Immunology, 1968, **15**, 323.

Immunoglobulin E: A New Class of Human Immunoglobulin*

Studies of the nature of the antibodies associated with isologous skin sensitizing activity have indicated the presence of a previously unrecognized immunoglobulin in human serum. The immunoglobulin was identified by virtue of specific antigenic determinants. Independently, a protein with similar antigen characteristics was identified both in the serum of a patient with multiple myeloma and in normal serum. It is proposed that the normal protein and antigenically related myeloma proteins shall be designated IgE or γE, and the heavy polypeptide chains of these molecules be designated ε (epsilon)-chains, in accordance with *Nomenclature for Human Immunoglobulins.*† This replaces the previous usage of γE-globulin and IgND.

IgE has antigenic determinants in common with other immunoglobulin classes, as well as specific antigenic determinants. IgE from non-myeloma sources contained the determinants of light chains of Type K and Type L. The E myeloma protein had light chains of Type L. The specific antigenic determinants of IgE were not detectable in IgG, IgA, IgM and IgD. Antisera specific for IgE failed to react with immunoglobulins of these four classes and their presently recognized subclasses. Conversely antisera specific for these classes and their subclasses failed to react with IgE.

Studies on the E myeloma protein showed that it contained heavy and light polypeptide chains with molecular weights of approximately 75,500 and 22,500. The unique determinants of IgE were not present on its light chains. The IgE determinants have not yet been directly demonstrated on the isolated heavy chains, but are thought to be located there for the following reasons:

(a) Digestion of the E myeloma protein with papain produced two kinds of fragments, referred to as Fab- and Fc-fragments by analogy with the fragments produced by the action of papain on IgG. The Fab-fragment contained light chain determinants but no IgE determinants. The Fc-fragment lacked light chain determinants. The IgE specific determinants were found only on this fragment.

(b) Molecular weight data were consistent with the Fc-fragment being a portion of the heavy chains. The molecular weight of the intact molecule was found to be approximately 200,000. Following complete reduction and dissociation, 20 per cent of the protein was recovered as light chains of molecular weight approximately 22,500, indicating two light chains per molecule. Assuming two heavy chains per molecule the molecular weight of each heavy chain was calculated to be approximately 75,500. The Fc-fragment had an approximate molecular weight of 100,000 estimated from sedimentation and gel filtration data.

Consideration of the antigenic analysis and the physico-chemical data indicated that IgE determinants were located in the heavy chains of the molecule.

There is evidence for antibody activity in IgE. IgE from selected sera was shown to combine with a number of antigens using several techniques of radio-immunoassay. The specificity of these reactions was comparable to the specificity of antigen binding by other classes of immunoglobulins.

In studies of immediate-type hypersensitivity the binding activity of IgE for a given

* This memorandum was drafted by the signatories (see page 324) following discussions held at the WHO International Reference Centre for Immunoglobulins in Lausanne in February 1968.

† *Bull. Wld Hlth Org.*, 1964, **30**, 447–450.

allergen in various human sera correlated with the ability of these sera to passively sensitize human skin to that allergen. IgE non-reactive with specific allergen and the E myeloma protein blocked this sensitization. The ability to induce or block isologous passive skin sensitization may be a characteristic of the human IgE class.

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