O. T. Avery

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AVERY, OSWALD T. (*b.* Halifax, Nova Scotia, Canada, 21 October 1877; *d.* Nashville, Tennessee, 20 February 1955), *biology.*

Avery began his career as a physician. His father, a Canadian clergyman, had moved his family to New York in 1887, and Avery spent the next sixty-one years of his life there. He attended Colgate University, graduating A.B. in 1900, and received his medical degree from the Columbia University College of Physicians and Surgeons in 1904. He worked for a short time in the field of clinical medicine and then joined the Hoagland Laboratory in Brooklyn, New York, as a researcher and lecturer in bacteriology and immunology (his lectures at Hoagland won him the appellation "The Professor," by which he was known throughout his career). In 1913 he became a member of the staff of the Rockefeller Institute Hospital, where he remained until 1948.

At the time that Avery came to the hospital, an investigation of lobar pneumonia was in progress, and he joined with A. Dochez in work on the immunological classification of the pneumococcus bacterium. This research led to the announcement, in 1917, that the pneumococcus produced an immunologically specific soluble chemical substance during growth in a culture medium.[1] Dochez and Avery further established that the substance was not a disintegration product of cell mortality but a true product of its metabolic processes, and that the substance was also present in the serum and urine of animals and men suffering from lobar pneumonia.

Beginning in 1922, Avery and his colleagues studied the chemical nature of these "soluble specific substances," which Avery believed were closely related to the immunological specificity of bacteria. They were soon shown to be polysaccharides derived from the capsular envelopes of the bacteria and to be specific to each pneumococcal type. By relating differences in bacterial specificity to these chemical differences in the capsular substances produced, Avery was able to explain in chemical terms many of the anomalies of immunological specificities. He showed that immunology could be analyzed biochemically, in terms of specific cellular components rather than the entire cellular complex, and thus contributed to the development of the study of immunochemistry.

Because of his concern with the extracellular substances of the pneumococcus, Avery began work in 1932 on a phenomenon first reported by F. Griffith in 1928. Griffith had observed that heat-killed virulent pneumococci could convert a nonvirulent strain to a disease-producer *in vivo.* Later investigations showed that this change in immunological specificity could be brought about *in vitro,* and that the alteration was permanent. Avery set out to isolate and analyze the active factor in the transformation, and his conclusions were reported in a well-known 1944 paper.[2]

A culture of an unencapsulated, and therefore nonvirulent, variant (designated *R*) of Type II pneumococcus, when exposed to an extract derived from encapsulated, virulent (*S*) Type III pneumococcus, was found to be converted to a Type III *S* culture. The isolated transforming material, upon examination, tested strongly positively for desoxyribonucleic acid (DNA) by the diphenylamine reaction. Elementary analysis revealed close resemblances in element ratios between the transforming substance and sodium desoxyribonucleate. Transforming ability was not inhibited by protein-destroying and ribonucleate-destroying enzymes, but only by those enzyme-containing preparations also capable of depolymerizing DNA. Treatment with desoxyribonucleodepolymerase also produced complete inactivation, at all temperatures up to the point of inactivation of the enzyme. Serologically it was found that transforming activity increased with increasing purity while the

purified substance itself exhibited little or no immunological reactivity. On the basis of these and other tests, Avery and his collaborators concluded that the active fraction consisted principally, if not solely, of a highly polymerized form of desoxyribonucleic acid.

Avery thus showed that, in one instance at least, DNA was the active causative factor in an inherited variation in bacterial cells. The experiments showed that the preparations most active in bringing about transformation were those purest and most protein-free, thereby effectively casting doubt on the widespread and commonly accepted belief that proteins were the mediators of biological specificity and cellular inheritance. It was to a great extent through this work that the stage was set for the rapidly ensuing elaboration of the structure, function, and importance of DNA. Avery himself speculated about the mechanism of specificity determination and pointed out that "There is as yet relatively little known of the possible effect that subtle differences in molecular configuration may exert on the biological specificity of these substances,"[3] a situation that was well on the way to being remedied within ten years with the development of the Watson-Crick model for the DNA molecule.

NOTES

1. *J. Exp. Med.*, **26** (1917), 477–493; *Proc. Soc. Exp. Biol. Med.*, **14** (1917), 126–127.
2. *J. Exp. Med.*, **79** (1944), 137–158.
3. *Ibid.*, p. 153.

BIBLIOGRAPHY

I. ORIGINAL WORKS. Avery's major early work, on the immunological specificity of the pneumococcus involved in lobar pneumonia, is to be found in his two 1917 papers with A. Dochez, "The Elaboration of Specific Soluble Substance by Pneumococcus During Growth," in *Journal of Experimental Medicine*, **26** (1917), 477–493, also published in the *Transactions of the Association of American Physicians*, **32** (1917), 281–298, and "Soluble Substance of Pneumococcus Origin in the Blood and Urine During Lobar Pneumonia," in *Proceedings of the Society for Experimental Biology and Medicine*, **14** (1917), 126–127. The majority of his work on the chemical nature of the soluble specific substance appeared in a series of papers with M. Heidelberger: "Soluble Specific Substance of Pneumococcus," in *Journal of Experimental Medicine*, **38** (1923), 73–79; "The Specific Soluble Substance of Pneumococcus," in *Proceedings of the Society for Experimental Biology and Medicine*, **20** (1923), 434–435; and "The Soluble Specific Substance of Pneumococcus," in *Journal of Experimental Medicine*, **40** (1924), 301–316. The one paper for which Avery is best known reported his work with MacLeod and McCarty, "Studies on the Chemical Nature of the Substance Inducing Transformation of Pneumococcal Types. Induction of Transformation by a Desoxyribonucleic Acid Fraction Isolated from Pneumococcus Type III," in *Journal of Experimental Medicine*, **79** (1944), 137–158.

II. SECONDARY LITERATURE. Complete bibliographies of Avery's work can be found appended to two major biographical sketches written by former colleagues: R. J. Dubos, in *Biographical Memoirs of Fellows of the Royal Society*, **2** (1956), 35–48; and A. R. Dochez, in *National Academy of Sciences, Biographical Memoirs*, **32** (1958), 32–49.

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