

Acute Toxicity of Choline Chloride Administered Orally to Rats.*

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From the recent studies on the toxicity of choline chloride in rats and mice^{1,2} two pertinent facts may be reiterated: (a) The toxicity increases with increasing concentration when choline chloride solutions are given intraperitoneally to rats, (b) The toxicity following intraperitoneal administration is much higher than that following administration by stomach tube. The following experiments amplify those previously reported¹ on the oral toxicity and show that an increase of toxicity with concentration also occurred when the choline is administered by stomach tube.

Methods. 413 male and female albino rats weighing from 76 to 343 g were given 4 different concentrations of choline chloride solutions.

Groups of 5 to 30 rats each were fasted for 24 hours and then given by stomach tube various doses of each of the 4 concentrations of choline. Several doses of each of the 4 solutions administered on a single day gave fairly consistent results. A roughly linear relationship existed between dosage and percentage mortality. However, on different days marked differences were observed in the susceptibility of the rats; there was considerable scatter in the series as a whole. No explanation for this variation could be found;

no correlation existed between sex or weight and toxicity, and the solutions were freshly made for each test.

Results. The results for the 2 higher concentrations (670 and 500 mg/ml) were combined and the results for the 2 lower concentrations (200 and 400 mg/ml) were combined as illustrated in Fig. 1. These values show a significant increase in mortality with increase in concentration. The LD₅₀, calculated by the method of Bliss³ for the 2 higher concentrations was of the order of 3.4 g/kg body weight. For the 2 lower concentrations, the LD₅₀ was of the order of 6.1 g/kg body weight.

The action of choline was rapid; symptoms appeared within 5 to 10 minutes. In most cases, there was an initial excitement period, characterized by jerking movements and occasional convulsions. At this time, the bloody tears (chromodacryorrhea)⁴ appeared in 30 to 90% of the animals which succumbed. The excitement period was followed in a few minutes by a depression with complete relaxation and depressed respiration which finally terminated in respiratory paralysis after 15 to 30 minutes. Animals which lived longer than 30 minutes in most cases survived. A few animals which survived several hours were found dead 18 hours after the drug was given. This delayed response was not observed following the intraperitoneal administration of choline.

Summary. 1. 413 albino rats were given solutions of choline chloride by stomach tube. Four concentrations, viz., 670, 500, 400, and 200 mg/ml were used. A significant increase in the toxicity with increase in concentration was found after combining the results for the 2 higher and 2 lower concentrations.

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¹ Hodge, H. C., Goldstein, M. R., *Proc. Soc. Exp. Biol. and Med.*, 1942, **51**, 281.

² Hodge, H. C., *Proc. Soc. Exp. Biol. and Med.*, 1944, **57**, 26.

³ Bliss, C. L., *Ann. Appl. Biol.*, 1935, **22**, 134.

⁴ Tashiro, S., Badger, E., and Younker, W., *Proc. Soc. Exp. Biol. and Med.*, 1940, **45**, 377.

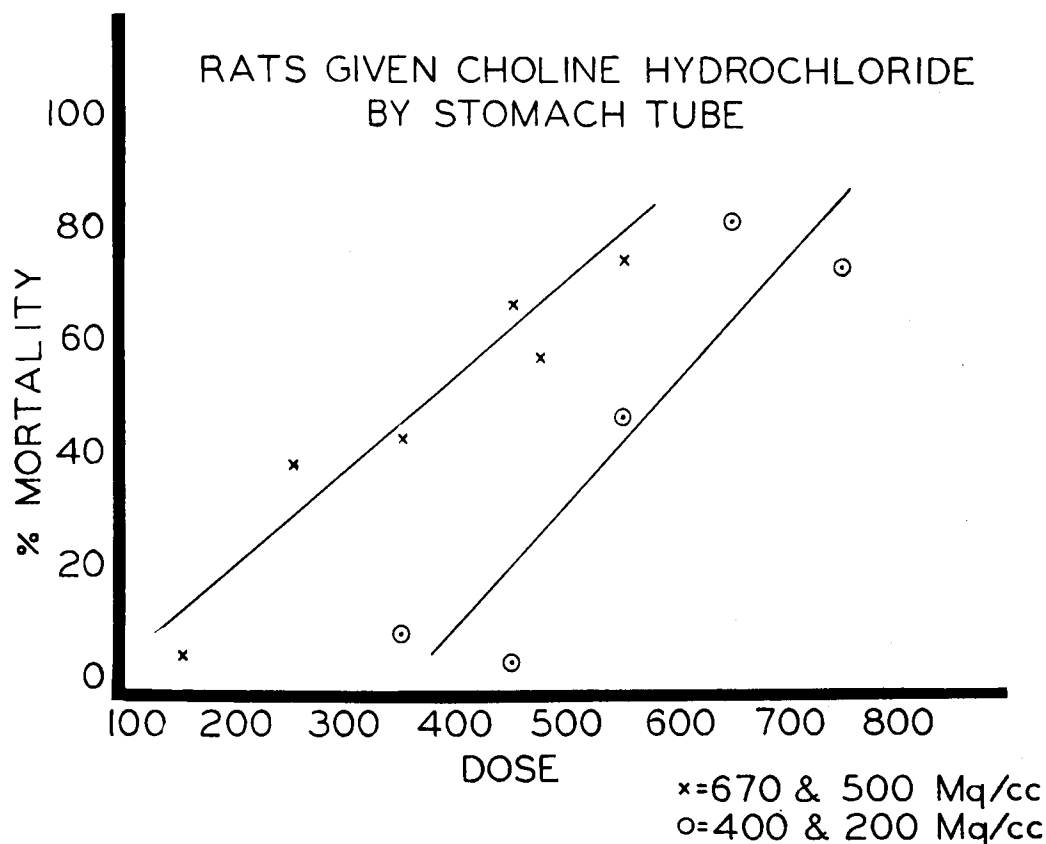


FIG. 1.

These two curves represent the average results obtained with rats given choline solutions containing 670 and 500 mg/ml and 400 and 200 mg/ml, respectively. The dose is represented as mg/100 g rat; expressed as g/kg, the abscissæ are 1.0 to 8.0, respectively.

2. The LD₅₀ for the 2 higher concentrations (average 580 mg/ml) was of the order of 3.4 g/kg body weight; for the 2 lower concentrations (average 300 mg/ml) was of the order of 6.1 g/kg body weight.