

This Week's Citation Classic

Johansson S G O, Mellbin T & Vahlquist B. Immunoglobulin levels in Ethiopian preschool children with special reference to high concentrations of immunoglobulin E (IgND). *Lancet* 1:1118-21, 1968. [Dept. Paediatrics and Blood Ctr., Univ. Hosp., Uppsala, Sweden and Children's Nutrition Unit, Addis Ababa, Ethiopia]

Immunoglobulin levels were determined in serum from Ethiopian children. The IgE concentrations were 16 to 20 times higher than in Swedish children and in a group with *Ascaris lumbricoides* infection the level was 28 times higher. Clinical investigations did not reveal a high incidence of atopic allergy. These findings favour the hypothesis that parasitic infestations are important factors in stimulating IgE production. [The SCI® indicates that this paper has been cited over 275 times since 1968.]

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"The allergy immunoglobulin, IgE, was discovered in the late 1960s¹ through the independent work of an American and a Swedish research group. I was, as a medical student, a young and inexperienced member of the latter team.

"From late-1966 to early-1967 we developed a radioimmunoassay for IgE, or IgND as our protein was tentatively named after the initials of a unique myeloma patient I had found.² After considerable initial problems we succeeded in the spring of 1967 in determining IgND (IgE) in human serum. The level was extremely low for an immunoglobulin. The first study of normal individuals, a group of 50 blood donors, showed that 49 of them had levels around a few hundred nanograms per ml while one girl had an IgND (IgE) concentration of 6,000 nanograms per ml. She was found to suffer from atopic allergy with asthma due to dog dander sensitivity.

"This finding initiated a study of IgND (IgE) concentrations in serum from patients with asthma.³ It was shown that patients with atopic, extrinsic asthma had on average six to

seven times higher IgND (IgE) concentrations than patients with intrinsic, endogenous asthma or healthy individuals. These data indicated that an IgND (IgE) determination would be useful for differentiation of atopic and nonatopic diseases. I guess one could say that the concept of IgE determination as 'an allergy specific sedimentation rate' was born and today many millions of IgE determinations are performed annually for that routine diagnostic purpose.

"The study on Ethiopian children appointed as a Citation Classic started in 1966 and the idea was to determine IgG, IgA, IgM, and IgD. I have to admit that I was not particularly crazy about the study. There were already a couple of papers on immunoglobulin levels in African communities. However, after the discovery of the high IgND (IgE) levels in atopic diseases the interest increased. The idea of looking for atopic diseases among Ethiopian children was of interest. The results that we obtained were surprising and not clearly explained. Despite clinical impressions that allergy is rare among these children, we found extremely high IgE values. Although it was not too obvious at that time it was not too farfetched to think about helminth infestations and we were quite impressed by the relationship we found between the degree of *Ascaris* infestation and the IgND (IgE) level. Attempts to detect specific IgND (IgE) antibodies to *Ascaris* antigens turned out to be more difficult than expected and had to be left with the usual phrase, 'further studies are in progress.'

"I really do not know why this publication has been so highly cited. It is true that many reports have confirmed and extended our findings about IgE in parasitic infestations. Parasites are also commonly used in experimental situations to study the mechanisms behind the production of IgE. However, the above mentioned article on IgE in asthma³ would in my mind better deserve to be a Citation Classic. IgE in parasitic infestations has been covered by several recent review articles, some stressing the clinical applications and others the experimental ones."⁴

1. Bennich H H, Ishizaka K, Johansson S G O, Rowe D S, Stanworth D R & Terry W D. Immunoglobulin E, a new class of human immunoglobulin. *Bull. WHO* 38:151-2, 1968.
2. Johansson S G O & Bennich H. Immunological studies of an atypical (myeloma) immunoglobulin. *Immunology* 13:381-94, 1967.
3. Johansson S G O. Raised levels of a new immunoglobulin class (IgND) in asthma. *Lancet* 2:951-3, 1967.
4. Johansson S G O & Foucard T. IgE in immunity and disease. (Middleton E, Jr., Reed C E & Ellis E F, eds.) *Allergy. Principles and practice* St. Louis. MO: Mosby. 1978. p. 551-62.