Structure and Biological Activity of Immunoglobulins

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I. Introduction

It seems clear that antibody activity is present in three classes of serum proteins. The major component, γ_2 or 7 S γ, comprises some 85–90% of the total, whereas the second, γ_{1M}, β_{2M}, or 19 S γ, has a much higher molecular weight, a higher electrophoretic mobility at pH 8.6, and contains about five times as much carbohydrate as the major component. The third protein in the group, γ_{1A} or β_{2A}, was not detected until the technique of immunoelectrophoresis was introduced by Grabar and Williams (1953) when it was realized that there was another protein which was antigenically related to 7 S γ and 19 S γ (Grabar *et al.*, 1956; Heremans *et al.*, 1959). It has been suggested that these proteins be col-

lectively known as immunoglobulins (Heremans, 1960) and, by analogy with the hemoglobin nomenclature, the 7 S, 19 S and γ_{1A} fractions be referred to as IgG, IgM, and IgA, respectively. Indication of the nature of the constituent peptide chains by a subscript may soon be possible. This terminology will be used throughout this article.

The association of antibody activity with IgG and IgM has been recognized for many years (Tiselius and Kabat, 1939; Heidelberger and Pedersen, 1937), but there was some doubt as to whether antibodies were present in IgA. It now seems probable that reagins—the skin-sensitizing antibodies—in human sera are associated with this fraction (Heremans and Vaerman, 1962; Fireman *et al.*, 1963; Yagi *et al.*, 1963), and Heremans *et al.* (1963) and Vaerman *et al.* (1963) showed that IgA prepared from the serum of patients recovering from infection with *Brucella abortus* contained antibody activity.

IgG and IgM are readily recognized in sera from all species examined, but IgA has only been clearly identified in human serum. However, Schultze (1959) and Heremans (1959) have suggested that the T- or β_2-globulin which contains most of the antitoxic activity of serum from a horse strongly immunized with diphtheria or tetanus toxoid (Kekwick and Record, 1941; Van der Scheer *et al.*, 1941) may be the equine equivalent to IgA. This component has a molecular weight of about 150,000, a higher electrophoretic mobility at pH 8.6, and a higher carbohydrate content than IgG from the same serum. Antigenically it is related to IgG and IgM, but is not identical with it and, hence, in all its properties the T- or β_2-globulin conforms with IgA. A rather similar protein has been reported present in guinea pig serum after prolonged immunization (Benacerraf *et al.*, 1963; White *et al.*, 1963). No carbohydrate analysis has been made, but from other properties this antibody-containing component also seems likely to be IgA. Rabbit colostrum shows the presence of a component which probably corresponds with IgA, but it was not detected in rabbit serum (Feinstein, 1963).

Schwick and Schultze (1961) have drawn attention to the presence, detected by immunoelectrophoresis, of other components in horse antiserum which are antigenically related to IgG. Kunkel and Rockey (1963) have found from ultracentrifuge studies that there are globulins containing anti-red-cell antibodies with sedimentation coefficient 8–15 S in some human sera and that these may be related to the IgA known to be present. There is, therefore, every prospect of further subdivision of the three main types of immunoglobulin.