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Intravenous Pentobarbital Anesthesia in Rabbits.

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Sixty mg./kg. of ethyl-l-methyl-butyl barbituric acid (pentobarbital, nembutal) one of the shorter-acting barbiturates is fatal to the majority of 10 rabbits when administered intraperitoneally. Forty mg./kg. (66.6%) of the lethal intraperitoneal dose produces surgical anesthesia for 40 to 50 minutes in a majority of instances within 20 to 40 minutes. Because of its safety this is the usual mode of administration of choice in most laboratory demonstrations and experiments. While the intravenous mode has the advantage of being virtually immediate in the induction of surgical anesthesia in rabbits and other small laboratory animals it is generally regarded as being too dangerous for routine laboratory employment. To this opinion we have never subscribed. Accordingly, we undertook to try to solve the supposed problem of danger incident to the intravenous employment of pentobarbital and thereby take advantage of its rapidity of action. In this work we were able to compile a large series of cases by employing pentobarbital intravenously over a period of 6 years in weekly operations on female rabbits as a part of the obstetrical and gynecological services of the Freedmen's Hospital in tests for early pregnancy (Schneider-Friedman Modification of the Aschheim-Zondek Test). This series supplemented by another large series in which this agency among others has been used in experimental pharmacology in our laboratory makes a total of 2,500 cases in which we have employed pentobarbital intravenously in surgical anesthesia in rabbits.

Correct dosage is a matter of prime importance. After numerous trials varying the single dose symptomatically the average optimal figure was found to be 20 mg./kg. We usually weigh out the barbiturate as the sodium salt because of its ready solubility. When the acid is weighed out and rendered soluble by the addition of sodium hydroxide allowance is made for the differences in molecular weights (110 mg. salt = 100 mg. acid). A 5% aqueous solution is usually employed.

The animal is either held down on its side by an assistant or strapped to a rabbit board on its back. The injection is made into the marginal ear vein at a slow rate (*circ.* 1 cc. per 30 sec.). As

soon as muscular relaxation sets in and the respiration slows, the rate of injection is reduced, the operator making brief pauses at intervals to gauge the latency and thereby avoiding the facile overdose. To measure grossly the degree of narcosis the tip of the ear or tail is pinched. Failure to resist by an outcry is determinative. The operative field can then be prepared and the incision made. Usually effective anesthesia has been obtained by this time (2 to 5 minutes). Occasionally a very small supplementary dose may be indicated just before making the incision.

The intravenous dose of pentobarbital necessary to produce good surgical anesthesia in rabbits varies in individual cases from 17.5 to 25 mg./kg. In our experience the optimal dose is 20 mg./kg. For the guidance of those who would want to use this procedure we advise injecting the first 15 mg./kg. at the rate of 1 cc. per 30 sec., then stopping for 10 sec., and following with 5 mg./kg. in 2, 3, or more squirts at intervals of 5 to 10 sec. p.r.n. The result in 98% of the cases will be satisfactory. If, on account of a too long latency as may occasionally happen an overdose has been given, an intravenous dose of picrotoxin invariably furnishes adequate protection. The optimal antidotal dose of picrotoxin is 1 mg. picrotoxin per 9 mg. nembutal, (Maloney, Fitch, and Tatum[1]). This dosage of picrotoxin is varied in accordance with the symptomatic response of the individual animal. Pentobarbital used as here described, is rapid, safe and satisfactory

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Production of Experimental Hypospadias in the Female Rat.

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It has been reported that the injection of large amounts of estrogenic substances into the pregnant rat during the last few days of her pregnancy caused an "hypospadias" in the female offspring.[1, 2] This same abnormality resulted when the mother rat was injected with large doses during the first 4 days of lactation.[3, 4] It was also

[1] Maloney, Fitch and Tatum, *J. Pharm. and Exp. Therap.*, 1931, **41**, 465.

[1] Hain, A. M., *Quart. J. Exp. Physiol.*, 1935, **25**, 131.

[2] Hain, A. M., *Quart. J. Exp. Physiol.*, 1935, **25**, 303.

[3] Hain, A. M., *Edin. Med. J.*, 1935, **42**, 101.

[4] Hain, A. M., *Quart. J. Exp. Physiol.*, 1936, **26**, 29.