REMARKS OF DR. MACLYN MCCARTY AT AVERY GATE MEMORIAL CEREMONY ON SEPTEMBER 29, 1965

It is not our purpose this afternoon to attempt a systematic analysis of Avery's scientific contributions and their impact on modern biological thought. Nor is it feasible to draw a comprehensive portrait of Fess and his extraordinary, multi-faceted personality. Rather, in this series of presentations, it is our hope that, in an informal and less structured manner, we can convey the essential spirit of the man, his work, and its scientific consequences.

There is much more of a central, unifying theme in Avery's career as an investigator than the simple fact that he was preoccupied for the greater part of it with a single group of microorganisms, the pneumococci. His intuitive ability to select significant problems for attack, the philosophy of his approach to their solution, and the stringent demands he made on scientific evidence before accepting his experimental findings as final are among the traits that give his work a special stamp. The questions he posed in dealing with the complex biological systems with which he worked were characteristically directed toward a fundamental understanding of the substances responsible for specificity. When faced with the necessity a year or so ago of preparing a paper with the rather forbidding title "Molecular Biology and Medicine", it occurred to me that, as much as he might have disliked the designation, Fess was a molecular biologist long before the term came into use. This assertion is adequately supported by the direction

and development of each of his major lines of investigation, involving as they did the isolation and characterization of biologically active molecules and efforts to establish the chemical basis for their specificity.

It is important to recognize that his explorations of the underlying biochemical basis involved in the phenomena he studied were motivated by a deep interest in broad biological problems, including, as Colin MacLeod will emphasize, clinical problems related to disease. One of the less well-known of the Professor's major interests was his concern with the host response to disease processes. This interest finds its most notable expression in his work on the human serum protein now known as C-reactive protein. This substance, which is not present in the blood of normal individuals but makes its appearance in response to a variety of inflammatory stimuli, was discovered in his laboratory by Tillett and Francis as a by-product of the pneumococcal work. The term "C-reactive" refers to the fact that the protein fortuitously reacts to form a precipitate with the somatic C polysaccharide of the pneumococcus. His studies of this substance with Abernathy and MacLeod led to its identification as a protein and characterization of many of its properties, and incidentally one of the first isolations of a humanprotein in a highly purified, homogeneous form. Thus, even his exploration of the host response to disease developed along the lines of molecular biology.

A long succession of students and collaborators had the intellectual stimulus of learning these approaches to scientific

investigation from him by precept. At the same time, there was the associated enriching experience derived from daily contact with a most exceptional personality. These latter experiences are perhaps the most difficult to recapture because of their subjective nature and personal flavor. Certainly, personal reminiscences are notoriously treacherous, particularly with respect to the accurate recollection of details and the temporal interrelationships of events as the years recede.

It is my impression that all of Fess's former associates have a similar picture of the major facets of his personality. It is not surprising, however, that there are differences of opinion and of interpretation with respect to many of his less familiar characteristics. These co-workers and friends concur in the broad outlines, but each has his own private view growing out of his own personal relationship with Avery. If these premises are correct, then it is clearly impossible for any one individual to advance a comprehensive analysis of his character that will fully satisfy all of his other former colleagues. In any event, I have no intention of attempting such an analysis. I would like, however, to touch upon one episode which both describes one of Avery's traits and illustrates my point concerning the inherent inaccuracy of personal recollections.

The success story recorded in the subsequent careers of a long series of Fess's boys establishes beyond doubt his preeminent talent for contributing to the molding and directing of promising young scientists. The techniques by which he achieved this -- and indeed whether anything qualifying as a technique was actually

involved -- has long been a subject of debate. Some of the things that happened to all aspiring investigators on arrival in Avery's laboratory are indisputable, however.

The neophyte was never under any circumstances given a problem by the Professor and put to work shortly after arrival on some aspect of pneumococcal bacteriology which fitted into the overall interests of the laboratory. The process was a much slower and more painful one -- most especially for those who by training and instinct felt dependent upon direction from above-- and was based on the firmly-held philosophy that every worker should select his own problem. This end was achieved through a combination of subtly directed reading and a series of discussions that frequently took the form of monologues.

As one gained a better integrated impression of the trend of investigation in his department over the years by reading -- chiefly from the collection of departmental reprints -- ones grasp of the pattern and interrelations of the research on the pneumococcus was greatly enhanced by his oral dissertations that have been referred to as Fess's Red Seal Records. They were virtuoso performances in which, with great logic and clarity, he would develop his theme, including historical background and the rationale of approaches used. The organization and phraseology of these vignettes had been composed in his mind at his leisure with great care and were used repeatedly in presenting the subject to various auditors.

The young hopeful, impatient to get to work at the laboratory bench, would at the same time be completely fascinated

by these discourses. Soon he would raise questions about certain aspects of the pneumococcus and ultimately would be gently maneuvered into suggesting his own problem by outlining his ideas for answering one of the questions he had himself raised. In this way, the beginner selected his own problem, and at the same time could be diverted through the medium of preliminary discussions from blind alleys and paths that had already been unsuccessfully followed.

In my own case, it was my recollection that this period of mixed frustration and intellectual stimulation went on for about two months. This proves to be a beautiful example of tricks that can be played by a faulty memory, and in this case the correction is supplied by a "diary" in the form of laboratory notes. I arrived at the Rockefeller Institute on September 1, 1941 and was greeted by Frank Horsfall who had just that summer returned to the Institute staff after his sojourn in the Rockefeller Foundation laboratories. Fess did not return from Maine until after the second week of September and so my indoctrination (which had been initiated with some reading material in the spring) was not begun in earnest until the middle of the month. This was the start of the period that I remember as having lasted many weeks, and yet the incontrovertible evidence of the laboratory notebook reveals that I had carried out my first tentative experiments in pneumococcal transformation before the end of September. By mid-October I was engaged in the growth of mass cultures of type III pneumococci for extraction of the crude transforming substance.

My distorted memory of this period probably has its basis in the rather special situation that obtained at this time. Colin MacLeod had left the Rockefeller Institute that summer to assume his duties as Professor of Microbiology at New York University, so that Fess was suddenly deprived of his close collaborator of the previous 7 years. Although I had at the outset a latent interest in pneumococcal transformation, and this interest had been sharply increased by reading and by the Red Seal Records on the subject, I was much too diffident to propose to Fess that I join him on the problem. On his part, he was restrained from enlisting my aid as a collaborator not only by his policy of insisting that the newcomer select his own problem but also, I am sure, by the unknown nature of my abilities as a laboratory worker. How could he be sure that I would not be more of a hindrance than a help? It was this impasse that must have been responsible for the aberration of memory which causes me to recall as several weeks what could not have been more than several days. I have no clear recollection of precisely how the impasse was broken, and here the laboratory notes are of no help.

There are many other respects in which these old laboratory notebooks prove their inadequacy, and although they seem quite thorough and adequately descriptive of experimental procedure they are not very useful in delineating the evolution of ideas or the origin of certain approaches. In particular, I had hoped to piece together from them a clear record of the origin and growth of the idea that the pneumococcal transforming principle

is composed of DNA. There is some information on the point, to be sure, but not enough to reconstruct from this source alone an accurate picture of all stages in the development of the idea. Nor is there any reflection of the negative factors that were introduced on discussion with others, such as the prevailing biochemical dogma of the time that nucleic acids from various sources were monotonously alike in composition and thus unlikely candidates as carriers of specific information.

There are rewards of a different nature to be derived from a return to the old notebooks, however, and thumbing through their pages again after twenty-odd years tends to conjure up memories of episodes and the daily laboratory routine of the period. One of the gratifying minor aspects of the work with the pneumococcal transforming system was that each morning on arrival in the laboratory the results of the experiment of the day before were waiting in the incubator to be read. Thus, when things were going well, each day began with a new bit of information that provided the stimulus and direction for further experiments. Fess and I had an unspoken agreement that prevented either of us from obtaining a sneak preview of the results before the other had arrived. (The old protocols serve to recall the image of Fess as we converged on the incubator each morning, and in particular I see his expression, which was a curious mixture of eager anticipation and of apprehension for fear something had gone wrong with our complex biological test system -- which, alas, was all too frequently the case.)

A multitude of such pictures remain in my memory as I am

sure they do in the memory of others. Despite the fact that they may be distorted and blurred by the passage of time, they remain as testimony of the lasting impact of his personality on his associates. This legacy is inextricably enmeshed in our minds with the more durable and objective legacy of his scientific accomplishments.

In closing, I would like to express the personal pleasure that I have derived from the intensified reminiscences of Dr. Avery stimulated by this occasion and from the opportunity to talk again with many of his old friends and with his brother and sister-in-law, Dr. and Mrs. Roy Avery. I must say, however, that the endless variety of these reminiscences has renewed my conviction that it is virtually impossible in a brief discourse to recapture more than a small portion of his attributes as a scientist and as a friend.

MMcCarty
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