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Aas K & Johansson S G O. The radioallergosorbent test in the in vitro diagnosis of multiple reaginic allergy: a comparison of diagnostic approaches.
J. Allerg. Clin. Immunol. 48:134-42, 1971.
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The results of the radioallergosorbent test (RAST) were compared with those used for the clinical allergy diagnosis (case history, skin tests, and provocation tests). The study confirmed that RAST was a reliable method, but the degree of reliability depended very much on the quality of the allergenic material used to produce the allergosorbent. The overall reliability of RAST was 73 percent. With acceptable allergen extracts, the *in vitro* test was found to be of value as a screening method before provocation tests. [The *SCI*® indicates that this paper has been cited in over 160 publications.]

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The invitation from *Citation Classics* has given me the opportunity to comment on my paper as an example of clinical work, clinical investigation, and basic research performed as a sort of intellectual triathlon.

Such a combination is in many ways very rational and rewarding. The scientist who works in a basic research laboratory must go through a long series of trials and failures in order to find and provide evidence for the one correct answer among a large number of hypotheses. The one who at the same time sees patients, however, can filter the hypotheses through a network of practical life observations, experiences, and logical thinking.

It was in this manner that I selected fish allergy as a model for allergen research. An infant with severe atopic symptoms was admitted to my department. He had been given nothing but breast milk but suffered from atopic eczema, bronchial asthma, and bouts of severe angiedema and diarrhea, which were exacerbated when his mother ate fish. The allergenic molecules in question had resisted cooking, digestion in the mother's intestines (proteolysis), passage through membranes, and a second digestion in the infant's intestines and were still active when reaching the reaginic antibodies in the tissues. From these observations, the allergenic activity of this molecule had to be associated with a sequential unit of amino acids and could probably be found on rather short fragments. From other clinical observations, I also thought that it should be possible to identify, characterize, and isolate the major allergens and responsible antigenic determinants in codfish. I wanted a model—and the allergic infant pointed out a suitable one.

I had very large amounts of a quite pure allergen at my disposal and a large number of human sera from patients with fish allergy and other proven allergies in the freezer. Moreover, in my clinical department in Oslo much had been done to characterize and improve allergenic material for diagnostic tests.

A few years earlier Kimishige Ishizaka had demonstrated that immediate hypersensitivity reactions were mediated by a distinct class of immunoglobulin (IgE),[1] and shortly afterwards Gunnar O. Johansson had found an IgE myeloma by screening myeloma sera.[2] This made it possible to produce large amounts of sheep and rabbit antibody to IgE. With this, Johansson, H. Bennich, and L. Wide in Uppsala developed the radioallergosorbent test (RAST) for the detection and quantitation of allergen-specific IgE antibodies in human sera.[3]

It was then quite natural that we established a collaboration concerning both basic and clinical aspects of allergy: they had the antibody test, and I had the purified antigen, the appropriate patients, and the appropriate biological tests.

We introduced a scoring system for the combined use of case history, skin testing, and RAST. With the use of RAST as a supplement to a carefully collected case history and correctly performed and critically evaluated skin tests, provocation tests were considered superfluous in 82 percent of the patients in the study. At the same time, we confirmed that skin tests were also highly reliable but only with good allergenic material. The codfish model is still the only one with detailed information about the major allergenic determinant (epitope). We had not reached that far in 1970-1971 but had been able to crystallize and further purify the major allergen in codfish.

In addition to showing the value of RAST as a diagnostic method, this paper was among those that contributed to the quality, characterization, and standardization of allergen extracts and to more precision in clinical work in allergy. It opened up a field of research full of challenges and rewarding progress, not the least of which was in allergen research.[4]

1. Ishizaka K, Ishizaka T & Hornbrook M H. Physico-chemical properties of human reaginic antibody IV Presence of a unique immunoglobulin as a carrier of reaginic activity *J. Immunology* 97:75-85, 1966. (Cited 340 times)
2. Johansson S G O & Bennich H. Studies on a new class of human immunoglobulins. Parts I & II. (Killander J. ed.) *Gamma globulins: structure and control of biosynthesis. Proceedings of the Third Nobel Symposium*, 12-17 June 1967, Södergarn, Sweden. Stockholm. Almqvist & Wiksell, 1967 p 193-205. (Cited 70 times.)
3. Wide L, Bennich H & Johansson S G O. Diagnosis of allergy by an in-vitro test for allergen antibodies. *Lancet* 2:1105-7, 1967. (Cited 840 times.) [See also: Wide L. Citation Classic *Current Contents/Life Sciences* 28(3):19, 21 January 1985.]
4. Aas K. Fish allergy and the codfish allergen model. (Brostoff J & Challacombe S J, eds.) *Food allergy and intolerance* London: Bailliere Tindall, 1987 p. 356-66.

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