THE VALUE OF ARTIFICIAL RESPIRATION IN PENTOBARBITAL POISONING OF RABBITS *

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BURSTEIN and Rovenstine have stated that the only proven resuscitative measure in the combating of lethal doses of barbiturates is effective artificial respiration (1, 2). More recently, Eckenhoff, Schmidt, Dripps and Kety (3), discussing the use of analeptics in drug depressions, emphasized the inclusion of artificial respiration in any schedule of therapy.

These observers have based their opinions upon clinical experience and observation. Recently, during the course of a laboratory study of analeptic agents, we were impressed by the efficacy of adequate pulmonary ventilation in overcoming acute barbiturate depression.

We have attempted to verify this impression and evaluate in a quantitative fashion the extent to which artificial respiration can affect the course of acute barbiturate depression in the rabbit.

METHOD

The general plan of the experiment was as follows: A dose of pentobarbital sodium in excess of 35 mg per kilogram, the LD_{50}, was injected into the marginal ear vein of the animal. Following this, the animal was placed upon an animal board in the supine position. When voluntary respirations ceased (usually one to three minutes following the barbiturate injection) the animal board was placed over a fulcrum and tipped through an arc of 90 degrees, in effect, acting as an Eve rocking apparatus (4). The board was tipped to give a respiratory rate approximately two-thirds as rapid as that of the normal unanesthetized animal. Artificial respiration was continued until the animal resumed spontaneous breathing. Following this, the animal was removed from the board and the time until spontaneous resumption of the prone position, "awakening," was noted.

Blood specimens were obtained by cardiac tap before, during, on completion of the artificial respiration, and upon "awakening." The blood was analyzed for barbiturate content by the method of Goldbaum (5).

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RESULTS

The data are summarized in table 1 and figure 1. The rate of metabolism of pentobarbital, as judged by its disappearance from the circulating blood, is rapid in the rabbit while under artificial respira-

TABLE 1

THE METABOLISM OF PENTOBARBITAL BY THE RABBIT MAINTAINED BY ARTIFICIAL RESPIRATION

Rabbit, No.	Dose, mg./kg.	Duration of Artificial Respiration, minutes	Blood Level of Pentobarbital		Pentobarbital Metabolized during Artificial Respiration, per cent
			At Beginning of Artificial Respiration, mg./100 cc.	At Conclusion of Artificial Respiration, mg./100 cc..	
2	35	20	3.80	2.95	22.3
X-1	35	20	3.25	2.95	9.2
M40	40	40	3.80	2.30	39.5
P51	40	30	5.90	4.10	30.5
13	40	15	4.00	3.00	25.0
14	50	53	6.10	2.70	55.7
17	50	27	5.70	3.30	42.1
18	50	25	5.40	3.60	33.3
21	50	27	4.40	2.90	34.1
132	60	40	6.20	3.10	50.0
Mean		29.7	4.86	3.10	34.1

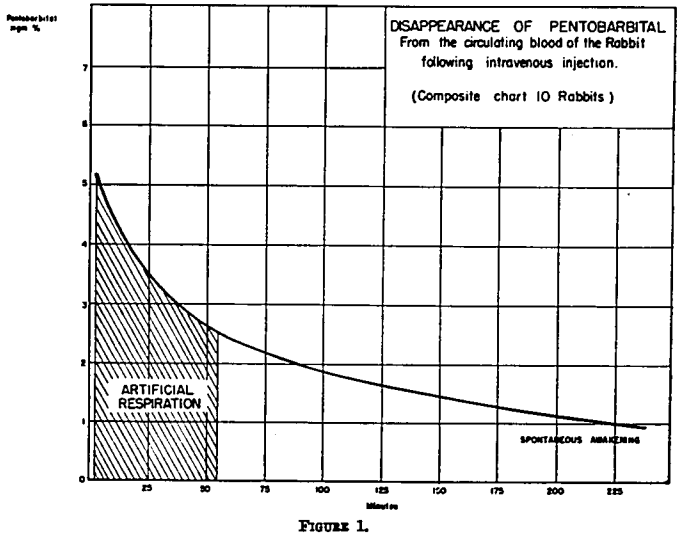

FIGURE 1.

tion. Between 9.2 and 55 per cent (mean = 34 per cent) of the pentobarbital was metabolized during the first thirty to forty minutes of anesthesia. This period includes most of the time spent under artificial respiration. A comparable group of rabbits receiving a nontoxic (30 mg. per kilogram) dose of pentobarbital metabolized 26 per cent of the barbiturate during the same time interval. The blood level at the time of awakening was 1.20 ± 0.1 mg. per 100 cc. This agrees closely with the 1.16 ± 0.04 mg. per 100 cc. obtained as awakening blood level in a large series of animals which had received nontoxic doses of pentobarbital.

Furthermore, when the blood level had fallen to 3.1 ± 0.5 mg. per 100 cc. all of the animals resumed normal spontaneous respiration and continued to "awakening" without further aid. No mortality studies were attempted, but it should be noted that although these animals received a dose of barbiturate at or above the LD_{50} level they all survived merely by the insurance of adequate pulmonary ventilation. In our experience, when artificial respiration was not undertaken within one to two minutes following the cessation of respiration the animals invariably died.

SUMMARY

The breakdown of pentobarbital following intravenous injection in the rabbit has been studied.

It has been found that the rabbit will tolerate toxic doses of pentobarbital providing adequate pulmonary ventilation is maintained. It has been further demonstrated that the metabolism of pentobarbital, as evidenced by the disappearance of the drug from the circulating blood, continues while the animal is maintained under artificial respiration.

The basic importance of maintenance of adequate pulmonary ventilation in the therapy of barbiturate depression is affirmed.

We wish to express our appreciation to the Abbott Pharmaceutical Company for the sodium pentobarbital used in this study.

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