Professor R R A Coombs

(Immunology Division, Department of Pathology, University of Cambridge)

Detecting IgE Antibody (Reagin) by the Red Cell Linked-antigen Antiglobulin Reaction [Abstract]

Professor Coombs began by discussing the various stages in the development of this reaction, which affords an *in vitro* measure for reaginic antibody. He then reported an investigation in which this method was used to investigate reaginic antibodies in the sera of persons with allergic asthma to castor bean allergen (Coombs *et al.* 1968). Finally, mention was made of the difficulties still to be overcome in the production of suitable reagents for the test. The analogy was pointed out between this test and the radio-allergosorbent test of Wide *et al.* (1967).

REFERENCES Coombs R R A, Hunter A, Jonas W E, Bennich H, Johansson S G O & Panzani R (1968) Lancet i, 1115 Wide L, Bennich H & Johansson S G O (1967) Lancet ii, 1105

Dr S G O Johansson (The Blood Center, University Hospital, Uppsala, Sweden)

IgE in Allergic Diseases

The new class of immunoglobulins, IgE (γ E), was characterized through the finding of myeloma protein ND (Johansson & Bennich 1967) and its counterpart in normal serum (Johansson, Bennich & Wide 1968). Its relation to the human skinfixing antibodies, reagins, was established by its antigenic identity with the γ E-globulin of Ishizaka et al. (1966) and by its capacity to inhibit the Prausnitz-Küstner reaction (Stanworth et al. 1967). The concentrations of IgE in serum from healthy individuals and from patients with various types of diseases have shown some characteristic differences. This paper presents a review of what is at present known of IgE levels in allergic diseases and their clinical importance.

IgE Levels in Health

The concentration of IgE in serum from healthy adults is extremely low, about 50,000 times lower than that of IgG and about 50 times lower than the lower limit of detection by gel-diffusion methods. To measure such small amounts the radio-immunosorbent technique (Wide & Porath 1966) was applied (Johansson, Bennich & Wide

1968). By this method it is possible to detect as little as 1 ng/ml of IgE and the standard error of the mean is 10-15%. Since the labelled protein, the reference standard solution and the antiserum used in the technique all emanate from a single myeloma protein, it is possible that the concentration of IgE given may have to be changed when other sources of IgE are available.

The mean IgE concentration in cord serum was 36 ng/ml which is about 10% of mean adult level (Johansson 1968). No correlation was found between the IgE levels in the serum of a mother and her newborn when about thirty paired samples were studied; this probably indicates de novo synthesis by the foetus. Restriction in ability to cross the placenta is similarly known for reagins.

The development of serum IgE levels during childhood is closely similar to that of IgA (Berg & Johansson 1969b). A slow but even increase was found during childhood and puberty. The highest values were seen in young adults. A slow but not significant decrease was found in adults with increasing age (Johansson 1968). No sex difference was found in any age group with respect to the IgE concentrations. The mean IgE level for all adults was 248 ng/ml with the two SD confidence limits, calculated on the logarithmic values, of 60-1,000 ng/ml.

IgE Levels in Asthma, Hay-fever and Atopic Dermatitis

The serum IgE levels were studied in an unselected group of adult patients suffering from asthmatic bronchitis (Johansson 1967). All patients with positive skin and provocation tests to at least one allergen were classified as 'allergic asthma' and the others, with a negative allergologic investigation, were classified as 'nonallergic asthma'. In the latter group some cases with other types of non-allergic, obstructive lung diseases might have been included. The mean IgE level in the allergic group was 1,590 ng/ml which is about six times higher than that in healthy adults and in the non-allergic group. Between 50% and 60% of the allergic patients had raised IgE levels. No difference was found between the two groups in concentrations of immunoglobulins G, A, M and D.

Similar results were found in children with allergic asthma (Berg & Johansson 1969a). However, some allergens, although causing severe asthma, seem to stimulate IgE production to a much lesser extent. Children with allergic asthma to moulds and dust, allergologically investigated by Dr K Aas of Oslo, were found to have normal IgE concentrations in serum (Berg & Johansson 1969a).

Patients with allergic rhino-conjunctivitis were found to have raised serum IgE levels to a lesser extent than patients with asthma (Berg & Johansson 1969a). The mean IgE level was only 2-3 times that of healthy controls and raised levels were found only in about 30% of the individuals. However, in all ten children with hay-fever, serially analysed during the summer season, a significant rise in IgE concentration was found.

The highest serum IgE levels were seen in patients with atopic dermatitis. In a group of adults with typical skin lesions a mean IgE value of 2,730 ng/ml was found, i.e. about ten times higher than that of normal individuals (Juhlin et al. 1969). More than 80% of the patients had raised levels. There was no difference between the IgE level in patients with pure atopic eczema and those also having symptoms of asthma, or hayfever or both. Patients with other types of eczema had normal levels and the same was true for patients with various types of urticaria.

IgE Levels in Other Conditions

Very high concentrations of IgE were found in serum from Ethiopian children (Johansson, Mellbin & Vahlquist 1968). In an unselected group a mean value 16–20 times higher than that of healthy Swedish children was found. Atopic manifestations such as asthma, hay-fever and eczema are said to be rare in Africa. The most probable explanation, therefore, is parasitic infestation and in a group selected for ascariasis the mean IgE concentration was about thirty times higher than that of healthy Swedish children.

Several non-atopic diseases such as pneumonia, hepatitis, autoimmune disorders, coeliac disease and ulcerative colitis have been investigated. Very limited, if any, changes of the IgE levels have been seen. It is probable that, if IgE is involved in those states, it is of minor importance, at least on a quantitative basis.

Conclusions

Raised serum levels of IgE have, so far, been found only in atopic diseases and in suspected parasitic disorders. When IgE is elevated it is often elevated to a considerable degree compared to what is usually seen among the other immunoglobulins. In allergic asthma and atopic dermatitis 50-80% of the patients had raised levels. These facts favour the value of the IgE determination as a diagnostic tool in allergology.

Acknowledgments: I wish to express my sincere thanks to Dr H Bennich, Institute of Biochemistry, University of Uppsala for the IgE preparations. This work was in part supported by the Swedish Medical Research Council, Grant No. B70-16X-105-06B.

REFERENCES Berg T & Johansson S G O (1969a) Int. Arch. Allergy (in press) (1969b) Acta pædiat. scand. (in press) Ishizaka K, Ishizaka T & Hornbrook M M (1966) J. Immunol. 97, 840 Johansson S G O (1967) Lancet ii, 951 (1968) Int. Arch. Allergy 34, 1

Johansson S G O & Bennich H (1967) Immunology 13, 381 Johansson S G O, Bennich H & Wide L (1968) Immunology 14, 265 Johansson S G O, Mellbin T & Vahlquist B (1968) Lancet i, 1118 Juhlin L, Johansson S G O, Bennich H, Högman C & Thyresson N (1969) Arch. Derm. (in press) Stanworth D R, Humphrey J H, Bennich H & Johansson S G O (1967) Lancet ii, 330 Wide L & Porath J (1966) Biochem, biophys. Acta (Amst.) 130, 257

The following paper was also read:

IgE Antibodies – General Perspectives Dr J H Humphrey