demonstrated by Spielmeyer's stain. It was found in paralyzed guinea pigs using *N. asteroides* or *M. tuberculosis* or *M. butyricum* as potentiating agents.

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16491 P

Effect of Urethane, X-rays, Potassium Arsenite, Benzol, on Survival Time in Transplanted Mouse Leukemia.*

ARTHUR KIRSCHBAUM, SISTER TERESITA JUDD, CHEN SHAN LU,† RUBY M. ENGSTROM, AND HARRY MIXER.

From the Departments of Anatomy and Radiology, University of Minnesota Medical School, Minneapolis.

Urethane depresses the white blood cell count and decreases the size of infiltrated organs in certain cases of human leukemia.[1] Clinical improvement was more striking in chronic myeloid than in chronic lymphatic and acute leukemia.[2] Certain transplanted and spontaneous rodent leukemias were susceptible to the effects of urethane.[3-6]

In these experiments 5 transfer lines of mouse leukemia were studied. Four originated in the high leukemia F strain[7] and a fifth (line RE) was transplanted originally from a spontaneous case which arose in an F_1 hybrid mouse between strains F and NH. Three of these lines of leukemia (15, 686, and RE) were myeloid, and 2 (86 and 291) were lymphoid. The routine method of transfer was by intraperitoneal inoculation of 5,000,000 splenic cells suspended in isotonic saline. Inoculated mice were all F_1 hybrids (strain F × strain NH) approximately 6 weeks of age.

The methods of treatment with urethane were the following:

a) At the time of transfer an anesthetic dose was administered subcutaneously with no further treatment, or

b) 2, 3 or 4 anesthetic doses were given daily for the first 2, 3 or 4 days. No further treatment was given to these mice, or

c) one-third or one-fifth of an anesthetic dose (1 mg/g) was given daily from the time of inoculation, or

d) after inoculated mice had become leukemic, 2 daily anesthetic doses were given, these being followed by daily doses of 0.33 mg/g body weight.

Survival was significantly prolonged in transplanted myeloid leukemia by all methods of treatment with urethane except the single anesthetic dose at the time of transfer, and 2 doses in the first 2 days following transfer (see Table I); in 2 instances 2 doses increased survival.

Line 291 was a relatively chronic lymphatic leukemia. Although the white blood cell count count was depressed by urethane, survival was not appreciably prolonged by the same type of treatment effective for the lines of myeloid leukemia. Lymphoid line 86 responded similarly to line 291 (see Table I for data).

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† Fellow of the China Medical Board.

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TABLE I.
Data on the Effect of Urethane on Five Transfer Lines of Leukemia.

Line of leukemia and transfer generation	No. of mice	Daily* urethane, mg/g	Daily inj.	Days after transfer	Avg survival in days (after transfer)
T_3 Line 686-Myeloid	3	0	—	—	34.3 ± .4
	4	1	4	First 4	46-120+†
T_4 " " "	3	0	—	—	37.0 ± 1.4
	2	§	24	28-48	49.0 ± 0.0
	5	1	4	First 2, 8-10	50-95+†
T_5 " " "	5	0	—	—	32.5 ± 1.5
	3	1	1	First day	34.0 ± 1.0
	3	1	2	First 2	41.0 ± 1.4
	3	1	3	" 3	50.0 ± 8.9
	3	1	4	" 4	42-66+‡
	4	§	20	25-45	47.2 ± 1.2
	6	.33	28	First 28	46-66+†
T_5 " " "	3	0	—	—	29.6 ± 1.6
	2	1	1	First day	41.0 ± 4.0
	2	1	2	First 2	30-64+†
	2	1	3	" 3	64+‡
	2	1	4	" 4	51-64+†
	4	.33	25	" 24	47.7 ± 6.3
	3	§	17	26-40	37.3 ± 2.4
T_{11} " 15 "	5	0	—	—	25.6 ± 2.0
	3	1	1	First day	28.0 ± 1.4
	3	1	2	First 2	31.3 ± 3.8
	3	1	3	" 3	41-57+†
	3	1	4	" 4	51-57+‡
	3	§	17	18-35	36.0 ± 2.4
T_{10} " 15 "	6	0	—	—	26.0 ± 2.0
	6	.33	22	First 25	83.1 ± 15.5
T_{18} " RE "	6	0	—	—	18.8 ± .8
	5	.33	29	First 29	31.0 ± 2.4
T_5 " 291-Lymphoid	6	0	—	—	25.3 ± 6.8
	3	1	1	First day	22.6 ± 4.1
	3	1	2	First 2	20.6 ± .9
	3	1	3	" 3	20.6 ± 4.0
	3	1	4	" 4	29.3 ± 6.1
	6	§	9	15-23	24.8 ± 2.4
	6	.33	23	First 26	26.6 ± 1.9
T_7 " 86 "	4	0	—	—	15.7 ± 1.6
	5	.33	18	First 18	21.0 ± 0.0
	5	.2	16	" 16	18.8 ± 2.2

* Aqueous solution of urethane. Except where indicated in text injections were intraperitoneal. The dose per gram of mouse was contained in 0.1 cc distilled water.
† One animal living.
‡ Two animals living.
§ Combined—Daily anesthetic doses for 2 days followed by daily maintenance doses of 0.33 mg/g.

Survival time was increased in myeloid leukemia when treatment was begun even after white blood cell counts were elevated sufficiently to indicate systemic leukemia. However, if white blood cell counts were extremely high and anemia severe, urethane was ineffective in favorably altering the clinical course of the transplanted myeloid disease.

The urethane-treated mice were all growing animals (15-20 g), and failed to gain in weight. However, when growth was suppressed to a greater degree (in mice inoculated

TABLE II.
Comparative Effects of Several Agents on Survival Time in Transplanted Leukemia.

Agent	Daily dose	Line of leukemia	No. of mice	Survival in days
Urethane	0.1 mg/g B.W.*	T_{13}-Line 15-Myeloid	5	38-50
"	0.33 " "	"	5	44-67
Benzol (oral)	10 mg	"	5	30-39
Potassium arsenite	0.1 " (total)	"	4	87-103+†
X-rays (whole body)	50 r	"	5	30-41
None—Controls		"	5	20-24
Urethane	0.33 mg/g B.W.	T_8-Line 686-Myeloid	3	37-56
Benzol (oral)	10 mg	"	3	30-41
Potassium arsenite	0.1 " (total)	"	3	75-94+‡
X-rays (whole body)	50 r	"	5	36-42
None—Controls		"	4	30-34
Urethane	0.33 mg/g B.W.	T_{23}-Line RE-Myeloid	2	20-27
Benzol (oral)	10 mg	"	2	17-22
Potassium arsenite	0.1 " (total)	"	2	36-42
None—Controls		"	4	14-18
Urethane	0.33 mg/g B.W.	T_{10}-Line 86-Lymphoid	3	17-21
Benzol (oral)	10 mg	"	3	15-17
Potassium arsenite	0.1 " (total)	"	3	21-25
None—Controls		"	4	11-17
Urethane	0.1 mg/g B.W.	T_8-Line 291-Lymphoid	4	21-25
"	0.33 " "	"	4	25-29
Benzol (oral)	10 mg	"	5	21-26
Potassium arsenite	0.1 " (total)	"	4	22-28
None—Controls		"	5	20-21

* B.W. = Body Weight.
† 3 mice still living.
‡ 2 mice still living.

with line 15 leukemia) by feeding a diet containing 5% p-aminobenzoic acid, survival time was not prolonged.

Other agents (x-rays, benzol, potassium arsenite, carcinogenic hydrocarbons, colchicine) may increase survival time in certain lines of transplanted leukemia and lymphosarcoma.[8-10] The effects of x-rays, benzol, potassium arsenite, and urethane were compared, treatment with all agents being started at the time of transfer. Results are given in Table II.

Of the agents tested, potassium arsenite was the most effective in increasing survival time in the 3 transfer lines of myeloid leukemia, although it had little if any effect on the course of the lymphoid disease. Treatment with either benzol or x-rays also prolonged survival time in myeloid leukemia (Table II). Mice gained in weight during treatment with either potassium arsenite or benzol, whereas animals treated with urethane and x-rays were smaller (15 g and 17 g as contrasted with 23 g). All mice were of approximately the same weight at the time of transfer of leukemia.

As a result of passage through successive generations of hosts, leukemic cells are altered[11] so that results achieved with transplanted leukemia may not apply to the spontaneous disease. Apparently the efficacy of a particular compound may be determined by the type of leukemia, whether myeloid or lymphoid, and genetic differences in leukemias of the same type. Early transfer generations, where survival is relatively long, are probably more favorable for testing than the late trans-

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fer generations of lines which have become highly malignant as a result of numerous transfers. A variety of lines should be tested with agents offering encouraging results on particular lines.

Summary. Survival time was lengthened significantly in 3 transfer lines of mouse myeloid leukemia by treatment with either potassium arsenite, urethane, x-rays, or benzol in decreasing order of effectiveness. Two transfer lines of lymphoid leukemia grown in genetically identical hosts did not respond favorably to the same treatment with the chemical agents. Potassium arsenite was more effective than urethane on a weight basis, and in the effective dose range was tolerated better than urethane.

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Further Experiments on Bridging of Long Nerve Gaps in Monkeys.*

EBEN ALEXANDER, JR., ROBERT P. WOODS, PAUL WEISS.

From the Children's Hospital, Department of Surgery, Harvard Medical School, and the Department of Zoology, University of Chicago.

The method of bridging gaps in peripheral nerves by a fiber cable embedded in a tubulated blood bridge, as described by Weiss and Taylor[1] for lower mammals has been successfully extended to monkeys by Matson, Alexander and Weiss.[2] The nerve gaps in these experiments measured up to 14 mm in length. The present experiments were undertaken to determine the feasibility of bridging longer gaps (from 22 to 32 mm), by the same technic.

Experiments. Five adult *Macaca rhesus* monkeys were used. The technic was essentially the same as in the earlier experiments. A section of the tibial nerve was cut out and the stumps allowed to retract; a segment of internal jugular vein was threaded over the proximal stump; the desired length of the gap was fixed by a tantalum sling stitch without tension; the nerve stumps were connected axially by a cable of finest nylon fibers (.006 inch); a trough made from polyethylene tubing of nerve caliber was placed under the cable-spanned gap and filled with blood from the jugular vein; after firm clotting had occurred, the trough was removed; finally, the sleeve of the vein was pulled over the bridged gap and secured to each nerve stump by a silk stitch. After wound closure with silk, no further provisions were made for the protection of the site of operation. The animals were set free in large cages. All remained in good health.

No detailed records were kept of the course of nerve recovery, and all tests were left to the terminal exploration, which was made under intravenous nembutal anesthesia, 289 to 333 days after the operation. After measuring both calves and exposing the nerve, the responses of leg and foot muscles to faradic stimulation of the nerve were determined. Segments of the regenerated nerve and of the control nerve from the opposite side were removed for histological study. In 4 of the 5 cases, the weights of the gastrocnemius muscles of both sides were also recorded.

Results. There were no technical failures in this series. Wounds healed without infection. In no case had the activities of the animals during the early postoperative period disrupted the nerve bridge. On re-exploration, the nerve bridge, after being freed from moderate adhesions, presented itself as an elon-

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