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Circulatory Effects of Pentothal Sodium.

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Many of the early reports of the action of pentothal sodium indicated relatively little effect on heart and circulation as compared with the more conspicuous respiratory depression.¹ Since with most anesthetics it is usually not difficult to restore respiration if the circulatory apparatus is relatively intact, this drug would seem to be fairly safe when used with discretion.

Curiosity about the effects of overdoses and of repeated doses prompted the introductory experiments here briefly reported. The work was done on 12 dogs and 10 cats. No ether or other general preliminary anesthetic was used: carotid, tracheal and femoral canulae being introduced after careful procaine local analgesia and gentle operative procedure.

Minimal narcotic doses (0.020 per kg. intravenously) slowly given ordinarily do not arrest respiration or lower the blood pressure. The same dose given too rapidly may cause a cessation of breathing without any measurable effect on blood pressure. When a larger sublethal dose (0.025 per kg.) is administered there is usually an arrest of respiration, sometimes an appearance of cardiac irregularity, but without an essential fall in blood pressure. These mild effects usually disappear spontaneously, or more rapidly with the aid of artificial respiration. After restoration of breathing, no further deleterious effect on respiration or blood pressure appears.

In one instance a dog, after repeated doses, was "resuscitated" 18 times in the course of an hour and 50 minutes by artificial respiration. Eventually blood pressure dropped suddenly to 0, and we were unable to restore it.

When, however, the original dose (0.020 kg.) was repeated after the return of reflexes, there was not only a longer period of narcosis, but respiration was arrested for a longer time, there was a more pronounced heart arrhythmia and sometimes a slight fall in blood pressure. After return of reflexes, repeated doses of the same size have a more pronounced effect on the blood pressure curve, showing

¹ Lundy and Tovell, *Proc. Mayo Clinic*, 1935, 10, 557, 743, 791; Pratt, Tatum, et al., *Am. J. Surg.*, 1936, 31, 464; Gruhzit, Dax, et al., *J. Pharm. and Exp. Therap.*, 1937, 60, 125.

definitely the slow, deep rhythm described by Gruber,² and ascribed by him after electrocardiographic studies to the development of ventricular ectopic beats interspersed with long compensatory pauses.

After the administration of a minimal narcotic dose, 4 of the dogs were carried along as nearly as possible at the level of abolition of corneal and joint reflexes by saline-diluted fractional doses (0.003-0.005) of pentothal sodium as indicated. There was a progressively longer narcotic effect after each successive administration. In each case, death followed an unwarned sudden drop of blood pressure to the base line, sometimes before respiration had ceased. The suddenness of the blood pressure fall and the previous appearance of ectopic ventricular contractions suggest the development of ventricular fibrillation.

It is of interest that in cats with 2 or 3 repeated minimal anesthetic doses intraperitoneally, respiration continued for as long as 2 to 5 days before the unconscious animals finally died.

Summary. The first undesirable effect of a single sublethal dose of pentothal sodium is sudden cessation of respiration. Repeated administration of small amounts, sufficient to maintain light anesthesia, suddenly produces signs of heart muscle poisoning. There seems to be a definite cumulative action. Whether this is due to damage of liver tissue, or whether the drug is changed into simpler, larger dose, and longer acting forms (diethyl-barbiturate?) we are not prepared to suggest. The longer the administration is continued, the more does the threat seem to shift to the more fatal circulatory side.

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Bleeding Tendency of Obstructive Jaundice: Prothrombin Deficiency and Dietary Factors.*

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Hawkins and Whipple¹ have described in bile fistula dogs a bleeding tendency which is prevented by feeding whole bile. Hawkins and Brinkhous² showed that the bleeding is due to a prothrom-

² Gruber, Charles M., *J. Pharm. and Exp. Therap.*, 1937, **60**, 143.

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¹ Hawkins, W. B., and Whipple, G. H., *J. Exp. Med.*, 1935, **62**, 599.

² Hawkins, W. B., and Brinkhous, K. M., *J. Exp. Med.*, 1936, **63**, 795.