

TABLE III.
Effect of Actinophage of Streptomycin-producing *S. griseus* on Various Strains of This Organism.

Culture No.	Nature of strain	Spot test* for phage		Submerged growth effect† Phage per ml $\times 10^7$, after days of incubation			
		Nutrient agar	Dextrose-asparagine agar	0	3	5	7
3326	N. J. culture of 1915 isolate	—	—	6	3	4	4
3326a	Holland culture of 1915 isolate	—	—	6	<0.4	<0.04	0.004
3326b	Kelner's mutant of 1915 isolate	+	+	6	100	105	186
3463	Streptomycin-producing soil culture of 1943	+	+	6	30	31	119
3464	Streptomycin-producing chicken throat culture of 1943 isolate	+	+	6	210	320	570
3464a	Spore isolate of last	+	+	6	34	260	204
3478	Grisein-producing culture	—	—	6	2	2	3
3481	More recent independent isolate of a streptomycin-producing culture	+	+	6	257	420	400
3482	Non-streptomycin-producing culture	—	—	6	0.2	0.01	0.03

* Phage placed on 24-hour vegetative streaks growing on nutrient and dextrose-asparagine agars, incubated an additional 24 hours, and examined for lysis.

† Phage added to freshly inoculated flasks of medium, grown under submerged conditions.

the culture upon artificial media for more than 30 years. When irradiated, this culture yielded a mutant that was as potent a producer of streptomycin as the streptomycin-yielding strains of *S. griseus* isolated in 1943.

This assumption was fully confirmed by the characteristic antibiotic spectrum of the two cultures, their behavior to streptomycin-dependent and streptomycin-resistant mutants of *E. coli* and other bacteria, and sensitivity of the two cultures to the same actinophage.

These results further point to the accuracy of the identification of the streptomycin-pro-

ducing cultures of *S. griseus* with that of the original 1915 isolate, based on literature description alone, in spite of the fact that the type culture available in two collections showed distinct changes from the original description.

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17146. Effect of Tetraethylammonium Bromide on Adrenal Medulla.

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Acheson and Moe¹ have shown that tetraethylammonium ion will block autonomic ganglia. Since the adrenal medulla is generally accepted as ganglionic in nature, the transmission of impulses across the ganglion and subsequent release of epinephrine should be blocked by the injection of tetraethylammon-

ium bromide. Some evidence for this has been shown by the action of tetraethylammonium on morphine hyperglycemia in dogs,² which closely resembles the effect on such hyperglycemia produced by surgical removal of the adrenal medulla.³ In both cases mor-

² Morrison, J. L., *Fed. Proc.*, 1947, 6, 359.

¹ Acheson, G. H., and Moe, G. K., *J. Pharm. and Exp. Therap.*, 1946, 87, 220.

³ Bodo, R. C., Co Tui, F. W., and Benaglia, A. E., *J. Pharm. and Exp. Therap.*, 1931, 61, 48.

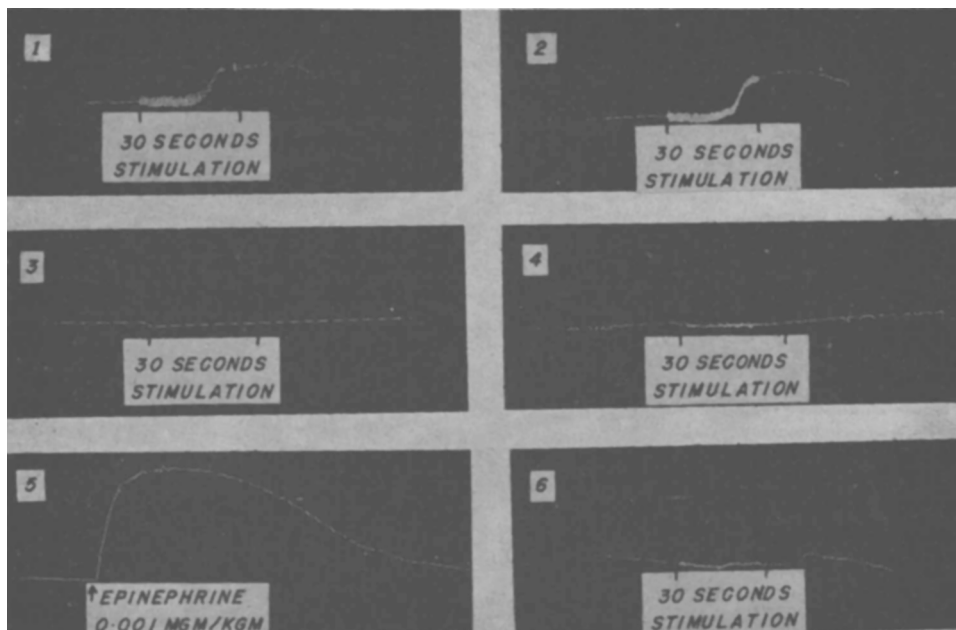


Fig. 1.

Cat C. Effect of stimulation of splanchnic nerve on retraction of nictitating membrane. (1) Initial stimulation in anesthetized cat. (2) Thirty minutes after first stimulation. (3) Ten minutes after tetraethylammonium bromide 10 mg/kg I.M. (4) Thirty minutes after injection of tetraethylammonium bromide. (5) Effect of epinephrine hydrochloride I.V. 45 minutes after tetraethylammonium bromide. (6) Seventy-five minutes after I.M. injection of tetraethylammonium bromide.

phine hyperglycemia is abolished or greatly diminished. A more direct method of determining blockade of the adrenal medulla is desirable than shown by blood sugar levels. Sensitivity of the denervated nictitating membranes of cats to circulating epinephrine offers a convenient biological test of such a blockade.⁴

Method. In a series of 6 cats the superior cervical ganglion on the left side was removed. During a recovery period of 4 days the nictitating membrane becomes sensitized to circulating or injected epinephrine. The cats were anesthetized and the following preparations made. Through an incision in the body wall, shielded electrodes were placed over the splanchnic nerve just before it enters the adrenal gland in order to provide for stimulation. The eyelids were retracted after cutting the lateral canthus and the nictitating membrane was connected to an isotonic lever mag-

nifying its movement several times and recording them on a revolving smoked drum. Splanchnic nerves were stimulated using a Bird Stimulator before and after intramuscular injection of a 10% solution of tetraethylammonium bromide. In all cases after full effect of the tetraethylammonium bromide had been shown, epinephrine was injected in order to demonstrate the action of epinephrine on the nictitating membranes. Either dial solution* or pentobarbital sodium was used as the anesthetic. We could find no appreciable difference in the response of the animals to these barbiturates. Doses of tetraethylammonium bromide ranged from 3 mg/kg up to 10 mg/kg. Maximum action was obtained in 10 to 15 minutes and lasted for about an hour after which time it began to wear off. Intravenous injections of varying amounts of epinephrine hydrochloride at any time during the maxi-

⁴ Rosenblueth, A., and Cannon, W. B., *Am. J. Physiol.*, 1932, **99**, 398.

* Dial Solution furnished through courtesy of Dr. Frederick F. Yonkman, Ciba Pharmaceutical Products, Inc.

mum effects of tetraethylammonium indicated that tetraethylammonium had no demonstrable effect on the action of epinephrine at the effector cells of the nictitating membrane.

Results. Tracings illustrating a typical experiment in Fig. 1 show that tetraethylammonium compound blocks the release of epinephrine from the adrenal medulla.

In all of the 6 cats used in this study the nictitating membrane was stimulated to contract as a result of electrical stimulation of the splanchnic nerve. Repetition of stimuli at intervals over a period of 30 minutes to one hour produced similar contractions. Retraction usually persisted for several minutes.

After administration of tetraethylammonium bromide, stimulation of the splanchnic nerve was not followed by retraction of the membrane. Injection of 3 mg/kg abolished retraction in most of the animals but 10 mg/kg abolished it in all animals. However, intravenous injection of .001 mg/kg of epinephrine hydrochloride at the peak of the tetraethylammonium effect produced marked retraction of the nictitating membrane.

Summary. 1. Tetraethylammonium bromide blocks the release of epinephrine from the adrenal medulla.

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17147. Tumorous Growths in the Pituitary and Trachea Following Radio-toxic Dosages of I^{131} .*

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The possible occurrence of thyroidal tumors after partial beta-ray destruction of the thyroid gland has prompted the investigation of long-term effects of high dosages of I^{131} . No thyroidal growths have been observed in our experiments with mice, but tumors of the trachea and hypophysis have been found. This report deals with the incidence of such tumors and provides a description of the growths as well as the conditions under which they are obtained. A detailed characterization of the cytological properties of the hypophyseal tumors is being prepared separately.

Methods and materials. Most of the work included in this report was done with adult mice of the C_{57}^+ strain. Smaller numbers of the A ,[†] I^+ and CFW^+ strains also were em-

ployed. Although more than 500 animals have been utilized in different phases of this study, the present report concerns 158 mice observed for a period of time sufficient to show the metaplastic and atypical growth changes, as well as 34 untreated control mice. Purina Laboratory Chow and water comprised the exclusive *ad libitum* diet of the mice, and they were kept at controlled temperature ($72^\circ \pm 2^\circ F$), humidity 65% ($\pm 5\%$), and illumination (12 hours per day).

Radioactive iodine was given subcutaneously as NaI without carrier, in neutral aqueous solution in dosages of 10, 50, 80, 100, 160, 200, 300, 400, 500 and 1000 microcuries.[§] At least 10 animals were included in each dosage group for the C_{57} and CFW strains, and in most cases, especially with the 100, 200 and 300 microcurie dosages, there were 40 or more animals.

Calibration and measurement of the dosages was done with a Geiger counter and standards

[§] 100 μc in normal adults produces almost complete, and 200 μc complete, thyroidal destruction.¹

¹ Gorbman, A., *PROC. SOC. EXP. BIOL. AND MED.*, 1947, **66**, 212.

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[†] Breeding stock of these strains originally obtained from colony of L. C. Strong, Yale University.

[‡] Purchased from Carworth Farms, New City, N. Y.