

Asthma

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Definition

- 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

- Airway inflammation
- Intermittent airflow obstruction
- Bronchial hyperresponsiveness

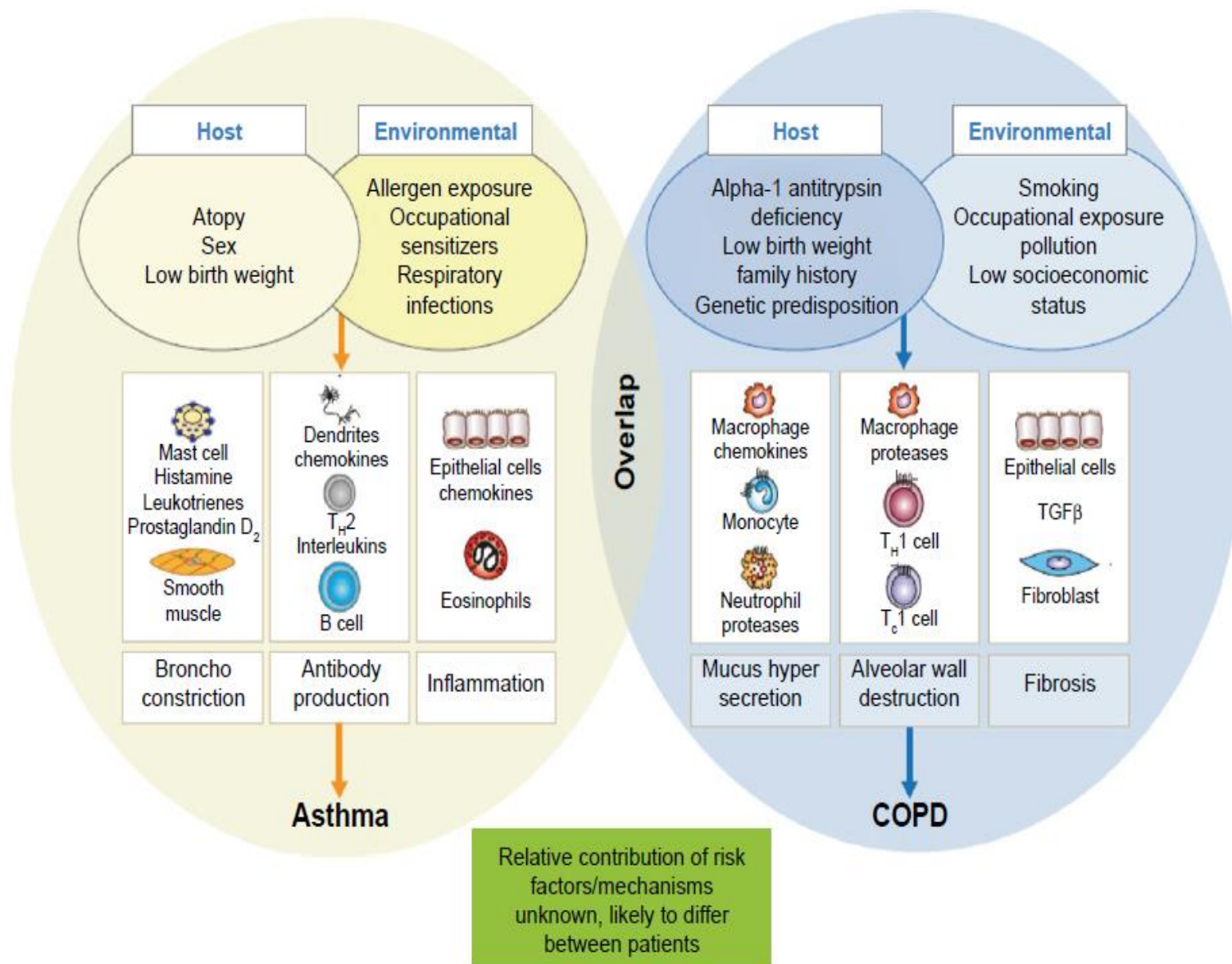
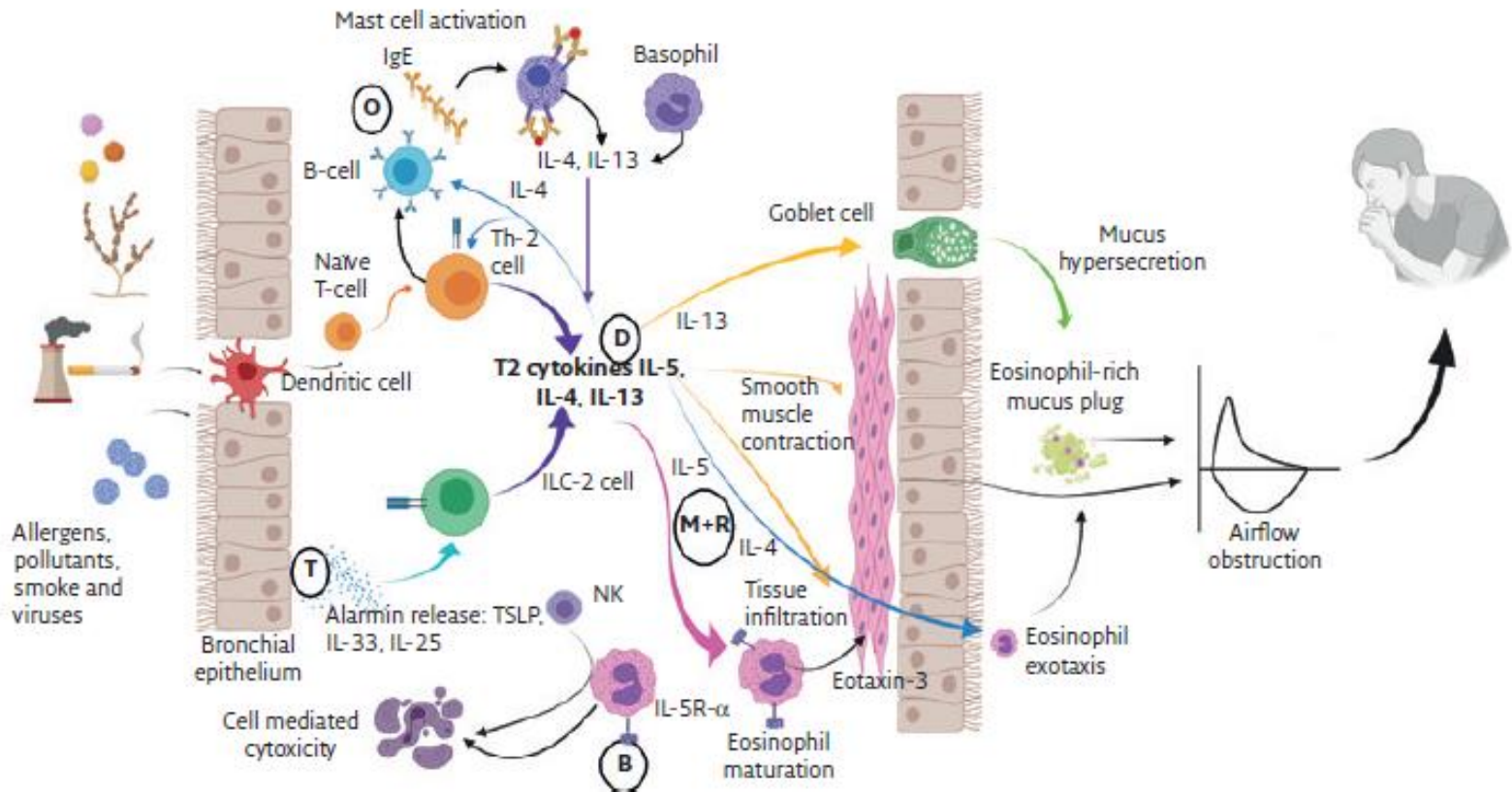


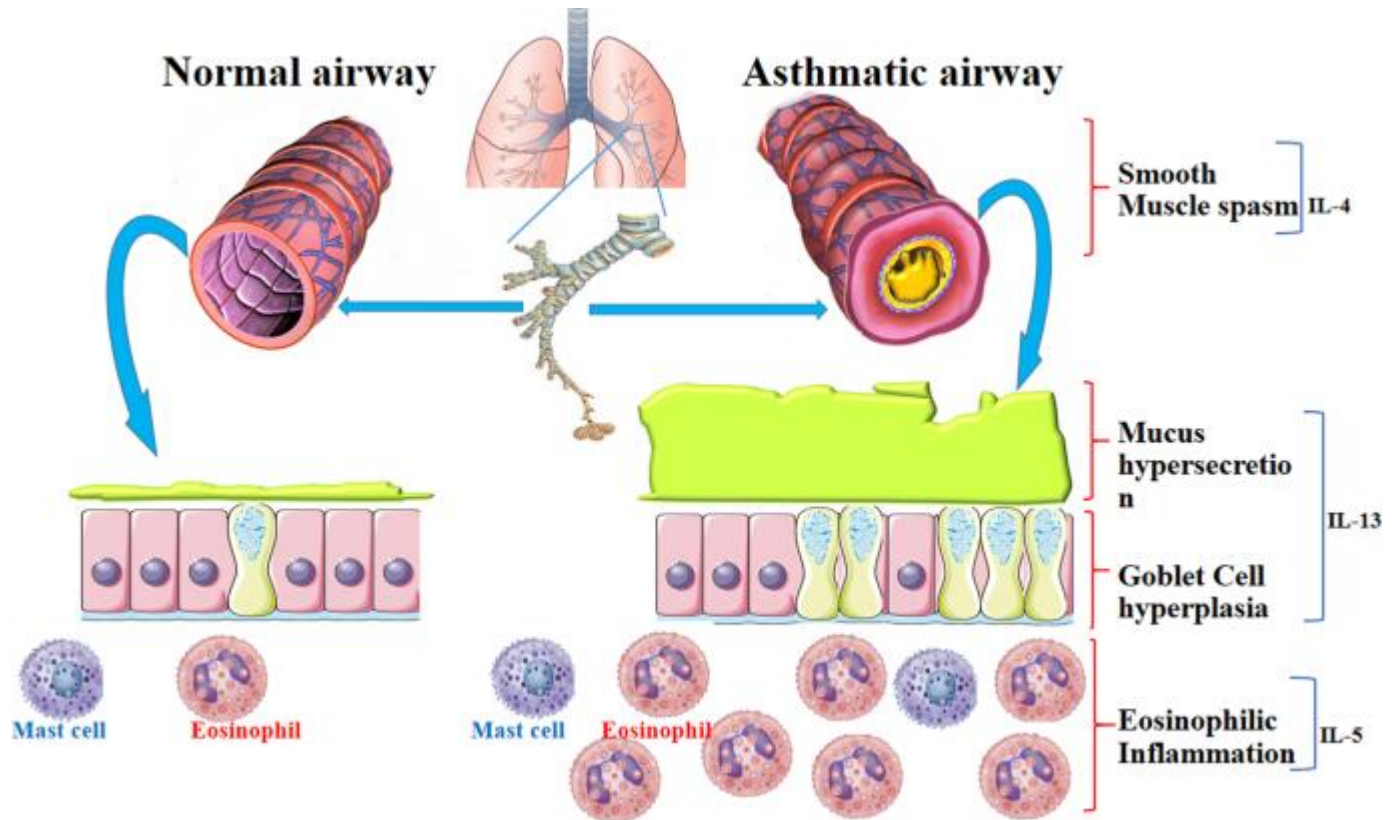
Figure 2 Pathophysiology of asthma, COPD, and overlap.

Notes: Data taken from Postma et al²⁵ and Barnes et al.²⁷

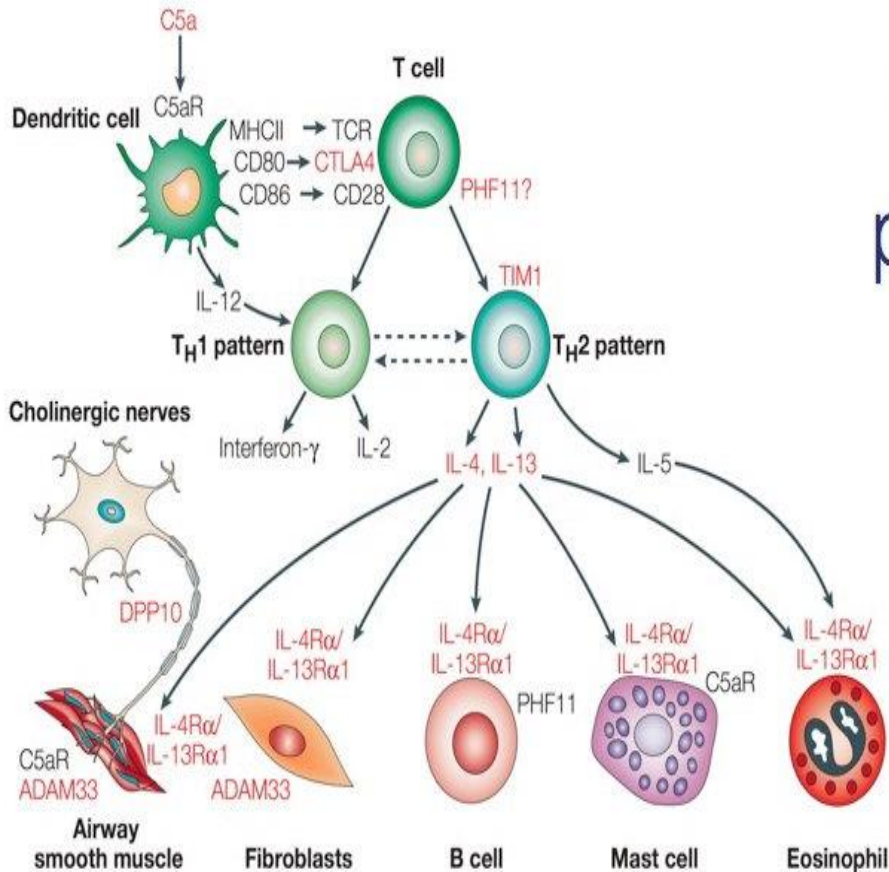
Abbreviations: TGFβ, tumor growth factor β; T_H1, T-helper 1; T_C1, type 1 cytotoxic T cells.

Pathophysiology:





Pathways in the pathogenesis of asthma



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

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 ₂	PaO ₂
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)

Etiology

- 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.
- 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
- 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.
- 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
- 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
 - O₂ 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)
 - O₂ 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)
- O₂ 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 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 ₁ or PEF
STEP 4 Severe Persistent	Continuous Limited physical activity	Frequent	< 60% predicted Variability > 30%
STEP 3 Moderate Persistent	Daily Attacks affect activity	> 1 time week	60 to 80% predicted Variability > 30%
STEP 2 Mild Persistent	> 1 time a week but < 1 time a day	> 2 times a month	> 80% predicted Variability 20 to 30%
STEP 1 Intermittent	< 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 baseline¹
- 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:
 - ❖ Atopic dermatitis.
 - ❖ Allergic bronchopulmonary aspergillosis.
 - ❖ EGPA
 - ❖ Eosinophilic pneumonia
 - Use mepolizumab (anti-IL-5 antibody) if counts 150 cells/ μ L or an eosinophil count of 300 cells/ μ 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
 - Observed also in: (allergic bronchopulmonary aspergillosis, EGPA)
 - 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 FEV₁/FVC (airway obstruction)
- Reversibility: increase of 12% and 200 mL after the administration of a short-acting bronchodilator

Bronchodilator Response PFT

ID: AKC1991

Date: 21/06/04

Gender: Male

Age: 40

Weight(kg): 96.0

Height(cm): 189

BMI: 26.87

PB: 745 Temp:

21

	Pre	Pre	Post	Post	Post	
Spirometry	Ref	Meas	% Ref	Meas	% Ref	% Chg
FVC	5.71	6.05	106	6.31	110	4
FEV ₁	4.27	3.74	88	4.27	100	14
FEV ₁ /FVC	74.0	62.0		68		
FEF ₂₅₋₇₅ %	4.19	(1.99)	(47)	2.66	63	33
PEF	10.27	10.19	99	9.4	91	-8

Lung Volumes

TLC

RV

RV/TLC

FRC PL

ERV

VC

Resistance

Raw

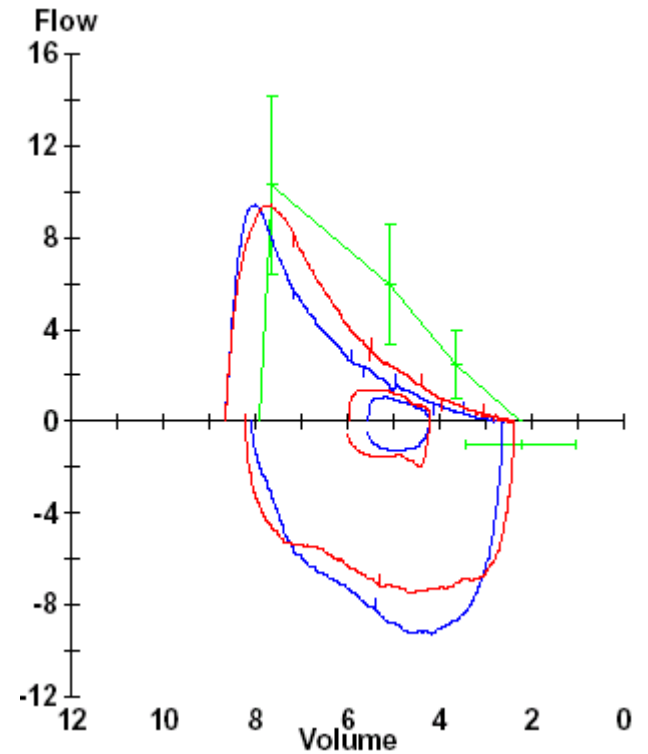
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Diffusion

D_{LCO}

D_{LCO} / V_A

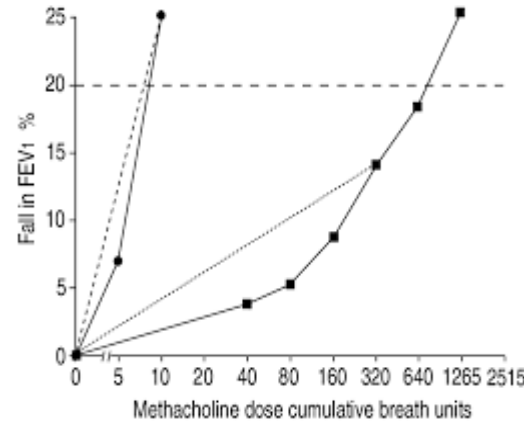
V_A



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.
- 20% decrease in FEV₁, up to the 4 mg/mL level, is considered a positive test result.
- The presence of airflow obstruction with an FEV₁ less than 65-70% at baseline is generally an indication to avoid performing the test.

Exercise testing

- 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
- Variability of 20% between morning and night .
- 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.

Asthma Treatment & Management

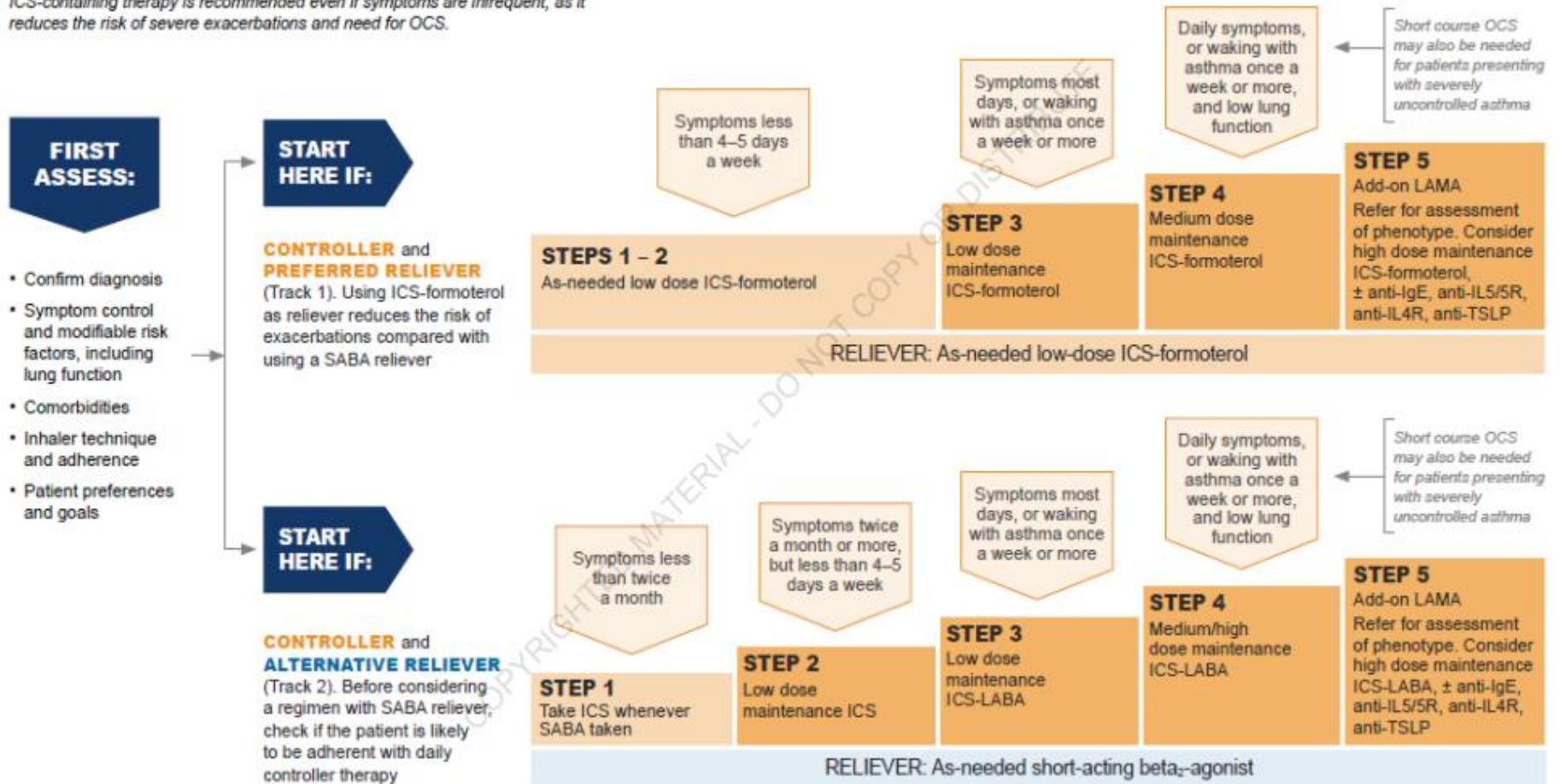
Goals for treating asthma

- 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(Exacerbations)

- A stepwise (step-up/step-down) approach
- For all patients: quick-relief medications include rapid-acting beta₂ agonists as needed for symptoms
- Intensity depends on the severity of symptoms
- If rapid-acting beta₂ agonists are used more than 2 days a week for symptom relief (not including use of rapid-acting beta₂ agonists for prevention of exercise-induced symptoms), stepping up on treatment may need be considered

GINA 2022 guidelines:

ICS-containing therapy is recommended even if symptoms are infrequent, as it reduces the risk of severe exacerbations and need for OCS.



Environmental control

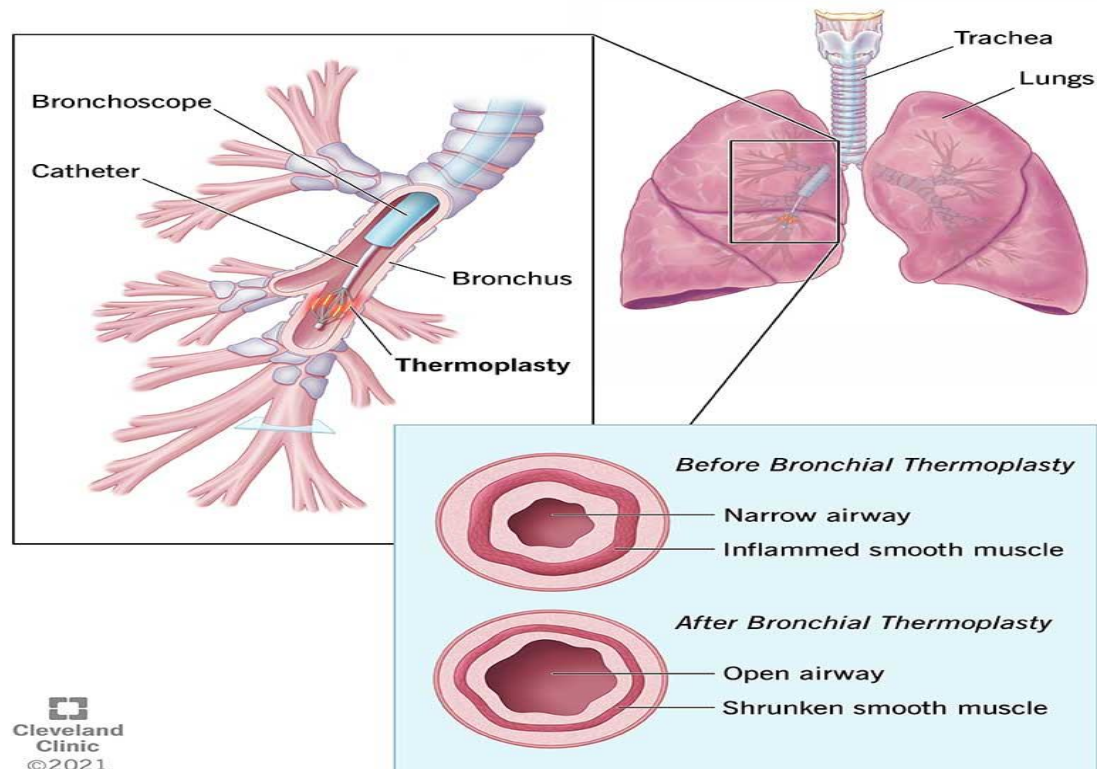
- Avoid smoking
- Control dust mites
- Pets: effect may last up to 6 months after pet removal
- Cockroaches
- Mold
- Pollen

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 :
 - prematurity,
 - low birth weight
 - perinatal mortality
- Maintain adequate oxygenation of the fetus by prevention of hypoxic episodes in the mother

THANK YOU!