Pharmacotherapy of allergic rhinitis

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INTRODUCTION

Allergic rhinitis is characterized by sneezing, rhinorrhea, and nasal obstruction as well as pruritus of the nose and palate. It is also frequently associated with postnasal drip, cough, irritability, and fatigue. Some patients have concomitant allergic conjunctivitis and/or asthma. Symptoms can be present year round, seasonally, or episodically upon exposure to specific allergens.

The pharmacologic management of allergic rhinitis is presented in this topic review. The clinical manifestations, diagnosis, differential diagnosis, and pathogenesis of allergic rhinitis are discussed separately. (See "Allergic rhinitis: Clinical manifestations, epidemiology, and diagnosis" and "Pathogenesis of allergic rhinitis (rhinosinusitis)".)

OVERVIEW OF TREATMENT

The management of allergic rhinitis involves the following components:

- **Pharmacotherapy**, which is the focus of this review. Most patients with allergic rhinitis require pharmacotherapy for satisfactory symptom control. As more medications become available without a prescription, patients can extensively self-treat, although the side effects of some over-the-counter allergy medications, particularly the excessive sedation and anticholinergic effects caused by older antihistamines, can be significant. In general,

patients who self-treat tend to underutilize glucocorticoid nasal sprays and overutilize older, sedating antihistamines. The challenge for clinicians is to educate patients about the relative efficacy of different therapies and assure that patients with significant symptoms are adequately treated with medications that do not cause undue side effects.

The management of allergic rhinitis in a specific patient is influenced by the frequency and severity of symptoms, the age of the patient, and the presence of concurrent conditions [1-9]. In this review, an approach to specific patient groups is presented initially, followed by a detailed discussion of available medications. (See 'Approach to specific patient groups' below and 'Commonly used therapies' below.)

- **Allergen avoidance**, which is reviewed separately. (See "Allergen avoidance in the treatment of asthma and allergic rhinitis".)

- **Allergen immunotherapy** (when appropriate), which is reviewed separately. Immunotherapy can be given as subcutaneous injections or as sublingual tablets (available for a limited number of allergens) or drops. Indications for immunotherapy include severe symptoms that are only partially controlled with medications, a preference on the part of the patient to minimize the use or cost of medications, and, particularly in an older child or young adult, prevention of progression to asthma [1]. (See "Subcutaneous immunotherapy (SCIT) for allergic rhinoconjunctivitis and asthma: Indications and efficacy" and "Sublingual immunotherapy for allergic rhinitis and conjunctivitis: SLIT-tablets".)

Consensus guidelines have been published for the management of allergic rhinitis [1-12]. The recommendations in this topic review are consistent with these guidelines. (See 'Society guideline links' below.)

APPROACH TO SPECIFIC PATIENT GROUPS

Young children (<2 years of age) — The development of allergic rhinitis requires repeated exposure to inhaled allergens and is therefore less prevalent in children under two years of age. If a child under two years appears to have persistent nasal symptoms, other disorders should be considered, such as "daycare syndrome" (ie, repeated viral infections of the upper respiratory tract), adenoidal hypertrophy, or chronic rhinosinusitis. (See "Chronic rhinosinusitis: Clinical manifestations, pathophysiology, and diagnosis" and "The pediatric physical examination: HEENT", section on 'Adenoidal hypertrophy'.)

If a child under two years of age is determined to have allergic rhinitis after an evaluation for other causes, treatment options include the following:

- **Minimally sedating antihistamines** (cetirizine, loratadine, and fexofenadine) are available in liquid formulations. Cetirizine is approved for children ≥6 months of age. (See 'Minimally sedating agents' below.)

  Sedating antihistamines (eg, diphenhydramine, chlorpheniramine, others) should be **avoided** in young children because these agents can cause paradoxical agitation and may be dangerous in infants [13]. (See 'Sedating antihistamines' below.)

- **Cromolyn (sodium cromoglycate) nasal spray** is available without a prescription and has essentially no adverse effects because it is not absorbed systemically. It is a good choice for parents who are very concerned about the potential side effects of other medications and are willing to administer something regularly. The authors use cromolyn extensively in infants and small children and find it very useful when applied consistently. However, cromolyn is less effective than glucocorticoid nasal sprays and more difficult to administer than oral antihistamines. (See 'Cromolyn sodium' below.)

Moderate-to-severe symptoms — Changing to a glucocorticoid nasal spray is the next step for children with severe symptoms not responsive to the above measures (table 1). Mometasone furoate, fluticasone furoate, and triamcinolone acetonide are approved by the US Food and Drug Administration (FDA) for use in children ≥2 years [14,15]. All choices are safe in young children with little differences between them, except some have more scent and volume than others (eg, fluticasone) and therefore may be less accepted by young children. The dose for each of these agents in young children is 1 spray per nostril once daily. If necessary, 2 sprays per nostril can be tried for a limited period (we limit to two weeks and reassess symptoms) in view of the age-limited dose approval and the concern for potential systemic side effects (eg, adrenal suppression) in children at the higher dose.

Older children and adults — For children ≥2 years of age, the approach to pharmacotherapy is essentially the same as that in adults and depends upon the severity and persistence of symptoms.

Mild or episodic symptoms — Patients with mild or episodic symptoms that are related to predictable allergen exposures (visiting a relative's house with a pet) can be managed with one of the following options:

- **A minimally sedating oral antihistamine** – This can be administered regularly or as needed (ideally two to five hours before an exposure for cetirizine and fexofenadine, while

loratadine peaks eight hours after administration). Cetirizine (approved for children ≥6 months), loratadine, and fexofenadine (both approved for children ≥2 years) are similarly efficacious and are available in syrups. (See 'Minimally sedating agents' below.)

- **An antihistamine nasal spray** (eg, azelastine or olopatadine) – The FDA has approved the use of intranasal azelastine in children >6 years of age and the use of intranasal olopatadine in children >12 years of age (its safety and efficacy have not been evaluated in younger children). (See 'Antihistamine nasal sprays' below.)

- **A glucocorticoid nasal spray** (more effective than antihistamines) – Administered regularly or as needed (table 1). For predictable exposures, we suggest initiating therapy two days before, continuing through, and for two days after the end of exposure [16,17]. Mometasone furoate, fluticasone furoate, and triamcinolone acetonide are approved by the US FDA for use in children ≥2 years of age [14,15].

- **Cromolyn nasal spray** – Administered regularly or as needed (ideally 30 minutes before an exposure). Taken in this manner, cromolyn is helpful for brief exposures (minutes to hours). For prolonged exposures, administration should ideally begin four to seven days in advance. Some parents and clinicians prefer to try cromolyn first in children because of its excellent safety profile. (See 'Cromolyn sodium' below.)

It should be explained to patients that each of these therapies is more effective when taken regularly, although as-needed use may be sufficient for very mild symptoms.

Persistent or moderate-to-severe symptoms

- **Glucocorticoid nasal sprays** are the most effective pharmacologic therapy for allergic rhinitis and are recommended by guidelines as the best single therapy for patients with persistent or moderate-to-severe symptoms, including seasonal symptoms [10,12]. All of the available preparations are similarly effective, although the newer agents (sometimes called second generation) are more convenient and probably safer for long-term use than the older agents because of lower bioavailability (table 1). Glucocorticoid nasal sprays with low bioavailability and once-daily dosing (all except flunisolide, which is not commonly used) may have a theoretical advantage in children, although this has not been proven. Mometasone and fluticasone furoate are approved by the US FDA for use in children ≥2 years of age [14]. Fluticasone propionate is approved for children ≥4 years of age. (See 'Glucocorticoid nasal sprays' below.)

For patients with moderate-to-severe symptoms and/or in those who fail to respond adequately to initial therapy with glucocorticoid nasal sprays, a second agent can be added. Options

include an antihistamine nasal spray, oral antihistamines, and antihistamine/decongestant combination products. There are few clinical trials directly comparing different combinations of these therapies, and the choice of additional agents should be based upon the patient's residual symptoms, preferences, and coexistent conditions:

- **Addition of an antihistamine spray –** Antihistamine nasal sprays include azelastine and olopatadine (see 'Antihistamine nasal sprays' below). Sprays containing both a glucocorticoid and an antihistamine (eg, azelastine hydrochloride/fluticasone propionate) are convenient and may provide additional benefit over either therapy alone, especially for breakthrough symptoms [18,19]. (See 'Combination corticosteroid/antihistamine sprays' below.)

- **Addition of a minimally sedating oral antihistamine** – The combination of glucocorticoid nasal sprays and oral antihistamines has not shown clear advantage over glucocorticoid sprays alone in most studies [1,20]. (See 'Dosing of commonly used agents' below.)

- **Addition of a minimally sedating oral antihistamine/decongestant combination** – These provide better symptom relief than antihistamines alone, although the adverse effects of the decongestant component limit their use in some patients (table 2). Adverse effects of oral decongestants are discussed below. (See 'Oral antihistamine/decongestant combinations' below.)

- **Injection immunotherapy** – (See "Subcutaneous immunotherapy (SCIT) for allergic rhinoconjunctivitis and asthma: Indications and efficacy".)

With comorbid conditions

Allergic conjunctivitis — In patients with both allergic rhinitis and allergic conjunctivitis, we prefer a combination of a glucocorticoid nasal spray and ophthalmic antihistamine drops, such as epinastine, azelastine, emedastine, or olopatadine, rather than glucocorticoid sprays plus oral antihistamines (table 3). A small number of randomized trials have shown the addition of antihistamine eye drops to be more effective and cause less ocular drying than the addition of oral antihistamines [21,22]. However, oral antihistamines can be more practical in children, who often object to administration of eye drops.

Some glucocorticoid nasal sprays (eg, mometasone furoate and fluticasone furoate) have been shown to have a small but statistically significant effect on allergic eye symptoms [23-26]. However, many patients require an additional agent for adequate relief.

Cromolyn sodium is available in ophthalmic preparations and may also be useful as prophylactic therapy before predictable allergen exposures (ie, visiting a home with cats).

Further information about the management of allergic conjunctivitis is found separately. (See "Allergic conjunctivitis: Management", section on 'Antihistamines with mast cell-stabilizing properties'.)

Moderate-to-severe asthma — Up to 40 percent of patients with allergic rhinitis are believed to have concomitant asthma. Although there are no biologic therapies approved specifically for allergic rhinitis, these agents are available for moderate-to-severe asthma that is not controlled with high doses of inhaled glucocorticoids and also improve the symptoms of allergic rhinitis [27].

- Omalizumab, an anti-IgE monoclonal antibody that is approved for asthma and chronic urticaria, was shown in a systematic review and meta-analysis of 11 studies of 2870 patients to reduce daily nasal symptoms, rescue medication use, and improve quality of life in patients with uncontrolled allergic rhinitis [28].

- Dupilumab, an anti-interleukin (IL) 4 receptor alpha monoclonal antibody that is approved for asthma and chronic rhinosinusitis with nasal polyposis, also improves symptoms of allergic rhinitis. A post-hoc analysis of dupilumab trial data involving patients with perennial allergic rhinitis and concomitant uncontrolled persistent asthma demonstrated significant improvement in rhinitis-associated symptoms of congestion, rhinorrhea, sneezing, and postnasal drainage [29].

Use of biologics for asthma is reviewed separately. (See "Treatment of severe asthma in adolescents and adults", section on 'Selecting among biologic agents'.)

Pregnancy — The treatment of allergic rhinitis in pregnant people is summarized in the algorithm and reviewed in detail separately (algorithm 1). (See "Recognition and management of allergic disease during pregnancy", section on 'Allergic rhinitis/conjunctivitis'.)

Breastfeeding — LactMed is an online database of information on medications and lactation hosted by the US National Library of Medicine [30]. The safety of various medications during lactation is summarized in the table (table 4). General guidelines have been proposed [31]:

- All patients should practice allergen avoidance. (See "Allergen avoidance in the treatment of asthma and allergic rhinitis".)

- Nasal saline sprays or irrigation can always be tried for any nonspecific relief it can provide. (See 'Nasal saline' below.)

- Intermittent congestion (symptoms less than four days per week) may be treated judiciously with a topical decongestant spray. (See 'Therapies requiring caution' below.)

- Mild persistent symptoms (symptoms more than four days/week and more than four weeks/year) may be treated with intranasal budesonide or cromolyn and supplemented by cetirizine or loratadine.

- Moderate-to-severe persistent symptoms may be treated with maintenance intranasal budesonide and/or immunotherapy injections and supplemented as needed with cetirizine or loratadine.

Older adults — Glucocorticoid nasal sprays are the first-line agents for older adults with allergic rhinitis (table 1). Minimally sedating antihistamines can be used safely in some older adult patients, although a few may experience adverse effects, and slowed metabolism may warrant lower starting doses [32]. Antihistamine nasal sprays are also a good option. We avoid first-generation sedating antihistamines in older adults [33]. (See 'Adverse effects and safety' below.)

COMMONLY USED THERAPIES

Nasal saline — Nasal saline sprays or irrigation with larger volumes of saline can wash allergens from the nasal passages. Saline can be used alone for mild symptoms or just before other topical medications, so that the mucosa is freshly cleansed when the medications are applied. Nasal irrigation with saline can be performed as needed only, daily at baseline, or twice daily for increased symptoms. Many brands of saline nasal sprays are available over the counter. Large-volume irrigations (>200 mL per side) should only be suggested to patients old enough to perform the irrigation themselves.

For large-volume irrigation, a variety of over-the-counter devices, including squeeze bottles, neti pots, and bulb syringes are effective, provided the system delivers an adequate volume of solution into the nose.

Nasal irrigation carries little risk if properly performed. Instructions for patients are provided (table 5). Patients can make their own irrigation solutions or buy commercially prepared solutions or kits. The saline solution may be warmed or used at room temperature. Patients should use distilled, sterilized, or previously boiled water because a small number of cases of primary amebic meningoencephalitis (PAM) have been contracted from using tap water that was contaminated with the amoeba *Naegleria fowleri* to perform sinus irrigation [34,35]. Although rare, PAM is usually fatal. *N. fowleri* is found worldwide and is usually contracted from

swimming in freshwater lakes and rivers, geothermal heated bodies of water, or inadequately chlorinated pools [36]. Irrigation devices can also become contaminated with the bacteria present in the patient's nasal cavities, although it is not clear that this causes any clinically significant problems. Still, irrigation devices should be cleaned as directed and replaced regularly [37].

Saline irrigation is associated with improvement in a variety of rhinitis conditions. Direct evidence for benefit in allergic rhinitis specifically includes the following:

- One randomized study of the impact of nasal irrigation in children with acute sinusitis found that, among those with concomitant allergic rhinitis, nasal irrigation significantly improved rhinorrhea, nasal congestion, throat itching, sleep quality symptoms, and nasal air flow [38]. A second study in children found that the effects of nasal irrigation were additive with those of intranasal glucocorticoids [39]. Nasal irrigation is particularly helpful when there are crusted nasal secretions due to chronic, thick drainage.

- Another randomized study of pregnant people found nasal saline irrigation to be beneficial for treatment of allergic rhinitis [40].

Overview of medications — The most effective single therapy for patients with persistent and significant nasal symptoms is a glucocorticoid nasal spray. Other therapies include oral antihistamines, antihistamine nasal sprays, mast cell stabilizers (the cromoglycates), leukotriene modifiers, and ipratropium. The features and efficacy of the various agents are reviewed in this section.

In contrast, nasal decongestant sprays (eg, phenylephrine, oxymetazoline, others) and systemic glucocorticoids should **not** be used for routine treatment of allergic rhinitis. (See 'Therapies requiring caution' below.)

Glucocorticoid nasal sprays — Glucocorticoid nasal sprays are the most effective single maintenance therapy for allergic rhinitis and cause few side effects at the recommended doses [10,12]. These agents are particularly effective in the treatment of nasal congestion, which often does not respond to oral antihistamines. Specific agents include beclomethasone, flunisolide, budesonide, fluticasone propionate, mometasone furoate, fluticasone furoate, and ciclesonide, and doses are shown in the table (table 1). A limited number of comparative studies among different glucocorticoid nasal sprays have not demonstrated significant differences in efficacy nor is there any evidence that doses greater than the recommended maximum for each preparation provide additional benefit [41,42]. Several glucocorticoid nasal sprays are available without a prescription.

Efficacy and onset of action — Glucocorticoid nasal sprays are more effective than oral antihistamines for relief of nasal congestion and blockage, nasal discharge, sneezing, nasal itch, postnasal drip, and total nasal symptoms, as demonstrated in randomized trials and a meta-analysis [1,16,43,44].

Glucocorticoid nasal sprays have also been shown to be more effective than antihistamine nasal sprays in most studies, as reviewed below. (See 'Antihistamine nasal sprays' below.)

Most glucocorticoid nasal sprays have an onset of action of a few hours [45-47]. However, maximal effect may require several days or weeks in patients with longstanding untreated symptoms.

Optimal use — Our approach is to start therapy with the maximal dose for age. Once symptoms are adequately controlled, the dose can be "stepped down" at one-week intervals to the lowest effective dose. Patients with severe symptoms will require daily use on a chronic basis. Some patients can reduce the frequency of use gradually and maintain symptom control with every-other-day or as-needed use. Newer preparations act within 3 to 12 hours, and as-needed use may be sufficient, particularly in patients with mild or episodic symptoms [16]. (See 'Mild or episodic symptoms' above.)

Clinicians should become comfortable with several preparations since each has its advantages and disadvantages relating to added fragrances, taste, and/or irritation.

To optimize the effects of this therapy and compliance with treatment, we suggest the following (figure 1):

- Preparations with **once-daily dosing** are convenient and can help optimize compliance. All formulations have a once-daily recommended dosing, except for one, flunisolide (which is twice daily).

- **Proper positioning of the head** can prevent the spray from draining down the throat. With the aqueous (nonaerosol) glucocorticoid nasal sprays, the patients should be instructed to keep their head pointed slightly downward during spraying and avoid tilting the head back. In addition, they should avoid pointing the spray at the septum, which can become irritated. A patient education topic on rhinitis, which reviews techniques for use of nasal sprays, is provided separately. (See "Patient education: Allergic rhinitis (Beyond the Basics)".)

- If mucous crusting is present, patients can rinse the nose with a saline **nasal spray or irrigation before the nasal glucocorticoid** is administered. Treatment failures can occur

if mucus or other debris prevent the medication from coating the nasal mucosa. (See 'Nasal saline' above.)

- For patients who are so obstructed that the spray will not penetrate significantly into the nostril, we suggest use of a decongestant spray 10 minutes before the nasal glucocorticoid, but this should only be done for five days to avoid the complications of decongestant sprays. After that, the glucocorticoid spray should be continued alone. If the nasal decongestant spray is not effective in relieving the obstruction, a very short course of oral glucocorticoids may be used. (See 'Combined with decongestant sprays' below and 'Refractory symptoms' below.)

"Dry" aerosol formulations — In the United States, two products are available that use a "dry" aerosol delivery system, beclomethasone dipropionate hydrofluoroalkane (HFA; Qnasl [brand name]) and ciclesonide HFA (Zetonna [brand name]). These may be more agreeable to patients who dislike the wet run-off or taste side effects that are experienced with some of the aqueous sprays (table 1).

With the aerosol products, patients should be instructed to tilt the head back slightly, dispense the spray, hold the breath for a few seconds, and then exhale through the mouth. The product insert also advises to avoid blowing the nose for 15 minutes after use. The nosepiece should be wiped with a clean, dry tissue weekly, although not cleaned with water.

Safety and adverse effects — Concerns with long-term use of many glucocorticoid preparations include adrenal suppression, slowed growth in children, decrease in bone mineral density, glaucoma, and cataract formation. With nasal sprays, the risk of these long-term complications appears to be small because of the relatively low doses involved, as discussed below. A practice guideline on rhinitis concluded that studies in both children and adults have failed to demonstrate that these adverse effects are consistent or clinically relevant to the use of glucocorticoid nasal sprays [1]. However, epistaxis and nasal septal perforation are potential adverse effects that are unique to nasal sprays. Because adverse effects are possible, glucocorticoid nasal sprays of any type should be tapered to the lowest effective dose in all patients once symptoms are controlled. (See 'Optimal use' above.)

Glucocorticoid nasal sprays may be divided into first- and second-generation preparations. **Second-generation agents are preferred** because they are equally efficacious but theoretically carry a lower risk of systemic effects because of markedly lower total bioavailability (oral and nasal) compared with first-generation agents [48-51]:

- **First generation** – Beclomethasone, flunisolide, triamcinolone, and budesonide (10 to 50 percent bioavailability)

- **Second generation** – Fluticasone propionate (<2 percent), mometasone furoate (<0.1 percent), ciclesonide (<0.1 percent), and fluticasone furoate (<1 percent)

Potential systemic effects with long-term use — The potential for systemic absorption of glucocorticoid nasal sprays, with effects on the hypothalamic-pituitary axis (HPA) and growth in children, has been evaluated in many studies. Most have shown no or limited HPA suppression at recommended doses, especially with second-generation agents [52-58]. However, studies have suggested a small effect on growth with both first-generation and second-generation agents [59-62]. As an example, reduction in growth velocity of -0.27 cm/year (95% CI -0.48 to -0.06 cm/year) was demonstrated in one large study of 474 prepubescent children, ages 5 to 8.5 years at screening, randomized to fluticasone furoate or placebo for 52 weeks for the treatment of perennial allergic rhinitis [62]. However, the dose of active agent was 110 mcg daily, which is the maximum recommended dose for this age group, and the protocol used in this study did not allow for dose reduction once symptoms were controlled, which is the desired approach to therapy. There was no detectable change in 24-hour urinary cortisol excretion to suggest adrenal suppression. Agents that are dosed once daily are preferred in growing children, since these are believed to (although not documented to) be less likely to impact the HPA and growth [48]. (See 'Optimal use' above.)

Drug interactions between intranasal fluticasone and strong inhibitors of CYP3A4 enzymes (eg, ritonavir, itraconazole, nefazodone) can effectively raise the dose of glucocorticoid and result in clinically significant adrenal suppression [63]. Although it is unclear how frequently this adverse outcome occurs, we suggest that patients receiving treatment with ritonavir, azole antifungals, or other strong inhibitors of CYP3A4 be treated with a glucocorticoid nasal spray **other** than fluticasone at the lowest effective dose or that the treating clinician at least be vigilant for signs and symptoms of Cushing syndrome. Budesonide, beclomethasone, triamcinolone, and flunisolide appear to be safer options.

Growth in children should be monitored when any glucocorticoid-containing medication is prescribed, especially if additional glucocorticoid-based medications are given, such as inhaled agents for asthma or topical corticosteroids for atopic dermatitis [64]. Longer-term studies of the effects on growth caused by inhaled glucocorticoids administered for asthma treatment (which deliver higher doses per actuation) are reassuring, although caution is still warranted. (See "Major side effects of inhaled glucocorticoids", section on 'Growth deceleration'.)

A small number of studies have examined the effects of glucocorticoid nasal sprays on other adverse effects, such as bone mineral density, intraocular pressure, or cataract formation [65-67]. A meta-analysis of 10 randomized controlled trials comprised of 2226 adult and adolescent patients with allergic rhinitis revealed no significant risk of elevated intraocular pressure or

development of posterior subcapsular cataracts after treatment for one year with glucocorticoid nasal sprays [68]. Some studies have demonstrated detrimental effects, although it is unclear whether these are large enough to result in clinically important outcomes over time.

Local irritation — Local irritation of the nasal mucosa including drying and burning and discomfort from the run-off into the throat of the liquid medication is reported by 2 to 10 percent of patients using sprays [69]. Formulations containing alcohol or propylene glycol are more irritating than aqueous preparations (table 1). Sometimes patients can minimize these complications by using proper administration technique and by gradually reducing the dose once symptoms are controlled to the lowest effective dose for that individual. It is helpful to demonstrate proper use of all inhaled medications at the time of initial prescription and again at follow-up visits. Aqueous pump and dry aerosol sprays have different instructions for use (see 'Optimal use' above). A patient education topic on rhinitis, which reviews techniques for optimal use of nasal sprays, is provided separately. (See "Patient education: Allergic rhinitis (Beyond the Basics)".)

Epistaxis — There are two types of nosebleed problems with the use of glucocorticoid nasal sprays, which are scant blood found in the nasal mucus (common) and frank epistaxis (uncommon):

- Mucosal irritation may lead to traces of blood in the mucus, which is often remedied by simply stopping treatment on the side of the nose where bloody mucus has been noted for a few days and then restarting therapy. Proper administration technique should be reviewed.

- Significant epistaxis is reported with both glucocorticoid nasal sprays and placebo in clinical trials and may therefore partly result from mechanical trauma of repeated spraying, although, when placebo rates were subtracted, nosebleed was still noted in 2 to 12 percent of patients using different glucocorticoid preparations. This can be particularly bothersome for older patients, who may do better with azelastine spray if the problem persists. Frank epistaxis is often hard to prevent, and, once it occurs, it may require future avoidance of glucocorticoid nasal sprays.

- Recurrent or chronic epistaxis, even mild in degree, requires evaluation for chronic nasal inflammation, which can occur in a number of conditions. These include vasomotor rhinitis, chronic nasal staphylococcal infection, and unusual disorders, such as Behçet syndrome, granulomatosis with polyangiitis (GPA), or chronic invasive fungal rhinosinusitis. In our experience, episodic epistaxis also occurs in any dry nose syndrome,

such as rhinitis associated with continuous positive airway pressure (CPAP) therapy, sicca syndrome associated with Sjögren's disease, or atrophic rhinosinusitis. The drying effects of cigarette smoking, caffeinated beverages, and medications with anticholinergic properties can also predispose to bleeding. Recurrent or chronic epistaxis should prompt rhinoscopy to determine the origin of the bleeding, even in patients thought to have epistaxis induced by installation of various medications, since malignancy of the nasal mucosa is also in the differential diagnosis.

Rare septal perforation — Nasal sprays should always be directed away from the septum. There are rare reports of nasal septal perforation with glucocorticoid nasal sprays [70,71]. However, long-term studies of large numbers of patients have not found evidence of damage to the nasal mucosa, despite years of use in the majority of patients [1,71].

Mechanisms of action — Glucocorticoids inhibit allergic inflammation in the nose at many levels [72,73]. These agents downregulate inflammatory responses by binding to intracellular glucocorticoid receptors in the cytoplasm of inflammatory cells. The receptors undergo conformational changes upon activation, entering the cell nucleus where they bind with glucocorticoid response elements located on anti-inflammatory genes. These activated genes transcribe messenger ribonucleic acid (RNA) for antiinflammatory proteins. At the same time, activated glucocorticoid receptors suppress the transcription of most cytokine and chemokine genes, whose products promote inflammation. (See "Glucocorticoid effects on the immune system".)

Combined with decongestant sprays — The use of decongestant sprays alone for more than a few days should be avoided due to the risk of rhinitis medicamentosa. However, there may be a role for once-daily treatment with the combination of a glucocorticoid nasal spray plus a decongestant spray in adult patients who do not respond optimally to glucocorticoid alone. Combined therapy was evaluated in a randomized trial of 60 adult subjects with perennial allergic rhinitis [74]. Participants were randomly assigned to receive once-nightly treatment with fluticasone furoate, oxymetazoline hydrochloride, the combination of both, or placebo for four weeks of treatment. Both symptom scores and objective nasal volume (determined with acoustic rhinometry) improved with combination therapy relative to placebo or oxymetazoline alone. Nasal symptoms were less in the combination group compared with the fluticasone monotherapy group, although nasal volumes were not statistically different. There was no evidence of rhinitis medicamentosa in the combination group. Further study is needed, although we have noted preliminary success in several adult patients in our clinical practice. We attempt to discontinue the vasoconstrictor spray once symptoms are controlled. (See 'Therapies requiring caution' below.)

Oral antihistamines

Minimally sedating agents — Antihistamines typically reduce itching, sneezing, and rhinorrhea but are less effective for nasal congestion compared with glucocorticoid sprays. H1 antihistamines are divided into first- and second-generation agents. The second-generation antihistamines are minimally sedating and are preferred over first-generation agents because they have similar efficacy and fewer central nervous system effects. Second-generation antihistamines are a popular option for many patients, especially those with mild or intermittent symptoms. Patients who experience adverse effects with the second-generation antihistamines (which is rare) or who prefer a local therapy are also better treated with glucocorticoid nasal sprays. We prefer glucocorticoid nasal sprays for patients with chronic or more significant symptoms because of their superior efficacy.

Second-generation agents include cetirizine and loratadine. These lipophobic agents were developed primarily to avoid the unwanted anticholinergic and central nervous system effects of the first-generation drugs [75-77]. Metabolites of second-generation agents, such as fexofenadine (metabolite of terfenadine), desloratadine (metabolite of loratadine), and levocetirizine (purified isomer of cetirizine) were designed to have fewer central nervous system effects than their parent compounds, although confirmatory evidence is lacking [75,78-80].

Onset of action of the oral second-generation agents is within one hour for most, and peak serum levels are attained in two to three hours [81,82]. They are dosed once or twice daily and appear to be similarly efficacious to each other [1,83-86]. There is no convincing evidence that doses of second-generation antihistamines greater than those maximally recommended provide additional benefit for allergic rhinitis, and higher-than-recommended doses are associated with sedation in some cases [87]. However, many clinicians find that using minimally sedating antihistamines twice daily when symptoms are severe is helpful with little sedation.

H1 antihistamines are not actually receptor antagonists but rather inverse agonists. They bind the H1 receptor and downregulate its constitutive activity, shifting the equilibrium from the active form of the H1 receptor to the inactive form [88]. Some antihistamines also reduce eosinophil survival [89]. Second- and third-generation antihistamines also have a variety of antiinflammatory properties [90-92].

Dosing of commonly used agents

- **Cetirizine** – The standard dose of cetirizine 10 mg once daily is appropriate for adults and children ages ≥6 years.

The usual dose for children ages two to five years is 5 mg once daily. Smaller children ages six months to two years may be given 2.5 mg once daily. The maintenance dose for patients with significant kidney and/or hepatic insufficiency should be reduced by one-half.

- **Levocetirizine** – Levocetirizine is an active enantiomer of cetirizine and produces effects equivalent to cetirizine at approximately one-half of the dose. For adults and children ≥12 years, the standard dose is 5 mg once daily. For children ages 6 to 11 years, the standard dose is 2.5 mg once daily. For children six months to five years, the dose is 1.25 mg once daily. Levocetirizine is unlikely to be effective as an alternative for patients who do not respond adequately to cetirizine. Significant dose alteration is necessary in kidney insufficiency. The small percentage of patients who experience sedation can take cetirizine in the evening.

- **Loratadine** – Loratadine is a long-acting selective H1 antihistamine chemically distinct from cetirizine and has a standard dose of 10 mg once daily for ages ≥6 years.

  For children ages two to five years, the usual dose is 5 mg once daily. For patients with significant kidney and/or hepatic insufficiency, the usual dose is administered every other day.

- **Desloratadine** – Desloratadine is the major active metabolite of loratadine and produces effects equivalent to loratadine at approximately one-half of the dose. For adults and children ≥12 years, the standard dose is 5 mg once daily.

  For children ages 6 to 11 years, the dose is 2.5 mg once daily, and, for those ages 1 to 5 years, the dose is 1.25 mg once daily. A lower dose of 1 mg once daily is approved in the United States for small children ages six months to one year. For patients with significant kidney and/or hepatic insufficiency, the usual dose is administered every other day.

- **Fexofenadine** – The suggested dose of fexofenadine is 180 mg daily for ages ≥12 years or 30 mg twice daily for children ages 2 to 11 years. A lower dose of 15 mg twice daily is approved in the United States for small children ages six months to two years. For patients with significant kidney insufficiency, the adult dose should be reduced to 60 mg once daily. It is best taken without food and specifically not with fruit juices.

Efficacy — The following general statements can be made concerning the efficacy of second- and third-generation antihistamines:

- Antihistamines are less effective than glucocorticoid nasal sprays, especially for the relief of nasal congestion, as previously presented [16,44]. (See 'Efficacy and onset of action'

above.)

- Second-generation antihistamines are equally or more efficacious than cromolyn in relieving symptoms. (See 'Cromolyn sodium' below.)

There is no evidence that pharmacologic tolerance develops to antihistamines [93]. In addition, the specific allergic sensitivities a patient has does not impact the antihistamine that is prescribed, although agents are sometimes marketed as effective for perennial or seasonal or indoor or outdoor allergies. This marketing simply reflects the clinical trials that were performed.

Adverse effects — The second-generation antihistamines are less sedating than the first-generation agents, although cetirizine is sedating for approximately 10 percent of patients [94,95]. Loratadine is nonsedating for most adults at the customary dose of 10 mg once daily, although sedation can occur at higher doses [95]. Fexofenadine is nonsedating at recommended doses and even at higher than recommended doses [94,96,97].

- Second-generation antihistamines have varying degrees of anticholinergic effects. Drying of the eyes, in particular, is noticeable to some patients [98].

- Some oral antihistamines may be associated with weight gain, although it is unclear if this is due to stimulation of appetite or reduced activity secondary to sedation and fatigue. Like other central nervous system effects, weight gain is more prominent with the older, first-generation agents, although it can occur in some patients with the second-generation agents [99]. Weight gain would be predicted to be minimal with fexofenadine [100], although we are aware of no studies directly assessing the second-generation agents for this particular untoward effect. Our experience suggests that increased hunger and weight gain with nonsedating antihistamines is minimal to none in most patients.

- St. John's wort may decrease loratadine and fexofenadine levels, making these antihistamines less effective [101-104]. However, the magnitude and significance of the interaction is uncertain.

Sedating antihistamines — First-generation antihistamines are all sedating and include diphenhydramine, chlorpheniramine, hydroxyzine, brompheniramine, and others. These agents have a limited role in the treatment of most patients because of their numerous adverse effects. We strongly prefer second- and third-generation antihistamines when oral preparations are desired. Most of these agents are available over the counter, both as single agents and in combination with other drugs. They are similarly efficacious, compared with each other, with only minor differences [1].

Adverse effects and safety — First-generation antihistamines cause significant sedation because they are lipophilic and easily cross the blood-brain barrier [105]. Central nervous system symptoms are reported by 20 percent or more of patients, and adverse effects on intellectual and motor function are well documented, even in the absence of subjective awareness of sedation [75,106,107]. Adverse effects are summarized in the table (table 2).

- Impairments affect driving performance and have been implicated in fatal motor vehicle accidents [75,108-111]. First-generation antihistamines are prohibited in many states for some transportation workers (eg, pilots, bus drivers), and individuals taking these agents are considered to be under the influence of drugs [112]. Despite this, a report from the Federal Aviation Administration noted increasing pilot use of these drugs over the past 15 years and reported detection of these agents in 4 and 11 percent of fatalities/accidents in 1990 and 2004, respectively [113]. Other measures of cognitive effects include performance defects on tests of divided attention, working memory, vigilance, and speed [1,114,115].

- First-generation antihistamines are problematic in children. In school-aged children, both untreated allergic rhinitis and the use of sedating antihistamines are associated with impaired school performance [108,115]. In very young children, first-generation antihistamines can cause paradoxical agitation, and over-the-counter cold remedies containing them have been linked to a small number of deaths in children <2 years of age [13]. (See "The common cold in children: Management and prevention", section on 'Over-the-counter medications'.)

- First-generation antihistamines may also be problematic in older adults who are more susceptible to their anticholinergic effects, including dry mouth and eyes, urinary hesitancy, and confusion (table 2) [116].

Antihistamine nasal sprays — Azelastine and olopatadine are available as nasal sprays and are similarly effective [117-119].

Azelastine is available in two strengths, 0.1% or 0.15%. The 0.15% became available over the counter in the United States in 2021.

- Only the lower strength should be used in children six months to six years of age. The dose is 1 spray per nostril twice daily.

- Children 6 to 12 years can use either strength at a dose of 1 spray per nostril twice daily.

- In older children and adults, the dosing of both strengths is the same: 1 or 2 sprays per nostril once or twice daily. We favor titrating to the lowest effective dose.

Olopatadine (available without a prescription) is available in one strength.

- The dose for children 6 to 11 years is 1 spray per nostril twice daily.
- The dose for children ≥12 years and adults is 2 sprays per nostril twice daily.

These agents appear to have some antiinflammatory effect and can improve nasal congestion [120-122]. Antihistamine nasal sprays have a rapid onset of action (less than 15 minutes) and can be administered "on demand" [2]. The onset of action is somewhat faster than that of glucocorticoid nasal sprays [46]. However, azelastine has a bitter taste that can be bothersome to some patients (which has been corrected in newer preparations) and was mildly sedating in some clinical trials, although not in others [123].

Guidelines generally suggest glucocorticoid nasal sprays in preference to antihistamine sprays based upon the fact that the majority of comparison studies favor glucocorticoids [5,124]. In noninferiority trials, both olopatadine and azelastine compared favorably with fluticasone propionate [19,125,126].

Combination corticosteroid/antihistamine sprays — The combination of a topical antihistamine and a topical corticosteroid may be helpful for patients who do not obtain sufficient relief with one agent [127]. Two such products available in the United States and several other countries are:

- Azelastine-fluticasone 137 mcg-50 mcg (Dymista [brand name]) – Approved for children older than six years and adults. The dose is 1 spray per nostril, twice daily.
- Olopatadine-mometasone 665 mcg-25 mcg (Ryaltris [brand name]) – Approved for children ≥12 years and adults. The dose is 2 sprays per nostril, twice daily.

In a randomized trial, 3398 patients with moderate-to-severe allergic rhinitis were treated for two weeks with either the combination of azelastine-fluticasone, fluticasone alone, azelastine alone, or placebo, with complete or near-complete resolution of total symptoms in 12, 9, 7, and 4 percent of patients, respectively [18].

Oral antihistamine/decongestant combinations — Nonsedating antihistamines combined with the decongestant pseudoephedrine provide better symptom relief than either agent alone [128]. Available second-generation combination agents include loratadine-pseudoephedrine, cetirizine-pseudoephedrine, and fexofenadine-pseudoephedrine. There are numerous first-

generation antihistamine/decongestant combination products that have been available without a prescription for years, although we generally avoid them because of the adverse effects of oral decongestants (see next section).

Adverse effects of decongestants — Decongestants have a variety of adverse effects, including hypertension, insomnia, irritability, and headache (table 2). In the United States, increasing abuse of pseudoephedrine (both as a stimulant in athletics and in the illegal production of methamphetamines) has led to the substitution of phenylephrine for pseudoephedrine in many over-the-counter first-generation combination preparations. However, the effects of phenylephrine at the 10 mg dose that is commonly available over the counter appear similar to those of placebo [129-132].

Decongestants are relatively contraindicated in patients with hypertension, contraindicated in those receiving monoamine oxidase inhibitor therapy, and should be used with caution in patients with closed angle glaucoma, cardiovascular or cerebrovascular disease, hyperthyroidism, or bladder neck obstruction.

LESS-USED THERAPIES

Less-used therapies include cromolyn sodium nasal spray, ipratropium bromide nasal spray, and therapies requiring caution (montelukast, nasal decongestant sprays, and systemic glucocorticoids).

Cromolyn sodium — Cromolyn sodium is a mast cell stabilizer. The dose is 1 to 2 sprays, three to four times daily. It inhibits mast cell release of histamine and other inflammatory mediators by inhibiting the intermediate conductance chloride channel pathways of mast cells, eosinophils, epithelial and endothelial cells, fibroblasts, and sensory neurons [133].

Cromolyn sodium is more effective than placebo in the treatment of seasonal allergic rhinitis. It also has no serious side effects and is available over the counter as a nasal spray. However, most studies show it to be less effective than glucocorticoid nasal sprays or second-generation antihistamines [134].

Cromolyn blocks symptoms associated with the immediate- and late-phase nasal allergen challenge and is effective in doing so, even when used shortly before allergen inhalation. This makes cromolyn particularly useful for individuals who experience episodic symptoms to allergens, such as a cat, where it may be used 30 minutes prior to exposure. For seasonal allergic rhinitis, it is most effective when initiated just prior to the pollen season, rather than

after symptoms have begun. Frequent dosing is required to attain a good effect in seasonal allergic rhinitis. Dose frequency can be reduced after the first two to three weeks of treatment.

In summary, cromolyn sodium is very safe, but its utility is limited by the need for frequent dosing and lower efficacy relative to other agents. It may be tried if other agents are not well tolerated.

Ipratropium bromide — Ipratropium bromide in the form of a 0.03% nasal spray can be useful for decreasing rhinorrhea. The dose is 2 sprays per nostril two to three times daily. Ipratropium bromide is a congener of atropine and may act by decreasing the release of substance P. However, it is less effective than glucocorticoid nasal sprays for sneezing, pruritus, or nasal obstruction [135]. Ipratropium bromide is also available in a stronger formulation (0.06%), although this is specifically labeled for reduction of rhinorrhea associated with colds.

Ipratropium is not recommended as a first-line drug in allergic rhinitis. It is sometimes useful in children or adults who have profuse rhinorrhea not otherwise controlled with topical nasal corticosteroids, a complaint most commonly observed in adult patients with concomitant allergic and nonallergic (or vasomotor) rhinitis. (See "Chronic nonallergic rhinitis", section on 'Prominent rhinorrhea without other symptoms'.)

Therapies requiring caution

- **Montelukast** – Montelukast is a leukotriene receptor antagonist that is used in the management of asthma and also has efficacy for allergic rhinitis, although the effects are modest. In experimental allergic rhinitis, nasal congestion correlates best with leukotriene C_4 (LTC_4) levels, whereas sneezing and nasal itching correlate with histamine levels. For the symptoms of allergic rhinitis, montelukast is similarly effective to oral antihistamines but less effective than glucocorticoid nasal sprays [44,136-139].

  Concerns about the risk/benefit ratio of montelukast are increasing. Neuropsychiatric changes have been reported in association with montelukast, including dream abnormalities, insomnia, anxiety, depression, suicidal thinking, and, in rare cases, suicide. A boxed warning was added to the product insert in 2020 with a recommendation from the US Food and Drug Administration (FDA) to avoid the use of montelukast in patients with allergic rhinitis or mild asthma in favor of other treatments.

  We typically restrict the use of montelukast for allergic rhinitis to patients with coexisting asthma who do not tolerate or refuse nasal sprays. We inform all patients about the potential side effects and advise them to stop the medication if they perceive adverse

mood effects. (See "Antileukotriene agents in the management of asthma", section on 'Adverse effects'.)

The dose of montelukast is 4 mg daily for children aged 6 months to <6 years, 5 mg daily for children between 6 and <15 years of age, and 10 mg daily for patients 15 years of age and older.

- **Nasal decongestant sprays** – Topical vasoconstrictor decongestants available include phenylephrine, oxymetazoline, xylometazoline, and naphazoline. Oxymetazoline is particularly popular due to its 12-hour duration of effect. Nasal decongestant sprays are highly effective for nasal congestions, but they are **not recommended as monotherapy** in the chronic treatment of allergic rhinitis because they can cause rhinitis medicamentosa. Rhinitis medicamentosa is a disorder arising from the downregulation of alpha-adrenergic receptors, resulting in rebound nasal congestion. It typically arises after three to seven days of use and can lead to a cycle of nasal congestion both caused by and temporarily relieved by the medication, resulting in escalating use and eventual dependency. (See "An overview of rhinitis", section on 'Nasal decongestant sprays'.)

  In contrast, the combination of a topical nasal decongestant and topical corticosteroid may effectively treat symptoms without causing rhinitis medicamentosa. (See 'Combined with decongestant sprays' above.)

  Nasal decongestants are helpful when used just before air travel in patients who have difficulties with middle ear and/or sinus equilibration with flying or in patients who have problems with altitude changes. The long-acting agent, oxymetazoline, is administered twice per day and is approved for limited use in children older than six years and adults.

- **Systemic glucocorticoids** — Short courses (ie, a few days) of oral glucocorticoids usually abolish symptoms of allergic rhinitis and may be indicated for severe allergic rhinitis symptoms that are preventing the patient from sleeping or working [5]. This approach was more widely used before nasal glucocorticoids and nonsedating antihistamines became available. However, systemic glucocorticoids should not be given repeatedly or for prolonged periods of time for the management of allergic rhinitis [140]. Similarly, we do not endorse injections of long-acting glucocorticoids for this condition, because of unpredictable absorption and the inability to dose adjust if side effects occur. (See "Major adverse effects of systemic glucocorticoids" and "Prevention and treatment of glucocorticoid-induced osteoporosis".)

ALTERNATIVE AND COMPLEMENTARY THERAPIES

Several alternative and complementary therapies are available for the treatment of allergic rhinitis and are reviewed separately. (See "Complementary and alternative therapies for allergic rhinitis and conjunctivitis".)

Patients with allergic rhinitis who are taking herbal therapies for other reasons should be aware of the following:

- St. John's wort may decrease loratadine and fexofenadine levels, making these antihistamines less effective. (See 'Adverse effects' above.)
- Patients with weed pollen allergies should be cautious about taking *Echinacea purpurea*, which has extensive homology with ragweed pollen and has been implicated in anaphylaxis in atopic patients [141].

REFRACTORY SYMPTOMS

Suspicion for chronic rhinosinusitis or rhinitis caused by other etiologies should be raised if a patient with presumed allergic rhinitis fails to improve significantly as a result of one to two months of consistently used pharmacotherapy and appropriate allergen avoidance. Evaluation for other conditions should be performed prior to pursuing allergen immunotherapy. (See "Chronic rhinosinusitis: Clinical manifestations, pathophysiology, and diagnosis" and "Allergic rhinitis: Clinical manifestations, epidemiology, and diagnosis", section on 'Differential diagnosis'.)

REFERRAL

Referral to an allergist/immunologist should be considered for the following patients:

- Children with moderate-to-severe allergic rhinitis. Referral should be considered because allergen immunotherapy has been shown to alter the progression of allergic disease and subsequent development of asthma. (See "Subcutaneous immunotherapy (SCIT) for allergic rhinoconjunctivitis and asthma: Indications and efficacy", section on 'Preventive effects'.)
- Patients with prolonged or severe symptoms of rhinitis or significant residual symptoms despite pharmacologic therapy and avoidance measures.

- Patients whose management might be enhanced by identification of allergic triggers.
- Patients with coexisting asthma or nasal polyposis. (Referral to a pulmonologist or otolaryngologist, respectively, are other options for such patients.)
- Patients with significant complications of allergic rhinitis, such as recurrent otitis media or recurrent sinusitis.
- Patients with intolerable adverse effects from medications or side effects that interfere with school/work productivity.
- Patients who are interested in immunotherapy as a treatment option.
- Patients who have required systemic glucocorticoids to control symptoms.

Patients who are able to discontinue antihistamines without experiencing intolerable symptoms should do so at least one week prior to their appointment, in case skin testing is indicated at the initial visit. Intranasal glucocorticoids and asthma medications do not interfere with skin testing and should **not** be discontinued. Patients with questions concerning which medications to continue or withhold should be instructed to contact the specialist's office prior to their appointment. (See "Overview of skin testing for IgE-mediated allergic disease".)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Rhinitis".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or email these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient education" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Environmental allergies in adults (The Basics)" and "Patient education: Giving your child over-the-counter medicines (The Basics)" and "Patient education: Environmental allergies in children (The Basics)")

- Beyond the Basics topics (see "Patient education: Allergic rhinitis (Beyond the Basics)" and "Patient education: Trigger avoidance in allergic rhinitis (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- **The role of medications in management** – In most patients, allergic rhinitis is a persistent condition that requires ongoing therapy over a period of years. Management combines allergen avoidance and pharmacologic therapy, with allergen immunotherapy added for refractory or severe cases. Many medications are available without a prescription, but some have significant adverse effects (ie, sedating oral antihistamines). (See 'Overview of treatment' above.)

- **Glucocorticoid nasal sprays** – Glucocorticoid nasal sprays are the most effective single-agent maintenance therapy for allergic rhinitis and cause few side effects at the recommended doses. They are particularly effective in relieving nasal congestion. Specific agents and usual doses are summarized in the table (table 1). Mometasone furoate, fluticasone furoate, and triamcinolone acetonide are approved by the US Food and Drug Administration (FDA) for use in children as young as two years of age. (See 'Glucocorticoid nasal sprays' above.)

- **Oral antihistamines** – Newer, nonsedating antihistamines are preferred over older, sedating agents because they are equally effective and have fewer side effects. However, patients often initially self-treat with older agents because they are familiar with them. (See 'Oral antihistamines' above.)

  - Second-generation agents include cetirizine, levocetirizine, loratadine, desloratadine, and fexofenadine. (See 'Minimally sedating agents' above.)

  - First-generation sedating antihistamines, such as diphenhydramine, chlorpheniramine, hydroxyzine, brompheniramine, and others, have significant adverse effects, including sedation and impairment of cognitive function, paradoxical agitation in young children,

and anticholinergic side effects in older adults. We generally avoid the use of these agents. (See 'Sedating antihistamines' above.)

- **Specific patient groups** – An approach to treating specific patient groups is provided. (See 'Approach to specific patient groups' above.)

  - **Children younger than two years** – Allergic rhinitis takes time to develop and is uncommon in children younger than two years of age. In this age group, other disorders should be considered, such as "daycare syndrome" (ie, repeated viral infections of the upper respiratory tract), adenoidal hypertrophy, or chronic rhinosinusitis. (See 'Young children (<2 years of age)' above.)

  - **Older children and adults with mild or intermittent symptoms** – For this group of patients, we suggest a glucocorticoid nasal spray, used regularly or only as needed (**Grade 2A**). We start at the maximal recommended dose for age and then taper to the lowest effective dose once symptoms are controlled (table 1). (See 'Older children and adults' above.)

  - **Additional options** – Some patients with mild symptoms may prefer other agents because of oral administration or desire to avoid glucocorticoids. Thus, the following are appropriate choices as well:

    - An antihistamine nasal spray, such as azelastine or olopatadine, administered regularly or as needed. Combination sprays, containing both an antihistamine and a glucocorticoid, can make administration simpler. (See 'Antihistamine nasal sprays' above and 'Combination corticosteroid/antihistamine sprays' above.)

    - A second-generation oral antihistamine, administered regularly or as needed. (See 'Minimally sedating agents' above.)

    - Cromolyn nasal spray, administered regularly or as needed. This is often preferred by parents of young children because of its excellent safety profile, although it is less effective than other agents. (See 'Cromolyn sodium' above.)

  - **Persistent or moderate-to-severe symptoms** – For this group of patients, we recommend a glucocorticoid nasal spray used regularly (**Grade 1A**). Several agents, such as fluticasone propionate, mometasone furoate, and fluticasone furoate, have minimal systemic bioavailability and are conveniently dosed once or twice daily (table 1). We start at the maximal recommended dose for age and then taper to the

lowest effective dose once symptoms are controlled. (See 'Persistent or moderate-to-severe symptoms' above and 'Glucocorticoid nasal sprays' above.)

- **Additional options** – If glucocorticoid nasal sprays alone are not sufficient to control symptoms, we suggest adding an antihistamine nasal spray (such as azelastine or olopatadine) in preference to other agents (**Grade 2B**). Nasal sprays containing both agents are available in the United States and some other countries. Another option is the addition of an oral antihistamine/decongestant combination, although we discourage regular use of these medications. (See 'Combination corticosteroid/antihistamine sprays' above and 'Persistent or moderate-to-severe symptoms' above.)

- **Patients with concomitant allergic conjunctivitis** – For patients with both allergic rhinitis and allergic conjunctivitis whose symptoms are not fully controlled with a glucocorticoid nasal spray, we suggest the addition of an antihistamine eye drop (table 3), rather than the addition of an oral antihistamine (**Grade 2B**). However, patients with severe symptoms may require all three agents to attain adequate relief. (See 'Allergic conjunctivitis' above.)

- **Pregnant and breastfeeding patients** – An approach to treating allergic rhinitis in pregnancy is depicted in the algorithm (algorithm 1). During breastfeeding, glucocorticoid nasal sprays are preferred, and the safety of other agents in summarized in the table (table 4). (See "Recognition and management of allergic disease during pregnancy", section on 'Allergic rhinitis/conjunctivitis' and 'Breastfeeding' above.)

- **Failure to improve** – Chronic rhinosinusitis should be suspected if a patient with presumed allergic rhinitis fails to improve significantly as a result of pharmacologic therapy and appropriate allergen avoidance. Referral to an allergist or otolaryngologist may be helpful. (See 'Refractory symptoms' above.)

REFERENCES

1. Dykewicz MS, Wallace DV, Amrol DJ, et al. Rhinitis 2020: A practice parameter update. J Allergy Clin Immunol 2020; 146:721.
2. van Cauwenberge P, Bachert C, Passalacqua G, et al. Consensus statement on the treatment of allergic rhinitis. European Academy of Allergology and Clinical Immunology. Allergy 2000; 55:116.

3. Bousquet J, Khaltaev N, Cruz AA, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). Allergy 2008; 63 Suppl 86:8.
4. Bousquet J, van Cauwenberge P, Aït Khaled N, et al. Pharmacologic and anti-IgE treatment of allergic rhinitis ARIA update (in collaboration with GA2LEN). Allergy 2006; 61:1086.
5. Brozek JL, Bousquet J, Baena-Cagnani CE, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines: 2010 revision. J Allergy Clin Immunol 2010; 126:466.
6. Angier E, Willington J, Scadding G, et al. Management of allergic and non-allergic rhinitis: a primary care summary of the BSACI guideline. Prim Care Respir J 2010; 19:217.
7. Siow JK, Alshaikh NA, Balakrishnan A, et al. Ministry of Health clinical practice guidelines: Management of Rhinosinusitis and Allergic Rhinitis. Singapore Med J 2010; 51:190.
8. Scadding GK, Durham SR, Mirakian R, et al. BSACI guidelines for the management of allergic and non-allergic rhinitis. Clin Exp Allergy 2008; 38:19.
9. Okubo K, Kurono Y, Fujieda S, et al. Japanese guideline for allergic rhinitis. Allergol Int 2011; 60:171.
10. Dykewicz MS, Wallace DV, Baroody F, et al. Treatment of seasonal allergic rhinitis: An evidence-based focused 2017 guideline update. Ann Allergy Asthma Immunol 2017; 119:489.
11. Seidman MD, Gurgel RK, Lin SY, et al. Clinical practice guideline: Allergic rhinitis. Otolaryngol Head Neck Surg 2015; 152:S1.
12. Wallace DV, Dykewicz MS, Oppenheimer J, et al. Pharmacologic Treatment of Seasonal Allergic Rhinitis: Synopsis of Guidance From the 2017 Joint Task Force on Practice Parameters. Ann Intern Med 2017; 167:876.
13. Centers for Disease Control and Prevention (CDC). Infant deaths associated with cough and cold medications--two states, 2005. MMWR Morb Mortal Wkly Rep 2007; 56:1.
14. Cutler DL, Banfield C, Affrime MB. Safety of Mometasone Furoate Nasal Spray in Children with Allergic Rhinitis as Young as 2 Years of Age: A Randomized Controlled Trial. Pediatr Asthma Allergy Immunol 2006; 19:146.
15. Weinstein S, Qaqundah P, Georges G, Nayak A. Efficacy and safety of triamcinolone acetonide aqueous nasal spray in children aged 2 to 5 years with perennial allergic rhinitis: a randomized, double-blind, placebo-controlled study with an open-label extension. Ann Allergy Asthma Immunol 2009; 102:339.
16. Kaszuba SM, Baroody FM, deTineo M, et al. Superiority of an intranasal corticosteroid compared with an oral antihistamine in the as-needed treatment of seasonal allergic

rhinitis. Arch Intern Med 2001; 161:2581.

17. Dykewicz MS, Kaiser HB, Nathan RA, et al. Fluticasone propionate aqueous nasal spray improves nasal symptoms of seasonal allergic rhinitis when used as needed (prn). Ann Allergy Asthma Immunol 2003; 91:44.
18. Carr W, Bernstein J, Lieberman P, et al. A novel intranasal therapy of azelastine with fluticasone for the treatment of allergic rhinitis. J Allergy Clin Immunol 2012; 129:1282.
19. Ratner PH, Hampel F, Van Bavel J, et al. Combination therapy with azelastine hydrochloride nasal spray and fluticasone propionate nasal spray in the treatment of patients with seasonal allergic rhinitis. Ann Allergy Asthma Immunol 2008; 100:74.
20. Can D, Tanaç R, Demir E, et al. Is the usage of intranasal glucocorticosteroids alone in allergic rhinitis sufficient? Allergy Asthma Proc 2006; 27:248.
21. Lanier BQ, Abelson MB, Berger WE, et al. Comparison of the efficacy of combined fluticasone propionate and olopatadine versus combined fluticasone propionate and fexofenadine for the treatment of allergic rhinoconjunctivitis induced by conjunctival allergen challenge. Clin Ther 2002; 24:1161.
22. Ousler GW 3rd, Workman DA, Torkildsen GL. An open-label, investigator-masked, crossover study of the ocular drying effects of two antihistamines, topical epinastine and systemic loratadine, in adult volunteers with seasonal allergic conjunctivitis. Clin Ther 2007; 29:611.
23. Prenner BM, Lanier BQ, Bernstein DI, et al. Mometasone furoate nasal spray reduces the ocular symptoms of seasonal allergic rhinitis. J Allergy Clin Immunol 2010; 125:1247.
24. Kaiser HB, Naclerio RM, Given J, et al. Fluticasone furoate nasal spray: a single treatment option for the symptoms of seasonal allergic rhinitis. J Allergy Clin Immunol 2007; 119:1430.
25. Martin BG, Ratner PH, Hampel FC, et al. Optimal dose selection of fluticasone furoate nasal spray for the treatment of seasonal allergic rhinitis in adults and adolescents. Allergy Asthma Proc 2007; 28:216.
26. Ratner P, Van Bavel J, Mohar D, et al. Efficacy of daily intranasal fluticasone propionate on ocular symptoms associated with seasonal allergic rhinitis. Ann Allergy Asthma Immunol 2015; 114:141.
27. Licari A, Castagnoli R, De Filippo M, et al. Current and emerging biologic therapies for allergic rhinitis and chronic rhinosinusitis. Expert Opin Biol Ther 2020; 20:609.
28. Yu C, Wang K, Cui X, et al. Clinical Efficacy and Safety of Omalizumab in the Treatment of Allergic Rhinitis: A Systematic Review and Meta-analysis of Randomized Clinical Trials. Am J Rhinol Allergy 2020; 34:196.

29. Weinstein SF, Katial R, Jayawardena S, et al. Efficacy and safety of dupilumab in perennial allergic rhinitis and comorbid asthma. J Allergy Clin Immunol 2018; 142:171.
30. Drugs and Lactation Database (LactMed). https://www.ncbi.nlm.nih.gov/books/NBK501922/ (Accessed on February 20, 2020).
31. Incaudo GA, Takach P. The diagnosis and treatment of allergic rhinitis during pregnancy and lactation. Immunol Allergy Clin North Am 2006; 26:137.
32. Kaliner MA. H1-antihistamines in the elderly. Clin Allergy Immunol 2002; 17:465.
33. Slavin RG. Treating rhinitis in the older population: special considerations. Allergy Asthma Clin Immunol 2009; 5:9.
34. Louisiana Department of Health and Hospitals. North Louisiana woman dies from rare ame ba infection. December 6, 2011 Available at: http://new.dhh.louisiana.gov/index.cfm/newsr oom/detail/2332 (Accessed on January 22, 2012).
35. US Food and Drug Administration. Is Rinsing Your Sinuses With Neti Pots Safe? http://www. fda.gov/ForConsumers/ConsumerUpdates/ucm316375.htm (Accessed on September 04, 20 12).
36. United States Centers for Disease Control and Prevention. Naegleria fowleri: Sources of Inf ection & Risk Factors. http://www.cdc.gov/parasites/naegleria/faqs.html#how_infect (Acces sed on February 02, 2012).
37. Psaltis AJ, Foreman A, Wormald PJ, Schlosser RJ. Contamination of sinus irrigation devices: a review of the evidence and clinical relevance. Am J Rhinol Allergy 2012; 26:201.
38. Wang YH, Yang CP, Ku MS, et al. Efficacy of nasal irrigation in the treatment of acute sinusitis in children. Int J Pediatr Otorhinolaryngol 2009; 73:1696.
39. Li H, Sha Q, Zuo K, et al. Nasal saline irrigation facilitates control of allergic rhinitis by topical steroid in children. ORL J Otorhinolaryngol Relat Spec 2009; 71:50.
40. Garavello W, Somigliana E, Acaia B, et al. Nasal lavage in pregnant women with seasonal allergic rhinitis: a randomized study. Int Arch Allergy Immunol 2010; 151:137.
41. Berger WE, Kaiser H, Gawchik SM, et al. Triamcinolone acetonide aqueous nasal spray and fluticasone propionate are equally effective for relief of nasal symptoms in patients with seasonal allergic rhinitis. Otolaryngol Head Neck Surg 2003; 129:16.
42. Mandl M, Nolop K, Lutsky BN. Comparison of once daily mometasone furoate (Nasonex) and fluticasone propionate aqueous nasal sprays for the treatment of perennial rhinitis. The 194-079 Study Group. Ann Allergy Asthma Immunol 1997; 79:237.
43. Juel-Berg N, Darling P, Bolvig J, et al. Intranasal corticosteroids compared with oral antihistamines in allergic rhinitis: A systematic review and meta-analysis. Am J Rhinol

Allergy 2017; 31:19.

44. Pullerits T, Praks L, Ristioja V, Lötvall J. Comparison of a nasal glucocorticoid, antileukotriene, and a combination of antileukotriene and antihistamine in the treatment of seasonal allergic rhinitis. J Allergy Clin Immunol 2002; 109:949.
45. Patel P, Patel D, Kunjibettu S, et al. Onset of action of ciclesonide once daily in the treatment of seasonal allergic rhinitis. Ear Nose Throat J 2008; 87:340.
46. Patel D, Garadi R, Brubaker M, et al. Onset and duration of action of nasal sprays in seasonal allergic rhinitis patients: olopatadine hydrochloride versus mometasone furoate monohydrate. Allergy Asthma Proc 2007; 28:592.
47. Couroux P, Kunjibettu S, Hall N, Wingertzahn MA. Onset of action of ciclesonide once daily in the treatment of seasonal allergic rhinitis. Ann Allergy Asthma Immunol 2009; 102:62.
48. Juniper EF, Ståhl E, Doty RL, et al. Clinical outcomes and adverse effect monitoring in allergic rhinitis. J Allergy Clin Immunol 2005; 115:S390.
49. Zitt M, Kosoglou T, Hubbell J. Mometasone furoate nasal spray: a review of safety and systemic effects. Drug Saf 2007; 30:317.
50. Daley-Yates PT, Price AC, Sisson JR, et al. Beclomethasone dipropionate: absolute bioavailability, pharmacokinetics and metabolism following intravenous, oral, intranasal and inhaled administration in man. Br J Clin Pharmacol 2001; 51:400.
51. Derendorf H, Meltzer EO. Molecular and clinical pharmacology of intranasal corticosteroids: clinical and therapeutic implications. Allergy 2008; 63:1292.
52. Schenkel EJ, Skoner DP, Bronsky EA, et al. Absence of growth retardation in children with perennial allergic rhinitis after one year of treatment with mometasone furoate aqueous nasal spray. Pediatrics 2000; 105:E22.
53. Allen DB, Meltzer EO, Lemanske RF Jr, et al. No growth suppression in children treated with the maximum recommended dose of fluticasone propionate aqueous nasal spray for one year. Allergy Asthma Proc 2002; 23:407.
54. Galant SP, Melamed IR, Nayak AS, et al. Lack of effect of fluticasone propionate aqueous nasal spray on the hypothalamic-pituitary-adrenal axis in 2- and 3-year-old patients. Pediatrics 2003; 112:96.
55. Benninger MS, Ahmad N, Marple BF. The safety of intranasal steroids. Otolaryngol Head Neck Surg 2003; 129:739.
56. Kim KT, Rabinovitch N, Uryniak T, et al. Effect of budesonide aqueous nasal spray on hypothalamic-pituitary-adrenal axis function in children with allergic rhinitis. Ann Allergy Asthma Immunol 2004; 93:61.

57. Kim K, Weiswasser M, Ruediger N. Safety of once daily ciclesonide nasal spray in children 2 to 5 years of age with perennial allergic rhinitis. Pediatr Asthma Allergy Immunol 2007; 20:229.
58. Murphy K, Uryniak T, Simpson B, O'Dowd L. Growth velocity in children with perennial allergic rhinitis treated with budesonide aqueous nasal spray. Ann Allergy Asthma Immunol 2006; 96:723.
59. Hoover RM, Erramouspe J, Bell EA, Cleveland KW. Effect of inhaled corticosteroids on long-term growth in pediatric patients with asthma and allergic rhinitis. Ann Pharmacother 2013; 47:1175.
60. Skoner DP, Rachelefsky GS, Meltzer EO, et al. Detection of growth suppression in children during treatment with intranasal beclomethasone dipropionate. Pediatrics 2000; 105:E23.
61. Skoner DP, Berger WE, Gawchik SM, et al. Intranasal triamcinolone and growth velocity. Pediatrics 2015; 135:e348.
62. Lee LA, Sterling R, Máspero J, et al. Growth velocity reduced with once-daily fluticasone furoate nasal spray in prepubescent children with perennial allergic rhinitis. J Allergy Clin Immunol Pract 2014; 2:421.
63. Foisy MM, Yakiwchuk EM, Chiu I, Singh AE. Adrenal suppression and Cushing's syndrome secondary to an interaction between ritonavir and fluticasone: a review of the literature. HIV Med 2008; 9:389.
64. Gupta R, Fonacier LS. Adverse Effects of Nonsystemic Steroids (Inhaled, Intranasal, and Cutaneous): a Review of the Literature and Suggested Monitoring Tool. Curr Allergy Asthma Rep 2016; 16:44.
65. Passalacqua G, Albano M, Canonica GW, et al. Inhaled and nasal corticosteroids: safety aspects. Allergy 2000; 55:16.
66. Bui CM, Chen H, Shyr Y, Joos KM. Discontinuing nasal steroids might lower intraocular pressure in glaucoma. J Allergy Clin Immunol 2005; 116:1042.
67. Opatowsky I, Feldman RM, Gross R, Feldman ST. Intraocular pressure elevation associated with inhalation and nasal corticosteroids. Ophthalmology 1995; 102:177.
68. Valenzuela CV, Liu JC, Vila PM, et al. Intranasal Corticosteroids Do Not Lead to Ocular Changes: A Systematic Review and Meta-analysis. Laryngoscope 2019; 129:6.
69. Blaiss MS. Safety considerations of intranasal corticosteroids for the treatment of allergic rhinitis. Allergy Asthma Proc 2007; 28:145.
70. Salib RJ, Howarth PH. Safety and tolerability profiles of intranasal antihistamines and intranasal corticosteroids in the treatment of allergic rhinitis. Drug Saf 2003; 26:863.

71. Seidman MD, Gurgel RK, Lin SY, et al. Clinical practice guideline: allergic rhinitis executive summary. Otolaryngol Head Neck Surg 2015; 152:197.
72. Borish L. Allergic rhinitis: systemic inflammation and implications for management. J Allergy Clin Immunol 2003; 112:1021.
73. Barnes ML, Menzies D, Fardon TC, et al. Combined mediator blockade or topical steroid for treating the unified allergic airway. Allergy 2007; 62:73.
74. Baroody FM, Brown D, Gavanescu L, et al. Oxymetazoline adds to the effectiveness of fluticasone furoate in the treatment of perennial allergic rhinitis. J Allergy Clin Immunol 2011; 127:927.
75. Verster JC, Volkerts ER. Antihistamines and driving ability: evidence from on-the-road driving studies during normal traffic. Ann Allergy Asthma Immunol 2004; 92:294.
76. Bielory L. Update on ocular allergy treatment. Expert Opin Pharmacother 2002; 3:541.
77. Bielory BP, O'Brien TP, Bielory L. Management of seasonal allergic conjunctivitis: guide to therapy. Acta Ophthalmol 2012; 90:399.
78. Deruaz C, Leimgruber A, Berney M, et al. Levocetirizine better protects than desloratadine in a nasal provocation with allergen. J Allergy Clin Immunol 2004; 113:669.
79. Simons FE, Prenner BM, Finn A Jr, Desloratadine Study Group. Efficacy and safety of desloratadine in the treatment of perennial allergic rhinitis. J Allergy Clin Immunol 2003; 111:617.
80. Layton D, Wilton L, Boshier A, et al. Comparison of the risk of drowsiness and sedation between levocetirizine and desloratadine: a prescription-event monitoring study in England. Drug Saf 2006; 29:897.
81. Berkowitz RB, McCafferty F, Lutz C, et al. Onset of action of fexofenadine hydrochloride 60 mg/pseudoephedrine hydrochloride 120 mg in subjects aged 12 years with moderate to severe seasonal allergic rhinitis: a pooled analysis of two single-dose, randomized, double-blind, placebo-controlled allergen exposure unit studies. Clin Ther 2006; 28:1658.
82. Berkowitz RB, McCafferty F, Lutz C, et al. Fexofenadine HCl 60 mg/ pseudoephedrine HCl 120 mg has a 60-minute onset of action in the treatment of seasonal allergic rhinitis symptoms, as assessed in an allergen exposure unit. Allergy Asthma Proc 2004; 25:335.
83. Kakutani C, Ogino S, Ikeda H, Enomoto T. [Comparison of clinical efficacy and cost-quality of antihistamines in early treatment for Japanese cedar pollinosis]. Arerugi 2006; 55:554.
84. Stübner P, Zieglmayer R, Horak F. A direct comparison of the efficacy of antihistamines in SAR and PAR: randomised, placebo-controlled studies with levocetirizine and loratadine

using an environmental exposure unit - the Vienna Challenge Chamber (VCC). Curr Med Res Opin 2004; 20:891.

85. Horak F, Zieglmayer PU, Zieglmayer R, et al. Levocetirizine has a longer duration of action on improving total nasal symptoms score than fexofenadine after single administration. Br J Clin Pharmacol 2005; 60:24.
86. Day JH, Briscoe MP, Rafeiro E, et al. Randomized double-blind comparison of cetirizine and fexofenadine after pollen challenge in the Environmental Exposure Unit: duration of effect in subjects with seasonal allergic rhinitis. Allergy Asthma Proc 2004; 25:59.
87. Hansen GR. Loratadine in the high performance aerospace environment. Aviat Space Environ Med 1999; 70:919.
88. Church MK. H(1)-antihistamines and inflammation. Clin Exp Allergy 2001; 31:1341.
89. Hasala H, Moilanen E, Janka-Junttila M, et al. First-generation antihistamines diphenhydramine and chlorpheniramine reverse cytokine-afforded eosinophil survival by enhancing apoptosis. Allergy Asthma Proc 2007; 28:79.
90. Gentile DA, Friday GA, Jr Skoner. Management of allergic rhinitis: Antihistamines and decongestants. Immunol Allergy Clin North Am 2000; 20:355.
91. Schroeder JT, Schleimer RP, Lichtenstein LM, Kreutner W. Inhibition of cytokine generation and mediator release by human basophils treated with desloratadine. Clin Exp Allergy 2001; 31:1369.
92. Meltzer EO, Malmstrom K, Lu S, et al. Concomitant montelukast and loratadine as treatment for seasonal allergic rhinitis: a randomized, placebo-controlled clinical trial. J Allergy Clin Immunol 2000; 105:917.
93. Simons FE. Advances in H1-antihistamines. N Engl J Med 2004; 351:2203.
94. Vacchiano C, Moore J, Rice GM, Crawley G. Fexofenadine effects on cognitive performance in aviators at ground level and simulated altitude. Aviat Space Environ Med 2008; 79:754.
95. Newer antihistamines. Med Lett Drugs Ther 2001; 43:35.
96. Hindmarch I, Shamsi Z, Kimber S. An evaluation of the effects of high-dose fexofenadine on the central nervous system: a double-blind, placebo-controlled study in healthy volunteers. Clin Exp Allergy 2002; 32:133.
97. Ridout F, Shamsi Z, Meadows R, et al. A single-center, randomized, double-blind, placebo-controlled, crossover investigation of the effects of fexofenadine hydrochloride 180 mg alone and with alcohol, with hydroxyzine hydrochloride 50 mg as a positive internal control, on aspects of cognitive and psychomotor function related to driving a car. Clin Ther 2003; 25:1518.

98. Ousler GW, Wilcox KA, Gupta G, Abelson MB. An evaluation of the ocular drying effects of 2 systemic antihistamines: loratadine and cetirizine hydrochloride. Ann Allergy Asthma Immunol 2004; 93:460.
99. Ratliff JC, Barber JA, Palmese LB, et al. Association of prescription H1 antihistamine use with obesity: results from the National Health and Nutrition Examination Survey. Obesity (Silver Spring) 2010; 18:2398.
100. Yanai K, Rogala B, Chugh K, et al. Safety considerations in the management of allergic diseases: focus on antihistamines. Curr Med Res Opin 2012; 28:623.
101. Borrelli F, Izzo AA. Herb-drug interactions with St John's wort (Hypericum perforatum): an update on clinical observations. AAPS J 2009; 11:710.
102. Chen C, Hanson E, Watson JW, Lee JS. P-glycoprotein limits the brain penetration of nonsedating but not sedating H1-antagonists. Drug Metab Dispos 2003; 31:312.
103. Katta A, Dhananjeyan M, Bykowski C, et al. Verapamil, but not probenecid, co-administration can convert desloratadine to a sedating antihistamine in mice. Drug Metab Lett 2007; 1:7.
104. Whitten DL, Myers SP, Hawrelak JA, Wohlmuth H. The effect of St John's wort extracts on CYP3A: a systematic review of prospective clinical trials. Br J Clin Pharmacol 2006; 62:512.
105. Simons FE, Simons KJ. Clinical pharmacology of new histamine H1 receptor antagonists. Clin Pharmacokinet 1999; 36:329.
106. Starbuck VN, Kay GG, Platenberg RC, et al. Functional magnetic resonance imaging reflects changes in brain functioning with sedation. Hum Psychopharmacol 2000; 15:613.
107. Weiler JM, Bloomfield JR, Woodworth GG, et al. Effects of fexofenadine, diphenhydramine, and alcohol on driving performance. A randomized, placebo-controlled trial in the Iowa driving simulator. Ann Intern Med 2000; 132:354.
108. Church MK, Maurer M, Simons FE, et al. Risk of first-generation H(1)-antihistamines: a GA(2)LEN position paper. Allergy 2010; 65:459.
109. O'Hanlon JF, Ramaekers JG. Antihistamine effects on actual driving performance in a standard test: a summary of Dutch experience, 1989-94. Allergy 1995; 50:234.
110. Ray WA, Thapa PB, Shorr RI. Medications and the older driver. Clin Geriatr Med 1993; 9:413.
111. Cimbura G, Lucas DM, Bennett RC, et al. Incidence and toxicological aspects of drugs detected in 484 fatally injured drivers and pedestrians in Ontario. J Forensic Sci 1982; 27:855.
112. United States Department of Transportation, National Highway Traffic Safety Administratio n: Digest of Impaired Driving and Selected Beverage Control Laws, 29th ed, April 2016.

113. Sen A, Akin A, Craft KJ, et al. First-generation H1 antihistamines found in pilot fatalities of civil aviation accidents, 1990-2005. Aviat Space Environ Med 2007; 78:514.

114. Kay GG. The effects of antihistamines on cognition and performance. J Allergy Clin Immunol 2000; 105:S622.

115. Bender BG, Berning S, Dudden R, et al. Sedation and performance impairment of diphenhydramine and second-generation antihistamines: a meta-analysis. J Allergy Clin Immunol 2003; 111:770.

116. Busse PJ. Allergic respiratory disease in the elderly. Am J Med 2007; 120:498.

117. Shah SR, Nayak A, Ratner P, et al. Effects of olopatadine hydrochloride nasal spray 0.6% in the treatment of seasonal allergic rhinitis: a phase III, multicenter, randomized, double-blind, active- and placebo-controlled study in adolescents and adults. Clin Ther 2009; 31:99.

118. LaForce CF, Carr W, Tilles SA, et al. Evaluation of olopatadine hydrochloride nasal spray, 0.6%, used in combination with an intranasal corticosteroid in seasonal allergic rhinitis. Allergy Asthma Proc 2010; 31:132.

119. van Bavel J, Howland WC, Amar NJ, et al. Efficacy and safety of azelastine 0.15% nasal spray administered once daily in subjects with seasonal allergic rhinitis. Allergy Asthma Proc 2009; 30:512.

120. De Weck AL, Derer T, Bähre M. Investigation of the anti-allergic activity of azelastine on the immediate and late-phase reactions to allergens and histamine using telethermography. Clin Exp Allergy 2000; 30:283.

121. Lee TA, Pickard AS. Meta-analysis of azelastine nasal spray for the treatment of allergic rhinitis. Pharmacotherapy 2007; 27:852.

122. Berger W, Hampel F Jr, Bernstein J, et al. Impact of azelastine nasal spray on symptoms and quality of life compared with cetirizine oral tablets in patients with seasonal allergic rhinitis. Ann Allergy Asthma Immunol 2006; 97:375.

123. US Food and Drug Administration. Azelastine hydrochloride ANDA 207411. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=207411 (Accessed on February 20, 2020).

124. Yáñez A, Rodrigo GJ. Intranasal corticosteroids versus topical H1 receptor antagonists for the treatment of allergic rhinitis: a systematic review with meta-analysis. Ann Allergy Asthma Immunol 2002; 89:479.

125. Carr WW, Ratner P, Munzel U, et al. Comparison of intranasal azelastine to intranasal fluticasone propionate for symptom control in moderate-to-severe seasonal allergic rhinitis. Allergy Asthma Proc 2012; 33:450.

126. Kaliner MA, Storms W, Tilles S, et al. Comparison of olopatadine 0.6% nasal spray versus fluticasone propionate 50 microg in the treatment of seasonal allergic rhinitis. Allergy Asthma Proc 2009; 30:255.

127. Berger WE, Meltzer EO. Intranasal spray medications for maintenance therapy of allergic rhinitis. Am J Rhinol Allergy 2015; 29:273.

128. Pleskow W, Grubbe R, Weiss S, Lutsky B. Efficacy and safety of an extended-release formulation of desloratadine and pseudoephedrine vs the individual components in the treatment of seasonal allergic rhinitis. Ann Allergy Asthma Immunol 2005; 94:348.

129. Hatton RC, Winterstein AG, McKelvey RP, et al. Efficacy and safety of oral phenylephrine: systematic review and meta-analysis. Ann Pharmacother 2007; 41:381.

130. Horak F, Zieglmayer P, Zieglmayer R, et al. A placebo-controlled study of the nasal decongestant effect of phenylephrine and pseudoephedrine in the Vienna Challenge Chamber. Ann Allergy Asthma Immunol 2009; 102:116.

131. Day JH, Briscoe MP, Ratz JD, et al. Efficacy of loratadine-montelukast on nasal congestion in patients with seasonal allergic rhinitis in an environmental exposure unit. Ann Allergy Asthma Immunol 2009; 102:328.

132. Meltzer EO, Ratner PH, McGraw T. Oral Phenylephrine HCl for Nasal Congestion in Seasonal Allergic Rhinitis: A Randomized, Open-label, Placebo-controlled Study. J Allergy Clin Immunol Pract 2015; 3:702.

133. Norris AA, Alton EW. Chloride transport and the action of sodium cromoglycate and nedocromil sodium in asthma. Clin Exp Allergy 1996; 26:250.

134. Pitsios C, Papadopoulos D, Kompoti E, et al. Efficacy and safety of mometasone furoate vs nedocromil sodium as prophylactic treatment for moderate/severe seasonal allergic rhinitis. Ann Allergy Asthma Immunol 2006; 96:673.

135. Milgrom H, Biondi R, Georgitis JW, et al. Comparison of ipratropium bromide 0.03% with beclomethasone dipropionate in the treatment of perennial rhinitis in children. Ann Allergy Asthma Immunol 1999; 83:105.

136. Ratner PH, Howland WC 3rd, Arastu R, et al. Fluticasone propionate aqueous nasal spray provided significantly greater improvement in daytime and nighttime nasal symptoms of seasonal allergic rhinitis compared with montelukast. Ann Allergy Asthma Immunol 2003; 90:536.

137. Nathan RA. Do leukotriene receptor antagonists have a place in pharmacotherapy of allergic rhinitis? Ann Allergy Asthma Immunol 2003; 90:466.

138. Wilson AM, O'Byrne PM, Parameswaran K. Leukotriene receptor antagonists for allergic rhinitis: a systematic review and meta-analysis. Am J Med 2004; 116:338.

139. Nayak A, Langdon RB. Montelukast in the treatment of allergic rhinitis: an evidence-based review. Drugs 2007; 67:887.

140. Aasbjerg K, Torp-Pedersen C, Vaag A, Backer V. Treating allergic rhinitis with depot-steroid injections increase risk of osteoporosis and diabetes. Respir Med 2013; 107:1852.

141. Mullins RJ, Heddle R. Adverse reactions associated with echinacea: the Australian experience. Ann Allergy Asthma Immunol 2002; 88:42.

Topic 7526 Version 61.0

GRAPHICS

Glucocorticoid nasal sprays for treatment of rhinitis

Name	Common brand name(s) and strength	Generic available	Available without a prescription (OTC)	Usual adult dose per nostril	Lower age limit when used in children (years)*	Us ped dos no
Second-generation (systemic bioavailability <1% or undetectable)						
Ciclesonide	Omnaris (50 mcg/spray)	No	No	Two sprays once daily	2 years	2 to years or tw spra once ≥12 Two once
	Zetonna (37 mcg/spray)	No	No	One spray once daily	12 years	≥12 One once
Fluticasone furoate	Flonase Sensimist (OTC) (27.5 mcg/spray)	No	Yes	Two sprays once daily	2 years	One spra once in ch 2 to years with spra daily
Fluticasone propionate	Flonase Allergy Relief (OTC) (50 mcg/spray)	Yes	Yes	Two sprays once daily or one spray twice daily	4 years	4 to years spra daily ≥12 Two once or or

						spra daily
Mometasone	Nasonex 24HR Allergy (OTC) (50 mcg/spray)	Yes	Yes	Two sprays once daily	2 years	2 to years spra daily ≥12 Two once
First-generation (systemic bioavailability 10 to 50%)						
Beclomethasone	Beconase AQ (42 mcg/spray)	No	No	One or two sprays twice daily	6 years	One spra twice in ch 6 to years with spra daily
	Pediatric: Qnasl Children's (40 mcg/spray) Adolescent/adult: Qnasl (80 mcg/spray)	No	No	Two sprays once daily using 80 mcg/spray product	4 years	4 to years spra daily 40 mcg/ prod ≥12 Two once usin mcg/ prod
Budesonide	Generic (formerly Rhinocort Allergy) (OTC) (32 mcg/spray)	Yes	Yes	One to two sprays once daily	6 years	One spra once in ch 6 to years with spra daily
Flunisolide	Generic (formerly Nasalide) (25	Yes	No	Two sprays two	6 years	6 to years

	mcg/spray)			or three times daily (maximum two sprays four times daily)		spray three time or tw spray twice ≥15 Two two three time (max two four daily
Triamcinolone	GoodSense Nasal Allergy (OTC), Nasacort Allergy 24 Hr (OTC) (55 mcg/spray)	Yes	Yes	Two sprays once daily	2 years	2 to years spray daily ≥6 y One spray once in ch 6 to years with spray daily

Nasal sprays work best when they are administered properly and the medication remains in the nose rather than draining down the back of the throat. Note that the recommended techniques for the aqueous and aerosol sprays are different. If the nose is crusted or contains mucus, it should first be cleaned with a saline nasal spray prior to use of intranasal sprays. Some people find that holding the other nostril closed with a finger improves their ability to draw the spray into the upper nose.

Once symptoms are controlled, the daily dose can be reduced to the lowest dose that maintains control.

Dosing and product descriptions are based upon products available in the United States and some other countries. Product descriptions in other countries may differ in some detail. Consult the Lexicomp drug monographs and local product information for additional detail.

OTC: over-the-counter (available without a prescription in the United States and some other countries).

* Lowest age use may differ from approved product labeling.

¶ Alcohol may contribute to dryness or irritation.

Graphic 55833 Version 39.0

Some adverse effects of antihistamines and decongestants

Antihistamines
Anticholinergic effects
Dry mouth and eyes
Impotence
Urinary hesitancy
Glaucoma
Central nervous system effects
Sedation
Rarely stimulation (usually children)
Confusion (older patients)
Cognitive impairment
Miscellaneous effects
Weight gain
Hypersensitivity
Prolonged QT interval
Ventricular arrhythmias
Decongestants
Nervousness
Irritability
Insomnia
Headache
Urinary hesitancy
Tachycardia/palpitations
Hypertension
Nausea

Graphic 65742 Version 4.0

Ophthalmic medications for the treatment of allergic conjunctivitis

Pharmacologic class	Usual adult dosing	Pediatric dosing
Antihistamines with mast cell-stabilizing properties: Decreased itching should be evident within 24 to 72 hours; may result in dry eye sensation or burning		
Olopatadine 0.1% and 0.2% (OTC Pataday, generics), 0.7% (OTC Pataday)	One drop per eye twice daily (0.1%); one drop per eye once daily (0.2% and 0.7%)	≥2 years: One drop per eye twice daily (0.1%); one drop per eye once daily (0.2% and 0.7%)
Alcaftadine 0.25% (OTC Lastacaft)	One drop per eye once daily	≥2 years: One drop per eye once daily
Bepotastine 1.5% (Bepreve, generics)	One drop per eye twice daily	≥2 years: One drop per eye twice daily
Cetirizine 0.24% (Zerviate)	One drop per eye twice daily	≥2 years: One drop per eye twice daily
Epinastine 0.05% (generics)	One drop per eye twice daily	≥2 years: One drop per eye twice daily
Ketotifen 0.025% (multiple OTC products)	One drop per eye twice daily	≥3 years: One drop per eye twice daily
Azelastine 0.05% (generics)	One drop per eye twice daily	≥3 years: One drop per eye twice daily
Emedastine 0.05% (not available in US but may be available in other countries)	One drop per eye up to 4 times daily	≥3 years: One drop per eye up to 4 times daily
Vasoconstrictor/antihistamine combination: Increased redness can occur temporarily when medication is stopped		
Naphazoline 0.25% and pheniramine 0.3% (OTC Naphcon-A, OTC Visine, OTC Visine-A) Naphazoline 0.27% and pheniramine 0.315% (OTC Opcon-A, generics)	One to two drops per eye up to 4 times daily	≥6 years: One to two drops per eye up to 4 times daily
Mast cell stabilizers: Decreased itching may be evident within a few days or may take up to four weeks		
Cromolyn sodium 4% (generics)	One to two drops per eye up to 6 times daily	≥4 years: One to two drops per eye up to 6 times daily
Nedocromil 2% (Alocril)	One to two drops per eye twice	≥3 years: One to two drops per

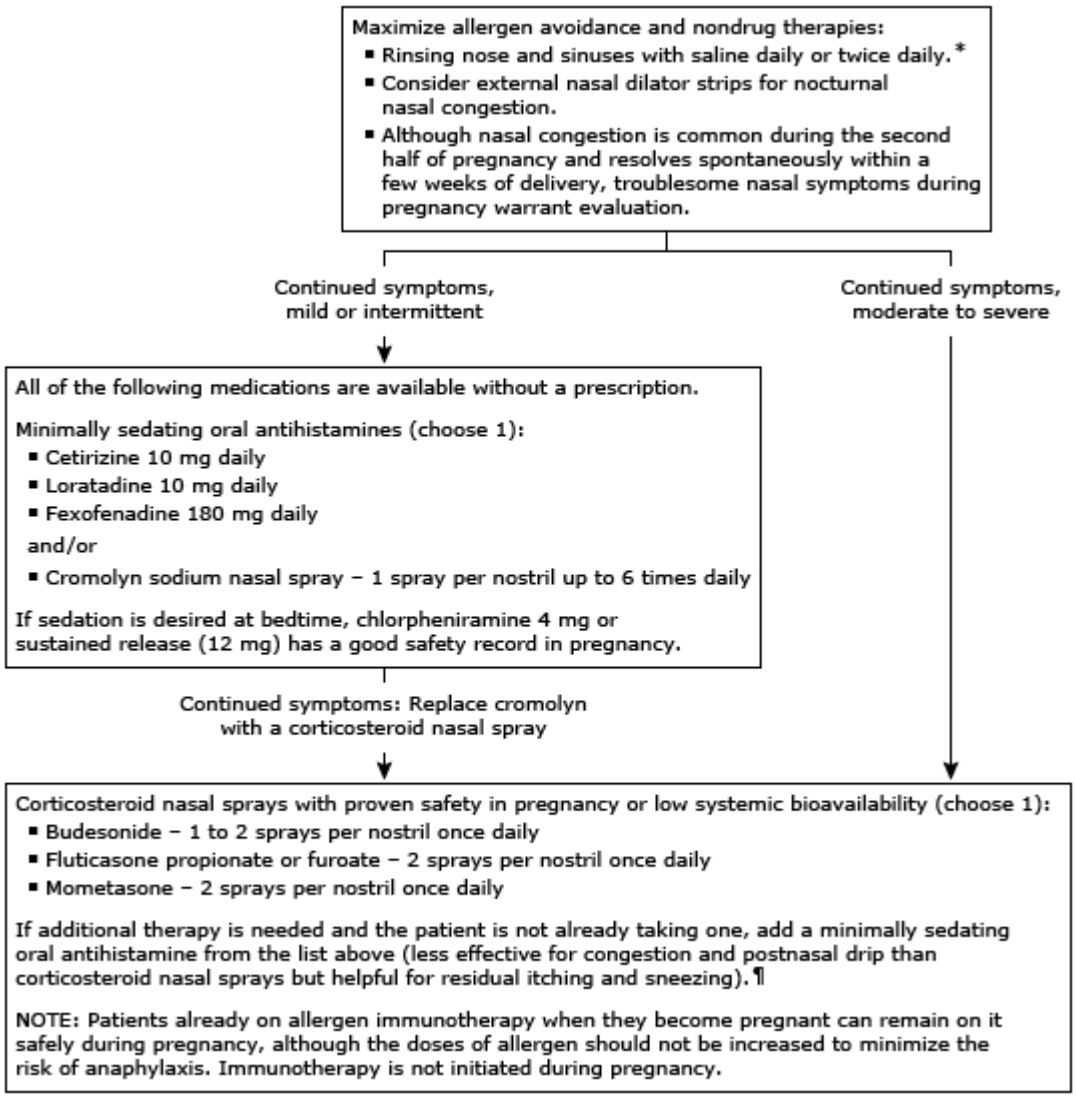
	daily	eye twice daily
Lodoxamide 0.1% (Alomide)	One to two drops per eye 4 times daily for up to 3 months	>2 years: One to two drops per eye 4 times daily for up to 3 months
Pemirolast 0.1% (not available in US but may be available in other countries)	One to two drops per eye up to 4 times daily for up to 4 weeks	≥3 years: One to two drops per eye up to 4 times daily for up to 4 weeks

United States trade names are shown in parentheses following generic name.

OTC: over the counter (available without a prescription).

Graphic 91098 Version 15.0

Treatment of allergic rhinitis in pregnancy



* The nasal passages can be rinsed with a saline spray or the lower sinuses can be rinsed with larger volumes using a neti pot or squeeze bottle. Refer to UpToDate content on pharmacotherapy for allergic rhinitis, discussion of nasal saline.

¶ Medications that are generally avoided in pregnancy include oral decongestants (especially in the first trimester), antihistamine nasal sprays (due to lack of human data), and herbal therapies (not regulated and thus could contain contaminants).

Graphic 134600 Version 3.0

Therapies for allergic rhinitis in lactating women

Drug category	Amount passed to infant in breast milk	Conclusions about maternal use during breastfeeding
Intranasal glucocorticoid sprays (budesonide preferred)	Minimal	Compatible.
Second-generation oral antihistamines		
Cetirizine	Minimal to small amounts	Large doses or prolonged use may cause sedation in nursing infant. May decrease milk supply if combined with a sympathomimetic.
Loratadine	Minimal to small amounts	Compatible but might reduce milk supply if combined with a sympathomimetic, such as pseudoephedrine.
Antihistamine nasal sprays	Minimal	Probably compatible. Use intranasal glucocorticoid preferentially.
Oral decongestants		
Pseudoephedrine	Passes into milk	Use short-acting preparations only and take just after breastfeeding to minimize amount entering milk. Use intranasal glucocorticoid preferentially fo persistent congestion. Use topical vasoconstrictor nasal spray for therapy of less than four days.
Phenylephrine	Little information available	Not recommended.
Cromolyn nasal spray	Insignificant	Compatible.
Leukotriene-receptor antagonists		
Montelukast	Unknown	Use only if other compatible agents are not sufficient and symptoms are significant. Avoid in newborn or preterm infant.
Zafirlukast	About 20%	Use only if other compatible agents are not sufficient and symptoms are significant. Avoid in newborn or preterm infant.
Ipratropium nasal spray	Unknown; maternal serum levels are negligible and milk levels will be very low, if at all; any drug in milk	Probably compatible.

	would not be absorbed by the infant	

References:

1. *Incaudo AF, Takach P. The diagnosis and treatment of allergic rhinitis during pregnancy and lactation. Immunol Allergy Clin N Am 2006; 26:137.*
2. *Briggs GG, Freeman RK, Yaffe SJ. Drugs in pregnancy and lactation, 10th ed, Lippincott Williams & Wilkins, Philadelphia 2015.*
3. *LactMed: United States National Library of Medicine. https://www.ncbi.nlm.nih.gov/books/NBK501922/.*

Graphic 58772 Version 7.0

How to perform nasal irrigation

Buffered normal saline nasal irrigation

The benefits

- Saline (saltwater) washes the mucus and irritants from your nose.
- The sinus passages are moisturized.
- Studies have also shown that a nasal irrigation improves the function of cilia (tiny hair-like structures on cells that move the mucus).

The recipe

1. Use a one-quart glass jar that is thoroughly cleansed.
2. You may use a large medical syringe (30 cc), water pick with an irrigation tip, squeeze bottle, or Neti pot. Do not use a baby bulb syringe. The syringe or pick should be sterilized frequently or replaced every 2 to 3 weeks to avoid contamination and infection.
3. Fill with water that has been distilled, previously boiled, or otherwise sterilized. Plain tap water is not recommended, because it is not necessarily sterile.
4. Add 1 to 1½ heaping teaspoons of pickling/canning salt. Do **not** use table salt, because it contain a large number of additives.
5. Add 1 teaspoon of baking soda (pure bicarbonate).
6. Mix ingredients together and store at room temperature. Discard after 1 week.
7. You may also make up a solution from premixed packets that are commercially prepared specifically for nasal irrigation.

The instructions

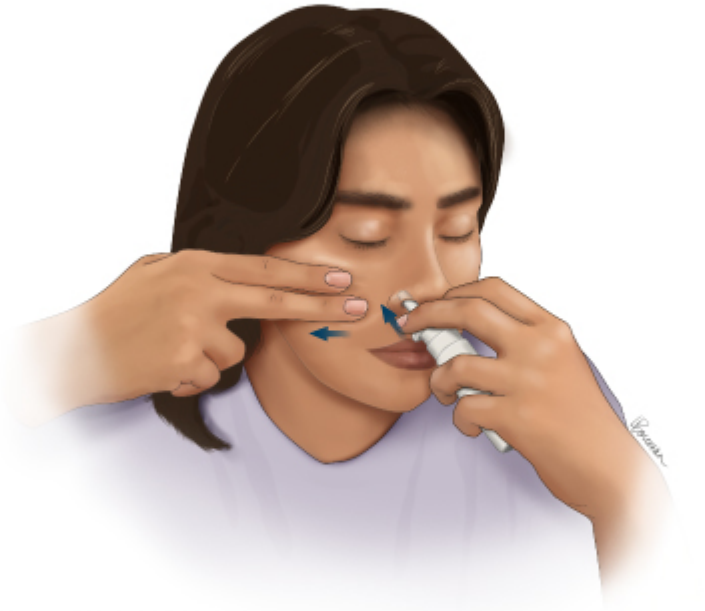
Irrigate your nose with saline 1 to 2 times per day.

- If you have been told to use nasal medication, you should always use your saline solution first. The nasal medication is much more effective when sprayed onto clean nasal membranes, and the spray will reach deeper into the nose.
- Pour the amount of fluid you plan to use into a clean bowl. Do **not** put your used syringe back into the storage container, because it contaminates your solution.
- You may warm the solution slightly in the microwave but be sure that the solution is **not hot**.
- Bend over the sink (some people do this in the shower) and squirt the solution into each side o your nose, aiming the stream toward the back of your head, **not** the top of your head. The solution should flow into one nostril and out of the other, but it will not harm you if you swallow a little. Avoid blowing your nose for about 15 minutes (this is especially helpful if the solution sometimes gets trapped in your ears).
- Some people experience a little burning sensation the first few times that they use buffered saline solution, but this usually goes away after they adapt to it.

Graphic 71059 Version 17.0

How to use a nasal spray properly

1. Blow your nose gently.
2. Shake the spray bottle to make sure the medicine is well mixed. Remove the cap.
3. Spray once or twice into the air until a good mist is dispensed.
4. Tuck your chin in and tip your head forward slightly.
5. To spray in the left side, use 1 or 2 of your left fingers to widen your left nostril slightly by pulling the skin near the nostril to the side. Use your right hand to hold the nasal spray. Put the nozzle into the left nostril, and spray away from the membrane in the middle of the nose (called the nasal septum). Spraying at the septum can cause irritation and sometimes minor bleeding. Think of aiming the spray towards the outside corner of your left eye. If this hand positioning feels awkward, you can skip the step of pulling the nostril open and just spray with either hand, but it is important not to spray directly at the septum.



6. Do not sniff until the medicine is dispensed, but you can close your mouth and inhale gently to keep the medicine from running out of the nose. If you sniff too vigorously, the medicine will go down your throat, where it does nothing for your nasal symptoms.
7. To spray the right side, use 1 or 2 of your right fingers to pull your right nostril slightly open and use your left hand to hold the nasal spray. Follow the same instructions as above, pointing the spray towards your right ear.

If you are also doing saline nasal irrigations, do those first and then wait 5 to 10 minutes before using your nasal spray medication. Waiting allows the irrigation to drain completely from the nose and increases the chance that medicine sprayed into the nose afterwards will be absorbed as fully as possible by the clean nasal lining.

Graphic 141563 Version 2.0