commercial typing serum. Our results showing that 19 of 23 separate group 4 types readily adsorb heterophile antibody may be compared with those of Bailey and Shorb,[1] showing that 32 of 35 "type IV" strains adsorb heterophile antibody. In all probability, however, Bailey and Shorb used larger adsorbing doses of pneumococci than we did.

In addition to the tests herewith reported we have had occasion to test the heterophile-antibody-adsorbing capacity of several pneumococcal strains belonging to types 1, 2, and 3. The type 1 strains have adsorbed a large amount, the type 2 strains a very small amount or none, while the type 3 strains adsorbed an intermediate amount of heterophile antibody. These results agree in the main with those reported by Bailey and Shorb.[1]

Conclusion. Heterophile antigen has a wide distribution in the various types of pneumococci. It is logical to assume, therefore, that heterophile antigen is at least part of the complex species-antigenic structure of most pneumococci.

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Excretion of Mercury Following Administration of Mercurial Diuretics with and without Theophylline.

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It has recently been shown that the addition of theophylline to the mercurial diuretics Mercurin and Salyrgan practically prevents their local toxic action[1, 2] and promotes their absorption after intramuscular injection.[3] Although Mercupurin (Mercurin with theophylline) has been found to have a somewhat greater diuretic efficiency than Salyrgan,[4-7] it remains to be proven unequivocally, however,

[1] DeGraff, A. C., and Batterman, R. C., PROC. SOC. EXP. BIOL. AND MED., 1935, **32**, 1546.

[2] DeGraff, A. C., Batterman, R. C., and Lehman, R. A., *ibid.*, 1938, **38**, 373.

[3] DeGraff, A. C. Batterman, R. C., and Lehman, R. A., *J. Pharm. Exp. Therap.*, 1938, **62**, 26.

[4] Thompson, W. A. R., *Quart. J. Med.*, 1937, **30**, 321.

[5] Crawford, J. H., and McDaniel, W. S., *Ann. Int. Med.*, 1935, **8**, 1266.

[6] Fulton, M. N., and Bryan, A. H., *J. Lab. Clin. Med.*, 1935, **20**, 1252.

[7] DeGraff, A. C., Nadler, J. E., and Batterman, R. C., *Am. J. Med. Sci.*, 1936, **191**, 526.

that theophylline exerts any influence after the drug has reached the circulation. It was therefore decided to study the excretion of mercury by laboratory animals after the administration of these diuretics with and without theophylline. It is fully realized that results thus obtained cannot necessarily be referred to man. Nevertheless, it was felt that information concerning the pharmacology of drugs of this type could more readily be obtained by using animals whose food, salt and water ingestion could be kept perfectly constant.

A total of 24 albino rabbits weighing between 2 and 3 kg were used in these experiments. All the animals had been raised on a diet of alfalfa hay and oats and had received a constant daily supply of water. On the day of the experiment each rabbit was tied to an animal board and 75 cc of water at body temperature administered by stomach tube. One hour later the animal was catheterized (French No. 10 catheter), the urine discarded and 0.10 cc of the drug to be studied was injected with a tuberculin syringe and 26 gauge needle either into the tibialis anterior muscle or one of the marginal veins of the ear. This was equivalent to 3.71 mg of mercury in the case of Salyrgan or Salyrgan with theophylline and 3.80 mg in the case of Mercurin or Mercupurin. The catheter was strapped in place with adhesive tape and all the urine excreted within the next 6 hours collected in 25 cc graduates. Since the rates of excretion vary considerably for the different drugs and methods of administration, it was necessary to space the collection of samples so that the time at which maximum excretion occurred could easily be determined. The mercury content of each sample of urine was then determined by the method of Winkler,[8, 9] modified by Gettler and Lehman.[10]

The protocols are given in condensed form in Table I and the results are summarized in Fig. 1 and Table II. In Fig. 1 is shown the influence of theophylline upon the total amount of mercury excreted in the urine of the rabbit within 6 hours. The experiments were not continued beyond this point since in all cases the amount of mercury in the urine dropped during the last hour of the period to less than 5% of that administered. Three bars are plotted for each drug and represent the values obtained from 3 animals treated identically. It will be seen that the variation between animals is

[8] Winkler, W. O., *J. Assn. Off. Agric. Chemists*, 1935, **18**, 638.

[9] Winkler, W. O., *ibid.*, 1936, **19**, 233.

[10] Gettler, A. O., and Lehman, R. A., *Am. J. Clin. Path.*, Tech. suppl., 1938, **8**, 161.

moderate and that the trend is unmistakable. Theophylline increases the total mercury excretion 30 to 40% after intravenous injection and 100 to 300% after intramuscular injection. The effect is so much greater by the intramuscular route because of the slower absorption of the preparations not containing theophylline. In fact it has been shown[3] that while, on the average 55% of the injected Salyrgan, and 57% of the Mercurin, are absorbed within the first 6 hours, Mercupurin and Salyrgan with theophylline are completely absorbed during the same time interval. It would be more logical,

TABLE I.
Mercury Excreted After Various Time Intervals.

Time after injection	Mg. of mercury found in urine*			
	Mercurin		Salyrgan	
	intravenous	intramuscular	intravenous	intramuscular
min.				
15	.374	—	.468	—
30	.389	.055	.321	.028
45	.619	—	.587	—
60	.481	.112	.361	.084
90	.399	.101	.290	.095
120	.244	.131	.106	.075
150	—	.088	—	.064
hr.				
3	.157	.070	.150	.047
4	.069	.150	.083	.078
5	.020	.112	.032	.050
6	.048	.152	.063	.046
	Mercupurin		Salyrgan with theophylline	
	intravenous	intramuscular	intravenous	intramuscular
min.				
7	.308	—	.475	—
15	.671	.181	.898	.054
22	.518	—	.695	—
30	.327	.539	.442	.867
45	.483	.455	.539	.414
60	.384	.579	.216	.554
90	.365	.319	.228	.412
120	.292	.306	.111	.223
150	—	.158	—	.105
hr.				
3	.164	.189	.120	.256
4	.118	.140	.097	.123
5	—	.091	.052	.112
6	.041	.059	.060	.132

*Each value represents the average of 3 experiments.

therefore, to express the excretion of Mercurin and Salyrgan as percentage of absorbed mercury which is excreted, rather than percentage of administered mercury. This calculation was made and its effect is shown graphically by the dotted lines in Fig. 1. It will be seen that theophylline still distinctly increases the total urinary ex-

TABLE II.
Maximum Excretion Rates.

	Intravenous				Intramuscular			
Drug	Mercurin	Mercupurin	Salyrgan	Salyrgan with theophylline	Mercurin	Mercupurin	Salyrgan	Salyrgan with theophylline
Max. excretion rates in % of administered mercury excreted per min.*	1.2	2.4	1.2	3.0	0.13	0.72	0.09	1.2
Min. after injection at which max. excretion rates occur.*	33	14	43	14	85	43	75	25

*Mean of 3 experiments.

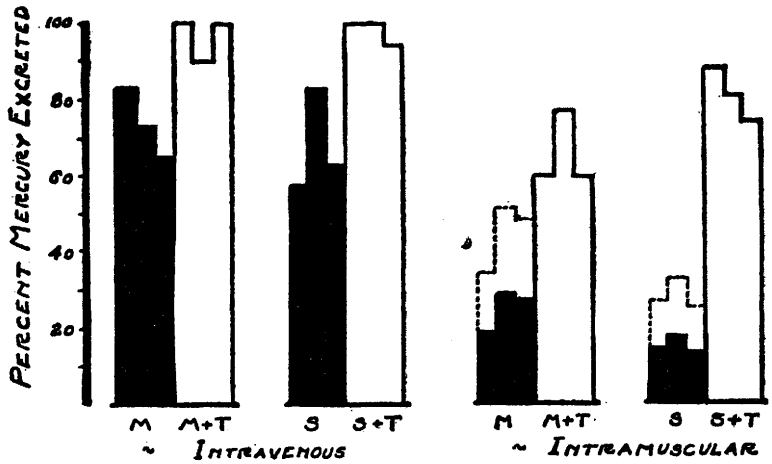

FIG. 1.

Diagrams showing the influence of theophyline upon the percentage of the injected mercury which is excreted in the urine of the rabbit within 6 hours. Dotted lines show the percentage of absorbed mercury which is excreted in the cases where absorption is incomplete. Abbreviations: M—Mercurin; M + T—Mercurin with theophylline or Mercupurin; S—Salyrgan; S + T—Salyrgan with theophylline.

cretion of mercury. By taking this factor into account it is possible to conclude that theophylline continues to influence the action of mercurial diuretics after their absorption into the blood.

It necessarily follows that if the total mercury excreted is increased by theophylline, then the rate of excretion must also be increased. The excretion rates over the time intervals given in Table I were calculated and the averages of the 3 maximum values for each 3 identical experiments are listed in Table II.* The average time after injection at which these maxima occur is also given and it will be seen that theophylline increases the mean maximum excretion rate to the same relative degree as it increased the total mercury excretion, while at the same time it causes the maxima to occur somewhat sooner.

Summary of Results. Theophylline was found to influence the urinary excretion of mercury following the injection of Mercurin or Salyrgan in the following ways: 1. The percentage of the administered mercury which is excreted within 6 hours increased 30 to 40% after intravenous injection and 100 to 300% after intramuscular injection. 2. The maximum rates of excretion increased greatly in all cases and by all methods of administration. 3. The maximum excretion rates occurred somewhat earlier.

* This procedure is used instead of determining the peak of the excretion rate curve since it requires no subjective estimate.

The results demonstrate that the combination of theophylline with these mercurial diuretics modifies their action after absorption as well as before.

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Recovery in the Rat from the Diabetes Insipidus Caused by Posthypophysectomy.

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Richter[1] and Pencharz, Hopper and Rynearson[2] have shown that after removal of the posterior lobe of the hypophysis ("posthypophysectomy") of the rat. with minimal damage to the anterior lobe, there ensues a profuse diabetes insipidus. Both were of the opinion that the condition was permanent; Richter followed the water intake of his rats for about 60 days and Pencharz, *et al.*, for 100 days. White,[3] using rats posthypophysectomized by Pencharz, reported 3 animals to be clearly diuretic a year after operation. In our experience, however, recovery from the diabetes insipidus produced by the same operation customarily occurs in time. Fig. 1 shows the

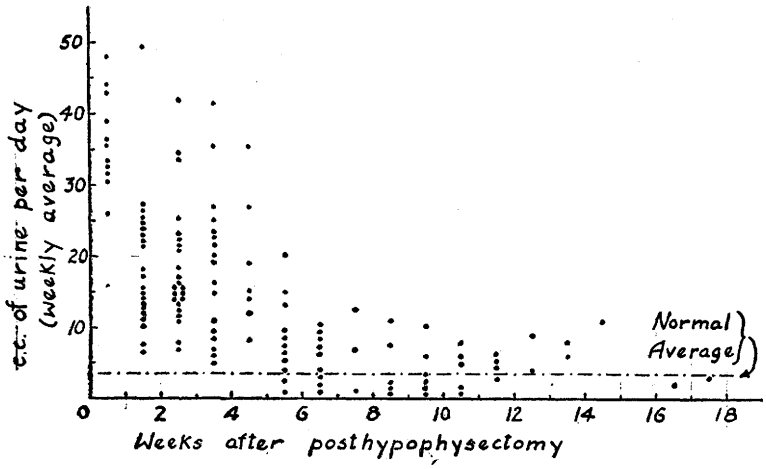

FIG. 1.
Urinary excretory rates after posthypophysectomy in the rat.

1 Richter, C. P., *Am. J. Physiol.*, 1934, **110**, 439.

2 Pencharz, R. I., Hopper, J., and Rynearson, E. H., PROC. SOC. EXP. BIOL. AND MED., 1936, **34**, 14.

3 White, H. L., *Am. J. Physiol.*, 1937, **119**, 5.