10806 P

On the Administration of Heparin *Per os.*

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In view of the possibility of using heparin in the prevention of thrombosis any information concerning the physiology of that substance is of considerable importance. For the inhibition of the clotting of blood *in vivo* heparin is applicated by intravenous injection.[1] With reference to the chemical resistance of heparin and the reported excretion of it in the urine[2] it was thought possible to apply it orally.

Heparin with the activity k = 3,4 and prepared as described before[3] was dissolved in water (10 mg per cc). Mice were then given 0.5 cc from a syringe with a special glass tube inserted through the mouth in the stomach. Blood was obtained by cutting the tail. None of the mice in the experiments showed any delayed clotting of the blood, notwithstanding the great amounts of heparin given. There were, therefore, the following two possibilities: (1) Heparin is inactivated in the alimentary tract, or (2) it is not absorbed by the organism.

To prove which is the case, mice were given heparin in the same manner as before, and during the following 5 days the feces was collected at intervals. It was then extracted with 0.50 cc of water per 10 mg of feces, centrifuged and the supernatant liquid tested for inhibitory action in the usual manner. To 5 drops of chicken plasma one drop of the fluid was added, and the clotting time by the addition of a drop of chicken thrombokinase was observed in a water-bath at 39°.[4]

In Table I two of the 9 experiments are described. The chicken plasma clotted, with the addition of thrombokinase only, in 1½ min. The experiments show that the heparin passes the alimentary tract without deterioration. The feces of the control mice showed no delayed blood-clotting. Two of the heparin mice showed also no inhibitory action of the feces, but this might be due to vomiting of the heparin solution.

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1 Murray, D. W. G., and Best, C. H., *J. Am. Med. Assn.*, 1938, **110**, 118.

2 Wilander, O., *Skand. Arch. Physiol.*, 1939, **81**, Suppl., 48.

3 Astrup, T., and Behrnts Jensen, H., *J. Biol. Chem.*, 1938, **124**, 309.

4 Astrup, T., and Behrnts Jensen, H., *Skand. Arch. Physiol.*, 1938, **79**, 290.

TABLE I.

Day and hour	Mouse A		Mouse B	
	Feces, mg	Clotting-time min	Feces, mg	Clotting-time
1st 900	3	1½	45	1½
" 1500	47	>10	65	>10
2nd 900	13	>10	110	>10
" 1600	68	>10	84	1½
3rd 900	41	4	64	1⅓
5th 900	136	1½	132	1⅓

Heparin in mice is not absorbed from the alimentary tract by the animal organism, but is excreted undisturbed with the feces in the course of about 2 days.

10807

Coagulation Time of Blood in Normal and Adrenal-Demedullated Rats.

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Vosburg and Richards,[1] von den Velden,[2] Cannon and Gray,[3] Cannon and Mendenhall,[4] and Mendenhall,[5] have presented evidence that adrenalinemia hastens the coagulation time of blood. Nice, Irwin and Kraft[6] observed that there was a decrease in the clotting time of blood following emotional excitation in normal rats and that this decrease was largely abolished by adrenalectomy. They concluded that this difference between normal and adrenalectomized rats was due to the loss of the adrenal medulla. In their experiment the samples of blood were obtained under ether anesthesia. Mendenhall[5] observed that coagulation processes were hastened by ether anesthesia.

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1 Vosburg, D. H., and Richards, A. N., *Am. J. Physiol.*, 1903, **9**, 35.

2 Von den Velden, R., *Therap. Monatschr.*, 1911, **25**, 279.

3 Cannon, W. B., and Gray, H., *Am. J. Physiol.*, 1914, **34**, 232.

4 Cannon, W. B., and Mendenhall, W. L., *Am. J. Physiol.*, 1914, **34**, 243.

5 Mendenhall, W. L., *Am. J. Physiol.*, 1915, **38**, 33.

6 Nice, L. B., Irwin, O. C., and Kraft, R. M., *Am. J. Physiol.*, 1931, **96**, 305.