

Respiratory Tract Infections

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Learning objectives

- ✓ Discuss the etiology, pathogenesis and clinical presentation of otitis media, sinusitis, pharyngitis and pneumonia
- ✓ Discuss common pathogens associated with pneumonia in various clinical areas
- ✓ Select appropriate antimicrobial agents based on the clinical setting and the respective dominating pathogens for these infections
- ✓ Propose strategies to prevent or reduce the occurrence of infections

Introduction

- Upper Respiratory Tract Infections includes
 - Otitis media
 - Sinusitis
 - Pharyngitis
 - Common cold
- N:B Most URIs are caused by viruses, have nonspecific symptoms, and resolve spontaneously

Acute otitis media (AOM)

- is an inflammation of the middle ear
- involves the rapid onset of signs and symptoms of inflammation in the middle ear
- **Otitis media with effusion** differs from acute otitis media in that signs and symptoms of an acute infection are absent

Epidemiology

- Otitis media occurs in all age groups
 - But is most common in children between 6 months and 2 years of age.
- By 3 years of age, up to 85% of children have had at least one episode of otitis media,
- Up to 20% have recurrent infections by 12 months of age.

Risk factors

- The winter season,
- Attendance at a daycare center,
- Early age at first infection,
- Nasopharyngeal colonization with middle ear pathogens,
- Genetic predisposition (siblings in the home)
- Lower socioeconomic status
- Exposure to tobacco smoke
- Male gender
- Immunodeficiency
- Allergy
- Urban population
- Non–breast-feeding in infants

Etiology

- Although AOM occurs frequently with viral URIs, bacteria are isolated from middle ear fluid in up to 90% of children with AOM
- *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis*
- All can possess resistance to β -lactams.
 - *S. pneumoniae* through alteration of penicillin-binding proteins,
 - *H. influenzae* and *M. catarrhalis* produce β -lactamases.

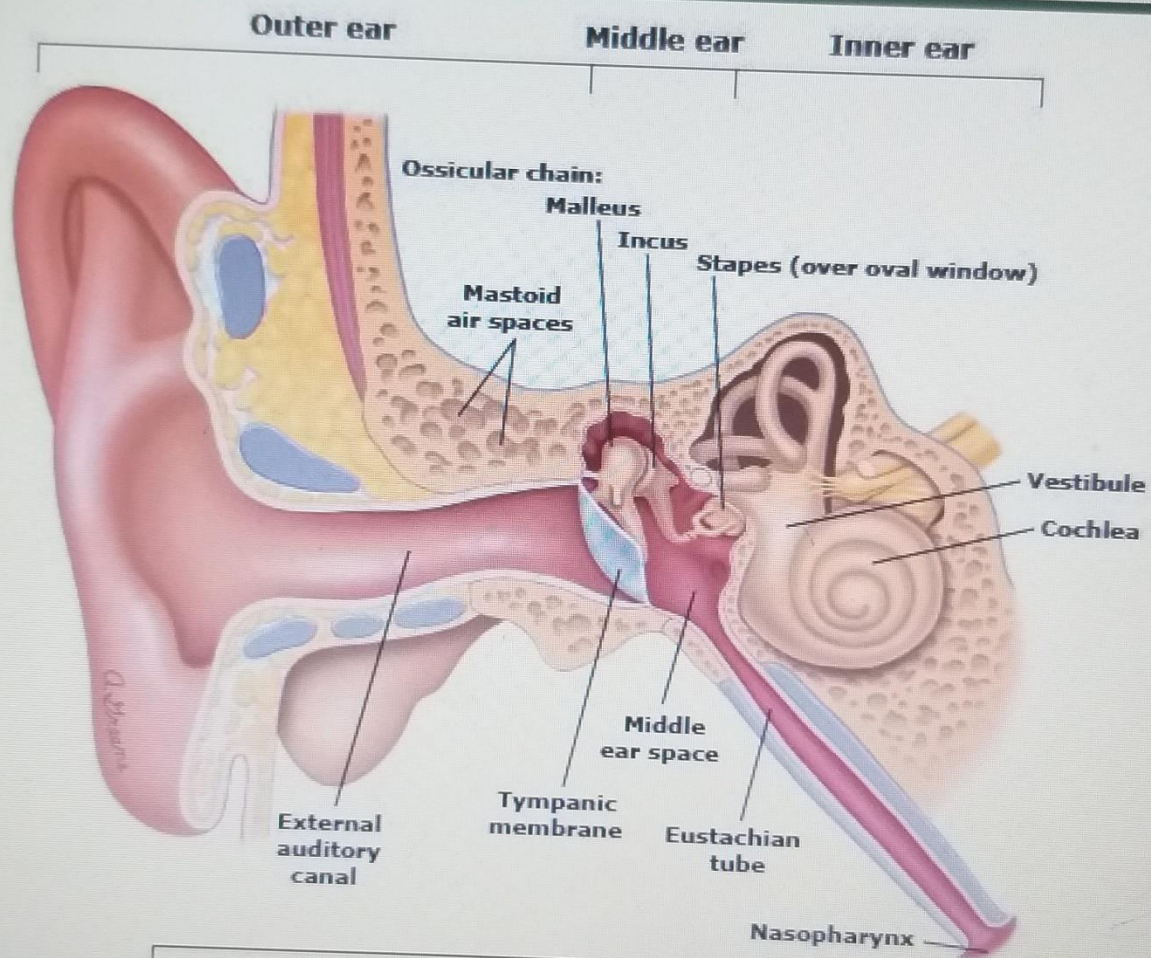
Pathophysiology

- AOM usually follows a viral URTIs that impairs the mucociliary apparatus and causes Eustachian tube dysfunction in the middle ear
- The middle ear is the space behind the tympanic membrane, or eardrum
- A noninfected ear has a thin, **clear** tympanic membrane
- In OM, this space becomes blocked with fluid, resulting in a bulging and erythematous tympanic membrane

Cont.....

- Bacteria that colonize the nasopharynx enter the middle ear and are not cleared properly by the mucociliary system
- The bacteria proliferate and cause infection
- Children are predisposed to AOM because the eustachian tube is shorter and more horizontal, facilitating bacterial entry into the middle ear

Anatomy of the adult ear



Clinical presentation

- Ootalgia (ear pain)
- Otorrhea
- Fever
- Bulging of the tympanic membrane
- Pneumatic otoscopy or tympanometry demonstrates an immobile eardrum; **50% of cases are bilateral**
- **Otitis media with effusion:** fluid in the middle ear w/out bulging eardrum

Diagnosis

- Otitis media is usually diagnosed clinically
- Bulging tympanic membrane(otoscopy)
- If the membrane ruptures, a sample of the exudate can be analyzed by Gram stain and culture

Case, part 1

- A 22-month-old boy presents to the pediatric clinic with 2 days of fever (38.6°C), nasal congestion, and fussiness. His mother reports that he was rubbing his left ear throughout the day. She states that he is more irritable than usual and was crying intermittently throughout the night last night. He is not eating as much as usual today. He attends daycare 5 days a week and has a 4-year-old sister who recently had a cold.
 - What information is suggestive of acute otitis media (AOM)?
 - What risk factors does this child have for AOM?
 - Is there any additional information you need to know before recommending a treatment plan?

Treatment

- **Desired outcome**
 - Pain management
 - Eradication of infection
 - Prevent complication
- General Approach
 - Differentiate acute otitis media from **otitis media with effusion** or **chronic otitis media**, as the latter two types do not benefit substantially from antibiotic therapy.
 - Address pain with oral analgesics

Cont.....

- Nonpharmacologic therapy
 - Children with recurrent AOM or chronic OME with impaired hearing or speech may benefit from surgery (tympanostomy tube placement with or without adenoidectomy)

Cont.....

- **Pharmacologic therapy**
- **First line**
 - ❖ **Amoxicillin**,
 - ❖ High-dose amoxicillin (80 to 90 mg/kg/day) is preferred over conventional doses (40 to 45 mg/kg/day)
 - ❖ **Amoxicillin /Clavulanate**, 1g BID for 10 days for adults, 90 mg/kg/day orally of amoxicillin plus 6.4 mg/kg/day orally of clavulanat for children
 - ❖ In cases of concurrent conjunctivitis, recurrent AOM, Hx amox. use
- **Second line**
 - **Cefuroxime** 30mg/kg/d BID, **cefpodoxime** 10mg/kg/day BID
 - **Ceftriaxone** 50 mg/kg IM or IV for 1–3 days (max 1 g/dose)

Cont.....

- **Duration**
- 10-day regimens are recommended for all severe infections and for children less than 2 years.
- 7-day regimens can be considered for mild to moderate AOM in children 2 to 5 years
- 5-7 days regimens for those children 6 years and older
- **Prevention**
- Vaccination (PCV and influenza vaccine)

Cont.....

- **Complication of otitis media**
- **Infectious:**
 - mastoiditis, meningitis, osteomyelitis, intracranial abscess
- **Structural:**
 - perforated eardrum
- **Hearing** and/or impairment

Case part 2

- On further questioning, He was treated for pneumonia with amoxicillin one months back., and this is his first ear infection.
- Immunizations: up-to-date
- Meds: Acetaminophen drops 120 mg orally every 4 to 6 hours as needed for fever
- ROS: (+) rhinorrhea and fever, (–) vomiting, diarrhea, or cough
- **PE:**
- Gen: Irritable child
- VS: BP 100/64 mm Hg, P 130 beats/min, RR 22 breaths/min,
- T 39.1°C (102.4°F)
- HEENT: Erythema and severe bulging of the left tympanic membrane

Case part 2

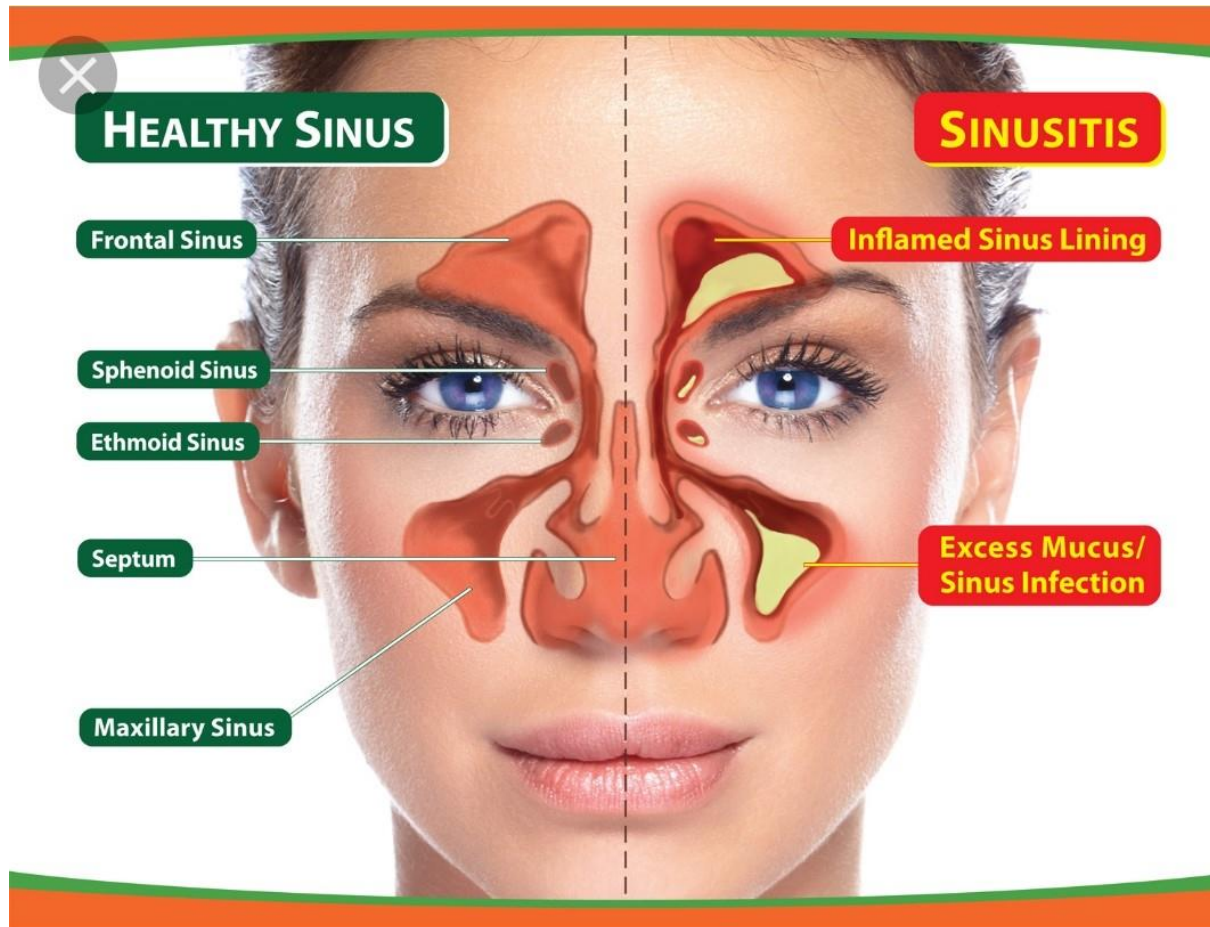
- Identify your treatment goals for this child?
- Given this information, what pharmacologic and supportive treatment do you recommend?

Chronic otitis media

- Chronic **suppurative** otitis media is characterized by persistent or recurrent **purulent otorrhea** in the setting of tympanic membrane perforation.
- Usually, there is also some degree of conductive hearing loss.
- Treatment of chronic active otitis media is surgical;
 - ❖ Mastoidectomy
 - ❖ Tympanoplasty
- Can be performed as outpatient surgical procedures

RHINOSINUSITIS

- **Sinusitis** refers to an inflammatory condition involving the four paired structures surrounding the nasal cavities.
- Although most cases of sinusitis involve more than one sinus, the **maxillary** sinus is most commonly involved; next in frequency are the **ethmoid**, **frontal**, and **sphenoid** sinuses.
- It is called **rhinosinusitis** because it involves inflammation of contiguous nasal mucosa,



Cont.....

- **Acute rhinosinusitis** is characterized by symptoms that persist for up to 4 weeks,
- **Chronic rhinosinusitis** manifests as cough, rhinorrhea, and/or nasal obstruction for more than 12 weeks.

Etiology

- Most rhinosinusitis infections have a viral etiology,
- Acute bacterial rhinosinusitis is caused by *S.pneumoniae*, *H.influenza* (50-70%)
- *M. catarrhalis* , GAS, *S.aures*, g-ves, anerobes

Pathophysiology

- Is caused by mucosal inflammation and mucociliary dysfunction from viral infection or allergy.
- Increased mucous production and reduced clearance lead to blockage of the sinus ostia
- This is ideal for bacterial growth and promotes mucosal injury characterized by increased in ILs, histamine, and TNF

Sign and symptom

- **Acute**

- Adults

- Nasal discharge/congestion
 - Maxillary tooth pain, facial or sinus pain that may radiate (unilateral in particular)
 - Severe or persistent (>7 days) signs and symptoms are most likely **bacterial** and should be treated with antibiotics

- Children

- Nasal discharge and cough for longer than 10 to 14 days or **severe signs** and symptoms such as temperature above **39°C** or **facial swelling** or **pain** are indications for antibiotic therapy

Cont.....

- **Chronic**
 - Symptoms are similar to acute sinusitis but more nonspecific
 - Rhinorrhea is associated with acute exacerbations
 - Chronic unproductive cough, laryngitis, and headache may occur
 - Chronic/recurrent infections occur three or four times per year and are unresponsive to steam and decongestants

Diagnosis

- Clinical diagnosis of sign and symptom
- Radiographic studies: Useful for assessing presence of complications
- Paranasal sinus puncture: not routine but can be useful in complicated or chronic cases
- Laboratory studies/nasopharyngeal cultures: not recommended
 - Unless there is cardio respiratory compromise, those with orbital complications, immunocompromised children, children with recurrent bacterial sinusitis

Treatment

- Desired outcome
 - Relieve sign and symptom
 - Limit antibiotic treatment to those who may benefit,
 - Eradicate the microorganism
 - Prevent complication
 - Prevent progression to chronic disease

Cont.....

- **Supportive therapy**
- nasal decongestant sprays : reduce inflammation by vasoconstriction
- saline and steam inhalation
- mucolytics (eg, guaifenesin) may be used to decrease the viscosity of nasal secretions
- Intranasal corticosteroids for patients with a history of allergic rhinitis

Pharmacologic therapy

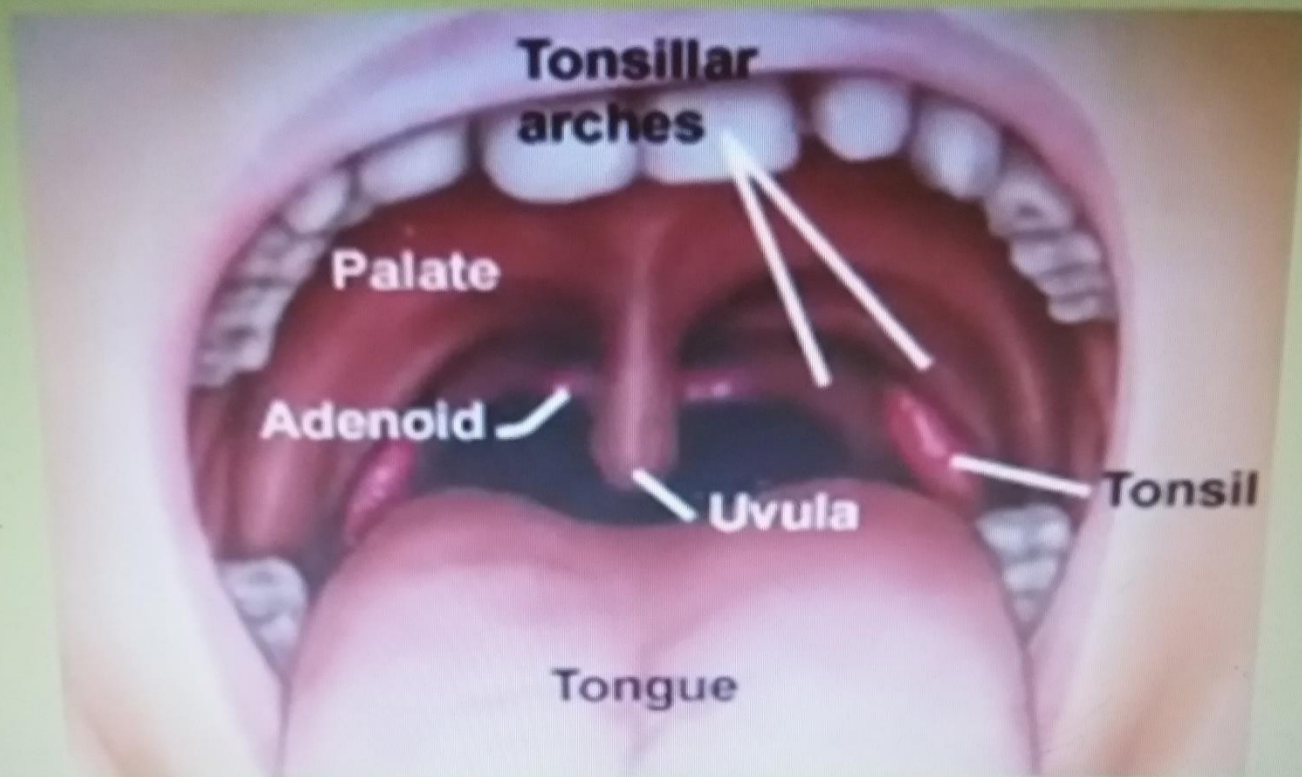
- **Amoxicillin-clavulanate** is first-line treatment for acute bacterial sinusitis (45mg/kg/d of amoxicillin component)
- Alternatives (allergy, resistance)
 - High dose Amoxicillin-clavulanate
 - Cephalosporin
 - Respiratory quinolones
 - doxycycline
- Cotrimoxazole and macrolides are not recommended due to high pneumococcal and H.influenza resistance
- Treatment duration ranges from 5 to 10 days in adults and 10 to 14 days in children

Complications

- Orbital cellulitis or abscess, periorbital cellulitis, meningitis,
- ethmoid or frontal sinus erosion,
- chronic sinusitis, and exacerbation of asthma or bronchitis

Acute Pharyngitis

- Pharyngitis is an acute infection of the oropharynx or nasopharynx
- Although viral causes are most common, **group A beta-hemolytic streptococci** (GABHS; also known as *S. pyogenes*), is the primary bacterial cause
- It spreads easily through direct contact with contaminated secretions.

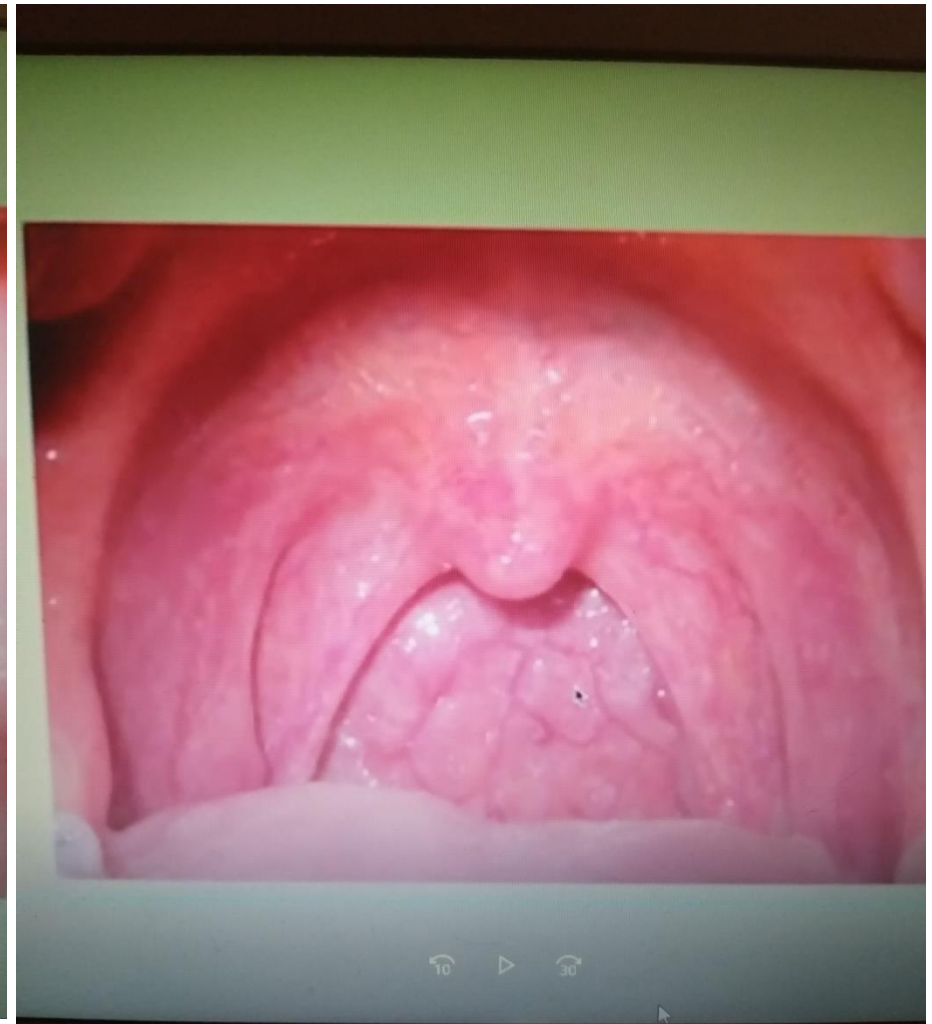
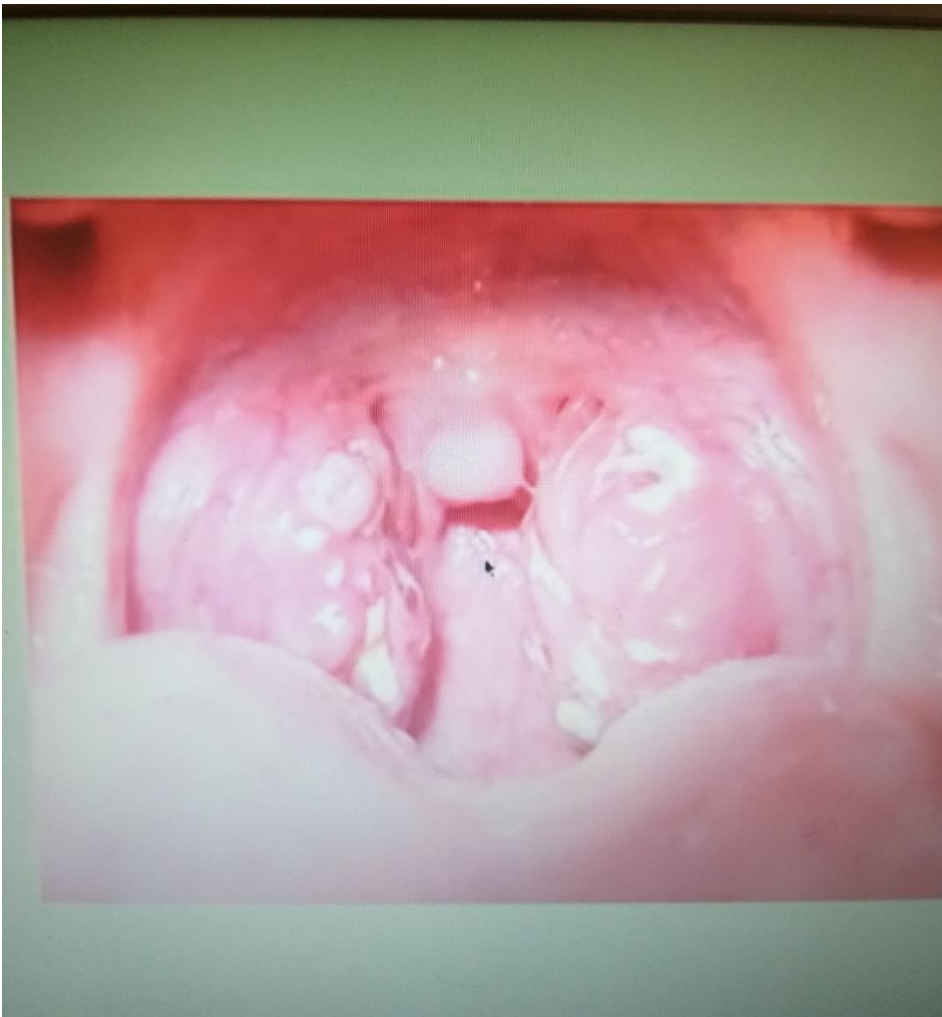


Epidemiology and etiology

- Children ages 5 to 15 years are most susceptible;
- parents of school-age children and those who work with children are also at increased risk.
- Viruses:
 - Rhinovirus, Coronavirus, Adenovirus, Herpes simplex virus, Influenza virus, Parainfluenza virus, and Epstein-Barr virus
- Bacterial: GABHS

Clinical presentation

- Sore throat
- Pain on swallowing
- Fever
- Headache, nausea, vomiting, and abdominal pain
- Erythema/inflammation of the tonsils and pharynx with or without patchy exudates
- Enlarged, tender lymph nodes
- Red swollen uvula, petechiae on the soft palate, and rash
- **Sign suggestive of viral origin** are cough, conjunctivitis and coryza



Treatment

- **Desired Outcome**
 - To improve clinical signs and symptoms,
 - Minimize adverse drug reactions,
 - Prevent transmission to close contacts, and
 - Prevent complications
- **Supportive care**
 - Antipyretic medications and nonprescription lozenges and sprays containing menthol and topical anesthetics for temporary relief of pain
 - Analgesics: paracetamol

Pharmacologic therapy

- Viral: Only symptomatic therapy
- Bacterial:
 - Penicillin benzathine-single dose (IM)
 - 0.6 mIU (if ≤ 27 kg); 1.2 mIU (if > 27 kg), 1.2 mIU for adults
 - Amoxicillin 50mg/kg once daily for 10 days
- Penicillin is the drug of choice due to safety, efficacy and low cost
- Amoxicillin is an alternative
- N:B Penicillin resistance has not been documented in group A streptococci,

Cont....

- Recurrent infections or treatment failures can be retreated with
 - the same initial antibiotic or
 - treated with amoxicillin-clavulanate, a first-generation cephalosporin, clindamycin, or penicillin G benzathine
- Duration of treatment
- 5-day courses of some cephalosporins are as effective for streptococcal eradication as 10 days of penicillin

Complications

- **Nonsuppurative complications:**
 - acute rheumatic fever,
 - acute glomerulonephritis, and
 - reactive arthritis
- **Suppurative complications:**
 - Peritonsillar abscess,
 - Retropharyngeal abscess,
 - Cervical lymphadenitis,
 - Mastoiditis,
 - Otitis media,
 - Sinusitis, and
 - Necrotizing fasciitis.

Case study

- A 6-year-old girl presents to the pediatrician with a sore throat and fever of 39.1°C for the past 12 hours. She has pain while swallowing. She has no other symptoms and takes no medications. Her mother reports that her litter sister had “strep throat” recently. Physical examination reveals pharyngeal and tonsillar erythema with exudates.
- Question
 1. Does this child have bacterial streptococcal pharyngitis?
 2. Is antibiotic therapy indicated? If so, what agent should be initiated and for how long?
 3. What education should be provided to her mother regarding treatment?

Lower respiratory Tract Infections

Introduction

- The most common infections involving the LRT are:
 - Bronchitis
 - Bronchiolitis
 - Pneumonia

Cont....

Host Defenses Protecting the Lungs

- **Innate defense:**
 - Anatomical features:
 - Nasal turbinates
 - Glottis
 - Mucociliary transport system
 - Coughing
 - Surfactant
 - Alveolar macrophages, lysozymes
- **Acquired immunity**
 - Epithelial cells
 - Macrophages

Bronchitis

- **Bronchitis** and **bronchiolitis** are inflammatory conditions of the large and small elements, respectively, of the tracheobronchial tree.
- The inflammatory process does not extend to the alveoli.
- Bronchitis frequently is classified as
 - **Acute**: individuals of all ages
 - **Chronic**: adults

Acute Bronchitis

- Acute bronchitis occurs most commonly during the winter months, similar to other acute RTIs
- **Etiology**
 - ⊙ **Respiratory viruses:** the most common (85-95%)
 - ❖ RSV, influenza virus, Parainfluenza viruses (most common)
 - ❖ Cold viruses (rhinovirus and coronavirus) – rare
 - ⊙ **Bacteria**
 - ❖ *M. pneumoniae*, *S. pneumoniae* and *H.influenza*
 - ❖ *C. pneumoniae*, *B. pertussis* (rare)

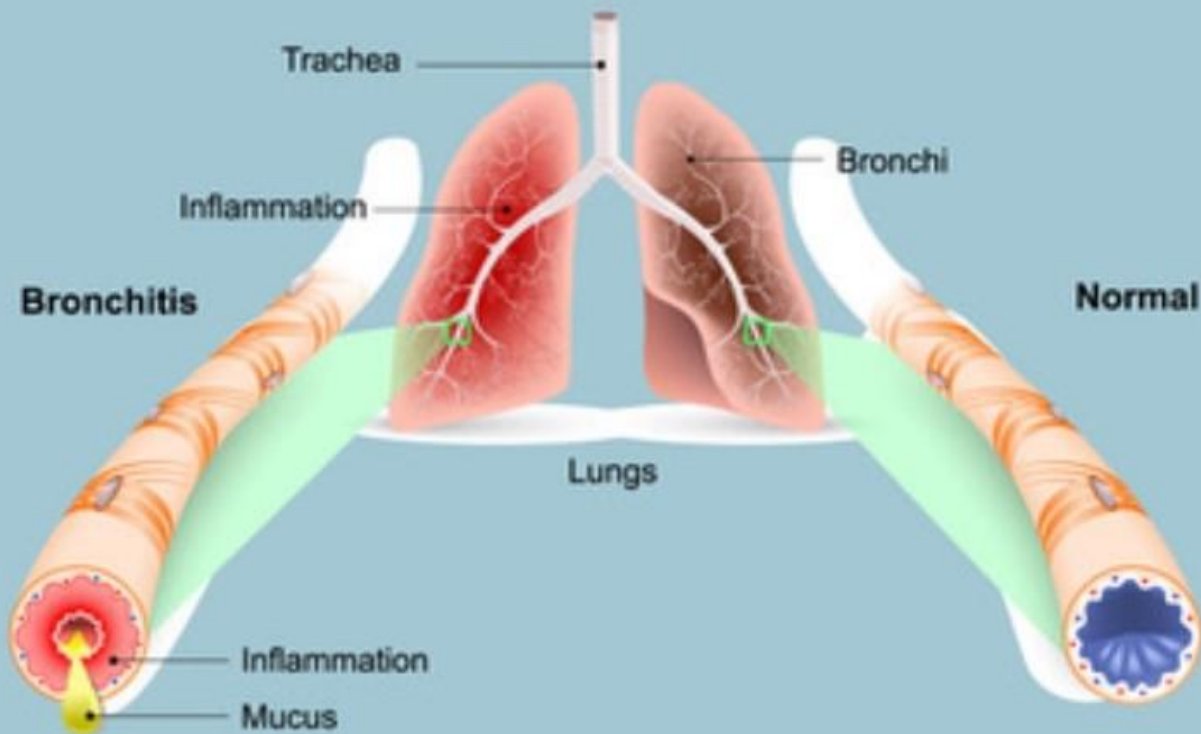
Pathogenesis

- Infection of the trachea and bronchi yields inflammation-induced hyperemic and edematous mucous membranes with an increase in bronchial secretions
- Destruction of respiratory epithelium can range from mild to extensive and may affect bronchial mucociliary function

Clinical presentation

- Cough persisting for 3 or more weeks
- mucopurulent sputum
- Dyspnea, cyanosis, or signs of airway obstruction(underlying lung disease)
- Fever rarely $>39^{\circ}\text{C}$
- Coryza, sore throat,

BRONCHITIS



Treatment

- **Desired outcome**
- Acute bronchitis, almost always, is self-limiting
 - To provide comfort to the patient
 - to treat associated dehydration and respiratory compromise
- **Supportive**
 - Reassurance and antipyretics
 - Bed rest for comfort
 - Fluids to prevent dehydration and possibly to decrease the viscosity of respiratory secretions.

Cont....

- Mist therapy (use of a vaporizer)
- Cough and cold remedies containing various combinations of antihistamines, sympathomimetics, and antitussives
- Routine use of antibiotics for treatment of acute bronchitis should be **discouraged**
- When possible, antibiotic therapy should be directed toward anticipated respiratory pathogen(s)

Chronic bronchitis

- Is a component of COPD
- a chronic cough productive of sputum for most of the days lasting more than 3 consecutive months of the year for 2 consecutive years
- R:F **cigarette smoking** (predominant factor)
 - exposure to occupational dust, fumes and
 - environmental pollution

Pathogenesis

- In chronic bronchitis, the bronchial wall is thickened, and the number of **mucus-secreting goblet cells** on the surface epithelium of both larger and smaller bronchi is increased
 - More mucus in their peripheral airways, further impairing normal lung defenses
 - Mucous plugging of the smaller airways.
 - residual scarring of small bronchi and airway obstruction

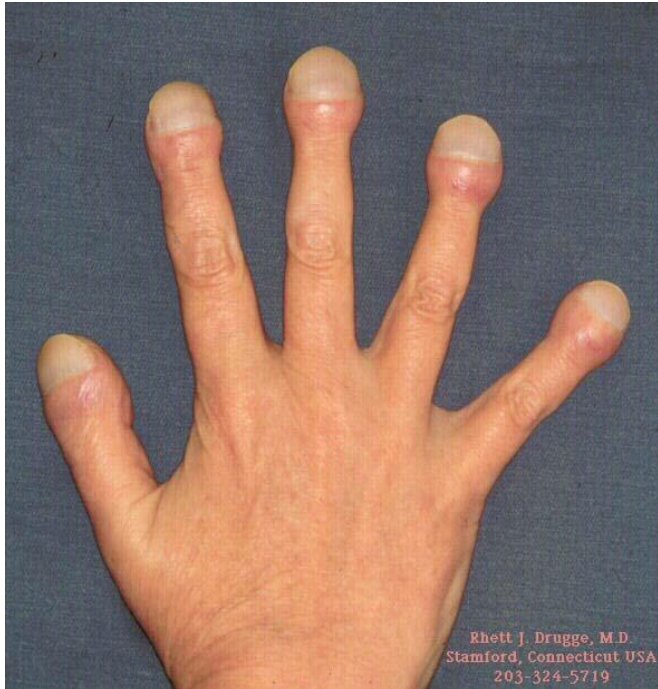
Clinical presentation

- Sign and symptom
 - Productive cough (hallmark)
 - Expectoration of largest quantity of sputum
 - Cyanosis (advanced disease)
- Physical examination
 - ✓ chest auscultation usually reveals inspiratory and expiratory **rales**, **rhonchi**, and mild **wheezing** with an expiratory phase that is frequently prolonged;
 - ✓ **Hyperresonance** on percussion with obliteration of the area of cardiac dullness

Cont....

- ✓ Normal vesicular breathing sounds are *diminished*
- ✓ **Clubbing** of digits (advanced disease)
- **Chest radiograph**
 - Increase in anteroposterior diameter of the thoracic cage (observed as a **barrel chest**)
 - Depressed diaphragm with limited mobility
- **Laboratory tests**
 - Erythrocytosis (advanced disease)
- **Pulmonary function tests**
 - Decreased vital capacity
 - Prolonged expiratory flow

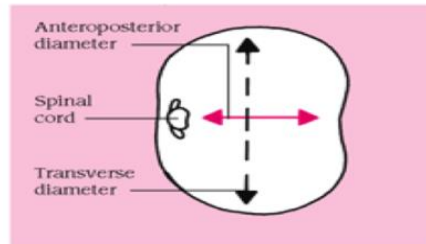
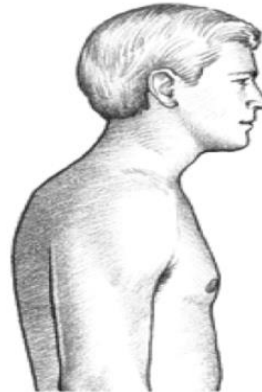
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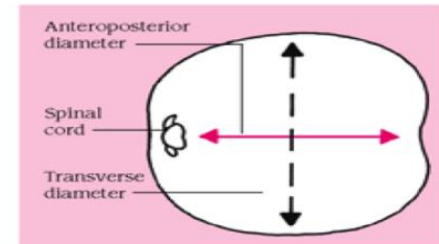
Recognizing barrel chest

In a normal adult chest, the ratio of anteroposterior to transverse (or lateral) diameter is 1:2. In patients with barrel chest, this ratio approaches 1:1 as the anteroposterior diameter enlarges.

NORMAL CHEST



BARREL CHEST



Cont....

- **Common bacterial pathogens isolated from sputum of patients with acute exacerbation of CB**
 - ✓ *Haemophilus influenzae*
 - ✓ *Moraxella catarrhalis*
 - ✓ *Streptococcus pneumoniae*
 - ✓ *Escherichia coli*, *Enterobacter* species, *Klebsiella*, *Pseudomonas aeruginosa*

Treatment

- **Desired outcome**
 - The goals of therapy for chronic bronchitis are twofold:
 - To reduce the severity of chronic symptoms and
 - To ameliorate acute exacerbations and to achieve prolonged infection-free intervals

Cont....

- **General Principles**

- Exposure to bronchial irritants should be reduced.
- Reduce or eliminate cigarette smoking.
- Postural drainage

- **Pharmacologic Therapy**

- Oral or aerosolized bronchodilators (e.g., albuterol aerosol)
- Combination therapy of SABA and corticosteroid
- Antimicrobials: Fluoroquinolones(levofloxacin, moxifloxacin), Amoxicillin/clavulanate, macrolides and **Cotrimoxazole** (mild disease)

Cont....

- Chronic antibiotic therapy is rarely indicated
- But long term therapy with macrolides associated with reduction in acute exacerbation
 - Due to their antibacterial, anti-inflammatory, and immunomodulatory activity
 - These drugs reduce bacterial adherence and toxin production, inhibit biofilm function,
 - reduce the generation of oxygen free radicals
 - control mucus hypersecretion and
 - improve mucociliary clearance

Bronchiolitis

- Is an acute viral infection of the lower respiratory tract
- Affects approximately 50% children (≤ 2 yrs)
- Incidence is more common in males
- Respiratory syncytial virus is most common etiology
 - parainfluenza, adenovirus, and influenza virus

Clinical presentation

- Signs and symptoms
 - Irritability, restlessness, and mild fever
 - Cough and coryza
 - Vomiting, diarrhea, noisy breathing, and increased respiratory rate (as symptoms progress)
 - Labored breathing with retractions of the chest wall, nasal flaring, and grunting

Cont....

- Physical examination
 - Tachycardia and Tachypnea
 - Wheezing and inspiratory rales
 - Mild conjunctivitis in one third of patients
- Diagnosis
- Based on history and clinical findings
- Routine use of chest radiography is not recommend

Treatment

- **General approach to treatment**
 - Bronchiolitis usually is a self-limiting illness
 - antipyretics, and adequate fluid intake
 - oxygen therapy and IV fluid (severe disease)
 - aerosolized bronchodilators (bronchospasm)
- **Pharmacologic therapy**
 - Routine use of corticosteroids is discouraged
 - Ribavirin (RSV, influenza A, B, parainfluenza, and adenovirus)
 - Reserved for severely ill children

Pneumonia

- **Definition**
- Pneumonia is an inflammation of the lung parenchyma
- To **the pathologist**, pneumonia is an infection of the alveoli, distal airways, and interstitium of the lung that is manifested by:
 - ↳ Increased weight of the lungs,
 - ↳ Replacement of normal lung's sponginess by consolidation, and
 - ↳ Alveoli filled with white blood cells, red blood cells and fibrin

Cont....

- To **the clinician**, pneumonia is a constellation of symptoms and signs:
 - ↳ Fever, chills, cough, pleuritic chest pain,
 - ↳ Sputum production,
 - ↳ Increased respiratory rate,
 - ↳ Dullness to percussion, bronchial breathing,
 - ↳ crackles, wheezes, pleural friction rub
- In combination with at least one opacity on CXR

Classification of pneumonia

1. Community-acquired pneumonia

- Cases of infectious pneumonia in patients living independently in the community
- Patients who have been hospitalized for other reasons for **less than 48 hours** before the development of respiratory symptoms

2. I. Hospital-acquired pneumonia

- Patients who have been hospitalized for **at least 2 days**

II. Ventilator-associated pneumonia

- Patients contracting pneumonia **>48 hours** after the institution of **endotracheal intubation and mechanical ventilation**

Epidemiology and Etiology

- It remains one of the most common causes of severe sepsis and infectious cause of death in children and adults
- Etiology varies with type of pneumonia
- *S. pneumoniae* colonizes the nasopharyngeal flora in up to 50% of healthy adults (CAP)
- *Mycoplasma pneumoniae* is 2nd common cause
- nontypeable *H. influenzae* causing pneumonia increases in COPD patients
- Viruses are a common cause of CAP in children

Common Pathogens by Type of Pneumonia

Type of pneumonia	Common pathogen
Community	<i>S. pneumoniae</i> , <i>H. influenzae</i> , <i>M. catarrhalis</i> , Atypical, viruses
Aspiration	Oral contents: Anaerobes, Viridans streptococci GI contents: Enteric gram-negative bacilli
Hospital Early onset	<i>S. pneumoniae</i> , MSSA, <i>E. coli</i> , <i>K. pneumoniae</i> ,
Late onset	MRSA, extended-spectrum β -lactamase-producing <i>K. pneumoniae</i> , <i>P. aeruginosa</i> , <i>Acinetobacter</i> spp.

Pathogenesis

- **Local host defense**

- URT defenses include nasal hair, normal bacterial flora, IgA, and complement.
- LRT defense include cough, mucociliary apparatus of the trachea and bronchi, IgA, IgM, and IgG, complement, and alveolar macrophages
- Mucous lines the cells of the respiratory tract, forming a protective barrier for the cells
 - Minimizes the ability of organisms to attach to the cells

Cont....

- Particles greater than 10 microns (μm) are removed from the nasopharynx by swallowing or expulsion.
- particles that are 2 to 10 μm in size are trapped by mucociliary apparatus of the trachea and bronchi
- Particles in the range of 0.5 to 1 μm may consistently reach the alveolar sacs of the lung.
 - Microorganisms fall within this size range, and if they reach the alveolar sacs, then infection may result if alveolar macrophages cannot eliminate them.

Cont....

- Route of entry of microorganisms
 - Inhaled as aerosolized particles,
 - Hematogenous spread from extrapulmonary site
 - aspiration of oropharyngeal contents
 - altered mental status and neuromuscular disease
- Lung infections with **viruses** suppress the antibacterial activity of the lung by **impairing alveolar macrophage** function and **mucociliary clearance**
 - resulting in **secondary bacterial** pneumonia
- Mucociliary transport is also depressed by ethanol and narcotics and by obstruction of bronchi by mucus or tumor

Cont....

- **Host Factors**

- Hypogammaglobulinemia: low level of antibodies
- Defects in phagocytosis or ciliary function, neutropenia, functional or anatomical asplenia, or a reduction in CD4⁺ T lymphocyte counts
- Anatomical defects such as obstructed bronchus

Cont....

- Once organisms invade the lung tissue, an **inflammatory** response is generated either by the organism or the host immune response
- The alveolar macrophages release cytokines which result in increased mucus production
 - associated with cough and sputum production
- If TNF- α and IL-1 and -6 are released systemically, the symptoms become more severe and include hypotension, organ dysfunction, septic-shock.

Pathology

- The pathology of pneumonia manifests as four general patterns:
 - Lobar pneumonia
 - Bronchopneumonia
 - Interstitial pneumonia
 - Miliary pneumonia

Lobar Pneumonia

- Classically involves an entire lung lobe relatively homogeneously
- Four stages of lobar pneumonia may exist simultaneously in the same lung
 - **Congestion:** vascular congestion and alveolar edema
 - **Red hepatization:** airless, noncrepitant firmness (like the liver), many erythrocytes, neutrophils, epithelial cells and fibrin in the alveoli
 - **Gray hepatization:** dry, friable, gray brown to yellow (RBC breakdown)
 - **Resolution:** enzymatic digestion of the alveolar exudate

Bronchopneumonia

- A patchy consolidation involving one or several lobes, usually involves the dependent lower and posterior portions of the lung
- a pattern attributable to the distribution of aspirated oropharyngeal contents by gravity.
- The consolidated areas are usually poorly demarcated

Interstitial Pneumonia

- Is defined by histopathologic identification of an inflammatory process
 - involving the interstitium, including the alveolar walls and the connective tissue around the bronchovascular tree.
- The inflammation may be patchy or diffuse

Miliary Pneumonia

- The resemblance of the diffusely distributed 2- to 3-mm lesions of hematogenous tuberculosis to millet seeds
- Numerous discrete lesions resulting from the spread of the pathogen to the lungs via the **bloodstream**

Complications

- Lung abscesses (necrotizing pneumonia)
- Vascular invasion with infarction
- Cavitation
- Empyema
- Bronchopleural fistula
- Emphysema
- Pneumothorax
- ARDS

Community acquired pneumonia

- Documented microbial causes of CAP include bacteria, fungi, viruses, and parasites
- Most cases of pneumonia are caused by
 - **S.pneumoniae**, H. influenzae, S. aureus(young infant or patient with CF)
 - M. pneumoniae, C. pneumoniae, Legionella spp,
 - Moraxella catarrhalis, aerobic gram-negative bacteria(chronic disease like DM. alcoholics)
 - GAS rare (if occur follows viral RTIs)
 - influenza viruses, adenoviruses, and respiratory syncytial virus

Cont....

- Overall, *S. pneumoniae* accounts for 50% of all cases of CAP requiring admission to the hospital
- Predictors of pneumonia due to gram-negative bacteria (including *Pseudomonas aeruginosa*)
 - Probable aspiration,
 - Previous hospital admission,
 - Previous antimicrobial treatment

Risk factors

- Age (elderly)
- Diabetes mellitus
- Smoking/alcohol use
- Chronic cardiovascular, pulmonary, renal and/or liver disease
- Aspiration, COPD, ARDS

Clinical presentation

- **Sign and symptom**

- Abrupt onset of fever, chills, dyspnea, and productive cough
- Pleuritic chest pain
- Rust-colored sputum or hemoptysis (due to destruction of blood vessels)

- **Physical examination**

- Tachypnea and tachycardia
- Dullness to percussion
- Chest wall retractions and grunting respirations
- Diminished breath sounds over affected area
- Inspiratory crackles during lung expansion

Cont....

- Chest radiograph
 - Dense lobar or segmental infiltrate
- Laboratory tests
 - Leukocytosis (neutrophil predominance)
 - Low oxygen saturation on pulse oximetry
- **Etiologic diagnosis**
 - Gram stain of sputum (presence of WBC in sputum)
 - Culture of sputum
 - Blood culture
 - Antigen tests
 - PCR
 - Serology (IgM, IgG) to determine presence of atypical org.
 - Bronchoscopy (tracheal secretion)

Treatment

- Desired outcome
 - Eradication of the offending organism through selection of the appropriate antibiotic
 - Complete clinical cure
 - Minimize complication

General approach to treatment

- **Oxygen** or, in severe cases, mechanical ventilation
- Administration of **bronchodilators** (albuterol) when bronchospasm is present,
- Chest physiotherapy with postural drainage if evidence of retained secretions
- Adequate hydration (IV if necessary), optimal nutritional support, and control of fever

Pharmacologic therapy

- **Selection of Antimicrobial Agents**

- ↳ Initially involves the empirical use of a relatively broad-spectrum antibiotic that is effective against probable pathogens

- ↳ **Therapy should be narrowed to cover specific pathogens after the results of cultures are known.**

- **Factors to define the potential pathogens:**

- ↳ Patient age,

- ↳ Previous and current medication history,

- ↳ Underlying disease(s),

- ↳ Major organ function, and

- ↳ Present clinical status

Empiric treatment

Clinical setting	Usual pathogen	Empiric therapy
Previously healthy / no AB use in the past 3 month	<i>S. pneumoniae</i> , atypical, <i>H.influeza</i> ,	Macrolides/tetracycline
Comorbidities (DM, COPD, chronic heart, liver or renal disease, malignancy, alcoholism) or recent antibiotic use	MDR <i>S.pneumoniae</i> , atypical, <i>H.influenza</i>	Respiratory quinolone or high dose β -lactam (amoxicillin, ceftriaxone) plus macrolide
Inpatient non ICU	<i>S. pneumoniae</i> , atypical, <i>S.aures</i> , <i>Legionella</i> sp, G-ve bacili, <i>H.influenza</i>	Fluoroquinoloned or β -lactam plus macrolide or Piperacillin/tazobactam or meropenem
Inpatient ICU	<i>P.aurginosa</i> suspected	+ Quinolone/ceftazidime
Viral	CA-MRSA suspected	+Vancomycin/linezoild Oseltamivir or zanamivir

Cont....

Antibiotic	Pediatric dose/day	Adult dose/day
amoxicillin	45-100mg/kg/day	1.5-3g/day
Piperacillin/tazobactam	200-300mg/kg/day	12-18g/day
Ceftriaxone	50-75mg/kg/day	1-2g/day
Ceftazidime	90-150mg/kg/day	4-6g/day
Cefepime	100-150mg/kg/day	2-6g/day
Clarithromycin	30-50mg/kg/day	1-2g/day
Azithromycin	10mg/kg then 5mg/kg/day	500mg then 250mg/day
Moxifloxacin		400mg/day
Levofloxacin	8-20mg/kg/day	750mg/day
Doxycycline	2-5mg/kg/day	100-200mg/day
Vancomycin	45-60mg/kg/day	2-3g

Criteria for Hospitalization

- ➡ Age >65
- ➡ Comorbidity
- ➡ Leukopenia ($<5000/\mu\text{l}$)
- ➡ *S. aureus* , G-ve bacilli, anaerobes suspected causes of pneumonia
- ➡ Suppurative complications
- ➡ Failure of PO treatment
- ➡ RR >30', PR >120', SBP < 90/mmHg
- ➡ $\text{PO}_2 < 60\text{mmhg}$,
- ➡ Acute alteration in mental status
- ➡ Multiple lobe involvement

Criteria to switch from IV to PO

- Switching from IV to PO antibiotics can be done safely when:
 - ➡ The white blood cell count is returning toward normal,
 - ➡ There are two normal temperature readings (37.5°C) 16 hr apart, and
 - ➡ There is improvement in cough and shortness of breath.

Criteria to discharge from the hospital

- Once physiologic stability is achieved:
 - ➔ An oral temperature of $<37.5^{\circ}\text{C}$ for 24 h,
 - ➔ A heart rate of $<100/\text{min}$
 - ➔ A respiratory rate of $<24/\text{min}$
 - ➔ A systolic blood pressure of $>90\text{ mmHg}$,
 - ➔ An oxygen saturation of $>90\%$ while breathing room air
 - ➔ The ability to eat and drink well enough to maintain hydration,

Hospital acquired pneumonia

- Hospital acquired pneumonia (HAP)
 - is seen most commonly in critically ill patients and is usually caused by bacteria
- Risk factors for the development of HAP/VAP fall into four general categories:
 - intubation and mechanical ventilation,
 - aspiration,
 - oropharyngeal colonization, and
 - hyperglycemia

Cont....

- ❖ Intubation serves as a direct conduit for bacterial introduction into the lower respiratory tract
- ❖ risk of aspiration is increased in hospitalized patients due to supine positioning of the patient
- ❖ Oropharyngeal colonization is affected by the use of antibiotics or oral antiseptics which may decrease normal flora and allows pathogenic organism to colonize the oral cavity
- ❖ Hyperglycemia promote infection by
 - Inhibiting phagocytosis
 - Providing additional nutrient to bacteria

Microbiologic Causes of HAP/VAP

Non-MDR Pathogens/ early onset	MDR Pathogens/ late onset
<i>Streptococcus pneumoniae</i>	<i>Pseudomonas aeruginosa</i>
<i>Haemophilus influenzae</i>	MRSA
MSSA	<i>Acinetobacter</i> spp.
Antibiotic-sensitive Enterobacteriaceae	<i>Enterobacter</i> spp.
✓ <i>Escherichia coli</i>	Antibiotic-resistant Enterobacteriaceae
✓ <i>Klebsiella pneumoniae</i>	✓ ESBL producing <i>Klebsiella</i> spp.
✓ <i>Proteus</i> spp.	<i>Legionella pneumophila</i>
✓ <i>Enterobacter</i> spp.	

Cont....

- Patients who are more likely to develop MDR organisms are
 - patients with longer lengths of hospital admission
 - Medical comorbidities, alcoholism,
 - Immunosuppressive disease/ therapy
 - Beta-lactam, macrolide, or fluoroquinolone therapy within the past three month
- Diagnosis of HAP usually is established by
 - the presence of a new infiltrate on chest radiograph, fever, worsening respiratory status, and the appearance of thick, neutrophil-laden respiratory secretions

Cont....

- VAP: is pneumonia occurring more than 48 hours postendotracheal intubation.
- The risk is exacerbated by the wide use of acid-reducing drugs (promote proliferation of microorganisms in the GI)
- Pneumonia that develops early in hospitalization are more likely to be caused by antibiotic sensitive microorganism
- **Diagnosis**
- a new infiltrate on chest radiograph, fever, purulent tracheal secretions, leukocytosis or leucopenia

HAP /VAP Treatment

Patients without Risk Factors for MDR Pathogens	Patients with Risk Factors for MDR Pathogens
Ceftriaxone or cefotaxime or	1. A β-lactam:
Moxifloxacin, ciprofloxacin, or levofloxacin or	Ceftazidime (2 g IV q8h) or cefepime (2 g IV q8–12h) or
Ampicillin/sulbactam (3 g IV q6h) or	Piperacillin/tazobactam, (4.5g q 6hr) plus
Ertapenem (1 g IV q24h)	2. A second agent active against gram-negative bacteria:
	Gentamicin (5-7 mg/kg IV q24h) or
	Ciprofloxacin (500mg q 8hr) or levofloxacin (750mg q 24hr) plus
	3. An agent active against gram-positive bacteria: (if MRSA suspected)
	Vancomycin (15 -20mg/kg q12h) or Linezolid (600 mg IV q12h)

Cont...

- **Duration of antibiotic**
- Adult outpatient CAP:
 - 5-day duration of therapy: levofloxacin (the 750-mg dose) and azithromycin
 - 7 to 10 days for other therapies
- Admitted to the hospital: 7 to 10 days
- HAP : 10 to 21 days.

Aspiration pneumonia

- **Risk factors**
- Dysphagia
 - (stroke, alcoholism, seizure and aging)
- Change in oropharyngeal colonization
 - (oral/dental disease, poor oral hygiene, tube feedings)
- GERD
 - acid suppressant therapy allow enteric Colonization of gastric content by gram-negative bacilli
- Decreased host defenses.
 - impaired mucous production or cilia function and decreased immunoglobulin in secretions

Cont..

- If the patient aspirates oral content: anaerobes and *Streptococcus* spp. are the primary pathogens
 - Treatment : penicillin G, ampicillin/sulbactam, or clindamycin
- If the patient aspirates oral and gastric contents, anaerobes and gram-negative bacilli are the primary pathogens
 - tt:ampicillin/sulbactam, amoxicillin/clavulanate, piperacillin/tazobactam, or ticarcillin/clavulanate)

PNEUMONIA IN PEDIATRICS

Etiologies

AGE GROUP	PATHOGENS
Neonates (<4 wk)	GBS, <i>E coli</i> , other Gram-negative bacilli, <i>S pneumoniae</i> , <i>H influenza</i>
4 wk-3 mo	RSV, other respiratory viruses (rhinoviruses, parainflenza virus, influenza virus, adenovirus), <i>S. pneumoniae</i> , <i>H. influenzae</i> ;
4 mo-4 yr	RSV, other respiratory viruses (rhinoviruses, parainflenza virus, influenza virus, adenovirus), <i>S. pneumoniae</i> , <i>H. influenzae</i> , <i>M. pneumoniae</i> , group A streptococcus
≥5 yr	<i>M. pneumoniae</i> , <i>S. pneumoniae</i> , <i>C. pneumoniae</i> , <i>H. influenzae</i> , influenza viruses, adenovirus, <i>Legionella pneumophila</i>

Cont....

- Pneumonia in children is classified as
 - Severe pneumonia
 - Non-severe pneumonia
- The management is based on the classification

Severe pneumonia

- **Diagnosis:**
- Cough or difficulty in breathing, plus at least one of the following:
 - Central cyanosis or oxygen saturation $< 90\%$ on pulse oximetry
 - Severe respiratory distress
 - Signs of pneumonia with a general danger sign:
 - Inability to breastfeed or drink,
 - Lethargy or unconscious,
 - Convulsions.

Cont....

- In addition, some or all of the other signs of pneumonia may be present, such as:
- Cough
- Fast breathing:
 - age < 2 months, $\geq 60/\text{min}$
 - age 2–11 months, $\geq 50/\text{min}$
 - age 1–5 years, $\geq 40/\text{min}$
 - Chest indrawing: lower chest wall indrawing (i.e. lower chest wall goes in when the child breathes in)

Cont....

- Investigations
 - Measure oxygen saturation with pulse oximetry in all children suspected of having pneumonia.
 - If possible, obtain a chest X-ray to identify
 - Pleural effusion,
 - Empyema,
 - Pneumothorax,
 - Interstitial pneumonia or
 - Pericardial effusion

- **Treatment**
- Admit the child to hospital.
- *Oxygen therapy*: To all children with oxygen saturation < 90%
- Antibiotic therapy
 - Give intravenous ampicillin and gentamicin.
 - **Ampicillin** 50 mg/kg and **Gentamicin** 7.5 mg/kg IM or IV once a day for at least 5 days
- If no improvement within 48 h and staphylococcal pneumonia is suspected, switch to
 - gentamicin 7.5 mg/kg IM or IV once a day and **Cloxacilline** 50 mg/kg IM or IV every 6 h
- Use **ceftriaxone** (80 mg/kg IM or IV once daily) in cases of failure of first line treatment.
- *Supportive Care*
 - If the child has fever ($\geq 39^{\circ}\text{C}$), give paracetamol.
 - If wheeze is present, give a rapid-acting

Pneumonia/ Non severe

- **Diagnosis**
- Cough
- Fast breathing:
 - age < 2 months, $\geq 60/\text{min}$
 - age 2–11 months, $\geq 50/\text{min}$
 - age 1–5 years, $\geq 40/\text{min}$
 - Chest indrawing

Cont....

- **Treatment**
- Treat child as outpatient.
- Advise care givers to give normal fluid requirements plus extra breast milk or fluids if there is a fever.
- Antibiotic therapy
 - Oral amoxicillin 40 mg/kg per dose twice a day for 5 days
- Supportive care
 - maintaining hydration, antipyretics

Prevention of pneumonia

- Children should be vaccinated against *S. pneumoniae*, *H. influenzae* type b, pertussis, and influenza
- Immune prophylaxis for RSV is only recommended for high-risk infants during RSV season
- To minimize the risk of developing HAP, healthcare providers should seek to minimize colonization of the aerodigestive tract, prevent aspiration (head raised 45 degree)

Case study 1

- A 65-year-old man was admitted to ED secondary to car accident. One day after admission he developed respiratory failure and was intubated. He has remained intubated and on day 7 the chest x-ray revealed bilateral lower lobe infiltrates. His temperature is 38.9°C ,BP is 110/75 mm Hg, and WBC is $20.4 \times 10^3/\text{mm}^3$ ($20.4 \times 10^9/\text{L}$)
 1. What are the suggestive signs and symptoms of pneumonia?
 2. What are the top three bacterial organisms that could be causing the pneumonia?
 3. What could be goal of therapy and ab choice

Case study 2

- B.L is a 10 day years old male neonate who was born from a 28 years old P I mother at a GA of 37 week. The delivery was by SVD. The neonate has inability to breastfeed , cough, fever, fast breathing, chest in drowning and grunting of 3 days duration. On physical examination, PR 185, RR 75, oxygen saturation 85 with atmosphere and has intercostal retraction.

Question

1. What are the suggestive sign and symptom of severe pneumonia?
2. What are the common bacterial organisms that could be causing the pneumonia?
3. Describe Nonpharmacologic and pharmacologic treatment for the patient

Case 3

- A 65-year-old man presents to ED complaining of difficulty breathing and shortness of breath of 5 days duration
- **PMH:** CHF for 5years and COPD for 4 years
- **SH:** Denies alcohol use, smokes 1 pack per day for 11 years. Lives alone and has 2 children.
- **Allergies:** NKDA
- **Meds:** enalapril 10mg/d, metoprolol 25mg/d mg orally; fluticasone/salmeterol 250/50 mcg one inhalation twice daily; albuterol inhaler as needed for SOB
- **ROS:** (+) difficulty breathing, SOB and chest pain; (–) N/V/D, change in appetite

- **PE:**
- VS: BP 90/80, P 110, RR 32, T 38.6°C (101.5°F)
- **Lungs:** Decreased breath sounds with rales and crackles in the left lower lobe
- **Neuro:**confused
- Diagnostic Tests: Chest x-ray: left lower lobe infiltrates; oxygen saturation 84% (0.84) on room air
- **Labs:** WBCs $18.2 \times 10^3/\text{mm}^3$ ($18.2 \times 10^9/\text{L}$) with a cell differential of 70% (0.70) neutrophils, BUN 67mg/dL , SCr 1.3 mg/dL , sputum Gram stain: moderate gram-positive cocci, few gram-negative bacilli, many WBC

Questions

1. Given the information what are the suggestive sign and symptom of severe pneumonia?
2. What are the likely microorganism that cause the pneumonia?
3. do you think the patient should be admitted?
4. What is the drug of choice for this patient?

THE END