TABLE I. Frequency of Defecation, Nausea and Vomiting in Dogs After Subcutaneous Injections of Dromoran and Morphine.

Dromoran, mg/kg	Defecation	Nausea	Vomiting	Morphine, mg/kg	Defecation	Nausea	Vomiting
.5	8/27 (29.8%)	—	1/27 (3.7%)	2.5	4/7 (57.2%)	—	3/7 (42.9%)
1	27/39 (69.3%)	22/39 (56.4%)	1/39 (2.6%)	5	27/51 (53%)	13/19 (68.3%)	23/51 (45.1%)
2	5/11 (45.4%)	2/11 (18.2%)	0/17 (0%)	10	4/7 (57.2%)	5/7 (71.5%)	3/17 (17.7%)

injection. A total of 83 injections of Dromoran and 75 injections of morphine were made subcutaneously using concentrations of 1% and 4%, respectively. The animals were watched for not less than one-half hour after injection, at which time all of the animals were depressed except one. This dog was excited by both Dromoran and morphine. At first the animals were watched only for vomiting, but later in the experiment observations were also made on defecation and nausea, as expressed by vomiting or salivation.

Results. Only 2 animals (or 2.4%) of the entire group receiving Dromoran vomited, whereas 29 (or 38.7%) of those receiving morphine vomited. Dromoran and morphine caused defecation in 52% and 54% of the animals, respectively (Table I).

Conclusions. In doses calculated to have about the same analgesic effect Dromoran produces much less vomiting in dogs than does morphine. These doses produce defecation in equal frequency.

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Initial Effects of Pentobarbital Sodium on Water Diuresis in Dogs. (19226)

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Although experimental data have appeared in the literature concerning the effects of pentobarbital sodium and other barbiturates on water diuresis no mention has been made of the early effects of the drugs when administered rapidly in anesthetic doses. In previous studies the urine rate was determined over prolonged periods and these long collection periods masked any early response of the kidney that may have occurred. A method of recording urine rates accurately over short periods is necessary if the immediate effects of the drugs on urine output are to be studied. Such a method was employed in the present study. It has been possible, therefore, to analyze the results in terms of immediate and delayed responses.

Methods. Trained female dogs, weighing 12-14 kg, were used in these experiments. The animals had access to water up to the time of the experiment but had been without food for 24 hours. Approximately 40 minutes before recording data on urine flow the dog was given 250 cc of water by stomach tube and a short time later was loosely restrained on a dogboard in a supine position in a cool, quiet room. One ureter was catheterized according to the method described previously(1) and the urine rate was determined by observing the drops of urine issuing from the catheter and recording on a kymograph. With high urine rates the volume output was determined by measuring the urine at 2-minute intervals in a 10 cc graduate. After the diuresis was

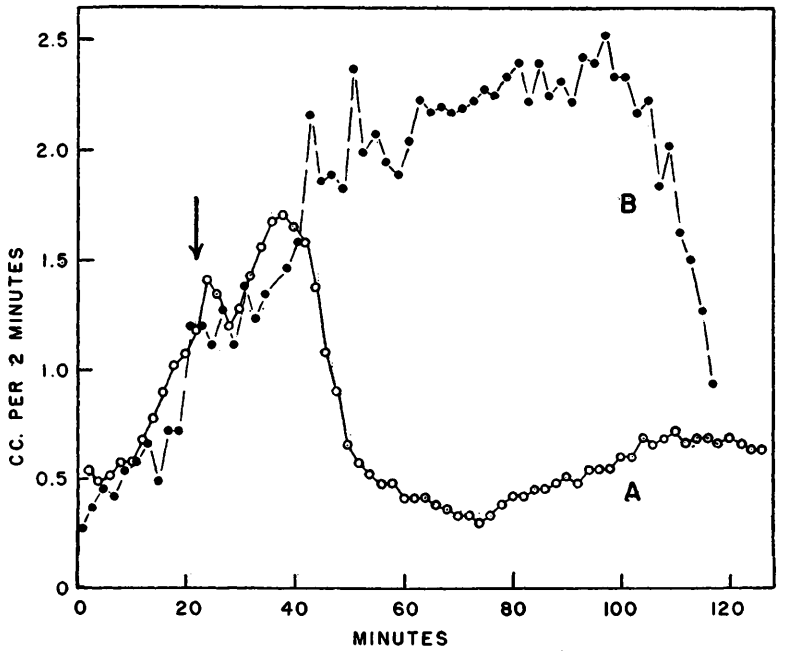

FIG. 1. Effect of pentobarbital sodium on water diuresis in dog. Curve A: Animal received 27 mg of anesthetic per kg intravenously at arrow. Curve B: Water diuresis in same dog without anesthesia. Animal received 250 cc water by stomach tube in both experiments at minus 37 min. Each point on curve is urine output from one kidney for preceding 2 min.

well-established pentobarbital sodium (Nembutal, Abbott) in a dose of 27 mg per kg body weight was administered intravenously within a period of 10 seconds. At no time during the injection was the determination of the urine rate interrupted. The recording continued until the animal showed definite signs of recovering consciousness. Because both kidneys normally respond alike to water diuresis, a response verified in these same dogs earlier (1), only one ureter was catheterized and the urine rate from one kidney determined. By alternating the ureter catheterized in a series of experiments it was possible to use a dog more often because with less frequent catheterization trauma to a ureter was minimized.

Results. A total of 24 experiments were carried out on 5 dogs, 20 studying the effects of the anesthetic on water diuresis and four controls without anesthesia. Curve A of Fig. 1 presents the data from a representative experiment. Shortly after the anesthetic was injected an inhibition of the diuresis occurred. This initial inhibition was temporary and gave way to a continuation of the diuresis. A second and prolonged inhibition occurred which gradually disappeared as the dog recovered consciousness. Fourteen of the 20 experiments with anesthesia showed the initial temporary antidiuresis which was followed by the prolonged antidiuresis. In the remaining 6 experiments the animals responded with the prolonged antidiuresis only. This delayed and prolonged inhibition of diuresis was so pronounced in 8 of the experiments that no recovery of urine rate was noted even though the recording continued in some experiments for 160 minutes after the anesthetic was administered.

Curve B represents the diuretic response in the same dog to an equal volume of water but without anesthesia. Although the urine rate showed fluctuations the diuresis lasted for more than 120 minutes without any definite temporary or permanent inhibition. Considering the fact that the animal was unanesthetized during the entire period and that the rate was determined every 2 minutes, the urine output followed a fairly smooth curve, a response which was the general rule provided

the animal remain quiet and undisturbed.

In 4 experiments on 2 dogs in this series blood pressure was recorded with a mercury manometer by direct femoral arterial puncture before, during and for a short time after the injection of the anesthetic. No urine rates were determined in these experiments. A precipitous fall in pressure of from 20 to 40 mm occurred immediately after each injection but the hypotension periods did not persist longer than 20 minutes. This temporary hypotension is the response generally seen when anesthetic doses of pentobarbital sodium are given quickly by vein.

Discussion. That anesthetic doses of barbiturates generally inhibit water diuresis in animals has been reported previously. But the mechanism of this inhibition is still a debatable issue. From the review of the literature by deBodo and Prescott(2) it appears as if the usual response of the water diuretic dog to anesthetic doses of barbiturates is an inhibition of the diuresis. From their own experiments deBodo and Prescott(2) reported that phenobarbital sodium given intravenously to water diuretic dogs in doses of 40, 80, and 110 mg per kg inhibited the diuresis in every normal dog studied; but when amytal sodium or pentobarbital sodium was given, even in full anesthetic doses, the inhibition of water diuresis occurred in only some of the dogs. The antidiuretic effect of the barbiturates was not present in dogs with the entire neurohypophysis destroyed and which showed a permanent diabetes insipidus. Silvette(3) reported that anesthetic doses of pentothal sodium inhibited the diuresis resulting from intraperitoneal injections of 0.2% NaCl solution in normal and hypophysectomized rats. He attributed the antidiuretic effect to the hypotension produced by the anesthetic and not to any increased secretion of the antidiuretic hormone (ADH). deBodo and Prescott(2) contend that in Silvette's animals not all of the neurohypophysis was removed because no permanent polyuria occurred in the animals and an increased secretion of ADH could still take place with anesthesia.

Just how the increased secretion of ADH during anesthesia occurs is a moot point. Fee(4) postulated that in the normal animal there is a mechanism which inhibits the secretion of the ADH and that anesthesia removes this inhibition and brings about an increased secretion of the hormone. Pickford(5) concludes that the inhibition of water diuresis in most cases of anesthesia is due, in part, to an increased secretion of the ADH.

Because of the rapidity with which the diuresis was initially and temporarily inhibited, and with the simultaneous fall in blood pressure, it is probable that the first antidiuresis in the present work is the result of a hypotension as suggested by Silvette(3). Although only 4 blood pressure determinations were made in these trained animals the hypotension which results from quick intravenous injections of pentobarbital sodium has been verified repeatedly in laboratory animals. The delayed and more prolonged antidiuresis can be attributed to an increased secretion of the ADH since it is present even though the general systemic blood pressure is at or near normal levels.

Summary. The intravenous injection of an anesthetic dose of pentobarbital sodium into 5 trained dogs showing a water diuresis produced a quick temporary inhibition of the diuresis in 14 of 20 experiments. The urinary rate recovered and approached the diuretic rate but a second and more prolonged inhibition of the diuresis occurred. The remaining 6 of the 20 experiments showed an immediate and prolonged inhibition of the diuresis. In 12 of the 20 experiments the urinary rate at the time the experiment was concluded was beginning to recover. The immediate temporary antidiuresis could be correlated in time of onset and duration, with a period of hypotension that followed each dose of anesthetic. The delayed prolonged antidiuresis was not correlated with hypotension and is believed to be due to increased liberation of antidiuretic hormone.

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