EFFECT OF PENTOBARBITAL SODIUM ON HEMOGLOBIN AND HEMATOCRIT VALUES IN GUINEA PIGS

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THE USUAL hypnotic doses of barbiturates seem to have little effect upon the cardiovascular system. There may be a slight fall in blood pressure and heart rate, but this may be due to the quieting action or sleep induced by the drug. It has been held, generally, that neither the cell counts, hematocrit determination, nor hemoglobin values of blood change significantly under hypnotic doses of these drugs. Searles (1) and others (7, 8) report significant decreases in hemoglobin, erythrocyte count and cell volume in dogs anesthetized with amobarbital, while Graca and Garst (2) later report transient decreases only after pentobarbital.

We wanted to learn whether any changes in hemoglobin content and cell volume might be occurring in our pregnant guinea pigs during delivery under pentobarbital at dosage levels sufficient to induce surgical anesthesia.

METHOD

Pregnant and nonpregnant, adult guinea pigs weighing between 500 and 1,100 Gm. were divided into the following four categories: group 1, 14 nonpregnant animals each given a single dose (28 mg./kg.) of pentobarbital (Veterinary Pentobarbital Sodium, Abbott); group 2, 7 pregnant animals given the same amount of the drug one to two days before expected delivery; group 3, a control group of 8 nonpregnant animals given 0.44 cc. of normal saline per kilogram of body weight; and group 4, 7 nonpregnant, splenectomized animals given the same single dosage of drug (28 mg./kg.) 5 days after splenectomy.

Before intrathoracic injection of the drug, or the saline, a blood sample (0.4 to 0.7 cc.) was drawn from the left side of the heart of each animal. After allowing thirty to forty-five minutes for drug action, a second sample was drawn from the heart. The thoracic cavity was never opened so that all animals were intact and continued to live with no untoward results after the experiment.

For hemoglobin determinations, 0.1 cc. of blood was diluted to 50 cc. with distilled water to which had been added 3 drops of potassium ferrocyanide, 3 drops potassium cyanide, 2 drops of concentrated ammonium hydroxide, and 5 cc. of phosphate buffers at *p*H 6.8. Readings were made in an Evelyne colorimeter. Hematocrit values were determined in the standard clinical manner using micro methods.

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Results

Table 1 gives the mean values, as well as the range of values, found in each of the groups for both hemoglobin and hematocrit determinations. Groups 1 and 2 show a consistent decrease in mean values after drug administration. Only one animal (see notation in group 1 of the table) showed an increase in hematocrit over its control value. The differences between the group means before and after drug administration are significant at the 2 per cent level of confidence. The decrease is greater in pregnant animals than in any of the other groups.

The saline control group showed no changes in values with passage of time. On the other hand, the splenectomized group continued to

TABLE 1

Effect of Pentobarbital Sodium on Hematocrit and Hemoglobin Values in Guinea Pigs

Group Number	Hematocrit (per cent)				Hemoglobin (Gm./100 ml.)			
	Normal		Anesthetic		Normal		Anesthetic	
	Mean	Range	Mean	Range	Mean	Range	Mean	Range
1	39.71	35.3–44.5	36.40	31.7–48.2*	13.28	12.18–14.96	12.24	10.33–13.96
2	43.40	39.2–48.3	36.82	31.0–43.0	14.29	13.00–16.03	12.51	9.55–14.86
3	40.35	37.5–43.5	40.23	36.7–†45.5	13.59	12.45–14.45	13.67	12.36–†15.06
4	38.60	32.5–44.7	34.10	31.0–42.1	12.64	10.33–14.86	11.59	10.09–14.35

* The value 48.2 represents the sole instance where the hematocrit value after drug showed an increase over the control level.

† No anesthetic. Second sample values forty-five minutes after placebo injection.

register decreases both in hematocrit and hemoglobin after drug administration. These latter differences were significant at less than 2 per cent level of confidence.

Discussion

Alterations in the blood solids after the administration of various anesthetics have been noted by various workers for some time. Hamburgher and Ewing (3) in 1908 pointed out that a hemoconcentration of 10 to 15 per cent occurred routinely in dogs after ether anesthesia. In 1924, Barbour and Bourne (4) showed that the increase in blood solids after ether was not this pronounced if the experimental dogs were fasted but allowed their drinking water. Later, Bourne (5) demonstrated that increases in environmental temperature to 33 C. or the

prior injection of morphine protected dogs entirely against the hemoconcentration effects of ether. Drabkin and Edwards (6) could find no change in blood solids with the administration of sodium amobarbital, but Bourne, Bruger and Dreyer (7), in 1930, did find a definite decrease in blood solids in both dogs and man when sodium amobarbital was used. They also observed what they took to be splenic enlargement when phenobarbital was the anesthetic employed. They suggested, therefore, that the decreases in cell counts, hematocrit, and hemoglobin that were noted under sodium amobarbital were probably due to splenic dilatation effected by the drug. Adolph and Gerbasi (8), in 1933, confirmed the decrease in blood solids with sodium amytal.

In 1939, Searles (1) investigated the effects of splenectomy upon these blood changes after anesthesia and concluded that the increase in solids after ether was inhibited somewhat by splenectomy, but that the decrease with sodium amytal failed to occur in splenectomized dogs. The entire experiment, however, was run on only 3 dogs, and sodium amobarbital administration always followed some days after ether administration in the same dog both before and after the same animal had been splenectomized. One might wish for a greater population and a division of the population into clear-cut ether and sodium amytal groups before accepting the hypothesis that decreases in blood solids after amobarbital are due to splenic dilatation in response to the drug. Hargis and Mann (9) were unable to abolish splenic contraction after ether in dogs with denervated spleens. However, it may be that Emerson (10) is correct when he suggests that the splenic reflex under ether may not be dependent upon neural mechanisms but rather upon the action of adrenalin on the spleen when the adrenal is stimulated by the anesthetic.

More recently, Graca and Garst (2) studied the early blood changes in 12 dogs after intravenous pentobarbital anesthesia. The chief finding was a striking leukopenia, with cells 20 per cent below control value within ninety minutes of drug administration. There were transient decreases in red blood cell counts, hematocrit, and hemoglobin determinations all of which were back to normal levels or greater than normal levels in 190 minutes. This is a far earlier recovery than the six and one-half hours that Hausner, Essex, and Mann (11) report necessary for the spleen to return to normal size after ether, pentobarbital sodium, or pentothal sodium anesthesia.

These studies in the dog make us suspect that our decreases in hemoglobin and hematocrit in guinea pigs are valid, and that they are not due to a splenic reflex mechanism. Certainly, we cannot confirm Searles' (2) findings on splenectomy in our guinea pigs. For some reason, the effects are greater in pregnant animals. It is doubtful whether any great shift in electrolyte balance or blood acidity occurred in the interval between our blood samplings to offer some alternate explanation for these decreases.

Summary

In a group of 14 nonpregnant guinea pigs given a single dose (28 mg./kg.) of pentobarbital, ample for the induction of surgical anesthesia, there was a consistent and significant decrease in hemoglobin and hematocrit values forty-five minutes after intrathoracic injection of the drug as compared with predrug values. Similar results were obtained from a group of 7 pregnant guinea pigs (65 days gestation; term 67 days) except that postdrug values were even lower than in nonpregnant animals. The group of 8 nonpregnant animals receiving a placebo injection of physiological saline showed no changes in hemoglobin or hematocrit forty-five minutes after injection.

A group of 7 splenectomized, nonpregnant animals continued to register significantly decreased values after drug administration. If splenic dilatation is a mechanism which accounts for decreases in cell count and cell volume after administration of phenobarbital, pentobarbital, pentothal, and amobarbital in some animals, and if splenectomy prevents such decreases from occurring, this mechanism is not functioning in the guinea pig.

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