Fu/Fu.) When the posterior axial region is sufficiently defective, it fails to provide the normal inductive stimuli which regulate the development of the posterior gut and urinary ducts, and particularly the separation of the urogenital sinus from the rectum. This assumption is based not on embryological evidence but on the evident connection between abnormalities of the posterior spine and urogenital system.

The hypothesis implies that the mutations studied (*u, Sd, Ki, T, Fu,* t^0 or t^1) have some effect in common which underlies the process or processes leading to the abnormal connection between gut and urinary duct. They apparently differ in their effects on certain other processes since each mutant probably has peculiar effects on tail form by which it can be identified. Further study may, of course, reveal differences in the urogenital effects of the different mutants, but the essential features of the syndrome, failure of posterior gut and urinary duct and absence of anus, appear to be the usual type of response of the embryo to anatomical defects brought about by a number of independent mutations.

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[2] Dunn, L. C., *Growth*, **5**, 141–161 (1941).
[3] Dunn, L. C., and Caspari, E., these PROCEEDINGS, **28**, 205–210 (1942).
[4] Reed, S. C., *Genetics*, **22**, 1–13 (1937).

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*CAN SPECIFIC MUTATIONS BE INDUCED BY SEROLOGICAL METHODS?**

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It has been suggested by Haldane (1935) and by Irwin (1939) that many of the erythrocyte antigens of birds and mammals are rather direct gene products. The reason for this view is that (if we except a portion of the antigens present in species-hybrids of doves) there is a one-to-one correspondence between the presence of specific single genes and specific antigens (see summaries for man by Boyd, 1939, and Wiener, 1935, for rabbits by Castle and Keeler, 1933, for fowls by Todd, 1935, for doves and pigeons by Irwin, 1939). In these cases there is—with the exception noted —no evidence for gene interaction, either between allelomorphs or between genes at different loci.

The same conclusions may be applied to the genes and antigens responsible for the specificity of transplantation compatibility in mammals. The results of Loeb and Wright (1927) with guinea pigs show that transplantation is successful only if all the specific genes of the donor are present in the host. This evidently means that the host forms antibodies to any antigen present in the donor tissue, unless the same antigen is present in the host also. The genetic results mean further that these antigens are numerous, and that here also there is no gene interaction. Similar conclusions may be drawn from the experiments on tumor transplantation in mice.

As pointed out by Haldane (loc. cit.), this conclusion suggests that there may be some common configuration in the molecular structure of an antigen and that of the gene responsible for it. If this common configuration concerns that part of the antigen that is responsible for its specificity—and such a relation is implied in the suggestion—there are certain further possibilities to be investigated.

As is well known (see discussion by Landsteiner, 1936), there are two distinct properties of an antigen—that of inducing the formation of a specific antibody, and that of reacting with the specific antibody. These two properties evidently depend on the same specific configuration; but for the first it is usually (probably always) necessary that the specific configuration be present in or chemically attached to a protein, while for the reaction with the antibody such an association is not necessary.

These considerations lead to the supposition that, if a particular gene is responsible for the formation of a given antigen, then there is a possibility that the antibodies induced by this antigen may react with the gene. If this possibility exists there is a series of consequences that are of interest to the geneticist.

One such consequence is that it becomes possible to interpret the old experiments of Guyer and Smith (1920, 1924) with rabbit lenses. As is well known, the lens protein has specific antigenic properties. Guyer and Smith reported that they immunized fowls to rabbit lenses, and injected the immune sera into rabbits. There resulted lens defects in the offspring, and these defects were inherited, both through females and through males. These experiments have been criticized, and Finlay (1924), Huxley and Carr-Saunders (1924) and Ibsen and Bushnell (1934) have failed in attempts to confirm them. I am, however, informed by Professor R. R. Hyde that his experiments (still in progress) have given confirmatory evidence. On the basis here suggested, the mechanism of such a result is clear: The lens protein does not ordinarily get into the circulation, so the animal neither forms antibodies to it nor binds them when immune serum is injected. These antibodies are, therefore, free in the circulation in the injected rabbits, and some of them combine with the specific genes (in the

germ cells) that are responsible for lens antigen—presumably inactivating them. If the results can be confirmed, and if this interpretation is correct, we have here a method for the induction of a specific mutation.

Guyer and Smith interpreted their results as demonstrating the inheritance of an acquired character. On the interpretation here suggested, it becomes a matter of terminology whether they are properly to be so described. It does appear, however, that other cases cited in support of the Lamarckian view should be reëxamined with the gene-antigen-antibody possibility in mind. A casual survey of the literature leads me to suppose that the most likely additional example is that reported years ago by Brown-Sequard. In this case the interpretation might be that guinea pigs are capable of producing antibodies to their own nervous tissue when it is injured.

* This manuscript was written in 1940, and was submitted to Dr. Hyde, whose experiments are referred to as forming much of the basis for the conclusions. Dr. Hyde gave his permission for the reference to his work; but I felt that he would prefer to wait until he could carry out more experiments, and I therefore did not publish. Two factors now influence me to publish the note: Dr. Hyde's death in 1943, without his having published his results; and the results of Dr. Emerson, described in the accompanying paper. The note stands as written in 1940, though a few minor changes might now be desirable. For more recent references, see the paper of Dr. Emerson.

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