of a 1% solution of nicotinic acid was followed by no hyperemia or ulceration. The substance has therefore little irritating action. Since nicotinic acid is often prepared from nicotine,[16] caution should certainly be exercised to eliminate any possibility of contamination by the alkaloid. Simple animal tests will detect such an impurity.

Summary. Nicotinic acid is at least several hundred times less toxic in mice, rats, and guinea pigs than nicotine. Nicotinic acid is devoid of action upon the autonomic ganglia. Nevertheless, repeated administration of large doses, 2 gm. daily, in dogs has resulted in poisoning and deaths.

9807

Renal Excretion of Exogenous Creatinine in the Aglomerular Toadfish, *Opsanus tau.*

JAMES A. SHANNON.

From the Marine Biological Laboratories, Woods Hole, and the Department of Physiology, New York University College of Medicine.

We have presented elsewhere a quantitative analysis of the relationship between plasma concentration and urine flow, and the tubular excretion of phenol red by the aglomerular fishes, *Lophius piscatorius* and *Opsanus tau.*[1] It was shown, in each of these species, that above 6.0 mg. % plasma phenol red there was no significant increase in the rate of excretion and that this maximal rate was not influenced by the extent or direction of the diffusion gradient. The present study represents an attempt at a similar analysis of the tubular excretion of exogenous creatinine by *Opsanus.* Marshall and Grafflin[2] have shown in this species that the fraction of injected creatinine which is excreted in an 18-hour period decreases progressively with increasing amounts of injected creatinine; furthermore, the fraction of a small injection excreted in a given period of time increases with increasing urine flow.

The present experiments may be divided into 2 groups. In the first group one urine collection period, 10 to 12 hours in duration and beginning 8 to 12 hours after the injection of creatinine, was made after single doses of 50 to 1500 mg. per kg. Under these con-

[16] McElvain, S. M., *Organic Synthesis,* 1925, **4**, 49.

[1] Shannon, J. A., *J. Cell. and Comp. Physiol.,* 1938, in press.

[2] Marshall, E. K., Jr., and Grafflin, A. L., *J. Cell. and Comp. Physiol.,* 1932, **1**, 161.

ditions the rate at which the plasma concentration falls is so slow that a single blood sample drawn at the end of the urine collection period suffices for the calculation of the clearance. Observations of this nature on 81 fish are given in Fig. 1 and summarized in Table I. In the second group of experiments, an effort was made to obtain in the same fish 2 urine collection periods at high plasma creatinine levels but at different rates of urine flow. An initial period was taken as described above, after which a second injection of creatinine (400 to 1000 mg. per kg.) was usually given and the second urine collection period started about 10 hours later. Blood was drawn at the end of each period. The initial periods of these experiments, 16 in number, are included in Fig. 1 and Table I. Blood and urine collections were made as previously described.[1] Creatinine was determined on Folin Wu filtrates of plasma and diluted urine by the Folin method.[3]

In confirmation of Marshall and Grafflin, we find that the rate of excretion of creatinine does not increase in direct proportion to the plasma concentration, and that the rate of excretion is related to urine flow. The data presented in Fig. 1 and summarized in Table I suggest the presence of an excretion maximum, but this is not as

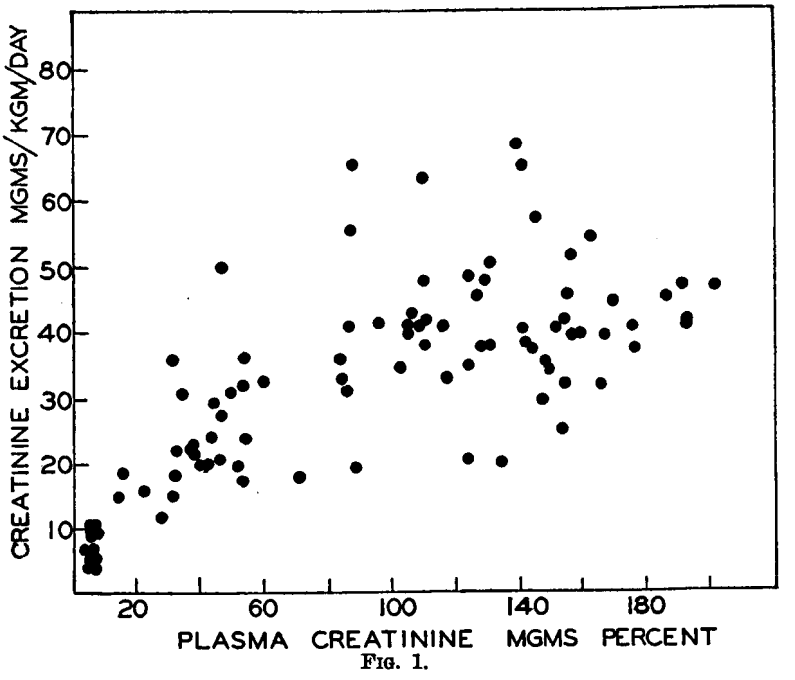

FIG. 1.

[3] Folin, O., *J. Biol. Chem.*, 1919, **38**, 81.

TABLE I.
Summary of the data shown in Fig. 1.

No. of periods	Mean plasma concentration, mg. %	Mean rate of excretion, mg. per kg. per day
9	4.81	6.28
11	16.6	17.02
11	38.5	23.9
11	56.0	28.4
11	93.4	41.3
11	117.2	41.9
11	136.5	45.0
11	154.0	41.5
11	181.0	43.0

sharply defined as in the case of phenol red. The scatter of the data is not due primarily to differences in urine flow since this does not vary widely; rather it appears that there is considerable variation in the capacity of the kidneys of similarly sized fish to secrete creatinine. The variation observed here is no greater than that previously reported for the tubular excretion of phenol red in this species and in *Lophius*, where urine flow has no demonstrable effect upon the rate of tubular excretion.

There is no doubt that an increase in urine flow is accompanied by an increase in creatinine excretion. This fact is evident not only in individual experiments but also in the summary in Table II. In view of this relationship it was not possible to utilize two-period experiments for the study of the excretion maximum, since the second period invariably had a higher urine flow. But the two-period experiments do show that the increase in creatinine excretion, with increased urine flow, is greatest when an increase in plasma concentration accompanies the increase in urine flow, and is greater than would be expected from either the increase in urine flow (Group 2, Table II) and the increase in plasma concentration (Fig. 1, Table I).

It is not known why urine flow influences the rate of tubular ex-

TABLE II.
Summary of Data Showing Effect of Urine Flow on Rate of Creatinine Excretion.

No. of Experiments in each group	Urine Flow cc. per kg. per day		Plasma Creatinine mg. %		Creatinine Excretion mg. per kg. per day		Ratio Second Period / First Period
	First Period	Second Period	First Period	Second Period	First Period	Second Period	
4	5.79	25.3	147.7	87.8	45.1	55.3	1.23
7	8.63	18.6	145.3	164.3	43.4	69.7	1.61
5	5.16	14.8	103.0	235.0	46.0	118.8	2.58

cretion of creatinine, but it may be noted that the aglomerular tubule must excrete its own water, this water moving in the same direction as the excreted solutes. Whether this circumstance imposes a relationship upon the mechanism of transfer which is absent in the glomerular nephron cannot be determined at present. If the transport of creatinine and water are independent functions, it is possible that the concentration of creatinine in the final tubular urine imposes a limitation upon its excretion. There would appear to be no reason to postulate a different mechanism of excretion in the aglomerular and glomerular nephron; but if such a relationship exists in the latter it may not be discoverable since the creatinine is excreted into a relatively large quantity of glomerular filtrate which subsequently undergoes concentration by the tubular reabsorption of water.

9808 P

Action of High Pressures on Plant Viruses.

J. BASSET, A. GRATIA, M. MACHEBOEUF AND P. MANIL. (Introduced by J. H. Northrop.)

From the Institut de Bacteriologie de l'Universite de Liege, Institut Pasteur de Paris, Institut Agronomique de l'Etat à Gembloux.

Two of us (J. Basset and M. Macheboeuf) with the help of several coworkers[1] have submitted different biological samples to the action of an apparatus devised several years ago by Basset[2] which realizes enormous pressures (beyond 20,000 atmospheres). Non-sporulated bacteria were killed after 45 minutes of exposure to a pressure around 5,000 atmospheres, while sporulated bacteria resist as high pressures as 20,000 atmospheres. Certain viruses and bacteriophages, on the contrary, are inactivated at pressures around 3,000-4,000 atmospheres, while some enzymes are inactivated at about 13,000 atmospheres and toxins at 17,000-19,000 atmospheres. Thus, if toxins behave much like enzymes, bacteriophages behave more like viruses. Globulins are denatured around

[1] Basset, J., Macheboeuf, M., and coworkers, *Compt. rend.*, 1932, **195**, 1431; 1933, **196**, 67, 1138, 1540; **197**, 796; 1935, **200**, 496, 1072, 1247, 1882; 1936, **202**, 121; *Bull. soc. philomath.*, 1933, 575; *Ergebnisse der Enzymforschung* (Leipsig), 1931, **8**, 304; *Bull. soc. chim. biol.*, 1936, **18**, 1181.

[2] Basset, J., *Compt. rend.*, 1927, **185**, 343; 1930, **191**, 928.