Respiratory agents: A nutshell

Edilberto A. Raynes, MD, PhD

Upper Respiratory Infections: Otitis Media and Otitis Externa

Viral Upper Respiratory Infections

- Rhinovirus most common virus
  - Adenovirus
  - RSV
  - Coronavirus
  - Enteroviruses
- Children get 6 to 8 colds a year
  - More if in daycare
- Adults average 2.5 URIs per year
- Last 7-9 days
- Significant runny nose and cough on days 1 to 4 predictive for viral origin

URI Symptoms

- Nasal congestion
- Rhinorrhea
- Malaise
- Scratchy or sore throat
- The nasal discharge typically starts out thin and clear and then thickens and progresses to a green or yellow color
- Generalized muscle aches
- Adults usually don’t have a fever
- Children may have low-grade fever

URI Treatment

- Symptomatic care
  - Fluids, antipyretics
  - Nasal bulb suctioning in infants
  - Decongestants in older children and adults
- No antibiotics
  - No difference in clinical outcomes

Decongestants

- Systemic Sympathomimetics
  - Pseudoephedrine
  - Phenylephrine
- Topical decongestants
  - Phenylephrine (Neosynephrine)
  - Oxymetazoline (Afrin)

Oral Decongestants

- Action: vasoconstriction of capillary vessels, theoretically decreasing congestion
- ADRs
  - Tachycardia
  - Hypertension
  - Anxiety/restlessness/irritability
- There is no evidence for the efficacy of either systemic decongestant in the treatment of URI in children
- Use may be hazardous
  - In 2004-05 1,519 children aged <2 years were treated in U.S. emergency departments for adverse events from cough/cold medications
  - Deaths in infants and young children

Cough Suppressants

- Dextromethorphan
- Codeine
- Action: centrally acting cough suppressant
- Evidence:
  - Codeine no more effective than DM or placebo
  - Little efficacy in cough d/t URI
  - Approximately 5-10% of Caucasians are poor DXM metabolizers
  - DXM + antidepressants may induce serotonergic syndrome
- Potential for abuse

Expectorants

- Guiafenesin (Robitussin)
- Action: stimulates respiratory tract secretions, decreases viscosity of respiratory secretion
- Evidence:
  - No evidence for efficacy in chronic cough or cough d/t URI

Sinusitis

- Bacteria isolated in 70% of patients with sinusitis
  - Strict criteria: persistent, not improving for at least 10 days
- Common pathogens
  - *S. pneumoniae* 30%
  - *H. flu* 20%
  - *Moraxella catarrhalis* 20%
  - rarely, *Staphylococcus*

Sinusitis: Goals of Treatment

- Absence of infection
- Resolution of all symptoms

Antibiotic choices for Sinusitis

- Amoxicillin first line
  - Dose at 80-90 mg/kg/day in high-risk children
    - 45 mg/kg/day in low risk children
  - Adults 500 mg TID
  - Or high-dose Augmentin
- For PCN allergic patients
  - Children: cefdinir, cefuroxime, or cefpodoxime
  - Adults: doxycycline or respiratory fluoroquinolone (levofloxacin)

Sinusitis: Worsening after 72 hrs

- Consider bacterial resistance
- Switch to Augmentin if amoxicillin was first choice
- If started on Augmentin:
  - Adults: consider respiratory fluoroquinolone (levofloxacin)
  - Children: cefdinir, cefuroxime, cefpodoxime

Acute Otitis Media (AOM)

- Caused by eustachian tube dysfunction
  - Negative pressure causes reflux of bacteria into middle ear
- Pathogens
  - *S. pneumoniae*
  - Nontypeable *H. influenzae*
  - *M. catarrhalis*
  - Microbiology is changing due to PCV vaccine
    - *H. flu* increasing, *S. pneumoniae* decreasing
    - Respiratory viruses account for 40 to 75% of AOM cases in children

AOM Diagnosis

- Diagnosis of AOM requires
  1. Moderate to severe bulging of TM or new onset of otorrhea
  2. Mild bulging of TM and < 48 hrs of ear pain or intense erythema of TM
- Bullous myringitis
  - thin-walled bulla

AAP/AAFP Guidelines for AOM in Children

- Initial observation without antibiotics for 48 to 72 hours in children > 2 years with non-severe illness
- If treating AOM with antibiotics, amoxicillin dosed at 80 to 90 mg /kg/day is first choice

Criteria for Initial Antibacterial-Agent Treatment or Observation in Children With AOM (AAP, 2013)

	Otorrhea with AOM	Unilateral or bilateral AOM with Severe Symptoms	Bilateral AOM without otorrhea	Unilateral AOM without Otorrhea
6 mo to 2 yr	Antibiotic therapy	Antibiotic therapy	Antibiotic therapy	Antibiotic therapy or additional observation
≥ 2 yrs	Antibiotic therapy	Antibiotic therapy	Antibiotic therapy or additional observation	Antibiotic therapy or additional observation

AOM Antibiotic Choices

- Amoxicillin is first choice
- Or amoxicillin/clavulanate 90mg/kg/day of amoxicillin

AOM antibiotics for PCN Allergic

- cefdinir (14 mg/kg per day in 1 or 2 doses)
- cefpodoxime (10 mg/kg per day, once daily)
- cefuroxime (30 mg/kg per day in 2 divided doses)
- Ceftriaxone 50 mg IM 1 day or x 3 days

AOM Initial observation for 48 hrs

- Low risk patient
  - > age 2 years
  - Mild otalgia
  - Temp < 39 degrees
- Adequate pain management is essential
- "Safety net" prescription
  - WASP "Wait and See Prescription"

AOM treatment failure at 48-72 hrs

- If initially treated with amoxicillin or other first line therapy:
  - Augmentin
  - Ceftriaxone IM/IV x 3 days
- PCN allergic:
  - Clindamycin plus third generation cephalosporin

AOM Patient Education

- Proper use of the prescribed antibiotic
- The predicted course of the infection once antibiotics are started
- Follow up in 2 to 3 days if no improvement
- Pain control

Asthma and COPD

Asthma

- Pathophysiology
  - Chronic inflammatory disorder of the airways
  - Recurrent episodes of wheezing, breathlessness and chest tightness
  - Airflow obstruction is reversible
- National Asthma Education and Prevention Program *Expert Panel 3 Guidelines* (2007) are used for management of all types of asthma

- Classification of Asthma
  - Mild intermittent
  - Mild persistent
  - Moderate persistent
  - Severe persistent
- Adult and children definitions differ slightly

Asthma

- Goals of Therapy
  - Reduce Impairment
    - Prevent chronic symptoms
    - Reduce use of inhaled short-acting beta agonists
    - Maintain normal or near normal pulmonary function
    - Maintain normal activity levels
    - Meet patient/family expectations of asthma care
  - Reduce Risk
    - Prevent recurrent exacerbations and minimize ED visits and hospitalizations
    - Prevent loss of lung function
    - Provide optimal therapy with minimal ADRs

Mild Intermittent Asthma

- Step 1 Therapy
- Use short-acting beta$_2$ agonists as needed for symptoms
- Patients have symptoms when exposed to triggers (URIs, allergens, chemical inhalents)
- Exercise can be mild intermittent
- Need an annual Flu shot

Beta$_2$ Receptor Agonists

- Short-acting beta agonists
  - Albuterol (ProAir, Ventolin, Proventil)
  - metaproterenol (Alupent)
  - terbutaline (Brethine, Brethaire)
  - bitolterol (Tornalate)
  - pirbuterol (Maxair)
  - levalbuterol (Xopenex)
- Long-acting beta agonists
  - salmeterol (Serevent)
  - formoterol (Foradil)
  - Indacaterol (Arcapta Neohaler)
  - arformoterol (Brovana)

Albuterol

- Selective $beta_2$ agonist with minor $beta_1$ activity
- Levalbuterol is where the (S)-isomer from racemic albuterol is removed

Salmeterol

- Salmeterol is more selective for $beta_2$ receptors than albuterol and has minor $beta_1$ activity
- 12 hour half life

Beta Agonists Clinical Use

- Exercise induced bronchospasm
  - Albuterol 2 puffs 15 min before exercise
  - Salmeterol 2 puffs 30 to 60 min before exercise
    - Do not use if already on daily dose of salmeterol
  - Leukotriene modifiers taken daily may decrease EIB symptoms in 50% of patients, but pt will still need to use albuterol before exercise

Beta$_2$ Agonists

- **Precautions and Contraindications**
  - Cardiac arrhythmias
  - Diabetics: potential drug-induced hyperglycemia
  - Long-acting beta agonists:
    - Black Box warning: the risks of salmeterol (Serevent) and formoterol (Foradil) outweighed the benefits and should not be used singly in asthma for all ages
    - 2-fold increase in catastrophic events (asthma related intubations and death)
  - Terbutaline Pregnancy Category B (others Cat C)
  - Children:
    - Albuterol safe for all age children
    - Salmeterol should not be used in children < age 4 yrs and never singly

Beta Agonists: Drug Interactions

- Digitalis glycosides: increased risk of dysrhythmia
- Beta adrenergic blocking agents: direct competition for beta sites resulting in mutual inhibition of therapeutic effects
  - Including beta blocker eye drops
- TCAs and MAOIs potentiate effects of beta agonist on vascular system

Monitoring

- Once control is achieved, the patient is seen every 1 to 6 months to determine if a step up or step down in therapy is indicated
- The Expert Panel III guidelines recommend the dose of inhaled corticosteroids be reduced about 25% to 50% every 2 to 3 months to lowest possible dose to maintain control

Managing Exacerbations

- Treat with oral steroids to regain control
- Use a short burst
  - Adults: 40 to 60 mg/day x 5 to 10 days
  - Children: 1 to 2 mg/kg daily (max 60 mg/day) x 3 to 10 days
- If not effective then step up in therapy

Mild Persistent Asthma

- Step 2 Therapy
- Treat with one long-term control medication daily
  - Low dose inhaled corticosteriods are the mainstay for all age patients
  - Cromolyn or a leukotriene modifier are alternative
  - See dosage charge for low dose schedule of each inhaled corticosteroid
- Use beta agonists as needed, if using more than ≥ 2 days per week then step up in therapy

Moderate Persistent Asthma

- Step 3 Therapy
- Treat with medium-dose inhaled corticosteroids
  - Or low-dose inhaled steroids plus long-acting beta agonists (adults)
  - Alternative: medium dose inhaled steroid plus leukotriene receptor modifier
- May use short acting beta agonists
- Exacerbations may require oral corticosteroids

Severe Persistent Asthma

- Step 4 Therapy
  - Medium-dose inhaled inhaled corticosteroids plus long-acting beta agonist
  - Or medium-dose inhaled corticosteroid and a leukotriene modifier or theophylline
- Step 5 Therapy
  - High-dose inhaled corticosteroids plus long-acting beta agonists
- Step 6 Therapy
  - High dose inhaled corticosteroids plus long-acting beta agonists and oral corticosteroids
- Severe persistent asthma requires consultation with asthma specialist