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Comment on the position paper of the European Academy of Allergy and Clinical Immunology on allergen immunotherapy

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Allergen immunotherapy (AI), or allergen specific therapeutic vaccination has had a chequered history. It was started in 1911 by Noon and Freeman using grass pollen in seasonal allergic rhinitis patients, but was only proved to be effective in a placebo-controlled trial some 40 years later. In 1986 the procedure largely disappeared from the United Kingdom when the Committee on Safety of Medicines, having noted the number of fatalities produced guidelines suggesting that allergen immunotherapy should only take place in a centre where full cardio-respiratory resuscitatory facilities were available, and that the patient should be watched for 2 hours following each injection. However the practice continued in mainland Europe and the USA and in 1998 the World Health Organisation published a position paper at the European Academy of Allergy and Clinical Immunology meeting in Birmingham. This paper was chaired by John Bousquet, Richard Lockey and Hans Jorgen Malling, from France, USA and Denmark respectively. The key points are that:

- specific immunotherapy should be used for proven IgE mediated disease involving 1 or 2 well characterised allergens where allergen extracts of good and reproducible quality are available.
- it should be prescribed by specialists and administered by physicians who are trained to recognise and treat anaphylaxis.
- Immunotherapy with inhalant allergens reduces symptoms and/or medication needs for patients with allergic asthma and rhinoconjunctivitis.
- Hymenoptera venom immunotherapy is the only effective treatment of insect sting-induced anaphylaxis.
- sublingual immunotherapy may be indicated in pollen and in mite-induced rhinitis.

Classical immunotherapy involves subcutaneous injection of allergen, usually with an induction phase of weekly injections for about 12 weeks with incremental doses until a maintenance dose is reached. This is then given at monthly intervals for between 3 and 5 years.

It is important to take a careful history prior to each injection of any recent illness or infection, medication change, allergen exposure or disease exacerbation. The reaction to the previous injection needs to be documented, particularly whether there was any delayed effect. If any of these factors are present then the next dose should either be reduced or omitted. Allergen must be given slowly subcutaneously, not intravenously. Afterwards the patient is asked to report any adverse effects immediately since anaphylaxis is easier to treat if tackled quickly. Patients must be under medical supervision for 1 hour post injection in the UK.

The mechanism of action of classical immunotherapy is unknown but there is some evidence that it involves a switching of T-cells from the TH2 (allergy promoting) type to the TH1 (allergy inhibiting), type or to unreactivity (anergy). This may involve the cytokine IL-10.

There is evidence of long term benefit following discontinuation of treatment and in childhood AI has been associated with the reduced risk of new allergic sensitisations. Thus it appears to have disease-modifying properties.

As the commitment of both clinician and patient to regular subcutaneous injections needs to be high this is obviously not a treatment for the majority of patients who are well controlled on allergen avoidance and conventional pharmacotherapy. At present it is largely reserved for patients who are not controlled by these methods. However the advent of trials suggesting efficacy with sublingual application of allergen and with peptide fragments, which do not cause anaphylaxis, the place of immunotherapy in rhinitis and asthma treatment needs to be reassessed.

Priorities include:

- assessment of the relative risk/benefit value of AI in asthma and rhinitis as compared with best conventional medical management, and any additional value of allergen immunotherapy as added to such management.
- the influence of AI upon natural history of allergic disease, in particular on the progression from rhinitis to asthma.
- better standardisation of allergen extracts and refining of dose regimes and durations to maximise efficient efficacy and safety.
- the mechanisms of action of successful AI.

- Identification of patients who are likely to derive particular benefit from AI.

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