Asthma

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Definition

- Asthma: Asthma is a chronic disease characterized by recurrent attacks of shortness of breath and wheezing.

the hallmark of asthma: + chest tightness

↳ Feels normal b/w the attacks / triggered by certain exposures and resolve spontaneously or with use of inhaler bronchodilator

ما صار معه هيك من قبل ؟
كيف خلصت الـ attack ؟

  - Vary in severity and frequency from person to person.
  - May become worse during physical activity or at night. {feeling better in morning}

↳ It's variable b/w pts. & variable in one pt. , peak flow variability

بنطلب منه يعملها الصبح والمسا

وبنشوف الـ variation in symptoms

Factors contributing to the rise of bronchial asthma in the region

It's not heridetary anymore,

Multifactorial disease, enviroment have an essential role

- Factors contribute in the developing of bronchial asthma:
  - 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*)

Asthma = airway disease

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)

Main pathophysiological features : airway resistance + Chronic inflammation +

smooth muscle abnormality

Pathophysiology

- Structure:
  - Mucosa: epithelial cells: capable of specialized mucous production and transport

↳ mucous gland hypertrophy, ↑ mucous production

  - Basement membrane

↓ changes in the

  - A smooth-muscle matrix extending to the alveolar entrances
  - Supporting connective tissue: fibrocartilaginous or fibroelastic

↳ In later stages of Asthma, the repeated inflammation leads to fibrous formation & remodeling of the airways → chronic asthma → irreversible airway obstruction → these prs. behave like prs. with COPD

Pathophysiology

↳ collection of inflammatory cells in the mucousa

- Cellular elements
  - * mast cells — most common
  - – Basophils
  - * Eosinophils — most common
  - ← Neutrophils → neutrophilic asthma is well documented in obese asthmatic → that's why they respond poorly to inhaled corticosteroids

more common in COPD

  - – 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, chest tightness

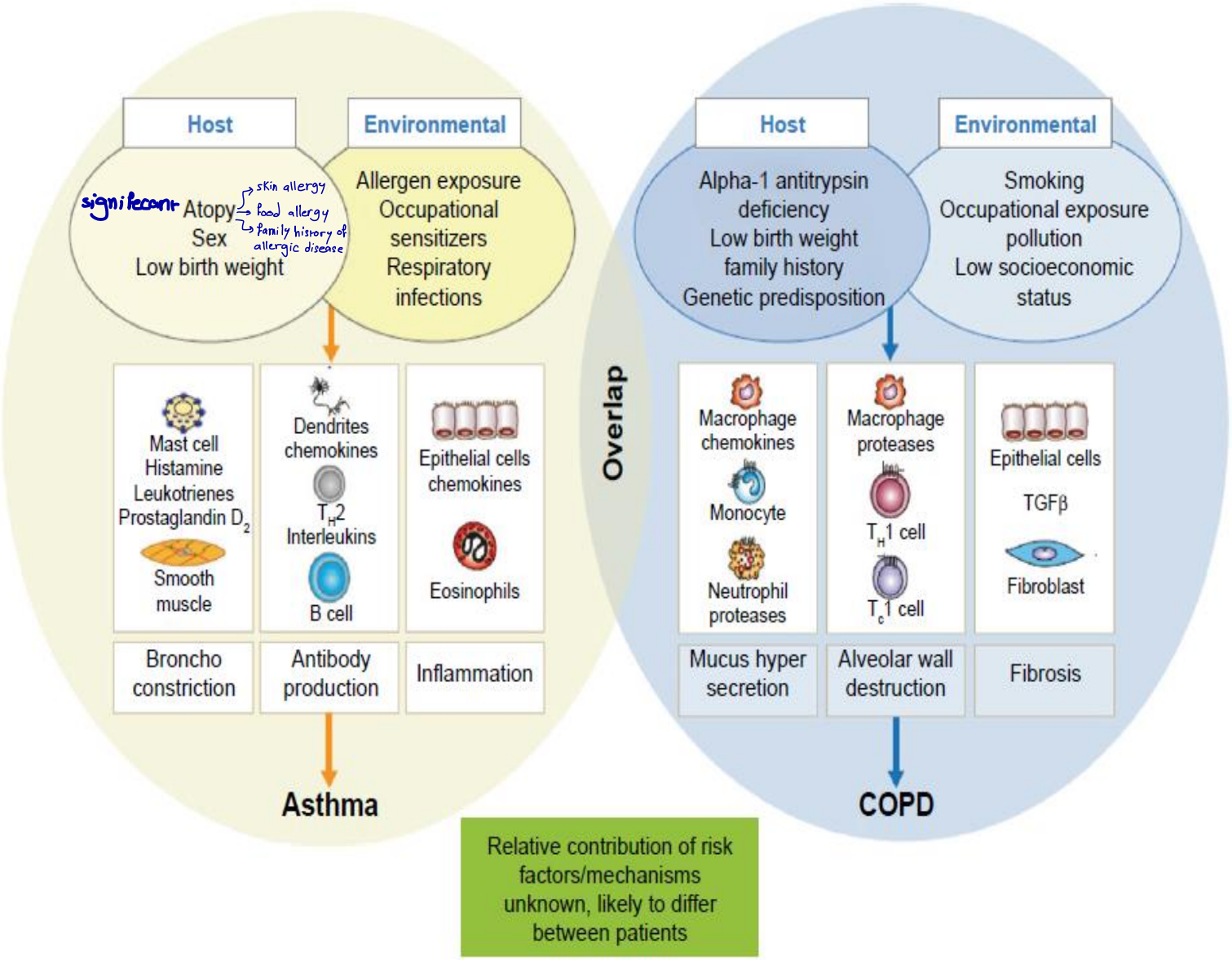
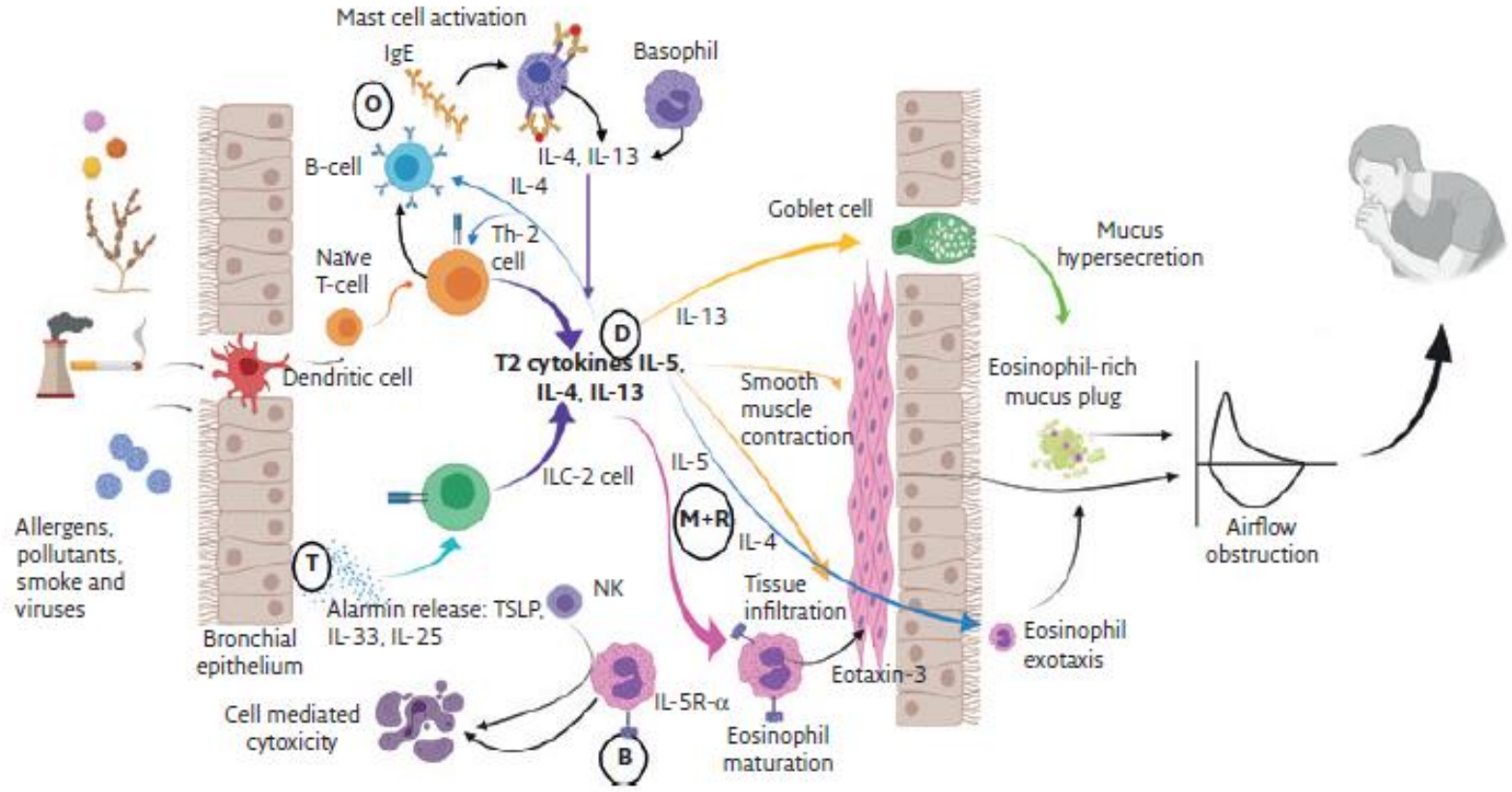


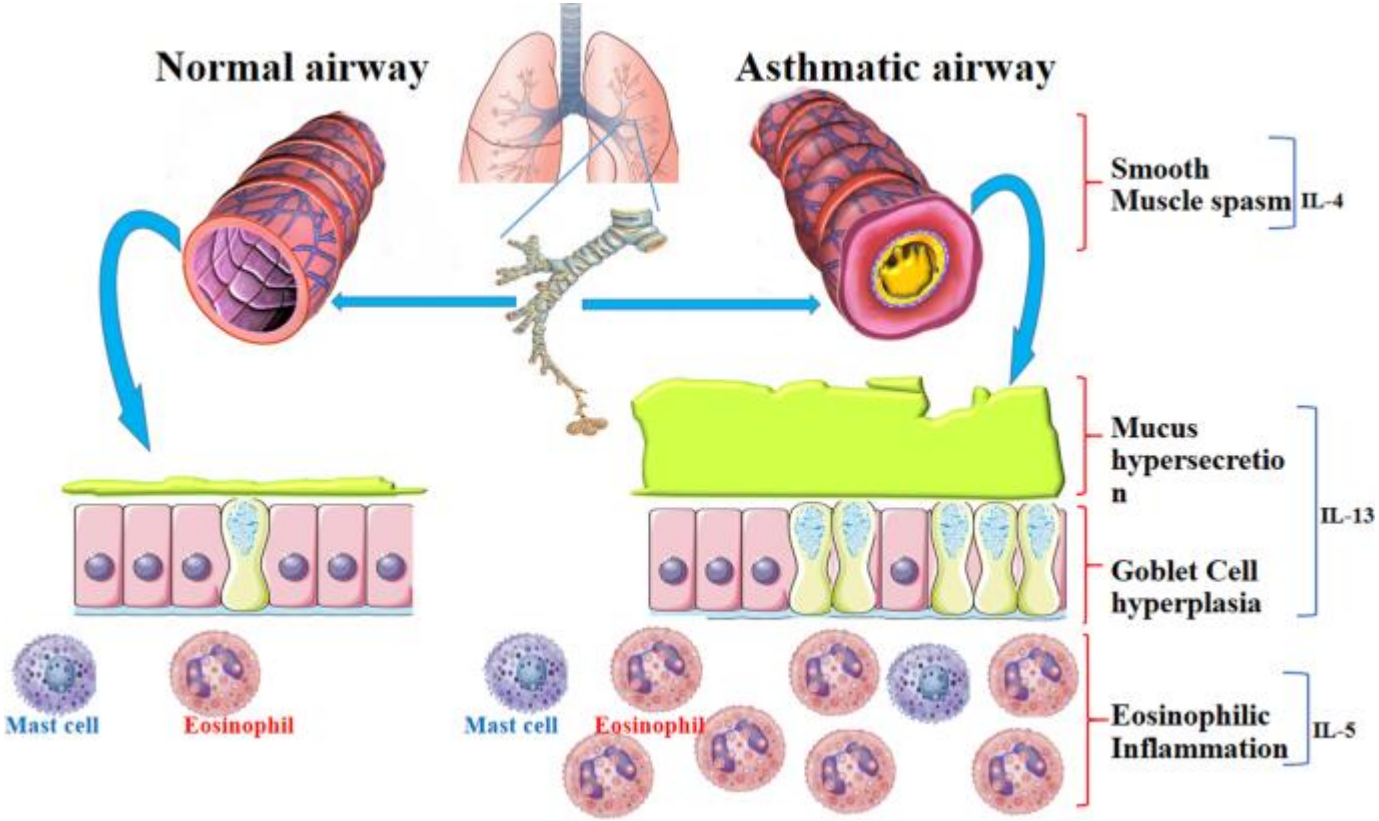
Figure 2 Pathophysiology of asthma, COPD, and overlap.

Notes: Data taken from Postma et al[25] and Barnes et al.[27]

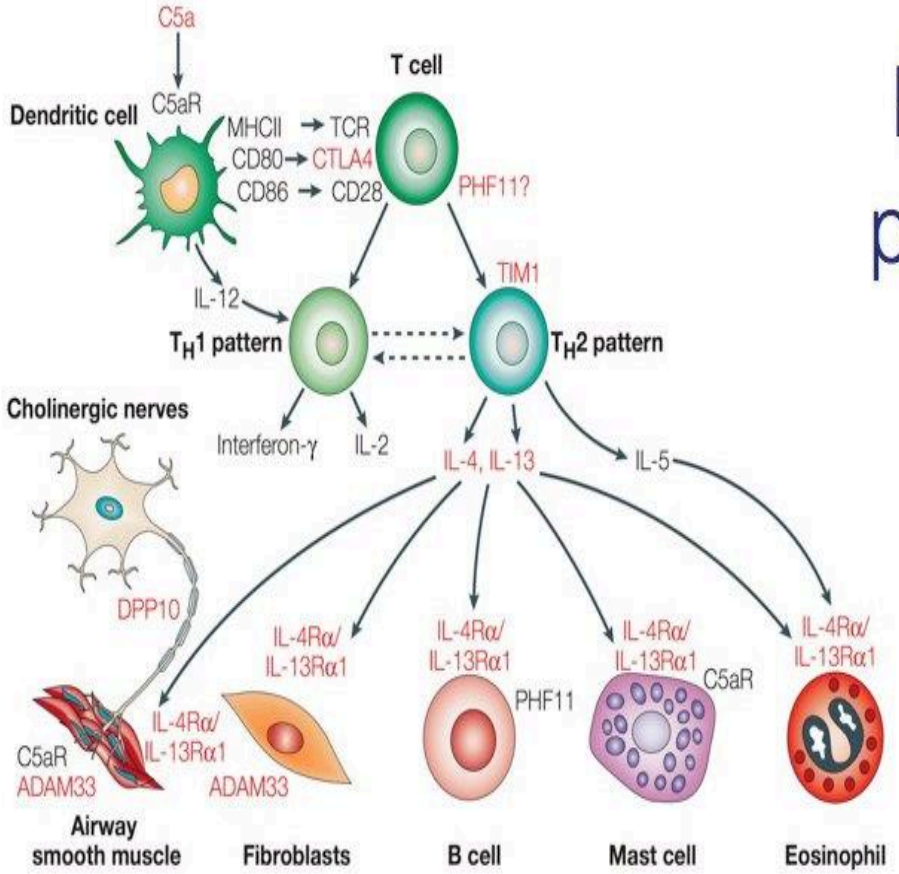
Abbreviations: TGFβ, tumor growth factor β; T_HI, T-helper I; T_CI, type I cytotoxic T cells.

Pathophysiology:




Normal airway
Asthmatic airway
Smooth
Muscle spasm
IL-4
Mucus
hypersecretio
n
Goblet Cell
hyperplasia
IL-13
Mast cell
Eosinophil
Mast cell
Eosinophil
Eosinophilic
Inflammation
IL-5

Pathways in the pathogenesis of asthma



anti – IL-4 → beneficial in eosinphilic asthma pts.

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

Airway Obstruaction (causes)

1. Acute bronchoconstriction: IgE-dependent mediator release following exposure to allergens (early asthma response) → exposed for fumes, dust, detergent
2. Airway edema: 6-24 hours following allergen challenge (late asthma response). → due to airway edema
   IgE is less likely to be involved
3. Chronic mucous plug formation: exudate of serum proteins and cell debris, may take weeks to resolve
4. Airway remodeling: due to structural changes due to long-standing inflammation, affects the extent of reversibility of airway obstruction Fibrosis in airway → irreversible

Bronchial Hyperresponsiveness

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

4 stages of blood gas progression with status asthmaticus

	$PaCO_2$	PaO_2
Stage 1	Decrease (< 35)	Normal
Stage 2	Decrease	Decreased
Stage 3	NORMAL ↑ hypoventilation	Decreased very tired / chest muscles not compensating
Stage 4	High (> 35)	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 → cause asthma excerbation

nor all

- Chronic sinusitis or rhinitis have asthma
- ASA,NSAID hypersensitivity, sulfite sensitivity
- Perinatal factors (prematurity and increased maternal age; maternal smoking and prenatal exposure to tobacco smoke

3 most common causes of uncontrolled asthma?
1. non compliance to inhalers
2. GERD
3. Chronic sinusitis & chronic rhinitis

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

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Aspirin-Induces Asthma

- Asthma, aspirin sensitivity, and nasal polyps
- 5-10% of patients with asthma
- Third to fourth decade
- Can occur with other NSAIDS but most commonly with aspirin
- Caused by an increase in eosinophils and cysteinyl leukotrienes after exposure
- Management:
  - Avoidance of these medications
  - add
  - Leukotriene antagonists, may allow patients to take daily aspirin for cardiac or rheumatic disease -if you can't stop aspirin-
    ↳ under medical observation
  - Aspirin desensitization decreases sinus symptoms, allowing daily dosing of aspirin
    small doses

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 → build up of exposures over the time
    - 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 variations helps in diagnosis

- 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

chronic sinusitis → needs nasal steroids

Exercise-induced asthma

Dry - inhaled air (cold air)

- 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
  bronchoalveolar lavage
- Refractory period, during which a second exercise challenge does not cause a significant degree of bronchoconstriction

management:

- Warm up and B2 agonist before exercise

بختين فتوتين قبل ما تلعب رياضة

Obesity

- Significant association between asthma and abnormal lipid and glucose metabolism.
- High BMI: worse asthma control weight loss improve asthma
- 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

Flares

↳ worsening of the base line respiratory symptoms that leads to change in medication

- 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

↳ Cardiac Wheeze → congestion in lung paranchyma causes → bronchiolitis

Cough

worse at night
dry cough (least sputum production)

- 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

Excerbation of Asthma classification:

1

- 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 of10-20 mm Hg)
  - O2 sat is 91-95%
  - Sitting position

Physical Examination

3

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.

4 Impending Respiratory Failure

- Drowsy and confused abnormal level of conscience
- 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 they become tachypnic & then → bradypnic
- 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

stable

Asthma Classification

Pt. come to the clinic fine, normal ..

- 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

In asthma pts. : FEV1 / FVC = < 70%.

	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

Forigen bodies, vocal cord dysfunction, tracheal bronchial lesion

- 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]
- 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

} can be causes of poor control

Asthma Workup

- Blood and sputum eosinophilia:
  - Greater than 4% (blood) supports the diagnosis of asthma
  - Its absence does not exclude asthma IL-5
  - 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/µL or an eosinophil count of 300 cells/µL within the past 12 months
  - ~~*~~ Adjust ICS with sputum eosinophilia → means pt. is not taking his inhaler

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)

↑ serum IgE level pt.

Chest Radiography

does not help

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

Chest CT Scanning

can be useful but not a part of diagnosis

- 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

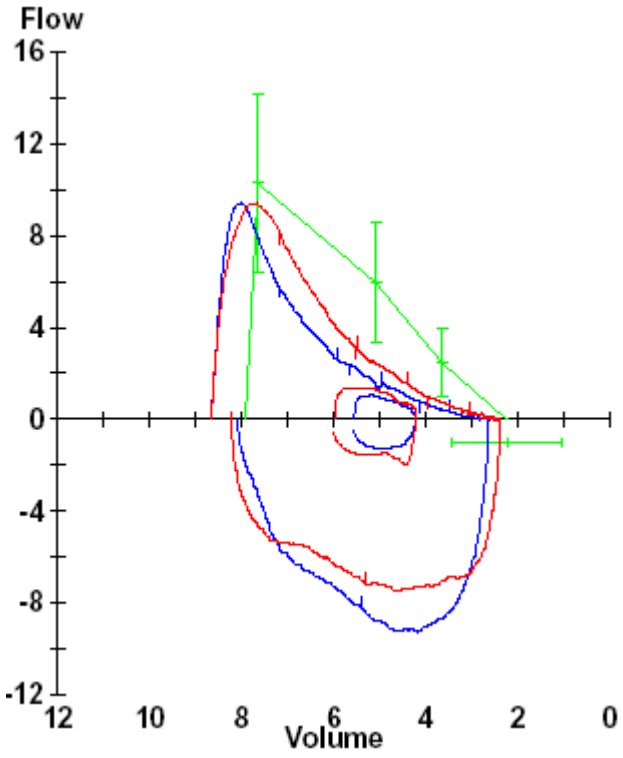
↳ Important + spirometry

- Establish asthma diagnosis
- Prior to initiating treatment
- Should include measurements before and after inhalation of a short-acting bronchodilator
- Reduced FEV_1/FVC (airway obstruction) → < 70%
- Reversibility: increase in FEV1/FVC of 12% and 200 mL after the administration of a short-acting bronchodilator (ventolin)

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

Spirometry	Pre Ref	Pre Meas	Post % Ref	Post Meas	Post % 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						
sRaw						
Diffusion						
D_{LCO}						
D_{LCO} /V_A						
V_A						



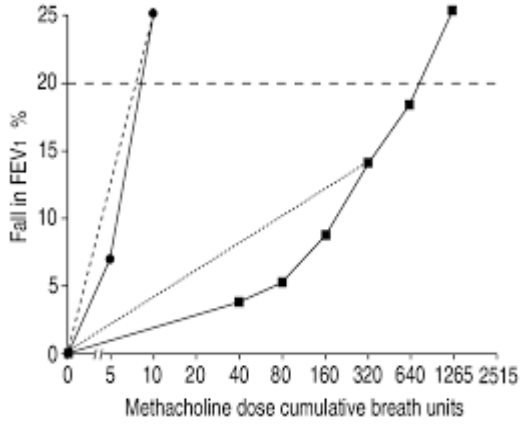
We induce acute asthma attack by:

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

- Mannitol

Methacholine/histamine challenge



- Methacholine is administered in incremental doses up to a maximum dose of 16 mg/mL.
- 20% decrease in FEV_1, up to the 4 mg/mL level, is considered a positive test result.
- The presence of airflow obstruction with an FEV_1 less than 65-70% at baseline is generally an indication to avoid performing the test.

Exercise testing

↳ For exercise induced asthma

- 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

بنخلي المريض يراقبه بالبيت ويكتبه على ورقة ويجبلنا اياه

- Common in the ED
- Serial measurements document response to therapy
- Variablity 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

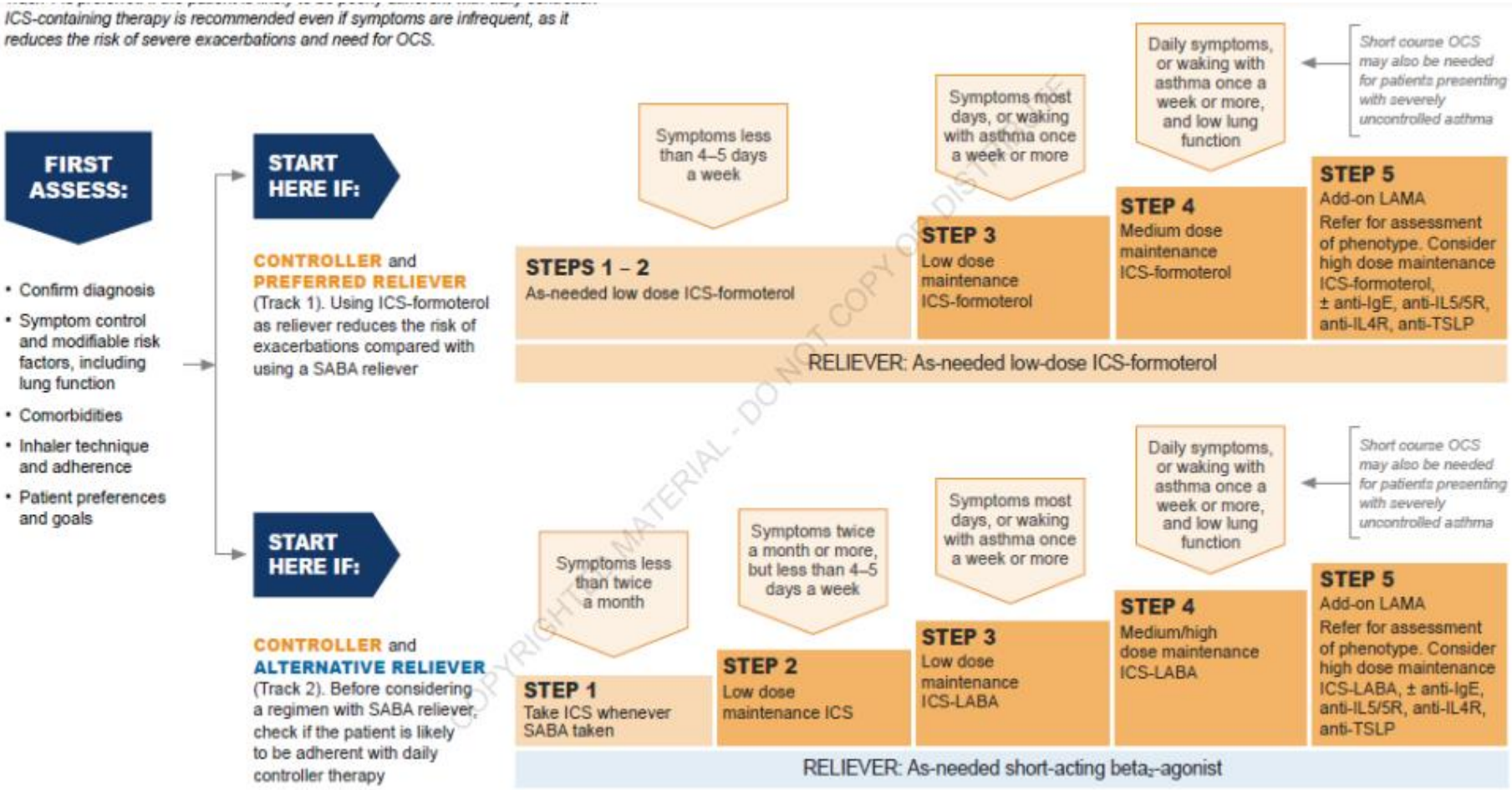
Goals for treating asthma

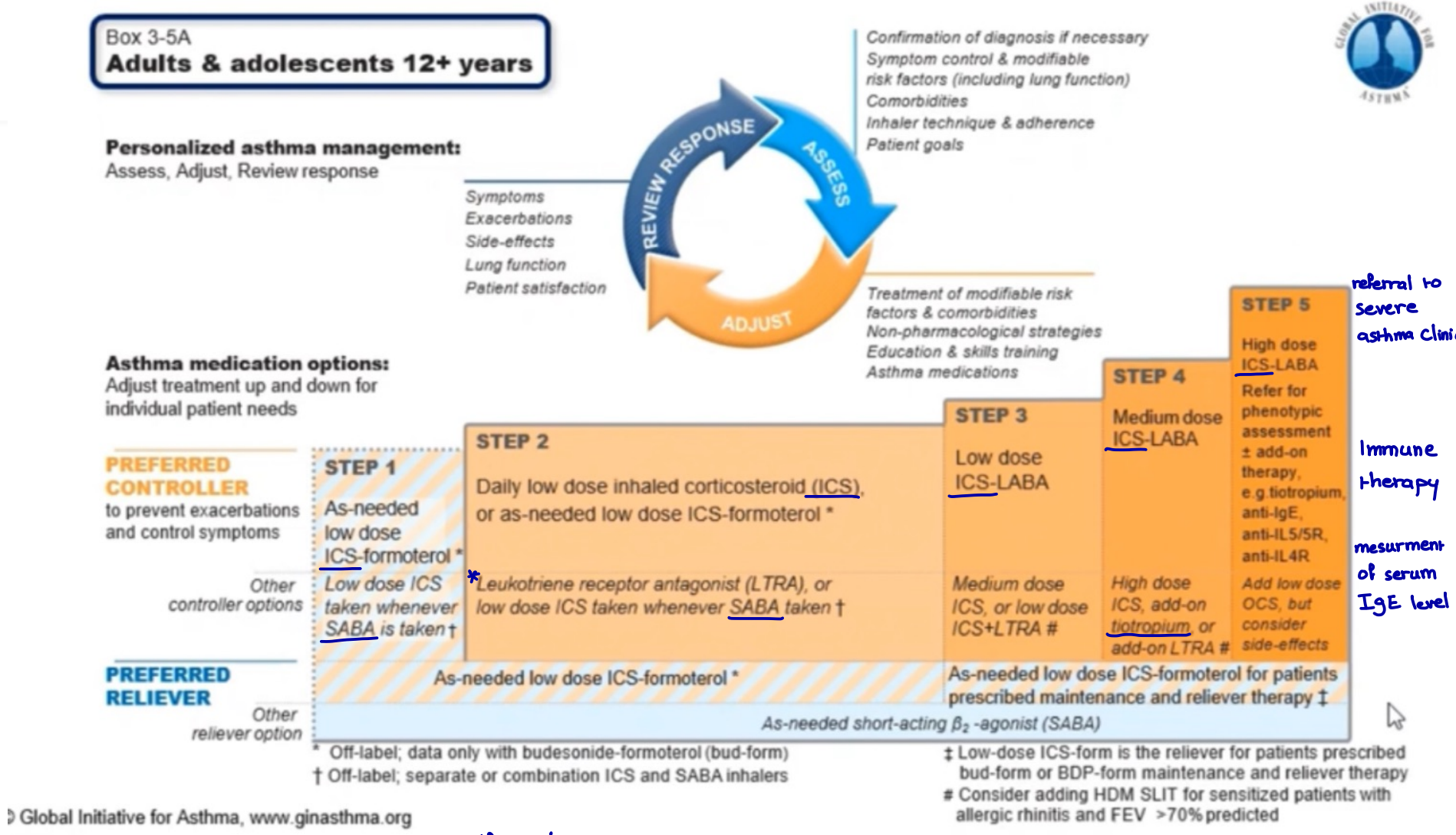
- Avoid troublesome symptoms night and day
- Use little or no reliever medication
- Have productive, physically active lives
- Have (near) normal lung function
- Avoid serious attacks(Exacerbations)

maintain Lung function

- A stepwise (step-up/step-down) approach
- For all patients: quick-relief medications include rapid-acting beta$_2$ agonists as needed for symptoms
- Intensity depends on the severity of symptoms
- If rapid-acting beta$_2$ agonists are used more than 2 days a week for symptom relief (not including use of rapid-acting beta$_2$ agonists for prevention of exercise-induced symptoms), stepping up on treatment may need be considered

GINA 2022 guidelines:





referral to severe asthma clinic

Immune therapy

mesurment of serum IgE level

GINA

* If asthma pt. is diagnosed → given inhaled corticosteroid

Tiotropium → spiriva

Environmental control

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

Monoclonal Antibody Therapy

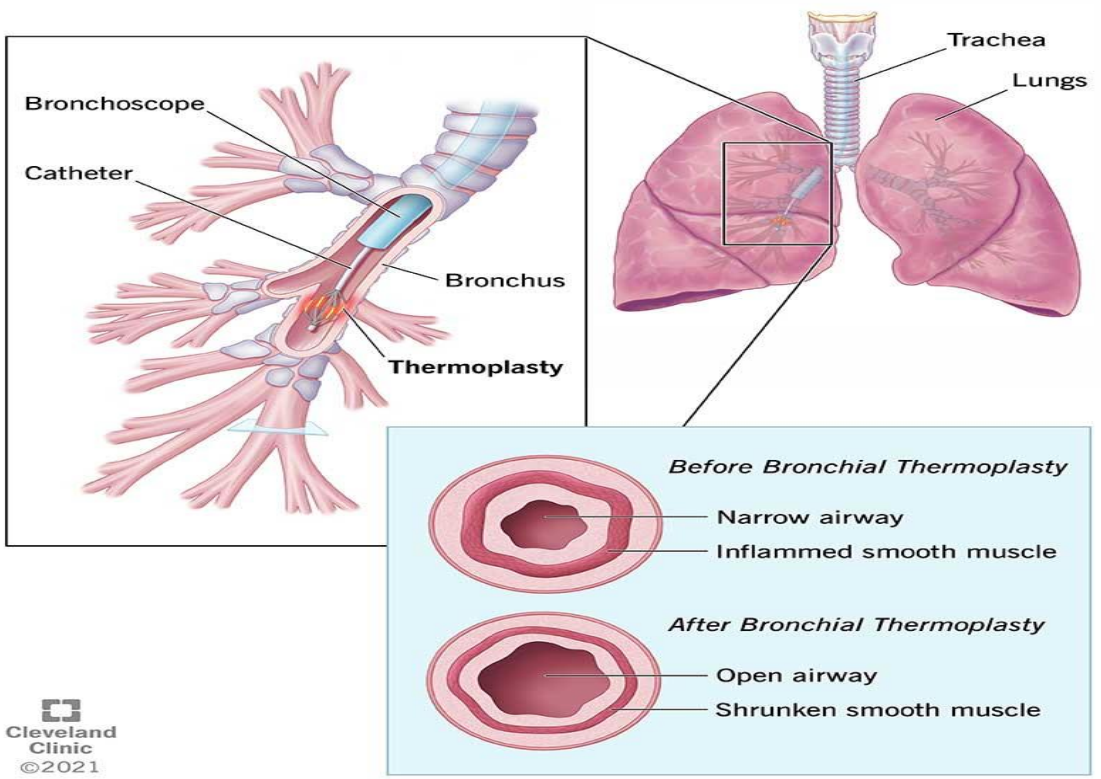
- Omalizumab:
  - IgG antibody against IgE
  - Given by subcutaneous injection every 2-4 weeks
  - moderate-to-severe persistent asthma
  - Positive skin test result or in vitro reactivity to a perennial aeroallergen
  - Symptoms are inadequately controlled with inhaled corticosteroids
  - IgE levels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

Bronchial Thermoplasty

burning the hypertrophied smooth muscles

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

↳not very good outcome



Acute Exacerbation

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

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

Definitions

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]

بطل موجود

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.

THANK YOU!