Chapter 77: Allergic Rhinitis

INTRODUCTION

- *Allergic rhinitis* involves inflammation of nasal mucous membranes in sensitized individuals when inhaled allergenic particles contact mucous membranes and elicit a response mediated by immunoglobulin E (IgE). There are two types: seasonal and persistent (formerly called “perennial”) allergic rhinitis.

PATHOPHYSIOLOGY

- Airborne allergens enter the nose during inhalation and are processed by lymphocytes, which produce antigen-specific IgE, sensitizing genetically predisposed hosts to those agents. On nasal reexposure, IgE bound to mast cells interacts with airborne allergens, triggering release of inflammatory mediators.
- An immediate reaction occurs within seconds to minutes, resulting in rapid release of preformed and newly generated mediators from the arachidonic acid cascade. Mediators of immediate hypersensitivity include histamine, leukotrienes, prostaglandin, tryptase, and kinins. These mediators cause vasodilation, increased vascular permeability, and production of nasal secretions. Histamine produces rhinorrhea, itching, sneezing, and nasal obstruction.
- A late-phase reaction may occur 4–8 hours after initial allergen exposure due to cytokine release from mast cells and thymus-derived helper lymphocytes. This inflammatory response causes persistent chronic symptoms, including nasal congestion.

CLINICAL PRESENTATION

- Seasonal (hay fever) allergic rhinitis occurs in response to specific allergens (eg, pollen from trees, grasses, and weeds) present at predictable times of the year (spring and/or fall) and typically causes more acute symptoms.
- Persistent allergic rhinitis occurs year-round in response to nonseasonal allergens (eg, dust mites, animal dander, molds) and typically results in less variable, chronic symptoms.
- Many patients have a combination of both types, with symptoms year-round and seasonal exacerbations.
- Symptoms include clear rhinorrhea, sneezing, nasal congestion, postnasal drip, allergic conjunctivitis, and pruritic eyes, ears, or nose.
- In children, physical examination may reveal dark circles under the eyes (allergic shiners), a transverse nasal crease caused by repeated rubbing of the nose, adenoidal breathing, edematous nasal turbinates coated with clear secretions, tearing, and periorbital swelling.
- Patients may complain of loss of smell or taste, with sinusitis or polyps the underlying cause in many cases. Postnasal drip with cough or hoarseness can be bothersome.
- Untreated rhinitis symptoms may lead to disturbed sleep, malaise, fatigue, and poor work or school performance.
- Allergic rhinitis is associated with other conditions, including asthma, chronic rhinosinusitis, otitis media, nasal polyposis, respiratory infections, and dental malocclusions.
- Complications include recurrent and chronic sinusitis and epistaxis.

DIAGNOSIS

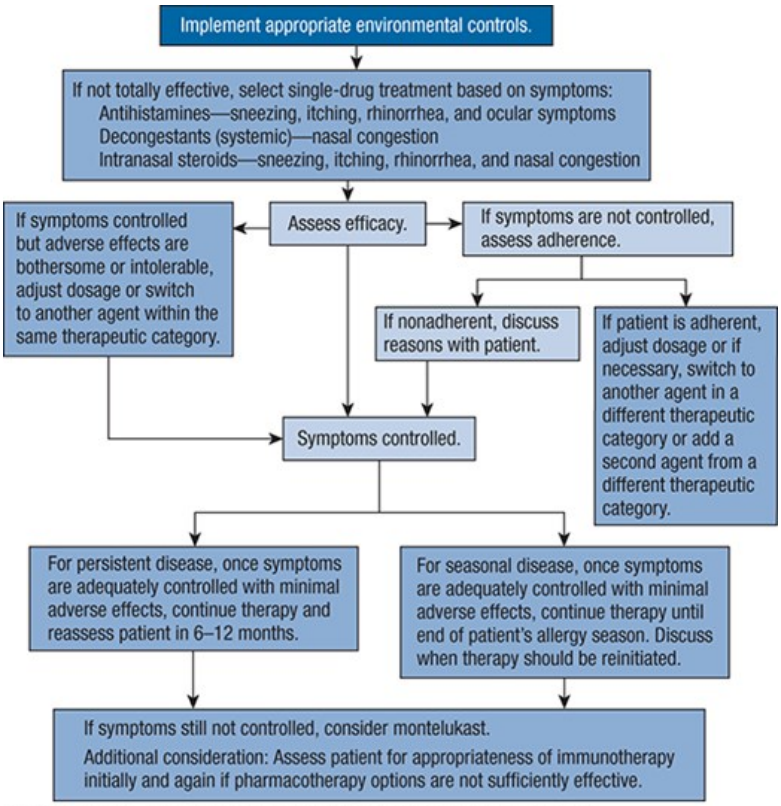
- Medical history includes careful description of symptoms, environmental factors and exposures, results of previous therapy, use of medications, previous nasal injury or surgery, and family history.
- Allergy testing can help determine whether rhinitis is caused by immune response to allergens. Immediate-type hypersensitivity skin tests are commonly used. Percutaneous testing is safer and more generally accepted than intradermal testing, which is usually reserved for patients requiring confirmation. The radioallergosorbent test (RAST) can detect IgE antibodies in the blood that are highly specific for a given antigen, but it may be slightly less sensitive than percutaneous tests.

TREATMENT

- Goals of Treatment: Minimize or prevent symptoms, prevent long-term complications, avoid or minimize medication side effects, provide economical therapy, and maintain normal lifestyle.
- **Figure 77-1** depicts a treatment algorithm for allergic rhinitis.

FIGURE 77-1

Treatment algorithm for allergic rhinitis.



Source: Terry L. Schwinghammer, Joseph T. DiPiro, Vicki L. Ellingrod, Cecily V. DiPiro: *Pharmacotherapy Handbook, 11e*

Nonpharmacologic Therapy

- Avoiding offending allergens is important but difficult to accomplish, especially for perennial allergens. Mold growth can be reduced by keeping household humidity below 50% and removing obvious growth with bleach or disinfectant.

- Patients sensitive to animals benefit most by removing pets from the home, if feasible. Reducing exposure to dust mites by washing bedding on a hot cycle, replacing carpets with hard flooring, and using vacuum cleaners with HEPA filters has not been shown to provide a clinical benefit. Only encasing bedding in impermeable covers has some clinical benefit in children but not adults.
- Steps to prevent poor air quality in homes include avoiding wall-to-wall carpeting, using moisture control to prevent mold accumulation, and controlling sources of pollution such as cigarette smoke.
- Patients with seasonal allergic rhinitis should keep windows closed and minimize time spent outdoors during pollen seasons. Filter masks can be worn while gardening or mowing the lawn.
- Nasal saline irrigations may improve nasal symptoms and reduce medicine consumption. Adhesive nasal strips can facilitate breathing and reduce nasal obstruction.

Pharmacologic Therapy

Antihistamines

- Histamine H_1-receptor antagonists bind to H_1 receptors without activating them, preventing histamine binding and action. They are effective in preventing the histamine response but not in reversing its effects after they have occurred. Antihistamines antagonize increased capillary permeability, wheal-and-flare formation, and itching.
- *Oral antihistamines* are divided into two categories: (1) nonselective (first-generation or sedating antihistamines) and (2) peripherally selective (second-generation or nonsedating antihistamines). However, individual agents should be judged on their specific sedating effects because variation exists among agents within these categories (**Table 77-1**).
- Antihistamines help control symptoms of sneezing, rhinorrhea, itching, and conjunctivitis. Symptom relief is caused in part by an anticholinergic drying effect that reduces nasal, salivary, and lacrimal gland hypersecretion.
- Antihistamines are only fully effective when taken 1–2 hours before anticipated exposure to the offending allergen. For seasonal allergic rhinitis, start treatment before the expected allergy season begins. Guidelines recommend that nonsedating agents be tried first, but tolerance to sedation from first-generation agents can develop after 4 days of treatment. If nonsedating agents are ineffective or too expensive, first-generation agents may be used. For persistent allergic rhinitis, use an intranasal corticosteroid as an alternative to or in combination with systemic antihistamines.
- Drowsiness is the most frequent antihistamine side effect, and it can interfere with driving ability or adequate functioning. Sedative effects can be beneficial in patients who have difficulty sleeping because of rhinitis symptoms.
- Adverse anticholinergic such as dry mouth, difficulty in voiding urine, constipation, and cardiovascular effects may occur (Table 77-1). Antihistamines should be used with caution in patients predisposed to urinary retention and in those with increased intraocular pressure, hyperthyroidism, and cardiovascular disease.
- Other side effects include loss of appetite, nausea, vomiting, and epigastric distress. Taking medication with meals or a full glass of water may prevent gastrointestinal (GI) side effects.
- **Table 77-2** lists recommended doses of oral agents.
- *Intranasal antihistamines*: **Azelastine** is a prescription-only intranasal antihistamine that relieves sneezing, rhinorrhea, and nasal pruritus of seasonal allergic rhinitis. The 0.1% product can be used in children for seasonal allergies, whereas the 0.15% product is labeled only for adults with either type of allergic rhinitis. However, guidelines favor use of intranasal antihistamines for seasonal but not persistent allergic rhinitis. Caution patients about the potential for drowsiness because systemic availability is ~40%. Patients may also experience drying effects, headache, and diminished effectiveness over time. **Olopatadine** is another intranasal antihistamine; it may cause less drowsiness because it is a selective H_1-receptor antagonist.
- *Ophthalmic antihistamines*: **Levocabastine**, **olopatadine**, and **bepotastine** are ophthalmic antihistamines that can be used for conjunctivitis

associated with allergic rhinitis. Systemic antihistamines are also usually effective for allergic conjunctivitis. Ophthalmic agents are a useful addition to nasal corticosteroids for ocular symptoms.

TABLE 77-1

Relative Adverse-Effect Profiles of Antihistamines

Medications	Relative Sedative Effects	Relative Anticholinergic Effects
Alkylamine class, nonselective		
Brompheniramine maleate	Low	Moderate
Chlorpheniramine maleate	Low	Moderate
Dexchlorpheniramine maleate	Low	Moderate
Ethanolamine class, nonselective		
Carbinoxamine maleate	High	High
Clemastine fumarate	Moderate	High
Diphenhydramine hydrochloride	High	High
Phenothiazine class, nonselective		
Promethazine hydrochloride	High	High
Piperidine class, nonselective		
Cyproheptadine hydrochloride	Low	Moderate
Phthalazinone class, peripherally selective		
Azelastine (nasal only)	Low to none	Low to none
Bepotastine (ophthalmic only)	Low to none	Low to none
Piperazine class, peripherally selective		
Cetirizine	Low to moderate	Low to none
Levocetirizine	Low to moderate	Low to none
Piperidine class, peripherally selective		
Desloratadine	Low to none	Low to none
Fexofenadine	Low to none	Low to none
Loratadine	Low to none	Low to none
Olopatadine (nasal only)	Low to none	Low to none

TABLE 77-2

Medication Dosing for Allergic Rhinitis

Drugs	Brand Names	Dosage for Adolescents[a] and Adults	Recommended Pediatric Doses
Antihistamines			
Oral			
Nonselective			
Chlorpheniramine maleate	Various	Plain: 4 mg every 6 hours Extended release: 12 mg every 12 hours	6–11 years: 2 mg every 4–6 hours 2–5 years: 1 mg every 4–6 hours
Clemastine fumarate	Tavist	1.34 mg (1 mg base) twice daily, up to 2.68 mg 3 times daily; max. 8.04 mg/day (6 mg base/day)	6–11 years: syrup 0.67 mg (0.5 mg base) twice daily; max. 4.02 mg/day (3 mg base/day)
Diphenhydramine HCl	Benadryl, others	25–50 mg every 4–6 hours (max. 300 mg/day)	6–11 years: 12.5–25 mg every 4–6 hours; max. 150 mg/day
Peripherally selective			
Loratadine	Alavert, Claritin	10 mg once daily	6–12 years: 10 mg once daily or 5 mg twice daily 2–5 years: 5 mg once daily
Fexofenadine	Allegra	60 mg every 12 hours or 180 mg once daily	2–11 years: 30 mg once daily
Cetirizine	Zyrtec	5–10 mg once daily	6–11 years: 5–10 mg once daily 6 mo. to 5 years: 2.5 mg once daily
Levocetirizine	Xyzal	5 mg once daily (in the evening)	6–11 years: 2.5 mg once daily (in the evening) 6 months–5 years: 1.25 mg once daily (in the evening)
Nasal			
Azelastine	Astelin, Astepro	1–2 sprays per nostril once or twice daily	2–11 years: 1 spray per nostril twice daily
Olopatadine	Patanase	Two sprays per nostril twice daily	6–11: 1 spray per nostril twice daily
Ophthalmic			
Bepotastine	Bepreve	1 drop into the affected eye(s) twice daily	2–11 years: 1 drop into the affected eye(s) twice daily
Levocabastine	Livostin	1 drop into the affected eye(s) 4 times daily	(Safety and efficacy not established)
Olopatadine	Patanol	1 drop into the affected eye(s) twice daily at intervals of 6–8 hours	3–11 years: 1 drop into the affected eye(s) twice daily at intervals of 6–8 hours
Decongestants			
Oral			

Pseudoephedrine	Various	60 mg every 4–6 hours Sustained release: 120 mg every 12 hours Controlled release: 240 mg once daily	6–11 years: 30 mg every 4–6 hours 2–5 years: 15 mg every 4–6 hours
Phenylephrine	Various	0–20 mg every 4 hours	6–11 years: 5 mg every 4 hours 2–5 years: 2.5 mg every 4 hours
Nasal			
Oxymetazoline	Various	2–3 sprays twice daily	6–11 years: 2–3 sprays twice daily
Phenylephrine	Various	2–3 sprays every 4 hours (0.25%–1%)	6–11 years: 2–3 sprays every 4 hours (0.25%) 2–5 years: 2–3 sprays every 4 hours (0.125%)
Nasal corticosteroids			
Beclomethasone	Beconase AQ Qnasl	1–2 sprays in each nostril twice daily 2 sprays in each nostril once daily	6–11 years: 1 spray in each nostril twice daily 4–11 years: 1 spray in each nostril once daily
Budesonide	Rhinocort Aqua	1 spray in each nostril once daily	6–11 years: 1 spray in each nostril once daily
Flunisolide	Various	Two sprays in each nostril twice daily	6–14 years: 2 sprays in each nostril twice daily
Fluticasone	Flonase	1–2 sprays in each nostril daily once daily	2–11 years: 1 spray in each nostril once daily
Mometasone	Veramyst, Nasonex, Nasacort	2 sprays in each nostril once daily	2–11 years: 1 spray in each nostril once daily
Triamcinolone	Nasacort AQ	2 sprays in each nostril once daily	2–11 years: 1 spray in each nostril once daily
Other nasal medications			
Cromolyn	Nasalcrom	1 spray in each nostril 3–4 times daily	2–11 years: 1 spray in each nostril 3–4 times daily
Ipratropium	Atrovent	2 sprays in each nostril 4 times daily	5–11 years: 2 sprays in each nostril 4 times daily
Leukotriene receptor antagonist			
Montelukast	Singulair	10 mg orally once daily	6–14 years: 5 mg chewable tablet once daily 2–5 years: 4 mg chewable tablet or oral granules once daily 6–23 months: 4 mg oral granules once daily

[a]Adolescent age is ≥12 years except for flunisolide and montelukast (≥15 years).

Decongestants

- Topical and systemic decongestants are sympathomimetic agents that act on adrenergic receptors in nasal mucosa to produce vasoconstriction,

shrink swollen mucosa, and improve ventilation. They should only be used when nasal congestion is present. Decongestants work well in combination with antihistamines when nasal congestion is present.

- Topical decongestants are applied directly to swollen nasal mucosa via drops or sprays (**Table 77-3**). They result in little or no systemic absorption.
- Treatment should not exceed 3–5 days to avoid rhinitis medicamentosa (rebound vasodilation with congestion). Patients with this condition use more spray more often with less response. Abrupt cessation is an effective treatment, but rebound congestion may last for several days or weeks. Nasal corticosteroids have been used successfully but take several days to work. Weaning off the topical decongestant can be accomplished by decreasing dosing frequency or concentration over several weeks. Combining the weaning process with nasal corticosteroids may be helpful.
- Other adverse effects of topical decongestants are burning, stinging, sneezing, and dryness of the nasal mucosa.
- These products should be used only when absolutely necessary (eg, at bedtime) and in doses that are as small and infrequent as possible. Duration of therapy should be limited to 3 days or less.
- **Pseudoephedrine** (Table 77-2) is an oral decongestant that has a slower onset of action than topical agents but may last longer and cause less local irritation. Rhinitis medicamentosa does not occur with oral decongestants. Doses up to 180 mg produce no measurable change in blood pressure or heart rate. However, higher doses (210–240 mg) may raise both blood pressure and heart rate. Systemic decongestants should be avoided in hypertensive patients unless absolutely necessary. Severe hypertensive reactions can occur when pseudoephedrine is given with monoamine oxidase inhibitors. Pseudoephedrine can cause mild CNS stimulation, even at therapeutic doses. Because of misuse as a component in the illegal manufacture of methamphetamine, pseudoephedrine is restricted to behind-the-counter sale with a limit on monthly purchases.
- **Phenylephrine** has replaced pseudoephedrine in many nonprescription antihistamine–decongestant combination products because of legal restrictions on pseudoephedrine sales.
- Combination oral products containing a decongestant and antihistamine are rational because of different mechanisms of action. However, antihistamines must be taken on a regular schedule, but decongestants should only be used when needed. Consumers should read product labels carefully to avoid therapeutic duplication and use combination products only for short courses.

TABLE 77-3

Duration of Action of Topical Decongestants

Medications	Durations of Action (hours)
Short acting	
Phenylephrine hydrochloride	Up to 4
Intermediate acting	
Naphazoline hydrochloride	2–6
Tetrahydrozoline hydrochloride	
Long acting	
Oxymetazoline hydrochloride	Up to 12
Xylometazoline hydrochloride	

Nasal Corticosteroids

- Intranasal corticosteroids reduce inflammation by reducing mediator release, suppressing neutrophil chemotaxis, reducing intracellular edema, causing mild vasoconstriction, and inhibiting mast cell–mediated, late-phase reactions.
- They relieve sneezing, rhinorrhea, itching, and nasal congestion (Table 77-2). Blocked nasal passages should be cleared with a decongestant or saline irrigation before administration to ensure adequate penetration of the spray. Advise patients to avoid sneezing or blowing their nose for at least 10 minutes after administration. Some patients improve within a few days, but peak response may require 2–3 weeks. The dosage may be reduced once a response is achieved.
- These agents are an excellent choice for persistent rhinitis and can also be excellent for seasonal rhinitis, especially if begun before exposure and the onset of symptoms. Recent guidelines suggest that nasal corticosteroids should be recommended as initial therapy for allergic rhinitis.
- Side effects are minimal and include sneezing, stinging, headache, epistaxis, and rare infections with *Candida albicans*.

Cromolyn Sodium

- **Cromolyn sodium**, a mast cell stabilizer, is available as a nonprescription nasal spray for symptomatic prevention and treatment of allergic rhinitis. It prevents antigen-triggered mast cell degranulation and release of mediators, including histamine. The most common side effect is local irritation (sneezing and nasal stinging).
- Nasal passages should be cleared before administration, and inhaling gently through the nose during administration enhances distribution to the entire nasal lining. Dosing must be repeated at 6-hour intervals to maintain the effect (Table 77-2).
- For seasonal rhinitis, treatment should be initiated just before the start of the offending allergen's season and continue throughout the season.
- In persistent rhinitis, improvement may not be seen for 2–4 weeks; antihistamines or decongestants may be needed during this initial phase of therapy.

Ipratropium Bromide

- **Ipratropium bromide** nasal spray is an anticholinergic agent that exhibits antisecretory properties when applied locally. It provides symptomatic relief of rhinorrhea associated with allergic and other forms of chronic rhinitis.
- It is not included in current treatment guidelines for allergic rhinitis and should be reserved for patients who fail or cannot tolerate other therapies. The optimal dose should be determined based on the specific patient's symptoms and response.
- Adverse effects are mild and include headache, epistaxis, and nasal dryness.

Montelukast

- **Montelukast** is a leukotriene receptor antagonist approved for treatment of persistent allergic rhinitis in children as young as 6 months and for seasonal allergic rhinitis in children as young as 2 years (Table 77-2).
- Montelukast is a third-line choice after antihistamines and nasal corticosteroids. Monotherapy is no more effective than peripherally selective antihistamines and is less effective than intranasal corticosteroids; however, the combination of montelukast and an antihistamine is more effective than an antihistamine alone. Montelukast monotherapy has been recommended for children with mild persistent asthma and coexisting allergic rhinitis.

Immunotherapy

- Immunotherapy is the process of administering doses of antigens responsible for eliciting allergic symptoms into a patient with the intent of inducing tolerance to the allergen when natural exposure occurs. Until recently, immunotherapy was only available for subcutaneous injection; sublingual dosage forms are now available for a limited number of allergens.

- Beneficial effects of immunotherapy may result from induction of IgG-blocking antibodies, reduction in specific IgE (long-term), reduced recruitment of effector cells, altered T-cell cytokine balance, T-cell anergy, and alteration of regulatory T cell activity.
- Good candidates for immunotherapy include patients with a strong history of severe symptoms unsuccessfully controlled by avoidance and pharmacotherapy and patients unable to tolerate adverse effects of drug therapy. Poor candidates include patients with medical conditions that compromise the ability to tolerate an anaphylactic-type reaction, patients with impaired immune systems, and patients with a history of nonadherence.
- For subcutaneous immunotherapy, very dilute solutions are given initially once or twice weekly. The concentration is increased until the maximum tolerated dose or highest planned dose is achieved. This maintenance dose is continued in slowly increasing intervals over several years, depending on clinical response. Better results are obtained with year-round rather than seasonal injections.
- Sublingual immunotherapy is available for ragweed, certain grasses, and house dust mite allergen. Ragweed and grass allergens are started 12 weeks before the allergen season and continued throughout the season. Because house dust mites cause persistent allergic rhinitis, this treatment is given year-round. The first dose is administered in the physician's office to allow observation of the patient for 30 minutes for hypersensitivity reactions. The patient places the tablet under the tongue where it dissolves; patients should not swallow for at least 1 minute. After the first dose is administered without incident, patients can take sublingual immunotherapy at home, but an autoinjectable epinephrine must be prescribed and available for immediate use.
- Adverse reactions with subcutaneous immunotherapy include mild induration and swelling at the injection site. More severe reactions (generalized urticaria, bronchospasm, laryngospasm, vascular collapse, and death from anaphylaxis) occur rarely. Severe reactions are treated with epinephrine, antihistamines, and systemic corticosteroids. The most common reactions with sublingual immunotherapy are pruritus of the mouth, ears, and tongue; throat irritation; and mouth edema. Sublingual immunotherapy is only approved for persons age 18 year and older.

EVALUATION OF THERAPEUTIC OUTCOMES

- Monitor patients regularly for reduction in severity of identified target symptoms and presence of side effects.
- Ask patients about their satisfaction with the management of their allergic rhinitis. Management should result in minimal disruption to their normal lifestyle.
- The Medical Outcomes Study 36-Item Short Form Health Survey and the Rhinoconjunctivitis Quality of Life Questionnaire measure symptom improvement and parameters such as sleep quality, nonallergic symptoms (eg, fatigue and poor concentration), emotions, and participation in a variety of activities.

See Chapter e13, Allergic Rhinitis, authored by J. Russell May, for a more detailed discussion of this topic.