

TABLE I.
Blood Iodine Values in Leukemia.

Patient	Sex	Age	Type of leukemia	Blood Iodine μ /100 cc
W.B.	M	56	lymphatic	17.9
M.S.	M	69	"	17.8
A.J.	M	64	"	14.1
A.D.	F	46	"	13.2
E.C.	M	56	"	11.7
R.T.	M	73	"	10.5
J.H.	M	61	"	9.3
C.B.	M	56	"	8.6
F.deG.	M	27	myeloid	7.4
S.T.	F	63	lymphatic	5.2
A.A.	M	75	"	4.7
I.L.	M	55	"	4.6
J.L.	M	54	"	4.3
J.P.	M	31	myeloid	3.8
N.M.	F	56	"	2.5
A.D.	F	52	"	1.7
M.P.	M	42	"	1.3

It seemed possible that the variation noted might be due to a difference in the iodine content of the white blood cells. However, in a few instances, when we made a crude attempt to separate the red cells from the white cells and plasma by means of a separating funnel, no difference could be demonstrated between the iodine content of whole blood and of the white cell-plasma fraction.

In 2 cases of lymphosarcoma the blood iodine was found to be high and it seems possible that this may be of some diagnostic value. The blood iodine was slightly elevated in 2 cases of Hodgkin's disease and normal in 2 others.

10090 P

Effect of Histamine Pretreatment upon Adrenalectomized Rats.

EATON M. MACKAY AND W. G. CLARK.

From the Scripps Metabolic Clinic, La Jolla, California.

There are many features of histamine "shock" and the "intoxication" of adrenal insufficiency which are similar. Karady has found¹ that the incidence and severity of surgical shock or histamine shock in the rat may be reduced by previous treatment with histamine. We have found that pretreatment with increasing doses of

¹ Karady, St., *Am. J. Physiol.*, 1938, **121**, 194.

histamine will increase the resistance of adrenalectomized rats to certain procedures to which they are ordinarily very susceptible.

Bilateral nephrectomy causes a marked decrease in the survival time of rats from which both adrenals have been removed.^{2, 3} Sixteen male albino rats weighing from 144-193 g were divided into 2 groups with an average weight of 170 g. The histamine-treated group was given a 10% suspension of finely ground crystals of histamine dihydrochloride in olive oil so that its action might be more protracted.⁴ Ten mg were administered subcutaneously daily for 6 days, followed by 20 mg per day for 8 days more, a total of 220 mg per rat. At this time the 2 groups still weighed about the same but the histamine-treated rats appeared to be in the poorer condition. Sixty hours after discontinuing the histamine treatment the adrenals and the kidneys were removed from all of the rats. In the histamine-treated group the cortex of the adrenal gland had become hypertrophied so that the adrenals of this group weighed 31% more than those of the controls. The survival time of the 2 groups of rats was quite at variance with their appearance. The untreated controls survived for from 28 to 41 hours with an average of 34.6 hours. The histamine-treated group, on the other hand, lived from 43 to 73.5 hours with an average of 56.8 hours, an increase in the average survival time of 64%.

Adrenalectomized animals are usually very sensitive to the effect of ingested potassium salts.⁵ Pretreatment with histamine before the removal of the adrenal glands raises the resistance of adrenalectomized rats to potassium salts. Twelve adult male rats were divided into 2 groups, 6 controls (266 g) and histamine-treated (262 g), of approximately equal weight. The rats of the histamine-treated group were given 360 mg histamine dihydrochloride per rat over a period of 17 days, starting with 10 mg daily for 5 days, then 20 mg for 8 days, 40 mg for 1 day and 100 mg for 1 day, all in aqueous solution. Twenty-four hours after the last injection both groups were adrenalectomized. As in the first experiment there was marked hypertrophy of the adrenals in the histamine-treated group, apparently limited to the cortex. Nine, 19, 22, 24, and 26.5 hours after adrenalectomy both groups received 2% KCl by stomach tube in a dose of 1 cc per dcm^2 of body surface, averaging 94 mg of KCl per

² Ingle, D. J., and Kendall, E. C., *Am. J. Physiol.*, 1936, **117**, 200.

³ MacKay, E. M., Bergman, H. C., and MacKay, L. L., *Am. J. Physiol.*, 1937, **120**, 83.

⁴ Keeney, E. L., *Bull. Johns Hopkins Hosp.*, 1938, **62**, 227.

⁵ Allers, W. D., Nilson, H. W., and Kendall, E. C., *Proc. Staff Meet. Mayo Clinic*, 1936, **11**, 283.

dose for the control group and 92 mg per dose for the histamine-treated group. The rats in the control group survived for 24.7-32 hours with an average of 27.5 hours after the operation while the rats pretreated with histamine survived 32-56 hours with an average of 41.0 hours after the operation.

The bearing of these results on the interpretation of adrenal function proposed by Selye⁶ is of interest. He concluded that one of the most important functions of the adrenals is to increase the resistance to "alarming stimuli" such as variable temperature, excessive muscular exertion, toxic drugs, etc. The adrenals are conceived to play an important rôle in the first stages of such adaptations, while later resistance is acquired by the peripheral tissues; the stimulus ceases to be alarming and the adrenal hormones are no longer required for adaptation. He further assumes that the symptoms of the alarm reaction are due to liberation of a toxic metabolite such as histamine and that the adrenal detoxifies this substance. Our data is the first experimental evidence directly supporting Selye's theory. The activity of the histamine destruction mechanism of the organism is greatly reduced after adrenalectomy⁷ and there is every reason to believe that this mechanism is much more active following pretreatment with increasing doses of histamine. It is of importance that adrenalectomized dogs can acquire a tolerance toward potassium salts⁸ and Selye has found⁹ that histamine adaptation is not lost after adrenalectomy.

The decrease in survival time of adrenalectomized rats produced by nephrectomy^{2,3} may well be due to an important decrease in the histamine-destroying activity of the organism, for the renal tissue has by far the highest histaminase content of any tissue^{10,11} and this organ destroys the most histamine *in vivo*.⁷

⁶ Selye, H., *Science*, 1937, **85**, 247.

⁷ Rose, B., and Browne, J. S. L., *Am. J. Physiol.*, 1938, **121**, 175.

⁸ Kendall, E. C., and Ingle, D. J., *Science*, 1937, **86**, 18.

⁹ Selye, H., *Arch. internat. Pharmacodynamie.*, 1937, **55**, 431.

¹⁰ McHenry, E. W., and Gavin, G., *Biochem. J.*, 1932, **26**, 1365.

¹¹ Edlbacher, S., and Zeller, A., *Helv. Chim. Acta.*, 1937, **20**, 717.