of seizures and that it may be a contributory factor in its relation to the chief or primary cause.

Thiouracil has been used in morphological experiments but not, as far as can be ascertained in the literature, has it been used for the direct purpose of protecting an animal from convulsive seizures.

Summary. The effects of feeding 0.1% 6n-prophylthiouracil in the food for 9 days to an inbred strain of mice, DBA/2, recognized for its high susceptibility to sound-induced convulsive lethal seizures, were observed. One hundred and fifty-one mice were started the drug feeding at 21 days of age and 30 animals at 25 days. The animals were tested for sound-induced seizures at 30 days when the susceptibility was normally highest. Practically 100% protection from lethal seizures was produced by the use of the drug. Approximately 68% of the individuals showed no form of convulsion. The 32% which had some form of convulsive spasm did not show the severe seizures exhibited by the controls. In this convulsive group the influence of the drug was manifested by a temporary paralysis of the front legs causing hopping movements or the behavior took the form of a trance-cataleptic posture which lasted for 2 to 3 minutes. Also the spasmic convulsion was shortened in duration and the preconvulsive period was lengthened. It may be that the thyroid gland has some important role, even if secondary, in the onset or prevention of convulsive seizures as elicited by sound in the mouse.

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Effect of Bacteriophage on Virulence of *Corynebacterium diphtheriae*. (19204)

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For many years the question as to whether or not virulent (toxigenic) *Corynebacterium diphtheriae* can become wholly avirulent (non-toxigenic) has vexed the public health official and the microbiologist alike. A view widely held for years was that, in persons convalescent from diphtheria, virulent diphtheria bacilli revert to an avirulent state with passage of time. No sound evidence has ever supported this belief. On the contrary, extensive studies(1-7) showed that if the change from the virulent to avirulent state occurs in nature, it must do so very rarely. Until very recently, attempts in the laboratory to alter the virulence of *C. diphtheriae* have failed completely, with the possible exception of the instance cited by Morton(8). No evidence has yet been offered that virulent strains become avirulent in nature.

On the other hand, all views on the stability of *avirulence* of *C. diphtheriae* must now be revised, and all epidemiological considerations concerning diphtheria must be altered in view of the demonstration by Freeman(9) in 1951 that certain bacteriophages readily induce certain strains of avirulent diphtheria bacilli to become definitely toxigenic and virulent for animals. We regard this discovery as one of the most fundamental in the field of diphtheriology since Loeffler's work. Dr. Freeman kindly sent us his avirulent strains and his bacteriophages. Two phages, A_6 and B_6, and five cultures, 324, 325, 326, 334, and 337B, were received. It is to be noted, as a pecu-

liarity of these avirulent strains, that all were isolated from 1 clinically typical case of diphtheria and one unrelated contact. The isolation of avirulent cultures from cases of diphtheria has been previously reported(10). Using these and other materials, attempts have been made to repeat Freeman's experiments in this laboratory. The procedures described by Freeman were modified in these preliminary experiments. Technical details will be described fully elsewhere.

Attempts to isolate any *C. diphtheriae* from the supposedly bacteria-free phage suspensions failed. The 5 strains of *C. diphtheriae* as received from Freeman showed no evidence of virulence. They were plated and about 100 individual colonies were subcultured and tested individually for virulence. None was virulent. Four of the 5 strains were then cultivated in Difco heart-infusion broth in contact with the original phages as received from Freeman. Phage B_6 produced partial lysis of all strains; phage A_6 produced no perceptible lysis. *In vitro* virulence tests made with the broth cultures at this stage showed definite lines indicating virulence of the strains 324, 326, 334, and 337B in contact with phage B_6. The same strains in contact with phage A_6 showed no evidence of virulence at this time. When phage B_6 was applied to young growth of the original strains on agar plates, clear zones appeared in which resistant colonies were observed. Subcultures of these resistant colonies were found to be virulent.

On further culture-to-culture passage of phage A_6, it acquired sufficient potency to produce complete lysis and to induce the change from avirulence to virulence in four of the strains—324, 326, 334, and 337B—in the same manner as phage B_6. In Freeman's laboratory, phage A_6 had not developed this degree of activity. We have also induced these changes in Freeman's avirulent cultures with a phage isolated here by us.

There is no reason not to regard all of these changed strains as true, toxigenic *C. diphtheriae*. Virulence was confirmed in animals.

Attempts to repeat these experiments with strains of avirulent *C. diphtheriae* isolated, not from cases but from healthy carriers, have so far been unsuccessful. However, the change from avirulence to virulence has been readily induced in 2 of our own cultures isolated from what appeared to be clinically typical cases of diphtheria. It is suggested that there may be some significance in the fact that the change may be induced readily in avirulent cultures from cases but not (up to the present) in those from healthy carriers.

Summary. The finding by Freeman that certain bacteriophages can induce certain strains of wholly avirulent *C. diphtheriae* to change into fully virulent, typical *C. diphtheriae,* has been fully confirmed in this laboratory. Preliminary data obtained here suggest that avirulent strains from clinical cases of diphtheria may be more susceptible to this change than strains from healthy carriers.

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