cm penetration of the beta radiation, then 1 liter of Kr-87 will deliver about 300 rep to the gastric mucosa. However, half the total energy is absorbed in the first 0.15 cm of mucosa (half value thickness—0.032 $E_M^{1.33}$); this means about 2,000 rep were absorbed by this superficial initial portion.

Krypton is inert and balloon breakage would cause no serious damage. The length of each treatment and number of treatments required are reasonable. Blood counts in all animals remain normal. The chief difficulty is that at present the work must be confined to the neighborhood of a nuclear reactor.

Further more quantitative animal work and long time observation are required before advocating this treatment in hyperacidity associated with peptic ulcer. At present no contraindications have appeared.

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2. Ricketts, W. E., *et al., Ann. Int. Med.*, 1949, v30, 24.

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Effect of Substituted Hydrazines and Related Compounds on Myeloid Mouse Leukemia C-1498.*† (19969)

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Other investigators(1-5) have extensively studied basic nitrogen compounds comprising free amines, diaryl and dialkyl amines, guanidines and amidines in the chemotherapy of cancer. No comprehensive study has been made with compounds incorporating the hydrazine group. The ease with which hydrazines form hydrazones by conjugation with carbonyl compounds might possibly upset biological systems important for the promotion of tumor growth, particularly oxidation systems such as the citric acid cycle, wherein hydroxy-containing compounds are enzymatically oxidized to the corresponding carbonyl. It is possible that this hydrazone, resulting from the interaction of the hydrazine with the carbonyl group, might interfere with an essential oxidation-reduction process in the cell. Likewise, hydrazines react readily with glucose; in this way they might also interfere with intracellular carbohydrate metabolism. Sixty-six hydrazine and hydrazide derivatives are reported, including the following parent structures: phenyls, biphenyls, stilbenes, quinolines, naphthalenes, aliphatic as well as a few cyclic hydrazides. The compounds were chosen to give the greatest variations of chemical and physical-chemical properties.

Materials and methods. C-57 black mice were implanted subcutaneously with myeloid leukemia C-1498. Therapy was started the same day. Dosage was approximately one-half the maximum tolerated dose. Seven mice were used to evaluate each compound; in doubtful cases the experiment was repeated. The controls died in 12-14 days. The drugs were usually dissolved or suspended in 4% gum acacia solution; when necessary sorethitan monooleate was added to aid solution. Peanut oil was occasionally used. Drugs administered orally were given by stomach tube.

Results and discussion. The results are summarized in Table I, which is self-explanatory. None of the compounds showed any significant prolongation of life of the animals.

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† With the technical assistance of D. Balcom, D. Morrison, E. Girdish and L. Horne.

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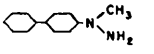
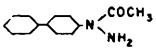
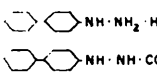
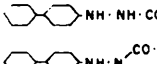
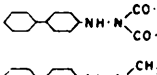
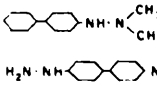
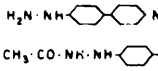
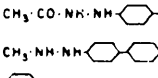
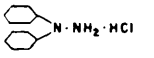
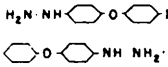
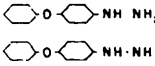
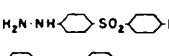
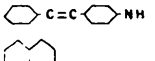
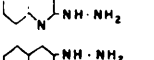
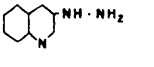
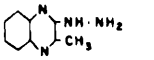
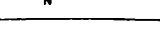
Some of the compounds are of particular interest as they are or resemble active biological agents. No. 58 is the hydrazine analogue of urethane; Nos. 52 and 56 are amino acid analogues; Nos. 29-39 inclusive, represent derivatives of phenylhydrazine. Nos. 42, 45, 50 and 51 are the hydrazides of *p*-aminobenzoic acid, *p*-aminosalicylic acid, isonicotinic acid and nicotinic acid, respectively. Nos. 53 and 59 are urea analogues. 3,5-Dioxo-1,2 diphenyl, 4n-butyl-pyrazolidine (No. 66) (Butazolidin[R]) has recently been introduced in the therapy of arthritis.

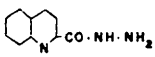
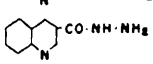
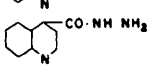
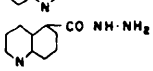
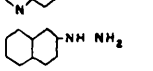
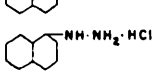
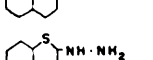
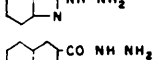
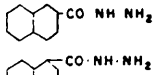
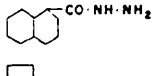
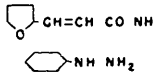
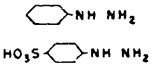
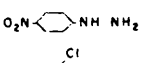
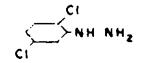
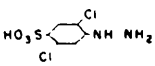
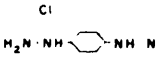
These hydrazines were prepared in order to examine a large range of physio-chemical properties. With the exception of Nos. 63-66 inclusive, all of the molecules are planar, and cover a large range of basicity. Although none of these compounds are surface acting agents, varying degrees of solubility in both aqueous and lipid medium are noted. This series therefore represents a gradation of partitian coefficients from high to low values. Aliphatic, aromatic and heterocyclic series with their diverse properties are also represented. A number of position isomers are noted, but the exact geometrical requirements of some important enzyme systems probably could not be met. Unfortunately no clue was obtained from these considerations.

Summary. Sixty-six compounds were tested for activity against myeloid mouse leukemia in C-57 mice. These included hydrazines, hydrazides, hydrazones and related com-

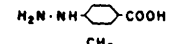
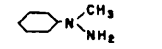
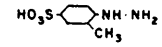
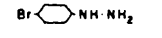
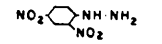
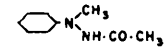
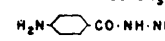
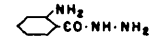
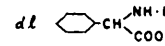
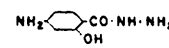
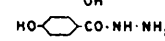
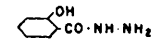
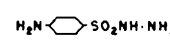
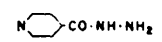
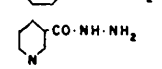
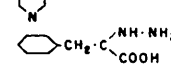
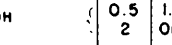
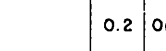
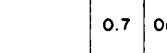
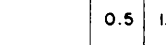
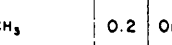
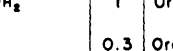
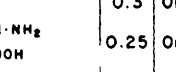
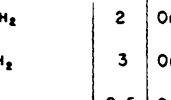
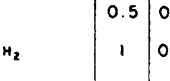
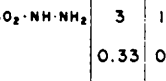
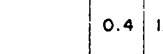
TABLE I

EFFECT OF SUBSTITUTED HYDRAZINE AND RELATED COMPOUNDS ON MYELOID LEUKEMIA - C1498

No	Formula	Dosage mg. per animal	Route	No. of treat. per wk.	Increase of life over contr in days
1		1.2	I.P.	3	0
2		2	I.P.	3	0
3		1	I.P.	3	1
4		2	I.P.	3	0
5		2	I.P.	3	0
6		1.5	I.P.	3	0
7		0.5	I.P.	3	0
8		2	I.P.	3	0
9		0.3	I.P.	3	0
10		1	I.P.	3	1
11		1	I.P.	3	0
12		1	I.P.	3	0
13		1	I.P.	3	0
14		1	I.P.	3	0
15		3	I.P.	6	0
16		0.22	I.P.	3	0
17		0.5	I.P	3	0
18		1	I.P	5	0

No.	Formula	Dosage mg. per animal	Route	No. of treat. per wk.	Increase of life over contr in days
19		0.5	I.P.	5	-1
20		2	Oral	6	-1
21		1.4	Oral	5	-2
22		0.4	Oral	6	-1
23		1 1	I.P. Oral	3 3	-1 -1
24		1	Oral	3	0
25		0.66	I.P.	3	0
26		3	Oral	4	-2
27		0.2	Oral	6	0
28		2	Oral	5	-1
29		0.15	Oral	5	1
30		6	Oral	6	1
31		0.15	Oral	5	0
32		0.7	Oral	5	0
33		6	Oral	6	0
34		8	Oral	6	-1

(Table I continued)

No.	Formula	Dosage mg. per animal	Route	No. of treat. per wk.	Increase of life over contr. in days
35		0.5 2	I.P. Oral	3 3	0 0
36		0.2	Oral	6	1
37		3	I.P.	5	0
38		0.7	Oral	3	0
39		0.5	I.P.	5	0
40		0.2	Oral	5	0
41		1	I.P.	3	0
42		1	Oral	3	-1
43		0.3	Oral	5	-2
44	*dl* 	0.25	Oral	3	-1
45		2	Oral	6	-1
46		3	Oral	6	-2
47		0.5	Oral	6	-2
48		1	Oral	6	0
49		3	I.P.	3	0
50		0.33	Oral	6	-2
51		0.4	I.P.	6	0
52		2	Oral	6	-1
53		0.4	Oral	5	0
54		1	Oral	3	0
55		0.17	Oral	3	0
56		0.5	Oral	3	1
57		6	Oral	6	-1
58		0.07	Oral	5	1
59		1	I.P.	5	0
60		0.5	I.P.	3	0
61		4	I.P.	3	1
62		12	I.P.	6	0
63		2	Oral	6	1
64		1	I.P.	6	1
65		2	I.P.	5	0
66		4	Oral	6	-2
*	Urethane	8	I.P.	3	2.4
*	Potassium Arsenite	0.1	I.P.	3	0

* Both Urethane and Potassium Arsenite were included for comparison.

The compounds were prepared in this laboratory with the following exceptions:- Nos. 3, 10, 29, 36, 38 were obtained from Distillation Products Corp., No. 37 from General Dyestuff Corp., No. 65 from the Dow Chemical Co., and No. 66 from the Geigy Chemical Co.

pounds. None was found active.

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2. ———, *Biochem. J.*, 1946, v40, 55.
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Sugar Alcohols. XXIX. Sorbitan Polyoxyethylene Fatty Acid Esters and Polyoxyethylene Monostearate and Respiration of Kidney. (19970)

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For many years our studies(1) have been designed to elucidate the fate of the sugar alcohols and their derivatives(2) in the animal body. The widespread use of the derivatives of sorbitol as non-ionic emulsifiers in such common components of the human diet as ice cream, bread and other bakery products has focused attention upon the effects of these