



IMMUNOLOGICAL FUNCTION IN ATOPY AND OTHER DISORDERS

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A THESIS SUBMITTED TO THE UNIVERSITY OF ADELAIDE FOR

THE DEGREE OF DOCTOR OF MEDICINE

September, 1974.

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## SUMMARY

The methods used to assess various parameters of humoral and cellular immunity are described. These include the establishment of the radioactive single radial diffusion assay for Immunoglobulin E; measures of serum levels of other major immunoglobulin classes; antibody responses to tetanus toxoid and S. typhi H antigen; delayed hypersensitivity reactions to intradermal antigen and dinitrochlorobenzene sensitization; lymphocyte tritiated thymidine uptake in whole blood culture, both spontaneous and when stimulated with phytohaemagglutinin; lymphocyte production of a cytotoxin for pigeon red cells; T and B lymphocyte numbers in the peripheral blood; and serum autoantibodies. Methods for performing faecal hookworm egg counts, blood eosinophil counts and detecting Australia Antigen are described.

Parameters of humoral and cellular immunity were measured in 91 asthmatics. Mean serum levels of IgG were raised, especially in those with a family history of atopy. Mean serum levels of IgE were raised, especially in those with a past history of eczema. There was a correlation between serum IgE levels and the absolute eosinophil count. Eighteen percent of patients failed to respond to tetanus immunization while only one patient failed to respond to typhi H antigen. Tetanus non-responders had a raised mean serum IgA level, reduced spontaneous lymphocyte tritiated

thymidine uptake and reduced thymidine uptake of phytohaemagglutinin-stimulated lymphocytes cultured in foetal calf serum when compared with tetanus responders. Nine percent of patients failed to mount delayed hypersensitivity reactions to a battery of five intradermal antigens. Three of four such patients could not be sensitized to dinitrochlorobenzene. The tritiated thymidine uptake of lymphocytes stimulated with phytohaemagglutinin was measured. When all subjects were considered, the mean uptake was normal for lymphocytes cultured in autologous serum, but depressed when cultured in foetal calf serum. Intrinsic asthma could not be differentiated from extrinsic asthma by any of the parameters.

Similar abnormalities were found in a study of 35 patients suffering from atopic eczema. Ten percent of patients failed to respond to tetanus immunization and 14% failed to mount delayed hypersensitivity reactions. The elevation of IgE levels was greater than that seen in asthma. IgG levels and the phytohaemagglutinin-stimulated uptake of lymphocytes cultured in foetal calf serum were normal, as were T and B lymphocyte numbers.

In a series of asthmatics receiving treatment with corticosteroids, antibody responses were marginally worse. Delayed hypersensitivity reactions were suppressed in patients receiving large doses of corticosteroids. The phytohaemagglutinin-stimulated tritiated thymidine uptake

was grossly depressed when cultured in either autologous or foetal calf serum. The mean spontaneous uptake by lymphocytes was elevated.

It is suggested that the data support the hypothesis that immune deficiency is important in the development of the atopic state in some people. It is envisaged that impaired response to antigen by the humoral or cellular immune systems results in increased stimulation of the IgE antibody system, leading to clinical disorder. The variations in the abnormalities detected between asthmatics and patients with atopic eczema may be chance variations or reflect the different clinical manifestations of the disease.

A study was carried out in the Eastern Highlands District of Papua New Guinea to test the hypothesis that a function of IgE antibodies is to assist in the control of helminth infestation. Subjects were divided into asthmatic, non-asthmatic atopic and non-atopic groups on the basis of clinical features and immediate hypersensitivity reactions to prick testing with a range of allergens. Serum IgE and blood eosinophil levels were elevated in all groups as compared with values found in temperate zones. Hookworm infestation was universal. Faecal egg counts were lower and IgE and eosinophil levels higher in the asthmatic and non-asthmatic atopic groups compared with the normal group. It is suggested that these findings are consistent

with the hypothesis that a function of the IgE immune system is to protect against helminth infestation.

A study was undertaken to investigate the effect of treatment for hookworm on IgE levels. In contrast to a previous report, IgE and blood eosinophil levels fell after treatment with anthelmintics. This accords with the general observation in other immunoglobulin classes that antibody levels fall after removal of the antigenic stimulus.

IgE levels were measured in a variety of conditions according to the availability of sera. No abnormalities were detected in patients with coeliac disease, aplastic anaemia, paraproteinaemia or with a positive serum anti-nuclear factor. There was a suggestion that levels may be elevated in alcoholic liver disease, Hodgkin's Disease and Sjogren's Syndrome.

Immunological function was also assessed in two other groups. Fifteen patients with dystrophia myotonica were studied. Although no abnormalities were detected in serum levels of the five major immunoglobulin classes, there was a rise in the serum  $\beta_1A$  complement level. Fifty four percent of patients failed to make a secondary IgG response to tetanus toxoid, while 13% failed to make a primary IgM response to S. typhi H antigen. Thirteen percent failed to make DHS reactions to intradermal antigen. The phytohaemagglutinin-stimulated lymphocyte uptake of tritiated

thymidine was normal, but the spontaneous uptake was depressed. It is suggested that there may be a wider derangement of immunological function in dystrophia myotonica than previously thought.

A simplified battery of tests of immune function was used to investigate normal Papua New Guinea Highlanders. Normal delayed hypersensitivity reactions, but raised immunoglobulin levels, low albumin levels and impaired antibody responses to both tetanus toxoid and S. typhi H antigen were found. Albumin levels were lower and antibody responses more impaired in the group with the more adverse environmental circumstances. It is suggested that mass immunization campaigns in the tropics should be carefully assessed.