

Asthma and IgE levels in rural and urban communities of The Gambia

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Summary

Two hundred and thirty-one randomly selected schoolchildren and adults from rural Gambian villages showed no evidence of asthma, nor could any case of asthma be found in three rural villages with a total population of over 1200. In contrast, asthmatic patients were identified without difficulty in the capital town. The geometric mean serum IgE level of 131 rural schoolchildren was 962 u/ml, whereas that of sixty age-matched urban schoolchildren was 368 u/ml ($P < 0.001$). Forty-four asthmatics, all from the capital town, had a mean serum IgE level of 405 u/ml, not significantly different from that of urban schoolchildren.

Twenty-one asthmatics showed skin sensitivity to house dust mite antigen, but their IgE levels were not significantly higher than asthmatics without skin sensitivity. The incidence of positive skin tests to mite antigen amongst normal Gambians, both rural and urban, was around 1%.

The findings are discussed in relation to the hypothesis that parasite-induced IgE may prevent the development of atopic illness.

Introduction

The immune response to certain parasites is characterized by greatly increased host production of IgE (Ogilvie & Jones, 1973), and it is now known that over-production of IgE also plays an essential part in the genesis of atopic disease (Ishizaka, Ishizaka & Hornbrook, 1966; Berg & Johansson, 1969). This shared feature has prompted the hypothesis that infection with certain parasites may mitigate against the development of atopic disease (Preston, 1970).

The hypothesis rests on the fact that binding of specific IgE to mast cells and basophils is necessary for subsequent triggering of vasoactive amine release by environmental allergens (Ishizaka *et al.*, 1970). If all available binding sites were already occupied by IgE directed against unrelated antigens, then the likelihood of developing atopic reactions to environmental allergens would be diminished. This concept of mast cell saturation has been supported by experimental work in man (Stanworth

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et al., 1967; Ogawa *et al.*, 1971; Bazarel, Orgel & Hamburger, 1973) and laboratory animals (Jarrett, Orr & Riley, 1971; Ohman & Block, 1972). Moreover, it has proved possible to enumerate occupied IgE binding sites on isolated basophils, and to show that exposure of basophils to high concentrations of myeloma IgE leads to a maximum occupation of about 100,000 sites/cell (Ishizaka, Soto & Ishizaka, 1973). Since IgE levels can be extremely high in some parasitic infections, it is possible that basophils and tissue mast cells may become saturated with parasite-induced IgE, leading to a low incidence of atopic illness. As a clinical test of the hypothesis, information was sought on the prevalence of asthma amongst a highly parasitized population in The Gambia, West Africa, and the serum IgE levels of asthmatics compared with those of the general population. As a further measure of atopy, the incidence of immediate hypersensitivity to house dust was ascertained by skin tests.

Methods

The Gambia (Lat. 13°50'N, Long. 16°W) lies in the Savannah belt of West Africa (Fig. 1). European influence is increasing in the capital town, Banjul (population 44,000) but elsewhere there has been relatively little development. A description of the country and of the pattern of disease in the community has been published by workers at the MRC Laboratories in The Gambia (Thomson *et al.*, 1968). In the present study (February 1974) the following groups of indigenous Gambians were examined.

(1) One hundred and ninety-one schoolchildren, sixty-six from School A, sixty-five from School B, and sixty from School C (Fig. 1). Schools A and B were in typical rural communities; the only relevant difference was that School B was in a schistosomiasis endemic area. School C was in the capital town. All children were aged between 8 and 14 and were selected by taking whole classes at a time. Schooling is not yet compulsory and there were five boys to each girl in this sample.

(2) One hundred rural villagers from Manduar (Fig. 1), the first to present them-

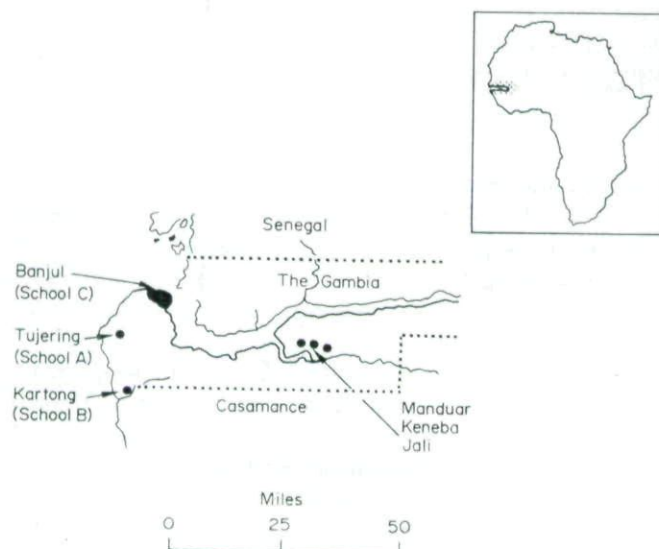


Fig. 1. Geographical location of groups studied.

selves during the MRC annual survey of the whole village population. Their ages ranged from 9 to 70 years and males outnumbered females two to one. The whole population of Manduar, together with the neighbouring villages of Keneba and Jali, has been studied by the MRC in detail (Thomson *et al.*, 1968; McGregor, Billewicz & Thomson, 1961); clinical records are kept of every person and these were examined to identify cases of asthma.

(3) Forty-four patients referred with a diagnosis of bronchial asthma and thought to have sufficient clinical evidence to justify the diagnosis. Twenty-nine patients fulfilled one or more of the following criteria; wheeze and more than 20% improvement in peak flow (measured with a Wright's Peak Flow meter) after inhalation of salbutamol, wheeze and more than 20% fall in peak flow after running 200 m, or a history of sensitivity to house dust confirmed by positive skin tests. The remaining fifteen patients gave a history of attacks of wheezing relieved by intravenous injections (of aminophylline).

Of the forty-four asthmatics, twenty were judged by their dress and education to come from economically privileged homes. Their mean age was 25 years (range 6–64 years) whereas that of the less privileged group was 34 years (range 6–67 years). All came from Banjul or its urban surroundings.

Skin tests with commercial preparations of house dust and *Dermatophagoides farinae* (Bencards Ltd) were performed on all subjects by the prick method, together with positive and negative controls (histamine 0.05% and carbol saline respectively).

Bedding dust was collected from four separate homes in Tujering and Manduar and sent for examination to the Pest Control Infestation Control Laboratories, Slough.

Blood was taken by venepuncture or by finger prick from all subjects barring two young asthmatics. After clotting, serum was collected and stored at -20°C . Serum IgE was measured in the Department of Immunology, Institute of Child Health, London, using the double antibody radioimmunoassay described by Gleich, Averbek & Swedlund (1971), with minor modifications. Estimations were made in duplicate on sera from asthmatics and rural villagers; single estimations were made on the schoolchildren's sera.

IgE levels were expressed as units relative to World Health Organization IgE Standard 68-341 (Rowe *et al.*, 1970). Because the IgE values fell in a normal distribution when plotted logarithmically, geometric means are quoted. Statistical analysis was performed by Student's *t*-test on logged data; *P* values of less than 0.05 were considered significant.

Results

Incidence of asthma in the rural communities

No cases of asthma were found amongst the 131 rural schoolchildren or the 100 Manduar villagers. In addition, MRC files revealed one case only of bronchial asthma amongst the population of over 1200 in the three villages of Manduar, Keneba and Jali. (This patient, a woman of 35, stated that she had had no chest trouble for many years and was normal on clinical examination.)

Incidence of asthma in the urban community

No cases of asthma were found amongst the sixty randomly selected urban schoolchildren who were examined and bled. Amongst the urban community forty-four

Table 1. The incidence of positive skin tests to house dust and *Dermatophagoides farinae* antigens

Group	No. tested	Skin test positive
Rural villagers (Manduar)	100	0
Rural school A	66	2
Rural school B	65	0
Urban school C	60	1
Asthmatics		
(a) economically privileged	20	13
(b) less privileged	24	8

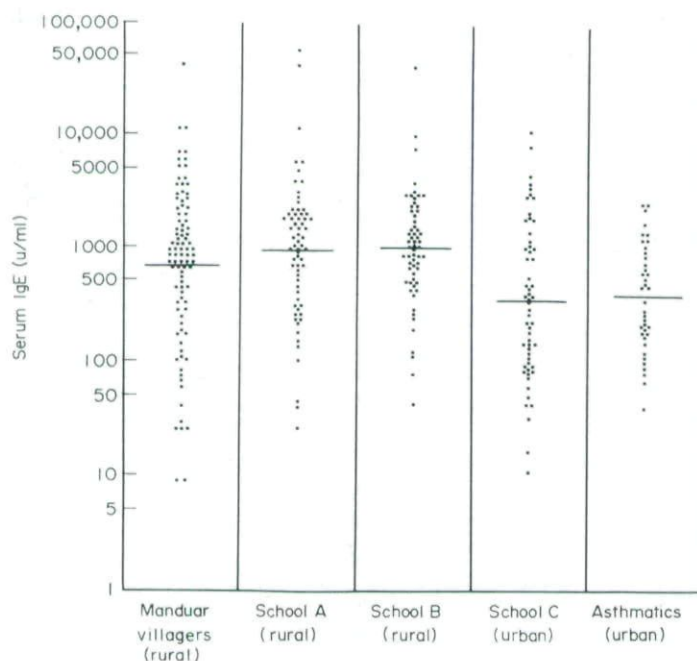
asthmatics were positively identified; most of these knew of other similar patients. At the Royal Victoria Hospital, Banjul, an average of eight patients are seen daily for treatment of asthma, the majority being fairly regular attenders.

Skin tests

The incidence of positive skin reactions in the various groups is shown in Table 1. In each positive case the size of the reactions to house dust and to *Dermatophagoides farinae* were identical.

Dust samples

All samples contained *Dermatophagoides pteronyssinus*; the samples from Manduar contained 58 and 114 mites/g; those from Tujering contained 12 and 942 mites/g.

**Fig. 2.** Serum IgE levels of the groups studied. Results are plotted on a logarithmic scale and geometric means are indicated.

IgE levels

Figure 2 shows the results of serum IgE estimations in the various groups. There were significant differences between urban and rural schoolchildren ($P < 0.001$) and between asthmatics and rural villagers ($P < 0.05$). The mean serum IgE levels of the two groups of rural schoolchildren were similar (923 u/ml and 1001 u/ml), whereas that of age-matched urban schoolchildren was only 368 u/ml. The mean level of the asthmatics, also from the town, was 405 u/ml. The lower mean of the rural villagers compared with rural schoolchildren probably reflects the wide scatter of ages amongst the villagers; analysis by age showed that the highest levels were present in those under 20 years of age. The mean serum IgE levels of thirty-seven villagers aged under 20 years was 895 u/ml, whereas that of the whole group was 683 u/ml. Figure 2 shows that the scatter of IgE levels was less amongst the asthmatic patients than in other groups; no asthmatic had a serum IgE level above 3000 u/ml. The mean serum IgE levels of skin test positive and negative patients (453 u/ml and 364 u/ml) were not significantly different, but the difference between mean levels of economically privileged and less privileged patients (287 u/ml and 537 u/ml) was more marked ($0.1 > P > 0.05$).

Discussion

Two observations of interest were made in this study. The first was that asthma was virtually absent from rural communities in The Gambia, not 100 miles from the capital town where asthmatics were readily identified. The second was that the IgE levels of rural schoolchildren were significantly higher than those of urban children; this difference was perhaps related to improved nutritional status and a reduced incidence of parasite infection in urban Gambians, factors which were shown by Johansson, Mellbin & Vahlquist (1968) to be important in lowering the serum IgE levels of Ethiopian children. Even so, the mean serum IgE levels of all groups of Gambian schoolchildren were several times higher than the mean of 53 u/ml for English schoolchildren, measured by the same radioimmunoassay (M. W. Turner, personal communication).

The rarity of asthma and the high IgE levels in rural Gambians are facts compatible with the hypothesis that high levels of IgE, presumably with specificity for various parasites, help to prevent the development of atopic illness. But the findings may be no more than coincidental and the hypothesis remains open to disproof, for example by clinical demonstration of asthma during active infection with an IgE stimulating parasite, or by laboratory demonstration of high levels of specifically parasite-directed IgE in serum from an asthmatic. Skin testing in this study was not helpful in supporting the hypothesis, for the incidence of positive skin tests was no greater in urban than rural children, despite their lower IgE levels.

Other factors may lie behind the observed difference in prevalence of asthma in Gambian communities. Local ethnic differences were present, but their importance is difficult to assess; in first and second generation immigrant children Morrison Smith (1973) demonstrated that environmental, rather than racial, factors were important in determining the prevalence of atopy. Differences in exposure to allergens may have existed between town and country, but dust mite was shown to be plentiful in rural homes. Natural selection may have operated against asthmatic children, although studies of childhood mortality in rural Gambia by McGregor, Billewicz & Thomson (1961) have not shown asthma to be a cause of death. However, there is now evidence

that transient IgA deficiency may play a part in the development of atopic illness (Taylor *et al.*, 1973; Stokes, Taylor & Turner, 1974); if so, natural selection might well operate against potential asthmatics, who would be likely to fall victim to infection during a period of immunodeficiency in the harsh environment of an African village.

Because of its possible therapeutic implications (Stanworth, 1971) the hypothesis that high circulating IgE levels may block the development of atopy needs to be pursued. The idea that allergic disorders may represent the continuing activity of an immune system made redundant by man's cleanliness has attraction. If true, it is perhaps not too fanciful to look forward to the treatment of allergic disorders by a harmless preparation of parasite antigen able to stimulate IgE.

Acknowledgments

The help of Dr I. A. McGregor (ex-Director) and Dr R. S. Bray (Director) of the MRC Laboratories, Fajara, The Gambia, in arranging this study is gratefully acknowledged.

Dr M. W. Turner very generously gave time, technical help and laboratory space to enable the IgE estimations to be made at the Institute of Child Health, London, and Dr A. M. Cunningham kindly examined the dust samples. The study was supported by a Wellcome Trust Travelling Fellowship.

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