TABLE I.
Effect of GH and ACTH on Blood Ketone Bodies of Fasted Normal Rats.

Injection	Initial blood	3-hr blood	Change	P‖
Controls, no inj. (12)†	7.9 ± 0.94‡	8.0 ± 1.06	+ 0.1 ± 0.85	
3 mg Albumin (5)	6.8 ± 1.45	6.1 ± 1.54	— 0.7 ± 0.18	.55
½ '' ACTH (7)	7.8 ± 1.41	13.0 ± 2.18	+ 5.2 ± 1.83	.01
1½ '' '' (6)	6.9 ± 0.79	16.3 ± 2.52	+ 9.3 ± 2.25	.01
3 '' '' (9)	7.9 ± 1.52	25.6 ± 1.97	+17.7 ± 2.65	.01
½ '' GH (8)	6.4 ± 0.85	10.1 ± 1.25	+ 3.7 ± 0.57	.01
1½ '' '' (7)	7.0 ± 0.84	11.4 ± 1.32	+ 4.4 ± 0.80	.01
3 '' '' (8)	7.4 ± 1.48	16.2 ± 2.00	+ 8.8 ± 1.70	.01
1½ '' ACTH + 1½ mg GH (6)	7.5 ± 0.87	21.5 ± 1.25	+14.0 ± 1.27	.01 .01§ .06*
3 '' '' + 3 '' '' (6)	9.8 ± 1.27	21.5 ± 0.86	+11.8 ± 1.21	.01 .20§ .09*

* Compared with the same dose of ACTH alone.
† Figure in parentheses indicates number of animals.
‡ Standard deviation of the mean.
§ Compared with the same dose of GH alone.
‖ From Fisher's[5] table of t. A value of 0.05 or less is considered significant.

mal rats is confirmed. 2. Under the experimental conditions used, the degree of ketonemia produced is correlated with the amount of hormone administered.

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Effect of Age upon Toxicity of Methadon.*

FRANCIS G. HENDERSON AND K. K. CHEN.
From the Lilly Research Laboratories, Indianapolis, Ind.

It has been mentioned that infants are highly susceptible to morphine as compared with adults.[1-3] This statement has been substantiated in animals by Döbeli,[4] Sollmann,[5] Gibbs and Bobb,[6] and Chester and associates.[7] Further, Eddy[8] and Chen and Robbins[9] showed that morphine was more toxic to both very young and aged rabbits, and rats, respectively, as compared with adults. The ages of their animals were accurately recorded.

Methadon is a drug of German origin, picked up by the Technical Industrial Committee[10] of the U. S. Government. Pharmacologic studies by Scott and Chen,[11,12] and

* The material used in this investigation was 'Dolophine' (Methadon, Lilly).

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6 Eddy, N. B., *J. Pharm. and Exp. Therap.*, 1939, **66**, 182.

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10 Kleiderer, E. C., Rice, J. B., Conquest, V., and Williams, J. H., Report No. 981, Office of the Publications Board, Dept. of Commerce, Washington, D. C.

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TABLE I.
Median Lethal Dose ± Standard Error of Methadon by Intravenous Injection in Female Albino Rats of Different Ages.

Age		No. of rats injected	LD_{50} ± S.E. mg per kg
Mo.	Days		
	14	40	14.62 ± 1.58
1		39	13.71 ± 1.49
1½		37	10.43 ± 1.19
2		38	11.45 ± 1.26
4		30	10.36 ± 1.30
6		26	13.56 ± 1.83
12		26	10.71 ± 1.45

Isbell and associates[13] reveal that this product has analgesic action and addiction liabilities similar to morphine. For further comparative studies, the effect of age upon the toxicity of methadon was investigated.

Albino rats were used for the toxicity studies with age groups varying from 14 days to 12 months. The animals were of the same sex, females—just as in our morphine work,[9] and from the same source. A total of 26 to 40 rats were used for each age group. The drug was administered by the tail vein. Different dose increments were given for the purpose of determining the median lethal dose (LD_{50}). The LD_{50} was calculated according to the combined slope method of Miller, Bliss, and Braun.[14]

Table I lists the median lethal doses of methadon for the various age groups. There is apparent evidence that rats 14 days and 1 month of age are less susceptible to methadon than those 1½ to 4 months old. Statistical analysis shows this difference to be barely significant at the 5% point. This is just opposite to morphine.[9] Also, rats 12 months old succumbed to methadon in approximately the same dosage as those of 1½ to 4 months of age. Morphine is relatively more toxic to 1-year-old rats than to young adults. For sake of clearness, the LD_{50}'s of methadon for different age groups in the present work are contrasted in Fig. 1 with those of morphine for corresponding age groups published previously.[9]

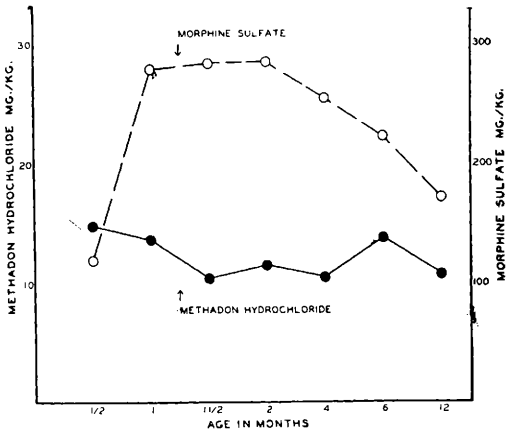

FIG. 1.
Graphic comparison of the effect of age upon the toxicity of morphine and methadon.

Summary. In contrast with morphine, methadon does not show a higher toxicity in very young or 1-year-old rats than in young adults, following intravenous injection.

[12] Scott, C. C., Robbins, E. B., and Chen, K. K., *Science*, 1946, **104**, 587.

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[14] Miller, L. C., Bliss, C. I., and Braun, H. A., *J. Am. Pharm. A.*, 1939, **28**, 644.