

Letter to the Editor

Specific immunotherapy in children is safe and effective

Dear Sir,

while reading the Special Report on specific immunotherapy (SIT) by Professor Frew on behalf of the British Society for Allergy and Clinical Immunology Working Party¹, we thought that the title should read more appropriately "Banishment of SIT except for venom hypersensitivity". Obviously allowing this form of treatment also to patients with rhinoconjunctivitis is unexpected, since most and most cases of this condition respond very favourably to second-generation H₁-receptors antiallergic drugs. While we appreciate the aims of the working party and the ensuing recommendations insuring scientific basis for SIT and optimization of allergic patients' management, especially for prevention and minimisations of untoward effects, we think that the special characteristics of childhood allergy are very different from adult allergy in several respects².

However what surprises us a great deal is that most reviews dealing with SIT, including that of Dr Larsen³ appear to apply to children the results of studies employing only adult patients. Several authors judged that the SIT results are controversial, especially in allergic rhinitis (AR), many cases of which can be effectively cured with drug therapy³⁻⁵. A thorough evaluation based on experience concludes that the critics to SIT are often supported by statements resembling clichés, such as the controversial results of well-controlled studies, the limits of its efficacy, the improvement of drug therapy, and the potential dangers. These clichés often recall the statements of various experts, for example the expert panels of a WHO/IUIS Working Group⁶ and the English Forum⁷ stress without proofs the high prevalence of severe reactions even fatal in childhood⁶, or practically suggest to eliminate SIT as a therapeutic option for allergic patients, since the risks associated with SIT are higher than the possible positive effects⁷. In addition, a recent work stated that children under 5 years of age present a significantly greater risk of systemic reactions⁸, however the authors failed to specify that:

1. The children were subjected to a rush protocol, which is known to provoke more reactions;
2. The children had neither premedication nor preventive measures; the authors were conscious of the risks, therefore the patients were hospitalized for the first night of treatment;
3. The authors hypothesized that the hospitalization increased the rate of severe reactions due to its psychologic impact⁹.

The Special Report¹ and Dr Naclerio⁴ are concerned with a supposed lack of studies comparing drug therapy with SIT. We have elsewhere discussed whether control children should be injected with placebo solutions or treated with all available medications, as we did¹⁰. However the differences between SIT- and drug-treated children are statistically very significant in our studies^{10,11}. These included 87 children (aged 2-14 years) with grass-pollen asthma and/or AR¹⁰, and 39 children (aged 5-14 years) with monoallergy to *Alternaria alternata*¹¹. The diagnosis in these children, as well as in the groups of controls, was established by careful clinical evaluation, including family and personal history, physical examination, and skin prick tests. Challenges were not used as an end point, but all individuals were highly positive by skin tests to allergen extracts. In both studies the 57 and 40 age- and sex-matched controls had a comparable severity and prognosis of the disease, and there was also a similar distribution as regards medical treatment prior to the trial. None of the children in the study- and control-group had previously received SIT. The children in study

Table I. Data in favour of early treatment with SIT I.

- The most severe cases with asthma have an early onset of the disease;
- The allergic component of asthma is most pronounced in children and adolescents;
- It has been suggested that SIT of children with hay-fever reduces the risk of development of asthma;
- Even slight asthma is accompanied by desquamation of bronchial epithelium probably due to the ongoing allergic inflammation in the bronchial mucosa;
- Elastic fibres in the bronchial wall are destroyed in cases with long-standing asthma.

received SIT with a pollen or *Alternaria alternata* extract (alum precipitated pyridine extract) over a 3-year period. The controls were regularly treated with all available medication. During both trials all children were seen in our Department at 3-month intervals.

Among children with both pollen-asthma and -rhinitis¹⁰, 39% of SIT-treated had excellent (marked improvement since onset of trial), 55% good (definitely better than at the trial onset), 6% poor (unchanged), results. Children suffering only from rhinitis showed comparable results (30, 60, and 10%, respectively). Only about 10% of both groups of controls improved ($p = 0.0033-0.0001$). The children with monoallergy to *Alternaria alternata*¹⁰ were evaluated and treated for 3 years as above. The SIT results were excellent in 80% and good in 20% of patients (and in 0-2.5% of controls) ($p = 0.0001$). This study was recently quoted by Dr Salvaggio in a recent AAAI Syllabus on mold allergy¹². Our studies have demonstrated that the improvement is dose-dependent: at a dose of 40,000 PNU 1.5% of children had excellent results, at a dose between 40,000 and 80,000 they were 18%, and at dose > 80,000 39% had excellent and 55% good results¹⁰. Recently we have prospectively observed during three years 300 children with correctly diagnosed asthma, and demonstrated that in pediatrics the SIT is remarkably safer and almost always effective¹³.

Up to now we have treated with SIT 1313 children aged 2-14 years¹⁰⁻¹⁴, we observed SR in 0.09% injections and only one case of shock = 0.0016% of injections and in 0.089% of 1119 treatments¹⁴. It is very striking that the children in our studies had only modest reactions which remitted without complications.

To the distinguished experts^{6,7} we answer that coronaropathies and related conditions are unlikely to present clinically in children, who can therefore benefit from adrenalin administration, and in addition, no fatal case in children is included by the English experts in their outstanding review, as we have thoroughly discussed¹³. We have also documented that severe adverse reactions during SIT are almost non-existent in children¹³. Several additional controlled studies have demonstrated the effectiveness of SIT in children¹⁵⁻²⁵. Considering the worldwide prevalence of allergic

Table II. Data in favour of early treatment with SIT II.

- Rhinitis symptoms are reduced for many years after a three years course;
 - Symptoms are reduced in a dose dependent manner;
 - Asthmatic symptoms are reduced early in the course of SIT of patients with pollinosis, *but not in chronic asthmatics*;
 - Reduces the allergic component of rhinitis and asthma as measured by mast cell release (skin response), provided doses high enough are used.
- Conclusions*
- Therapeutic subcutaneous IT:*
- Should be given to patients with severe rhinitis despite correct medication;
 - Should be given early in the course of asthma, before permanent damage to the bronchi has developed;
 - May induce allergic reactions, why proper monitoring is most important;
 - Prophylactic treatment would be of the greatest interest in neonates, infants and children at high risk of developing allergy.

disease which increases in a geometric way, the best results are certainly obtained when SIT is associated with effective preventive measures²⁶.

In conclusion SIT is the only treatment able to influence the natural history of respiratory allergic diseases; if early started and carefully conducted it remains a cornerstone in the treatment of childhood AR and asthma²⁷ (Tables I and II). In addition drug therapy may continue for the whole life-span²⁸, whereas after a 3-5-year SIT course the effect of therapy lasts for several if not countless years (10-14). It is of note that cessation of long-term drug treatment in children with asthma results in clinical deterioration²⁹.

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