

Immunoglobulin E and eosinophil levels in atopic and non-atopic populations infested with hookworm

D. I. GROVE, T. O. BURSTON and I. J. FORBES

Department of Medicine, University of Adelaide, South Australia, and
Papua New Guinea Institute of Medical Research, Goroka

Summary

Measurements of serum IgE and blood eosinophil levels were carried out on subjects in the Eastern Highlands District of Papua New Guinea, an area of universal hookworm infestation. Subjects were divided into asthmatic, non-asthmatic atopic, and normal groups on the basis of clinical features and immediate hypersensitivity reactions to skin prick testing with a range of allergens. Serum IgE levels and blood eosinophils were elevated in all groups as compared with values found in temperate zones. Both parameters were significantly higher in the asthmatic and non-asthmatic groups compared with the normal group. These findings are consistent with the hypothesis that a function of the IgE immune system is protection against helminth infestation.

Introduction

Raised serum levels of Immunoglobulin E (IgE) were initially found in the atopic disorders (Johansson, 1967; Johansson *et al.*, 1970). Increased IgE levels were subsequently shown in a variety of helminth infestations including *Ascaris lumbricoides*, (Johansson, Mellbin & Vahlquist, 1968), *Toxocara spp* (Hogarth-Scott, Johansson & Bennich, 1969), *Trichinella spiralis* (Rosenberg, Polmar & Whalen, 1971), *Capillaria philippinensis* (Rosenberg *et al.*, 1971) *Schistosoma japonicum*, *Wuchereria bancrofti* and hookworm (Ito, Sawada & Sato, 1972). Similarly, eosinophilia has been observed for many years in allergies and parasitic infections.

We have reported increased resistance to hookworm infestation (*Necator americanus*) in an atopic population as assessed by faecal egg counts (Grove & Forbes, 1974). It was suggested that while heightened ability to produce reaginic antibodies may result in the development of one of the atopic disorders, it may also carry with it increased efficiency in controlling helminth infestation. This paper reports serum IgE levels and blood eosinophil levels in atopic and non-atopic populations infested with hookworm.

Subjects and methods

The investigation was carried out in the Goroka Subdistrict of the Eastern Highlands District of Papua New Guinea. The location and its inhabitants have been described in detail elsewhere (Grove & Forbes, 1974). Hookworm infestation was universal but other intestinal helminthiasis was rare. There were no significant differences in intensity of hookworm infestation between villages.

Skin testing for immediate hypersensitivity reactions was carried out by the prick method on 500 villagers using the following range of allergen preparations: *Dermatophagoides farinae*, *Candida albicans*, *Ascaris lumbricoides*, Sudan Grass (Bencard, England); *D. pteronyssinus*, Mosquito, *Alternaria*, *Cladosporium*, *Penicillium*, Kangaroo Grass, Pennisetum Grass, Pig Hair, Dog Hair, Hen Feathers (Commonwealth Serum Laboratories, Australia). A subject was considered atopic if a weal of 2 mm or more was produced by at least one allergen. It was not intended that the procedure should be exhaustive, but that there would be a reasonable chance of identifying a large proportion of the atopic population. Ten per cent of the villagers were identified as atopic on this criterion.

In addition, inpatients at the Goroka Base Hospital in whom a clinical diagnosis of asthma was made were studied. Pulmonary function tests were performed on most patients and demonstrated reversible airways obstruction.

Atopic and non-atopic subjects were taken in similar proportions from each of the villages. Ages could only be estimated, but the distribution was similar in the 3 groups: asthmatics, 38 ± 10 years; atopics, 33 ± 15 years and controls, 39 ± 14 years.

Serum IgE levels were measured by using the radioactive single radial diffusion method described by Rowe (1969). The standard was from a batch of pooled human serum, 69/204, supplied by the World Health Organization.

Blood eosinophil levels were measured by the counting chamber method described by Dacie (1968) using eosin-acetone diluting fluid and a Neubauer counting chamber. Venepuncture was always performed early in the morning.

Results

Both serum IgE levels and blood eosinophil levels were substantially greater than those found in temperate zones without endemic hookworm infestation (Johansson, *et al.*, 1968; Dacie, 1968).

Serum IgE levels are shown in Fig. 1. There was significant elevation in the non-asthmatic atopic group when compared with non-atopic villagers ($P < 0.02$, *t* test). Similarly, levels were elevated in asthmatic subjects ($P < 0.05$, *t* test). When both groups were combined and compared with non-atopic villagers, there was increased statistical significance ($P < 0.005$, *t* test). Tests of significance were calculated using logarithmically transformed values.

Blood eosinophil levels are shown in Fig. 2. There was significant elevation in the asthmatic plus non-asthmatic atopic group when compared with the non-atopic group ($P < 0.05$, Wilcoxon's Sum of Ranks test).

A significant correlation was established between serum IgE levels and blood eosinophil levels in both non-atopic subjects ($r = 0.3492$, $n = 94$, $P < 0.001$) and in the asthmatic plus non-asthmatic atopic group ($r = 0.3068$, $n = 66$, $P < 0.05$, Fig. 3).

Discussion

The relationship between reaginic antibodies and protective immunity in animals is

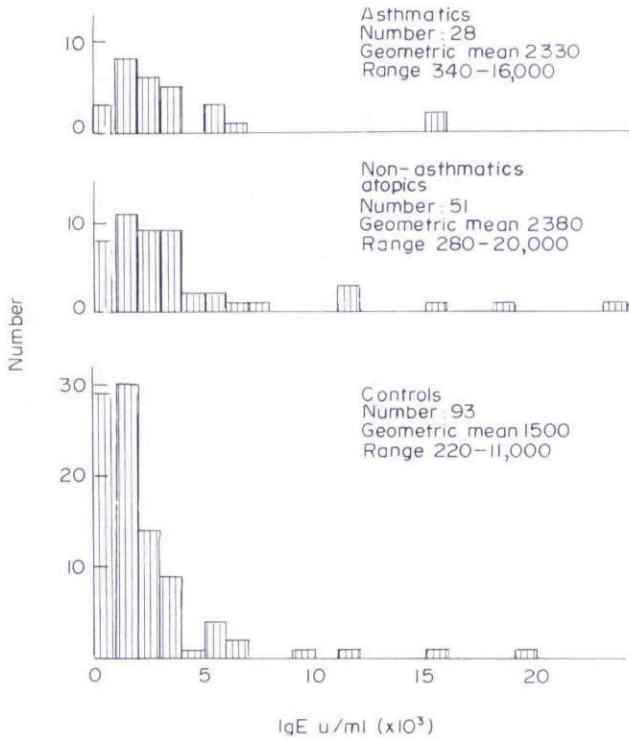


Fig. 1. Serum IgE levels in asthmatics, non-asthmatic atopics and normal subjects.

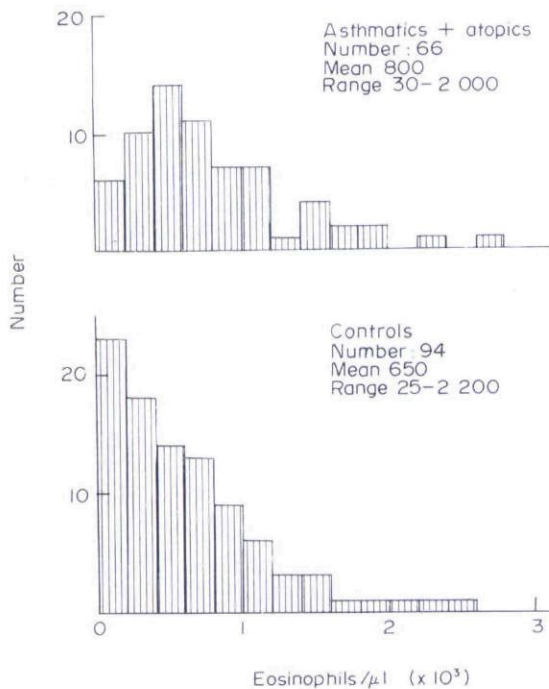


Fig. 2. Blood eosinophil counts in asthmatics plus non-asthmatic atopics and normal subjects.

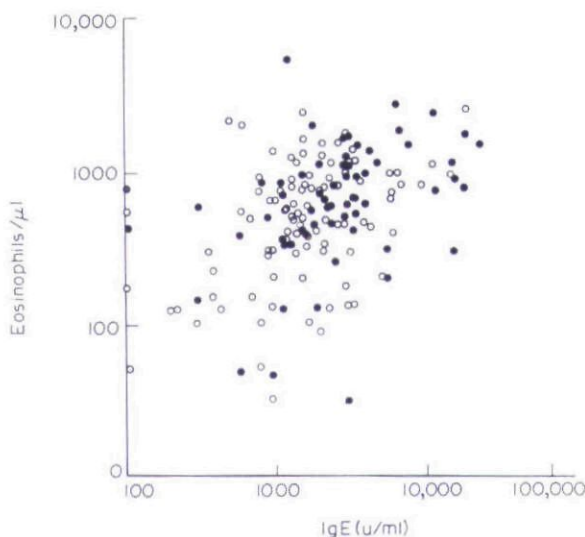


Fig. 3. Correlation between serum IgE and blood eosinophil counts; ● represents normal subjects; ○ represents asthmatic and atopic subjects.

not clear (Sinclair, 1970; Kelly, 1973). Helminth infestation in animals, in addition to inducing a reaginic response to helminth antigens, potentiates antibody responses to non-helminth antigens (Orr & Blair, 1969; Jarrett & Stewart, 1972). The role of IgE in human helminthiasis is obscure despite a constant relationship (Somei, Muneco & Tomio, 1972).

Although blood levels do not necessarily reflect tissue activity, the raised serum IgE levels may represent increased immediate hypersensitivity reactions in the tissues. The relatively higher IgE levels in the non-asthmatic atopic and asthmatic groups may represent increased titres of antibody to non-helminth antigens, hookworm-specific antigens, or both. The non-asthmatic atopic and asthmatic populations presumably respond in greater degree to non-helminth antigens as in other parts of the world. The raised IgE levels in these groups may thus simply represent the addition of helminth antibodies to an already high IgE level. Alternatively, the raised IgE levels may result from higher titres of hookworm-specific antibodies as a manifestation of increased reaginic responsiveness to any antigen. If so, this may have no functional significance. When taken in conjunction with reduced hookworm egg output in these groups, however, the higher IgE levels are consistent with the hypothesis that atopic individuals are more successful in controlling helminth infestation by virtue of an increased efficiency in IgE responsiveness to helminth antigens.

The mechanism of this resistance may be the release of biologically active amines, e.g. histamine and 5 hydroxytryptamine which render the environment unsuitable for the parasite (Kelly, 1973). Atopic individuals may produce more specific IgE with increased release of amines.

Speculation continues as to the role of the eosinophil (leading article, *Lancet*, 1971). It has been shown that eosinophils phagocytose antigen-antibody complexes (Sabesin, 1963). Biologically active amines are chemotactic to eosinophils (Archer, 1963). The eosinophilic response to histamine may be less in non-atopic than atopic individuals (Feinberg, Feinberg & Lee, 1966). It has been stated that eosinophilia and antiparasite

immune reactions are separable phenomena (leading article, *Lancet*, 1971). There is, however, a correlation between eosinophilia and IgE levels in both the normal and atopic-asthmatic groups. Furthermore, the relatively higher IgE levels in the asthmatic and non-asthmatic atopic groups are paralleled by a relatively greater eosinophilia in these groups. The eosinophilia could be a direct response to an antigenic stimulus or may be a second order phenomenon, such as a consequence of the presence of free amines, antigen-antibody complexes, or release of lymphokines.

These results are consistent with the hypothesis that a function of the IgE-mediated immune system is to assist in control of helminth infestation, but carrying with it a propensity to atopic disease.

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