Address of the President Sir Henry Dale, O.M., G.B.E., at the Anniversary Meeting, 30 November 1945

The annual number of *Obituary Notices of Fellows of the Royal Society* published today, and the names which have just been read to us, remind us of the losses from its Fellowship which the Society has suffered during the year now closing.

I propose on this occasion to proceed next to the presentation of the Medals for 1945.

Awards of Medals, 1945

The COPLEY MEDAL is awarded to Dr OSWALD THEODORE AVERY for his contributions to knowledge of the chemical basis of the specific properties of bacteria, particularly of the types of the pneumococcus. His researches in this field have appeared in unhurried and orderly sequence over the course of a long and distinguished career, and they have furnished a large and essential constituent of the framework now available for a fundamental science of immunochemistry.

We allow ourselves here to claim Avery as Canadian by birth, though with acknowledgment that his life's work has been accomplished in the United States of America, and in the Rockefeller Institute of New York in particular, of which he has held the Membership since 1913.

It was in 1917 that Dochez and Avery demonstrated that cultures of different strains of the pneumococcus yielded different 'soluble specific substances'. From 1923 onwards appeared a remarkable series of papers by Avery, with Heidelberger and other collaborators, in which it was shown that these specific substances had the nature of complex polysaccharides of highly individual characters. These were present in the regular capsular envelope characteristic of the pneumococcus in its virulent forms; and each type of such virulent pneumococci, distinguishable by its immunological specificity, was shown to have its own distinct polysaccharide. Each of these reacted, with a like specificity, with the corresponding immune body. Not that these polysaccharides, the soluble specific substances isolated in chemical purity, had antigenic properties by themselves. It was only when they were artificially linked to proteins foreign to the reacting animal body, or retained their natural linkage with proteins of the bacterial strains producing them, that they elicited, on injection, the appearance in the blood of specific immune substances, causing agglutination or lysis of the corresponding organisms; but, with the immune substances thus evoked, the pure, separated polysaccharides now exhibited the same specific affinities, each forming a precipitate with the corresponding anti-serum.

Here, then, in chemically definite form, were separable, prosthetic, combining groups such as Paul Ehrlich had long earlier envisaged and prophetically named 'haptenes'. Here also was one of the principal foundation stones of a great building of immunological chemistry, which, in the hands of Avery's contemporaries and followers, notably in those of a distinguished fellow-Member of the Rockefeller Institute, the late Karl Landsteiner, has rapidly included an ever-widening range of studies of artificial and natural antigens. Fellows of this Society may recall that last year we were privileged to hear Bakerian and Croonian Lectures, by Professor Haworth and Dr Harington respectively, both dealing, from somewhat different angles, with experiments in immunochemistry, and each contributing its own important extension to a structure of knowledge founded so largely on Avery's pioneer discoveries.

Meanwhile, in the hands of Avery and his co-workers, knowledge of the specific characters of the pneumococci, and of the manner in which these are acquired, had been moving quietly to a new pinnacle of achievement. They had long ago shown that pneumococci, which, in artificial culture, have lost the capsules endowing them with virulence and containing the specific polysaccharides, have reverted to avirulent non-specific types, growing in the rough, wrinkled colonies characteristic of such defective strains. It had been shown also, by the late Fred Griffith, that such a degenerate, non-specific pneumococcus, from whatever specific type it had its provenance, could be induced by cultivation in a medium prepared from a complete, virulent type to reacquire a capsule conferring the corresponding specificity. And now, only last year, Avery, with Macleod and McCarty, has been able to isolate and to characterize a chemical principle acting in minute dosage as the specific stimulus to such a transformation. An unencapsulated, avirulent, typeless pneumococcus derived from a specific strain of type II, responds to this stimulus by acquiring and retaining the capsule and specific polysaccharide, with the virulence and the cultural characters, of a fully specific strain of type III. [Here surely is a change to which, if we were dealing with higher organisms, we should accord the status of a genetic variation; and the substance inducing it—the gene in solution, one is tempted to call it—appears to be a nucleic acid of the desoxyribose type. Whatever it be, it is something which should be capable of complete description in terms of structural chemistry.]

It has been a matter for rejoicing to his many admirers, friends and followers in many countries that Avery, a veteran now among investigators, should thus, on the eve of his retirement, have attained this new peak of discovery—a fitting climax to a devoted career of such wide influence on the progress of science. Many, we feel with assurance, in his own country and far beyond it, will welcome and approve our award to Dr Avery in this year of the Royal Society's highest recognition, its Copley Medal.