

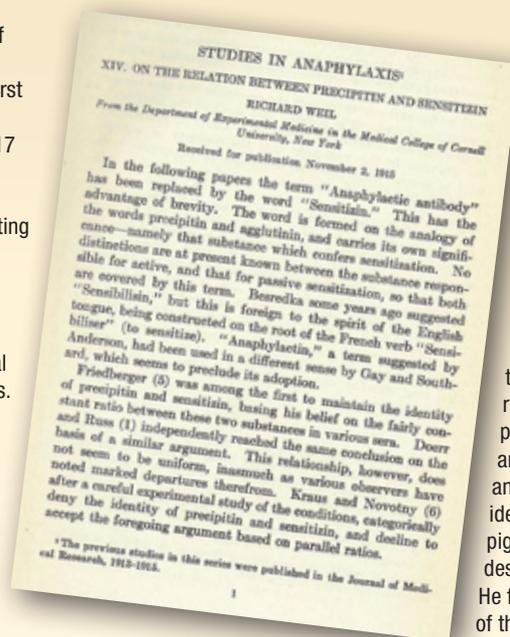
# The First Article in *The Journal of Immunology* “Studies in Anaphylaxis”

In February 1916, The American Association of Immunologists and the New York Society for Serology and Hematology jointly published the first issue of *The Journal of Immunology*. (See “The Founding of *The Journal of Immunology*”, page 17 of this newsletter) The goal for the new journal was to advance the field of immunology, already recognized to be vital to understanding and treating disease, by publishing the newest research in “immunity, serology, and bacterial therapy” and discussing the “problems of immunology.”<sup>1</sup> With these aims in mind, the editors chose for the first article a study on a major immunological debate of the day, the mechanism of anaphylaxis.

The article was “XIV. Studies in Anaphylaxis: On the Relation between Precipitin and Sensitizin” by Dr. Richard Weil, chair of Department of Experimental Medicine, Cornell Medical College.<sup>2</sup> The article is of interest for more than just its scientific content as it also demonstrates the scientific milieu and conventions of the time. Weil was well placed to publish his paper, for he was a founding member and future president of The American Association of Immunologists and also a member of the New York Society for Serology and Hematology. Unlike most modern research papers, his article had only a single author, lacked defined Abstract, Methods, Results, and Discussion sections, and was written in an almost conversational style. Further, the article was the 14th in a series, with the first 13 published in the *Journal of Medical Research* — the 15th, 16th, and 17th (the final) in the series were published simultaneously with the 14th in *The JI*. In this first *JI* article, and throughout his larger series of articles, Weil persuasively argued for a cellular mechanism of anaphylaxis.

Although the phenomenon of anaphylaxis had been described earlier, the seminal experiments were reported by Richet and Portier in 1902. In attempting to vaccinate experimental animals including pigeons and dogs against the toxin of the Portuguese man-of-war or, later, sea anemones, they were shocked to note the opposite effect. The animals injected with a second vaccinating dose became violently ill and died. Richet and Portier created a new term for this observed hypersensitivity: “anaphylaxis,” which literally means “against protection.” Following previous demonstrations of natural and artificially induced immunity to infection, the description of anaphylaxis was the first comprehensive demonstration of harmful effects caused by the immune system. This discovery changed the conception of immunology and earned Richet the Nobel Prize in Physiology or Medicine in 1913.

By the time of the publication of Weil’s article in *The JI*, scientists were divided in their views on whether the cause of anaphylaxis was humoral or cellular — a divide firmly entrenched in early immunology itself. While both sides agreed that interaction between antigen and antibody caused anaphylaxis, proponents of the humoral theory asserted that antigen and antibody combined in the blood to form a chemical toxin. In his Nobel address, Richet touched upon this idea as a simple explanation for the ‘toxin’ produced by *in vitro* incubation of immune serum and antigen. He explained that “there exists in anaphylactized blood a substance harmless in itself but which releases a strong poison when mixed with the antigen.”<sup>3</sup> Weil was unconvinced that events in a test tube emulated the situation *in vivo* and was one of the first



supporters of the cellular theory. This theory hypothesized that antibodies became bound to cells and that antigen-antibody binding induced the cell to produce the anaphylactic reaction. In a talk in January 1916, just prior to publication of his article in *The JI*, he stated that the difference between these two theories was not “merely scholastic,” but that the “entire philosophy of immunity is involved in the choice between them.”<sup>4</sup>

In Weil’s article, he described how, through a series of injections of immune rabbit serum and horse serum into guinea pigs, he concluded that “precipitating antibody” and “sensitizing antibody” (i.e., antibody responsible for anaphylaxis) were identical. (Interestingly, by studying the guinea pig as a model, he primarily would have been describing IgG1, rather than the classic IgE.) He further stated that the precipitating function of the antibody could be destroyed (by heat or chemical treatment) without affecting the sensitizing value, presuming this to be due to the retained antigen-binding capacity of the antibody. In his concluding statements, Weil firmly asserted his belief regarding the mechanism of anaphylaxis: “Anaphylaxis therefore consists simply in the cellular reaction due to the fixation of antigen by cellular antibody.”

Of course, we know today that Weil would ultimately be proven correct in his cellular theory of anaphylaxis. The discovery of IgE in the 1960s spurred impressive progress in the field. It is now well established that antigen crosslinking of IgE on mast cells and/or basophils triggers their degranulation to induce anaphylaxis and that prompt treatment with epinephrine reverses the life-threatening effects. Nevertheless, the frequency of anaphylaxis seems to be increasing, and patients look toward current researchers for new solutions. A century following the experiments of Richet and Weil, investigators continue to shed light on signaling events which occur during anaphylaxis, identifying potential new therapeutic targets.

From its launch in February 1916, *The JI* was intended to advance the field of immunology as a whole. But the editors of the journal and, by extension, the members of AAI also wanted to represent the contributions of preeminent scientists in the U.S. and England in particular. Given their attempt to define themselves as a group, their choice of the first article was perhaps not so surprising. The publication of Weil’s article placed *The JI* on one side of a hotly debated issue, ensuring the relevance of the journal to the field and positioning the young society as an emerging forum for discussion and dissemination of discoveries advancing immunology.

<sup>1</sup> Announcement. *The Journal of Immunology* vol. 1.

<sup>2</sup> Richard Weil, “Studies in anaphylaxis. XIV. On the relation between precipitin and sensitizin,” *The Journal of Immunology* vol 1 (1916): 1–18.

<sup>3</sup> Charles Richet, “The Nobel Prize in Physiology or Medicine 1913 - Award Ceremony Speech,” Nobelprize.org, [http://nobelprize.org/nobel\\_prizes/medicine/laureates/1913/press.html](http://nobelprize.org/nobel_prizes/medicine/laureates/1913/press.html) (accessed August 10, 2011).

<sup>4</sup> Richard Weil, “Anaphylatoxin and the mechanism of anaphylaxis” in *Proceedings of the second Pan American scientific congress*, vol 10, sec 8, part 2, ed. Glen Levin Swiggett (Washington, DC, GPO, 1916), 308–313.