7872 P

Inhibition of Leucogenic Activity in the Rabbit by Certain Cyclic Compounds.

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The leucopoietic apparatus of the rabbit under ordinary circumstances is an organ in a delicate state of equilibrium and the threshold for leucopoietic stimuli is low. It has been shown[1] that the intravenous injection of even a small quantity of distilled water may be capable of producing a stimulation characterized by a transient leucocytosis which is the result of a true bone marrow reaction, for it is accompanied by a sudden increase in the number of juvenile cells in the peripheral circulation. The more potent stimulating agents will produce a more profound reaction. Nucleic acid, or sodium nucleinate, are examples of such potent stimulating agents and the parenteral introduction of either of these substances into a normal rabbit will invariably be followed by a transient leucocytosis which is accompanied by a marked increase in the percentage of juvenile cells in the peripheral circulation.

During the course of an investigation into the action of certain cyclic compounds on the haematopoietic tissues, it was observed that the capability of the leucogenic tissues to respond to normal stimuli was lost long before any change could be observed in the cellular constituents of the peripheral circulation. These compounds which include amidopyrin, antipyrin, a-dinitrophenol, phenylhydrazine hydrochloride, catechol and o-quinone, have been described as possible etiological agents in the production of human agranulocytic angina.[2, 3, 4]

With the exception of the reaction given to a-dinitrophenol, the reaction to amidopyrin may be regarded as typical of the reactions to the entire group; the quantities of these substances which were required to inhibit the irritability of the leucogenic tissues varied greatly, phenylhydrazine being the most potent agent and antipyrin the least active.

For the sake of brevity, only one set of results is presented, but the action of each substance was investigated on a group of 8

[1] Climenko, D. R., *Quart. J. Exp. Physiol.*, 1930, **20**, 369.

[2] Kracke, R. R., and Parker, F. P., *J. Lab. Clin. Med.*, 1934, **19**, 799.

[3] Silver, S., *J. Am. Med. Assn.*, 1934, **102**, 1213.

[4] Madison, F. W., and Squier, T. L., *J. Am. Med. Assn.*, 1934, **102**, 755.

experimental animals with a control animal in each group. The results show a high degree of consistency and any one animal may be regarded as being typical of its group.

Rabbit 5 of Group I showed the following steady state

Date	r b c	Hb	w b c	% granulocytes	Polynuclear Count I	II	III	IV	V	Weighted Mean
9/20	6,200,000	75	9,200	28	23	33	29	12	3	2.39
9/21	6,200,000	75	8,100	30	22	33	31	11	3	2.40
9/22	6,400,000	75	10,400	28	22	31	30	12	5	2.47

Following the intramuscular injection of 5 mg./kg. of nucleic acid, the following results were obtained:

Hours after injection	r b c	Hb	w b c	% granulocytes	Polynuclear Count I	II	III	IV	V	Weighted Mean
0	6,400,000	75	8,200	29	24	32	30	12	2	2.36
1	———	—	8,800	31	30	38	23	8	1	2.12
2	———	—	14,200	37	41	28	21	10	0	2.00
4	———	—	15,100	34	42	28	18	12	0	2.00
8	6,300,000	74	10,600	34	40	29	20	11	0	2.02
24	———	—	8,600	36	31	39	21	9	0	2.17
48	6,280,000	75	7,800	32	27	43	23	7	0	2.10
96	6,100,000	75	8,000	27	25	33	32	9	1	2.28
240	6,200,000	75	6,800	29	21	32	30	14	3	2.46

At the end of this period of 10 days this animal received amidopyrin (0.2 gm./kg./day) orally for a period of 18 days. At the end of this time an intramuscular injection of 5 mg./kg. of nucleic acid failed to evoke the normal response as may be observed by an examination of the following data. The steady state for this animal was:

Date	r b c	Hb	w b c	% granulocytes	Polynuclear Count I	II	III	IV	V	Weighted Mean
10/22	5,800,000	79	9,200	28	25	35	27	9	4	2.32
10/23	6,050,000	75	8,600	31	24	36	24	11	5	2.32
10/25	5,900,000	75	11,400	27	27	34	28	9	2	2.25

The nucleic acid was injected and the following results were obtained:

Hours after injection	r b c	Hb	w b c	% granulocytes	Polynuclear Count I	II	III	IV	V	Weighted Mean
0	6,100,000	74	8,200	27	28	37	27	8	2	2.25
1	———	—	6,800	26	28	36	26	8	4	2.30
2	———	—	7,200	27	26	38	25	9	2	2.23
4	———	—	7,600	28	27	33	27	10	3	2.29
8	———	—	8,600	30	26	34	28	9	3	2.31
24	6,300,000	71	8,400	29	25	36	24	11	4	2.33
48	6,000,000	73	7,600	30	29	32	25	12	2	2.26
96	6,050,000	73	6,800	27	26	35	27	9	3	2.28
240	5,850,000	76	9,400	29	24	34	28	10	4	2.36

At the same time an animal that had been used as a control for this group responded to the second injection of nucleic acid in the same manner as it did to the original injection which had been given 28 days earlier. Similar inhibition was obtained after the administration of antipyrin, phenylhydrazine hydrochloride, o-quinone and catechol. The reaction to a-dinitrophenol differed slightly in that the quantity (20 mg./kg.) which was required to produce the inhibition of the leucogenic tissues, produced a preliminary stimulation which was characterized by an increase in the percentage of juvenile cells in the circulation without a concomitant leucocytosis. After the drug had been administered for a few days this reaction was lost and the proportions of the cellular elements in the peripheral circulation returned to normal. Shortly after this return to normal, the administration of nucleic acid failed to evoke a response.

The bone marrows of the experimental animals showed a marked degree of hyperplasia, with an increase in the number of primitive haemocytoblasts.

7873 C

The Influence of Sodium Thioglycollate on the Glycolytic Enzyme System of Muscle Extract.

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It has been suggested by Lipmann[1] that the enzyme (or one component of the enzyme system) of muscle extract which is capable of converting glycogen into lactic acid is reversibly oxidizable and reducible and is active as an enzyme only in its reduced state. This hypothesis was seemingly confirmed by Michaelis and Runnström.[2] The evidence presented by the latter authors for the reactivation of a muscle extract which had become partially or completely inactive by standing exposed to the air was as follows. If such an extract was treated with a neutralized solution of thioglycollic acid and then subjected to a manometric experiment, with the addition of sodium bicarbonate and a suitable partial pressure of CO_2, a definite and sus-

[1] Lipmann, F., *Biochem. Z.*, 1933, **265**, 133.

[2] Michaelis, L., and Runnström, J., PROC. SOC. EXP. BIOL. AND MED., 1934, **32**, 343.