PULMONARY/RESPIRATORY SYSTEM

Function: respiration (inhalation/exhalation of respiratory gases)
→ Site of gas exchange (O_2 – for energy (ATP) production) & CO_2 – waste product)

Structure: 3 segments
1. Upper respiratory tract: nose & nasal passages; paranasal sinuses; pharynx
2. Respiratory airways: voice box (larynx); trachea; bronchi/large bronchioles
3. Lungs: respiratory (small) bronchioles; alveolar ducts & sacs; alveoli

Gas exchange

Alveoli: hollow cavity (200 µm)
> Collagen & elastin (stretches upon inhalation)
> Capillary net/mesh (single layer epithelium → gasses diffuse max 2 cell distance)
> 700 million alveoli →surface area = 70 m^2

Respiratory Surface: 2 gasses are transferred in opposite directions (diffusion)
> Continuous blood flow (steep concentration gradient & saturated blood already moved on)
> Gas needs to be in FLUID (therefore moist environment in lungs)

Impaired by: pneumonia, pulmonary edema, anemia (lack of Hb to bind O_2)

Airways

		Structure	Function
Conducting	Trachea, L & R bronchus, bronchi	• Cartilage • Smooth muscle • Ciliated pseudostratified columnar epithelium • Mucus secreting goblet cells	• Conduct air to respiratory airways • Warm & humidify inspired air • NO GAS EXCHANGE
	Bronchioles, terminal bronchioles	• No cartilage • Smooth muscle • Cuboidal epithelium • Mucus secreting goblet cells	
Respiratory	Respiratory bronchioles, alveoli	• Simple squamous epithelium	• Gas exchange with blood • O_2 IN / CO_2 OUT

Ventilation/Perfusion (V/Q) Ratio: measures efficiency & adequacy
> V (ventilation) = air that reaches alveoli
> Q (perfusion) = blood that reaches alveoli

- Oxygen inhaled just enough to SATURATE
- Ideal V/Q = 1 Reality V/Q = 0.8

Low V/Q: impaired gas exchange
> Low paO_2
> Bronchitis, asthma, pulmonary edema

= Perfusion, no ventilation

High V/Q: wasted ventilation (unoxygenated blood)
> High paO_2 (low $paCO_2$)
> COPD, pulmonary embolism

= Ventilation, no perfusion

Impaired by: pulmonary hypertension; MI

Definition of asthma: heterogeneous disease, usually characterized by chronic airway inflammation
> Variable & recurring symptoms
> REVERSIBLE airflow obstruction/ bronchospasm

Asthma risk factors:
- Genetic burden (inheritance doubles risk)
  - > Neither parent = 15-20% risk
  - > One parent = 30-40% risk
  - > Both parents = 80-90% risk
- History of exposure to cigarette smoke
- History of allergies/dermatitis
- Intense allergy in infancy (mold, dust mites)

Asthma Triggers:
- Allergens
- Irritants
- Weather changes
- URTIs
- Cold air
- Strong emotions
- Exercise

Diagnosis of asthma: based on history of characteristic sx patterns & evidence of variable airflow limitation (bronchodilator reversibility testing or other tests)

> Asthma is usually characterized by airway inflammation & hyper responsiveness, but these are not necessary/sufficient to make dx of asthma

Physical examination: often normal

> Most frequent finding: wheezing on auscultation (esp. on forced expiration)

> Wheezing may be absent during severe asthma exacerbations ("silent chest")

Increased % asthma sx	*Decreased % asthma sx*
• > 1 type of sx • Sx often worse at night or early morning • Sx vary over time & in intensity • Sx are triggered	• Isolated cough w/ no other respiratory sx • Chronic production of sputum • SOB associated with dizziness, light-headedness or peripheral tingling • Chest pain • Exercise-induced dyspnea with noisy inspiration (stridor)

REVIEW – TYPE 1 HYPERSENSITIVITY

PRISH:

- Pain: release of nerve stimulating chemicals
- Redness: increased blood flow
- Immobility: multisource including swelling
- Swelling: accumulation of fluid
- Heat: blood flow from body core is warm

Not all sx may be present – depends on location

> Internal (organs) vs. external (skin)

> Pain receptors vary greatly + personal thresholds

Hypersensitivity: results when immune response is harmful to host

> Occurs when antigen recognition is exaggerated or inappropriate

> Requires presensitization (priming of immune system)

Chemical mediators of T1 Hypersensitivity

Pre-existing in leukocytes	Newly synthesized in hypersensitivity I rxns
• Histamine • Serine proteases • Chemokines (eosino- & neutro- phils) used to recruit leukocytes	• Leukotrienes • Prostaglandins • Platelet-activating factor • Interleukins • Tumor necrosis factor

Mechanism of ACUTE PHASE:

1. Antigen presentation: MHC II + antigen presents to helper T cell → T cell differentiates becoming TH2 (cytokine mediated)
2. T cells & B cells see same antigen → co-stimulus of B & T cells → secrete cytokines (IL2 & IL4) = cell proliferation, activation & differentiation
   > B cell activation is T-cell dependent pathway
3. B cells become PLASMA CELL: antibody & cytokine production

Inappropriate pathway: B-cell isotype switching

1. IL-4 production SWITCHES antibody type → results in **IgE** not IgA, IgG, or IgM
2. IgE circulates with antigen specific recognition
3. IgE binds to innate cell Fc receptors on circulating mast cells & basophils → leukocyte sensitization
4. Re-exposure to antigen activates sensitized cells (IgE recognizes antigen) → degranulation → proinflammatory cytokines produced

Mechanism of LATE PHASE:

1. Mast cells & basophils produce cytokines
2. Cytokines recruit eosinophils
3. Re-exposure and recognition – IgE binds allergen (antigen)
   > Eosinophils Fc receptors are bound to IgE antivodies
4. Eosinophil degranulates – proteolytic enzymes & proinflammatory cytokines are released

ASTHMA PATHOPHYSIOLOGY:

> Inflammation

> Bronchial hyperresponsiveness

> Mucus hypersecretion

> Airway remodeling

ASTHMATIC RESPONSE:

Early phase: BRONCHOCONSTRICTION – smooth muscle contraction *in airway*

> Inflammatory mediators (histamine, leukotrienes, prostaglandins)

> Peaks in 30-60 minutes

Late phase: INFLAMMATION – bronchial edema, epithelial cell lining damage, mucus hypersecretion, bronchospasm

> Eosino- & neutro- phils infilitrate airway tissues

> Peaks in 5-6 hours

GOALS OF ASTHMA MANAGEMENT

- Symptom control & maintain normal activity levels
- Risk reduction of exacerbations, fixed airflow limitation & medication side-effects

> Achieving these goals requires partnership between pt & HCPs

ROLE OF LUNG FUNCTION IN ASTHMA:

- Diagnosis: demonstrate variable expiratory airflow limitation
  - > Reconsider Dx if sx & lung fxn are discordant
    - Frequent sx but normal FEV_1: cardiac disease, lack of fitness?
    - Few sx but low FEV_1: poor perception, restriction of lifestyle?
- Risk assessment: low FEV_1 is an independent predictor of exacerbation risk
- Monitoring progress: measure lung function at Dx, 3-6 months after starting txt (to identify personal best), then periodically
  - > Consider long-term PEF monitoring for pts with severe asthma or impaired perception of airflow limitation
- Adjusting treatment??
  - > Limited by between-visit variability of FEV_1 (15% yr-yr)

ASSESSING ASTHMA SEVERITY: assessed retrospectively from level of txt required to control sx & exacerbations

> Assess asthma severity after pt has been on controller txt for several months

> Severity is not static – may change over months or years, or as different txts become available

Categories of asthma severity:

- Mild asthma: well-controlled with Steps 1 or 2 (as-needed SABA or low dose ICS)
- Moderate asthma: well-controlled with Step 3 (low dose ICS/LABA)
- Severe asthma: requires Step 4/5 (moderate or high dose ICS/LABA ± add-on) or remains uncontrolled despite txt

ASSESSMENT OF ASTHMA

1. Asthma control
   a. Assess sx control over last 4 weeks
   b. Assess risk factors for poor outcomes
      (incl. low lung fxn)
2. Treatment issues
   a. Check inhaler technique & adherence
   b. Side effects
   c. Does pt have written asthma action plan?
   d. Pt's attitudes & goals for their athma?
3. Comorbidities – may contribute to sx & poor QOL
   > Rhinosinusitis, GERD, obesity, obstructive sleep apnea, depression, anxiety

DISTINGUISH BETWEEN UNCONTROLLED & SEVERE ASTHMA:

1. Watch pt using their inhaler. Discuss adherence & barriers to use.
2. Confirm the diagnosis of asthma.
3. Remove potential risk factors. Assess & manage comorbidities.
4. Consider treatment step-up.
5. Refer to a specialist or severe asthma clinic.