GENETICS AND THE ORIGIN OF SPECIES

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Griffith, Dawson, Heidelberger, Avery, and many other bacteriologists, biochemists, and immunologists have in the last twenty years worked out a fascinating story of diversity and protean instability in the pneumonia microörganisms, pneumococci (a review in White, Robinson and Barnes 1938). The species *Diplococcus pneumoniae*

is subdivided into at least thirty-two types distinguishable chiefly through immunological, physiological, and biochemical tests. Each of these types is supposed to preserve its identity when reproducing in infected hosts or on artificial culture media which give optimum growth. The core of the pneumococcus cell consists of nucleoproteins, lipids, complex polysaccharides and other substances, which, as far as the present data go, appear to be essentially similar in all the types. The surface of the cell has, however, an envelope consisting chiefly of polysaccharides which are chemically specific for each type and which are presumed to be responsible for the differences in the behavior of these types. In the process of reproduction each type of cells is able to synthesize its proper polysaccharide envelope, which is, hence, an hereditary trait by definition.

If, however, the bacteria are cultivated on media containing homologous immune sera, or on media which are otherwise unfavorable to their growth, they undergo what is described as "degradation" or "dissociation." Their normal virulence is largely lost, and the shape of the colonies growing on agar plates is changed from the normal "smooth" to a degenerate "rough." The most important fact is, however, that the polysaccharide envelope, which is present in the "smooth" form, is not detectable in the "rough" state, and with its loss the specificity of the thirty-two types likewise disappears. Immunization by the rough phase causes the formation of "antirough" antibodies, which are absorbed by the rough as well as by the smooth cells, while immunization by the smooth phase develops the "antirough" as well as the type-specific "antismooth" antibodies. A reversal of degradation can be accomplished by a passage through a susceptible host, or by addition of the antirough serum to the culture medium. The speed of this reversion is greater if the process of degradation has not been completed; it seems, however, not to have been thoroughly established whether a reversion from rough to smooth can be accomplished by these methods if a rough clone is used to start with.

With the exception of a single feature, the phenomena so far outlined are not unduly surprising from the standpoint of genetics. Mutations from smooth to rough and vice versa may take place at all times with finite low frequencies; depending on the environment in

which a strain lives, one of the phases is selected and displaces the other. The unique feature is the convergence observed in the rough phase resulting in an apparent loss of the distinctions between the types. The mutations from smooth to rough seem to be physical losses of the distinctive features of the cells expressed in the polysaccharide envelope, as though the germ plasm of this organism contained a certain stable nucleus and a variable periphery which may be disposed of altogether. Still more extravagant, and yet conclusively proved, phenomena are enacted if a culture of the rough phase is added to a vaccine consisting of dead cells of the smooth phase with a trace of the antirough serum. For in this case rough reverts to smooth of the same type to which the cells in the vaccine had belonged. Thus, if a small amount of the rough culture derived from the normal (smooth) line of Type II is added to a suspension of smooth cells of Type III devitalized by heating, a smooth line of Type III, not of Type II, is produced. By this method it seems to be possible to convert at least many of the thirty-two types of the pneumococci into many other types. The transformation of the rough into the smooth of the same type from which the rough had been originally derived is, of course, also accomplished by the same method, if a vaccine of that type is used. The vaccines lose their transforming effectiveness after being heated to the boiling point, but cell suspensions heated to 60°C. and subsequently frozen and thawed are effective.

The strains "transformed" from one type into another retain their new properties after cultivation on suitable media or after passage through animal hosts. Hence, they acquire not merely a temporary polysaccharide envelope of a kind different from that which their ancestors have had, but are able to synthesize the new polysaccharide indefinitely. If this transformation is described as a genetic mutation—and it is difficult to avoid so describing it—we are dealing with authentic cases of induction of specific mutations by specific treatments—a feat which geneticists have vainly tried to accomplish in higher organisms. Admittedly, there are many obscurities in the situation which ought to be cleared up. For example, it seems to be unknown whether the transformation affects every cell in the culture or whether only some cells mutate and others are destroyed; whether

the mutation takes place in connection with the division of the cells or can be accomplished without reproduction taking place; and whether all the possible transformations of the types can be induced with equal ease. Nevertheless, geneticists may profit by devising experiments along the lines suggested by the results of the pneumococcus studies.