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Intravenous Saline Tolerance in Mice.

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In the course of investigating the comparative toxicity of certain sparingly soluble compounds in mice, it was necessary to inject as much as 5 cc per 20 g of body weight of hypotonic and isotonic solutions. In order to determine the effects of injecting such large volumes without the influence of any drug, the intravenous toxicity of sodium chloride solutions at different osmotic concentrations was investigated. In addition the rate of injection was varied to determine the maximum speed permissible for safe administration.

Male mice of the CF 1 strain, weighing from 19 to 30 g were used and all animals surviving the initial injection were observed one week for delayed deaths. The solutions were administered into one of the lateral veins of the tail at a given rate by means of a constant speed infusion pump.

In the first experiment physiological saline (0.85% NaCl, 0.15N) was administered until death occurred. At the rate of 0.9 cc per minute, an average of 6.9 $\pm$ 0.71‡ cc per 20 g was found to be the fatal dose. Although increasing the rate of administration above 1 cc per minute (1 to 2.5 cc per min.) appeared to decrease the fatal dose to 5.9 $\pm$ 0.63‡ per 20 g, the difference between the 2 sets of data is not significant. After establishing the fatal dose for physiological saline, a second experiment was carried out in which various concentrations of sodium chloride were injected at different rates until the animals received 5 cc per 20 g or less if death occurred. Accordingly the animals were divided into 5 groups receiving one of the following solutions: distilled water, 0.425%, 0.85%, 1.70%, or 2.55% sodium chloride at rates ranging from 0.2 to 4.0 cc per minute. As is shown in Table I, half physiological saline (0.425%, 0.073N) is the least toxic; 5 cc per 20 g was tolerated by all animals at a maximum rate of 3.50 cc per minute. Increasing the rate above this point results in death. As the salt concentration was increased, tolerance to 5 cc per 20 g was reduced. With physiological saline, this volume was tolerated at a maximum rate of 2.5 cc per minute, but in the case of distilled water, 1.70 or 2.55% sodium chloride, 5 cc per 20 g could not be administered safely, for some deaths occurred even at the slowest rates. It would hardly be practical to administer 5 cc per 20 g at rates below 0.2 cc per minute because of the time required for the injection.

Both physiological and half physiological saline are well tolerated under the circumstances of this experiment whereas the hypertonic solutions are not "safe" since deaths occurred even at the slowest rates of administration. Although the half physiological saline appears to be slightly less toxic than the physiological saline this difference is not statistically significant. Therefore, when large volumes (5 cc per 20 g body weight) are required in intravenous toxicity studies in mice, it would seem most logical to use solutions with an osmotic concentration between the range of 0.073N to 0.15N. This is equivalent to 0.425% to 0.85% NaCl. In our studies we adjusted the solutions of the sparingly soluble compounds to 0.073N and injected up to 5 cc per 20 g at a rate of 1.5 cc per minute.

Summary. Mice tolerated intravenous injections of 5 cc per 20 g body weight of half physiological and physiological saline at maximum rates of 3.5 and 2.5 cc per minute respectively. The average lethal dose for physiological saline given at a rate of 0.9 cc per minute is 6.9 cc per 20 g.

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‡ Standard error.

TABLE I.
Toxicity of Various Sodium Chloride Solutions Administered Intravenously at Different Rates.

	Rate of administration cc/minute													
	4.0-3.5		2.9-2.5		2.4-2.0		1.9-1.5		1.4-1.0		0.9-0.5		0.5-0.2	
% NaCl	cc/20 g	D*	cc/20 g	D*	cc/20 g	D*	cc/20 g	D*	cc/20 g	D*	cc/20 g	D*	cc/20 g	D*
0	4.7†	4/4	4.6†	3/3	5.1	1/1	4.5†	1/1	4.2†	1/1	3.9†	1/1	4.6†	2/2
0.425	5	3/10	5	0/9	5	0/6	5	0/3	5	0/2	5	0/1		
									"Safe" range					
0.85	5	4/6	5	2/8	5	0/3	5	0/4	6.4‡	0/3	5.0	0/6	5.0	0/1
1.70	3.9†	1/1	4.0†	2/2					4.2†	1/1	5.0	1/3	5.0	1/3
2.55	2.2†	1/1					1.8†	1/1	2.6†	1/1	2.9†	3/3	5.1	2/2

* D = No. dead / No. dosed
† Death before 5 cc injected.
‡ Two of these animals received 7 cc per 20 g.

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Failure of Xanthopterin to Influence Hematopoiesis and Growth in Rats.*

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Tschesche and Wolf[1] reported that rats fed goats' milk develop an anemia which responds to xanthopterin. Simmons and Norris[2] and Simmons[3] observed that anemia in Chinook salmon responds to injections of xanthopterin. Totter and Day[4] reported that in rats with the deficiency induced by feeding a purified diet containing succinylsulfathiazole, administration of 20 μg of xanthopterin per day caused a leukocytosis and a marked weight gain, but in subsequent experiments they failed to confirm this observation. Wright and Welch,[5] Daft and Sebrell,[6] and Axelrod, *et al.*,[7] also failed to note any effect when xanthopterin was fed to rats deficient in pteroylglutamic acid (PGA). Totter and co-workers[8,9] reported that favorable hematopoietic responses occur when xanthopterin is given to vitamin M-deficient monkeys. In this laboratory, 2 macrocytically anemic swine have shown a submaximal hematopoietic response to large parenteral doses of xanthopterin (10 mg daily),[10] a phenomenon which is being investigated further.

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