

represent a secondary response to these processes, indicating neutrophil activation with enzyme release. Alkaline phosphatase² and proteinase C⁶ may be the target antigen of ANCA in vasculitis,² although this remains controversial.⁷ A neutrophil cytoplasmic enzyme may be the autoantigen, and the presence of ANCA may be an incidental finding related to the release of this enzyme into the blood, perhaps even having a protective role.

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Airborne mite allergen

SIR,—Dr Sporik and colleagues (Dec 15, p 1507) comment on our report (Oct 13, p 895). They defend their assertion that 2 µg *Der p* I/g dust is a "working value" of exposure to house-mite allergen, above or below which sensitisation will or will not take place.¹

We have always thought that the notion of threshold levels for allergen sensitisation is irrational. There are many underlying defects of immune response and a multitude of adjuvant factors that predispose to allergic sensitisation.² The quantity of allergen likely to sensitise will almost certainly differ according to the type of predisposing defect. Indeed, under some circumstances exposure to high concentrations might be more likely to induce tolerance than to sensitise.³

Equally, a threshold concentration of allergen (10 µg *Der p* I/g dust) that will produce disease in sensitised subjects, as Platts-Mills and de Weck suggested,¹ seems contrary to conventional views of immunology. The sensitised individual would be expected to react to far lower concentrations of antigen than would be necessary to sensitise the naive subject. Furthermore, in the case of asthma, non-specific bronchial hyperreactivity, which is affected by many factors such as viral infection as well as allergens, has a critical effect on acute responses to allergen.⁴ Thus, we believe it is appropriate to question the standards that were accepted by two international workshops, and were predominantly based on one North American study.⁵ The standards have yet to be proven by prospective study.

Sporik and colleagues cite their prospective investigation in support of their threshold concept.⁶ Among the 59 children born to atopic parents in their study, 31 of 56 aged between 1 and 2 years and exposed to more than 2 µg *Der p* I/g dust were not allergic to house mite at age 10, and only 3 were exposed to less than this value and were not allergic. Investigations of month of birth in relation to seasonal allergens suggest that the susceptible period of sensitisation is 0-3 months of age.⁷ The measurement between 1 and 2 years was probably too late.

We do not disagree with the suggestion that air sampling for allergen is fraught with difficulty; however, this is also true of dust collection. Should the latter be analysed by area or concentration sampling, and what are the standards for suction apparatus, filters, and elution procedures? The reservoir measurement can only be valid if release of allergen into the air is proportionate to its concentration. Our findings suggest that this is dependent on the

material in which the reservoir is contained, with synthetic carpets releasing much less than wool carpets.

Dr Tunon De Lara and colleagues (Dec 15, p 1508) draw our attention to the results of their study of airborne and dust levels of moulds, which support our contention. Furthermore, as Dr Preston and Dr Sinclair (same issue, p 1508) note, particle size of aeroallergen is critical for symptoms in sensitised individuals. Although dust sampling will take no account of mass median diameter of allergen, air sampling will, generally, only pick up smaller particles that remain airborne and can be inhaled. We found no difference in the results if mattress dust was substituted for carpet dust levels. Further details of our study are presented elsewhere.⁸

We believe that until large prospective investigations have been completed investigators should not be sanguine about threshold allergen exposure. We prefer the pragmatic approach of presence or absence of aerosolised allergen in relation to sensitivity in patients with rhinitis or asthma.

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Limb abnormalities after chorionic villus sampling

SIR,—I read with interest Dr Firth and colleagues' report (March 30, p 762) in which four cases of an oromandibular limb hypogenesis syndrome were described after chorionic villus sampling (CVS). I would like to describe a case that may contribute to discussion on this subject.

A 25-year-old woman with one previous normal pregnancy had labour induced for intrauterine death at 26 weeks' gestation. The pregnancy had been normal until then, and neither CVS nor amniocentesis had been undertaken. The mother received treatment for CIN2 in 1988, but had no other past medical history. The fetus was a stillborn male weighing 810 g and showing early maceration. There was micrognathia, a small mouth, absent fingers, and rudimentary digits on the feet. Internal examination was normal. There was no cardiac or brain anomaly. The placenta showed no gross abnormality (trimmed weight 205 g, cord 29 cm). However, microscopic examination revealed the presence of organised thrombi in the fetal stem vessels in all the sections that were examined (figure).

This case is one of oromandibular limb hypogenesis, a sporadic disorder with pathological findings similar to those described by Firth et al in their cases. The placental histology sheds light on the pathological process involved in this pattern of abnormality, in which both distal limb defects and micrognathia are associated. Proximal limb development is normal, but the digits and distal parts of the limbs have either failed to develop or have been destroyed earlier in gestation. The presence of organised thrombi in fetal stem vessels suggests that there had been an episode of thrombosis at some point before birth. Damage to the distal limbs could have resulted from an ischaemic or embolic event associated with placental fetal vessel thrombosis. This placental abnormality is