RHINITIS

INTRODUCTION

Nasal symptoms are experienced in most people at times as a normal defense mechanism, and the threshold at which such symptoms are perceived as a problem vary. The diagnosis of rhinitis is based on the subjective reporting of nasal complaints in the absence of upper respiratory tract infection, other diseases, or structural abnormalities. To date, investigations for rhinitis have low sensitivity and specificity and the diagnosis, therefore, must be made predominantly on the basis of the clinical history. Diary recording of symptoms and their circumstances over a 2-week period may be helpful in borderline cases.

CLASSIFICATION OF RHINITIS

Rhinitis occurs mostly in patients aged 15-25 years, however it does occur also in patients over 45 years old. As with other allergic diseases, the prevalence of rhinitis is steadily increasing (Fig. 1).

Patients present with nasal irritation, sneezing, rhinorrhea, and nasal blockage, symptoms which may be seasonal or perennial. In allergic rhinitis there is usually a clear relationship with exposure to known allergens, most frequently pollens in seasonal rhinitis, and house dust mite or household pets in perennial rhinitis. The identification of an allergic trigger in the latter group is often difficult. In some patients there is no evidence of allergy. Some of these have vasomotor (autonomic) rhinitis, the major symptom of which is rhinorrhea, and, in the remainder, no allergen can be detected even though their symptoms are similar to those of allergic rhinitis (Fig 2).

Allergic rhinitis

Atopy, defined as the ability to produce high levels of IgE directed against common allergens, is very prevalent among young adults, with approximately 20–30% of adults and children 25-35%. The prevalence of allergic rhinitis in United States is around 15% or 50-60 million people. The majority of these patients are consulting their PCP’s.

The important allergens in allergic rhinitis vary in different parts of the country: in the United States grass pollinosis is commonest, in some parts of ragweed predominates (Fig. 3). In tropical climates, allergenic pollens may be present all year round, consequently the symptoms of pollen allergy may be perennial. Conversely, classically perennial allergens, such as the house dust mite, provoke seasonal symptoms in temperate climates where there are increased levels of mite allergens during the autumn (see Fig. 3). molds are less common causes of allergic rhinitis, owing to their small size, as they are more likely to be deposited in the lower airway by gravity-dependent sedimentation or inertial impaction than in the upper airway by turbulent airflow.
Occupational agents also cause allergic rhinitis. In fact, rhinitis is a more common manifestation of sensitization than asthma, the nasal mucosa being more accessible to deposition of dusts and vapors (e.g., baker's flour, isocyanates, wood dusts, and animal allergens) all of which can be associated with an IgE-mediated allergic response. Food allergens can also be a source of symptoms. Some food additives, such as meta bisulfite, can also provoke generalized allergic symptoms, including rhinitis.

It is likely that much allergic sensitization occurs in very early life when the immune system is immature (Fig. 4). The inheritance of atopy is likely to be polygenic. Gene-linkage studies have suggested an autosomal-recessive inheritance for elevated total IgE levels, but there are several levels of genetic control for specific and total IgE, skin test positivity, and disease specificity.

Environmental influences in the first year of life are important in the onset of allergic disease. Rhinitis is more common in individuals born in spring and summer. This was initially thought to indicate the influence of tree or grass pollen exposure in the first weeks of life. However, nonatopic rhinitis is also more common in those born in spring and summer, indicating that factors other than environmental pollens are responsible for this seasonality. There is evidence that early respiratory infections have a role in initiating IgE dysregulation, a fundamental feature of allergic disease. As the onset of allergic disease in children born to atopic parents is temporally related to early respiratory infections, it has been proposed that exposure of infants born in spring or summer to winter viral respiratory infections occurs at a vulnerable time, (i.e., after protective maternal immunoglobulins have fallen to a low level but before the infant's own immune system has developed fully). This theory is supported by detailed studies of infants with respiratory syncytial virus bronchiolitis showing the presence of virus-specific IgE and raised total circulating IgE, suggesting a direct association of viral infection with IgE.

Socio-economic factors are also important. A strong inverse relationship between hay fever and family size has been noted, with first-born children being at greatest risk. This relationship is independent of the social class of the father. IgE production is enhanced by cigarette smoking and, in infants and young children, parental smoking contributes to allergic sensitization and is associated with wheezing and the risk of rhinitis. The relative risk of rhinitis is doubled for children who live in damp houses and have parents who smoke. Modern energy-efficient 'tight' buildings encourage the growth of house dust mites and molds, because of higher humidity and warmth, and so increase exposure to potential allergens. Environmental pollution may also contribute to allergic sensitization.

Nonallergic rhinitis

Nonallergic rhinitis is defined by the absence of positive skin-prick tests or radioallergosorbent test (RAST) to common allergens. In practice, the diagnosis is usually dependent on there being no offending allergen apparent from the clinical history. As advancing age is associated with reduced IgE levels and a reduced prevalence of positive skin-prick tests or RAST, this may be a confounding factor when assigning rhinitics into atopic and nonatopic subgroups. Such age-related changes contribute to the fall in the apparent prevalence of allergy among perennial rhinitics from around 80% in childhood to under 20% in elderly people. Epidemiologic
studies of a population of nearly 3000 patients in Tucson, Arizona, have shown that the prevalence of symptoms of rhinitis is as high as 30% even in those with very low age-adjusted serum IgE scores. This emphasizes that there is a nonallergic subgroup to rhinitis.

The contribution of environmental pollutants and occupational agents to nonallergic rhinitis is uncertain. It is likely that there are many unrecognized agents which may contribute to development of rhinitis. Nonallergic rhinitis may be subdivided into eosinophilic and vasomotor subgroups although some authorities have included all nonallergic rhinitics under the term vasomotor rhinitis. As 'vasomotor' implies a predominantly vascular component to the disease, it seems appropriate to reserve this term for those who cannot be shown to have features of an inflammatory process. The presence of eosinophils in nasal secretions may be demonstrated by light microscopy. Patients with a history of predominantly watery rhinorrhea, who do not have eosinophilic secretions, may be included in the vasomotor subgroup, although ideally this group should be defined by a therapeutic response to parasympathetic blockage. The eosinophilic subgroup is very similar to the allergic rhinitis group, except for the absence of an identifiable allergen.

PHYSIOLOGY OF THE NOSE
The nasal epithelium rests on the basement membrane (lamina lucida, lamina densa, and lamina reticularis), a layer of connective tissue composed of collagen types III, IV, and Y, laminin, and fibronectin. The underlying lamina propria is characterized by high vascularity (Fig. 5). The arterioles have no internal elastic lamina and a porous basement membrane, which increases permeability and allows greater access for pharmacologic agents. There is an extensive capillary network, and the capillaries are fenestrated, allowing rapid transit of fluid across the capillary wall. Large cavernous vascular sinusoids are present in the lamina propria on the turbinates. These contribute to heating and humidification of inspired air. Beneath the lamina propria are periosteum and bone.

Innervation of the nose
Sensory innervation
The trigeminal nerve supplies afferent (sensory) fibers to the nasal mucous membrane. Activation of these fibers produces the sensations of irritation or pain, which often result in sneezing (Fig. 6).

Vascular innervation
Sympathetic fibers, which mainly follow the blood vessels, predominate. Release of their co-transmitters -noradrenaline and neuropeptide Y (NP-Y) -causes vasoconstriction and maintains the sympathetic tone of the sinusoids. Sympathetic tone fluctuates throughout the day with an increase in patency in alternate nostrils every 2-4 hours (the nasal cycle).

Parasympathetic fibers, arising in the sphenopalatine ganglion to form the vidian nerve, control vasodilatation and glandular secretion. The parasympathetic co-transmitters are acetylcholine and vaso-active intestinal peptide. Axon reflexes can be powerful in the nasal mucosa, resulting in vasodilatation and transudation with thickening of the mucosa. These reflexes may be initiated by the effect of irritants and inflammatory
mediators at sensory nerve endings and the transmitters include sensory neuropeptides, substance P, neurokinin A, and calcitonin gene-related peptide (CGRP). Additionally, sensory nerve activation can cause vasodilatation via neural connections from the trigeminal to the sphenopalatine ganglia and via central nervous reflexes. There are also nasobronchial reflexes which may be activated in asthmatics to promote reflex bronchoconstriction in response to nasal obstruction.

Control of mucus secretion
Mucus is secreted by goblet and serous cells in the epithelium, by submucosal serous glands, and by deep nasal glands. It is diluted by transudate from the blood vessels. Secretion is controlled by parasympathetic cholinergic nerves, but sympathetic stimulation and axon reflexes also enhance secretion.

Functions of the nose
Aside from the sense of smell, the nose provides 'air-conditioning' of inspired air and filtration of potentially harmful particulate matter (Fig. 7). The nose has a remarkable capacity to humidify inspired air, raising the temperature of room air to 32°C, and humidifying it to 98% relative humidity before it reaches the lungs. This is effected by fluid shift across the highly vascular mucosa and increasing blood flow through the sinusoids.

The narrow, irregular shape of the nasal cavity promotes turbulent air flow, which contributes to impaction of inhaled particles in the upper airway, a protective function against the inhalation of potentially harmful particles into the bronchial tree. Pollen grains, which are around 10 μm in size, are largely deposited in the nose, whereas turbulent air flow is insufficient to deposit particles less than 2 μm in size, such as mold spores, in the nose. These particles will usually reach the distal airways. Particles trapped in the nose are moved into the pharynx by mucociliary transport within 10-30 minutes of impaction, and subsequently swallowed. Additionally, 99% of water-soluble gases, such as sulfur dioxide, are prevented from reaching the lower airways because of passage over the nasal mucosa.

Pathophysiology
Nasal responsiveness
Increased nasal responsiveness, which may be measured in terms of both symptoms and nasal airway resistance (NAR), can be demonstrated in rhinitics by the response to the inhalation of nonspecific challenge agents such as histamine and methacholine. Although there is considerable overlap, measurements of NAR show significantly greater histamine responsiveness in rhinitics than in both atopic and nonatopic nonrhinitics (Fig. 8). Methacholine does not increase NAR and it causes a significant increase in nasal secretion only in rhinitics. This contrasts with bronchial hyperresponsiveness, in which there is a much closer association with symptomatic asthma and a strong correlation between the response to histamine and methacholine. It is likely that the pathogenetic mechanisms of rhinitis and asthma are very similar, with hyper-responsiveness being a cardinal feature in both conditions. The difference in responsiveness of the upper and lower respiratory tract may be explained by the absence of a smooth muscle response in the nose. The action of histamine on the vascular network thus remains effective in reducing airway patency by causing hyperemia and edema of the mucosa.
whereas methacholine acts predominantly on glandular secretion, with a much less potent effect on vasodilatation because of the dominance of sympathetic vasoconstrictor nerves. The importance of vascular congestion as the mechanism of nasal obstruction is demonstrated by the rapid response to vasoconstrictor sprays, which is not a feature of bronchoconstriction in asthma.

**Allergen provocation**

Early-and late-phase responses may be demonstrated in the nose after inhalation of allergen by sensitized individuals. Late-phase responses, with associated increases in symptoms and NAR, occur in approximately 50% of patients between 2 and 8 hours after allergen provocation. The physiologic changes of the late phase can be very subtle compared to the intense blockage and symptoms of the early phase (Fig. 10). Small increases in NAR during the late phase may be obscured by the nasal cycle. Recent research suggests that platelet activation factor (PAF) and other mediators can increase the nasal response to bradykinin and histamine.

**Priming**

During the pollen season, sensitized individuals are exposed to low levels of pollen for a prolonged period. This differs markedly from the artificial conditions of allergen challenge in the laboratory where large doses of allergen over a short period of time are usually required to evoke a response. Thus, during the pollen season, a sensitized person may become increasingly responsive to allergen, a process known as priming. This may be simulated in the laboratory by repeated allergen challenge after which the dose of allergen required to elicit a response may be reduced by up to 100 times.

**Inflammatory cells and mediators**

**Mast cells**

Studies of the nasal mucosa have shown that the total numbers of mast cells are higher in atopic rhinitics when compared with nonrhinitics (Fig. 11). Moreover, in rhinitics the numbers of both mast cells and eosinophils in the mucosa increase during the pollen season (Fig. 12). The number of circulating mast cell and basophil progenitors is also increased in such patients and falls during the pollen season, suggesting that these cells are being recruited to the site of allergic inflammation.

Following allergen inhalation, evidence of mast cell degranulation can be seen in nasal mucosal biopsies and increased levels of mast cell products may be detected in nasal lavage fluid. Mast-cell mediators are responsible for many of the immediate symptoms of nasal allergy. A large number of inflammatory mediators have been identified (see Fig. 11).

**Histamine is the mediator which is most consistently found following allergen challenge.**

**Eosinophils**

Eosinophil numbers are increased in rhinitics, and rise during the pollen season in pollen-sensitive individuals (Fig. 13). Eosinophils increase transiently in nasal mucosal biopsies from pollen-sensitive rhinitics 30 minutes after allergen challenge, but the numbers in nasal secretions are persistently raised, and peak at 7-10 hours. This suggests rapid migration from the mucosa into the secretions. The chemo-attractants involved in
this process remain to be identified, although they may include leukotriene B4 (LTB4), PAF, eotaxin, and adhesion molecules (VCAM-1). The eosinophils are activated, with hypo dense granules, and can damage nasal epithelial cells slowing and disorganizing the ciliary beat. The influx of activated eosinophils results in the release of toxic granule products, particularly eosinophilic peroxidase (EPO) and major basic protein (MBP), which are toxic to cultured human nasal epithelial cells and cause lysis. Even at low concentrations, MBP can reduce ciliary beat frequency. Such damage may contribute to the inflammatory features of the late-phase response and subsequent nasal hyper-responsiveness.

Dendritic cells and T cells

The number of both dendritic (or Langerhans') cells and T cells at the surface of the nasal epithelium is increased in rhinitis. The interaction of dendritic cells (which process and present allergen) with T cells promotes differentiation of T cells towards the IL-4 and IL-5 producing the helper T cell type 2 (Th2) subtype, leading to IgE production by plasma cells and eosinophil activation respectively. In-situ hybridization studies have shown increased numbers of T cells from atopic rhinitics expressing mRNA for IL-4 and IL-5.

DIAGNOSIS OF RHINITIS

The diagnosis of rhinitis in a patient complaining of upper airway problems consists of obtaining a detailed history and performing a physical examination supplemented by critical tests (such as skin testing or RAST). Further laboratory, radiologic, and morphologic examinations may also be performed if considered necessary.

History

A detailed history augmented with specific questions, presented in the form of either a structured oral interview or a written questionnaire, is essential to distinguish rhinitis from upper respiratory infections or other nasal complaints. Such a questionnaire should cover the following:

- Is there a family history of atopy?
- What is the symptom profile - is there a dominant nasal symptom, such as blockage, sneezes, or nasal secretions?
- Are the nasal problems isolated or are there more extensive symptoms?
- Are there concomitant signs from other parts of the upper airways, such as sinuses or ears?
- Is there a history of lower airway, ocular, or dermatologic disease?
- How would you describe the symptoms and what is the chronology of their onset?
- Are there potential allergens in the house environment, e.g. bedding materials, any pets, low quality of housing?
- Are there any specific precipitating factors (e.g. flowers)?
- Is there any relationship to food or drink?
- What are the occupation and leisure activities, particularly those which aggravate symptoms?
- What is the impact of problems on lifestyle?

Symptom presentation

The traditional symptoms are as follows: nasal blockage, itching, sneezing bouts, and increased nasal surface fluid, but the dominant symptom may differ from one patient to another. There is also a wide individual variation
in terms of the tolerability of nasal symptoms. Some people may find a few bouts of sneezing troublesome, while others do not seek medical advice even when their nasal passage is completely blocked. A detailed symptom score registration may well prove helpful when it comes to assessing the severity of rhinitis.

The variability of symptoms may be a result of the difference in the pathogenesis of the major nasal symptoms. Nasal blockage is the result of a decrease in the tone of the capacitance vessels and, to a minor degree, tissue edema. The increase in nasal surface liquid is the result of glandular activity, the leakage of plasma, and the increase in fluids from other sources, such as the conjunctiva. Conjunctival symptoms of itching and increase in tear fluid are also very common in association with allergic rhinitis: the term rhinoconjunctivitis is often more relevant.

Physical examination
Several facial features are associated with the various symptoms of the nasal and ocular disease (Fig. 14 – The Allergy Salute). These include:
- ‘allergic shiners’ -infra-orbital dark circles, related to venous plexus engorgement;
- ‘allergic gape’ or continuous open-mouth breathing -a result of nasal blockage;
- ‘transversal nasal crease’ -a result of the frequent upward rubbing of the nose;
- dental malocclusion and overbite resulting from longstanding upper airway problems.

Rhinoscopy
A rhinoscopy is essential in the clinical workup of nasal problems, especially since there are several possible explanations of nasal problems. Simple inspection will reveal any external nasal deformities, but there may also be inner septal deformities. The rhinoscopic examination can be made using the traditional light-mirror (or light), and a nasal speculum to widen the nasal opening. The posterior rhinoscopy is performed with a mirror placed below the soft palate to permit the inspection of the epipharyngeal region. When possible this examination should be supplemented with an endoscopic examination of the nasal cavities and epipharyngeal region. This examination is performed using either a short rigid rhinoscope (or a short flexible rhinoscope, which is also useful for examining the posterior parts of the nasal cavity, as well as permitting examination of the epipharynx and larynx.

The following findings should be noted:
- any structural deformities, such as septal deviations. The site of any deformity should be specified and the presence or absence of polyps should be recorded (Fig. 15 Norma; Nose +16 small nasal polyp);
- the amount and the condition of nasal surface liquids (e.g. watery, mucoid, or purulent), which can be useful in differentiating infection from other conditions;
- the condition of the mucous membranes and the color, texture, and signs of scars and lesions should be specifically evaluated. An allergic condition might be indicated by the traditional bluish tint;
- unilateral nasal obstruction may also indicate a foreign body.
Additional tests
Tests for the presence of allergy

• The history and physical examination needs (mandatory) to be supplemented with an allergen-reactivity test.

Skin tests and RAST (Fig. 17)

The routine test for allergy of the upper airways is the skinprick test (SPT) or RAST. It should be carried out when there are no other obvious reasons for the nasal symptoms.

Differential diagnosis
The most common differential diagnosis is perennial non allergic rhinitis. The more common problems which the physician sees are endocrine disturbances, such as nasal congestion as a complication of pregnancy, oral contraceptives, or hypothyroidism, giving rise to a thickened and edematous nasal mucosa. Rhinitis medicamentosa with a rebound vasodilatation (side-effects of terbutaline and reserpine) often produce an edematous and red nasal mucosa which should not be confused with true rhinitis.

It is important to be aware of other diseases which may present with nasal symptoms. Uncharacteristic features, such as unilateral nasal blockage, bleeding, or pain, may suggest other pathologies (e.g. malignant tumors or Wegener's granulomatosis. In infants, unilateral nasal blockage and discharge may also be caused by the presence of a foreign body or, rarely, congenital choanal atresia. Septal deviation, whether congenital or traumatic, may cause nasal blockage, but it is unlikely to be noticed for the first time in adulthood unless there is superadded rhinitis. Chronic infective rhinosinusitis can usually be differentiated by its predominantly greenish secretions and infective exacerbations, although it can occur in association with perennial rhinitis because of impaired drainage from the sinuses.

Allergen avoidance
Avoidance regimens improve symptoms by decreasing the exposure to allergens which trigger the allergic reactions. This approach is usually successful, and should be strictly enforced when there is an allergic reaction to foods, drugs, or animals. Because seasonal pollens and molds have a widespread airborne distribution, complete avoidance of these allergens is difficult if not impossible. Sometimes a total change of environment might be of value.

Measures designed to reduce the degree of mite exposure in the home include covering mattresses, boxsprings, duvets, and pillows in vinyl or synthetic materials. Breathable allergen-proof covers are now available for mattresses, pillows, and duvets. More extreme measures include the removal of upholstered furniture, stuffed animals, carpeting, and wall hangings to eliminate dust traps. Superheated steam cleaners remove or denature house dust mite, mold, and pet allergens. However, the cost:benefit ratio of taking more drastic measures, such as major house renovation, is poor. Careful and regular cleaning with a wet mop is important. The benefit of local air filtration is limited, and calls for careful maintenance of the filters if it is to be useful. The effects of animal dander.
can be reduced by washing the animal once a week.

It is also important to try to eliminate other local irritants as much as possible. The importance of a nonsmoking environment cannot be stressed enough.

**Drug treatment**

Several pharmacologic agents are available for the treatment of hay fever symptoms, most of which have different efficacy profiles, as is shown in Figure 19. A combination of drugs with different effect profiles can be productive. The conjunctivitis which is often present, and as troublesome as the nasal symptoms, should also be treated.

**ALLERGIC CONJUNCTIVITIS**

Allergic inflammation of the ocular surface (the lid margins, conjunctiva and cornea; Fig. 20) is one of the commonest ocular disorders. In its mildest form, the conjunctiva becomes inflamed in response to a transient allergen (e.g. pollen in seasonal allergic conjunctivitis), or a persistent allergen (e.g. house dust mite in perennial allergic conjunctivitis) producing unpleasant symptoms but not threatening sight.

Seasonal and perennial allergic conjunctivitis

These disorders are the commonest forms of allergic conjunctivitis and are similar except in their time course, which is determined purely by the duration of exposure to the causative allergen. In seasonal allergic (hayfever) conjunctivitis (SAC), the offending allergens are plant pollens and spores and clinical manifestations occur only during the seasons in which high atmospheric concentrations of these allergens are reached). In perennial allergic conjunctivitis (PAC), the allergens (most commonly house dust mite, but also animal dander, mold, etc.) and, therefore, the symptoms and signs, are present year-round. In both conditions the eyes are itchy, watery, sticky and red but any visual disturbance is mild, caused by excessive tearing and production of mucus. Contact lens wearers may find that their lens tolerance decreases while the condition is active. The clinical appearance is of a mild conjunctival inflammation and clinical signs may be very slight. The bulbar and tarsal conjunctivae show mild to moderate hyperemia, edema and infiltration (loss of transparency and thickening resulting from inflammatory infiltration).