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**Production of Thyroid Hyperplasia in Rats and Mice by Administration of Methyl Cyanide.**

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The daily subcutaneous administration of small doses of aliphatic cyanides to young rabbits of either sex maintained on a diet of alfalfa hay and oats has been shown to produce thyroid hyperplasia within 21 days.<sup>1</sup> The most potent cyanide was found to be methyl cyanide. The use of methyl cyanide as a goitrogenic agent has now been extended to rats and mice.

*Rats.* Twelve female albino rats, 6 being litter mates aged 3 months, and 6 litter mates aged 5 months, were divided into 3 groups, 2 animals from each litter comprising each group. Their diet consisted of hominy 100 parts, rolled oats 25 parts, powdered skim milk 5 parts, dry meat 25 parts, salt 1½ parts and tap water; this was found to be nongoitrogenic. They were given daily subcutaneous injections of varying doses of methyl cyanide in water, the first group receiving 0.08 cc., the second 0.04 cc. and the third 0.02 cc. of methyl cyanide. One animal from each group was sacrificed at the end of 21 days, and all showed only very slight thyroid hyperemia. At the end of 28 days there was definite thyroid hypertrophy, but it was obvious that rats' thyroids were less reactive than rabbits'. During the next 8 days the doses were gradually increased on the remainder in each group, until that on the largest dose was receiving as much as 0.15 cc. of methyl cyanide daily without any clinical sign of cyanide poisoning. After 36 days of treatment the thyroids were larger and more hyperemic. As has been pointed out previously, there were individual variations, but in general the thyroid reactions were proportional to dosage. The results are given in Table I.

*Mice.* A batch of 12 mice on the same diet as the rats received similar treatment, and were divided into 3 groups, receiving daily 0.005 cc., 0.0025 cc., and 0.00125 cc. of methyl cyanide respectively. Their ages at the beginning of the experiment were 3½ weeks and their weights averaged 13 gm. Only a slight thyroid reaction was produced after periods varying from 11 to 34 days.

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<sup>1</sup> Marine, D., Baumann, E. J., Spence, A. W., and Cipra, A., *Proc. Soc. Exp. Biol. and Med.*, 1932, **29**, 772.

TABLE I.

No. of Rat	Age	Wt.	Methyl Cyanide	Duration of Treatment	Condition of Thyroid*
	mo.	gm.	cc.	days	
1	5	230	0.08	28	+ -
			0.1	4	
2	5	260	0.08	28	+ -
			0.1	4	
			0.15	4	
3	3	158	0.08	28	- +
4	3	144	0.08	21	- †
5	5	202	0.04	33	+
			0.1	3	
6	5	202	0.04	33	+ -
			0.1	3	
7	3	136	0.04	28	- +
8	3	118	0.04	21	- †
9	5	173	0.02	33	- +
			0.05	3	
10	5	145	0.02	33	- +
			0.05	3	
11	3	114	0.02	16	-
12	3	112	0.02	21	- +

\*+ = Twice normal size, moderately hyperemic.

+ - = One and a half times normal size, slightly hyperemic.

- + = Slightly enlarged, slightly hyperemic.

- = Not enlarged, not hyperemic.

Hunt and Seidell<sup>2</sup> demonstrated in "acute" experiments the high tolerance of rats for methyl cyanide, the minimum lethal dose being between 4 and 5 mg. per gm. of body weight. The thyroid reactions obtained in rats and mice by means of the administration of cyanide are far less than those produced in rabbits receiving relatively much smaller doses, and bear out the well-known fact that these animals possess considerable resistance to goitrogenic substances. Since age is such an important factor in both the thyroid response and the animals' resistance to methyl cyanide, it is probable that younger animals would have given better reactions.

<sup>2</sup> Hunt, R., and Seidell, A., Bull. No. 47, Hyg. Lab. U. S. Pub. Health and Marine Hosp. Serv., Washington, 1909.