

spontaneous fission is a certain mechanism which is quantitatively insufficient. However, by assuming sufficient segregation of uranium in the surface layer, this defect can be corrected. The mechanism involving residual primeval gases is based on analogy with the earth and is quantitatively too large. If a correction factor is applied to this mechanism, there is no good reason for not accepting data from meteors, which give values much too small.

The previous existence of iodine-129, while a matter of speculation, is well founded on present theories of element formation. If we accept this assumption, it is then possible to estimate the interval between element formation and the formation of the satellite in its present state. The interval of  $4 \times 10^8$  years would not appear to be contradicted by other observations.

The three alternatives lead necessarily to explicit predictions of the composition of the lunar atmosphere. These are given in Table 5. If iodine-129 is alone responsible, there will be only xenon-129; if spontaneous fission, there will be 5 percent krypton and 95 percent xenon; if primeval gases, 93 percent krypton and 7 percent xenon.

It would appear that only a gas sample would make it possible to distinguish between the alternatives. Since the scale height is only a few kilometers, it is not probable that initial grazing rocket orbits would come sufficiently close to permit the collecting of a gas sample.

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## Louis Pillemer, Immunochemist

The sudden death of Louis Pillemer, on 31 August 1957, came at a time when he had just received wide recognition for his work in the field of immunochemistry.

Dr. Pillemer was born in Johannesburg, Union of South Africa, in 1908, the son of Lithuanian parents. He was brought to the United States at the age of one and was naturalized in 1916. Although he had none of the aids which position and wealth can bestow, he managed to complete his undergraduate studies, in Kentucky, and received his B.S. degree at Duke University in 1932. While at Duke he came under the influence of the late W. A. Perlzweig, who stimulated his interest in biochemistry. On the advice of Perlzweig he came to Western Reserve University in 1935 to continue his studies, working toward a Ph.D. degree, with emphasis in immunology and biochemistry. While Pillemer was at Duke University he became interested in Perlzweig's attempts to purify

and to crystallize the enzyme urease. It was then a logical step to continue this work and to study the immunological specificity of the crystallized urease. This work became the basis for his doctoral thesis, in 1938. It was entitled, "Chemical and Immunologic Studies on the Effects of Radiant Energy and of Oxidation on Crystalline Urease."

During his studies in my laboratory at the Institute of Pathology, Western Reserve University, Pillemer's great interest in immunology was readily discovered and fired. He showed great capacity for absorbing and retaining information as well as for sustained concentration at the laboratory bench. He also possessed inductive and deductive potentialities, the latter being dominant. In addition, he had the ability to spend two and even three consecutive nights in the laboratory in order to complete a given unstable preparation, and it was not uncommon for him to do so. During this time he rose from the position of demonstrator of

immunology (1938-39) to that of associate professor of immunochemistry (1946-50), and to that of professor of biochemistry in 1950. Throughout these years, Pillemer's time was devoted primarily to research.

Early in his career at Western Reserve he showed great interest in our work on the elusive factor called "complement," an interest he maintained to the last days of his life. Realizing the need for more knowledge of protein separation, and being aware of the beautiful studies then under way in the laboratories of E. J. Cohn at Harvard, we decided, after consultations with Cohn, to send Pillemer to Boston to learn the basic techniques of the Harvard group. Before he left for Boston we were able to show, in collaboration with Chase Breeze Jones, that the complement complex was bound to certain globulins of the serum, but the newer methods of the Boston workers led to the separation and characterization of two of the four components of the complement complex.

In 1944 Pillemer was called to military service and was attached to the Army Medical School in Washington, D.C. Upon his discharge, he returned to Cleveland and undertook the problem of the purification of certain bacterial toxins. The support for these studies came first from John Wyeth and Sons of Philadelphia and then from Lederle Laboratories Division, in New York. By 1946, Pillemer, in collaboration with Wittler,

Burrell, and Grossberg, succeeded in purifying tetanus toxin to the point of crystallization and with high yields in toxicity. Concurrently, Lamanna and his associates, and Abrams and his associates, succeeded in crystallizing the toxin of *Clostridium botulinum* (A). These two toxins were, therefore, the first to be crystallized.

Purification work was extended to formaldehyde-detoxified tetanal and diphtherial toxoids. Partially purified preparations of these immunizing agents soon became commercially available and were also incorporated into diphtheria-pertussis-tetanus "triple vaccine." It was a natural extension of these studies to attempt to isolate the protective antigen of *Hemophilus pertussis* in order that it might be used to supplant the killed-organism vaccine then available. In collaboration with Blum and Lepow, Pillemer separated the antigen by a novel procedure involving sonic disintegration of the organisms followed by adsorption of the protective antigen on human red cell stromata. This preparation was highly effective in protecting mice against *H. pertussis* in the intracerebral challenge test. Furthermore, a beautifully planned and executed field trial, conducted by the British Medical Research Council, has demonstrated the efficacy of the Pillemer antigen in protecting human beings against whooping cough.

The importance of the isolation of the protective antigen of *H. pertussis* transcends its possible use in a purified "triple vaccine." This work has made it possible to show that the protective antigen is distinct from other, previously implicated, antigens, such as agglutinin; that the protective antigen does not give rise to a demonstrable circulating antibody (this finding rules out any protec-

tive effect of agglutinin and other, previously implicated, antibodies); that the mouse intracerebral challenge test, while "unphysiological," is a valid assay for establishing the potency of pertussis vaccines; and finally and perhaps most important, that the mechanism of immunity in *H. pertussis* and related infections remains to be explained.

By 1954 Pillemer had returned to our old problem on complement and, together with his associates—Blum, Lepow, Ross, Todd, and Wardlaw—made an important contribution in the field of natural immunity by demonstrating the existence of, and by isolating, a new serum protein named "properdin" and by demonstrating its role in immune reactions. These workers found that properdin, in conjunction with complement and  $Mg^{++}$ , participated in the destruction of certain bacteria, protozoans, and abnormal red cells, as well as in the inactivation of certain viruses. This new protein was found in normal human and other mammalian sera and appeared to be involved in infection and resistance. There was indeed shown to be a relationship between the properdin level and the resistance or susceptibility of experimental animals to infection. Properdin was purified and characterized as a euglobulin with an isoelectric point between pH 5.5 and 5.8. It was shown to contain lipid, carbohydrate, and phosphorus and, in the human being, to comprise not more than 0.02 percent of the normal serum proteins. A unit of this agent contains not more than 0.5 microgram of protein nitrogen. The molecular weight of properdin is over 1,000,000. Properdin was shown to differ from antibody in that it combined with various and unrelated substances. For its function it appeared to require the various components of the complement complex. Pillemer, then,

considered properdin to be a primordial form of antibody.

Since properdin was originally obtained after adsorption to an insoluble polysaccharide (zymosan) derived from yeast cell walls, a logical extension of these studies was the observation of whether or not polysaccharide complexes of microbial and mammalian origin would combine with properdin and thereby alter properdin levels *in vitro* as well as *in vivo*. This work was done by Pillemer together with Schoenberg, Blum, and Wurz; with Ross; and with Landy and other collaborators. The active polysaccharides contained both alpha and beta linkages, furanosidic and pyranosidic units, and interhexose linkages of 1.4, 1.6, 1.3, 2.1, and 2.6 types, as well as combinations of these within the same component. The properdin system thus comprised: (i) properdin; (ii) complement or factors resembling complement; and (iii) magnesium ions. Its primary role appeared to be in the natural defensive system of the host. Time will clarify this function.

Pillemer belonged to many scientific organizations, among them, the International Society of Hematology. In 1956 he received the R. E. Dyer lectureship award, in Washington, D.C.

He was an incorrigible individualist and cared little for honors. His only "hobby" was the elucidation of the biochemical aspects of immunology. He knew what he was looking for! Bernard once stated that "he who does not know what he is looking for will not lay hold of what he has found when he gets it." His contributions were the result of devotion to his field and of an unflagging industry.

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