Steroid-responsive nephrotic syndrome and allergy

Sir,

The large and detailed survey by Meadow et al.\(^1\)\(^2\) on the incidence of allergic features in steroid-responsive nephrotic syndrome (SRNS) differs in some ways from our recent findings.\(^3\) In 42 SRNS children associated with minimal glomerular changes we could not find a statistically significant difference between the frequency of allergic disorders, the serum levels of total IgE, and the incidence of allergen-specific IgE antibodies in serum as detected by RAST,\(^*\) and furthermore there were fewer positive skin prick tests. Our data do not support the hypothesis that IgE mediated hypersensitivity plays a general role in the pathogenesis of SRNS, but they strengthen the view that in a small group of children with SRNS who are characterised by the coincidence of a clear history of allergy, a positive skin prick test, and high specific IgE antibodies to certain allergens, this pathogenesis must be considered.

Some discrepancies between the results of Meadow et al. and our own study must be owing to differences in the selection of patients and control subjects as well as to the interpretation of skin tests and laboratory data. As in other investigations\(^4\)\(^5\) the great majority of children in the Leeds study had a SRNS characterised by frequent relapses, whereas 26% of our patients were non-relapsers or ones who seldom relapsed in whom the proportion of positive atopic histories or abnormal allergic tests was low. Of 16 cases in our steroid-dependent group (which had the highest number of relapses) five were labelled as atopic, a proportion similar to that in the whole British series.\(^1\)\(^*\) The control population studied by Meadow et al. may be biased by the exclusion of children with primary atopy, in contrast to our own controls.

Our criteria for accepting a skin test or RAST as pathological were stricter; a weal of 2 mm diameter regarded by Meadow et al. as a positive skin test was classified as 1+ (negative) by us. Results of RASTs were graded in our study, and classified as pathological only if

\* RAST = radioallergosorbent test.

at least 2+. Only 21% of SRNS patients were counted as having a positive skin test and 17% as having a RAST class 2 or higher, to at least one of 8 allergens used. A comparison between the two series is difficult because the spectrum of specific allergens applied for skin tests and RAST was different; the source of the allergens taken for skin tests differed in the two studies. Furthermore, no control data for RAST are given in the paper of Meadow et al.

A striking difference between the two investigations concerns the type of allergic manifestations observed in children with SRNS. Whereas in the British series only 4 of 26 children with a positive history of allergy had hay fever we found it in 6 of our 7 atopic cases. In our series we did not find a patient with a clear history of food allergy or eczema. However, we can confirm that the presence of an overt atopic disorder at the same time as a relapse of the SRNS is rare. In our experience most of the abnormal skin tests were produced by mixed grasses, rye, and oat, and high RAST titres mainly by pollin; in Meadow’s series these tests were found to be positive predominantly with house dust or *Dermatophagoides pteronyssinus.*

In contrast to the recent findings of the British authors and earlier results\(^6\)\(^7\)\(^8\) we failed to find a significant difference in levels of total serum IgE between nephrotic and control children and only 4 of our 7 patients with SRNS labelled as allergic presented with IgE concentrations higher than 500 U/ml. This discrepancy could be attributed to the fact that most of our patients were studied at the beginning of a relapse, whereas all British patients were in remission. However, this argument does not seem to be valid because in another series of patients with SRNS serum IgE levels were higher during treatment of a relapse than during remission.\(^6\) We agree with Meadow et al. that the association between high total serum IgE and allergy is not constant in SRNS; therefore the significance of raised serum IgE levels in nephrotic children is doubtful.

In our study we included 18 children with steroid-resistant nephrotic syndrome associated with focal-segmental glomerulosclerosis, but only one presented

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Figure. Two children with frequently relapsing steroid-responsive nephrotic syndrome treated with immunotherapy.
with atopic features. This low incidence compared with SRNS may indicate that the two main histopathological forms of the idiopathic nephrotic syndrome—that is, minimal glomerular changes and focal-segmental glomerulosclerosis—are two different disease entities. This hypothesis is supported by recent data on the frequency of HLA antigens in these groups of patients.

We found that HLA B8 was significantly more common in patients with SRNS and minimal glomerular changes when associated with atopy (38%) but not in those without atopy (28%), compared with controls (18%).

In contrast to an earlier report the frequency of HLA B12 in SRNS was the same as that in a control group but was significantly increased in patients with steroid-resistant focal-segmental glomerulosclerosis.

We found that HLA B8 was significantly more common therapy (preseasonal hyposensitisation by subcutaneous injections of specific allergen extracts) in 2 children with frequently relapsing SRNS (Figure). In both patients there was a rapid clearance of allergic airway symptoms, and in one child there was complete disappearance of proteinuria during a period of 3 years without further immunosuppressive therapy, followed by a relapse 8 months after immunotherapy was stopped. The other patient continued to have a similar SRNS relapse rate during immunotherapy as before it. Although the mechanisms of immunotherapy in SRNS remain unknown we believe that further trials are indicated in highly selected patients with SRNS and frequent relapses who have obvious clinical and laboratory symptoms of allergy.

References


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Professor Meadow comments:

This further study of nephrotic syndrome and allergy provides additional useful information. It seems that the excess of clinical and immunological features of allergy is associated particularly with the group of nephrotic children who relapse frequently. It is sad that this association does not lead to specific causes of relapse being identified for individual children; hence antiallergic management and therapy (other than corticosteroids) do not seem to be of benefit.

The German experience with immunotherapy (cure in one child, and no benefit in the other) emphasises the need for carefully controlled studies of therapy for a condition as variable and unpredictable as relapsing nephrotic syndrome.