

Antidiuretic Effects of Inactin and Pentobarbital in Chickens. (30676)

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A large number of drugs acting on the central nervous system produce an antidiuretic effect by causing the release of antidiuretic hormone (ADH) from the posterior pituitary. For instance, morphine inhibits water diuresis (1) and this action appears to be dependent upon a functional neurohypophysis since no antidiuretic effect is produced in cases of permanent diabetes insipidus resulting from the removal of neurohypophysis.

The effect of barbiturate derivatives on water diuresis and their mode of action are similar to that of morphine in the sense that barbiturate derivatives inhibit water-diuresis in dogs by causing the release of ADH (2). However, the level of antidiuretic effect seems to depend upon the type of derivative and the animal species concerned, *e.g.*, phenobarbital inhibited the water diuresis in all the normal dogs studied by De Bodo and Prescott (2), whereas Buschke (3) reported that the same compound decreased the water diuresis in only 2 out of 7 rabbits. Amytal sodium did not inhibit the water diuresis in all the dogs even when given in the large doses and pentobarbital sodium at half anesthetic dose (16 mg/kg) inhibited the excretion of water in 50% and at full anesthetic dose (32 mg/kg) in 66% of dogs (2).

Sandoptal has been reported to increase the water diuresis in rabbits (4) but decreased the water diuresis in dogs (5). Frey and Kumpiess (6), as early as 1914, reported that barbitol-sodium decreased the water diuresis in humans and in dogs (5) in contrast to the observation by Kugel (4) that the same compound in the rabbit either increased the water diuresis or did not have any effect.

The extent of antidiuretic effect of barbiturates seems to depend upon the animal species concerned and upon the type of barbiturate derivatives employed led us to investigate the effect of pentobarbital and 5-ethyl-5 (1-methyl propyl)-2-thiobarbituric

acid, or inactin[†] (whose effect on the water diuresis of any animal species is not yet reported) on the water diuresis of the domestic chicken. There are no previous reports of barbiturate effects in this species.

Methods and materials. Thirty White Leghorn roosters weighing approximately 2 kg each were divided into 3 groups of 10 each. One group served as the control, the second group was given inactin and the third was given pentobarbital sodium.

All animals were given a load of water (5% in cc/kg body weight) *via* stomach tube and gravity flow. Birds to receive the drugs were loaded with water 5 minutes before drug administration. Initially, pentobarbital (3%) at the rate of 30 mg/kg, and inactin (5%) at 35 mg/kg were administered by the intravenous route, but to maintain the same plane of anesthesia in both groups we found an additional amount of inactin at the rate of 50 mg/kg by the intraperitoneal route at 20-minute intervals, whereas birds in the pentobarbital group required only 30 mg/kg body weight over a period of 2 hours.

Criteria used to assess the comparable plane of anesthesia in the treated groups were the closure with the nictitating membrane, the rate of respiration and the ease of plucking the neck feathers (neck feathers may be plucked very easily in anesthetized birds). After the first dose of drugs birds were put on a canine surgery board fixed at an angle. This allowed the chickens to lie at an angle. The wings and legs were tied to the rack. Birds were adjusted to the proper height on the board so that a test tube inserted inside the cloaca would just touch the table.

In order to prevent contamination of urine with fecal material a cotton plug was in-

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[†] Inactin is a German product which has not been approved for clinical use in the U. S. In Germany it is used both in animals and humans to produce a quick and ultra short duration of anesthesia. The U. S. supplier of inactin is: Henley & Co., Inc., New York.

TABLE I. Average Amount of Urine in cc Excreted in 2 Hours Based on Per Kilogram Body Weight with Standard Error of Mean (S.E.).

Group	No. of birds	Avg wt in kg $\pm$ S.E.	Avg amt of urine in cc/kg/2 hr $\pm$ S.E.
Control	10	1.59 $\pm$.065	20.92 $\pm$ 1.8
Inactin	10	1.61 $\pm$.078	3.19* $\pm$.126
Pentobarbital	10	1.56 $\pm$.069	3.01* $\pm$.51

* P < .001.

serted into the region of the cloacal valves between the copradeum and urodeum which obstructed the fecal flow into the cloaca. Urine samples were collected, measured and recorded after every $\frac{1}{2}$ hour for 2 hours. The amount of urine collected in a period of 2 hours was reported as the average amount of urine (in cc) for each group on the basis of body weight with the standard error of mean (S.E.).

Results and discussion. Chickens in the control group showed a significantly greater amount of urine excreted than did the chickens in the inactin-treated and pentobarbital-treated groups, but there was no difference in the amount of urine excreted by the birds in the latter two groups (Table I).

Our results indicate that the barbiturate derivatives have an antidiuretic effect on the domestic chicken comparable to that reported in dogs and humans. The same degree of antidiuresis produced by inactin and pentobarbital is interesting in view of the fact that the former is an ultra short and the latter a short acting barbiturate. Thus, it seems that both drugs decrease the water diuresis in chickens by a common mechanism. This mechanism in the chickens might be the same

one as demonstrated by De Bodo *et al*(2) in dogs, namely, the release of ADH from the neurohypophysis after the administration of barbiturate derivatives. However, until the effect of the barbiturate derivatives can be tested in neurohypophysectomized birds, this mechanism is not clear. Barbiturates may also inhibit water diuresis by a decrease in the glomerular filtration rate, a decrease in the renal plasma flow as a combined result of systemic hypotension and intra-renal vasoconstriction(7,8). The present data do not permit a differentiation as to the site of action of inactin and pentobarbital.

Summary. 1. The present work provides the evidence for the antidiuretic effect of barbiturates in the chicken. 2. Inactin and pentobarbital produce the same level of antidiuretic effect in the chickens if the plane of anesthesia maintained by both drugs is the same.

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1. De Bodo, R. D., J. Pharmacol. Exp. Therap., 1944, v82, 74.
2. De Bodo, R. C., Prescott, K. F., *ibid.*, 1945, v85, 222.
3. Buschke, F., Arch. f. Exp. Path. U. Pharmacol., 1928, v136, 32.
4. Kugel, M. A., *ibid.*, 1929, v142, 166.
5. Bonsmann, M. R., *ibid.*, 1930, v156, 160.
6. Frey, W., Kumiess, K., Z. f. d. ges. Exp. Med., 1914, v2, 65.
7. Goodman, L. S., Gilman, A., The Pharmacological Basis of Therapeutics, 2nd Ed., Macmillan Co., 1955, p132.
8. Mylon, E., Winternitz, M. D., Sütönagy, D. J., Am. J. Physiol., 1943, v139, 313.

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