

NRSG 913 Applied Drug Therapy
Allergies and Upper Respiratory Infections
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OBJECTIVE: Understand the drug classes and specific agents used to treat allergic rhinitis and upper respiratory tract infection. The participant should be able to discuss the advantages and disadvantages of specific drugs or drug classes in regard to administration, adverse effects, drug interactions, monitoring parameters and cost considerations.

READING: Gourley DR, Herfindal ET, eds. Textbook of Therapeutics: Drug and Disease Management, 6th edition. Baltimore: Williams & Wilkins, 1996. pages 1251-1265.

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Oppenheimer RW. Sinusitis: how to recognize and treat it. Postgraduate medicine.1992;91(5):281-291.

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Allergic Rhinitis

I. Definition: Allergic rhinitis is caused by seasonal or chronic exposure of the mucous membranes to inhaled allergenic materials that elicit a specific immunologic response.

II. Predisposing Factors:

- family history
- allergen exposure
- socioeconomic class

III. Pathophysiology:

- nasal physiology
- IgE mediated immune response
 - histamine response
 - increase in vascular permeability
 - smooth muscle contraction
 - mucus secretion
 - influx of basophils, eosinophils and neutrophils

IV. Clinical symptomatology:

- sneezing
- pruritus
- conjunctival itching
- watery/sore eyes
- irritability, fatigue, depression
- nasal obstruction
- rhinitis
- lacrimation
- itchy ears, palate and/or throat

V. Characteristics of Seasonal vs. Perennial Allergic Rhinitis (Inflammation related rhinitis)

- | | | |
|------------|---|--|
| Seasonal: | Often quite predictable in onset related to the seasons of pollination of grasses, weeds, trees. | |
| Perennial: | Often symptoms are present year around, related to house dust, animal hair/dander, dust mites, feathers or tobacco smoke. | |
| Others: | Noninflammatory: | Vasomotor, medication induced and hormonal |
| | Structural: | Nasal polyps, septal deviations |

VI. Complications

- inability to sleep, chronic fatigue, malaise
- loss of smell and/or taste
- delayed development of language skills
- acute and/or chronic sinusitis
- decreasing work/school efficiency
- recurrent otitis media/chronic middle ear infections
- dental malocclusions/orthodontic problems
- upper respiratory tract infections

VII. Diagnosis

- A. Patient history
- B. Skin testing
 - 1. intradermal
 - 2. epicutaneous
- C. IgE measurements
 - 1. Radioallergosorbent test (RAST)

VIII. Treatment

- Goals of therapy:
1. prevent attacks
 2. reverse symptomatology of attacks
 3. avoid significant adverse effects
 4. increase patient's level of activity and avoid long-term complications of disease state

A. Avoidance of offending allergens

B. Antihistamines (H₁ receptor) - Competitive antagonist at the receptor by preventing the binding histamine.

1. Commonly used antihistamines:

<i>Agent (Generic)</i>	<i>Trade Name</i>	<i>Usual Adult Dose (PO)</i>	<i>Sedative Potential</i>	<i>Anticholinergic Effect</i>
"First generation Antihistamines"				
Chlorpheniramine	Chlor-Trimeton®	4mg q4-6 hours, q12h	Low	Moderate
Brompheniramine	Dimetane®	4mg q4-h hours	Low	Moderate
Diphenhydramine	Benadryl®	25-50mg q4-h hours	High	High
Clemastine	Tavist®	1.34-2.68mg q12h – TID	Moderate	High
Promethazine Rx	Phenergan®	12.5-25mg TID-QID	High	High
Carbinoxamine Rx	Histex CT, liquid	1 tablet (8mg) q12 H	High	High
Hydroxyzine Rx	Atarax®, Vistaril®	10-25mg QID	High	High
"Second generation Antihistamines"				
Terfenadine	Seldane®	60mg q12h	Low	Low to none
Loratadine OTC	Claritin®	10mg QD	Low	Low to none
Desloratadine Rx	Clarinex	5mg QD	Low	Low to none
Astemizole	Hismanal®	10mg QD	Low	Low to none
Cetirizine Rx	Zyrtec®	10mg QD	Mild	Low to none
Fexofenadine Rx	Allergra®	60mg q12h	Low?	Low?
TOPICAL ANTIHISTAMINES				
Azelastine	Astelin	2 sprays each nostril BID	None?	Low to None

2. Adverse Effects

a. CNS effects

- drowsiness and/or dizziness
- paradoxical excitement, particularly in children and the elderly

b. Anticholinergic effects

- dry mouth
- urinary retention
- blurred vision
- constipation
- dry mouth

c. Cardiac effects

- ventricular tachycardia, torsades de pointes... more common in patients taking second generation agents, see also "drug interactions" below

- d. Gastrointestinal intolerance
 - N/V -constipation
 - diarrhea

3. Precautions

- a. prostatic hypertrophy
- b. closed angle glaucoma
- c. preexisting heart disease

4. Drug interactions

- a. other CNS depressants

- b. Macrolides antibiotics (Not as significant of a problem since offending agents have been pulled from the market)

- c. azole type antifungals, ketoconazole (Nizoral), itraconazole (Sporonox)

5. Patient counseling

- a. alert of CNS depression
- b. alcohol
- c. tolerance to agent
- d. scheduled vs. timing prior to exposure

6. Selection of agent and cost considerations

C. Topical Decongestants

1. Topical decongestants are applied directly to swollen nasal mucosa via sprays, producing vasoconstriction, shrinking of swollen mucosa and improve ventilation.

2. Commonly used topical decongestants.

Agent (Generic)	Trade Name	Adult dosage, drops/spray	Duration of action
Phenylephrine .25%, .5%, 1%	Neo-Synephrine ®	2-3 drop/sprays q4-6 hour	4 hours
Xylometazoline 0.1%, 0.05%	Neo-Synephrine LA®, Otrivin®	2-3 drops/sprays q12 hours	12 hours
Oxymetazoline 0.05%, 0.025%	Afrin®, Duration®, Dristan®	2-3 drop/sprays q12 hours	12 hours

3. Adverse effects

- rhinitis medicamentosa

- burning, stinging, sneezing, dryness of the nasal mucosa

4. Patient counseling

- a. appropriate use
 - nasal drops

 - nasal spray

- b. duration of therapy and avoidance of rhinitis medicamentosa

D. Systemic Decongestants

1. Commonly used systemic decongestants

Agent (generic name)	Trade name	Usual adult dose	Duration of action
Pseudoephedrine Rx OTC	Sudafed®	30-60mg q4-6 hours, 120mg q12 hours	4 hours, 12 hours
Phenylephrine Rx	Combination Only		
Ephedrine			
Phenylpropanolamine	Combo only	25mg q4h, q8-12 hours sust. Release	4 hours, 12 hours

2. Comparison with topical agents

- lower incidence of rhinitis medicamentosa
- not as immediately effective
- may last longer

3. Adverse effects

- CNS stimulation, nervousness, restlessness, dizziness, insomnia, headache
- hypertension, cardiovascular stimulation

4. Patient counseling

E. Combination antihistamine/decongestant agents

1. Rational of use

2. Patient counseling

F. Topical Corticosteroids

1. Effects of topical steroids on nasal mucosa

- decrease in epithelial mediator cells -decreased in epithelial permeability
- reduction of the secretory response-partial inhibition of immediate allergen symptoms
- inhibition of the late phase response -questionable effectiveness in ocular symptoms

2. Commonly used nasally administered steroids

Agent (generic name)	Trade name	Usual adult dose
Beclomethasone	Beconase AQ®	1 spray each nostril 2 times daily
Flunisolide	Nasarel®, generic also	1 spray each nostril twice daily
Triamcinolone	Nasacort AQ®	1 spray each nostril daily
Fluticasone	Flonase®	1-2 sprays each nostril daily
Mometasone	Nasonex®	1-2 sprays each nostril daily
Budesonide	Rhinocort®	1-2 sprays each nostril daily

3. Adverse effects

- rarely has any effect on the hypothalamic-pituitary-adrenal axis
- more common- burning, nasal irritation, sneezing, epistaxis
- localized *Candidal* overgrowth (rarely)

4. Patient counseling

- a. requires regular use for up to 1 week for maximal effectiveness
not immediately effective continued use required for sustained effectiveness
- b. appropriate use, use with other topical decongestants
- c. educate and understand patients fears regarding “steroid phobia”

G. Cromolyn sodium (Nasal crom®)

1. Prevents the degranulation of mast cell and subsequent release of mediators of allergic reaction, including histamine.

2. Has no direct antihistamine, anticholinergic or anti-inflammatory properties
3. Side effect profile as steroids: local irritation most common
4. Dose: 1 spray into each “clean” nostril 4-6 times daily.
 Must come into contact with entire nasal mucosa, (> 90%)
MUST BE USED FOR UP TO FOUR WEEK BEFORE MAXIMAL EFFECTIVENESS
 Decrease the use of other agents when chromogen becomes effectiveness

H. Ipratropium (Atrovent® Nasal Spray)

- anticholinergic treatment for rhinorrhea associated with seasonal rhinitis
- use for runny nose not responding to conventional therapy or combination therapy
- does not improve other symptoms of allergic rhinitis (sneezing, congestion, postnasal drip)
- generally well tolerated, adverse effects: nasal dryness, epistaxis

I. Ophthalmic Preparations

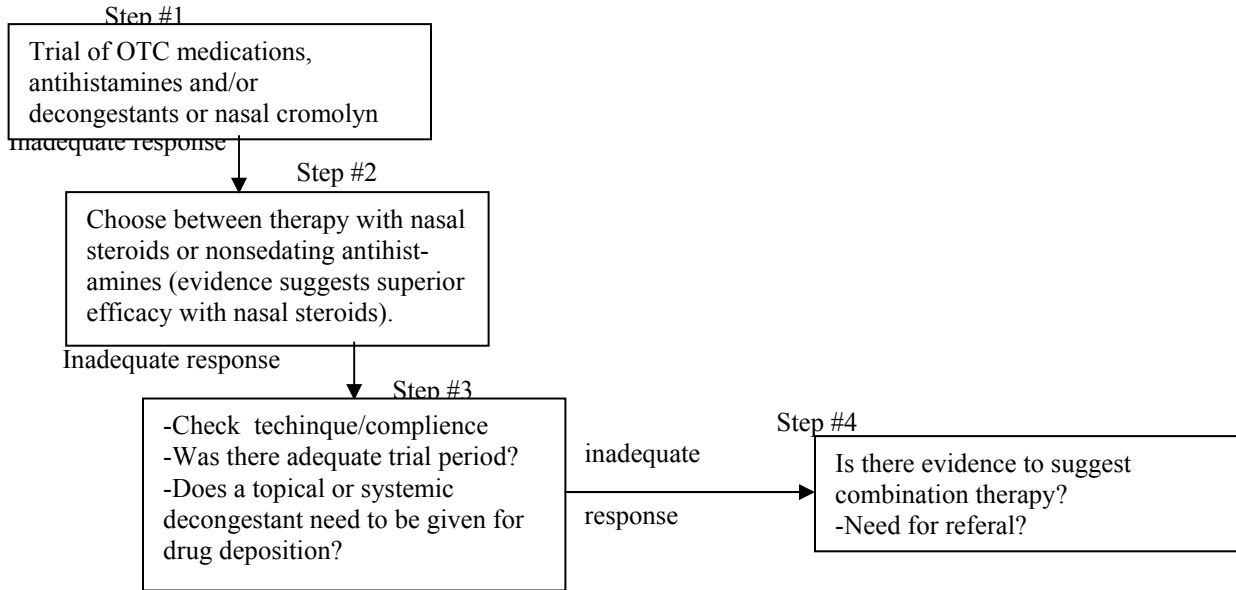
Systemic (antihistamines) and topical (steroids) may NOT provide adequate relief from significant ocular symptoms. Topical ophthalmic preparations may be an effective adjunctive therapy.

1. Antiinflammatory
 - Ketorolac (Acular®) ophth drops
 - Flurbiprofen (Ocufer® and generic) ophth drops
 - Suprofen (Profenal®) ophth drops
 - Diclofenac (Voltaren®) ophth drops
2. Mast cell stabilizers
 - Iodoxamide (Alomide®)
 - Cromolyn sodium (Crolom®)
3. Antihistamines
 - Levocabastine (Livostin®)
4. Vasoconstrictors
 - Naphazoline (Vasocon-A®, Opcon-A®)
 - Phenylephrine (Neo-synephrine Ophth, and others)
 - Tetrahydrozoline (Visine, Murine and others)
 - Oxymetazoline (OcuClear)

J. Immunotherapy

1. Effectiveness of antigen extracts continues to be controversial
2. Suppression of seasonal rises of IgE antibodies, decreased basophils, generation of antigen suppressor cells
3. Adverse effects
 - local reactions
 - allergenicity- bronchospasm, laryngospasms, vascular collapse
 - life-threatening anaphylaxis
4. Cost

K. Treatment Algorithm for Allergic Rhinitis



L. Allergic Rhinitis Medication Recommendations

(adapted from International Rhinitis Management Working Group, Allergy 1994;49:1-34)

Medication	Itching, Sneezing	Discharge	Blockage	Impaired Smell	Prophylaxis
Nasal corticosteroids	+++	+++	++	+	++
Oral decongestant	-	-	++	-	-
Oral antihistamines	+++	++	±	-	+
Nasal decongestants (3-7 days, max)	-	-	+++	-	-
Nasal cromolyn	+	+	±	-	+
Oral corticosteroids (short course, use caution)	+++	+++	+++	++	-
Ipratropium nasal spray	-	+++	-	-	-

Key: - not effective; ± questionably effective; + minimally effective; ++ moderately effective; +++ maximally effective

M. Indications for possible Allergy Specialist Referral

- Prolonged manifestations of rhinitis
- Complications of rhinitis (e.g. otitismedia, sinusitis, nasal polyposis)
- Comorbid conditions (eg. Asthma, COPD)
- Previous treatment with oral corticosteroids
- Symptoms interfere with functioning (eg. Sleep disturbances, impaired school or work performance)
- Symptoms significantly decrease quality of life
- Effective treatment produces adverse events
- Need for further definition of allergic or environment triggers
- Need for more intense education
- Multiple medications required over a prolonged period of time

UPPER RESPIRATORY TRACT INFECTIONS (URTI)

I. The Common Cold

A. Epidemiology

- cause of > 50 million lost work days per year
- Americans spend > \$2 billion yearly on > 800 cold remedies
- etiology included rhinoviruses, parainfluenza viruses, RSV and others
- 30% of colds are caused by rhinoviruses for which there are over 100 antigenically different serotypes

B. Symptomatology

- rhinorrhea, nasal congestion, sneezing, sore throat, and nonproductive cough
- nasal discharge may progress from clear and watery to purulent
- malaise, HA and chills (fever, if present, is usually low grade)
- dry, scratchy, sore throat
- differential diagnosis between group A streptococcal infection, seasonal/allergic rhinitis
- progression of disease to complication of sinusitis and otitis media

C. Treatment

1. FDA Categories of OTC products
 - a. Category I. agents that are recognized as being safe and effective for their claimed indication
 - b. Category II. agents are neither safe or effective
 - c. Category III. agents that have insufficient data for classification
2. Symptomatic treatment - same drugs used to treat allergic rhinitis
 - a. Antihistamines - dry up nasal secretions
 - b. Decongestants - relief of nasal congestion
 - c. Antitussives - suppress cough, generally through suppression of the medullary cough center
 - dextromethorphan 10-30mg q4-8h (DM in most antihistamine/cough combinations)
 - codeine 10-20mg q4-6h (other narcotics hydrocodone)
 - diphenhydramine 25-50mg q4h
 - benzonatate (Tessalon Pearls) 100mg tid. Act as a local anesthetic
 - d. Analgesics
 - acetaminophen
 - Nonsteroidal antiinflammatory drugs
 - Aspirin
 - e. Expectorants - decrease sputum viscosity and promote expectoration
 - **guaifenesin 200-400mg q4h (only Category I)** - terpin hydrate (not available)
 - potassium iodide (formerly in Organidin® products, replaced with guaifenesin)
 - **hydration (water, water, water, water)**
 - f. Anticholinergic agents - decrease in nasal secretions
 - ipratropium (Atrovent®) nasal spray
 - g. Antivirals -
 - amantidine 200mg daily at the first sign of symptoms
 - vitamin C (ascorbic acid)
 - zinc gluconate
 - Echinacea
 - h. Antibiotics - No scientific evidence to support the use of antibiotics

II. Sinusitis - Inflammation of the paranasal sinuses, usually precipitated by the effects of an upper respiratory infection (common cold), allergic rhinitis, hypertrophied adenoids, structural defects, swimming, cigarette smoking, environmental pollutants (just to name a few).

- Characterized as:
- acute - lasting less than 3 weeks
 - subacute - lasting 3 - 8 weeks
 - chronic - lasting longer than 8 weeks

A. Symptoms

- | | |
|---|--|
| -midfacial or periorbital pain/pressure | -congestion |
| - fever | - cheek and conjunctival swelling |
| - purulent anterior nasal discharge | - headache |
| - cough | - loss of smell and taste, voice changes |

- posterior nasal drainage
- B. Microbiology
 - viral causes (rhinovirus, influenza, parainfluenza) \approx 30%
 - *Streptococcus pneumoniae*
 - *Haemophilus influenzae* (beta lactamase producer)
 - streptococcal species
 - *Moraxella catarrhalis* (beta lactamase producer)
 - gram-negative and -positive anaerobes
- C. Treatment
 1. Considerations
 - resistance patterns and production of β -lactamase
 - lack of known definitive organism (generally empiric treatment)
 - even without antibiotics \sim 60%of patients will have symptoms resolve within 2 weeks. However, antibiotics do significantly increase the per cent of patient cured at 2 weeks treatment
 - efficacy, safety and cost of antimicrobial treatment (considering generally 2 weeks or greater of therapy)
 2. Adjunctive treatment
 - nasal sprays (Ocean® nasal spray), nasal toilet
 - topical and systemic decongestants
 - antihistamines - avoid due to increased viscosity of purulent drainage
 - analgesics
 - nasal inhaled steroids
 3. Antibiotics
 - empiric therapy should be effective for *S. pneumoniae* and *H. influenzae*
 - a. primary treatments
 - amoxicillin 250-500mg tid x 10-14 days
 - sulfamethoxazole/trimethoprim DS (Bactrim/Septra DS) bid x 10-14 days
 - Erythromycin 250-500mg qid x 10-14 days
 - Doxycycline 100mg bid x 10-14 days
 - b. Secondary therapies
 - amoxicillin/clavulanate (Augmentin) 250-500mg tid x 10 days
500mg - 875mg bid x 10 days
 - penicillin VK 250-500mg po x 10 days (for documented *S. pneumoniae*)
 - second generation cephalosporins (cefaclor (Ceclor®) 250-500mg tid x 10 days
(cefuroxime axetil (Ceftin®) 250mg bid x 10 days)
 - c. Monitoring parameters
 - improvement in symptoms after 3-4 days therapy
 - consider changing antibiotics
 - “long term” therapy

III. Pharyngitis - (or pharyngotonsillitis) - inflammation of the posterior oral cavity tissue

- A. Etiology
 - rhinovirus and adenovirus and others
 - Group A β -hemolytic streptococci (GABHS), *Streptococcus pyogenes* (5-30% of all pharyngitis)
 - peak prevalence during the colder months
 - often seen in conjunction with other URI's

B. Symptomatology

- fever
- anterior cervical adenopathies
- tonsillar exudate
- sore throat
- erythema of the pharynx
- lymphatic hyperplasia

C. Diagnostics

- family history
- rapid GABHS screen for antigen detection (differentiate viral vs bacterial)
- exposure to others with GABHS

D. Treatment

- drug of choice for GABHS - penicillin 250mg qid x 10 days
- treatment success may be limited by compliance.
 - Benzathine penicillin IM 25,000-50,000 units/kg x 1 dose
 - Available as 600,000, 1.2 million unit pre-filled syringes
- Penicillin allergy - TRUE ALLERGY?
 - Erythromycin 250mg qid x 10 days