Acute and Chronic Rhinitis
(Intermittent and Persistent Rhinitis)

Wayne Kradjan, Pharm. D., RPh
Dean and Professor
Oregon State University
College of Pharmacy
Rhinitis

• Inflammation of the mucous membranes in the nose
  – Nasal discharge (rhinorrhea) (“runny nose”)
    • Profuse watery discharge; excess mucous production
  – Congestion
    • Excessive blood flow (hyperemia)
    • Vasodilation and increased permeability contribute to localized edema
    • Lay terms: Swelling and enlargement (dilation) of the blood vessels in the nose
  – Post nasal drip
Similarities to asthma

- **Allergic rhinitis**
  - Same cascade of events as allergic asthma except affecting nasal mucosa instead of bronchioles.
  - IgE mediated, degranulation of mast cells, histamine release, recruitment of inflammatory mediators.

- **Early and late phase responses analogous to asthma**
  - Histamine is one of several mediators of early phase response and minor player in late phase response
  - Inflammatory mediators perpetuate symptoms in late phase
Sympathetic Nervous System

- Vasodilation causes edema and congestion
  - Beta adrenergic stimulation or Alpha-1 adrenergic blockade
- Vasoconstriction causes decongestion
  - Alpha-1 adrenergic agonists
Acute (Intermittent) Rhinitis

- < 4 days/ week or < 4 weeks duration
- Generally non-allergic
- Viral infections: “Colds”
  - Rhinovirus, adenovirus, cocksackie
  - No role for antibiotics
- Bacterial infections
  - Rhinosinusitis (Sinus infection)
  - Streptococcus, Pneumococcus, Staphylococcus
  - Discharge is thicker (more purulent) + systemic symptoms.
- Pregnancy
Drug induced rhinitis

- Oral contraceptives and estrogens replacement
- Overuse of alpha agonist decongestant sprays (rebound)
- Antihypertensives
  - Alpha-1 antagonists: prazosin, terazosin, clonidine, reserpine
  - Calcium channel blockers
- First generation antidepressants
  - Amitriptyline (Elavil)
Chronic (Persistent) Rhinitis

- > 4 days per week or >4 weeks duration
- Mild- Absence of:
  - sleep disturbance
  - Interference of usual daily activities, work, school
  - Troublesome symptoms
- Moderate and severe based on presence of symptoms above
- 30% of adults; 40% of children in U.S.
Chronic (Persistent) Rhinitis

• Allergic Rhinitis
  – Affects all ages. Onset most common in children or early adult
  – **Seasonal** (“hay fever”). May vary geographically
    • Grass, weed, ragweed, tree pollens
      (spring and fall, post snow melt)
  – **Perennial** (year round, continuous symptoms)
    • Mold, mildew, dust mites, animal dander and saliva
  – Mixed seasonal and perennial
  – High correlation to asthma
Common Symptoms
Allergic Rhinitis

• Sneezing. Often uncontrollably and repeated immediately upon exposure
• Congestion. Both immediate and chronic
  – Also conjunctivitis
• Clear watery nasal discharge, not thick or yellow
• Nasal pruritus (“allergic salute”)
  – Also eyes, ears, palate, back
• Post nasal discharge: discharge into posterior pharynx. A common asthma trigger.
• Headache. Differentiate from sinus infection.
Physical findings

• Nasal examination
  – Turbinates normally pale pink.
  – In allergy = swollen, moist (“boggy”), discolored (pale and erythematous or blue)
• Transverse crease over lower bridge of nose (secondary to chronic “allergic salute”)
• Dark discoloration below eyes (“allergic shinners”)
Long term effects of persistent allergic rhinitis

• Thickening of nasal epithelium and connective tissue proliferation.
  – Loss of epithelial cilia
• Nasal polyps
• Asthma development
• Asthma trigger via post nasal drip
• Otitis media and hearing loss in children
• Increased risk of bacterial sinus infections
Chronic (Persistent) Rhinitis
Non-allergic, perennial

• Hyperreactive nasal mucosa due to unknown stimuli.
  – Possible autonomic imbalance with excess cholinergic (parasympathomimetic) responses
    • Consider therapeutic implications

• Non-allergic rhinitis with eosinophilia (NARES)

• Unknown cause: Idiopathic (vasomotor) rhinitis
  – More congestion and headache; less itching and runny nose
  – Cigarette smoke, animals, perfumes (odors), stress trigger allergic like symptoms
Allergic Reactions

Exposure to allergens
(Dust, weeds, pollen, mold)

\[ \text{IgE} \]

Mast cells release of

**Histamine and other inflammatory mediators**

\[ \text{Histamine binds to “receptors” in nose} \]

Immediate response:
runny nose, congestion, sneezing;
itchy eyes, throat and ears;
red eyes (conjunctivitis), post nasal drip

Long term response:
inflammation,
chronic symptoms

(smoke, perfumes)
Environmental Control

- Allergic rhinitis same as for allergic asthma
- Impermeable covers on pillows, mattresses, box springs for dust mites (? benefit)
- Remove
  - Carpets
  - Stuffed animals
  - Pets
- Avoidance of allergens and triggers
- Humidity <50% to reduce molds, mildew
Antihistamines

• Block binding of histamine to receptors in nasal mucosa; do not block mast cell histamine release
  – Limited value in colds and non-allergic chronic rhinitis by drying secretions (anticholinergic);
    May reduce post nasal drip vs excess drying in others.
  – Short term prevention or rapid relief of allergy associated histamine symptoms
  – Most effective if taken before exposure and used continuously
  – Relieve nasal discharge (runny nose), sneezing, itching, conjunctivitis, and possibly post nasal drip
  – Minimal effect on congestion and headache

• Although they maintain some long term effect, they are best used as “short term relievers”. Albuterol analogy
Oral Antihistamines

– Traditional ("sedating"). All non-prescription
  
  • Diphenhydramine (Benadryl), Brompheniramine (Dimetane), chlorpheniramine (Chlortrimeton), clemastine (Tavist), doxylamine, tripolidine. Hydroxyzine (Atarax, Vistaril = Rx)

– Non sedating
  
  • Low lipid solubility, do not cross blood brain barrier.
  • Not anticholinergic
  • Fexofenadine (Allegra) 60 mg BID, 180 mg QD. Active metabolite of terfenadine (Seldane). No evidence of Torsade.
  • Loratadine (Claritin, Alavert)- now OTC. 10 mg Q 24 hr. also 10 mg RediTabs, 5 mg/5 ml syrup for children. also “D” formula with pseudoephedrine 5 mg/120 mg Q 12 hr and 10 mg/240 mg Q 24 hr.
  • desloratadine (Clarinex). Active metabolite of loratadine. 5 mg QD if over 12 years old
Antihistamines (continued)

– Intermediate sedation

• Cetirizine (Zyrtec)- Now available OTC
  Active metabolite of hydroxyzine
  5-10 mg QD (2.5 mg if age 2-5). Also Zyrtec D 12 hr

• Levocetirazine (Xyzal) – 5 mg tabs
  R-enatiomer (active form) of cetirizine
  Same indications and side effects as Zyrtec
  5 mg HS if over age 12; 2.5 mg age 6-11
Antihistamine Side Effects
(not Allegra, Claritin or Clarinex)

• Drowsiness
  – Less if taken at bedtime
  – May become tolerant
• Loss of mental alertness: driving risk, inability to concentrate at work or school.
• “Anticholinergic”:
  – Dry mouth, constipation, urine retention (caution in older adults, especially men)
  – Confusion, psychosis in older adults and paradoxical excitation in infants
  – NOT contraindicated in glaucoma or asthma
• Tachyphylaxis due to auto enzyme induction?
Antihistamine Controversies

• In allergic rhinitis
  – Which to use first: a cheaper sedating antihistamine or the more expensive non-sedating drug?
  – Are non-sedating agents or cetirizine any more effective than older agents?
  – Is Clarinex better than Claritin or Allegra? (Just how effective are these drugs vs placebo?)
  – Will nighttime dosing reduce daytime sedation and reduced attentiveness?
  – Should antihistamines be used before anti-inflammatory medications?

• In viral syndromes (colds)
  – Should antihistamines be used at all?
“Topical” antihistamines

- **Intranasal**
  - Azelastine (Astelin): 0.1% nasal spray, 125 μg per spray. 2 sprays twice daily in each nostril.
  - For symptoms of seasonal allergic rhinitis (rhinorrhea, sneezing, nasal pruritus) in adults and children > 12 years of age.
  - More effective in reducing nasal blockage and rhinorrhea than oral drugs?
  - May reduce eye itching via systemic absorption or accidental spray into eye.
    - 40% absorbed from the nose. T ½ = 22 hours. Also active metabolite (desmethylazelastine) with T ½ = 54 hours.
  - Bitter taste = 19.7% vs 0.6% placebo.
  - Sleepiness = 11.5% vs 5.4% placebo.
  - Headache = 14.8% vs 12.7% placebo.
  - Also nasal irritation and dry mouth.
Azelastine (Astelin)
Antihistamine Nasal Spray
Decongestants

- All are alpha-1 adrenergic agonists
- Vasoconstrictors (narrow blood vessels) to reduce fluid leakage into surrounding tissues ("edema")
- Effective for both allergic and non-allergic causes including colds and chronic rhinitis.
- Topical sprays very rapid acting with minimal side effects
  - Oxymetazoline (Afrin), phenylephrine (Neo-synephrine), tetrahydrozoline, xylometazoline
  - Caution: limit to maximum of 5-7 days to prevent "rebound congestion"
- Consider saline sprays for chronic congestion
Oral Decongestants

- Pseudoephedrine (Sudafed), phenylephrine
- Longer acting than sprays and little risk of “rebound”
- Sudafed: short acting (30-60 mg Q 4-6 hours) and long acting (SR 120-240 mg Q 12-24 hrs)
- Side effects
  - Raise blood pressure; increase heart rate
  - Stimulants (difficulty sleeping, nervousness, shaky); additive to caffeine; some abuse potential
- Phenylpropanolamine (also in diet pills) removed from market due to possible stroke risk
- Ephedrine 12.5-50 mg Q 4-6 hr in OTC combos Ephedra (Ephedrine), Ma Huang- removed 2004
Combination Products

• Antihistamine plus decongestant
  – Choose based on symptoms
  – Short acting or long acting
    • 6 vs 12 vs 24 duration
• Allegra D: 60 mg fexofenadine/120 mg sudafed BID
• Claritin D: loratadine 5 mg/120 mg sudafed BID
  loratadine 10 mg/sudafed 240 mg QD
• Clarinex-D 24 hr: desloratadine 5 mg/sudafed 240
• Zyrtec D: 5 mg cetirizine/120 mg sudafed BID
Important Principle

• Anti-inflammatory medications are the key to long term success of allergic rhinitis
• Chronic (persistent) allergic rhinitis is an inflammatory disorder
• The value of anti-inflammatory drugs in perennial non-allergic rhinitis is less clear
• Antihistamines and decongestants reduce symptoms, but do not reduce the cause of the problem
Intranasal Corticosteroids

- Beclomethasone (Beconase AQ 0.42% soln).
  - 42 mcg/spray. DS = 84 mcg. 1-2 spray BID
- Budesonide (Rhinocort Aqua)
  - 50 mcg/spray (32 mcg delivered).
    2 sprays BID or 4 sprays QD
- Flunisolide (generic, Nasalide?, Nasarel Aqueous?)
  - 0.025% soln, 25 mcg/spray. 2 sprays BID.
- Fluticasone (generic, Flonase AQ)
  - (fumarate = Veramyst 27.5 mcg/spray 1-2 QD)
  - 0.05% soln, 50 mcg/spray. 1 spray QD or 2 sprays BID
- Mometasone (Nasonex aqueous)
  - 0.05% soln, 50 mcg per spray. 2 sprays per nostril BID
- Triamcinolone (Nasacort HFA?, Nasacort AQ)
  - 55 mcg/spray. 2-4 sprays BID to QD
Intranasal Corticosteroids

- Most effective therapy available
  - blow nose before use; decongestant if needed
  - point applicator straight back; aim away from nasal septum)

- Must be used continuously
  - Onset 1-2 days to 3-5 days; Max effect at 2-3 weeks
  - Use thru allergy season or for many years

- Side effects
  - Burning, stinging, cold sensation (less with AQ formulas). All may be drying.
  - Nose bleeds (don’t spray toward septum)
    - Rare mucosal ulceration, septal perforation
  - Less often: sore throat, Candidal infection,
  - Growth suppression in children, osteoporosis in adults, cataracts? High doses, long term use
Recent changes

• Fluticasone and mometasone PRN?
• Fall 2003: CFC containing preparations removed from market
• Propylene glycol and polyethylene glycol preps being discontinued in favor of aqueous *suspensions*. 
Beclomethasone

Beconase AQ

Vancenase AQ - discontinued
Budesonide
(Rhinocort Aqua)
Flunisolide (generic)
Nasalide/ Nasarel no longer available?
Fluticasone Nasal

Furoate salt (Veramyst)

Propionate Salt (Flonase)
Mometasone
(Nasonex)
Triamcinolone
(Nasacort AQ)
Leukotriene Inhibitors

• Montelukast (Singulair) 10 mg QD
  – Leukotriene receptor blocker
  – FDA approved for allergic seasonal rhinitis in combination with intranasal steroids

• More consistent effect on nasal symptoms than on rhinorrhea or sneezing.

• Little indication of additive effect to antihistamines for total symptom scores
  – Replacement if intolerant of antihistamine SE’s?

• Inferior to corticosteroids as monotherapy
  – Good evidence for role as adjunct to intranasal steroids
Intranasal Cromolyn

- Nasalcrom (OTC): 40 mg/ml solution or 5.2 mg per spray in pump sprayer.
- Non-corticosteroid anti-inflammatory ("mast cell stabilizer" to block histamine release); for mild to moderate symptoms.
- Less effective and slower in onset (10-30 days) than corticosteroids.
- No harm to bones or eyes
- Inconvenience of four doses per day
  - 1 spray QID (4-6 X/day to start, later 2-3 X/day)
  - Inhalation for asthma
- Less nasal side effects: 10% burning, stinging
Persistent ocular symptoms

- Allergic conjunctivitis
  - Itching, burning, tearing
  - Conjunctival edema, swelling of eyelids
- Vernal keratoconjunctivitis
  - Giant papillae of the conjunctivae and associated with itching, tearing, keratitis and photophobia. Exacerbated by contact lens wear
- Cold compresses
- Normal saline or artificial tears
- Antihistamine eye drops if symptoms persist despite oral antihistamines and/or nasal steroids
  - Temporary relief of itching due to allergic conjunctivitis
Topical eye drop options

• Antihistamines (Rx only)
  – Azelastine (Optivar) 0.05%. 1 drop each eye Q 12 hr
  – Emedastine (emadine) 0.05%. 1 drop QID
  – Levocabastine (Livostin) 0.05%. 1-2 drops each eye QID

• Antihistamine/decongestant combinations (OTC)
  – Vasocon A (antazoline 0.5% + naphazoline 0.05%)
  – Naphcon-A, OcuHist, Opcon A (pheniramine 0.3% + naphazoline 0.025%)
Topical antihistamines
(Continued)

• Non-corticosteroid ("mast cell stabilizers")
  – Cromolyn 4% (Opticrom, Crolom) 1-2 drops 4-6x/day, Lodoxamide (Alomide), 0.1%, 1-2 drops QID Nedocromil (Alocril), Pemirolast (Alamast)

• Antihistamine with mast cell stabilizing properties
  – Olapatadine (Pantanol) 0.1%. 1-2 drops each eye BID (5-8 hours apart)
  – ketotifen (Zaditor) 0.025%. 1 drop Q 8-12 hr (OTC 2007)
    – Less stinging with olapatadine than levocabastine?

• Corticosteroid
  – Loteprednol (Alrex)

• Other (NSAID)
  – ketorolac (Acular)
Ipratropium (Atrovent) Nasal Spray

• A drying agent (anticholinergic) to reduce nasal discharge (runny nose, post-nasal drip)
  – No effect on congestion, itching, redness
• Allergic and non-allergic rhinitis
  – 2 sprays of 0.03% solution 2-3 times daily
• Common cold
  – 2 sprays of 0.06% solution 3-4 times daily
• Side effects: nasal dryness, burning, nose bleeds, sore throat in 4-8%
Ipratropium (Atrovent) Nasal Spray
Special Situations

• Severe worsening of allergic rhinitis not responding to antihistamines and topical corticosteroids
  – Prednisone “bursts” 40 mg daily for 3-7 days. Children: 1-2 mg/kg/day
    Do not exceed 2-3 times per year.

• Chronic symptoms not responding to usual therapies
  – Immunotherapy (desensitization) shots with specific allergens identified via skin testing.
Non drug therapies for cold

• Drink lots of fluids
• Humidifiers, vaporizers
• Salt water (saline) drops and sprays to soothe irritated tissues and moisturize nasal mucosa
  - ½ to 1 teaspoon per 6-8 ounces of water 4-6 x per day
Symptom relief of colds

Antipyretics

• Fever and body ache reduction
• Slow time to recovery via increased viral shedding?
• Acetaminophen (Tylenol)-
  – caution re liver damage
• Ibuprofen (Advil), naproxen (Aleve)
  – More effective than acetaminophen?
• Aspirin
  – Avoid in children: Reye’s syndrome
American College of Chest Physicians
Evidence Based Practice Guidelines
(Chest. January 2006, supplement)

• Cough associated with common cold is primarily the result of postnasal drip or inflammation of upper respiratory tract.
  – OTC cough suppressants do not treat the underlying cause.
  – First generation antihistamines and/or decongestants may be effective
  – Dextromethorphan, guaifenesin, second generation antihistamines, zinc **not proven to relieve cold-related coughs**.

• Cough and cold medications **inadvisable in children less than 15 years of age** because of lack of efficacy data in children under age 6, increased adverse effects, and even mortality risk (via accidental ingestion).
  – All products discontinued for < 2 year old
  – Age 2-11 still under review
Safety in Children

- FDA reports from 1969-2006
  - 54 child deaths from decongestants (primarily pseudoephedrine)
  - 69 child deaths from antihistamines (includes diphenhyramine, chlorpheniramine, brompheniramine)

- Centers from Disease Control (2006)
  - Estimated 1,500 children under age 2 treated in ER during 2004-2005 for ADRs from cough and cold products, including 3 deaths

- Oct 2007 14 pediatric products removed from market
  - www.aap.org/new/kidcolds.htm
  - Saline nasal drops, humidifiers, vaporizers recommended
Cough suppressants

- Avoid if productive cough
- Use if disturbing sleep, vomiting, chest pain
  - Blood in sputum or vomitus: Mallory Weiss tear
- Dextromethorphan (15-30 mg)
  - Benylin Adult Cough = Dextromethorphan 15 mg/5 mL without diphenhydramine
  - Robitussin Maximum Strength Cough = Dextromethorphan 15 mg/5 mL; **NO** guaifenesin
  - Vicks 44" Soothing Cough Relief” 10 mg/5 mL
  - Delsym extended release (ion exchange resin) = 30 mg/5 mL Q 12 hours
- Honey, lemon juice, whiskey
Expectorants

• Guaifenesin (100 mg/5 mL)
  – Questionable efficacy: 300-1000 mg
  – Nausea and vomiting at higher doses
  – “logic” of combination with dextromethorphan?
    • AC = Codeine
    • CF = Dextromethorphan and phenylpropanolamine
    • DC = Codeine and pseudoephedrine
    • DM = Dextromethorphan
    • PE = Pseudoephedrine

• Iodides

• Steam, hot shower, hot soup
Combination Products

- Antihistamine plus decongestant
  - Choose based on symptoms
  - Short acting or long acting

- Multi-symptom products
  - Fever reducer (acetaminophen, aspirin, ibuprofen)
  - Cough suppressant (dextromethorphan)
    - At least 15 mg short acting, 30 mg long acting
  - Expectorant (guaifenesin, Robitussin)

- Are all symptoms present?

- Additive to other medications already taking?
  - Especially high risk with acetaminophen-liver damage
Untangling Labels

• Allergy formula:
• Nighttime:
• Daytime:
• Non-drowsy formula:
• Sinus formula:
• Flu formula:
• Maximum strength:
• Cold formula:
Untangling Labels

- Allergy formula: has antihistamine, maybe decongestant
- Nighttime: has antihistamine, maybe decongestant
- Daytime: no antihistamine, probably has decongestant
- Non-drowsy formula: no antihistamine, does have a decongestant
- Sinus formula: has decongestant
- Flu formula: has acetaminophen (or ibuprofen)
- Maximum strength: 500 mg acetaminophen per dose
- Cold formula: no predicting
Nyquil, Multi-symptom Cold/Flu Relief

"The nighttime sniffling, sneezing, coughing, aching, stuffy head, fever so you can rest medicine."

Two tablespoonfuls at bedtime: doxylamine 12.5 mg, pseudoephedrine 60 mg, dextromethorphan 30 mg, acetaminophen 1000 mg (in 10% alcohol)
DayQuil Multi-Symptom Cold/Flu Relief

"The non-drowsy, stuffy head, congested chest, sore throat, coughing, fever so you can face your day medicine."

"Alcohol free/ antihistamine free"

2 tablespoonfuls up to four time daily:
- pseudoephedrine 60 mg
- dextromethorphan 20 mg
- guaifenesin 200 mg
- acetaminophen 650 mg
Echinacea

- May have immunostimulant properties to prevent and treat the common cold
- 300mg 3-4 times daily at first sign of symptoms using preparation made from herbal leaf portion of plant.
- Liquid extract preferred, but bad taste
- No value in long term prevention
- Related to sunflowers and ragweed: allergic potential?
- Avoid if taking immunosuppressive drugs or have autoimmune disease (lupus, rheumatoid arthritis)
Zinc

- May inhibit viral replication
- Conflicting evidence of benefit.
- Best data with 13-23 mg zinc gluconate or zinc acetate lozenges every 2 hours while awake
  - Cough, sore throat, nasal discharge respond differently
  - Zinc gluconate nasal spray not effective
  - Zinc gluconium nasal gel (Zicam): decreased duration and symptom severity
- Some sweetening agents and other additives may bind or inactivate the zinc
- Side effects: bad taste (80%), nausea, mouth or throat irritation (37-50%), diarrhea
Summary

• What symptoms are present?
  – Sore throat: salt gargle, hard candy, benzocaine
  – Headache or body aches: acetaminophen or ibuprofen
  – Stuffy nose: decongestant. Afrin or pseudoephedrine
  – Runny nose: antihistamines?

• Suspect allergies?
  – Antihistamines
  – Nasal corticosteroids
  – Nasal cromolyn