***Allergic Rhinitis***

**Pathophysiology and Therapeutics PY-2**

**Cardiopulmonary II Module**

**Spring 2012**

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**Purpose:** The goal of this self-learning topic is to help you understand the pathophysiology and treatment modalities available for allergic rhinitis. After independently reviewing the suggested readings, you will be able to answer the following learning objectives. **Please note that allergic rhinitis will be incorporated into exam #1 for this module. Allergic rhinitis will also be the main topic for the PY-2 spring recitation final written SOAP note.**

**Required Readings:**

1. Pharmacotherapy: A Pathophysiologic Approach, 8th Edition. Dipiro JT, Talbert RL, Yee GC et al. Chapter 104: Allergic Rhinitis, p. 1649-1660.
2. Melvin TA, Patel AA. Pharmacotherapy for Allergic Rhinitis. *Otolaryngol Clin N Am* 2011; 44:727-739.

**Objectives:**

1. Explain the pathophysiology of allergic rhinitis.

* In a sensitized individual, allergic rhinitis occurs when inhaled allergenic materials contact mucous membranes and elicit a specific response mediated by immunoglobulin E (IgE).
* This acute response involves the release of inflammatory mediators and is characterized by sneezing, nasal itching, and watery rhinorrhea, often associated with nasal congestion. Itching of the throat, eyes, and ears frequently accompanies allergic rhinitis.

1. Differentiate between seasonal and perennial rhinitis, including common allergen triggers associated with both. Also, distinguish between intermittent and persistent rhinitis.

* Allergic rhinitis may be regarded as seasonal allergic rhinitis, commonly known as *hay fever*, or perennial allergic rhinitis (increasingly called intermittent and persistent).
* Seasonal rhinitis occurs in response to specific allergens usually present at predictable times of the year, during plants' blooming seasons (typically the spring or fall). Seasonal allergens include pollen from trees, grasses, and weeds.
* Perennial allergic rhinitis is a year-round disease caused by nonseasonal allergens, such as house-dust mites, animal dander, and molds, or multiple allergic sensitivities. It typically results in subtler, chronic symptoms.

1. Identify the underlying risk factors that predispose patients to developing allergic rhinitis.

* The development of allergic rhinitis is determined by genetics, allergen exposure, and the presence of **other risk factors**.
* A family history of allergic rhinitis, atopic dermatitis, or asthma suggests that rhinitis is allergic.
* The risk of developing allergic disease appears to increase if one parent is atopic and further increases if two are allergic; however, small sample sizes and the lack of reproducibility prevent generalization.
* For allergic rhinitis to occur, an individual must be exposed over time to a protein that elicits the allergic response in that individual.
* Other predisposing factors include: an elevated serum IgE (>100 international units/mL [>100 kIU/L]) before the age of 6 years, eczema, and heavy exposure to secondhand cigarette smoke.

1. Compare and contrast immediate versus late-phase hypersensitivity reactions involved in allergic rhinitis.

* Both immediate and late-phase reactions are observed after allergen exposure.
* The immediate reaction occurs within seconds to minutes, resulting in the rapid release of preformed mediators and newly generated mediators from the arachidonic acid cascade as the mast cell membrane is disturbed.
  + These mediators of immediate hypersensitivity include histamine; leukotrienes C4, D4, and E4; prostaglandin D2; tryptase; and kinins.
* Four to 8 hours after the initial exposure to an allergen, a late-phase reaction occurs symptomatically in 50% of allergic rhinitis patients.
  + This response, thought to be caused by cytokines released primarily by mast cells and thymus-derived helper lymphocytes, is characterized by profound infiltration and activation of migrating cells. This inflammatory response likely is responsible for the persistent, chronic symptoms of allergic rhinitis, including nasal congestion.

1. Describe the clinical presentation of a patient with allergic rhinitis.

* The patient with allergic rhinitis typically complains of clear rhinorrhea, paroxysms of sneezing, nasal congestion, postnasal drip, and pruritic eyes, ears, nose, or palate.
* Symptoms of allergic conjunctivitis are associated more frequently *with seasonal than perennial* allergic rhinitis, because a majority of the perennial allergens, such as dust mites and molds, are indoors, where air velocity is too low for substantial deposition of allergenic particles on the conjunctivae.
* Symptoms secondary to the late-phase reaction, predominantly nasal congestion, begin 3 to 5 hours after antigen exposure and peak at 12 to 24 hours.
* For children, physical exam may reveal allergic shiners, a transverse nasal crease caused by repeated rubbing of the nose, and adenoidal breathing. Nasal turbinates are coated with thin, clear secretions. Tearing and periorbital swelling may be present.

1. Outline the different allergy skin tests available for diagnosing allergic rhinitis patients and identify the medications that must be avoided prior to this testing.

* Percutaneous skin tests with diluted allergen, positive control (histamine), and negative control are used to identify to what the patient has sensitivities.
  + Or by the intradermal route, where a small volume (0.01 to 0.05 mL) of diluted allergen is injected between the layers of skin.
  + Percutaneous tests are more commonly performed and are safer and more generally accepted, with intradermal tests reserved for patients requiring confirmation in special circumstances.
* Also, a radioallergosorbant (RAST) test can detect IgE antibodies in the blood that are specific for a given allergen. These tests are highly specific but may be slightly less sensitive than percutaneous tests.
* First-generation antihistamines should be stopped 3 to 5 days before testing, and second-generation, nonsedating antihistamines should be stopped for 10 days before testing.
* Medications with antihistamine properties (e.g., sympathomimetic agents, phenothiazines, and tricyclic antidepressants) should be discontinued before skin testing.

1. Recognize the complications of untreated allergic rhinitis and other disease states that may occur in these patients.

* Symptoms of untreated rhinitis may lead to disturbed sleep, chronic malaise, fatigue, and poor work or school performance.
* Patients often are plagued by loss of smell or taste, with sinusitis or polyps underlying many cases of allergy-related hyposmia.
* Postnasal drip with cough, hoarseness, and even vocal polyps also can be bothersome.
* Structural facial and dental problems can result from chronic allergic rhinitis.17,18 The chronic edema and venous stasis may contribute to the development of a high-arched, V-shaped palate.
* Children with allergic rhinitis appear to be at greater risk of otitis media conditions because of nasal obstruction and negative middle ear pressure.
* Constant upward rubbing of the nose (allergic salute) can cause a transverse crease across the lower nose; nasal congestion often leads to venous pooling and dark circles under the eyes known as allergic shiners.
* Recurrent sinusitis and chronic sinusitis are relatively common complications of allergic rhinitis.
* Epistaxis also can be a problem; it is related to mucosal hyperemia and inflammation.
* Allergic rhinitis is clearly a risk factor for asthma. The majority of asthma patients have nasal symptoms, whereas approximately 10% to 40% of rhinitis patients have asthma.

1. Establish environmental controls that may reduce allergic rhinitis symptoms.

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| |  |  | | --- | --- | | |  | | --- | | **Table 104-3 Environmental Controls to Prevent Allergic Rhinitis** | | | |  | | --- | | **Pollens**   * Keep windows and doors closed during pollen season * Avoid fans that draw in outside air * Use air conditioning * If possible, eliminate outside activities during times of high pollen counts * Shower, shampoo, and change clothes following outdoor activity * Use a vented dryer rather than an outside clothesline | | [**Molds**](javascript:PopupGlossaryTerm(2753490);)   * Use similar controls as above * Avoid walking through uncut fields, working with compost or dry soil, and raking leaves * Clean indoor moldy surfaces * Fix all water leaks in home * Reduce indoor humidity to <50% if possible | | **House-dust mites**   * Encase mattress, pillow, and box springs in an allergen-impermeable cover * Wash bedding in hot water weekly * Remove stuffed toys from bedroom * Minimize carpet use and upholstered furniture * Reduce indoor humidity to <50% if possible | | **Animal allergens (if removal of pet is not acceptable)**   * Keep pet out of patient's bedroom * Isolate pet from carpet and upholstered furniture * Wash pet weekly | | **Cockroaches**   * Keep food and garbage in tightly closed containers * Take out garbage regularly * Clean up dirty dishes promptly * Use roach traps | | **Other recommendations**   * Do not allow smoking around the patient, in the patient's house, or in the family car * Minimize the use of wood-burning stoves and fireplaces | | |  | |

1. List the treatment options for allergic rhinitis, including: dosages, adverse effects, OTC status and patient counseling points.

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| |  |  | | --- | --- | | |  | | --- | | **Table 104-5 Oral Dosages of Commonly Used Oral Antihistamines and Decongestants** | | | |  |  | **Dosage and interval*a*** | | | --- | --- | --- | --- | | **Medication** | **Availability** | ***Adults*** | ***Children*** | | **Nonselective (first-generation) antihistamines** |  |  |  | | [Chlorpheniramine maleate](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5875');), plain*b* | OTC | 4 mg every 6 h | 6–12 y: 2 mg every 6 h | |  |  |  | 2–5 y: 1 mg every 6 h | | [Chlorpheniramine maleate](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5875');), sustained-release | OTC | 8–12 mg daily at bedtime or 8–12 mg every 8 h | 6–12 y: 8 mg at bedtime | |  |  |  | <6 y: Not recommended | | [Clemastine fumarate](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5914');) *b* | OTC | 1.34 mg every 8 h | 6–12 y: 0.67 mg every 12 h | | [Diphenhydramine hydrochloride](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=393211');) *b* | OTC | 25–50 mg every 8 h | 5 mg/kg per day divided every 8 h (up to 25 mg per dose) | | **Peripherally selective (second-generation) antihistamines** |  |  |  | | [Loratadine](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6481');) *b* | OTC | 10 mg once daily | 6–12 y: 10 mg once daily | |  |  |  | 2–5 y: 5 mg once daily | | [Fexofenadine](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6195');) | Rx | 60 mg twice daily or 180 mg once daily | 6–11 y: 30 mg twice daily | | [Cetirizine](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5857');) *b* | OTC | 5–10 mg once daily | >6 y: 5 mg once daily Infants 6–11 month*c* | | [Levocetirizine](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=325477');) | Rx | 5 mg every evening | 6–11 y: 2.5 mg every evening | | **Oral decongestants** |  |  |  | | [Pseudoephedrine](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6868');), plain*b* | OTC*e* | 60 mg every 4–6 h | 6–12 y: 30 mg every 4–6 h 2–5 y: 15 mg every 4–6 h | | [Pseudoephedrine](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6868');), sustained-release*d* | OTC*e* | 120 mg every 12 h | Not recommended | | [Phenylephrine](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6768');) *f* | OTC | 10–20 mg every 4 h | 6–12 y: 10 mg every 4 h 2–6 y: 0.25% drops, 1 mL every 4 h | |  |  |  | 2–6 y: 0.25% drops, 1 mL every 4 h | | |  | |

1. **Given a patient case, identify rhinitis medicamentosa secondary to topical decongestant use and recommend how to manage it.**

* rhinitis medicamentosa: Nasal congestion associated with tolerance to and resulting overuse of topical decongestants. Also known as *rebound vasodilation or rebound congestion*.
* Patients should be instructed to use as small a dose as possible as infrequently as possible and only when absolutely necessary (e.g., at bedtime to aid in falling asleep). Duration of therapy always should be limited to 3 to 5 days.
* Combining the weaning process with nasal steroids may prove useful. Ultimately, the success of any plan depends on the patient's resolve and clear understanding of the importance of stopping the drug to end the problem.

1. **Identify the pregnancy categories for individual agents used to treat allergic rhinitis and recommend a safe and effective treatment strategy for a pregnant woman suffering from allergic rhinitis.**

**Nasal saline.** Rhinitis of pregnancy tends not to respond to anti-histamines or nasal sprays. This condition seems to respond temporarily to nasal saline (salt water), which is safe to use during pregnancy (it is not actually a drug). Nasal saline is available over the counter, is inexpensive, and can be used as often as needed. Generally 3 to 6 sprays are placed in each nostril, leaving the saline in the nose for up to 30 seconds, and then blowing the nose.

**Anti-histamines.** Older anti-histamines, such as chlorpheniramine and tripelennamine, are the preferred agents to treat allergic rhinitis during pregnancy, and are both category B medications. Newer anti-histamines such as over-the-counter loratadine (Claritin®/Alavert® and generic forms) and prescription cetirizine (Zyrtec®) are also pregnancy category B medications.

**Decongestants.** Pseudoephedrine (Sudafed®, many generic forms) is the preferred oral decongestant to treat allergic and non-allergic rhinitis during pregnancy, although should be avoided during the entire first trimester, as it has been associated with infant gastroschisis.  This medication is pregnancy category C.

**Medicated nasal sprays.** Cromolyn nasal spray (NasalCrom®, generics) is helpful in treating allergic rhinitis if it is used before exposure to an allergen and prior to the onset of symptoms. This medication is pregnancy category B and is available over the counter. If this medication is not helpful, one nasal steroid, budesonide (Rhinocort Aqua®), recently received a pregnancy category B rating (all others are category C), and therefore would be the nasal steroid of choice during pregnancy.

**Immunotherapy.** Allergy shots can be continued during pregnancy, but it is NOT recommended to start this treatment while pregnant. Typically the dose of the allergy shots is not increased, and many allergists will cut the dose of the allergy shot by 50 percent during pregnancy. Some allergists feel that allergy shots should be stopped during pregnancy, given the risk of anaphylaxis and possible danger to the fetus as a result. Other than anaphylaxis, there is no data showing that the allergy shots themselves are actually harmful to the fetus.

1. Explain the role of immunotherapy in reducing allergic rhinitis symptoms.

* The therapy was first called *desensitization*; however, this did not seem appropriate because skin reactivity sometimes remained. The name was later changed to *hyposensitization*. Although this term is still used today, immunotherapy is used more commonly.
* Immunotherapy is the slow, gradual process of injecting increasing doses of antigens responsible for eliciting allergic symptoms into a patient with the hope of inducing tolerance to the allergen when natural exposure occurs.
* Several mechanisms have been proposed to explain the beneficial effects of immunotherapy, including induction of IgG-blocking antibodies, reduction in specific IgE (long-term), reduced recruitment of effector cells, altered T-cell cytokine balance (a shift from T-helper type 1 to T-helper type 2), T-cell anergy, and induction of regulatory T cells.
* The effectiveness of immunotherapy for seasonal allergic rhinitis appears to be better than that seen with perennial rhinitis.
* Data indicate that for some patients 3 years of immunotherapy may be sufficient to give lasting benefit; however, many require longer treatment.
* Adverse reactions can occur with immunotherapy and range from mild to life threatening. Because of this potential risk, immunotherapy must not be given without adequate direct observation in a medical facility.