Effect of Aminopterin on Animals Receiving Myelokentric or Lymphokentric Acid. (18241)

RUGGERO CONTE MAROTTA* AND F. R. MILLER.

From the Charlotte Drake Cardeza Foundation, Jefferson Medical College and Hospital, Philadelphia, Pa.

In the past 2 years much has been written concerning the effect of Aminopterin on normal and leukemic cells(1). The remissions which occur in acute leukemia, especially acute lymphoid leukemia in childhood, are now well known. Because of this work it seemed to us of interest to discover whether this substance could in any way alter the pathologic changes we have obtained with myelokentric and lymphokentric acids(2,3).

Material and methods. Guinea pigs were given daily intramuscular injections of crude

TABLE I.

Animal No.	Aminopterin, total dose, mg	Teropterin, total dose, mg	Crude myelokentric acid (liters)	Crude lymphokentric acid (liters)	Result	Liver	Spleen	L.N.	Bone marrow	Adrenal
1	4		4		++M	++	++		+++ H	+
2	4		4		++M	++	++		+++ H	+
3	16		4		±M	—	+F		+++ HA	+
4	16		4		±M	—	+F		+++ HA	+
5	22		4		+M	+	+F		+++ HA	+
6	22		4		++M	++	++		+++ HA	+
7	16		2		—M	—	—F		+++ HA	—
8	14		2		—M	—	—F		+++ HA	—
9	14		4		—M	—	—F		+++ HA	++
10	14		4		—M	—	—F		++ HA	—
11		110	4		++M	++	++		+++ H	+++
12		110	4		++M	++	+++		+++ H	+
13		80	2		+M	+	++		+++ H	+
14		80	2		++M	++	+++		+++ H	++
15		130	4		+++M	+++	+++		+++ H	++
16		130	4		++M	++	++		+++ H	++
17		120	6		++M	++	++		+++ H	+++
18		120	5		++M	++	++		+++ H	++
19		100	4.5		++M	++	++		+++ H	+++
20	14			3	—L	—	F	—	h	—
21	4			0.5	—L	—	—	—	h	—
22	12			3	—L	—	—F	—	h	+
23	12			3	—L	—	—F	—	h	—
24		80		3	++L	+	+++	++	++ HB	++
25		60		3	++L	+	++	++	++ HB	+
26	20				neg.				Slight h	
27	20				neg.				Slight h	
28	22				neg.				Slight h	
29	22				neg.				Slight h	

F = Fibrosis.
A = Amaturation.
M = Myeloid.
L = Lymphoid.
B = Increase in erythropoiesis and eosinophils.
H = Hyperplasia.
h = hypoplasia.

* Fellow of the Institute of International Education.

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myelokentric or crude lymphokentric acid. 0.5 ml to 1.0 ml of urinary extract was given daily in aqueous suspension at a pH of 7.8 for 9 to 14 days. The total dose of extract given was made from 2 to 6 liters of urine. Ten guinea pigs, as well as receiving crude myelokentric acid, also were given varying amounts of Aminopterin, the daily dose being 2 mg; and as controls 10 animals were given 10 mg daily of Teropterin as well as crude myelokentric acid. Crude lymphokentric acid was given to 6 animals; to 4 of them 2 mg daily doses of Aminopterin were given, and the other two were given 10 mg daily doses of Teropterin. Four animals were given 2 mg daily doses of Aminopterin only.

Results. The results are summarized in the table, in which it will be seen that animals that received crude myelokentric acid are designated under result as being positive for extra medullary myelopoiesis, + to +++M; or if negative for this finding, –M; and equivocal animals are marked±. Liver, spleen and adrenals were examined for extra medullary myelopoiesis and are graded – to +++ under such headings. Animals that received crude lymphokentric acid were similarly graded as to the extent of lymphopoiesis in liver, spleen, lymph nodes, and adrenals and the results are tabulated for each animal as –L or ++L. Animals that received Aminopterin alone exhibited no myeloid or lymphoid stimulation, and these therefore are designated negative. The only change in this latter group is slight hypoplasia of the bone marrow.

It will be seen that animals 1 and 2 showed little effect of the drug on the extra medullary hematopoiesis. These 2 animals, however, were given only 2 doses of Aminopterin on the last two days of injection with urinary extract. All others that received Aminopterin and myelokentric acid, with the exception of 6, exhibited only minimal or no extra medullary blood formation. The bone marrows of this group showed hyperplasia, and in all except those from animals 1 and 2 there was some amaturation with little red cell formation. (Fig. 1). The spleens of all but 1, 2 and 6 were small and fibrotic.

All animals that were given Teropterin and myelokentric acid showed a fairly good response, *i.e.* extra medullary hematopoiesis in at least 3 organs. The bone marrows were hyperplastic in all elements. (Fig. 2)

The 4 animals that received Aminopterin and lymphokentric acid exhibited no lympho-

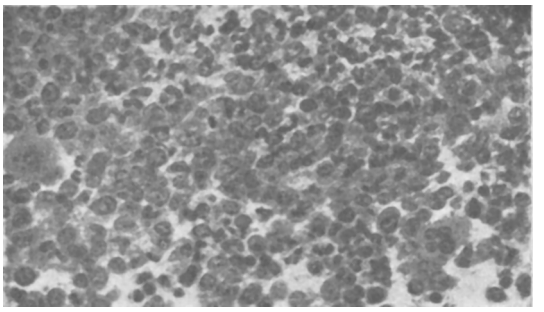

FIG. 1.
Section of bone marrow ×300, from animal that received crude myelokentric acid and Aminopterin showing hyperplasia with some amaturation of leukopoiesis. Erythropoiesis is less than normal.

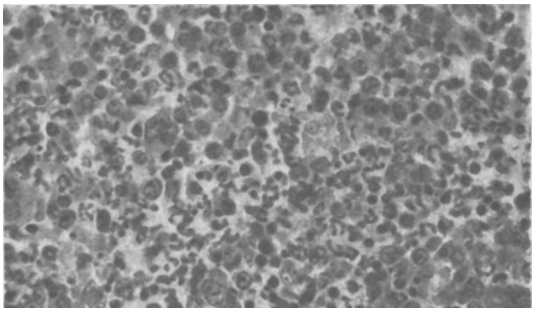

FIG. 2.
Section of bone marrow ×300, from animal that received crude myelokentric acid and Teropterin showing hyperplasia of all myeloid elements.

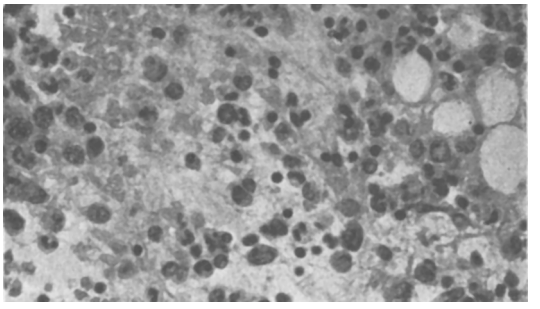

FIG. 3.
Section of bone marrow ×300, from animal that received crude lymphokentric acid and Aminopterin showing moderate hypoplasia of all myeloid elements.

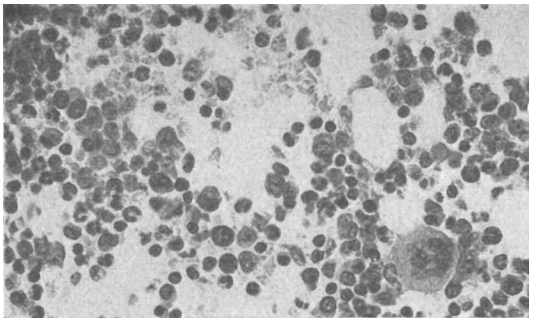

FIG. 4.
Section of bone marrow ×300, from animal that received Aminopterin showing mild hypoplasia of all myeloid elements, particularly the erythroid.

cytic stimulation. There was some fibrosis of the spleen in 20, 22, and 23, and all bone marrows were mildly hypoplastic and amaturative. (Fig. 3). The 2 control animals that received Teropterin and lymphokentric acid each showed a moderate increase in lymphopoiesis with, as well, an eosinophilia in the bone marrow and increased red cell production. Those animals that were given Aminopterin only exhibited mild hypoplasia of the bone marrow especially of the red cell elements. (Fig. 4). Otherwise these animals were negative. Fig. 1 to 4 represent the marrows from these four groups of animals.

Discussion. It would seem that Aminopterin interfered with the action of the lymphokentric acid more than that of myelokentric acid. This is evident in that the organs of animals 20, 21, 22, and 23 exhibited no increased lymphopoiesis; however, the bone marrows of these animals were more hypoplastic than those of animals that received Aminopterin only. In all animals the Aminopterin effected red cell formation more than white cell or platelet formation. It would be difficult to interpret the combined action of Aminopterin and these two acids, but the effects of Aminopterin on human leukemia are somewhat similar to the findings reported here.

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Auto-Interference Associated with Influenza B Virus.*† (18242)

VINCENT GROUPÉ AND LEONORA H. PUGH.‡

From the Department of Microbiology, New Jersey Agricultural Experiment Station, New Brunswick, N. J.

The phenomenon of auto-interference is characterized by the presence, in concentrated viral inocula, of material which exerts an antagonistic or inhibitory effect on multiplication of the same virus. In the case of the influenza viruses serial passage of low dilutions of infected allantoic fluid in embryonated eggs was found to result in markedly lower infectivity and hemagglutinin titers than those obtained when high dilutions of the same inoculum were employed(1). Carefully controlled exposure of infected allantoic fluids to ultra-violet light was found to destroy or greatly reduce their infectivity, without gross destruction of the property of interference (2,3). The material responsible for the property of interference in such fluids has been shown to be intimately associated or identical with inactive virus(2,4).

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