Alterations of pulmonary function
Advanced Pathophysiology

Acute respiratory failure

- acute or chronic impairment of gas exchange between the lungs and the blood causing hypoxia with or without hypercapnia
- Acute impairment in gas exchange between the lungs and the blood causing hypoxia with or without hypercapnia (caused by acute decompensation of chronic pulmonary disease)
    - Hypoxic respiratory failure (type 1 respiratory failure) is hypoxia without hypercapnia and with an arterial partial pressure of oxygen (PaO2) of <60 mmHg (<8 kPa) on room air at sea level
    - Hypercapnic respiratory failure (type 2 respiratory failure) is hypoxia with an arterial partial pressure of carbon dioxide (PaCO2) of >50 mmHg (>6.5 kPa) on room air at sea level

ARDS

- Most common symptoms and signs are dyspnea and hypoxemia, which progress to acute respiratory failure
- Acute respiratory distress syndrome (ARDS) is a non-cardiogenic pulmonary edema and diffuse lung inflammation syndrome that often complicates critical illness.
- diagnosis of ARDS is based on fulfilling 3 criteria:
    - acute onset (within 1 week)
    - bilateral opacities on CXR
    - PaO2/FiO2 (inspired oxygen) ratio of ≤300 on PEEP or CPAP ≥5 cm H2O.
- If no risk factor for ARDS is present, then heart failure as a cause of acute pulmonary edema should be ruled out

Pleura Alterations

Pneumothorax

- occurs when air gains access to, and accumulates in, the pleural space
- c/o dyspnea and chest pain
- In tension pneumothorax, patients are distressed with rapid labored respirations, cyanosis, profuse diaphoresis, and tachycardia
- Risk factors for the development of spontaneous pneumothorax, such as the presence of chronic respiratory diseases, should be assessed
- *Pneumocystis jirovecii* pulmonary infection can result in a pneumothorax, the patient should also be questioned about risk factors for HIV infection.

Pleural effusion

- fluid collects between the parietal and visceral pleural surfaces of the thorax
- A thin layer of fluid is always present in this space for lubrication and ease of movement of the lung during inspiration and expiration. If the normal flow of fluid is disrupted,

with either too much fluid produced or not enough removed, then fluid accumulates, resulting in a pleural effusion
- Patho: an imbalance of fluid production and removal
- fluid, under normal circumstances removed by lymphatics, local factors are altered
    - protein alterations, infection, inflammation
- the fluid is no longer regulated leading to excess fluid
- dyspnea, cough, and pleuritic chest pain
- typical exam findings
    - absent breath sounds
    - dullness to percussion
    - decreased or absent tactile fremitus
    - decreased vocal transmission over the base of the lung

Empyema
- presence of pus in the pleural space
- represents the end-stage of a progressive process evolving from a small amount of free-flowing, non-infected pleural fluid to a large amount of frank pus that can become loculated and result in thick pleural peel
- Risk factors: include pneumonia, iatrogenic intervention in the pleural space, diabetes, and alcohol abuse
- key sx: breathlessness (secondary to large pleural effusion or pneumonia); fever; and pleuritic chest pain
- Patho: pleural fluid accumulates secondary to inflammation and increased permeability of the visceral pleura. #3 stages include exudative, fibrinopurulent and organized

Restrictive lung Disorders

Atelectasis
- Definition: loss of lung volume due to collapsed lung tissue
- Classification 2/2 pathophysiological mechanisms
    - Obstructive
        - also called resorptive
        - A consequence of blockage of an airway
    - Non-obstructive
        - Loss of contact between parietal and visceral pleura
        - Many causes

Bronchiolitis
- acute viral infection of the lower respiratory tract
- Patho: characterized by epithelial cell destruction, cellular edema, and airway obstruction by inflammatory debris and mucus
- Respiratory syncytial virus (RSV) accounts for the vast majority of cases
    - Others include human metapneumovirus, influenza, rhinovirus, parainfluenza, and adenovirus

- Leading cause of hospital admission in infants under 1 year of age
- KEY sx : cough, wheeze, and labored breathing

Pulmonary fibrosis (idiopathic)

- rare form of fibrotic lung disease
- no known etiology
- progresses over several years and characterized by scar tissue formation within the lungs, dyspnea, and a significantly shortened lifespan after diagnosis
- history of progressive symptoms (typically dyspnea and cough) and evidence of radiographic findings
- restrictive pulmonary physiology (absence of findings that suggest an alternative diagnosis)
- Exposure as ?? etiology to IPF
- Occupational or environmental exposures have been studied extensively as possible causes of IPF
- exposure to metal dust, wood dust, and livestock farming
    - consistently shown risk factors for the development of IPF
- Other occupations w/ inhalation of organic/inorganic dust
    - stone cutting/polishing and raising birds
- Patho: inhalation of small organic/inorganic particles → induce injury → begins the cascade of events= ultimately leading to IPF

Obstructive pulmonary Disorders

Bronchiectasis

- form of obstructive lung disease
- Patho: permanent dilation of bronchi due to the destruction of the elastic and muscular components of the bronchial wall→ robust inflammatory response → structural damage → chronic inflammation
- acute exacerbation -worsening of cough, change in sputum color, increase in sputum volume, fever, and/or fatigue
- Features
- Key sx:
- present with recurrent pulmonary infections
    - (TB*, Hinflu, s aureus)*
- chronic daily productive cough with mucopurulent sputum production

Asthma (adult)

- Def: chronic inflammatory airway disease characterized by intermittent airway obstruction and hyperreactivity
- Many cellular components are involved in the asthmatic pathway
    - mast cells, eosinophils, T lymphocytes, macrophages, neutrophils, and epithelial cells.

- Patho: insult/inflammation = increased bronchial hyperresponsiveness and recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, which are usually associated with widespread but variable airway obstruction that is reversible either spontaneously or with treatment
- Symptomology: recurrent episodes of shortness of breath, chest tightness, wheezing, or coughing

Asthma (child)

- Same definition, but pediatric asthma differs from adult asthma
    - Most common chronic dz in resource rich countries
    - EIB may be the only manifestation in children
    - older children, as in adults, this may lead to permanent structural alterations of the airway wall (airway remodeling) and potentially a more severe asthma phenotype
- child-specific asthma guidelines should be used
    - Adult/ adolescent guidelines should not be extrapolated to younger age groups
- majority of asthmatic children have an intermittent symptom phenotype
- minority have persistent symptoms reflecting the underlying chronic inflammation
- Epidemiology
- Children
    - Prev 8.5%
        - Prepub males >
        - Postpub female > ?hormone related
        - AA>>Cauc
- Adults
    - Prevalence
        - 10.6% AA/8% cauc/6.5% hisp/13.1% nonhisp
- Etiologies
- Children & Adults
    - Multifactorial
    - Genetics
        - ADAM33/ch12q +many more
    - Environmental
        - Occupational
        - Food additives
        - Irritants/ASA
        - Viral/bacterial infections
- Defined as:
    - Daytime symptoms
    - Nighttime symptoms
    - Exacerbations
    - Peak expiratory flow
    - PEF variability

- Asthma Classifications
  - Infrequent intermittent
    (formerly infrequent episodic)
    - Daytime –none
    - Nighttime- none
    - Brief exacerbations
    - mild in severity, occurring less frequently than every 6 to 8 weeks
    - Peak expiratory flow
    - (PEF)/FEV1 >80% predicted value
    - based on age, sex, and height
    - PEF variability <20%

  - Frequent intermittent
    (formerly frequent episodic)
    - daytime symptoms between exacerbations
    - up to 2 days/week
    - No nighttime symptoms between exacerbations
    - up to 2 nights/month
    - Exacerbations occurring at intervals shorter than every 6 to 8 weeks
    - PEF/FEV1 80% > greater
    - predicted value based on age, sex, and height
    - PEF variability <20%

  - Mild persistent
    - Daytime symptoms
    - more than once per week but not every day (>2 times/week but 1 or fewer times/day)
    - Nighttime symptoms
    - more than twice per month but not every week (>2 nights/month)
    - Exacerbations may affect activity and sleep
    - PEF/FEV1 80% or greater of the predicted value
    - based on age, sex, and height
    - PEF variability 20% to 30%

  - Moderate persistent
    - Daily daytime symptoms between exacerbations
    - daily attacks affect activity
    - Nighttime symptoms
    - more than once per week (>1 night/week)
    - Exacerbations at least twice per week. Restricts activity or affects sleep
    - PEF/FEV1 80% or greater of the predicted value
    - based on age, sex, and height
    - PEF variability >30%

- Severe persistent
    - Continual daytime symptoms between exacerbations
    - continuous limited physical activity
    - Frequent nighttime symptoms
    - between exacerbations (frequent)
    - Exacerbations are frequent and restrict activity
    - PEF/FEV1 <60% of the predicted value based on age, sex, and height
    - PEF variability >30%

COPD

- Progressive disease state characterized by airflow limitation that is not fully reversible
- history of smoking, occupational and environmental risk factors, or a personal or family history of chronic lung disease
- Classic symptomology:
    - progressive shortness of breath, wheeze, cough, and sputum production, including hemoptysis
- COPD etiology
- Tobacco smoking is by far the main risk factor for COPD!!!
    - It is responsible for 40% to 70% of COPD cases
- exerts its effect by causing
    - inflammatory response
    - cilia dysfunction
    - oxidative injury
- Air pollution/occupational exposure are other common etiologies. Oxidative stress and an imbalance in proteinases and anti-proteinases are also important factors in the pathogenesis of COPD
- Alpha-1 antitrypsin deficiency= Autosomal dominate panacinar emphysema that usually presents at an early age d/t inhibition of elastase
- GOLD guidelines
    - uses a combined COPD assessment approach to group patients according to symptoms and previous history of exacerbations
    - Symptoms are assessed using the mMRC or CAT scale
        - **Group A:** low risk (0-1 exacerbation per year, not requiring hospitalization) and fewer symptoms (mMRC 0-1 or CAT <10)
        - **Group B:** low risk (0-1 exacerbation per year, not requiring hospitalization) and more symptoms (mMRC ≥2 or CAT≥ 10)
        - **Group C:** high risk (≥2 exacerbations per year, or one or more requiring hospitalization) and fewer symptoms (mMRC 0-1 or CAT <10)
        - **Group D:** high risk (≥2 exacerbations per year, or one or more requiring hospitalization) and more symptoms (mMRC≥ 2 or CAT≥ 10).

Chronic Bronchitis

- DEF: chronic productive cough >3 months in 2 successive years
- May precede or follow airway limitation
- May develop in smokers as early as 36 y/o
- Patho: excessive airway mucin production

Emphysema

- DEF: pathologic term used to describe the structural changes of COPD
- Abnormal and permanent changes of e the airspaces distal to the terminal bronchioles
- Exclusion of fibrosis
- Subtypes include proximal acinar, panacinar, and distal acinar

Alpha-1 antitrypsin (AAT)

- deficiency is an autosomal codominant genetic disorder
    - 1 allele is inherited from each parent and each allele is expressed equally
        - resulting from AAT allele mutations at the protease inhibitor (PI) locus
    - cause ineffective activity of the specific protease inhibitor alpha-1 antitrypsin
        - enzyme responsible for neutralizing neutrophil elastase and preventing inflammatory tissue damage in the lungs.
    - Variants of the enzyme may also polymerize and accumulate in the liver= hepatic failure
- Alpha-1 antitrypsin is also known as alpha-1 proteinase inhibition
- Pulmonary and hepatic manifestations
    - include emphysema, COPD, and cirrhosis

Pulmonary Infections

- Pneumonia
- 2/2 defect in host defenses, exposure to a particularly virulent microorganism, or a large inoculum size.
- Impaired immune response
    - caused by HIV infection or advanced age or dysfunction of defense mechanism
    - through current or passive smoking, COPD, or aspiration leads to greater susceptibility to respiratory infections in patients
    - Microbes that are present in the upper airways can enter the lower airways by microaspiration.
    - mechanisms of the lungs (innate and acquired) keep the lower airways sterile
- 4 mechanisms of infection
    - Inhalation
        - viral and atypical pneumonia in younger healthy patients
        - Infectious aerosols are inhaled into the respiratory tract
    - Aspiration
        - of oropharyngeal secretions into the trachea

        - primary route enter the lower airways
    - Hematogenous spread
        - from a localized infected site (right-sided endocarditis)
    - Direct extension
        - from adjacent infected foci (tuberculosis can spread contiguously from the lymph nodes to the pericardium or the lung
- Pneumonia Types
    - CAP- community acquired PNA
    - HAP-Hospital acquired PNA
    - Viral PNA
    - SARS
    - MERS
    - Atypical bacterial PNA
    - Aspiration PNA
    - Legionella
    - Chlamydia
    - Aspergillosis
    - Mycoplasma infection
    - Neonatal (meconium)
    - BOOP (Bronchial obliterans organizing PNA)

Pneumonia (CAP)

- Community Acquired
    - pneumonia acquired outside of hospital or healthcare facilities
- Clinical diagnosis:
    - respiratory tract infection
    - presence of fever >100ºF (>38ºC)
    - cough, expectoration
    - chest pain
    - dyspnea
    - signs of invasion of the alveolar space
- likely microbial causes of CAP differ according
    - differences in local epidemiology
    - setting (outpatients, hospitalized, or ICU)
    - severity of disease
    - patient characteristics (gender, age, and comorbidities)
- *Streptococcus pneumoniae* -most common causative
- ***CAP***
    - new lung infiltrate on chest x-ray
    - + 1 or more of the following:
        - fever/chills
        - cough
        - sputum production
        - dyspnea
        - myalgia/arthralgia

        - pleuritic pain
- ***HAP***
    - Alveolar shadowing on CXR or CT scan supports the diagnosis
    - presents with a combination of
        - fever (or hypothermia)
        - leukocytosis (or leukopenia)
        - increased tracheal secretions
        - poor oxygenation

Tuberculosis

- infection by *M tuberculosis* and inadequate containment by the immune system → requires inhalation of droplet nuclei
- Following deposition in the alveoli, *M tuberculosis* is engulfed by alveolar macrophages, but survives and multiplies within the macrophages → Proliferating bacilli kill macrophages and are released; this event produces a response from the immune system.
- Exposure may lead to clearance of *M tuberculosis*, persistent latent infection, or progression to primary disease
- TB pathogenesis:

- TB Risk
- HIGH SUSPICION for TB should be considered in any person with risk factors for TB exposure OR who have suggestive symptoms
    - fever, malaise, pleuritic chest pain, cough longer than 2-3 weeks, night sweats, and weight loss, hemoptysis, psychological symptoms, clubbing, erythema nodosum)
    - CXR abnormalities
- RISK FACTORS
    - high = exposure; birth in endemic country, immunosuppression, silicosis, atypical fibrosis
    - Lower= dense Populus settings, IVDA, ESRD, malignancy, low socioeconomic

Acute Bronchitis

- defined as a self-limiting lower respiratory tract infection
    - distinguish this condition from common colds and other upper respiratory ailments
- acute inflammation of the bronchial wall
    - which causes increased mucus production along with edema of the bronchus
- productive cough that is the hallmark of a lower respiratory tract infection
    - infection may clear in several days, repair of the bronchial wall may take several weeks
- <u>usually caused by a viral infection</u>

    - *coronavirus, rhinovirus, respiratory syncytial virus, and adenovirus*
    - Cough is typically worse at night or with exercise
    - lasts >2 weeks in 50% and 4 weeks in 25% of patients
    - may be associated with bronchospasm and/or excessive mucus production
      Diagnosis is primarily clinical
- Other causes for acute cough such as pneumonia, asthma, or postnasal drip should be ruled out if suspected

Pulmonary abscess/ cavitation

- Circumscribed collection of pus in the lung that leads to cavity formation, usually with an air-fluid level visible on CXR
- commonly occurs in patients with a predisposition to gastric content aspiration due to altered consciousness
- Mixed microbial flora (anaerobic bacteria and microaerophilic streptococci) are involved in the formation of abscesses related to the aspiration of gastric contents

Pulmonary artery HTN (PAH)

- Disease of the small pulmonary arteries characterized by vascular proliferation and remodeling
    - vascular changes are vasoconstriction, smooth-muscle cell and endothelial-cell proliferation, and thrombosis
    - Suggestive of predominance of thrombogenic, mitogenic, proinflammatory, and vasoconstrictive factors, probably as a consequence of pulmonary endothelial-cell dysfunction or injury
- It results in a progressive increase in pulmonary vascular resistance (PVR) and, ultimately, right ventricular failure and death.
- defined by a mean pulmonary arterial pressure >25 mmHg at rest
    - w/ pulmonary capillary wedge pressure <15 mmHg and PVR >3 Woods units, without a known cause

Pulmonary alterations Of Children

- Maternal Smoking
- RISK FACTOR for several adverse outcomes
    - Abnormal fetal lung development in the saccular and alveolar development stages- can have lasting effects/long term lung function issues
    - Can lead to development of asthma in children and lung dz in adults
    - Nicotine crosses breastmilk
    - Prevent prevent
    - Cannot use nicotine replacement therapy

Infectious Child- pulmonary

Croup (laryngotracheobronchitis)

- Common cause of acute respiratory distress
- Usually a result of viral infection (parainfluenza virus types 1 or 3)
- upper-airway obstruction due to generalized inflammation and edema of the airways
- Acute onset of seal-like barky cough, in moderate to severe cases accompanied by stridor and sternal/intercostal in drawing

Acute epiglottis

- Infection of the supraglottis that may cause airway compromise
    - classically *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Staphylococcus aureus*, and MRSA
    - Other rare bacterial pathogens =*Pasteurella multocida* have been reported
- An airway emergency, especially in children, and precautionary measures must be taken
- classically described in children aged 2 to 6 years of age
    - however, it may manifest at any age, including in newborns
    - It may now be more common in older children and adults due to the *Haemophilus influenzae* type B (Hib) vaccine

Tonsillar Infections

- Acute infection of the palatine tonsils
    - Can be difficult to distinguish clinically from viral pharyngitis
    - Common bacterial pathogens =beta-hemolytic and other streptococci, with the most common being group A beta-hemolytic streptococci
    - Commonly viral pathogens= rhinovirus, coronavirus, and the adenovirus
    - tonsillitis associated with infectious mononucleosis, the most common infective agent is the Epstein-Barr virus

Foreign body aspiration

- Inhalation of a foreign body into the larynx and respiratory tract
- symptoms include sudden onset of respiratory distress associated with coughing, gagging, or stridor.
    - Unilateral wheezing suggests partial obstruction of the main or distal bronchi
- Anticholinergics, antipsychotics, and anxiolytics can impair the cough reflex and/or swallowing
- Significant morbidity and mortality is seen in the younger age group (2 months to 4 years old) because of the narrow airways and immature protective mechanisms

risk is higher in children with mental retardation and swallowing difficulties and also in boys

Laryngomalacia

- Congenital abnormality of the larynx cartilage that predisposes to dynamic supraglottic collapse during the inspiratory phase of respiration, resulting in intermittent upper airway obstruction and stridor
- Most common laryngeal anomaly and most frequent congenital cause of stridor in infants
- Presents with inspiratory stridor
    - Some patients have upper airway obstruction with associated feeding difficulties
    - Frequently associated with GERD

Cystic fibrosis

- Genetic multisystem disease associated with abnormalities in salt and water transport across epithelial surfaces affecting primarily the respiratory and gastrointestinal tracts
- common manifestations
    - pancreatic dysfunction that results in calorie malabsorption
    - lung disease that results from a cycle of mucus retention, infection, and inflammation
- Although severely life-shortening, in the past 50 years average survival has increased dramatically to almost 40 years of age
- Most common genetic disease in US
- Affecting Caucasians mostly
- Newborn screening now routine
- Testing: Sweat chloride test (GOLD standard)
    - Genetic testing
    - CXRAY

Lung Cancer

- And other malignancies of the respiratory tract
- Laryngeal Cancer
- arises from progressive accumulation of genetic alterations that lead to selection of a clonal population of transformed cells
- Hoarseness, dysphonia, sore throat, difficulty swallowing, referred otalgia, vocal cord lesions on indirect laryngoscopy, and neck mass/adenopathy that persists for >3 weeks are sentinel signs that should be evaluated by an otolaryngologist
- alcohol use frequently associated with development of the disease

Small cell lung cancer (SCLC)

- is an aggressive malignancy
- Approximately 2/3 of patients have evidence of distant metastasis at presentation
- Primarily develops in older adult smokers
- common presenting symptoms are cough, chest pain, hemoptysis, dyspnea, and weight loss

Non-small cell lung cancer

- most common form of lung cancer, and comprises 3 major types:
    - adenocarcinoma
    - squamous cell carcinoma
    - large cell carcinoma
- common in older adult smokers and ex-smokers and presents w/ cough, chest pain, hemoptysis, dyspnea, and weight loss.
- Small tumors in the lung are often asymptomatic, so the majority of patients have either locally advanced or metastatic disease at diagnosis

Mesothelioma

- Malignant pleural mesothelioma accounts for most malignant mesotheliomas
- a rare malignancy with an annual incidence in the US of 3200
- Commonly caused by exposure to asbestos
    - 20- to 40-year latency period between exposure and development of malignancy
    - typical patient is in the sixth to ninth decade of life

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