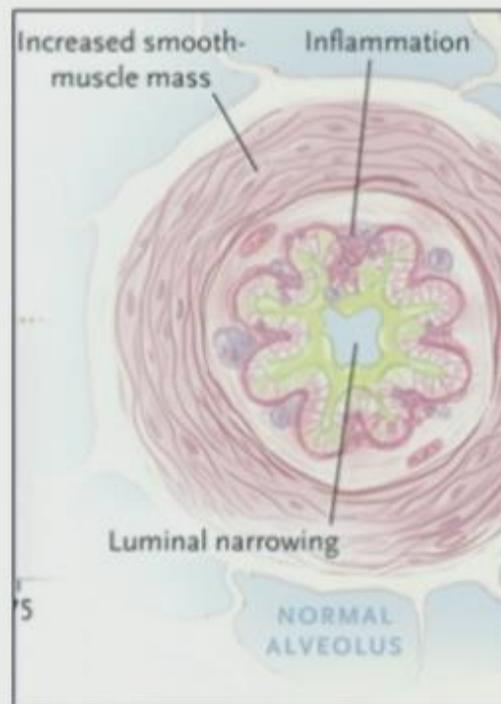
# COPD and asthma: two disease processes

## COPD



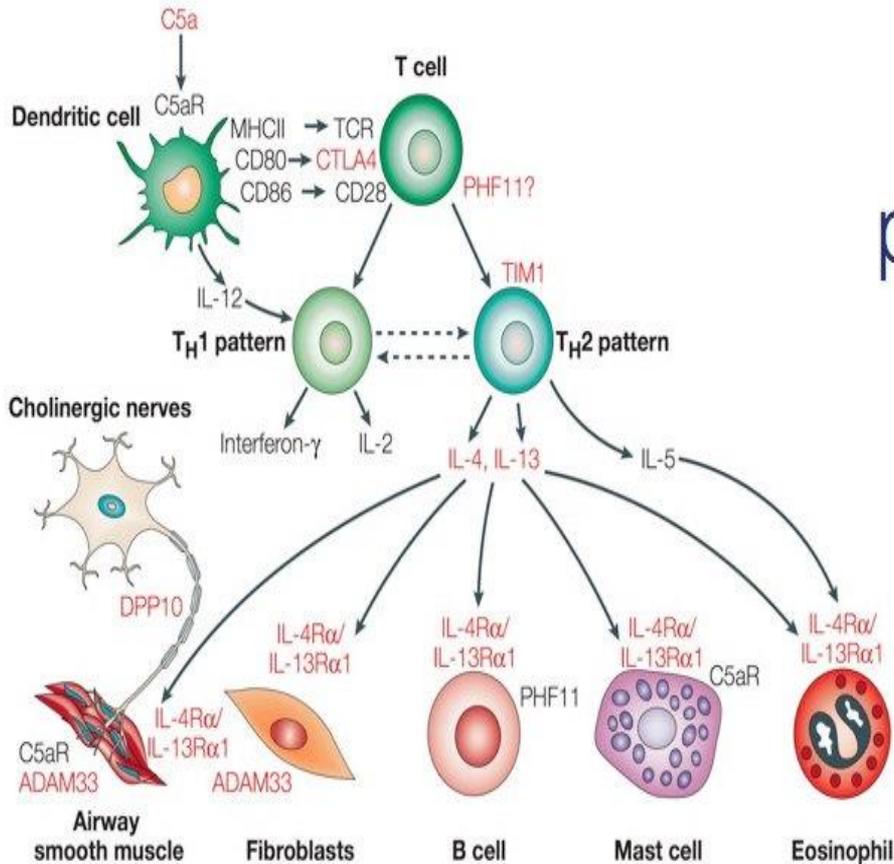
Obliterative bronchiolitis  
Mucus hypersecretion  
Emphysema

## Asthma



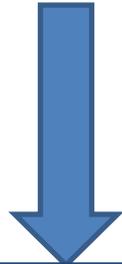
Increased smooth muscle mass  
Inflammation  
Luminal narrowing

# Pathways in the pathogenesis of asthma

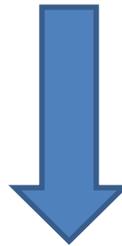


Wills-Karp et al,  
Nat Genet 5: 376-387, 2004

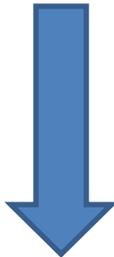
allergens, environmental irritants  
Viruses, cold air, exercise



Chronic inflammation



Bronchial hyperresponsiveness



Bronchospasm, wheezing, shortness of breath

# Airway Obstruction (causes)

- Acute bronchoconstriction: IgE-dependent mediator release following exposure to allergens (early asthma response)
- Airway edema: 6-24 hours following allergen challenge (late asthma response).
- Chronic mucous plug formation: exudate of serum proteins and cell debris, may take weeks to resolve
- Airway remodeling: due to structural changes due to long-standing inflammation, affects the extent of reversibility of airway obstruction

## Bronchial Hyperresponsiveness

- Hyperinflation compensates for the airflow obstruction leading to hypoventilation, vasoconstriction and ventilation-perfusion mismatch.

4 stages of blood gas progression with status asthmaticus

	PaCO <sub>2</sub>	PaO <sub>2</sub>
Stage 1	Decrease	Normal
Stage 2	Decrease	Decreased
Stage 3	NORMAL	Decreased
Stage 4	High	Decreased

# Etiology

- Environmental allergens (eg, house dust mites; animal allergens, especially cat and dog; cockroach allergens; and fungi)
- Viral respiratory tract infections
- Exercise, hyperventilation
- GERD
- Chronic sinusitis or rhinitis
- ASA, NSAID hypersensitivity, sulfite sensitivity
- Perinatal factors (prematurity and increased maternal age; maternal smoking and prenatal exposure to tobacco smoke)
- Beta-adrenergic receptor blockers (including ophthalmic preparations)
- Obesity
- Environmental pollutants, tobacco smoke
- Occupational exposure
- Irritants (eg, household sprays, paint fumes)
- Various high- and low-molecular-weight compounds (eg, insects, plants, latex, gums, diisocyanates, anhydrides, wood dust, and fluxes; associated with occupational asthma)
- Emotional factors or stress

# Aspirin-Induces Asthma

- Asthma, aspirin sensitivity, and nasal polyps
- 5-10% of patients with asthma
- Third to fourth decade
- Can occur with other NSAIDS
- Caused by an increase in eosinophils and cysteinyl leukotrienes after exposure
- Management:
  - Avoidance of these medications
  - Leukotriene antagonists, may allow patients to take daily aspirin for cardiac or rheumatic disease
  - Aspirin desensitization decreases sinus symptoms, allowing daily dosing of aspirin

# GERD

- A definite asthma-causing factor (defined by a favorable asthma response to medical antireflux therapy) in 64% of patients; clinically silent reflux was present in 24% of all patients
- Aggressive antireflux therapy may improve asthma symptoms, pulmonary function, or unexplained chronic cough.

# Occupational Asthma

- 10-15% of adult asthma cases
- High-risk jobs: farming, painting, janitorial work, and plastics manufacturing
- ACCP consensus statement: work-related asthmas as including occupational asthma (ie, asthma induced by sensitizer or irritant work exposures) and work-exacerbated asthma (ie, preexisting or concurrent asthma worsened by work factors)

# Occupational Asthma

- Types of occupational asthma:
  - Immune-related
    - Has a latency of months to years after exposure
  - Non-immune-related (irritant-induced asthma (reactive airway dysfunction syndrome))
    - Has no latency period and may occur within 24 hours after an accidental exposure to high concentrations of respiratory irritants
- Asthmatics with worsening of symptoms during the week and improvement during the weekends should be evaluated for occupational exposure.
- Peak-flow monitoring during work (optimally, at least 4 times a day) for at least 2 weeks and a similar period away from work is one recommended method to establish the diagnosis. [

# Viruses and Asthma

- Rhinovirus illness during infancy: significant risk factor for the development of wheezing in preschool children and a frequent trigger of wheezing illnesses in children with asthma
- 80-85% of childhood asthma episodes are associated with prior viral exposure
- Prior childhood pneumonia due to infection by respiratory syncytial virus, *Mycoplasma pneumoniae*, and/or *Chlamydia* species was found in more than 50% of a small sample of children aged 7-9 years who later had asthma.
- Treatment with antibiotics appropriate for these organisms improves the clinical signs and symptoms of asthma
- SH smoke exposure is associated with increased infection with RSV/ childhood asthma

# Sinusitis (United Airways)

- Of patients with asthma, 50% have concurrent sinus disease
- Important exacerbating factor for asthma symptoms
- Treatment of nasal and sinus inflammation reduces airway reactivity
- Treatment of acute sinusitis requires at least 10 days of antibiotics to improve asthma symptoms

# Exercise-induced asthma

- Exercise triggers acute bronchoconstriction in persons with heightened airway reactivity
- Any age
- Primarily in persons who have asthma
- Also in patients with normal resting spirometry findings with atopy, allergic rhinitis and cystic fibrosis
- In healthy persons: elite or cold weather athletes
- Often a neglected diagnosis
- The underlying asthma may be silent in as many as 50% of patients, except during exercise

# Exercise-induced asthma

- Pathogenesis:
- Water and/or heat loss from the airway
- BAL: no increase in inflammatory mediators
- Refractory period, during which a second exercise challenge does not cause a significant degree of bronchoconstriction
- Warm up and B2 agonist

# Obesity

- Significant association between asthma and abnormal lipid and glucose metabolism beyond body mass association
- High BMI: worse asthma control
- Sustained weight loss improves asthma control
- Accelerated weight gain in early infancy is maybe associated with increased risks of asthma symptoms

# Presentation

- History
  - Is this Asthma?
  - Family history: allergy, sinusitis, rhinitis, eczema, and nasal polyps
  - Asthma severity
  - Precipitating factors
  - Social history: smoking, workplace or school characteristics, educational level, employment, social support, compliance with medications, and illicit drug use

# Exacerbation History

- Prodromal signs or symptoms
- Rapidity of onset
- Associated illnesses
- Number in the last year
- Need for emergency department visits, hospitalizations, ICU admissions, intubations
- Missed days from work /school or activity limitation

# Symptoms

- Wheezing is one of the most common symptoms
- Mild: only end expiratory
- As severity increases: lasts throughout expiration
- Severe asthmatic episode: also present during inspiration
- Most severe: absent because of the severe limitation of airflow associated with airway narrowing and respiratory muscle fatigue.

# Asthma and Wheezing

- Asthma can occur without wheezing: obstruction involves predominantly the small airways
- Not necessary for the diagnosis of asthma
- Can be associated with other causes
  - Cystic fibrosis, heart failure
  - Vocal cord dysfunction (inducible laryngeal obstruction (ILO) Predominantly inspiratory wheeze , heard best over the laryngeal area in the neck.
  - Dynamic airway collapse: bronchomalacia, or tracheomalacia: expiratory wheeze heard over the large airways

# Cough

- May be the only symptom of asthma, especially in cases of exercise-induced or nocturnal asthma
- Nonproductive and nonparoxysmal
- In nocturnal asthma: after midnight and during the early hours of morning.

# Others

- Chest tightness/pain (with or without other symptoms of asthma) especially in exercise-induced or nocturnal asthma.
- Nonspecific symptoms in infants or young children:
  - Recurrent bronchitis, bronchiolitis, or pneumonia; a persistent cough with colds; and/or recurrent croup or chest rattling

## Exercise-induced bronchoconstriction

- Only with exercise
- Cough, wheezing, shortness of breath, and chest pain or tightness
- Sore throat or GI upset
- 10 minutes into the exercise
- Short exercise period: symptoms may develop up to 5-10 minutes after completion of exercise
- Higher intensity, more intense attack

# Physical Examination

- Mild episodes
  - Shortness of breath with physical activity
  - Can talk in sentences and lie down
  - May be agitated
  - Respiratory rate is increased
  - No use of accessory muscles
  - Heart rate is less than 100 bpm
  - Moderate expiratory wheezing
  - O<sub>2</sub> saturation is greater than 95%

# Physical Examination

- Moderately severe episodes:
  - Use of accessory muscles
  - In children: supraclavicular and intercostal retractions, nasal flaring, abdominal breathing
  - The heart rate is 100-120 bpm
  - Loud wheezing
  - **Pulsus paradoxus:** (fall in systolic blood pressure during inspiration of 10-20 mm Hg)
  - O<sub>2</sub> sat is 91-95%
  - Sitting position

# Physical Examination

## Severe episode

- Shortness of breath at rest
- Talk in words
- Respiratory rate: greater than 30/min
- Use of accessory muscles
- Heart rate is more than 120 bpm
- Loud biphasic (expiratory and inspiratory) wheezing
- Pulsus paradoxus is often present (20-40 mm Hg)
- O<sub>2</sub> sat less than 91%
- Sitting position: tripod position.

# Impending Respiratory Failure

- Drowsy and confused
- Thoracoabdominal movement
- Wheezing may be absent
- Severe hypoxemia, bradycardia
- Pulsus paradoxus may be absent: suggests respiratory muscle fatigue.
- Diaphoresis
- Rise in  $\text{PCO}_2$  and hypoventilation
- Life-threatening hypoxia, advanced hypercarbia, bradypnea, somnolence

# Nonpulmonary Manifestations

- Signs of atopy or allergic rhinitis, such as conjunctival congestion and inflammation, ocular shiners, a transverse crease on the nose due to constant rubbing
- Pale nasal mucosa
- Erythematous Turbinates
- Nasal polyps
- Atopic dermatitis
- Eczema

# Asthma Classification

- The severity of asthma is classified as the following:
  - Intermittent
  - Mild persistent
  - Moderate persistent
  - Severe persistent
- Patients with asthma of any level of severity may have mild, moderate, or severe exacerbations
- The presence of one severe feature is sufficient to diagnose severe persistent asthma

# CLASSIFY SEVERITY

## Clinical Features before Treatment

	Symptoms	Nocturnal Symptoms	FEV <sub>1</sub> or PEF
<b>STEP 4</b> <b>Severe</b> <b>Persistent</b>	Continuous Limited physical activity	Frequent	< 60% predicted Variability > 30%
<b>STEP 3</b> <b>Moderate</b> <b>Persistent</b>	Daily Attacks affect activity	> 1 time week	60 to 80% predicted Variability > 30%
<b>STEP 2</b> <b>Mild Persistent</b>	> 1 time a week but < 1 time a day	> 2 times a month	> 80% predicted Variability 20 to 30%
<b>STEP 1</b> <b>Intermittent</b>	< 1 time a week Asymptomatic and normal PEF between attacks	< 2 times a month	> 80% predicted Variability < 20%

# Asthma Differential Diagnoses

- Vocal cord dysfunction or inducible laryngeal obstruction (ILO): paradoxical adduction of the vocal cords during inspiration, and may disappear with panting, speech, or laughing
  - Direct laryngoscopy during symptomatic periods or after exercise
  - The presence of flattening of the inspiratory limb of the flow-volume loop may also suggest vocal cord dysfunction, but this is only seen in 28% of patients at baseline<sup>1</sup>
- Tracheal and bronchial lesions
- Foreign bodies

# Asthma Differential Diagnoses

- Congestive heart failure (cardiac asthma)
  - Engorged pulmonary vessels and interstitial pulmonary edema, which reduce lung compliance and contribute to the sensation of dyspnea and wheezing
  - Wheezing secondary to bronchospasm: related to paroxysmal nocturnal dyspnea and nocturnal coughing

# Asthma Differential Diagnoses

- Sinus disease
- Gastroesophageal reflux

# Asthma Workup

- Blood and sputum eosinophilia:
  - Greater than 4% (blood) supports the diagnosis of asthma
  - Its absence does not exclude asthma
  - Greater than 8% may be observed in patients with concomitant atopic dermatitis, should also prompt an evaluation for allergic bronchopulmonary aspergillosis, Churg-Strauss syndrome, eosinophilic pneumonia
  - Use mepolizumab (anti-IL-5 antibody) if counts 150 cells/ $\mu$ L or an eosinophil count of 300 cells/ $\mu$ L within the past 12 months
  - Adjust ICS with sputum eosinophilia

# Asthma Workup

- Serum Immunoglobulin E:
  - Total serum immunoglobulin E levels greater than 100 IU are frequently observed in patients experiencing allergic reactions
  - Not specific for asthma
  - Observed in patients with other conditions (eg, allergic bronchopulmonary aspergillosis, Churg-Strauss syndrome)
  - Normal levels do not exclude the diagnosis of asthma
  - Elevated levels are required for chronic asthma patients to be treated with omalizumab (Xolair)

# Chest Radiography

- Reveals complications
- Alternative causes of wheezing
- Normal or hyperinflation
- Exclude pneumothorax or pneumomediastinum

# Chest CT Scanning

- Bronchial wall thickening
- Bronchial dilatation
- Cylindrical and varicose bronchiectasis
- Reduced airway luminal area
- Mucoid impaction of the bronchi
- Centrilobular opacities, or bronchiolar impaction
- Linear opacities
- Airtrapping, as demonstrated or exacerbated with expiration mosaic lung attenuation, or focal and regional areas of decreased perfusions

# Pulmonary Function Testing

- Establish asthma diagnosis
- Prior to initiating treatment
- Should include measurements before and after inhalation of a short-acting bronchodilator
- Reduced FEV<sub>1</sub>/FVC (airway obstruction)
- Reversibility: increase of 12% and 200 mL after the administration of a short-acting bronchodilator

# Methacholine/histamine challenge

- When spirometry is normal or near normal
- In patients with intermittent or exercise-induced asthma symptoms
- Testing helps determine if airway hyperreactivity is present
- A negative test result excludes the diagnosis of asthma
- Methacholine: a direct stimulant that acts directly on acetylcholine receptors on smooth muscle, causing contraction and airway narrowing

## Methacholine/histamine challenge

- Methacholine is administered in incremental doses up to a maximum dose of 16 mg/mL, and a 20% decrease in FEV<sub>1</sub>, up to the 4 mg/mL level, is considered a positive test result for the presence of bronchial hyperresponsiveness
- The presence of airflow obstruction with an FEV<sub>1</sub> less than 65-70% at baseline is generally an indication to avoid performing the test.

# Exercise testing

- For exercise-induced bronchoconstriction
- 6-10 minutes of strenuous exertion at 85-90% of predicted maximal heart rate and measurement of postexercise spirometry for 15-30 minutes
- A positive test: a 15% decrease in  $FEV_1$  after exercise.

# Peak Flow Monitoring

- Common in the ED
- Serial measurements document response to therapy
- Helpful in determining whether to admit the patient to the hospital or discharge from the ED (if more than 70% 60 min post last treatment)
- A limitation of PEF is that it is dependent on effort by the patient
- FEV<sub>1</sub> is also effort dependent but less so than PEF
- Can be compared with asymptomatic (baseline) PEF if known

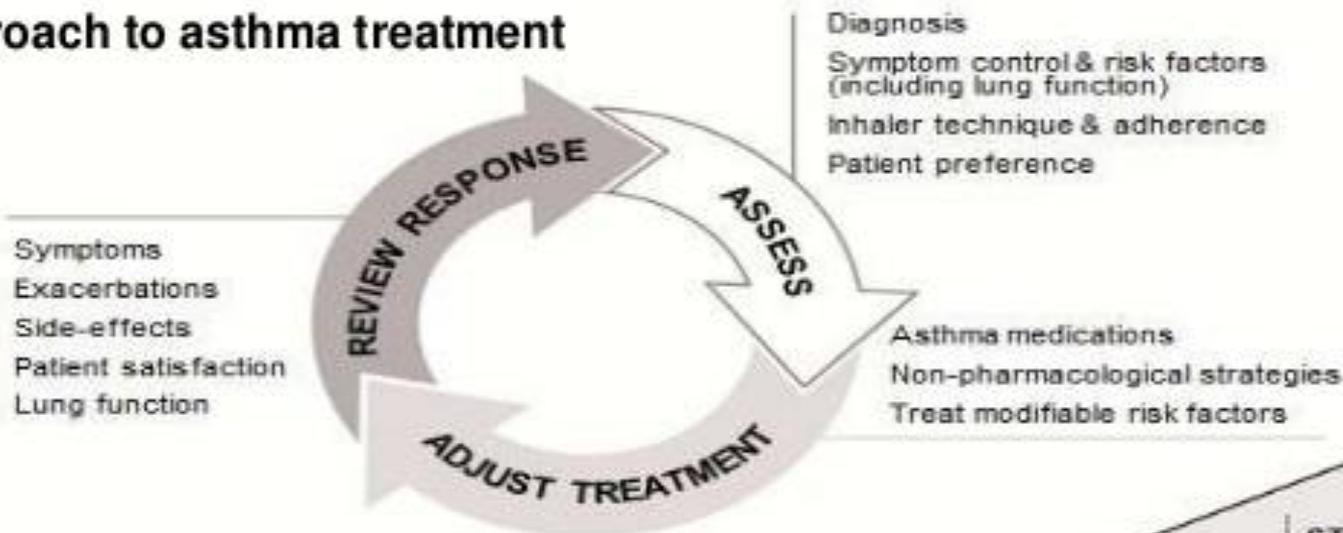
# Asthma Treatment & Management

# Goals for treating asthma

- Avoid troublesome symptoms night and day
- Use little or no reliever medication
- Have productive, physically active lives
- Have (near) normal lung function
- Avoid serious attacks

- A stepwise (step-up/step-down ) approach
- For all patients: quick-relief medications include rapid-acting beta<sub>2</sub> agonists as needed for symptoms
- Intensity depends on the severity of symptoms
- If rapid-acting beta<sub>2</sub> agonists are used more than 2 days a week for symptom relief (not including use of rapid-acting beta<sub>2</sub> agonists for prevention of exercise-induced symptoms), stepping up on treatment may need be considered

# Stepwise approach to asthma treatment



**PREFERRED CONTROLLER CHOICE**

*Other controller options*

**RELIEVER**

	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
<b>PREFERRED CONTROLLER CHOICE</b>		Low dose ICS	Low dose ICS/LABA*	Med/high ICS/LABA	Refer for add-on treatment e.g. anti-IgE
<i>Other controller options</i>	Consider low dose ICS	Leukotriene receptor antagonists (LTRA) Low dose theophylline*	Med/high dose ICS Low dose ICS+LTRA (or + theoph*)	Add tiotropium* High dose ICS + LTRA (or + theoph*)	Add tiotropium* Add low dose OCS
<b>RELIEVER</b>	As-needed short-acting beta <sub>2</sub> -agonist (SABA)		As-needed SABA or low dose ICS/formoterol**		

**REMEMBER TO...**

- Provide guided self-management education (self-monitoring + written action plan + regular review)
- Treat modifiable risk factors and comorbidities, e.g. smoking, obesity, anxiety
- Advise about non-pharmacological therapies and strategies e.g. physical activity, weight loss, avoidance of sensitizers where appropriate
- Consider stepping up if ... uncontrolled symptoms, exacerbations or risks, but check diagnosis, inhaler technique and adherence first
- Consider stepping down if ... symptoms controlled for 3 months + low risk for exacerbations. Ceasing ICS is not advised.

# Environmental control

- Avoid smoking
- Control dust mites
- Pets: effect may last up to 6 months after pet removal
- Cockroaches
- Mold
- Pollen

# Monoclonal Antibody Therapy

- Omalizumab:
  - IgG antibody against IgE
  - Given by subcutaneous injection every 2-4 weeks
  - moderate-to-severe persistent asthma
  - Positive skin test result or in vitro reactivity to a perennial aeroallergen
  - Symptoms are inadequately controlled with inhaled corticosteroids
  - IgE levels between 30 and 700 IU
  - Should not weigh more than 150 kg

# Bronchial Thermoplasty

- controlled thermal energy is delivered to the airway wall during a series of bronchoscopy procedures

# Acute Exacerbation

- Short acting bronchodilators .
- Steroids
- Heliox: 80:20
- Intubation

# Asthma in Pregnancy

- Complicates 4-8% of pregnancies
- Severe and poorly controlled asthma may be associated with increased prematurity, low birth weight and perinatal mortality
- It is safer to be treated with asthma medications than to have asthma symptoms and exacerbations
- Maintain adequate oxygenation of the fetus by prevention of hypoxic episodes in the mother

# Nocturnal Asthma

- Significant clinical problem
- Peak-flow meters should be used to allow objective evaluation of symptoms and interventions
- Sleep apnea, symptomatic GERD, and sinusitis should be controlled when present
- Medications should be appropriately timed, and consideration should be given to the use of a long-acting inhaled or oral beta<sub>2</sub>agonist, a leukotriene modifier, and inhaled corticosteroids
- Sustained-release theophylline preparation and changing the timing of oral corticosteroids to midafternoon can be also be used.

## Asthma

Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation. [GINA 2016]

## COPD

COPD is a common preventable and treatable disease, characterized by persistent airflow limitation that is usually progressive and associated with enhanced chronic inflammatory responses in the airways and the lungs to noxious particles or gases. Exacerbations and comorbidities contribute to the overall severity in individual patients. [GOLD 2016]

## Asthma-COPD overlap syndrome (ACOS) [a description]

Asthma-COPD overlap syndrome (ACOS) is characterized by persistent airflow limitation with several features usually associated with asthma and several features usually associated with COPD. ACOS is therefore identified by the features that it shares with both asthma and COPD.

A specific *definition* for ACOS cannot be developed until more evidence is available about its clinical phenotypes and underlying mechanisms.

# Step 3 - Spirometry



Spirometric variable	Asthma	COPD	ACOS
Normal FEV <sub>1</sub> /FVC pre- or post-BD	Compatible with asthma	Not compatible with diagnosis (GOLD)	Not compatible unless other evidence of chronic airflow limitation
Post-BD FEV <sub>1</sub> /FVC <0.7	Indicates airflow limitation; may improve	Required for diagnosis by GOLD criteria	Usual in ACOS
FEV <sub>1</sub> ≥80% predicted	Compatible with asthma (good control, or interval between symptoms)	Compatible with GOLD category A or B if post-BD FEV <sub>1</sub> /FVC <0.7	Compatible with mild ACOS
FEV <sub>1</sub> <80% predicted	Compatible with asthma. A risk factor for exacerbations	Indicates severity of airflow limitation and risk of exacerbations and mortality	Indicates severity of airflow limitation and risk of exacerbations and mortality
Post-BD increase in FEV <sub>1</sub> >12% and 200mL from baseline (reversible airflow limitation)	Usual at some time in course of asthma; not always present	Common in COPD and more likely when FEV <sub>1</sub> is low	Common in ACOS, and more likely when FEV <sub>1</sub> is low
Post-BD increase in FEV <sub>1</sub> >12% and 400mL from baseline	High probability of asthma	Unusual in COPD. Consider ACOS	Compatible with diagnosis of ACOS

**THANK YOU!**