and this may be the requisite for demonstrating a hyperglycemic response to CPZ since a depression of cellular metabolism in an animal normally functioning at a high metabolic rate would bring about more pronounced changes in the concentration of substances in the blood which are metabolized than would be expected in an animal with a lower normal rate of metabolic activity. Evidence in support of this concept would be the somewhat intermediate effect of CPZ on the blood sugar of the hamster which has a BMR somewhat intermediate to that of the mouse and rat (8,9).

The protection afforded by CPZ from the hypoglycemic convulsions and death following insulin injection in mice would be expected in view of the hyperglycemic state of these animals prior to insulin administration. Whether or not there is any direct antagonism of the insulin molecule cannot be said without further investigation.

Summary. The glycemic effects of chlorpromazine were studied in the mouse, hamster and rat. A hyperglycemic response was found in the mouse and hamster with the mouse having the greater response of the two No significant glycemic change was observed in the rat. An exacerbation of the diabetic state and decrease in survival time was found in alloxan diabetic mice treated with CPZ. A protection from hypoglycemic convulsions and death produced by insulin was afforded to mice which had been injected with CPZ 2 hours previous to the injection of insulin.

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Induction of Toxigenicity in Non-Toxigenic Strains of *C. diphtheriae* with Bacteriophages Derived from Non-Toxigenic Strains. (21948)

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Freeman(1,2) reported that some bacteriophages isolated from *C. diphtheriae* could induce totally non-toxigenic strains of *C. diphtheriae* to become toxigenic and that these transformed strains were indistinguishable in all respects from toxigenic strains occurring in nature. This observation has been confirmed in this laboratory(3,4) as well as in other laboratories(5,6). In each instance, toxigenicity was induced only by bacteriophages obtained from naturally-occurring toxigenic strains of *C. diphtheriae*.

Because of the epidemiological significance of this transformation, studies were undertaken to determine the relative frequency with which the change could be produced in non-toxigenic strains isolated from cases and carriers. Of the 52 strains tested so far the change has been induced in only 8 strains, all of which were the mitis or mitis-like type. While Hewett(7) has reported the transformation in gravis-type strains employing phages derived from toxigenic gravis strains, it has not been accomplished in this laboratory. However, definitions of the gravis type differ in different laboratories. During serial passage of one group of cultures with phages from toxigenic strains, complete lysis was obtained with 2 non-toxigenic strains, (A-8888, mitis-like North Dakota, and A-8782, gravis,

Alabama) without any demonstrable change in toxigenicity. It appeared probable that these strains were lysogenic in themselves. Therefore, experiments were planned to determin whether or not the bacteriophages isolated from strains A-8888 and A-8782 might induce toxigenicity in other non-toxigenic strains. Although the data presented here concerning these studies are not complete, sufficient evidence has accumulated to warrant a report.

Materials and methods. Details of the technics used in these experiments will be published elsewhere. The non-toxigenic strains used in these experiments were chosen from among those which had become toxigenic when treated with phages derived from toxigenic strains. All strains of *C. diphtheriae* from which bacteriophage was derived, as well as those strains in which toxigenicity was induced, were tested first for non-toxigenicity by subcutaneous inoculation in guinea pigs, by intracutaneous inoculation of rabbits, and by the *in vitro* toxigenicity plate method. None showed any evidence of original toxigenicity by any of the methods. The bacteriophages were obtained from atoxigenic strains A-8888 and A-8782 (later also A-8188) by inoculating heart-infusion-agar plates with 3 to 4-hour heart-infusion-broth cultures of the organisms, incubating overnight, followed by extraction of the phage by freezing the agar over CO_2 ice and thawing at room temperature. The expressed liquid was centrifuged at high speed and the supernatant fluid, after heating at 52-53° for 20 minutes, was used in serial passage.

Results. Serial passage of non-toxigenic Freeman strains F-324 and F-326, with phages obtained from A-8888 and A-8782, produced almost complete clearing after the third passage. Centrifuged sediments of the lysed broth cultures were streaked on the *in vitro* toxigenicity plate and gave the precipitation lines typical of toxigenic strains of *C. diphtheriae*. A portion of this same sediment, when streaked on heart-infusion-agar plates and incubated overnight, produced partially lysed colonies which also produced lines of precipitation on the *in vitro* toxigenicity plate. Similar centrifuged sediments when injected intradermally into a rabbit, produced reactions which were indistinguishable from those produced by typical, toxigenic strains of *C. diphtheriae*. The same results were obtained with 3 separate phage extracts from strains A-8888 and A-8782.

Attempts to induce toxigenicity in other non-toxigenic strains of *C. diphtheriae* with these same phages were not successful. Curiously, these strains, which failed to become toxigenic when treated with phages from A-8888 and A-8782, did become toxigenic when treated with phages derived from known toxigenic strains. This observation suggests that phages derived from non-toxigenic strains may differ from phages derived from toxigenic strains. However, phages derived from non-toxigenic strains A-8888 and A-8782 and adapted to atoxigenic strains F-324 and F-326 readily induced toxigenicity in non-toxigenic strains A-334, A-8613, and A-8630. The number of passages necessary to bring about this change varied both with the strain and the phage. Other strains are being passed with these phages but the results are incomplete as yet. The toxigenicity of these phage-changed strains has been tested on both the *in vitro* toxigenicity plate and intradermally in the rabbit.

In another experiment phage was isolated from non-toxigenic strain A-8188 by the method previously described. After 44 passages with atoxigenic strains F-324 and F-326 only partial lysis of these strains was observed and toxigenicity could not be demonstrated. The heated supernatants from the last passage were used for treatment of non-toxigenic strains A-8613 and A-8630. Complete lysis was obtained after the seventh passage and the centrifuged sediments were shown to be toxigenic on the *in vitro* plate and when injected intradermally into the rabbit.

The observations made during the course of the above experiments seem to suggest that there may be different races of diphtheria bacteriophage or that several factors are requisite for induction of toxigenicity not all of which are necessarily present in any given strain of *C. diphtheriae* or in any one bacteriophage.

Summary. It has been established that certain bacteriophages derived from naturally-

occurring non-toxigenic strains of *C. diphtheriae* will induce toxigenicity in certain non-toxigenic strains of *C. diphtheriae* as readily as will phages derived from naturally-occurring toxigenic strains.

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Tissue Conversion of Thyroxine to Triiodothyronine.* (21949)

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The isolation of a new thyroxine-like compound from the thyroid and plasma by Gross and LeBlond(1,2) and the subsequent identification of this substance as 3,5,3′-triiodothyronine by Gross and Pitt-Rivers(3,4), and Roche, Lissitsky and Michel(5) have stimulated a great deal of investigative work. Triiodothyronine has been shown to be about 5 times as potent as thyroxine in preventing thiouracil-induced goiter in rats(6,7,8) and to produce a much more rapid elevation in the oxygen consumption of hypothyroid animals and man than does thyroxine(8-11). These findings, along with the earlier reports by Gross and LeBlond(1) of isolation of the I^{131}-triiodothyronine from tissues and plasma of thyroidectomized animals given I^{131}-labeled thyroxine, led Gross and Pitt-Rivers(6) to postulate that thyroxine is enzymatically deiodinated to triiodothyronine in the tissues and that triiodothyronine is the active form of the hormone at the tissue level. Although Albright, Larson and Trust(12) reported the conversion of thyroxine to triiodothyronine by kidney slices and MacLagan and Sprott(13) made similar observations using liver homogenates, Roche, Michel, Michel and Lissitzky (14) have been unable to demonstrate the deiodination of thyroxine to triiodothyronine *in vitro*. More recently Roche and Michel(15), on the basis of *in vivo* work with thyroidectomized animals, found that the thyroid is the sole important source of plasma triiodothyronine and that there was no triiodothyronine or its derivatives in the bile or urine of such animals after the injection of labeled thyroxine. Kalant, Lee, and Sellers(16) reported that triiodothyronine was the major radioactive compound found in the skeletal muscle of propylthiouracil-treated rats given I^{131}-labeled thyroxine but Taurog(17) stated that his group did not find consistent conversion of thyroxine to triiodothyronine in liver, kidney, spleen or diaphragm.

With these conflicting observations in mind, the following experiments were devised in an attempt to demonstrate the *in vivo* conversion of thyroxine to triiodothyronine by the rat.

Methods. (a) Thirty-three male Sprague-Dawley rats, weighing 250 to 300 g and maintained at 80°F and on standard Purina Laboratory Chow were given 10 μc (0.5 to 0.7 μg) of I^{131}-labeled thyroxine† intravenously. (The stock solution of thyroxine consisted of this hormone in 50% propylene glycol in water: aliquots were diluted with 0.9% saline before administration.) At intervals of 30 minutes, one, 3, 6, 12, and 24 hours after injection, liver, kidney, and skeletal muscle were removed. Nine rats were studied at the 30-minute point, 3 at one hour, 7 at 3 hours, 3 at 6 hours, 4 at 12 hours and 7 at 24 hours.

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† Obtained from Abbott Laboratories, Oak Ridge, Tenn.