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Effect on Coagulation Time of Oral Administration of Rabbit Thrombin.

HENRY J. TAGNON* AND F. H. L. TAYLOR. (Introduced by George R. Minot.)

From the Thorndike Memorial Laboratory, Second and Fourth Medical Services (Harvard), Boston City Hospital, and the Department of Medicine, Harvard Medical School, Boston, Mass.

Parfentjev[1] recently described a method for the preparation of pseudoglobulin of rabbit plasma having a high clot-promoting activity. Parfentjev's preparation has been repeated and the activity associated with this pseudoglobulin was found to be thrombic in nature.[2] This was indicated by the ability of the pseudoglobulin fraction to coagulate pure fibrinogen solution in the absence of calcium and to coagulate citrated and oxalated plasma from which prothrombin had been removed. Evidence indicating that this material may have clinical applications as a powerful hemostatic when applied locally to small wounds has also been presented.[3]

The present communication reports the effect of the oral administration of relatively large amounts of pseudoglobulin from rabbit plasma, hereafter referred to as "rabbit thrombin", to dogs, normal subjects and patients suffering from hemophilia.

Methods. Coagulation times were determined on venous blood by the standard procedure formerly described.[4] In certain instances the blood was removed with an oiled syringe and determinations made both in glass tubes and in tubes made of a synthetic plastic "Lusteroid". This procedure prolongs the coagulation time,[5] which makes it possible to evaluate small changes in the coagulation time in glass. In the case of the animal experiments the thrombin was administered either in hamburg steak or milk or in aqueous solution by stomach tube. In the case of human subjects 10 g of the material were dissolved in tomato juice and ingested.

Results. The investigations were carried out on 2 dogs, 2 nor-

* Graduate Fellow of the Belgian-American Educational Foundation 1941-1942.

1 Parfentjev, I. A., *Am. J. Med. Sci.*, 1941, **202**, 578.

2 Taylor, F. H. L., Lozner, E. L., and Adams, M. A., *Am. J. Med. Sci.*, 1941, **202**, 585

3 Lozner, E. L., MacDonald, H., Finland, M., and Taylor, F. H. L., *Am. J. Med. Sci.*, 1941, **202**, 593.

4 Pohle, F. J., and Taylor, F. H. L., *J. Clin. Invest.*, 1937, **16**, 741.

5 Lozner, E. L., and Taylor, F. H. L., *J. Clin. Invest.*, in press.

mal human individuals and 2 patients suffering from hemophilia. When amounts of thrombin varying from 3 to 10 g were given to dogs by mouth there was a prompt fall in the coagulation time, reaching its maximum in about 2 hours, after which it returned toward its initial value. The results obtained in "Lusteroid" tubes paralleled those obtained in glass tubes.

In one normal human subject the results obtained were entirely similar to those found in dogs following oral administration of the material. There was a prompt fall in the coagulation time reaching a minimum in 2 hours with a return toward normal values which was complete in 24 hours. In the second normal subject the initial fall in coagulation time occurred promptly but the return to normal was somewhat delayed.

When 10 g of rabbit thrombin were administered to 2 patients with hemophilia, there was a prompt fall in the coagulation time of the venous blood both in glass and in "Lusteroid" tubes. The data for this observation are given in Table I; they are also illustrative of the effects in both dogs and normal human subjects. In both the hemophilic patients the minimum coagulation time occurred one hour after ingestion and a return to the original prolonged coagulation time had begun in 2 hours.

The results indicate that following the ingestion of large amounts of rabbit thrombin the coagulation time of the circulating blood of dogs, normal human subjects and patients with hemophilia when tested on both glass and Lusteroid tubes is reduced the effect is of short duration.

Comment. The administration of Mill's fibrinogen and McKhann's placenta extract by mouth has been known under certain circumstances to produce a fall in the coagulation time of the circulating blood. These materials are of unknown composition. In rabbit thrombin one has a defined protein which can be administered by mouth and its effect followed in the circulating blood. This phe-

TABLE I.
Effect of Oral Administration of Thrombin on Coagulation Time of Venous Blood of a Patient with Hemophilia in Glass and in "Lusteroid" Tubes.

Subject	Time, hr	Coagulation time, min		Amt. of thrombin administered, g
		Glass	Lusteroid	
	Control	73	125	
			←	10 g in tomato juice
Hemophilia (not fasting)	1	23	40	
	2	27	110	
	3	87	142	
	4	97	120+	

nomenon may have significance to the physiologist interested in the administration of a tagged protein.

So far as the practical use of the administration of rabbit thrombin is concerned, it must be pointed out that relatively large amounts of the material were used. The data indicate that in hemophilic individuals even larger amounts would be necessary to reduce the blood coagulation time to normal. Further studies, however, may produce a more potent material which might result in the production of beneficial effects.

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Metabolism and Food Utilization of Riboflavin-Deficient Chicks.

MAX KLEIBER AND THOMAS H. JUKES.*

From the Division of Animal Husbandry and Division of Poultry Husbandry, University of California, College of Agriculture, Davis.

Riboflavin deficiency, like most dietary deficiencies, lowers the growth rate of animals. This influence has been described for rats by György and his coworkers[1] and for chicks by Lepkovsky and Jukes.[2] The relation of this stunting of growth to the utilization of food energy and food protein is discussed in this paper.

Method. Five respiration trials of 10 days' duration were carried out with 5 groups of 10 chicks. At the age of 7-9 days the chicks were kept on a diet that was considered deficient in riboflavin, since it led to a stunting of growth and that stunting could be prevented by the addition of riboflavin.

At the age of 12 days 10 chicks in each of the 5 trials were placed in an open-air circulating respiration chamber at a temperature of 29 to 30°C. Food and water were kept before the chicks from 8 a.m. to 8 p.m. During the night the chicks had access only to water. The excreta were collected every 12 hours. Food and excreta were analyzed for nitrogen according to Kjeldahl and for energy in the bomb

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1 György, P., Kuhn, R., and Wagner, Jauregg, T., *Klin. Wochenschr.*, 1933, **12**, 1241.

2 Lepkovsky, S., and Jukes, T. H., *Science*, 1935, **82**, 326.