The inoculum, a saline suspension of organisms from a B.G. slant, was progressively diluted until no growth took place in the above medium. At this stage the addition of nicotinic acid or nicotinamid (0.5 to 0.001 γ per cc) would allow the organisms to grow.

The above medium is not complete as the addition of a small amount of hydrolyzed casein results in a heavier growth.

Summary. Nicotinic acid or nicotinamid favors the growth of Phase I *H. pertussis.*

11764

Effect of Diminishing Doses of Post-Pituitary Extract on Urinary Excretion of Water and Chlorides.

HERBERT SILVETTE. (Introduced by H. E. Jordan.)

From the Department of Pharmacology, University of Virginia.

Previous work has indicated that, when the dose of injected post-pituitary extract is progressively reduced, the excretion rates of water and chlorides were changed independently of one another.[1] The present experiments were designed to extend these observations by following the change in urinary excretion over a wide range of extract dosage. Thus the dose of extract was varied from 3000 milliunits per 100 g of body weight down to 2.5 milliunits. White rats were employed, weighing about 200 g. Each animal was used but once to prevent any possible complication due to sensitization

TABLE I.
Urine and Chloride Excretion After Various Doses of Post-Pituitary Extract.

Series	No. animals in series	Milliunits post-pituitary ext. injected	Avg 6-hour excretion	
			Urine, cc/100 g B.W.	Chlorides, mg/cc urine
A	24	0	7.4	0.32
B	16	2.5	7.1	0.29
C	12	5	6.6	1.22
D	24	10	6.0	2.40
E	17	25	5.4	3.14
F	21	50	4.2	3.98
G*	6	375	2.7	6.05
H*	6	750	2.7	8.50
I*	12	1500	2.2	9.45
J*	6	3000	2.5	9.35

*Data taken from Table 3, Silvette, *Am. J. Physiol.*, 1940, **128**, 747.

1 Silvette, H., *Am. J. Physiol.*, 1940, **128**, 747.

or tolerance to the pituitary extract. The animals were given intraperitoneal injections of 10 cc of 0.2% sodium chloride solution per 100 g of body weight with which had been mixed the calculated amount of pituitary extract.* They were then placed in metabolism cages for 6 hours, and the urine collected and analyzed for chlorides.[1]

The data are presented in Table I. These show that as the dosage of the extract was progressively decreased, the excretion of water gradually increased while that of the chlorides steadily diminished. The water excretion approached the normal level much more rapidly than the chloride excretion, however; and, when the dosage of the extract was reduced to 5 milliunits, it was observed that the urine excretion was now inhibited to the extent of only 11%, while the chloride output was still 280% above the normal level. When the amount of pituitary extract was reduced still further (*e.g.*, to 2.5 milliunits) no significant change from the control levels could be observed. This dosage, therefore, was concluded to be subminimal, at least in respect to the chloride and water changes. Analogously, the dose of 3000 milliunits was supramaximal, as its effect on urinary excretion was no greater than that produced by an injection of 1500 milliunits.

Theoretically it should be possible to find an extract dosage between 5 and 2.5 milliunits at which the water excretion would be normal while the chloride excretion would still be above control levels, but experimentally this has not proved possible because the available extracts are not standardized with respect to their antidiuretic potency, and may indeed vary otherwise to the extent of ±20%.†

The above observations lend additional weight to the conception of the duality of the response to post-pituitary extract; *i.e.*, that the injection of the extract leads to 2 separate and distinct effects on kidney function, the one concerned with changes in salt excretion and the other with water.[1, 2] They also indicate that the chloride-concentrating ability of the renal tubules, which is enhanced by the antidiuretic hormone,[1] is considerably more sensitive to this hormone than is the parallel water-resorbing power. This difference in sensitivity might be useful as the basis for a practicable method of standardizing the antidiuretic potency of pituitary extract, since

* Posterior Pituitary Solution Squibb (U.S.P. XI strength), kindly furnished by Dr. John F. Anderson of E. R. Squibb and Sons.

† *United States Pharmacopoeia*, XI revision, 1936, article "Liquor Pituitarii Posterii."

[2] Melville, K. I., *J. Physiol.*, 1936, **87**, 129.

under the conditions of the experiments described herein the rate of change of the chloride excretion is considerably greater than that of the water output over a practicable working range of 5-25 milliunits of U.S.P. post-pituitary extract.

11765 P

l-Proline and Tumor Incidence in Mice.

Frederick S. Hammett.

From the Research Institute of the Lankenau Hospital, Philadelphia.

It has been demonstrated that l-proline is a specific participant in some process concerned in differentiation expression of obelia.[1]

It is our purpose and practice to test the repeatability or non-repeatability of the uncomplicated and unequivocal findings from lower forms on growth of spontaneous mammary tumors in female mice. Such has been done with l-proline.

Preliminary trials for toxicity level were made on some 20 test and 20 control mice by Mr. McDevitt at the Marine Experimental Station in North Truro. More secondary tumors appeared in the proline mice. These were separate new tumors. The small number of animals and the changing dosage made this observation inadequate for conclusion.

The measure of non-toxicity commonly used in these growth studies is absence of body weight loss of tests in terms of controls on prolonged administration of the amino acid.

Having established the safe dosage the regular series of trials was run in the mouse colony at Philadelphia. Here 78 mice were daily given by intrascapular subcutaneous injection 0.2 cc of an M/125 solution of l-proline in distilled water from the time of appearance of the first tumor until death. Seventy-six untreated mice served as controls. These lived, grew, produced their tumors and died contemporaneously with the others under like environmental and nutritive conditions.

Here, too, the mice given l-proline had more multiple primary tumors than the controls. All mice, both tests and controls, had primary tumors of course. A second tumor appeared in 56.4% of the proline group, and in but 44.7% of the controls. A third tumor appeared in 20.5% of the proline series and in but 13.2%

[1] Hammett, F. S., and Collings, W. D., *Growth*, 1937, 285.