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This Week's Citation Classic

Ovary Z. Immediate reactions in the skin of experimental animals provoked by antibody-antigen interaction. *Progr. Allergy* 5:459-508, 1958.
[Department of Microbiology, Johns Hopkins University, Baltimore, MD]

This article described immediate type skin reactions in experimental animals emphasizing passive cutaneous anaphylaxis (PCA), which is a widely used, simple, very sensitive, and reliable method for detecting and quantifying sensitizing antibodies. It is especially useful for detecting antibodies of the IgE class. [The *SCI*® indicates that this paper has been cited over 520 times since 1961.]

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"In 1942, I learned from the great Hungarian pharmacologist, M. Jancsó, a technique used to visualize histamine action in the skin. In the late-1940s, while working at the University of Rome, Italy, I proposed to G. Biozzi to do experiments using this technique. Then Biozzi received a one-year fellowship to work in the prestigious laboratory of B. Halpern in Paris. He was so brilliant that the French never let him go back and he is still working in Paris. I remained in Rome and applied what we learned from our work to study histamine release during allergic reactions (my interest stemmed from my allergy to cats). That is how I discovered passive cutaneous anaphylaxis for which I coined the term PCA (a bad term, by the way, as it combines Latin and Greek words). To my amazement, I could detect 0.2 micrograms of rabbit antibody/ml. This was 200 times less than was detectable using other methods then available. I wrote, therefore, to P. Grabar, a professor at the Pasteur Institute in Paris (I worked there in the 1930s), to ask his advice and to see if I could be wrong. He invited me to the Pasteur Institute and gave me several sera to test, of which only he knew the antibody content. Each time I could detect about 200 times less than detectable by other methods known at that time. So, after all, I was right! M. Heidelberger, the dean of immunochemists, happened to be present and on his recommendation, M. Mayer invited me to Johns Hopkins University. It was there that I studied PCA more thoroughly. I made the observation in collaboration with F. Karush that the Fc fragment of the immunoglobulin molecule is necessary for 'skin fixation' (sensitization).[1] This observation led to the study of Ig receptors on cells.

"Monovalent haptens are generally ineffective for challenge of PCA.[2] This observation was at the basis of the bridging hypothesis for immunological triggering.

"In other investigations, concerning complement, the methods described in the *Citation Classic* paper were used, and it was shown for the first time that anaphylatoxin is derived from the last acting component of complement (C3 at that time).[3]

"At New York University with B. Benacerraf and other collaborators, we described that contrary to the unitarian theory, different classes of antibodies carry different biological activities.[4] These biological activities are therefore carried by the Fc fragment. Indirectly, this observation led A.G. Osler to show that two pathways of complement fixation are possible by antibodies[5] (today called classical and alternative) and thus rehabilitated the early work of L. Pillemer on properdin.[6] An unexpected use was later found in the enhancing and suppressing effect of anti-idiotypic antibodies of the IgG1 and IgG2 classes.[7]

"The article was written because P. Kallós, who read my publications, thought that it was time to write a review about the subject and that it would be of general interest to immunologists. It turned out that this happened to be the case, as judged by the frequent citations.

"I think that the article is highly cited because PCA is a very sensitive and reliable method for detection of certain classes of antibodies which sensitize for allergic reactions, especially IgE, and its use permitted the study of some fundamental aspects of many *in vivo* immunological reactions."

1. **Ovary Z & Karush F.** Studies on the immunologic mechanism of anaphylaxis. II. Sensitizing and combining capacity *in vivo* of fractions separated from papain digests of antihapten antibody. *J. Immunology* 86:146-50, 1961.
2. **Ovary Z.** Activité des substances à faible poids moléculaire dans les réactions antigène-anticorps *in vivo* et *in vitro*. *C.R. Acad. Sci.* 253:582-3, 1961.
3. **Osler A G, Randall H C, Hill B M & Ovary Z.** The participation of complement in the formation of anaphylatoxin. *J. Exp. Med.* 110:311-39, 1959.
4. **Ovary Z, Benacerraf B & Bloch K J.** Properties of guinea pig 7 S antibodies. II. Identification of antibodies involved in passive cutaneous and systemic anaphylaxis. *J. Exp. Med.* 117:951-64, 1963.
5. **Osler A G & Sandberg A L.** Alternate complement pathways. *Progr. Allergy* 17:51-92, 1973.
6. **Pillemer L, Blum L, Lepow I H, Ross O A, Todd E W & Wardlaw A C.** The properdin system and immunity: I. Demonstration and isolation of a new serum protein, properdin, and its role in immune phenomena. *Science* 120:279-85, 1954.
7. **Eichmann K & Rajewsky K.** Induction of T and B cell immunity by anti-idiotypic antibody. *Eur. J. Immunol.* 5:661-6, 1975.