Elementary analyses as well as crystallographic measurements will be reported in detail in a later publication.

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Acute Agranulocytosis of Kala-Azar: Negative Effect of Urea Stibamine and Neostibosan on Blood of Normal Rabbits.

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Acute agranulocytosis, an important complication of kala-azar, has been observed in 8 of 71 patients suffering from visceral leishmaniasis.[1, 2] Six of these 8 patients exhibited a sudden and marked drop in the granulocytes at some time during treatment for kala-azar with either urea stibamine or neostibosan. Both drugs contain the benzene ring in their complex molecule. Acute agranulocytosis following the administration of certain compounds containing the benzene ring has been reported.[3] The following experiment was made in order to observe the effect of intravenous injection of urea stibamine and neostibosan on the blood of normal rabbits.

Eight normal rabbits were taken from the stock without selection. After a control period during which regular blood counts were made, 3 of the rabbits were given intravenous injections of urea stibamine, 3 others were given neostibosan and the remaining 2 were held as controls. An appropriate amount of either drug was dissolved in sufficient volume of double distilled water to make a 5% solution. The injection was given daily, except Sundays, through the marginal vein of the ear. Since urea stibamine is believed to be more toxic than neostibosan, the former was given in smaller individual doses. The total amounts were the same in all except in one (rabbit 1) in which it was double that of the others. Nothing was given to the control animals.

Counts were made on the blood obtained from the tributaries of the marginal vein of the opposite ear. These counts were done twice weekly and they included hemoglobin estimation, enumeration of total red and white blood cells and differential count of the leucocytes by the supravital method.

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[1] Zia, L. S., and Forkner, C. E., *Am. J. Med. Sci.*, in press.

[2] Zia, L. S., and Forkner, C. E., Trans. F. E. A. T. M. Ninth Congress, Nanking, China, 1934, in press.

[3] Madison, F. W., and Squier, T. L., *J. Am. Med. Assn.*, 1934, **102**, 1213.

TABLE I.
Negative Effect of Urea Stibamine and Neostibosan on White Blood Cells in Rabbits.

Rabbit No.	Drug given	Total dose	Duration of Experiment	Total W.B.C. per cumm.				Total P.M.N. per cumm.			
				Before inj.		After inj.		Before inj.		After inj.	
				Max.	Min.	Max.	Min.	Max.	Min.	Max.	Min.
		gm.	days								
1	Neostibosan	4.79	65	18,100	6,100	15,150	5,200	10,220	3,782	10,756	2,028
2	,,	2.40	65	9,400	5,080	11,450	6,150	4,165	3,125	8,696	3,634
3	,,	2.40	65	28,000	6,100	24,000	6,000	9,526	5,022	15,277	3,151
4	None (Control)	—	65	11,700	4,750	8,400	6,000	6,515	2,277	6,048	2,948
5	,, ,,	—	54	11,750	11,750	12,800	7,350	—	—	7,710	3,825
6	Urea Stibamine	2.40	60	9,050	6,950	11,600	6,400	—	—	7,100	1,700
7	,, ,,	1.90	49	10,400	8,500	13,250	6,500	—	—	6,655	2,730
14	,, ,,	2.40	52	5,600	5,600	10,400	5,150	2,576	2,576	4,070	1,323

TABLE II.
Effect of Urea Stibamine and Neostibosan on the Hematopoietic Organs of Rabbits.

Rabbit No.	Drug given	Total dose	Duration of experiment	Histologic Findings				
				Spleen	Liver	Bone-Marrow	Lymph-nodes	
							Peripheral	Mesenteric
		gm.	days					
1	Neostibosan	4.79	65	Hyperplasia	Normal	Normal	Normal	Hyperplasia
2	,,	2.40	65	,,	,,	,,	Hyperplasia	
3	,,	2.40	65	,,	,,	Hyperplasia	Moderate hyperplasia	
4	None (Control)	—	65	Normal	,,	Normal	Normal	
5	,, ,,	—	54	,,	,,	,,	,,	
6	Urea Stibamine	2.40	60	Slight hyperplasia	,,	Slight hyperplasia	Hyperplasia	
7	,, ,,	1.90	49	Necrosis	Moderate cirrhosis, chiefly portal	Marked hyperplasia	,,	
14	,, ,,	2.40	52	Increased fibrosis and moderate hyperplasia	Extensive cirrhosis with proliferation of bile capillaries	Marked hyperplasia	Normal	

After the rabbits had received the prescribed amount of the drug, they were killed by intravenous injection of air. The liver, spleen, lymph-nodes and bone marrow were removed and immediately fixed in Zenker-formol solution (10% formalin). The sections were stained with hematoxylin and eosin. The results of the blood counts and histologic examination of the organs are shown in the accompanying tables. There was no appreciable effect on the body temperature or body weight as compared with the control animals.

It is to be noted that although the amount of either urea stibamine or neostibosan given to these experimental animals is far in excess of the usual amount given to patients for the treatment of kala-azar, yet neither the total white blood cells nor the granulocytes showed any significant decrease throughout the period of observation (Table I). On the other hand in these animals, there was hyperplasia of the spleen, lymph-nodes and bone marrow (Table II). In rabbits 7 and 14, there was cirrhosis of the liver and in rabbit 14 there was proliferation of the bile capillaries. Neither of the control animals presented similar changes. It should be pointed out that inasmuch as the controls did not receive the solvent of these drugs, this part of the experiment was not adequately controlled. Nevertheless, from the results obtained, it is concluded that repeated injections into normal rabbits of large amounts of urea stibamine and neostibosan did not produce in their peripheral blood anything resembling acute agranulocytosis.

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Blood Diastase as an Indicator of Liver Function.

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The method developed in this laboratory for the estimation of diastase in biological material satisfies 2 essential requirements: it yields accurate quantitative results, and is sufficiently sensitive to permit the determination of very small quantities of the enzyme.

The quantity of the enzyme we express as the amount of reducing matter, in terms of glucose, which is produced by a known amount of the enzyme-bearing material under standardized conditions. As applied to blood, when we state that the diastase value of human blood serum is on an average 120, this means that 100 cc.