PRACTICE GUIDELINES

Effective Allergy Practice: A Document on Standards of Care and Management for the Allergy Patient*

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INTRODUCTION

Since the late 1950s the prevalence of atopic allergy has approximately doubled every 10 years [1]: allergy has been referred to as the 'number one environmental disease' [2]. The vast increase in the environmental load of chemical pollutants over the last 40 years has been unparalleled in the evolution of humankind. Food, water and the indoor and outdoor environments are increasingly polluted. This places a huge strain on the capacity of humans to adapt to their present environment.

With well over 20% of the population being allergic, the cost to health and therefore to the exchequer is considerable. Drug therapy is crucial for the suppression of symptoms in some clinical situations, but elimination of the cause must, in the end, be more effective. The methods used by the physician members of the BSAEM/BSNM restore a considerable proportion of the patients to health, and allow them to discontinue drug therapy.

This document will outline the background of allergy services in the UK, the areas of medicine to which allergists can contribute, the techniques used in investigation and management and the individual conditions to which allergists with appropriate training can make a significant contribution.

The interventions outlined in this document are both clinically effective and cost effective in patients with a wide range of chronic and recurrent conditions. If they are not managed constructively, these patients often turn to alternative therapies for help. Physicians must make an accurate diagnosis for two reasons: to ensure that other serious conditions are not missed, and so that the patients receive effective management.

HISTORICAL BACKGROUND

The term allergy was coined by von Pirquet in 1906. His original wording (in translation [3]) was:

For this general concept of a changed reactivity I propose the term Allergy. Allos implies deviation from the original state . . . . A foreign substance which by one or more applications stimulates the organism to a change in reaction is an Allergen. This term traces its origin to the word Antigen, which implies a substance capable of giving rise to the production of Antibody. The term Allergen is more far-reaching. The Allergen comprises besides the antigen proper, the many protein substances which lead to no production of Antibodies, but to supersensitivity.

The concept was accepted, and has been an integral part of medical thought ever since.

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However, even in the early years there was a tendency among allergists in general to see allergy as having mainly immediate effects, and the evidence that avoidance of triggers could prevent subacute and chronic symptoms was largely ignored, in spite of accumulating clinical evidence in the US [4], particularly from AH Rowe [5]. Coca and Cooke recognized the hereditary aspects of allergy in 1923 and introduced the term atopy [6]. Coca (then editor of the Journal of Immunology) had a prolonged debate with Doerr of Switzerland, the latter insisting that all allergic reactions had to be shown to be dependent on antibody, and Coca standing up for von Pirquet’s original definition of allergy as a state of altered reactivity [3]. Coca lost the battle, and states of altered reactivity in which antibody has not been explicitly implicated have been excluded from classical allergy ever since, even those that respond to the same management as the so-called classical allergies. It was not until much later, 1966, that immunoglobulin E (IgE), the antibody which sensitizes cells and causes immediate reactions on contact with allergen, was isolated [7].

Coca’s stance is supported by logic, by the subsequent demonstration that T-lymphocytes can carry immunological specificity, and by the other types of immunological damage which have since been described [8]. During the course of reactions of all the Gell and Coombs types, inflammation may be induced, and mediators released with a variety of mainly physiological effects. Some of these mediators are many times more potent than histamine, with the potential for causing a wide range of symptoms and pathological consequences [9].

THE POSITION OF ALLERGY PRACTICE IN THE UK

During the last 30 years, allergy services in hospitals have usually been provided by consultants from a variety of specialties who have developed an interest in this field, particularly chest physicians, dermatologists and ENT surgeons. They have had a variable amount of support from pathologists, a few of whom are specialist immunologists. Clinical immunologists are still limited to a few centres, and are concerned with immunodeficiency, autoimmunity, transfusion and/or transplantation as well as allergy, with research interests mainly in the elucidation of immune mechanisms.

A few hospital-based clinics have offered wide-ranging allergy care, but these services have often not survived the retirement of the initiating consultant. There has been no formal training available. The vacuum has been recognized, and partly filled, by doctors who have specialized in allergy outside the hospitals, many outside the National Health Service.

Allergists in the UK are represented by two societies: the British Society for Allergy and Clinical Immunology (BSACI) (founded in 1947 as the British Allergy Society) which has a predominantly immunological membership, and the British Society for Allergy and Environmental Medicine (BSAEM) (founded in 1979 as the Clinical Ecology Group, and recently amalgamated with the British Society for Nutritional Medicine (BSNM)) with a predominantly clinical membership. Although the BSACI and the BSAEM/BSNM have interests in common, they have philosophical differences. The BSACI generally considers that allergists should restrict their practice to those conditions, and those techniques, associated with IgE-mediated allergic mechanisms. In contrast, the BSAEM/BSNM takes the pragmatic view that the sole criterion should be clinical, and that allergists should manage those conditions which are exacerbated by reactions to food or environmental factors, irrespective of whether the mechanism has been elucidated: their aim is to prevent symptoms rather than suppress them, as far as is consistent with a satisfactory life-style.

In spite of having implications for the care of patients, the 1992 report of the Royal College of Physicians [10] was written from an immunological rather than a clinical standpoint: it makes no reference to much of the work which has been published in relation to the environmental factors, chemicals and foods which affect health, as has been pointed out in a rigorous and well-referenced critique [11].
AREAS OF MEDICINE TO WHICH ALLERGISTS CONTRIBUTE

Reactions to environmental factors and foods can cause an extraordinary range of symptoms [12–15]. Two types of reaction which fulfil the original definition of allergy contribute to the symptoms: these must be clearly distinguished. Type A reactions include the classical acute allergic reactions whose distribution is determined by the mode of entry of the allergen. Type B reactions are not IgE-mediated, and have a distinctly different natural history. Type B reactions are often masked, so that the relationship between the allergen and the symptom is not apparent until after a break in exposure. Symptoms may be delayed, and occur with an organ distribution unrelated to the portal of entry of the allergen. Each of these types of reaction may result in a variable amount of secondary inflammation, and the resulting conditions are often treated with steroids or non-steroidal anti-inflammatory drugs.

The main symptoms and syndromes which can be relieved by environmental allergists are as follows:

‘Traditional’ allergies which may have an IgE-mediated component, including:

- allergic rhinitis and conjunctivitis (seasonal and perennial);
- asthma;
- skin disorders with allergic aspects (eczema, urticaria, angio-oedema);
- anaphylaxis;
- allergic reactions to insect bites and stings;
- allergic reactions to drugs and to other chemicals;
- food allergy.

Syndromes which may be induced or exacerbated by reactions to food or environmental factors, possibly allergic though probably not IgE-mediated, including:

- irritable bowel syndrome and Crohn’s disease;
- migraine (and epilepsy in migrainous children);
- arthritis;
- cerebral syndromes (anxiety/depression, mental confusion, panic attacks, hyperactivity, etc.);
- unexplained fatigue;
- abacterial cystitis and bladder pain;
- multi-system polysymptomatic illness.

Other physiological/pathological disorders frequently occurring in association with the above, including:

- enzyme anomalies;
- gut dysbiosis;
- nutritional deficiencies;
- chronic toxicity;
- hyperventilation, etc.

The traditional separation of the classical allergies from the other conditions mentioned above ignores the interactions between them, demonstrated experimentally and evident in clinical practice. Clinically, even localized allergic reactions often have generalized effects, such as the lethargy and malaise that accompany hay fever. Younger allergic patients may have single-system involvement, but this is rare in the older age groups who are usually polysymptomatic with several different aetiologies. Best results commonly require consideration of more than one modality of management. For example, nutritional deficiencies can predispose to allergies by their adverse effects on the immune system, and chronic or recurrent allergic reactions may cause further depletion of key minerals and vitamins.

In the view of the BSAEM/BSNM, management of patients with these conditions by the
same clinician is essential if an effective and cost-effective service is to be provided. The lead should clearly come from allergists since the major element in this complex of diseases is the patient's adverse reactions to foods and inhalant allergens, and to concentrations of chemicals which cause no adverse effects in unsensitized individuals. This service can be provided by other clinicians who accept the reality of multi-system disease, and are prepared to acquaint themselves with the techniques. This is starting to happen with children where increasing numbers of paediatricians are finding the value of these methods. General practitioners also are in a good position to carry out allergy investigations, and nurses can be trained to help. After allergic patients in general practice had been seen by a nurse practitioner trained in the detection of inhalant allergies and in avoidance techniques, they needed fewer consultations and fewer drugs [16].

INVESTIGATIVE METHODS USED BY ALLERGISTS

History
A good history has always been the cornerstone of all medical teaching, but the constraints of time in modern practice mean that it is now rarely observed. It is an essential part of good allergy practice, and time spent in obtaining a detailed picture of the patient, his experiences, background, illnesses, life-style and environment frequently saves future consultations. Allergists should allot a minimum of 1 h to each new patient, and this will sometimes be insufficient. The history may be backed up by the use of a questionnaire and/or a dietary diary or questionnaire filled up by the patient, but these cannot short circuit the essential requirement for a properly conducted medical history.

Skin Prick Testing
This has been the standard for evaluating IgE-mediated inhalant allergic responses for decades: it correlates highly with the Radio-Allergo-Sorbent-Test (RAST). Prick testing is cheap and with immediate responses it gives results within 15 min, in contrast to RAST testing which is intrinsically more expensive and slower, the clinician rarely getting a report in much under a week.

The procedure is fully described in standard works [17–19], but testers should have practical training in the clinical situation to ensure that it is carried out correctly. While it is generally safe, anaphylaxis from skin testing has occurred, and all allergists should have a basic training in resuscitation techniques, and have appropriate emergency drugs at hand.

The procedure is most reliable in young persons with inhalant problems. Skin prick testing is primarily used to assess IgE-mediated immediate responses to inhalants, but non-immediate responses can also be measured [18], and all skin tests should be monitored to extinction [17], and the patient instructed to record any additional reactions which occur in the next 48 h. At the present time, many clinics do not do this and miss clinically important data. Negative skin prick tests do not exclude reactivity to the inhalant allergen concerned [20]: prick tests may not correlate exactly with clinical challenge results.

Prick tests may be of use in IgE-mediated food allergy, but may under some circumstances induce anaphylaxis: this has been reported particularly in boys with eczema [21]. Skin prick tests are of no value in food intolerance. In particular, a negative skin prick test to a food cannot exclude intolerance to that food [22]. The practice of implying to patients that a negative prick test (or a negative RAST) shows that they do not react to that food is reprehensible.

Prick test allergens are usually used at a concentration of about 1:10 w/v. Standardization of allergen extracts is based on the major allergenic determinant; some patients, however, will be insensitive to this, and minor allergens may also be required. While standardization may be essential for incremental immunotherapy, for all other purposes
activity is more important. Allergists require too many different test materials for standard-
ization to be a realistic option at the present time. Allergen extracts should be of the highest
quality and lowest irritancy possible in the current state of knowledge [23].

Intradermal Skin Testing

This technique has been extensively used in allergy diagnosis in other countries, but is not
now recommended as a diagnostic tool in IgE-mediated hypersensitivity and should
therefore only be employed with inhalant allergens when prick tests are negative, or as part
of the titration of a therapeutic dose. It may be used as a single strength or as a series of
dilutions to assess other types of immunological reactions including delayed reactions,
provided that inspections are made at appropriate intervals. Intradermal tests are more likely
than prick tests to be positive when allergic mechanisms other than Gell and Coombs [8]
Type 1 are involved, and this may be why they have been regarded as more subject to
false-positive responses than prick tests by those whose main concern is atopy.

Allergens for intradermal use are more dilute, usually not more concentrated than 1:100
w/v. If used for diagnostic purposes, the use of more than one dilution is recommended, and
interpretation must take account of any irritation caused in more sensitive skins by the
higher concentrations of individual extracts, particularly of foods. The significance of
positive intradermal tests with foods is still a matter of some controversy [24].

Patch Testing

This is a technique for measuring contact dermatitis responses, and is carried out exten-
sively in dermatology clinics. Currently a standard European Test Battery is employed
which is well documented [25]. However, a much wider and changing range of chemicals
may be involved [26, 27], and use of specific batteries for patients in some occupations has
been recommended [27].

Many departments of dermatology with no other training in allergy perform this
procedure in a reliable fashion. While all allergists should have knowledge of the technique
and be able to prepare and test special extracts for patients not covered by the Standard
European Battery, the procedure does not require the special training of allergists. Its value
is limited to the investigation of contact hypersensitivity responses, but aero-allergens
giving a positive prick skin test should be included in the battery in eczema patients since
patch test positivity to aero-allergens was a good predictor of the clinical significance of the
allergen in this condition [28].

Challenge Testing with Inhalant Allergens

Challenge testing with inhalant allergens may involve administration to the conjunctiva,
nasal mucosa or bronchi: appropriate challenge testing may be of value in establishing the
diagnostic relevance of a positive skin test, providing clear evidence of local reactivity.
However, bronchial challenge testing should only be performed under controlled conditions.

Challenge Testing with Chemicals

Many patients who are sensitive to very low concentrations of chemicals give a clear
history, but the identity of the chemical concerned is not always apparent, and not all
chemically sensitive patients are aware of the extent of their problems. Avoidance, followed
by re-exposure may be sufficient to indicate the association in some.

Chemical challenge testing may be performed using serial dilutions administered sub-ling-
gually, intradermally or by inhalation of known concentrations (too low for recognition by
smell) in a specially designed booth [29]. Placebos should be included when testing. Each
method may show false-negative results in heavily exposed individuals, unless steps are taken to reduce exposure for several hours or days beforehand: this can sometimes be achieved during a holiday, and most reliably by admission to an environmentally controlled unit (see page 88), where special measures are taken to keep chemical contamination to an absolute minimum.

If it is necessary to confirm acute IgE-mediated reactions caused by drugs and other chemicals, this should be done by RAST tests where possible, otherwise by challenge under controlled conditions with resuscitation facilities available.

**Challenge Testing with Food**

When there is a history of IgE-mediated food allergy giving rise to severe reactions, food challenges should not be attempted, and confirmation should be obtained from RAST tests. Other cases of immediate food allergy may be submitted to challenge if confirmation is required, but the challenge may need to be done in hospital and should start with a small quantity of the food, proceeding to larger quantities if there is no response.

In food intolerance syndromes, challenge frequently gives a false-negative result unless preceded by a period of avoidance of at least 5 days and up to a few weeks. The standard procedure, established in the 1930s, is that the food(s) should be avoided for a test period to see whether symptoms improve. If so, the foods are reintroduced one at a time. If symptoms recur the test is positive.

Food intolerance has been demonstrated conclusively in a number of double-blind studies measuring parameters such as peak expiratory flow [30, 31] or observing clear signs such as urticaria, angio-oedema, vomiting and diarrhoea [32], or behavioural disturbance [33, 34]. A wide range of other symptoms have also been provoked by test foods but not by placebos in double-blind studies [35–39].

Intolerance to food additives has also been demonstrated [40–42] using objective criteria. Contributions from food contaminants have also been noted [43, 44].

In the view of some allergists [45, 46], clinical food challenge testing should always be performed or confirmed double-blind. This is theoretically sound, particularly for scientific studies, but unattainable at present because current methods of double-blinding result in challenges which are not sensitive enough to exclude reactivity. Other data support the validity of results from open testing.

The BSAEM/BSNM does not currently recommend double-blind testing as a routine in clinical management for the following reasons.

1. All the methods of blinding which have been devised reduce the sensitivity of the test, either by limiting the dosage that can be given, or eliminating contact with the buccal mucosa. The National Institutes of Health study concluded that blind administration was not sensitive enough to detect reactions in all patients [47, 48].

2. Since any food may cause reactions, the ‘safety’ of the placebo must be established for each patient individually: the choice of placebo has been unsatisfactory for some of the patients in a number of the published studies of double-blind challenge with foods, for instance the use of a chocolate cookie without pre-checking [49], or of glucose (usually derived from corn) in a patient who reacted to corn [32].

3. Clinically, well conducted open testing is effective: if patients avoid all the foods causing symptoms on open testing, most remain symptom-free.

4. Patients are usually surprised and displeased to find that the foods to which they react are their favourite and most commonly eaten foods: this makes an explanation of hypochondriasis unlikely.

5. Open food testing gives consistent results in almost all patients, both on retesting after an appropriate interval [30], and with recurrence of the symptom when the food could not be avoided, often because it was in a hidden form.
It is the view of the BSAEM/BSNM that it is the patient's clinical improvement that is of primary importance when considering the results of food avoidance and challenge testing. Food intolerance may be temporary [32] and tolerance may be re-established fairly rapidly if the food is avoided: a negative challenge test cannot rule out the possibility that the food caused symptoms previously, especially in infants and children [50].

For each patient with food intolerance, decisions must be taken about the appropriate duration of avoidance before challenge, which foods should be tested, and at what rate and in what order they should be tested, and the results must be evaluated. The procedure requires allergists thoroughly trained and experienced in the technique, or personnel trained and supervised by them. The allergist should have access to a dietician with a special interest in this area.

Exclusion diets and challenge testing are time consuming and depend on accurate clinical observations. For routine care, these usually have to be made by the patients or relatives: most do very well, but there are some who cannot manage for a variety of reasons. Lessof [51] has recently emphasized the importance of clinical observations in the elucidation of the problems of food intolerance, calling for more laboratory back-up. This should include a major effort to develop laboratory tests to detect all types of food intolerance accurately enough to replace in vivo tests.

Laboratory Tests

Like any doctor, the allergist will require access to routine investigations though in most instances these investigations will have been done before referral, and the previous reports may suffice.

Immunological testing will be required for some patients. This may include measurements of immunoglobulins IgG, A, M and E, either as totals or their fractions, and IgE RAST for specific allergens. Tests for IgG antibodies for specific allergens may also be of value. For some patients, tests for complement components, T cell subsets and other parameters may be needed.

IgE-mediated food and drug allergies are more safely tested using RAST than by clinical tests, and insect venom RAST tests are used in evaluating patients for incremental immunotherapy.

Patients with food intolerance may have secondary disorders of gut function and deficiencies of vitamin and mineral status for which investigations may be needed. Clinically, treatment of deficits in nutritional factors is effective and safe. It requires much further research, and should be based on reliable laboratory measurement of appropriate nutrients, but few of the tests required are currently available in hospital laboratories.

Although RAST tests are of value in IgE-mediated food allergy [47, 52, 53], they may mislead in cases of food intolerance. The chief laboratory test used in food intolerance is the leucocytotoxic test, the subject of an adverse report in the US [54], which has been repeatedly quoted without reassessment. The leucocytotoxic test and the derivative, the Alcat test, have been evaluated in three studies, two double-blind [55, 56] and one single-blind [57], all of which gave positive results. In the view of the BSAEM/BSNM, these tests require more study, and the occurrence of both false-positives and false-negatives means that the tests cannot at the present time satisfactorily replace food challenge in identifying trigger foods. The tests can have a role in the selection of foods for elimination dieting, or elimination prior to challenge. If the mechanism of the test involves some immunological component, which is suggested by experimental evidence [53, 57], positive findings would be limited to the various forms of food allergy, and negative results expected in conditions such as lactose intolerance.
MANAGEMENT METHODS

Avoidance

Avoidance of exposure is the prime method of management for inhalant allergies, food intolerance and chemical sensitivities, and allergists need to develop considerable expertise in advising patients about appropriate steps to take, and about equipment. For some patients, this is sufficient to keep them virtually symptom-free. For others, adequate avoidance is not possible, either because of the nature of their exposures or their life-style, or because they would have too few safe foods to achieve a reasonable varied diet or to allow an adequate social life. These patients need some additional protection.

Specific Prophylaxis

Allergists use specific prophylaxis with extracts of the allergen trigger to induce hypo sensitization, reducing the severity of symptoms provoked by exposure or even preventing them entirely.

Specific prophylaxis is effective in IgE-mediated allergy and must prevent symptoms by specific interference with immunological mechanisms, even if the precise ways in which this occurs are not entirely understood. When the same methods of specific prophylaxis also prevent non IgE-mediated symptoms from environmental factors or foods, it is reasonable to presume, as a working hypothesis, that immunological mechanisms are again involved.

Incremental immunotherapy. Incremental immunotherapy has been shown to confer specific prophylaxis in hay fever [58], bee and wasp venom allergy [59], rhinitis due to house dust mite allergy [60], and asthma due to mould [61]. However, incremental immunotherapy should not be undertaken lightly since most patients experience systemic side-effects, 5% of them severe. In the UK, it is not recommended for patients with severe asthma; stringent precautions must be taken with other patients; and its use is largely restricted to the management of IgE-mediated bee and wasp venom allergy in specialist centres. Allergists should base decisions to treat on assessments both of the risks of treatment and of the risks the patient would run if unprotected.

Enzyme-potentiated desensitization. Enzyme-potentiated desensitization (EDP) uses low dose antigen extracts and β-glucuronidase with an activating alcohol (1–3 diol): these are mixed together immediately before being administered by intradermal injection or by application to a skin scarification in a small plastic cup. The antigen extracts are very dilute, delivering a dose of pollens roughly equivalent to that in a prick test, the foods to one-hundredth of that. The amount of β-glucuronidase present in the vaccine is equivalent to that normally present in 1 ml of blood; it appears to work as a lymphokine. In the presence of antigen at the appropriate concentration, it is thought to stimulate the Langerhans cells to migrate to the local lymph glands and reprogramme T suppressor lymphocytes. If antigen is present at the wrong concentration, it may hypersensitize.

Patients are treated with mixed inhalant allergens and/or a food allergen mix as appropriate.

EPD has been in use for over 20 years: at least 100 000 treatments have been given by the cup method, and about 50 000 by injection in selected patients. Adverse reactions have been few, almost invariably symptoms similar to, and no worse than, those experienced previously. Anaphylaxis has occurred only once, after an injection in a patient with a 20-year history of occupational exposure to β-glucuronidase in powder form.

Though a single pre-seasonal EPD may be adequate for protection in pollen allergies, and one or two treatments usually effective against house dust mite, annual boosters may be needed for a year or two. Some patients with food intolerance respond early, but there may be no convincing evidence of desensitization to foods until after three or four EPD
treatments (about 1 year). When tolerance improves, the frequency of treatment is determined by how long it lasts after each treatment: this usually increases with time.

Early work on β-glucuronidase as a biological response modifier was laboratory based [62–67]. The first clinical trial of EPD in hay fever [68] was published in 1967, and in food allergy [69] in 1975; both were positive. There have been double-blind trials of EPD in ulcerative colitis [70], hay fever [71–73] and in food-induced hyperkinetic syndrome [74]. All the trials were positive with a notable absence of side-effects. All three hay fever trials [71–73] employed a single pre-seasonal dose and all showed significant benefit, although clinically a two-treatment schedule is more effective. Recently, effective management of canine atopic dermatitis using EPD has been reported [75].

In the ulcerative colitis trial, 27 patients were given five treatments with mixed food allergens at intervals of 2 months, without prior identification of trigger foods; 31 controls received placebo [70]. Treatment was single-blind but assessments were double-blind. There was no difference between the groups for the first 14 months, but in the next 14 months significantly more of the treated group reported improvement, and the treated group showed fewer relapses ($p < 0.025$) and used less steroids.

Children with hyperkinetic syndrome who had initially had a Conners score (short form) of more than 15, whose symptoms had been controlled by food avoidance following an exclusion diet, were subsequently entered in a double-blind EPD trial. After three 2-monthly injections, 16 out of 20 treated by EPD became tolerant of trigger foods compared to four of the 20 who received placebo injections ($p < 0.001$) [74].

Neutralization. Neutralization by the Miller technique [76] was introduced in the US over 30 years ago and is the desensitization technique of choice for a wide range of allergic conditions (excepting venom anaphylaxis) by members of three of the four American allergy societies, the American Academy of Environmental Medicine, the Pan American Allergy Association and the American Academy of Otolaryngic Allergy. It is used regularly by nearly 5000 doctors in the US, the vast majority board-certified allergists or board-certified ENT surgeons. It has been used in this country for 15 years. Hundreds of thousands of treatment doses are given annually with no reported case of serious adverse reaction. The exact mechanisms involved are not understood.

The technique involves intradermal endpoint titration of 0.05 ml of progressively weaker extracts (five-fold dilutions) of the offending food or inhalant at 10-min intervals to find the first dilution that does not cause increase in wheal size or thickness after 10 min, and/or relieves symptoms provoked by prior administration of that food (but not unrelated foods). This is termed the endpoint or treatment dose. When this dose is taken as prophylaxis it protects against symptoms from that food or allergen. Endpoints for a number of foods or inhalant allergens are combined in a ’vaccine’ which is taken regularly, usually by self-administered subcutaneous injections of 0.05 ml on alternate days, sometimes as sublingual drops taken more frequently. An adaptation of the method may be used for chemical sensitivity.

Neutralization usually gives immediate protection against symptoms from exposure to the trigger, though it may take some weeks for the maximal effect to develop [77]. Initially, prophylaxis depends on regular self-administered treatment with the endpoint vaccine. After a few months to several years, patients usually regain tolerance, and vaccine treatments may be spaced out or discontinued. If patients discontinue too early, tolerance may not be permanent and vaccines may be required again.

Some patients develop symptoms during the testing procedure, relieved by the treatment dose, but the provocation of symptoms is unreliable and attempts to use this for diagnosis have been a source of confusion. Trials of the two different uses of neutralization (for instance [78, 79]) are often not distinguished by reviewers, leading them to draw erroneous
conclusions. One trial of the symptom version has been given particular prominence [80, 81] in spite of serious methodological flaws [82].

The 1989 position paper of the American College of Physicians [54] identified two controlled studies of neutralization as a therapeutic technique (using the maximum tolerated dose), both of which had given positive results [83, 84], as had controlled studies of individual patients [35, 85, 86]. They included two others [87, 88] (one [88] lacking in detail), in the table of positive studies, and none among the negatives. The double-blind randomized cross-over trial by Scadding and Brostoff [84] compared the effectiveness of sublingual treatment doses of house dust mite allergen with placebo in allergic rhinitis due to house dust mite allergy. During treatment with active vaccine, 13 out of 18 patients showed an increase in morning inspiratory peak nasal flow ($p < 0.01$) (in some as much as 1000-fold), symptoms improved ($p < 0.03$), and a higher threshold dose of allergen was required to reduce peak nasal flow ($p < 0.05$).

However, several studies were not included in the position paper. Boris et al. [89] studied the effect of subcutaneous vaccine containing treatment doses of animal allergens in sensitive asthmatics: after active vaccine the dose of allergen needed to cause a 20% drop in $FEV_1$ was four times greater than after placebo. A double-blind seven-centre cross-over trial of subcutaneous food neutralization vaccines sponsored by the American Academy of Otolaryngic Allergy studied 33 patients and reported that symptoms overall (mainly rhinitis and headache) were relieved during the two active vaccine periods compared to the placebo period in 20 patients (76%, $p < 0.001$) [79]. In eight patients, symptoms were consistently aggravated by the vaccine, suggesting that the treatment dose had not been titrated correctly.

The efficacy of neutralization has been confirmed in two studies in horses with heaves (the equine equivalent of asthma): chronically affected horses too breathless to be ridden have been brought back into use [90], jumping and racing [91].

**Medication**

Medication, primarily bronchodilators, steroids, anti-histamines and other anti-allergy drugs [92] may be required, but allergists providing a wide-ranging service regard these drugs largely as back-up, needed particularly if specific prophylaxis cannot be arranged.

A history of intolerance of drugs is common in these patients. When chemical toxicity or sensitivities have played a part in the development of symptoms, drug medication may lead to further deterioration by increasing the load of xenobiotic chemicals requiring detoxification and excretion [94–96].

**SPECIAL FACILITIES**

Most patients with these conditions can be investigated satisfactorily as outpatients, but this is not possible for some of the more severely affected patients, either because challenge could be life-threatening, or because sensitivities to many different inhalants, foods and chemicals mask each other. It is often impossible to achieve a full allergy investigation of patients with life-threatening symptoms in an ordinary hospital ward because of the inevitable contamination from cleaning chemicals, newspapers and magazines, perfumed toiletries, flowers etc.

Environmental control units (ECUs) were pioneered in the US in the 1960s [97, 98]. The first purpose-built ECU was opened in the UK in 1985. It was constructed of, and furnished with, materials which do not give off volatile organic compounds, and high-level filtration of water and air installed to ensure minimal contamination by chemicals and inhalant allergens. It is managed to ensure strict exclusion of inhalant allergens and volatile chemicals (such as those from newspapers), and no one smelling of cigarette smoke, perfume, etc. is allowed in without showering. It specializes in the management of patients
with multiple allergies who need the care of a specialist staff, and a ‘clean’ environment [15, 99–105].

ECUs make it possible to test patients with multiple sensitivities and to provide them with specific prophylaxis. The standard regime of approximately 3 weeks usually starts with a 5-day fast to promote rapid clearing; if any symptoms do not clear substantially within 10 days, an environmental cause can usually be excluded. Patients are subsequently challenged with > 40 foods and 12–19 chemicals, tested with relevant inhalant allergens, and discharged on an individually designed 4-day rotation diet, self-administered neutralization vaccines to foods, inhalants and/or chemicals, nutritional supplements and information on avoidance measures. Patients are advised to keep to their regime strictly at first, relaxing when they can do so without relapse.

ECUs have an essential role to play in the investigation of severely affected patients, but an equally important role in establishing whether environmental reactions contribute to the aetiology of undiagnosed medical problems [99]. Such a possibility can only be confidently excluded if the patient has failed to improve after a fast in an ECU.

INDIVIDUAL CONDITIONS TO WHICH ALLERGISTS MAKE A CONTRIBUTION

Traditional Allergies

These conditions are most often due to inhalant allergy, and prior to 1987 many of the severe cases were managed using incremental immunotherapy. They still are in some other countries, but incremental immunotherapy is rarely used now in the UK except for insect venom allergies, most other cases being managed by drugs.

In conditions such as rhinitis and asthma, patients are generally regarded as having either allergic or intrinsic disease. However, the word intrinsic is usually a misnomer since Type B reactions, often due to foods, sometimes to chemicals or inhalants, can be demonstrated in many of these patients. Wide-ranging allergy care offers both a more complete diagnosis of which allergens to avoid, and the possibility of specific prophylaxis using one of the low-dose methods.

The care of allergic children is of particular concern [14], in view of the alarming increase in the use of inhalers in schools. Investigation of allergic children pays dividends [50, 104–106], for instance 91% of 322 children under 1 year of age with asthma or rhinitis and negative skin tests improved on a hypoallergenic diet [50]. Although many children present with asthma or eczema, others present with recurrent glue ear [107–109], enuresis [110], recurrent temperatures, colic or failure to thrive.

Allergic rhinitis. The common division of rhinitis into summer hay fever and perennial rhinitis is somewhat artificial. Patients with typical summer hay fever often progress to prolonged seasonal, even to perennial, symptoms. Others start with perennial symptoms and later develop a summer exacerbation. Although referred to as rhinitis, other organ systems are usually affected, with conjunctivitis, asthma, skin rashes, general malaise and tiredness, the latter first noted in 1873 [111]. Anti-histamines accentuate this tiredness, some 20% of patients experiencing some sedation even with the newer ones, and prescriptions have to carry a warning label. When drugs are used as the sole method of controlling symptoms, anti-histamines may have to be combined with eye drops, nasal cromoglycate and/or steroids, and inhaled cromoglycate, steroids and/or β-agonists if there is accompanying bronchospasm. This regime is satisfactory for mild cases without any need for specialist investigation, but if more than one drug is required, the patient ought to be monitored closely. This involves medical manpower costs in addition to the cost and possible ill-effects of the drugs. These patients, and those who dislike dependance on drugs, deserve an allergy investigation.

This should comprise an adequate history, appropriate physical examination and skin
testing. In addition to inhalant allergens, the role of environmental chemicals and food intolerance should be routinely explored. Specific and detailed programmes of allergen avoidance, when appropriate, can render a significant proportion of patients symptom-free without medication. Low-dose prophylaxis is effective [71–73, 79, 84] and should be available for all those who need it.

**Asthma.** Asthma is a multi-factorial complaint and attacks can be precipitated by non-specific factors such as exercise and infection in those with bronchial hyper-reactivity. However, if the specific causes of hyper-reactivity can be detected and eliminated, this may be substantially reduced, with a marked reduction in the need for medication [101, 112]. Asthma used to be regarded as a benign condition, but deaths increased in the 1960s, and, with ups and downs, have continued to be a major problem since. The condition is becoming more common [113], and appears to be more severe. The British Thoracic Society Guidelines [114] lay continuing and relentless stress on drug management, with very little mention even of methods of reducing exposure to inhalant allergens, and no mention of food intolerance, even though increased drug usage does not seem to have reduced the mortality. Indeed, regular therapy with selective β-agonists increases bronchial hyper-reactivity [115, 116], and β-agonists have been implicated in asthma deaths on theoretical, clinical and epidemiological grounds [117–119]. Long-term oral steroid therapy carries well-recognized risks, particularly for children.

The cost to the nation of asthma mortality, morbidity and medication is very high, with additional personal costs which are of greatest concern for asthmatic children. Allergy management can reduce this burden.

It is therefore time that allergy management of asthma was given a higher profile. Allergic factors contribute to most, if not all, cases of asthma: all asthmatics should receive effective counselling on the techniques of reducing exposure to inhalant allergens and chemicals. Patients on continuing regular medication involving more than one drug deserve a full allergy investigation, and may need specific prophylaxis, which is effective [89, 100, 101]. In a recent study, all asthmatics showed positive skin (prick and/or intradermal) tests to inhalant allergens, 18 out of 19 patients developed bronchospasm with food challenge and seven with very low doses of chemicals [100]. At follow-up, patients had fewer symptoms and were taking less medication [101].

Management of asthmatics will be similar to that for allergic rhinitis, although exploration of possible chemical sensitivity, both occupational and other, is more important in asthma. Some of the more severe cases of asthma should not undertake food challenge except under supervision, as severe bronchospasm may occur, even with foods whose effect had not previously been suspected [100].

**Skin disorders with allergic aspects.**

**Urticaria and angio-oedema:** acute urticaria may subside rapidly, and unless it is a recurring problem it is likely to remain in the province of the general practitioner. Chronic urticaria may require a considerable drug cocktail to achieve satisfactory suppression. The cost burden of this suppression may be considerable, whereas elucidation of the causes with subsequent avoidance can relieve the symptoms, without the need for medication [15]. Reactions to foods, inhalant allergens and chemicals [120], and gut dysbiosis [121] may all contribute.

Angio-oedema is frequently under-diagnosed, particularly when it occurs with urticaria, as it often does. When it causes respiratory obstruction, it becomes dangerous, and the allergist must ensure that such patients carry an emergency kit (see anaphylaxis). Drug prophylaxis is not effective in all cases, but with a full allergy investigation the cause(s) can usually be found.

**Eczema:** Infantile eczema may clear on palliative management after a few years, but is
is very distressing to children and their parents while it lasts, and significant numbers go on to develop chronic eczema. The main pharmacological treatment is steroids, usually topical. These are associated with significant absorption in most cases, a particular risk for small children: chronic steroid use causes skin damage, and may interfere with growth. Three studies have shown the importance of food intolerance in eczema [122–124]. Twelve of 13 children with severe chronic eczema attained complete remission on an exclusion diet [122], all relapsing when they returned to a normal diet: 73% of 37 children with refractory eczema improved on an elemental diet [123].

Aero-allergens (such as mites and animal danders) and chemicals also play a part in some cases of eczema, both through inhalation and by contact [28], and many cases can be totally relieved by an adequate avoidance programme.

Contact sensitivities are often of importance in eczema, and occasionally in other conditions. Any allergist dealing with skin disorders should be trained in and familiar with the techniques of patch testing, but, except perhaps for aero-allergens, this can often be left to the dermatologists, who usually achieve excellent results as avoidance is the treatment for other contact allergies.

The particular role of the allergist in relation to skin conditions is to detect the unsuspected triggers, usually foods or chemicals, and to initiate good avoidance regimes when triggers have been recognized: some cases also need specific prophylaxis or an assessment of nutritional status [125, 126]. Eczema in early childhood may be due to immediate food allergy, but more often it is mixed or Type B. For some patients with intolerance to multiple foods, specific prophylaxis using one of the low-dose methods will be needed: incremental immunotherapy is not used for food intolerance and is regarded as dangerous in patients with eczema [21].

Anaphylaxis. The inevitable consequence of major untreated anaphylaxis is death: this is preventable if the patient carries emergency medication, and knows how to use it, provided that the patient is not taking non-selective β-blockers, which may block the effects of adrenaline. Allergists should ensure that all patients who have had anaphylaxis, or angio-oedema with laryngeal involvement or serious involvement of the tongue, carry an emergency kit, have another in reserve, and be registered with Medic-Alert. The kits should include a source of adrenaline, anti-histamine (such as Piriton 4 mg, 2 stat and 1 4-hourly), and prednisolone (40 mg stat, repeated the next day). Patients should be taught to inject themselves with adrenaline (including hands-on experience) and/or provided with an adrenaline inhaler.

For immediate Type 1 angio-oedema of the throat from food contact the kit should also include isoprenaline tablets BP 10–20 mg, which can be taken sublingually and give a higher local concentration and quicker local response. Unfortunately, at present they are no longer manufactured or easily obtainable in the UK.

An adequate allergy investigation should be carried out. Anaphylaxis due to drugs is usually recognized, though the investigation may need to explore a number of drugs which were given concurrently. It should be possible for the drug responsible to be strictly avoided, especially if it is by prescription only. A bracelet with details should be worn to cover emergencies. Contact substances such as latex may also provoke anaphylaxis.

Anaphylaxis due to food allergy is of greater concern: it has been reported after a wide range of foods and only very small quantities may be needed to provoke it, amounts readily hidden in processed food. Anaphylaxis from foods represents a serious hazard, and regularly causes death [127].

The allergist will usually use RAST test to investigate anaphylaxis, as skin tests, particularly intradermal tests, may be dangerous. If clinical challenge tests are necessary, they should be performed in a hospital unit where full resuscitation facilities are available.

Patients should carry the emergency kit until the cause of the anaphylaxis is found, and
unless avoidance can be total, continue to do so until there is evidence of protection by specific prophylaxis.

**Allergic reactions to insect stings and bites.** Since allergy to wasp and bee venom may lead to anaphylaxis and death, patients who have had a generalized reaction to insect stings should be considered for specific immunotherapy to give protection against further stings. The standard method in use is incremental immunotherapy, which should be given in a specialist centre with full resuscitation facilities: decisions about treatment in individual patients require special experience, and depend on the clinical history and the demonstration of specific IgE antibody.

Severe reactions to the bites and stings of other insects are reported in the literature: allergists should be aware of them and prepared to investigate all adverse reactions of this sort.

**Allergic reactions to drugs and other chemicals.** Traditionally, allergists have looked for chemical sensitivity reactions almost solely in the workplace, where they are indeed responsible for considerable morbidity and absenteeism [26, 27, 128–130]. However, for housewives the home is the workplace, and most patients spend more time there than at work. Large numbers of chemicals are now used in the home, and the home is, in this respect, often as dangerous as the workplace. Indoor environments may be up to ten times as polluted as the outdoor atmosphere, even in cities [129]. Chemical sensitivities may be IgE-mediated [26, 128], but most are not, and give rise to a wide range of symptoms [128–130], particularly cerebral symptoms [94]. Allergists need to be prepared to investigate all types of adverse effects of very low doses of chemicals. An allergist is an essential member of teams investigating outbreaks of tight building syndrome [131, 132].

Many chemicals are widely distributed, and their involvement in the aetiology of symptoms is often unsuspected. Patients with chronic exposure frequently give false-negative results on challenge until after a period of avoidance: establishing the relationship may be difficult unless there is access to an ECU.

Protection against most chemical sensitivities can be achieved using the neutralization technique [100] or EPD, which implies that some sort of specific reactivity is involved, even in those not mediated by IgE. Effects of many xenobiotic chemicals (particular the herbicides and pesticides) on enzymes have been described [129] and are believed to contribute to the aetiology of chemical sensitivity [130].

IgE-mediated drug allergy requires facilities for specific testing, best done by indirect laboratory techniques when possible. Drug sensitivity reactions are common, but a number of reactions may be due to an excipient rather than to the drug itself, even to the small amounts of corn or lactose in pills, and preservatives in liquids. Tartrazine, sunset yellow and erythrocyn for instance, all used as pill colourants, are known allergens [133], and other chemically related dyes are in common use. In the UK, pharmaceutical manufacturers are permitted to keep medicine formulations confidential. Experience in assessing these reactions is largely confined to allergists. Responsible testing may enable the patient to take those drugs which have tested negative. It is important, however, to recognize that, as with foods, reactions to chemicals are of varying severity. Drugs causing Type B reactions might reasonably be used for short-term therapy if there were no adequate alternative: these need to be differentiated from drugs causing acute IgE-mediated reactions which should be avoided entirely.

**Food allergy.** Food allergy is an immediate, Gell and Coombs [8] Type 1, reaction to food. It is anaphylactic in nature, and therefore of rapid onset, and often severe. As the problem is IgE-mediated, laboratory testing by RAST is the method of choice for establishing the
diagnosis, and should be performed by a competent laboratory. Some patients with food allergy may subsequently have a sudden fatal anaphylaxis. This has occurred with a wide range of foods, particularly nuts and peanuts [127].

The term food intolerance is often used for all intolerance to foods which has not been shown to be IgE-mediated. This is confusing, since it includes both Type B food reactions, mediated by other immunological mechanisms (e.g. IgG or immune complexes) or with features suggesting that an immunological mechanism may be involved, and food intolerance due to toxicity, enzyme anomalies or gut dysbiosis. For clarity, the term intolerance should be reserved for biochemical intolerances.

Type B reactions occur mainly to foods eaten frequently. They have a distinct natural history, showing a tendency to masking, and for recovery (temporary or complete) to occur after variable periods of avoidance [32], often more quickly in infants [50]. The reality of many of these reactions has been demonstrated in double-blind food challenge (see page 84).

** Syndromes Which May Be Induced or Exacerbated by Reactions to Food or Environmental Factors **

Non IgE-mediated allergy to foods plays a large, but not exclusive role in these syndromes [13, 14], and reactions to inhalants and chemicals, and other mechanisms may also contribute [13, 14].

*Irritable bowel syndrome and Crohn’s disease.* Allergists manage irritable bowel syndrome (IBS), non-ulcer dyspepsia and related syndromes (including some cases with proven hiatus hernia) by the detection of food reactions (occasionally Type A but mainly Type B, with some contribution from enzyme anomalies), avoidance of trigger foods, encouraging less repetitive eating habits and specific prophylaxis when necessary: in occasional patients, inhalant allergies or chemical sensitivity may need to be explored. It is not unusual for patients to react to wheat: the condition of these patients deteriorates when treated with wheat bran.

A 50% success rate was obtained using a single dietary regime in IBS patients who had failed to respond to other treatments [134]. With more comprehensive dietary investigation, 70% responded well and on follow-up 2–3 years later 90% of these were well: most were keeping to their diets but a quarter could relax [135].

In most patients, Crohn’s disease can be brought into remission by restricting food intake to a hypo-allergenic elemental food only for 14 days: avoiding foods which gave symptoms on food challenge was as effective in maintaining remission as steroids [136]. In a more recent collaborative study [137] involving 93 patients, these findings were confirmed and there were significantly fewer relapses in patients maintained by diet.

*Migraine.* In patients attending a migraine clinic, many attacks of severe migraine were prevented by avoiding daily drugs (particularly ergotamine and exogenous hormones—the contraceptive pill and hormone replacement therapy (HRT)), and smoking, as well as cheese, chocolate, citrus fruit and alcohol [138], but most patients continued to have headaches: of those who also cooperated with an exclusion diet, 85% became headache-free, with a reduction of average tablet use from 115 per month before the diet to less than one [139]. Migraine was relieved by an exclusion diet in 70% of patients in another study [140]. Of 88 children who completed an exclusion diet, 89% recovered completely [38]. The foods causing migraine may include those implicated because of their amine content, but in very few cases would freedom from migraine have been achieved if amine-rich foods alone had been avoided [38, 139].

In Grant’s migraine study [139], 15 patients were also hypertensive: all 15 became
normotensive after the exclusion diet, and remained so if they avoided foods which caused symptoms. In 45 children with both epilepsy and migraine who followed an exclusion diet, the epilepsy improved in 80%; 25 recovered, 11 improved and only nine did not respond [39].

Arthritis. Type B reactions, mainly to foods, contribute to both rheumatoid arthritis [141–143] and osteoarthritis, and many patients remain well for many years if they avoid trigger foods or receive specific prophylaxis. However, not all such patients respond to a wide-ranging allergy investigation, possibly because reactions to auto-allergens or infective agents are also contributing. Many patients with rheumatoid arthritis suffer from poor nutrition, and may show considerable improvement when this is corrected.

Cerebral symptoms. The provocation of cognitive and emotional cerebral symptoms by sublingual application of weak extracts of foods was significantly greater than with placebo in a double-blind study in subjects who had symptoms previously [144]. Such symptoms as mood changes, panic attacks and variable difficulty in concentration, memory or speech are common in multi-symptomatic patients [15], and are seen particularly in chemically sensitive patients [129], or caused by nutritional deficiency [145], but may also be caused by reactions to foods. Symptoms are similar to those of psychological origin (though they tend to be more variable in severity) and have usually been attributed previously to psychological causes [146], but the prevention of symptoms by the avoidance of allergens and chemical triggers argues against this [105]. Allergists should seek to make a positive diagnosis in these cases: the criteria required for accepting a symptom as of psychological origin should be tightened to discourage this easy and quick diagnosis until the contribution of allergic and related reactions has been evaluated.

Two studies have reported marked improvement in hyperactivity in children on an exclusion diet, with recurrence of symptoms on blind challenge with some foods [33, 34]. In one [74], children subsequently given specific prophylaxis recovered tolerance to more foods than controls (see page 87).

Patients with mild cerebral symptoms present no particular management difficulties, but the investigation of patients with severe problems cannot be undertaken in the UK at present because there is no ECUs with facilities for caring for disruptive patients.

Unexplained fatigue. Chronic fatigue syndrome is a multi-factorial illness [147] in which there is often some degree of sensitivity to chemicals and to foods [148], though this may be a secondary phenomenon. Many are helped by detection of sensitivities, or of nutritional deficiencies [149], or management of gut dysbiosis. The multi-system nature of their symptoms means that allergists are the best group to undertake the management of these patients.

Abacterial cystitis and bladder pain. Recurrent cystitis in women (sometimes, if not each time, abacterial) and bladder pain frequently respond to a wide-ranging allergy investigation and food allergy has been postulated as a cause of nephrotic syndrome [110].

Multi-system polysymptomatic illness. Although patients may initially have had single-system disease, by the time they are referred to allergists they commonly have multiple symptoms. In a recent follow-up audit of two groups of the more seriously affected patients (370 in all), over 70% were ‘very much better’, 35% ‘well or almost well’: the patients reported medians of five and eight symptoms (graded as severe and frequent/constant), respectively on referral, but each group had a median of only one such symptom on
follow-up [15]. One of the groups had been asked the same questions both contemporane-
ously and retrospectively with similar results, showing that the difference was not due to
inaccurate recollection: relatives gave independent confirmation [105]. The symptoms had
previously been present for a median of over 10 years, and had resulted in a median of 2
(range 0–10) previous referrals per patient [105].

Management of these patients by single-system specialists is ineffective and expensive.
Patients referred to an allergist are relieved when they find a doctor interested in all their
symptoms. To achieve good results, allergists may have to explore a number of different
aetiological factors in these patients.

Other Physiological/Pathological Disorders

Other disorders are commonly seen in patients with allergies, particularly those with
multiple symptoms. The reasons for this seem to be complex since there is evidence that
immune factors have bidirectional interaction with stress [150–152], and nutrition [96, 129,
153] and indications of complex interactions with hormonal disorders [96, 154], chronic
toxicity [129, 155, 156], gut dysbiosis [157, 158] and hyperventilation. Narrow diets
predispose to food intolerance, and dismissal of genuine symptoms may contribute to
psychological overlay [159].

Gut dysbiosis. Some form of gut dysbiosis is common in this group of patients [158, 160,
161], but the precise details vary, and the condition overlaps with food intolerance. Patients
are often relieved of their symptoms by appropriate attention to diet and nutrition,
sometimes needing anti-fungal drugs for several months.

The reality of this syndrome has been demonstrated by the frequency with which these
patients have abnormal gut fermentation [162, 163], often associated with deficiencies in
B-vitamins and trace minerals [160].

Nutritional deficiency. The diet of large sections of the population falls far short of the
World Health Organisation recommendations [164–166], especially with regard to trace
minerals and vitamins. Depletion of trace minerals by the heavy use of chemical fertilizers
in modern intensive agriculture, treatment of foods to prolong shelf-life [94], and increased
processing of foods have all contributed. Cattle and sheep deficient in trace minerals
(mainly selenium, copper, cobalt and zinc) suffer from a range of conditions including
infertility and abortion: these can be prevented by treating the stock or the pastures with the
appropriate nutrients [167].

Deficiencies of trace minerals, vitamins and essential fatty acids also contribute to a wide
range of symptoms in humans [168–171], but doctors in general receive no training in the
use of nutritional methods of treatment. Nutrition research is mostly done on animals, or on
healthy humans, or as epidemiological studies, not on the individual patient, and very little
nutrition research is published in the journals commonly read by clinicians.

Drug treatment of the symptoms caused by nutritional deficiencies may compound the
problem by introducing additional xenobiotic material that has to be detoxified, thus
aggravating the deficiency [95]. In contrast, rectifying the deficiency prevents the symptom
at source, and improves general health. A range of conditions have responded to the
correction of nutritional deficiencies [168–171]. The nutritional approach has great potential,
and allergists should attempt to keep up to date with developments in this area.

It might be expected that dieticians would have a substantial contribution to make in this
area as well as in devising balanced diets for patients who have to avoid a variety of
different foods. However, to date this does not seem to be the case, and most are
ill-equipped to make the positive contribution needed. Active support from dieticians would
be essential if all patients who could benefit were to be managed adequately.
Other. There is very little published work on chronic toxicity: it is difficult to set up satisfactory studies, particularly in humans, and firm conclusions cannot be drawn from most unintentional human experiments because of their uncontrolled nature. Investigations indicate that exposures to chemicals at levels present in the environment have effects on enzymes with a wide range of functions [94–96, 129, 130]. Clinically, chronic toxicity tends to result in multi-system disease that may mimic Type B allergic illnesses, as well as predisposing to the development of allergic reactions.

Pesticides and herbicides have particularly been implicated in extensive evidence in other species. At normal environmental exposure levels, lethal toxic effects have been noted in peregrine falcons, sparrowhawks and buzzards which like humans are at the end of a food chain [172], and in foxes, otters, mink, badgers, etc. [173], and sublethal effects in other species of birds. Organochlorine timber treatment of loft habitats is thought to have caused fatalities in bats [173], a number of these compounds being found in the carcasses. None of this is surprising since pesticides and herbicides were synthesized precisely in order to interfere with essential biological systems [174]. Air contaminants may also be important, and, in humans, mercury in dental amalgam [175].

The extent and importance of biochemical individuality was recognized long ago [176, 177], but it is still under-appreciated. Enzyme anomalies seem to be particularly common in allergic patients [178], but it is not clear yet whether this is because individuals with certain anomalies are more likely to become allergic, or because the anomalies and the allergies are linked by the effects of chemical toxicity or nutritional deficiencies [129, 130]: a similar doubt exists about the relationship between allergies and the hyperventilation syndrome.

It is important for the allergist to be aware of these factors, particularly in relation to the management of the more severely affected patients.

ESTIMATING THE NEED FOR ALLERGISTS

Surveys of the prevalence of allergies, for instance asthma, indicate that they are rare in isolated primitive communities living a totally unsophisticated life-style [179]. The increase with westernization seems to be almost linear. A survey in the UK in 1979 showed an overall incidence of 30%, with a significant increase over the previous 5 years [180]. The rise has continued since then [1]: an alarmingly high proportion of primary school children in the UK now take inhalers to school.

Most allergic patients have chronic symptoms, using up considerable consultation time and other medical facilities, and consuming quantities of drugs [181, 182]. Many of the side-effects of drugs have allergic or pseudo-allergic mechanisms, and side-effects occur more frequently in allergic patients, particularly with long-term or repeated medication. Adequate allergy investigation and management has been shown to reduce expenditure on drugs, and can be cost effective [182–184], even without considering any saving of the potential cost of iatrogenic disease. During a 5-year follow-up of patients who had presented with chronic intractable phlebitis [184], the 10 control patients had 41 episodes requiring hospital admission and at least 60 lesser episodes involving total costs of $200 000, compared with 10 patients investigated in an ECU who had a total of two transient episodes only during the same period costing a total of $200: the treated patients could walk without pain in contrast to the control patients who remained incapacitated. The need for a variety of different types of surgical operation may also be reduced, for instance grommets [109], cholecystectomy [185], nasal polypectomy [12] or for the carpal tunnel syndrome [186]. Even a single consultation of allergy patients with a nurse practitioner, advising on little more than inhalant avoidance, reduced both drug use and consultations [16].

At the present time, only a very small proportion of patients who have chronic symptoms due to food and environmental factors find their way to doctors offering a wide-ranging
allergy service, and usually only do so after a number of other referrals. Most of these practitioners are in the private sector, though some general practitioners use these methods and find them cost-effective [182, 183]. Cox [183] found that his drug bill in general practice went down from 21% above the average for his area before he started to use the techniques of environmental medicine, to 31% below the average, 8 years later. Compared with the average for his area (per 1000 patients) he prescribed 40% fewer drugs for the nervous system, 50% fewer for the gastrointestinal system, 50% fewer anti-rheumatics, 44% fewer anti-allergy drugs and 53% fewer for the skin. Prescriptions for anti-fungals were 25% higher and nutritional supplements 129% higher.

Ten allergy training posts have recently been approved, but they will do little more than provide replacements for the allergists approaching retirement. If purchasers were to appreciate the potential savings in consultation and investigation costs, medication and sickness benefit which result from the transfer of only a fraction of the above conditions (for instance migraine, IBS and polysymptomatic illness) to allergists giving wide-ranging care, a major initiative would be required to provide appropriate training. In view of the excellent response of most patients with IBS and migraine to management by environmental medical methods [135, 139], and the enormously high cost to the country, and to the NHS, of these conditions, this must eventually happen.

THE ETHICS OF ALLERGY PRACTICE

In the view of the BSAEM/BSNM, it is curious that the medical profession should have scorned the methods of environmental allergy for so long, in the face of repeated reports of its efficacy. The main bone of contention seems to have been the topic of Type B food allergy, which in the experience of the society plays an important role in the aetiology of many chronic diseases.

The idiosyncratic nature of the adverse effects of foods was first noted by Hippocrates (460–377BC), who recommended dietary measures to treat and prevent a number of maladies [187], but also by Maimonides in the twelfth century [188], Sir John Floyer [189] in 1698, Sir Gilbert Blane in his ‘Medical Logick’ [190] in the early years of the last century, H. H. Salter [191] in 1868, G. W. Hare [192] in 1905 and Charles Richet [193] in 1911. A group of allergist physicians in the US [4] were very active from the early 1920s, and in the UK Sir Humphrey Rolleston [194] contributed to a symposium in 1921, Latham and Coke [195] published an important paper on asthma in 1922, and George Heam was actively using these methods in Birmingham from just after World War II. The similarity of the lists of syndromes found to respond is striking, and confirmed by recent studies [15]. This was so even when the physicians were unaware of each other’s work which was the case with Maimonides [188], Hare [192] and Rowe [5]. Each of the physicians may have influenced a few independent-minded colleagues through their publications or their teaching, but until recently they had failed to influence mainstream medical thought.

In the last 20–30 years, two opposing developments have resulted in active polarization. The development of potent drugs and other technologically based treatments has fostered the belief that the control of symptoms is a pharmacological or surgical matter. In contrast, over the same period, environmentally minded physicians have concentrated on preventing symptoms, with significant success. The logic of the latter view has been cogently expressed by Rapp [196].

Basically, if you have a sore on your foot caused by a nail in your shoe, the answer is to remove the nail, not to put a bandage on the sore.

As a result of this polarization, there is now a movement within pharmacological medicine not only to disparage any new management method which has not been tested by double-blind trials, but also to attempt to have such treatments disallowed [197]. Hallowing
the double-blind trial in this way is at odds with the facts. Has there ever been a double-blind trial in which every treated patient has done better than every control patient? It is unlikely: trials are only done because treatments only offer partial control of symptoms, or help some patients more than others. ‘Chance’ say the statisticians, but in this sense ‘chance’ is individual variability [176, 177, 198], and unless and until all the relevant facets of individual variability can be measured, trial results will continue to be applicable to the average patient, but not necessarily to the patient in front of you. Moreover, overemphasis on blinding unfairly penalizes those modalities of management which cannot be tested blind, including everything requiring active co-operation from the patient.

If the will were there, it would be possible to test the efficacy of wide-ranging allergy management by well designed randomized referral trials. In the opinion of the BSAEM/BSNM, such trials are long overdue. So certain is the society that the methods would stand up to investigation that members would be prepared for their methods to be compared with any other type of management in patients with the conditions discussed.

It is not only a physician’s right to attempt to find better ways of helping patients but also a duty: the imposition of restrictions on doctors who are genuinely trying to do this would result in the fossilization of medicine. The BSAEM/BSNM recalls that the Declaration of Helsinki [199] states that:

In the treatment of the sick person, the physician must be free to use a new diagnostic and therapeutic measure if in his or her judgement it offers hope of saving life, re-establishing health, or alleviating suffering,

and that the Declaration of Geneva [200] insists that for doctors “the health of my patient will be my first consideration”. The BSAEM/BSNM urges all physicians to listen to patients who have chronic symptoms and then ask themselves two questions: ‘Why does the patient have these symptoms?’ and ‘Might something in his/her life-style or exposures be contributing?’

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EFFECTIVE ALLERGY PRACTICE


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