Lower Respiratory Tract Viral Infections``

VL-5
Dec. 1st 2013

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Structures of the Respiratory System

Structures of the Upper Respiratory System,
- Nose
- Nasal cavity
- Pharynx
- Tonsils
- Mucus

Structures of the Lower Respiratory System
- Larynx
- Trachea
- Bronchi
- Alveoli
- Diaphragm
- Various protective components
  - Ciliated mucous membrane, alveolar macrophages, and secretory antibodies IgA
Viral Lower Respiratory disease

- Site of replication:
  - Turbinate "baffles"
  - Cervical lymph node
  - Trachea
  - Bronchi
  - Bronchioles
  - Bronchial lymph node
  - Alveoli
  - Alveolar macrophage

- Clinical manifestation:
  - Rhinitis (common cold)
  - Pharyngitis
  - Laryngitis
  - Tracheitis
  - Bronchitis
  - Bronchiolitis
  - Bronchopneumonia

- Virus:
  - Rhinovirus
  - Coronavirus
  - Parainfluenza virus
  - Respiratory syncytial virus
  - Influenza virus
  - Adenovirus
  - Herpes simplex virus
  - Epstein-Barr virus
  - Parainfluenza virus
  - Respiratory syncytial virus
  - Influenza virus
  - Adenovirus
VIRAL INFECTIONS OF THE LOWER RESPIRATORY TRACT

• 75-80% of all acute respiratory tract infections are of viral origin.
  – Everyone has 3 or 4 per year

• Incidence varies inversely with age.
  – Greatest in young children
VIRAL INFECTIONS OF THE LOWER RESPIRATORY TRACT

- Majority of acute viral infections are in the lower respiratory tract
- Common characteristics of infection are:
  - Short incubation period of 1 to 4 days.
  - Transmission from person to person.
- Transmission can be direct or indirect.
  - Direct - through droplets
  - Indirect - through hand transfer of contaminated secretions
Presentation

- Most often, LRTI is accompanied by fever and may be preceded by a typical viral URTI.

- It is important to assess all children with a fever accurately.

- Bacterial pneumonia should be considered in children when there is persistent or repetitive fever above 38.5°C together with chest recession and a raised respiratory rate.

- In all age groups be aware that:
  - Audible wheezing is not seen very often in LRTI (although it is common with more diffuse infections such as in *M. pneumoniae* and bronchiolitis).
  - Stridor or croup suggests URTI, epiglottitis or foreign body inhalation.
Pathophysiology

• There is no hard and fast definition of LRTI that is universally agreed upon.
• Essentially, it is inflammation of the airways/pulmonary tissue, due to viral or bacterial infection, below the level of the larynx.
• Remember that gastrooesophageal reflux may cause a chemical pneumonitis.
• Smoke and chemical inhalation may also cause pulmonary inflammation.
RESPIRATORY Syncytial VIRUS
(CONTINUED)

• Almost all children are infected by the age of four.
• May be fatal in children with heart and lung disease, and in the premature.
• One of only a few treatable viral syndromes.
• Ribavirin treatment is expensive, requires hospitalization and is reserved for only the most severe infections
MICROBIOLOGY

- Typically caused by viruses
  - RSV - most common
  - Parainfluenza
  - Human Metapneumovirus
  - Hantavirus
  - Influenza
  - Rhinovirus
  - Coronavirus
  - Human bocavirus

- Occasionally associated with Mycoplasma pneumonia infection
Viral Diseases of the Lower Respiratory System

- **Respiratory Syncytial Virus Infection**
  - Most common childhood respiratory disease
  - Signs and symptoms
    - Fever, runny nose, and coughing in babies or immunocompromised individuals
    - Mild cold-like symptoms in older children and adults
  - Pathogen
    - Respiratory syncytial virus (RSV)
  - Pathogenesis
    - Virus causes syncytia to form in the lungs
    - Immune response to RSV cause further damages to the lungs
Viral Diseases of the Lower Respiratory System

- **Respiratory Syncytial Virus Infection**
  - Epidemiology
    - Transmission occurs via close contact with infected persons
  - Diagnosis, treatment, and prevention
    - Diagnosis made by immunoassay
    - Supportive treatment for young children
    - Prevention includes aseptic technique of health care and day care employees
Parainfluenza virus

• Second only to RSV as cause of RTI in infants and young children.
• Most infections occur late fall and winter.
• Infection is often limited to the nasopharynx.
• Approximately 25% spread to the lungs.
• Approximately 2% get laryngo-tracheo-bronchitis, Croup
Hemagglutinin neuraminidase (PIV only) or attachment protein (RSV only)

Lipid bilayer

Fusion protein

Small hydrophobic protein (RSV only)

Matrix proteins

Large polymerase complex

Nucleoprotein

Phosphoprotein
Adenovirus

- Double stranded, naked DNA virus.
- Icosahedral symmetry with fibres projecting from each vertex
- Virus infects by direct contact or resp droplets
- Produces 5-10% of pediatric respiratory infections.

- Clinical syndromes include:
  - Febrile pharyngitis
  - Lower respiratory infections
  - Pharyngoconjunctival fever
  - Conjunctivitis
  - Diarrhea
Hantavirus Pulmonary Syndrome (HPS)

- **Epidemiology**
  - Human disease more likely as mouse population increases
  - Spread by inhalation of dust contaminated by mice
  - Person-to-person contact does not occur

- **Diagnosis, treatment, and prevention**
  - Diagnosis made based on characteristic symptoms
  - No specific treatment is available
  - Prevention requires control of rodents
Hantavirus Pulmonary Syndrome (HPS)

- **Signs and symptoms**
  - Symptoms progress to cough, shock, and labored breathing

- **Pathogen**
  - Caused by *Hantavirus*
  - Spread by inhalation of dust contaminated by mice

- **Pathogenesis**
  - Infection causes widespread inflammation, Infects capillary epithelium; blood vessel damage and shock
  - High fatality rate (40%)
Hantavirus

90–100 nm

Membrane glycoproteins

Lipid envelope

Three negative ssRNA molecules within capsids

- envelopeced,
- segmented,
- -ssRNA bunyavirus

Outer capsid

Negative ssRNA
Metapneumovirus

- First described in 2001 by van den Hoogen
  - Nasophargyngeal aspirates from 28 children over a 20 year period
  - Children had similar symptoms to RSV
  - World wide distribution: Has been isolated in US, Brazil, Japan, Australia and UK
Metapneumovirus Symptoms

- Cough, fever, dyspnea
- Can range from URTI → Respiratory failure
- Significant pulmonary inflammatory changes
  - Increased IL-8, foamy macrophages
- In temperate countries, hMPV has a seasonal distribution, overlapping with RSV with most cases reported during the winter/spring.
DIAGNOSIS OF RESPIRATORY VIRAL INFECTIONS

- Clinical syndrome
- Time of year
- What’s in the community?
- Virus isolation
- Virus antigen detection (not rhinovirus)
- Molecular methods eg. PCR
- Serology (not rhinovirus)
Diseases LRTI

- Lower respiratory illness (LRTI) most common serious illness in childhood
- 1/3 of all children develop LRI in first year of life
- Most common reason for hospitalization after neonatal period
- Presentation focuses on:
  - Croup
  - Bronchitis, bronchiolitis
  - Epiglottitis
  - Pneumonia
CROUP
Definition

• “A generic term”
• A heterogenous group of illnesses affecting the larynx, trachea, and bronchi: Laryngotracheobronchitis,
• Viral origin
• Characteristic cough, inspiratory stridor, hoarseness
Etiology

• Viral-mediated inflammatory condition
• Laryngotracheitis, laryngotracheobronchitis
• Affects vocal cords and subglottic airway
• Viral:
  ▪ 65% due to parainfluenza types 1, 2, 3
  ▪ Most hospitalized cases are type 1
  ▪ Others: adenovirus, RSV, varicella, measles, HSV, enteroviruses, Transmitted by inhalation via nasopharynx

• Spasmodic: viral associated, possibly allergic reaction to antigens
Infectious croup

Syndrome characterized by:

- Bark like cough
- Hoarseness
- Inspiratory stridor
- Respiratory distress of varying severity
- Preceded by coryza زكام and low grade fever for 12 to 72 hrs
PATHOGENESIS

• The viruses that cause croup typically infect the nasal and pharyngeal mucosal epithelia initially and then spread locally along the respiratory epithelium to the larynx and trachea.

• The anatomic hallmark of croup is narrowing of the trachea in the subglottic region.

• This portion of the trachea is surrounded by a firm cartilaginous ring such that any inflammation results in narrowing of the airway.

• In addition to this "fixed" obstruction, dynamic obstruction of the extrathoracic trachea below the cartilaginous ring may occur when the child struggles, cries, or becomes agitated.
PATHOGENESIS

- The dynamic obstruction occurs as a result of the combination of high negative pressure in the distal extrathoracic trachea and the floppiness of the tracheal wall in children.

- Laryngoscopic evaluation of patients during acute laryngotracheitis shows redness and swelling of the lateral walls of the trachea.

- In severe cases, the subglottic airway may be reduced to a diameter of 1 to 2 mm.

- In addition to mucosal edema and swelling, fibrinous exudates and, occasionally, pseudomembranes can build up on the tracheal surfaces and contribute to airway narrowing.

- The vocal cords and laryngeal tissues also can become swollen, and cord mobility may be impaired.
Autopsy studies in children with laryngotracheitis show infiltration of histiocytes, lymphocytes, plasma cells, and neutrophils into edematous lamina propria, submucosa, and adventitia of the larynx and trachea.

Patients with bacterial tracheitis have a bacterial super infection that causes thick pus to develop within the lumen of the subglottic trachea.

Ulcerations, pseudomembranes, and micro abscesses of the mucosal surface occur.

The supraglottic tissues usually normal.
Host factors

Underlying host factors that predispose to clinically significant narrowing of the upper airway include:

• Anatomic narrowing of the airway, such as subglottic stenosis or laryngeal web
• Hyperactive airways, perhaps aggravated by atopy or gastroesophageal reflux, as suggested in some children with spasmodic croup or recurrent croup
• Acquired airway narrowing from respiratory tract papillomas (human papillomavirus) or post-intubation scarring.
Epidemiology

- Incidence highest in 2nd year of life
- Parainfluenza virus (types 1, 2, and 3)
- RSV, influenza or adenovirus
- Bacterial tracheitis may complicate course: (staphylococcus, H. influenzae, S. pneumoniae or moraxella catarrhalis)
Epidemiology

• 15% of respiratory visits in children
• Most common cause of stridor in children
• Annual incidence: 6 cases per 100 children younger than 6yoa
• Affects children 6mos-12yoa, peak incidence at 2yoa
• Boys:Girls 1.5:1
• Fall and winter predominance
Clinical Presentation

• Prodrome: rhinorrhea, pharyngitis, low-grade fever, +/- cough over 12-48 hours
• Gradual development of barking cough, hoarseness, varying inspiratory stridor +/- fever
• May develop more severe obstruction with inspiratory stridor at rest, increased nasal flaring, retractions, progressive hypoxia and cyanosis
• Symptoms may worsen at night/with crying
• Mild course 3-7 days, more severe 7-14 days
Studies?

- Plain neck XR: “Steeple sign”
- CT: suspected other causes
- Laryngoscopy
Parainfluenza virus

Narrowing of air column

Steeple sign
Differential Diagnosis

- Epiglottitis
- Bacterial tracheitis
- Foreign body
- Subglottic stenosis
- Peritonsillar abscess
- Retropharyngeal abscess
- Diptheria
- Laryngomalacia

- Vocal cord paralysis
- Smoke inhalation
- Burns/Thermal injury
- Neoplasm
- Laryngeal fracture
Infectious croup: Treatment

- Management depends on severity of distress
  - **Mild cases**: barky cough, stridor with crying or agitation
  - **More severe**: increased work of breathing, tachypnea, retractions, stridor at rest
  - **Very severe**: hypoxia, lethargy, apnea
Infectious croup: Treatment (con’t)

- Home therapy for mild cases
- Cool mist: moistens secretions, comforting
- Steamy bathroom
- Exposure to cold air
- Can intensify bronchospasm if also wheezing
Infectious croup: Treatment (continued)

- Corticosteroids for moderate-severe cases
  - **Injected:** dexamethasone (0.3 - 0.6 mg/kg)
    - Onset 3-6 hours
    - Duration 36 - 54 hours
  - **Oral:** dexamethasone (0.3-0.6 mg/kg) or prednisolone or prednisone (1-2 mg/kg)
    - Onset 2-4 hrs
    - Duration 12-36 hrs
  - **Nebulized:** budesonide
    - Onset 2-4 hours
Infectious croup: Treatment (continued)

• Nebulized epinephrine for more severe cases
  ▪ Opens airway by reducing mucosal edema (vasoconstriction of precapillary arterioles leading to decreased hydrostatic pressure and fluid resorption)
  ▪ L-epinephrine gives same benefit and same adverse effect as the more expensive racemic epinephrine
  ▪ Doses: 0.5 ml of 2.25% racemic epinephrine or 5 ml of 1:1000 l-epinephrine
  ▪ To minimize irritation, dilute l-epinephrine with normal saline
Management

- Serial observation
- Mist therapy
- Steroids
- Epinephrine
Indications to Hospitalize

- Actual/expected epiglottitis
- Cyanosis
- Depressed sensorium
- Hypoxemia
- Pallor
- Progressive stridor
- Resp distress
- Restlessness
- Toxic-appearing
Complications

- Otitis media
- Bronchiolitis
- Pnemonia (rare)
- Bacterial tracheitis (rare)
- No ANTIBIOTICS?
Summary

- Croup is a common viral illness in children
- Treatment options include
  - Steroids – good evidence to support
  - Epinephrine – years of experience and trials support its use
  - Mist – years of use/no data to support
- Evidence supports outpatient treatment in mild to moderate croup
Bronchitis
What Is Bronchitis?

- Bronchitis is an inflammation of the bronchial tubes, or bronchi, that bring air into the lungs. Inflammation is a chemical reaction in the body that produces redness, swelling, and pain.
- Bronchitis can be caused by:
  - Viruses
  - Bacteria
  - Smoking
  - Breathing in certain kinds of irritating chemicals
- When the cells lining the bronchi are irritated, the tiny hairs (cilia) that normally trap and eliminate things from the outside stop working. Formation of material associated with irritation (inflammation) also increases; causing the passages to become clogged.
Bronchitis
(Chest infection)

Definition
• Bronchitis is an inflammation of the lining of bronchial tubes, which carry air to and from your lungs. Bronchitis may be either acute or chronic.
• A common condition, acute bronchitis often develops from a cold or other respiratory infection.
• Chronic bronchitis, a more serious condition, is a constant irritation or inflammation of the lining of the bronchial tubes, often due to smoking.
• Acute bronchitis usually improves within a few days without lasting effects, although you may continue to cough for weeks.
• However, if you have repeated bouts of bronchitis, you may have chronic bronchitis, which requires medical attention.
• Chronic bronchitis is one of the conditions included in chronic obstructive pulmonary disease (COPD).
• Treatment for bronchitis focuses on relieving your symptoms and easing your breathing.
There are two types of bronchitis:

- **Acute bronchitis** usually lasts only a few days. It is often caused by a viral infection and may begin after you develop a cold or sore throat. It usually produces no long-lasting, harmful effects.

- **Chronic bronchitis** is diagnosed when a person has too much phlegm in the airways, which leads to a persistent, productive cough. An individual is considered to have chronic bronchitis if cough and sputum (matter that is coughed up from the lungs) are present on most days for a minimum of three months for at least two successive years, or for six months during one year.
ACUTE BRONCHITIS

DEFINITION

• Inflammation of trachea and bronchi (larger airways) with cough being the predominant feature
• Usually lasts 1 to 3 weeks, peaks between October and March

Potential Causes

Viral infection: 90% of cases

• Influenza A or B, adenovirus, rhinovirus, para-influenzae, corona virus, Respiratory Syncytial Virus (RSV), human metapneumovirus

Bacterial infection: 10% of cases

• Mycoplasma pneumoniae, Chlamydia pneumoniae, Bordetella pertussis possible causes
• Streptococcus pneumoniae and H. Influenziae usually only causative organisms if there is underlying lung disease

Clinical features: cough and wheezing are the strongest positive predictors, less than 10% of patients are febrile
Predisposing Risk Factors

- Chronic sinusitis
- Chronic Obstructive Pulmonary Disease (COPD)
- Asthma
- Bronchiectasis
- Immunocompromised (chronic asthma)
- Smoking
- Second hand smoke
- Air pollutants, environmental factors
- Alcoholism
- Gastro Esophageal Reflux Disease (GERD)
- Wood stoves
Symptoms

For either acute bronchitis or chronic bronchitis, signs and symptoms may include:

- Cough
- Production of mucus (sputum), either clear or white or yellowish-gray or green in color
- Shortness of breath, made worse by mild exertion
- Wheezing
- Fatigue
- Slight fever and chills
- Chest discomfort

**Treatment**: studies have failed to show significant improvement with Ab therapy and at best may decrease duration of cough, decrease purulent sputum production.
BRONCHIOLITIS
BRONCHIOLITIS

• Common cause of illness in young children
• Common cause of hospitalization in young children
• Associated with chronic respiratory symptoms in adulthood
• May be associated with significant morbidity or mortality
Spread

- Humans only source of infection
- Direct or close contact with secretions
- Large-particle droplets <3 ft or fomites
- May persist hours on surfaces or 30 minutes on hands
- Viral shedding 3-8 days or longer
- Incubation period 2-8 days (4-6)
Epidemiology

- Most common lower respiratory tract infection in infants
- Most common etiology is RSV, most cases between December and March (75% of cases under 2)
- More common in crowded living conditions and smoke exposure
- Breastfeeding appears to confer a protective advantage
- Most severe symptoms in those under 2 years of age
- >50% affected by age 1, 80-90% by age 2, 40% have LRTI
- No permanent RSV immunity, reinfections common
- 1-2% require hospitalization (80% under 1 year)
- Cost of hospitalization infants under 1 year
- More likely to have respiratory problems when older
RISK FACTORS OF SEVERITY

- Prematurity
- Low birth weight
- Age less than 6-12 weeks
- Chronic pulmonary disease
- Hemodynamically significant cardiac disease
- Immunodeficiency
- Neurologic disease
- Anatomical defects of the airways
ENVIRONMENTAL RISK FACTORS

- Older siblings
- Concurrent birth siblings
- Native American heritage
- Passive smoke exposure
- Household crowding
- Child care attendance
- High altitude
PATHOGENESIS

- Viruses penetrate terminal bronchiolar cells--directly damaging and inflaming
- Pathologic changes begin 18-24 hours after infection
- Bronchiolar cell necrosis, ciliary disruption, peribronchial lymphocytic infiltration
- Edema, excessive mucus, sloughed epithelium lead to airway obstruction and atelectasis
Clinical Features

- Rhinitis, tachypnea, wheezing, cough, crackles
- Accessory muscle use and nasal flaring
- Apnea, grunting, cyanosis
- Poor feeding, difficulty sleeping, fussiness
- Tachycardia and dehydration may occur
- Natural course 7-10 days, peak on day 4
Diagnosis & Testing

- Clinical diagnosis on basis of Heart & Pulmonary
- Laboratory and radiologic studies should not routinely be ordered
- Nasopharyngeal swab for RSV ELISA may be used eg for cohorting
- Chest X-Ray to exclude other Dx, or if not improving as expected
DIFFERENTIAL DIAGNOSIS

- Viral-triggered asthma
- Bronchitis or pneumonia
- Chronic lung disease
- Foreign body aspiration
- Gastroesophageal reflux or dysphagia leading to aspiration
- Congenital heart disease or heart failure
- Vascular rings, bronchomalacia, complete tracheal rings or other anatomical abnormalities
Risk Factors for Severe Disease

- Age under 6-12 weeks
- History of prematurity esp < 28 weeks GA
- Underlying cardiopulmonary disease
  - Chronic lung disease
  - Complex congenital heart disease
  - Congenital airway abnormalities
- Immunodeficiency
- Severe neuromuscular disease
Management

- **Mainstay:** supportive care (hydration, oxygenation, nasal suction, respiratory support if needed)
- **No routine bronchodilator use** – may improve symptoms short-term but no effect on length of illness or LOS; potential for harm (SE, cost)
- **No routine corticosteroid use** – no benefit in RR, O2 sat, LOS though given to 60% of inpatients
- **No routine use of ribavirin** – variable results, may be appropriate for severely ill infants
- **Antibiotics** only if indication of concurrent bacterial infection
Prevention

- Palivizumab (anti-RSV) (Synagis®) prophylaxis for selected infants under 24 months
  - 15 mg/kg IM monthly November-March
- Hand washing
- Avoiding passive smoke exposure
- Promotion of breastfeeding