C. Salmonella: genetic transduction mediated by bacterial phage

In distinction to the sexual mechanism that has been demonstrated in Escherichia coli, a more restricted type of genetic transfer has been documented for Salmonella species, that is, genetic transduction. This term also embraces the very similar processes of genetic "transformation" in the pneumococcus, Hemophilus, and other bacteria. The main distinction is that in Salmonella, transduction appears to be mediated by particles of bacterial viruses, whereas in the other bacteria mentioned the transductions can be carried out by means of partially purified, chemically extracted, preparations of desoxyribonucleic acid. The salient features of transduction in Salmonella which distinguish it from sexual recombination in Escherichia coli are: (1) the role of a subcellular agent in transduction; intact cells are required for sexual recombination; (2) in general only one genetic trait can be transduced (at a frequency of about 1 per million phage particles) on any one occasion; in sexual recombination the entire genotypes of the two parents are potentially involved. In both cases the new forms that are produced are perfectly stable, genetically.

Considerable effort has been devoted to the characterization of the vector of transduction in Salmonella as bacterial phage. Earlier work had pointed to the role of small filterable particles, but these were at first confused with "L-forms". Whatever biological significance L-forms may have has not yet been shown but they now appear to be irrelevant to genetic transduction in Salmonella.

The first studies with transduction in Salmonella involve primarily the same kinds of biochemical, nutritional, drug resistance, and similar alterations as have been used before in the work with E. coli. We have had very little success

with transduction analysis of the somatic antigens, most likely due to technical difficulties. In view of their particular interest in those antigens most intimately concerned with the virulence of Salmonella typhi for man (the so-called Vi antigen) this problem has been since adopted by other workers at the Army Medical Service Graduate School, and our attention has been concentrated on the flagella. In these studies for which we have enjoyed the collaboration of Dr. Bruce Stocker now of the Lister Institute in London, and Dr. P. R. Edwards at the U. S. Public Health Service Communicable Disease Center at Chamblee, Georgia, three levels of genetic determination of the flagella have been demonstrated. There are several loci concerned with whether flagella will be formed at all, mutation at any one of them resulting in a so-called "O-form" or non-flagellated, non-motile mutant. Secondly, at least two kinds of mutants have been analyzed which are apparently "paralyzed", that is, while they possess flagella, these flagella are non-functional. And finally, there are at least two distinct loci concerned in the control of the serological structure of the flagella. Since the accepted taxonomy of the Salmonella group has been based primarily on the flagellar antigens, the recombinations which have been obtained by transduction in the laboratory have, so to speak, created and recreated many "species." That is to say, there is now a theoretical understanding of the mechanism by which so large a variety of serological types has no doubt been produced in nature. Our present studies are now emphasizing the fundamental biological basis of genetic transduction. Rare exceptions in which the linked transduction of distinct markers appears to occur suggest that transduction involves the inadvertent transfer of a broken piece of a bacterial chromosome by the phage particle which was initially responsible for the disruption of the nuclear material of its host cell. The most puzzling feature of this process is the mechanism by which the transduced chromosome fragment is capable of supplanting its previous homologue when a new host bacterium is symbiotically

infected by the vector bacteriophage. We are also concerned with a detailed analysis of the genetic control of the flagellar antigens, especially in so far as the total genotypic potentiality of a given Salmonella cell is never expressed all at once. There appears to be a qu[illegible] -hereditary differentiation which limits the expression of antigenic potentialities for considerable numbers of generations by a process whose genetic basis may be in some way analogous to that of embryonic differentiation.