

fects noted in the kidney were observed after the animals were on experiment for a longer time. Undoubtedly some of these trends may be attributable, in part, to the fact that the most susceptible animals died in the early phases of the study and consequently were not available for histological study.

Summary. A histological study of the duodenum, ileum, rectum, liver, kidney, testis and bone marrow of weanling hamsters fed on a basal diet containing 5 or 15% polyoxyethylene monostearates (Sta-soft or Myrj)

or lard was conducted. Marked changes were observed in the duodenum, ileum, liver, kidney, and testis of hamsters fed Myrj or Sta-soft after 2-10 weeks on experiment. Histological changes observed in the small intestine, particularly the ileum, consisted of a severe erosion of the mucosa. Necrosis of the liver, decreased spermatogenetic activity of the testis, and tubular degeneration of the kidney were also observed.

Received July 21, 1950. P.S.E.B.M., 1950, v75.

Studies on Urinary Histamine in Chronic Myelocytic Leukemia.*† (18193)

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It is now well established that there are increased amounts of histamine in the blood of patients with chronic myelocytic leukemia (1-5), and that the histamine resides mainly in the cells of the granulocytic series which are beyond the blast stage of development(5). Since blood histamine levels in chronic myelocytic leukemia as high as 25 $\mu\text{g./ml}$ (250 times normal) are found, and since the turnover of white blood cells is probably rapid(6) an in-

vestigation of the fate of this potentially active material seemed of interest. It has been shown that considerable amounts of histamine are excreted in the urine(7). In man this is conjugated, probably in the form of acetyl histamine. It has also been shown that histamine base fed by mouth to dogs is excreted in the urine in the form of acetyl histamine(8). The present studies were initiated to determine whether or not the endogenous blood histamine was removed by this urinary route in patients with chronic myelocytic leukemia.

Methods. Blood histamine was estimated according to the method of Code(9) using the terminal ileum of the guinea pig as the assay object. Urine histamine was determined following the bioassay procedure of Anrep *et al.*(7) with the modifications that charcoal adsorption with subsequent elution was eliminated and the amount of alumina was increased from 2 g to 5 g for 5 ml of urine in

* This paper is based on work performed under Contract No. AT-04-1-GEN-12 between the Atomic Energy Commission and the University of California at Los Angeles.

† The authors wish to express their appreciation to Mr. Charles Kim for valuable technical assistance in performing the histamine determinations and to the many members of the staff of Wadsworth General Hospital, Veteran's Administration, Los Angeles, whose cooperation made it possible to obtain the specimens.

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TABLE I.

Subject	WBC, $\times 1000$	Blood histamine, $\mu\text{g}/\text{ml}$	Fasting urine histamine, $\mu\text{g}/\text{hr}$
M. (8-19-49)	180	6.5	19.8
	105	15.0	99.0
P. (3-20-50)	421	25.0	84.7
	310	15.0	25.6
F.	59	8.9	28.6
T.*	35	0.31	9.1
H.	16	0.15	13.1
J.	32	0.59	7.8
T. (6-9-50)	712	8.5	26.0
	695	7.2	14.0
W.	46	N.D.†	11.2
Avg		8.7	30.8

* Polycythemia vera.

† No determination.

order to adsorb all the guinea pig ileum relaxins present in urine. Because it has been shown that the absorption of food, particularly meat, elevates the urine histamine levels (7), urine collections were made between 6 and 7:30 a.m., the subjects not having eaten since the previous evening meal.

Results. The urines of 25 fasting normal adults were examined and urine histamine excretions were found to range from 5.7-68.1 $\mu\text{g}/\text{hour}$ with an average of 27.0 $\mu\text{g}/\text{hour}$. Normal blood histamines in this laboratory average 0.075 $\mu\text{g}/\text{ml}$ with a range of 0.030-0.11 $\mu\text{g}/\text{ml}$ (5).

The data for seven patients with chronic myelocytic leukemia and one patient with polycythemia vera are shown in Table I.

It is seen that while blood values many times the upper normal limit occur in patients with chronic myelocytic leukemia the fasting urine values are quite similar to the normal average and range.

Comments. If the observations made in this laboratory indicating that the life span of the circulating granulocytes is 24 hours or somewhat less(6) are of the proper order of magnitude, then the average patient in this group (assuming 5 liters as the average blood volume) has 5000 $\times$ 8.7 μg or 43.5 mg of histamine turned over from this source in this period. This is about 100 times greater than in the normal subject. With an average fasting urine histamine excretion of 30.8 $\mu\text{g}/\text{hour}$ it can be seen that only 0.73 mg of histamine would leave the body through the urine in one day. This large discrepancy suggests that the fate of the histamine found in granulocytic leukocytes in chronic myelocytic leukemia is probably not conjugation followed by urinary excretion, or alternatively that the leukocytes in leukemia have a markedly longer life span than experimental evidence in normal animals would seem to indicate. Endogenous histamine of this type may, like injected histamine(10), be in some way destroyed in the body and appear in the urine, if at all, only in small amounts.

Summary. 1. While the blood histamine is markedly elevated in chronic myelocytic leukemia, fasting urine histamine excretion is in the normal range.

2. Assuming a 24 hour life span for the white blood cell it is shown that conjugation and urinary excretion is not the mechanism of removing the large amount of blood histamine present in patients with chronic myelocytic leukemia.

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Received July 24, 1950. P.S.E.B.M., 1950, v75.