

cortex of newborn rats and also rises to adult levels very slowly. (3) The slow increase in the choline oxidase activity of rat liver as a function of the weight of the animal is demonstrated.

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Surgical Anesthesia in Rabbit and Dog with Intravenous Amphenone B.* (19266)

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We have previously reported that Amphenone "B"(1) has a potent depressant action on the central nervous system of the rat (2). We now report the experimental use of intravenously administered aqueous solutions of this compound to induce complete surgical anesthesia in the rabbit and dog.

Female New Zealand White rabbits and small female mongrel dogs were maintained on a stock diet. Food was removed the evening preceding operation. No preoperative medication was employed. Either a 2% or 4% aqueous solution of Amphenone "B" was employed. All injections were given by intermittent intravenous infusion beginning with a sufficient volume to induce prompt anesthesia. The surgical procedures listed in Table I were immediately performed. Supplemental doses of drug were administered intravenously as required for maintenance of surgical anesthesia.

The behavior of these animals during the course of these observations warrants the conclusion that Amphenone "B" possesses a sufficiently profound depressant action on the central nervous system to abolish pain response in the rabbit and dog. The accompanying respiratory depression is sufficiently limited to afford a substantial margin of safety in the

performance of major surgical procedures. Complete relaxation of the abdominal muscles was noted during each operation. Visceral manipulation such as traction on the uterus and exterioration of the bladder and intestines was carried out with ease and without significant effect on respiration or on the depth of anesthesia. The blood retained a normal oxygenated appearance and only the expected amount of blood loss was observed.

The rate of recovery was recorded as the length of time required for each animal to spontaneously assume an upright position. The speed with which such recovery occurred suggests that the compound is rapidly cleared from the blood.

In the rat Amphenone "B" effects a marked enlargement of the thyroid and adrenal and exerts an atypical folliculoid action on the female genital tract(3-5). In the rabbit it exhibits a weak progestational action on the uterus(4). A number of steroid compounds, notably progesterone, have anesthetic properties when administered in high dosage either intraperitoneally or intravenously(6). Accordingly, the association of anesthetic and endocrine effects in a non-steroid compound such as Amphenone "B" presents a striking parallel to the biological phenomena observed with steroids.

Summary. Intravenously administered Amphenone "B" produces surgical anesthesia in the rabbit and dog. The margin of safety is

* 1,2 bis-(p-aminophenyl)-2-methylpropanone-1 dihydrochloride.

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TABLE I. Surgical Procedures Under Amphenone Anesthesia.

Animal	Body wt (kg)	Dose for induction (mg/kg)	Length of induction (min)	Total dose (mg/kg)	Duration of total injection (min)	Duration of anesthesia (min)	Surgical procedure*	Length of operation ^T (min)	Recovery (min)
Dog 1	10.15	118	5	197	22	70	1	30	140
2	2.39	119	4	218	26	46	1, 2	24	49
3	3.5	230	4	320	27	34	1	17	82
Rabbit 1	1.98	150	3	200	4	16	1, 2	11	16
2	2.20	153	4	254	7	9	1	9	19
3	1.69	118	3	213	7	13	1	7	39
4	2.82	84	3	200	5	17	1	10	32
5	3	195	4	293	11	20	1	12	—

* 1 = bilateral ovariectomy; 2 = subtotal hysterectomy.

^T = time from incision to closure. — = not observed.

sufficient to permit complete anesthesia without major respiratory depression and with rapid recovery. The combination of endocrinological and anesthetic properties of Amphenone "B" parallels that previously observed for progesterone and other steroids.

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Effect of Amphenone "B" on Adrenal, Thyroid and Testes.* (19267)

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Recent work by Allen, Hertz, and Tullner (1,2) has shown that when Amphenone "B"[‡] (3), a substituted desoxybenzoin, was injected subcutaneously into female rabbits or given intragastrically to female rats, it produced marked thyroid and adrenal enlargement as well as progestation. The adrenomegalic effects were prevented by the administration of cortisone without reducing the goitrogenic effect and, conversely, the administration of thyroxine inhibited thyroid enlargement with-

out affecting the adrenal enlargement (4).

These observations, and the fact that Amphenone "B" did not cause enlargement of the adrenal and thyroid in hypophysectomized animals, suggested that "These responses were brought about through a pituitary mechanism similar to that by which thiouracil induces thyroid hypertrophy" (5). Whereas, the evidence indicates that Amphenone "B" increases the secretion of ACTH and TSH, the data available do not preclude the possibility of an increased production of thyroid and adrenal hormones rather than a decreased production, as would be expected in the case of a blocking agent such as thiouracil. We have extended the foregoing studies in an effort to explain more fully the alterations of thyroid and adrenal size and function and are reporting the results in this paper.

Experimental. Sprague-Dawley rats were

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[‡] 1,2-bis-(p-aminophenyl)-2 methyl propanone-1 dihydrochloride, kindly supplied by Dr. E. J. Fellows of the Smith, Kline and French Co., Philadelphia, Pa.