

Allergen injection immunotherapy

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Although allergen injection immunotherapy (AII) has been around for nearly a century, many doctors are still not aware of the evidence for its efficacy. About 15 000 patients are treated by AII in Australia each year, with about 300 000 injections administered annually for a wide range of allergens. The 10 most commonly prescribed allergen vaccines in Australia are house dust mite; five-grass pollen mix; 12-grass pollen mix; cat; couch grass, ryegrass and plantain pollens; *Alternaria* mould; cockroach; and olive/privet pollen. Patients receive regular subcutaneous doses of the allergens to which they are allergic, often for 3–5 years.¹ Does the treatment work, and, if so, is it cost-effective and is it safe?

Does it work? To date, about 200 completed randomised controlled trials have examined the question of whether AII is an effective treatment for allergic airway disease. Based on National Health and Medical Research Council levels of evidence, AII significantly reduces symptoms and medication usage in both allergic rhinitis (Level I) and asthma (Level I), although the former is the usual indication in Australia for this intervention.

Improvements with AII are clinically as well as statistically significant. In asthma,² the number needed to treat (NNT) (ie, number of patients treated to avoid asthma worsening in one subject) is four, the NNT to avoid increasing medication in one patient is five, and there is a significant reduction in both specific and non-specific bronchial hyper-responsiveness. Data are homogeneous, and most studies are of medium to high quality. Further, AII may reduce the progression from allergic rhinitis to asthma in some children (Level II),³ and monotherapy for one specific allergen reduces the risk of development of new sensitisation to other allergens (Level II).⁴ Whether AII is effective for treating food allergy has not been established, but research in this area is continuing.

Is it cost-effective? AII is cost-effective for treating atopic airway disease. Two large, rigorous German studies^{5,6} examining the pharmacoeconomics of AII for treating atopic airway disease found that there are net savings 3–6 years after starting treatment. Other research from Italy and the USA supports these findings.

AII treatment is cost-effective because (a) allergen extracts are relatively cheap (about \$10–15 a month in Australia); (b) the tolerance induced persists for years after treatment has stopped (Level II);⁷ and (c) the reduction in new asthma and prevention of additional allergen sensitisation may reduce the incidence of new disease.^{3,4}

Is it safe? Most debate on AII centres on questions of safety and risk. Mild to moderate systemic effects (rhinitis, mild bronchospasm, urticaria) occur in one in 1500 injections, there is one severe (near-fatal) anaphylaxis per million injections, and one death per 2.5 million injections.⁸ An Australian general practitioner treating 10 patients with AII annually could expect one instance of a mild to moderate systemic reaction every 7 years. AII might cause one death in Australia every 8 years. Notwithstanding the tragedy of any treatment-related death, this statistic has to be compared with the rate of rare deaths associated with other treatments and balanced

Evidence-based practice tip

The incidence of mild immediate reactions to allergen injection immunotherapy is reduced by pre-medication with an oral antihistamine before each injection (Level II).*

*NHMRC levels of evidence.

against the proven reduction in development of asthma in most patients.

Most severe adverse events result from giving an incorrect dose, giving the wrong extract, or giving the vaccine to a patient who has unstable asthma or is taking β -blockers. As adverse reactions are not predictable, safety can be enhanced by adhering strictly to the requirement that patients remain in the

clinic for a minimum of 30 minutes (ideally, 45 minutes) after each injection (even maintenance doses). This facilitates early access to medical treatment if an adverse reaction occurs.

When should patients be referred? There are good reasons for referring a patient to an allergist or clinical immunologist before initiating AII: apart from obtaining a second opinion on contraindications and other safety issues, this allows the consultant to assist with management if problems arise.

Medical practitioners administering AII should be aware of the data on safety and compare these with data on the adverse effects of other interventions that they prescribe, and the disease itself, to put the issue into perspective. With proper selection of patients and vaccines, attention to contraindications, provision of a suitable administration milieu, strict adherence to the recommended waiting time after giving the injection, and a team approach with a consultant, AII can be a rewarding treatment for the patient.

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- 1 Specific allergen immunotherapy for asthma. A position paper of the Thoracic Society of Australia and New Zealand and the Australasian Society of Clinical Immunology and Allergy. *Med J Aust* 1997; 167: 540–544.
- 2 Abramson MJ, Puy RM, Weiner JM. Allergen immunotherapy for asthma. *Cochrane Database Syst Rev* 2003; (4): CD001186.
- 3 Moller C, Dreborg S, Ferdousi HA, et al. Pollen immunotherapy reduces the development of asthma in children with seasonal rhinoconjunctivitis (the PAT-study). *J Allergy Clin Immunol* 2002; 109: 251–256.
- 4 Pajno GB, Barberio G, De Luca F, et al. Prevention of new sensitizations in asthmatic children monosensitized to house dust mite by specific immunotherapy. A six-year follow-up study. *Clin Exp Allergy* 2001; 31: 1392–1397.
- 5 Schadlich PK, Brecht JG. Economic evaluation of specific immunotherapy versus symptomatic treatment of allergic rhinitis in Germany. *Pharmacoeconomics* 2000; 17: 37–52.
- 6 Martens P, Lobermeyer K. Krankheitskosten-Studie und Kosten-Nutzen-Analyse der spezifischen Immuntherapie bei Asthma. *Allergo J* 2001; 10: 341–347.
- 7 Durham SR, Walker SM, Varga EM, et al. Long-term clinical efficacy of grass-pollen immunotherapy. *N Engl J Med* 1999; 341: 468–475.
- 8 Amin HS, Liss GM, Bernstein DI. Evaluation of near-fatal reactions to allergen immunotherapy injections. *J Allergy Clin Immunol* 2006; 117: 169–175.

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