

CURRENT THERAPY IN ALLERGY AND IMMUNOLOGY 1983-1984

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PREFACE

The past decade has witnessed a virtual explosion in the awareness, knowledge, and understanding of diseases in which abnormalities in the expression of immune function play a proven or presumed role. Despite this rapid acceleration in understanding, a rational basis for the therapy of many of these diseases continues to elude us owing to the complexity of the immune system. There are several excellent textbooks devoted to immunological diseases; however, these almost invariably deal primarily with pathogenesis, basic mechanisms of disease expression, and clinicopathologic features. Therapy is not emphasized since, with regard to immune-mediated diseases, this information is often difficult to extract from the literature. As in any rapidly evolving field of medicine, significant differences of opinion often exist with regard to optimal therapy. This is compounded by the fact that therapeutic results which are reported for diseases which are usually chronic and with fluctuating courses are often divergent and can be misleading to the clinician. Thus, a summary of the literature is often not helpful since the information may tend to confuse the reader. In the present volume we have sought to fill the need for a concise but thorough guideline to the therapy of these diseases. We have left pathogenetic considerations and clinicopathologic manifestations of these diseases to be covered elsewhere and have assumed that the diagnosis has been well established at the point where the reader consults this text. Diagnostic considerations are only described when they influence the choice of therapeutic modalities.

Of critical importance to the success of this

venture is the quality and experience of the authors who participated. We have chosen authors who are widely recognized clinical investigators active in the study and treatment of the diseases about which they write. They are at the cutting edge of the therapeutic research relating to the diseases which they discuss. Since references to the literature have not been included, we have asked the authors to focus on the precise therapeutic approach which they themselves take toward a particular disease entity and have stressed that they supply precise details such that the readers can readily employ this approach in their own patients. We believe that our colleagues have done an admirable job, and we are greatly appreciative of the efforts that they have applied.

Since the knowledge and understanding of the immunologic diseases are still in a rather dynamic state, particularly with regard to therapeutic modalities, we plan to revise the text frequently in accordance with the information accrued.

We would like to acknowledge the encouragement and skillful assistance of our publisher, Mr. Brian Decker, as well as the editorial assistance of Ms. Margaret Askey and Ms. Ann London. Our major debt, however, is to the investigators who so graciously shared their knowledge with us and with their profession.

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January, 1983

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ALLERGIC RHINITIS

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Seasonal allergic rhinitis due to pollens (hay fever) is relatively easy to identify by a history of recurrent seasonal problems lasting a month or two at a time when specific pollens are known to be prevalent. In the eastern and midwestern United States, the spring season brings tree pollens from early February to May and grass pollens somewhat later in May and June. In August and September ragweed pollens appear and affect some 5 percent or more of the population. In the Rocky Mountain and Pacific states the seasonal picture tends to be blurred, because many plants have long and variable periods of pollination. In the Southwest, the mountain cedar tree pollinates in February, producing a syndrome peculiar to this area. A physician usually learns to recognize allergic rhinitis caused by the plants growing in his region.

Most patients will seek medical advice only after having tried over-the-counter drugs with little success. The common hay fever remedies that are so heavily advertised contain an antihistamine, either alone or in combination with a decongestant. While FDA rules at one time permitted antihistamine doses in over-the-counter preparations which were only about one-half the usual prescription dose, this rule has been relaxed in recent years and several preparations contain the same doses of these drugs as in products available on prescription. The patient may appear in the doctor's office either because of unsatisfactory control of symptoms or because symptomatic control is achieved only at the cost of unacceptable side effects. With these combinations, the most common side effect is drowsiness—a sensation of tiredness or a feeling of not being able to think straight—from the antihistamine, although some patients may have feelings of excitement or tension from the stimulants used as decongestants.

The suspicion of allergy should be confirmed by some objective means, such as a skin test. Introducing a small amount of extract of suspected allergens into the skin by intracutaneous injection,

scratch, or puncture leads to release of histamine and other mediators and the development of a wheal with surrounding erythema. This reaction is a reproduction of the manifestations of the disease in microcosm. Although the concept is simple, performance and accurate interpretation of skin tests is still something of an art and usually requires the specialist in allergy and immunology. Extracts for testing are subject to considerable variation in potency and are therefore difficult to standardize and store. Daily use of these materials by someone well versed in these problems is necessary to obtain diagnostically useful information.

The common allergic reactions are mediated by antibodies of the IgE class, and radioimmunoassay methods can detect these antibodies in serum. Although these techniques show considerable promise, they require so much technical expertise and such sophisticated reagents that results can be inaccurate. Laboratories that perform these tests are not effectively regulated at this time, hence the physician must be wary of quality. Considering that the price per test is five to ten times that of skin tests, these tests probably should be reserved for the occasional patient with unusual problems, or for those with skin diseases that preclude skin tests.

Once the physician is satisfied that a patient's rhinitis symptoms are due to allergy, the first question is whether exposure can be avoided. This consideration is often lost in a rush to prescribe drugs or employ immunotherapy. For widespread allergens such as pollens, which cannot be eliminated, exposure may be minimized by filtering the air in the house, office, or perhaps just the sleeping room. Ordinary room or home air conditioning, when the outside air is closed off and the inside cooled air is recirculated through a simple mechanical filter, removes most particles the size of pollen (10–25 μ), even though smaller dust particles and mold spores will be less efficiently removed. Electrostatic precipitators are much more efficient, can be added to forced air home heating and cooling systems, and will clean the air that passes through the device of essentially all particles larger than 0.1 μ . Tabletop units which clean the air in a single room are also available. Electrostatic precipitators lose efficiency as they become dirty and must be cleaned every few weeks. Windows and doors must be closed so that as little outside air enters as possible. These devices are to be distinguished from "air purifiers" and "ion generators" which add ions to the air but do not remove particulates. HEPA (high efficiency

particulate air) filters remove all but the smallest particles in one pass through a very fine pore replaceable paper filter and also are available in room size units.

When medications are needed, one may first try an antihistamine either alone or in combination with a decongestant. Patients have often used low potency over-the-counter preparations with little benefit or been put off by side effects of a particular agent. With the great variety of antihistamines available, it is sometimes possible to find a preparation that gives the patient little trouble. A trial of several different antihistamines is needed, as it is not possible to predict which agent will be most successful. Chlorpheniramine, 4 mg, is a good first choice and is effective for about 4 hours. Azatadine, 1 or 2 mg, is longer acting and requires only 2 doses a day. Antihistamines are most effective for hypersecretion, being less capable of relieving nasal congestion. Addition of a decongestant, such as pseudoephedrine, 30 or 60 mg, will help nasal stuffiness and also often counteract the drowsiness induced by an antihistamine. I prefer to give the two types of drug independently in order to vary the dosage of each to achieve a good balance.

Vasoconstrictor nose drops should be used infrequently because of the danger of habituation and rebound congestion requiring more frequent usage, with the eventual development of rhinitis medicamentosa. Topically applied antihistamines are essentially ineffective.

When antihistamines or decongestants are less than satisfactory, the physician can turn to corticosteroids topically applied in the nose. The three drugs available in the United States are flunisolide, beclomethasone, and dexamethasone. The brand names and recommended dosages of these drugs are listed in Table 1. They are simple to use and usually involve two sprays in each nostril by a freon-propelled unit (beclomethasone, dexamethasone) or a simple mechanical pump (flunisolide). In patients with seasonal problems, it is wise to initiate treatment at the first sign of symptoms, as control may take some days to achieve once severe nasal swelling has been allowed to develop. For severe cases, the recommended dosage can safely be increased either by using three sprays at a time or by using the steroid four times a day. Once symptoms are under control, usage can often be reduced to twice or even once a day for maintenance. Local side effects consist mainly of slight burning sensations immediately after spraying, a sensation that commonly disappears after a week of use. Moniliasis has been an exceedingly rare problem.

TABLE 1 Topical Nasal Corticosteroids Currently Available

Dexamethasone (Turbinaire), 100 mcg/spray (freon-propelled, micronized powder) Dosage: 2 sprays each nostril 3 times a day (1200 mcg/day)
Flunisolide (Nasalide), 25 mcg/spray (mechanical pump, propylene glycol solution) Dosage: 2 sprays each nostril 2 times a day (200 mcg/day)
Beclomethasone (Vancenase, Beconase), 42 mcg/spray (freon-propelled, micronized powder) Dosage: 1 spray each nostril 2 to 4 times a day (168–336 mcg/day)

When dexamethasone is used in the recommended dosage, systemic absorption of the steroid causes mild reductions in adrenal function; but, when tested, normal adrenal secretion has invariably returned within a few days after discontinuance of the drug. Even twice the recommended dosage of flunisolide and beclomethasone shows no evidence of causing adrenal suppression. Furthermore, a patient using the recommended dosage of orally inhaled beclomethasone for asthma can add nasal flunisolide or beclomethasone without inducing adrenal suppression.

Although these drugs are quite effective in controlling nasal symptoms, they may be less effective for eye symptoms. Vasoconstrictor eye drops may suffice (naphazoline, 0.025 percent) when the problem is not too severe, but dexamethasone, 0.1 percent ophthalmic solution, may be necessary for adequate relief. Corticosteroids in the eye are contraindicated if there is any suspicion of viral or bacterial infection.

When the patient appears in midseason with a disabling attack of allergic rhinitis accompanied by complete nasal blockage and distressing eye symptoms, rapid control may not be possible with the drugs previously mentioned. In such cases, a short course of systemic corticosteroid is in order and will make the patient feel better within 24 hours. Prednisone, in oral doses starting from 25 to 40 mg a day with rapid reduction (5 mg a day) will usually be sufficient. The entire daily dose can be given at one time upon awakening in the morning. The advantage of oral administration is that dosage can readily be controlled, whereas injected long-acting steroids offer little opportunity for variation and therefore have an increased risk of systemic side effects. Topical steroid should be added as soon as nasal block-

age begins to be relieved and continued for maintenance as the systemic steroid is withdrawn.

Whatever the drug treatment, long-term control by desensitization or immunotherapy should be considered. Immunologic study shows that allergy "shots" with extracts specific for the patient's allergies induce development of specific protective antibodies of the IgG class within several months, and over several years cause a gradual reduction of the IgE antibodies that confer the allergic reaction. Patients with simple, short, seasonal problems readily controlled by drugs may not consider the result worth the effort and expense. On the other hand, patients with multiple or severe allergies may wish to be relieved of the necessity of taking medicine several times a day for long periods during the

year and may find a course of injections a reasonable alternative. Clinically, in controlled study, relief of symptoms has been good, although often less than complete. Patients usually appreciate the results and do not find the injections onerous once the initial series is completed. Maintenance or booster injections every four or even six weeks will usually continue satisfactory control. Immunotherapy is specific, both immunologically and clinically, and treatment for one allergy will do little to control the manifestations of another allergy. Consequently, accurate identification of the allergens responsible for the patient's symptoms is essential to good results. The well-trained specialist can best prescribe and carry out this method of treatment.

RHINITIS DUE TO ALLERGY TO ANIMALS

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A cat is nothing to sneeze at
(with apologies to O. Nash)

This chapter will consider the treatment of IgE-mediated respiratory allergies due to emanations arising from non-human mammalian sources (exclusive of foodstuffs of animal origin), which, when inhaled, can cause allergic respiratory symptoms. These allergies are often referred to as "animal dander allergy" or "epithelial allergy." However, because there is still some uncertainty about the exact tissue sources of the allergic substances from animals, we prefer the more noncommittal term "allergy to animals."

Lists of animal species that cause allergy are usually topped by cats or guinea pigs or rats. This is probably because these are the species to which people are exposed most often, either as pets or as research animals. It is also possible that these species are in some way more allergenic than others. Even within a species, some breeds appear to be more allergenic than others, for example, Siamese

cats. In the general adult population, the prevalence of allergy to cats is about 8 percent, to dogs about 3 percent. Among allergic individuals, the reported frequency of allergy to cats has ranged from about 10 percent up to 34 percent. Allergy to animals thus ranks just after allergy to pollens and allergy to house dust mites in prevalence. For information on the frequency of allergy to a long list of animal species, consult the literature.

When exposure is most intense, for example, among laboratory workers, the onset of clinically significant allergic sensitivity usually requires 1 to 3 years of contact, although a month's exposure has been sufficient in some cases. Once established, allergy to an animal may persist for years, even in the absence of apparent contact. Each contact presumably serves to maintain or boost the level of sensitivity, as each pollen season does in pollen allergy.

The largest proportion of airborne particles in indoor air is derived from mammalian epithelium. These are mainly dander particles, that is, the dead skin scales that are continuously shed from the epidermis and trapped in the hair before being shed into the environment. Also present in indoor air and emanating from animals are droplets of moisture from expired air and, particularly in laboratory animal quarters, dust particles coated with urine and feces. Animal allergens are associated with all of these particles, many of which are sufficiently small to be respirable.