Toxicity of Dimethyl Selenide in the Rat and Mouse. (19333)

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(Introduced by M. Mason Guest.)

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The toxicity of inorganic selenium varies considerably according to its ionic state. According to Franke and Potter(1), the order of toxicity of the inorganic seleniums from the highest to the lowest is selenate, selenite, and selenide. Elemental selenium is almost nontoxic. The *minimum fatal dose** of sodium selenate injected intraperitoneally in the rat was found to be 5.25 to 5.75 mg Se per kg of body weight(2). Similarly, the toxicity of organo-selenium compounds is variable(3-6). A study of various seleniferous diets, as reported by Franke and Painter(7), showed the toxicity of selenium from different sources to be in the following order: wheat, >corn, >barley, >selenate, >selenite, >selenide, and >elemental selenium. They observed that there was little difference in the toxicity of selenium as it occurs in the different grains, but the naturally-occurring selenium was found to be definitely more toxic than inorganic selenium. Since naturally-occurring selenium has been shown to be in the protein fraction of seleniferous grains(8), and it has been postulated that selenium could replace sulfur in methionine and cystine(9), the toxicity of the selenium analogs of these amino acids is of particular interest. The *minimum fatal dose** of selenium in the form of selenium-cystine when injected intraperitoneally into the rat was found to be 4.0 mg Se per kg of body weight(4).

It was noted in previous experiments(10) in which studies were carried out to investigate the time-excretion of injected dimethyl selenide, that relatively large amounts of dimethyl selenide (600 mg Se per kg of body weight) could be administered to rats without any apparent deleterious effects. A systematic search of the literature revealed that no toxicity studies of dimethyl selenide had been reported. Therefore, it was the purpose of the experiments presented here to determine the *median lethal dose* (L.D. 50) of dimethyl selenide in the rat and mouse.

Experimental. Dimethyl selenide was prepared according to the method of Bird and Challenger(11). Elementary carbon and hydrogen analyses† revealed the following results:

$(CH_3)_2Se$ (109.03)	Carbon, %	Hydrogen, %
Theoretical	22	5.55
Found	23.3	5.69

The mercuric derivative $(CH_3)_2Se \cdot HgCl_2$ (12) melted at 151-153°C. The $(CH_3)_2Se$ had a boiling point at 53°C and had a specific gravity of 1.41 at 15°/4°C. The preparation was injected intraperitoneally into the animals, using a tuberculin syringe for the rats and a syringe specially constructed from a narrow bore serological pipette for the mice. Sixty-three mice of mixed sex with an average weight of 25 g, and 34 male rats with an average weight of 311 g were administered doses of dimethyl selenide which are recorded in Table I. The mortality was determined at

TABLE I. Mortality of Mice and Rats Injected with Dimethyl Selenide.

Dose $(CH_3)_2Se$, g/kg	No. of animals	Mortality—24 hr, %	Mortality—48 hr, %
1.4	15 m*	26.7	33.3
1.4	5 r	0	0
2.1	15 m	66.7	100
2.1	11 r	45.5	54.5
2.8	15 m	86.7	93.3
2.8	5 r	80	80
3.5	14 m	92.9	92.9
3.5	13 r	84.6	84.6
7	4 m	100	100

1 ml $(CH_3)_2Se$ = 1.018 g Se as $(CH_3)_2Se$, or 1.408 g $(CH_3)_2Se$ at 15°/4° C.
* m = mice, r = rats.

* The minimum fatal doses were taken as the smallest doses which would kill 75% or more of the animals in less than 2 days.

† Analyses by the Clarke Microanalytical Laboratory, Urbana, Ill.

24 and 48 hours after the time of injection.

Results and discussion. Within one to 2 minutes following injection of dimethyl selenide near the median lethal dose, the animals entered a state of hyperpnea with the elimination of an overwhelming garlic-like odor on the breath. Convulsions in the mice, but not in the rats, were common. This was usually followed by exitus within a few hours, with the fatal doses, although some animals died as late as 36 hours after injection. In all cases, the signs of hyperpnea were gone after the first 2 or 3 hours.

Median lethal doses (L.D. 50) for the rat and mouse at 24 hours were determined (13,14) by plotting per cent mortality on probit against log dosage graph paper. It was found that the L.D. 50 for 24 hours for the mice was 1.3 g Se as dimethyl selenide (1.8 g dimethyl selenide) per kg of body weight. That for the rats was 1.6 g of Se as dimethyl selenide (2.2 g dimethyl selenide) per kg of body weight. It will be noted that these figures are several times greater than the minimum fatal doses for either sodium selenate (5.25 to 5.75 mg Se per kg)(2), or selenium-cystine (4 mg Se per kg of body weight)(4).

In relation to the selenium detoxification mechanism, it is of particular interest to point out that after the administration of sodium selenate, which is a relatively toxic compound, selenium rapidly appears in the respiratory gases(15) in the form of dimethyl selenide (10), which is a sparingly toxic compound. Thus, it would appear that the animal organism when treated with a toxic form of selenium, converts it in part to a less toxic compound which is readily excreted via the lungs.

Summary. The median lethal dose (L.D. 50) of dimethyl selenide was determined for the mouse and rat. It was found, after intraperitoneal injection of dimethyl selenide, that the median lethal dose for the mouse was 1.3 g of Se as dimethyl selenide (1.8 g dimethyl selenide) per kg of body weight, and 1.6 g Se (2.2 g dimethyl selenide) per kg of body weight for the rat.

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Leucocytosis in Vitamin E Deficient Rabbits.* (19334)

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Previous reports from this laboratory have indicated an effect of vit. E deficiency on nucleic acid metabolism(1,2). It was also noted that E-deficient monkeys exhibited a leucocytosis which responded to therapy with alpha tocopherol(1). This paper reports the results of a study of the effect of vit. E deficiency on the peripheral leucocytes of rabbits. The data to be presented show that E-deficient rabbits exhibit a leucocytosis which