

Allergy: conventional and alternative concepts

SUMMARY OF A REPORT OF THE ROYAL COLLEGE OF PHYSICIANS COMMITTEE ON CLINICAL IMMUNOLOGY AND ALLERGY

Introduction

The RCP booklet on *Allergy—conventional and alternative concepts* has been written for doctors and patients alike [1]. Its aim is to provide a brief summary of how the common allergic diseases are diagnosed and treated by conventional allergists using scientific and validated techniques and remedies. The approaches of practitioners of alternative allergy have also been appraised.

The introductory section lays emphasis on the definition of allergy. Allergy must be regarded as a form of exaggerated sensitivity (hypersensitivity) in which there is a specific alteration of the immune system. However, there is still confusion amongst the general public, and many doctors, as to what constitutes a true allergic disease. For this reason allergy (and its mimics) is divided in the booklet into four broad categories. *Category 1* includes the common atopic allergic diseases such as allergic rhinitis (including hayfever), allergic (atopic) asthma, and immediate anaphylactic reaction to foods. These are all IgE-mediated and involve mast cells, histamine and other pharmacological agents. *Category 2* contains the non-IgE-mediated hypersensitivity diseases such as contact dermatitis, extrinsic allergic alveolitis (eg farmer's lung, bird fancier's lung) and coeliac disease. Here a variety of other immunological mechanisms are proposed such as T-cell-mediated hypersensitivity and immune complex disease. There is a third group (*category 3*) in which conditions are attributable to external agents but are non-immunological. Food intolerance is an example (see below). *Category 4* consists of conditions such as chronic fatigue syndrome and certain psychological disturbances which have been incorrectly attributed to allergy. Most conventional doctors do not consider that there is an allergic basis to these disorders; but they have attracted the attention of practitioners of 'alternative allergy'. It may be the failure of

conventional medicine to classify, diagnose and treat these conditions satisfactorily that has frustrated many patients and led them to take recourse to unproven forms of treatment.

Allergic diseases are common, and although training in clinical immunology and allergy has only recently been introduced into the National Health Service, there are facilities for allergy testing at most major hospitals. A comprehensive and regularly updated list of allergy clinics in the NHS can be obtained from the British Society for Allergy and Clinical Immunology (BSACI Secretariat, Conference Associates, Congress House, 55 New Cavendish Street, London W1M 7RE).

[*Added in proof*] Because allergic reactions affect different parts of the body, the BSACI is conducting courses for doctors to improve their knowledge and treatment of these disorders. Courses are designed not only for general practitioners, who in the first instance see most of the people with allergic disorders, but also for specialists whose primary interest is in diseases which often manifest allergic reactions affecting specific organs such as the eyes, nose, lungs, gut and skin.

Scope of allergic diseases

The most common allergic disease is *summer hayfever*—affecting about 10 to 15 per cent of the population. Although the pollen counts have been steadily falling, for some unknown reason the incidence of hayfever seems to be increasing. Many believe that atmospheric pollution may contribute, especially since the presence of sulphur dioxide in the atmosphere has been shown to potentiate other allergic conditions such as allergic asthma. The diagnosis is usually readily obtained from the clinical history and confirmed by the 'skin prick test'.

There is particular concern about the apparent increase in *allergy to the house dust mite*. Central heating and poor ventilation in modern houses provides the warm moist environment for mites to flourish. Allergy to the house dust mite is the most common cause of chronic allergic rhinitis. It is also associated with worsening of asthma and aggravation of atopic eczema after direct skin contact.

Allergy to animals is also an important cause of allergic disease, particularly chronic rhinitis and asthma. Wherever the pet population increases, allergy to

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domestic animals appears to be more prevalent. Cat allergens seem to be a common cause of asthma in sensitised subjects but dogs, horses, mice, rats, guinea pigs, hamsters and gerbils are all potent sources of allergenic material. Birds can also give rise to allergic disease, including extrinsic allergic alveolitis.

The role of *allergy in asthma* is difficult to define precisely since asthma can be triggered by a variety of agents including allergens, viral infections, exercise, exposure to fumes and other irritants, certain drugs, food and drink, and occasionally food additives. Allergy is a common cause of childhood asthma. The importance of a specific allergen in a single individual is usually suspected from the clinical history. Many mould spores are allergenic but may be difficult to incriminate since other factors may also be involved. The precise contribution of allergy, as opposed to other triggers, is of practical importance, however, where the allergenic substance or substances can be easily identified and avoided.

Occupational asthma is triggered by sensitising agents inhaled in the workplace. The important agents are platinum salts, isocyanates, epoxy resins, colophony fumes, proteolytic enzymes, laboratory animals and grain (or flour) dust. Pharmaceutical products, wood dusts and castor bean dust may also be involved. Occupational asthma is an important cause of ill-health and time off work.

Allergy to stinging insects (particularly wasps and bees) is a rare but potentially serious problem. A few deaths from general anaphylaxis following wasp and bee stings are still reported in the United Kingdom each year. In proven cases allergen immunotherapy gives effective protection against further stings.

Allergy to drugs represents only a small proportion of all adverse reactions to drugs since reactions must be distinguished from drug overdose, side effects, toxicity, intolerance and idiosyncratic reactions. True allergic reactions are relatively common with antibiotics (mainly penicillins and cephalosporins) and muscle relaxants used in anaesthesia. Many other agents such as local anaesthetics and aspirin cause typical hypersensitivity reactions but the precise immunological nature of these remains uncertain.

Although swelling, itching and redness are found in many different skin disorders, a clear association between *allergy and the skin* is often very difficult to establish. Despite a large literature and much debate it appears that allergy plays a role in a minority of cases of chronic urticaria and atopic dermatitis. Atopic eczema is often made worse by food in very young children but this is less common in older children and adults. Contact dermatitis may be due to allergy, irritation, or both. Patch tests are the standard methods for testing for allergic contact sensitivity.

Food allergy is one of the most controversial subjects in the practice of allergy because there are no

universally agreed definitions and diagnostic criteria for it. Since many adverse reactions to foods do not involve the immune system the more embracing term *food intolerance* is often preferred [2]. Food allergy, intolerance and aversion have been divided in the RCP report on allergy into five groups. In *group 1* there are the undisputed allergies which involve immunoglobulin E. These examples include the immediate, sometimes violent, reactions which occur in susceptible subjects after ingestion of nuts, eggs, milk, fish and shellfish. *Group 2* consists of food allergy associated not with IgE but with strong evidence that the immune system is altered. Examples are coeliac disease and cow's milk protein enteropathy. *Group 3* includes non-allergic food reactions (food intolerance) to foods affecting certain susceptible individuals. Examples include some types of irritable bowel syndrome, food-induced migraine, reactions to sulphites or nitrites as well as those due to a lack of digestive enzymes (hypolactasia, low aldehyde dehydrogenase) or due to more complex mechanisms (eg tartrazine, red wines and cheeses). In *group 4* are the established and well recognised intestinal diseases where the role of foods in causation is sometimes suspected but still *unproven*. Examples include chronic ulcerative colitis and Crohn's disease. In *group 5* are the food aversions which occur in subjects where non-specific symptoms to food are not confirmed by double-blind testing.

Treatment of allergy and asthma

The basic principles in the treatment of common allergic diseases are: (1) allergen avoidance; (2) drugs; and (3) allergen immunotherapy (desensitisation or hyposensitisation).

Allergen avoidance is sometimes relatively easy for those who are sufficiently motivated (eg avoidance of pets). Avoiding dust mites is more difficult, but regular cleaning can be useful and chemicals which kill mites (acaricides) are under trial. Pollen grains are virtually impossible to avoid. Work-related allergies result from exposure to occupational agents, which good work practices can prevent.

Drugs used in hayfever include the new non-sedating antihistamines and corticosteroid nasal drops and sprays. Systemic corticosteroids should only be considered in patients with severe continuous symptoms. Sodium cromoglycate spray can be used as an alternative to corticosteroids. Sodium cromoglycate eye drops are also useful for allergic conjunctivitis.

Drugs used in asthma include those for relief, ie symptomatic treatment, the most effective drugs being the β -agonists. β -Agonists are particularly useful for relief of wheeze and are also very effective in protecting against exercise-induced asthma. There has been concern that β -agonists used without other forms of treatment in moderate to severe asthma might mask

the presence of underlying inflammation. Most patients with chronic asthma require preventive treatment in the form of inhaled corticosteroids or, particularly in children and young adults, sodium cromoglycate. In adults intermittent or long-term treatment with corticosteroids has become the mainstay of therapy in all but mild asthma.

Immunotherapy (desensitisation or hyposensitisation) has been used for about 70 years and is a form of treatment for selected patients with proven atopic allergy. It aims to provide some protection from the effects of natural exposure by giving increasing doses (usually by injection) of the antigens which induce allergic symptoms. Immunotherapy is not without risk and, while this is so, many allergists believe that it should only be used in (a) patients with severe summer hayfever who have failed to benefit sufficiently from anti-allergic drugs and (b) patients hypersensitive to wasp and bee venom. Because immunotherapy is relatively expensive and requires considerable commitment by both doctor and patient, its use should be carefully assessed in each case. Immunotherapy is not recommended for chronic asthma because it rarely works and may lead to severe reactions.

In the United Kingdom allergen injection immunotherapy for the treatment of IgE-mediated disease, including summer hayfever, has generally been discontinued as a result of the recommendations of the Committee on Safety of Medicines (CSM) in October 1986 [3]. Concerned about deaths from severe bronchospasm and anaphylaxis, the CSM recommended that injections should only be given where facilities for full cardiorespiratory resuscitation are immediately available and patients are kept under medical observation for at least two hours after treatment. Thus successful immunotherapy depends on: (1) careful selection of patients; (2) the use of standardised vaccines; and (3) a skilled operator, ie a person who has had formal training in this form of treatment and is aware of the potential dangers, particularly anaphylaxis.

Alternative concepts of allergy

The rival claims of mainstream and alternative practitioners of allergy bewilder many patients and doctors. Conventional doctors are worried that many of the claims of alternative practitioners are unsubstantiated. They are disappointed that there are very few properly conducted double-blind placebo-controlled trials and believe that the benefit claimed by many alternative practitioners is the result of suggestion or the placebo response. Before a new form of investigation or treatment can be accepted, the claims made for it should be confirmed on several occasions and should be repeatable by other researchers. According to the RCP document many of the claims made for alternative methods of diagnosing and treating allergy do not stand up to scrutiny.

Clinical ecologists believe in the concept of a disease which they describe as 'environmental illness' or 'chemical hypersensitivity syndrome' which is held to be responsible for a wide range of symptoms. When multiple hypersensitivities, hypersensitivity to candida infection, or food-associated myalgic encephalomyelitis are diagnosed on arbitrary grounds and in patients with very similar symptoms, this itself raises questions about their validity.

The main criticism raised against clinical ecology relates to the lack of a clear, critical and objective approach and the frequent use of unproven methods in diagnosis and treatment. The much publicised provocation-neutralisation test (the Miller technique) is subject to particular criticism, especially as its interpretation is often subjective and open to bias. In this procedure test substances are administered at successively higher doses by intradermal or subcutaneous injection until there is an increase in the size of the cutaneous weal where the substance has been injected. Different doses are then given serially until the weal response disappears. When carried out under careful double-blind conditions the responses of patients to active and control injections were indistinguishable. The frequency of so-called positive responses to injected extracts appeared to be the result of suggestion and chance [4].

Clinical ecologists treat some of their patients in environmental control units constructed from inert material. There is no evidence, however, that they confer any clinical benefit apart from filtering the air for removal of certain recognised allergens and avoiding conditions which favour the house dust mite and the effect of passive smoking.

Several other diagnostic tests and treatments are used by practitioners of alternative allergy. They include the leukocytotoxic test which involves mixing the patient's leukocytes on a microscope slide with an extract of specific food and inspecting the cells for evidence of damage. This test has been heavily criticised and can be very misleading.

The Vega test (an 'electrical' or 'black box' test) is widely used but its value is unproven and there are no controlled trials to substantiate the claims made for its use.

Hair analysis is used by practitioners of alternative methods either to identify elevated levels of toxic heavy metals or low levels of selenium, zinc, chromium, manganese and magnesium (where replacement therapy is often advised). There are no scientific data to substantiate these hypotheses. A completely different form of hair analysis is dowsing in which a pendulum is swung over a hair sample. Many commercial laboratories claim to diagnose allergic diseases from samples of hair. Studies have concluded that these are 'unscientific and economically wasteful'.

Other unusual methods include applied kinesiology and auriculo-cardiac reflex methods. These have either failed to withstand a double-blind study or are unsupported by any objective data.

Enzyme-potentiated desensitisation involves mixing a minute amount of allergen with β -glucuronidase and applying it to the skin in an attempt to desensitise to pollens and food allergens (for ulcerative colitis). Some trials have been published but lack sufficient detail for subjective appraisal.

While homoeopathy has been claimed to benefit hayfever sufferers (using a solution of grass pollen diluted to a point where no molecules remained) [5], no attempt has been made to compare the effects with those of conventional anti-allergic drugs.

Other areas of interest to practitioners of alternative allergy include *Candida* hypersensitivity syndrome, mercury hypersensitivity from dental fillings, allergy to electricity, and chronic fatigue or postviral syndrome (often called myalgic encephalomyelitis). While the persistence of symptoms after a viral infection can at times cause concern, there is no convincing evidence to suggest that these conditions are allergic disorders or that the proposed methods of treating them are valid. There is no case for asking the National Health Service or medical insurance companies to pay for any of the reported procedures.

Not all the evidence concerning alternative medical procedures is wholly negative. There are some areas in which valid conclusions cannot be drawn on the available evidence. Hypnosis was popularised as a method of therapy in the late eighteenth century for conditions which can now be recognised as largely psychosomatic. It has been claimed to help some asthmatics and deserves further evaluation. Similar claims have been made in respect of acupuncture.

Herbal remedies have also been claimed to be of value for allergies but, in general, there is no evidence that they work. A possible exception is the use of traditional Chinese medicinal plants in the treatment of atopic eczema in childhood. One carefully designed placebo-controlled double-blind trial has reported substantial benefit [6]. This study has generated considerable interest and will need to be confirmed.

The subject of allergy seems to be particularly suitable for promoting unorthodox treatments. Why do patients seek out such therapy? Is this because of a failure of orthodox medicine to recognise and respond to their needs and anxieties? In part this must be true. In comparing the conventional and the unorthodox approaches we should however also be concerned about the reliability of the alternative diagnostic tests in use and the validity of the diagnoses made and treatment given. Some of the test methods, in particular, can be seriously misleading [7,8].

Diagnosis and treatment are also important. Medical practitioners are very familiar with patients who express psychological illness as physical symptoms and who are then convinced that they have a physical disease. The number of patients in a doctor's surgery with anxiety symptoms can rise sharply when there is intense media interest in a currently fashionable disease. The misdiagnosis of such patients as having an

allergic disease can be unfortunate, especially in those who are depressed. Such errors can also delay the diagnosis of conditions which may become fatal if neglected, including cancers which can begin with relatively non-specific symptoms [9]. By recommending unhealthy diets, reinforcing obsessional behaviour or encouraging social isolation further damage is caused.

Vulnerable people should be aware that there are some laboratories and practitioners who rely on controversial and unproven procedures such as leukocytotoxic testing, provocation and neutralisation injections, and sublingual provocation tests which are not considered by independent observers [10] either to be effective or to have a scientific basis. Better evidence of efficacy is needed before these procedures can be accepted as valid.

Summary and conclusions

Allergy is an exaggerated response of the immune system to external substances. It plays a role in a wide range of diseases. In some, such as summer hayfever, the symptoms are entirely due to allergy. In other conditions, particularly asthma, eczema and urticaria, allergy plays a part in some patients but not all. In these situations, allergy may either have a major role or provide just one of many triggers. In an individual patient's illness, the importance of allergy may change with time.

The most common allergens (substances causing allergy) are grass and tree pollens, the house dust mite, products from pets and other animals, agents encountered in industry, wasp and bee venom, drugs, and certain foods. Food allergy presents a particularly difficult problem. Some individuals who react to food suffer from true food allergy but in others there is no evidence of an alteration in the immune system. Here the term 'food intolerance' is preferable.

Conventional doctors treat allergy by allergen avoidance—where this is possible—and drugs that relieve symptoms. In a few selected cases, in which other methods have failed, immunotherapy (desensitisation or hyposensitisation) is recommended.

Patients who consult practitioners of alternative allergy often do so because they are dissatisfied with the conventional approach to diagnosis and treatment, and sometimes because they have conditions which conventional doctors do not accept as having an allergic basis. There is a very wide range of alternative approaches to allergy, including the methods used by clinical ecologists, acupuncturists and homoeopaths. Hypnosis may have a small role to play in asthma, and similar claims for acupuncture need to be evaluated. Furthermore, it is likely that there are many active ingredients in medicinal plants used by herbalists which need to be clearly identified and purified so that their usefulness can be properly assessed. Apart from these situations, none of the other evaluated areas of alternative allergy has been shown to be of

value. There have, however, been many false and misleading claims and serious harm may be caused by misdiagnosis or delays in appropriate treatment. The public should be warned against costly methods of diagnosis and treatment which have not been validated.

It is clear that many patients improve as a result of suggestion or the 'placebo response'. The placebo response can be very powerful and for this reason it requires further scientifically based research since a better understanding of the interplay between the brain and allergy associated symptoms might result in improved forms of therapy. On the other hand, the placebo response must be clearly distinguished from the effects claimed for a particular form of treatment.

Allergic diseases are common and the cause of much ill health. Improvements in diagnosis and treatment of allergy, like other branches of medicine, can only be made by rigorous clinical scientific studies.

References

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Copies of the full report can be obtained from the publications department of the Royal College of Physicians, price £10.00 + £1.00 p&post, Overseas £13.00 (including postage).

Errata

We apologise to authors and readers for the misprints that appeared in the April issue of the Journal.

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Domiciliary oxygen therapy for children

A report of a working group of the Royal College of Physicians' Committee on Thoracic Medicine.

Table 3 should read as follows (the third item has been corrected):

Table 3. Essential domiciliary oxygen equipment

- Low-flow oxygen meter (0.1–1 l/min) or ultra-low-flow meter (25–200 ml/min) for infants and young children
- Appropriate cylinder heads
- Appropriate devices for administration of oxygen, such as nasal cannulae catheters and extension tubing
- Bubble humidifier for those receiving nasal or nasopharyngeal supply at flow rates more than 0.1 l/min
- Non-kinking extension tubing to allow mobility without restricting oxygen supply
- Simple resuscitation equipment

P 177–180

Medical audit: the differing perspectives of managers and clinicians

Helen E. Smith *et al*

The Figures in this paper did not print satisfactorily. Correctly printed reprints are available from the College or from **Dr Helen E. Smith**, Department of Public Health Medicine, District Headquarters, North Staffs Royal Infirmary, Prince's Road, Stoke-on-Trent ST4 7JN.

P 204–214

Molecular studies of viral pathogenesis in the central nervous system

Peter G. E. Kennedy

A printing error occurred on Figure 5(c) on page 21. Correctly printed reprints are available from **Professor Kennedy**, Glasgow University Department of Neurology, Institute of Neurological Sciences, Southern General Hospital, Glasgow G51 4TE.