While inactivation in these experiments appears to be complete the method of carrying out the test involves the possibility of a small residuum of active phage escaping detection, for the inactivated solution is diluted 1:1000 with broth before titrating it. This step is necessary in order to bring the KCN concentration down to a level (1/10,000,000) which will not interfere with the titration reaction. However, even should some phage not be inactivated the maximal theoretical amount that might be overlooked would be very small indeed; at most not more than two hundred thousandths of one per cent of the original phage titre.

Conclusions. 1. The inactivation of antistaphylococcal bacteriophage suspended in infusion broth at pH 7.6 by CN^- can be completely reversed by converting CN^- to $Ag(CN)_2^-$. 2. The previously reported reversible inactivation of phage by Hg^{++} therefore appears to be not a special case but rather one example of a more or less general property of phage.

7181 P

Effect on Total Thyroidectomy on Response to Adrenalin.

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The following observations have been carried out as a part of the study concerning the therapeutic value of total thyroidectomy in angina pectoris. It was noted a few years ago[1] that intramuscular injections of adrenalin, when given to patients suffering with angina pectoris would provoke attacks of anginal pain. As a result of clinical observation, it was found that when total thyroidectomy was performed in patients who were having daily attacks of angina, these attacks disappeared immediately following the operation and long before any changes had taken place either in the basal metabolism or in the rate of blood flow. It was therefore suspected and, in fact, predicted[2] that removal of the thyroid gland might be producing a fundamental alteration in the response of the circulation to

[1] Levine, S. A., Ernstene, A. C., and Jacobson, B. M., *Arch. Int. Med.*, 1930, **45**, 191.

[2] Levine, S. A., Cutler, E. C., and Eppinger, E. C., *New Eng. J. Med.*, 1933, **209**, 667.

adrenalin and that a previously positive response might possibly become negative after such an operation.

Five patients were given intramuscular injections of adrenalin varying from 0.3 to 0.5 cc. of a 1-1000 solution before and 2-3 days after operation. In the first of these cases, which was operated upon August 22, 1933, 0.5 cc. before the operation induced a maximum rise of the pulse rate of about 20 and the blood pressure rose from 188/88 to a maximum of 226/94 in a few minutes. Typical substernal anginal pain also resulted. On August 23, 1933, 0.5 cc. of adrenalin produced no pain, a rise in the pulse rate of only 10 and the blood pressure was hardly changed. On August 26 0.5 cc. of adrenalin again produced no chest pain, although the systolic blood pressure rose about 30 mm. On August 27, 1.0 cc. of adrenalin again failed to produce anginal pain and the effect on the pulse and blood pressure was slight. Here, although twice the original amount of adrenalin was given, the effect on the pulse rate and blood pressure was less and there was no chest pain.

In a second case, preoperatively 0.5 cc. of adrenalin produced a rise in the pulse rate of about 18 with no change in the blood pressure. Definite anginal pain resulted. Three days after the operation the same dose of adrenalin caused no pain nor appreciable changes on the pulse rate or blood pressure. In a third case, 0.4 cc. preoperatively produced severe anginal pain with a rise in the pulse rate of about 35 and a change in the blood pressure from 140/85 to 165/95. Two days after operation, the same dose of adrenalin caused no anginal pain although the pulse rate and blood pressure increased almost as much as before. In the fourth instance, slight anginal distress was produced by 0.4 cc. before operation and the pulse rate and blood pressure showed moderate increases. Two days after the operation a similar amount of adrenalin produced no chest distress whatever and very slight elevations in pulse rate and blood pressure. In a fifth case, 0.3 cc. of adrenalin reproduced typical anginal pain. The pulse rate rose slightly and the blood pressure moderately. Two days after operation the same dose of adrenalin caused practically no change in the pulse rate but the blood pressure rose moderately. Definite anginal pain resulted, however, but the patient stated that the distress was much less than on the previous occasion.

Preoperatively, the average basal metabolism of these 5 patients was —4% and the rate of blood flow, 18 seconds, whereas 2 to 3 days after the operation the corresponding figures were +4% and 19 seconds. Further observations on the effect of adrenalin in our

patients with angina pectoris were discontinued because of the hazard involved. More detailed studies along this same line are, therefore, being carried out in animals.

This study suggests that the complete removal of the thyroid gland alters the response of the cardiovascular system to adrenalin and that this effect is independent of changes in the basal metabolism or the rate of blood flow. We also believe that it is the alteration of this mechanism which may in a measure be responsible for the relief of anginal pain in these patients.

7182 C

Loss of Sensitivity to Anterior Pituitary-like Hormone of Pregnancy Urine.

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It has been shown that the greatly enlarged ovaries of rats injected with extract containing the anterior pituitary-like hormone of pregnancy urine (A.P.L.) will decrease in weight after a certain period even though administration of the hormone be continued. Such ovaries will finally return to a normal weight level.[1, 2, 3]

We have recently repeated these experiments on a series of 12 rats, continuing the A.P.L. injections for a longer time, and we found that after prolonged administration of the hormone the ovaries of some of these rats became actually subnormal in size, weighing as little as 7 mg. after 4 months' treatment (increasing doses of 25-200 units of A.P.L. daily). The ovaries of 8 out of 10 rats, however, were still normal in size at this time (30-45 mg.), but they lost their sensitivity to A.P.L., for 200 units per day of this hormone did not have any luteinizing effect upon them. Histologically they showed numerous corpora lutea in retrogression, but no mature follicles.

In 4 similarly treated rats we performed a laparotomy, inspected the ovaries after 4 months of treatment with A.P.L. and found them normal or subnormal in size. We then injected these rats over a

[1] Collip, J. B., *Internat. Clinics*, 1932, **4**, 51.

[2] McPhail, M. K., *J. Physiol.*, 1933, **80**, 105.

[3] Zondek, B., *Die Hormone des Ovariums und des Hypophysenvorderlappens*, Julius Springer, Berlin, 1931.