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Blood Histamine in the Rabbit During Anaphylactic Shock.

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It has been shown by Code¹ that there is an increase in the whole blood histamine of the dog and guinea pig during the stage of acute symptoms in anaphylactic shock. In the dog, this increase was shown to occur mostly in the plasma. Plasma histamine was not determined in the guinea pig. Code and Hester² have demonstrated a diminution of the whole blood histamine in the horse and calf during anaphylactic shock.

During the course of investigations on anaphylactic shock in the rabbit, blood histamine determinations were made on the whole blood, and on the plasma.

Two groups of 4 rabbits each were sensitized by the administration of 3 successive doses of 2 cc of horse serum intraperitoneally at 4-day intervals. On the day of the experiment, 3 to 4 weeks after the last sensitizing dose, control specimens of blood were taken from all the animals. In the first group, both whole blood and plasma histamine were determined. In the second group, whole blood histamine alone was estimated.

The shock dose consisted in each case of 6 cc of horse serum given intravenously. Four of the animals were given a dose of cortin one-half hour before the shock dose was administered.

Following the administration of the shock dose of horse serum, a second specimen of blood was removed by cardiac puncture at a time interval varying from 4 to 15 minutes.

The blood samples were obtained by cardiac puncture, and clotting was prevented by the use of heparin (Connaught Laboratories) in all specimens. Blood histamine was determined by the Code³ modification of the Barsoum and Gaddum method. All assays were carried out on the isolated guinea pig ileum suspended in Tyrode solution containing atropine sulphate in a concentration of 1×10^{-6} . Histamine values are given in terms of the base.

In all cases a marked decrease in the whole blood histamine as

* Aided by a grant from the Banting Research Foundation.

¹ Code, C. F., *Proceedings Am. Phys. Soc.*, 1938, p. 40.

² Code, C. F., and Hester, H. R., *Am. J. Phys.*, 1939, **127**, 71.

³ Code, C. F., *J. Phys.*, 1937, **89**, 257.

TABLE I.
Histamine Content of Whole Blood and Plasma of Sensitized Rabbit Before and During Anaphylactic Shock.

Rabbit No.	Y Histamine/cc Blood		Y Histamine/cc Plasma		Reaction
	Control specimen	Specimen after inj. of antigen	Control specimen	Specimen after inj. of antigen	
20	2.5	0.3	0.1	0.3	Mild
21	3.0	0.75	0.35	0.125	"
22*	3.0	1.1	0.175	0.4	Severe, died
23*	1.35	0.5	1.0	0.4	" "
24*	5.0	0.7			" "
25	2.75	1.0			"
26	2.0	0.4			Mild
27*	3.0	0.6			Severe, died

* Animals given cortin before receiving antigen.

TABLE II.
Histamine Content of Whole Blood and Plasma of Normal Rabbit.

Rabbit No.	Y Histamine/cc	
	White Blood	Plasma
2	2.5	0.5
3	2.75	0.3
4	2.0	0.5
6	2.75	1.0
7	2.5	0.45
8	2.5	0.75
9	3.5	7.0
10	2.5	1.0

compared with control values was observed. (Table I.) In the 4 animals in which plasma histamine was determined along with the whole blood histamine, minor changes were noted but these were not consistent and did not differ markedly from the control values or from plasma histamine found under normal conditions. (Table II.)

A curious phenomenon was observed in that the animals which received cortin all died within 7 minutes of the injection of the shock dose in acute anaphylactic shock. The other animals exhibited mild to severe symptoms, but did not die.

The results obtained in this experiment differ from those reported by Code¹ in which an increase of the total blood and plasma histamine was observed. They are, however, similar to the changes occurring in the total blood histamine during anaphylactic shock in the horse and calf, which Code and Hester² have recently reported.

It is difficult to interpret such results at the moment. Code⁴ has shown that the white blood cell layer of the blood of the rabbit con-

⁴ Code, C. F., *J. Phys.*, 1937, **90**, 485.

tains up to 80% of the total blood histamine, and this has been confirmed by one of us.⁵ It may be that during anaphylactic shock, such histamine is liberated into the plasma where it is free to exert its effect, and from which it is rapidly removed by various tissues, such as occurs in the rat (Rose and Browne⁶) or that the rapid disappearance is coincident with the sudden withdrawal of white blood cells from the circulation during anaphylactic shock in the rabbit. It should be noted that there is no correlation between the severity of the symptoms and degree of change in the histamine content of the blood as observed in these preliminary experiments. The relationship of the cortin to anaphylaxis will be discussed elsewhere.

Summary. During acute anaphylactic shock in the rabbit, a marked decrease in total blood histamine occurs. No increase of plasma histamine is observed.

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Effect of Cyanide on Cerebral Metabolism.*

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Loevenhart¹ suggested the use of small doses of cyanide intravenously in the treatment of schizophrenia. Since many methods now employed for treating schizophrenia (metrazol,² insulin,³ and nitrogen⁴) depress cerebral metabolism the present study was made to determine the effect of small concentrations of cyanide on cerebral metabolism *in vivo*. In addition a comparison was made between the effects of intravenous cyanide on cerebral and muscular metabolism.

Method. Dogs were anesthetized with pentobarbital and the superior longitudinal sinus, femoral vein and artery were exposed. Blood was drawn before and for various periods after the intra-

⁵ Rose, B., unpublished results.

⁶ Rose, B., and Browne, J. S. L., *Am. J. Phys.*, 1938, **124**, 412.

* Aided by a grant from the Child Neurology Research (Friedsam Foundation).

¹ Loevenhart, A. S., Lorenz, W. F., Martin, H. G., and Malone, J. F., *Arch. Int. Med.*, 1918, **21**, 109.

² von Meduna, L., *Z. f. g. ges. Neur. u. Psychiat.*, 1935, **152**, 235.

³ Sakel, M., *Nerv. and Ment. Dis.*, Monograph No. 62, New York, 1937.

⁴ Himwich, H. E., Alexander, F. A. D., and Lipetz, Basile, *Proc. Soc. Exp. Biol. and Med.*, 1938, **39**, 367.