CIRCULATORY COLLAPSE FOLLOWING THE COMBINED USE OF PITUITRIN* AND PENTOTHAL†‡

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The fact that barbiturate anesthesia has a definite catalytic effect in the production of collapse when combined with pituitrin has been verified experimentally. Raginsky and his associates noted that several animals under barbiturate anesthesia succumbed to comparatively small doses of pituitrin (1). Koppanyi stated that in his work with barbiturates he had noticed an increased incidence of pituitrin shock (2). Melville found that dogs under phenobarbital were especially sensitive to pituitrin (3). With the popularity of pentothal anesthesia alone or in combination with other agents for many obstetrical and gynecologic procedures in which pituitrin is used, this experimental evidence assumes added importance.

Pituitrin shock, as this state of collapse has been identified previously, has been shown to be a definite clinical entity (4). Its occurrence has been recorded for the most part in patients undergoing anesthesia and operation. We have had, in our experience, 2 patients in whom severe shock developed in the presence of the combination of pituitrin and pentothal and undoubtedly there were many others which were unidentified. These patients received only 10 units (1 cc.) of a standard posterior pituitary preparation (pituitrin) while under pentothal hypnosis. Repeated injections of similar amounts after recovery from pentothal showed no recurrence of the shock.

MECHANISM OF ACTION

Pituitrin, posterior pituitary extract, contains an oxytocic and a pressor factor. The oxytocic factor, called pitocin, stimulates the myometrium while the pressor factor, called pitressin, constricts capillaries and small arterioles. Pituitrin shock appears to be the end result of the pressor factor on the coronary arteries (5–8). The myocardium undergoes an anoxic dilatation (9) which decreases cardiac output, and

* Posterior pituitary extract.
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produces a clinical picture of primary shock, that is, hypotension with bradycardia. The peripheral effect of the pressor factor is noted clinically in the pale skin but the hypertensive state, usually seen in peripheral vasoconstriction, is overbalanced by the central cardiac depression.

The role of pentothal in precipitating pituitrin shock is not specific. The experimental evidence of Raginsky (1) and Melville (3) and the more recent work of Masson (10), who showed pentothal anesthesia to be prolonged twofold with pituitrin, does not too clearly define the action. Phenobarbital, which differs from pentothal chiefly in duration of action (11), seems to have a direct depressant action on the myocardium. It has been shown that the force of ventricular contractions decreases when the cardiac muscle is perfused with barbiturate solution (1). Phenobarbital also dilates the heart which in turn weakens contractions. Furthermore, pentothal anesthesia may decrease the oxygen saturation of the blood by causing respiratory depression (12).

From the evidence presented it would seem that there are two factors producing myocardial anoxia: (1) pituitrin action through coronary constriction and (2) pentothal acting through direct myocardial depression. Together, in clinical dosage, they may produce shock. Two case reports of such an incident are presented.

**Reports of Cases**

**Case 1.**—A 25-year-old white woman was admitted to the U. S. Naval Hospital, Bethesda, Maryland, on February 9, 1948, with a history of intermittent vaginal bleeding following a spontaneous abortion on December 14, 1947. Physical findings revealed the blood pressure to be 130 mm. systolic and 75 mm. diastolic, pulse 80 and respirations 18. Erythrocytes numbered 3,200,000, leukocytes 10,050 per cubic millimeter and hemoglobin 9.75 Gm. per 100 ml. of blood. On February 11, 1948, at 6:30 a.m. the patient was given nembutal, 3 grains (0.180 Gm.). At 8 a.m. the patient was taken to the operating room and at 8:25 a.m. anesthesia was induced with pentothal. The dilatation was begun at 8:30 a.m. and ergotrate 1 cc. and pituitrin 1 cc. (10 units) were administered by intramuscular injection. The procedure required approximately five minutes and 15 cc. of a 2.5 per cent solution (375 mg.) of pentothal was given. The patient was responding when she left the operating room. Upon her return to the ward at 9 a.m. her blood pressure was 90 mm. systolic and 45 mm. diastolic. At this time the nurse noted that the patient would not respond, her color was poor, her pulse was weak and her respirations were shallow. At 9:05 a.m. the blood pressure was not perceptible. Analgesics, caffeine sodium benzoate and euramine, were given with slight transient improvement in general appearance, and an intravenous infusion of 5 per cent glucose in physiologic saline solution was begun. At 10 a.m. the blood pressure was recorded at 96 mm. systolic and 68 mm. diastolic and the patient was responding. Beginning at 3 p.m. that day pituitrin, 1 cc. (10 units) was given every four hours for six doses without untoward effect. The patient was discharged the following day with no complaints.

**Case 2.**—A 28-year-old white woman was admitted to the U. S. Naval Hospital, Bethesda, Maryland, on February 10, 1948, with a chief complaint of menor-
Rhabia and dysmenorrhea. Physical findings were essentially normal, the blood pressure was 128 mm. systolic and 84 mm. diastolic, and the laboratory findings showed a negative urine and 4,500,000 erythrocytes, 750 leukocytes per cubic millimeter and hemoglobin 13 Gm., per 100 ml. of blood. On February 13, 1948, she was given the following premedication: nembutal, 3 grains (0.180 Gm.) at 8:15 a.m., morphine sulfate, 1/6 grain (0.010 Gm.), and scopolamine, 1/200 grain (0.003 Gm.), at 9:15 a.m. At 10:15 a.m. the patient was taken to the operating suite. At 10:25 a.m. anesthesia was induced with pentothal. Ergotrate and pituitrin, 1 cc. each, were administered intramuscularly and dilatation and curettage was performed. Pentothal 12 cc. of a 2.5 per cent solution (300 mg.) was given. The patient returned to the ward at 10:40 a.m., responding readily. At 11:10 a.m. the patient looked very pale. The blood pressure was 77 mm. systolic and 48 mm. diastolic, the pulse was 78, and respirations were shallow and slow. At 11:15 a.m. the blood pressure was unobtainable, the pulse was 60 and very faint. The patient's color was white, but she was not cyanotic and she made no response to painful stimuli. The nurse, fearing the patient to be near death, instituted artificial respiration. The condition was diagnosed as "acute barbiturate poisoning" and coramine was given intravenously and intramuscularly. An infusion was started. The patient remained in the condition for approximately sixty minutes before she began to respond. At 12:30 p.m. the blood pressure was 88 mm. systolic and 32 mm. diastolic and the pulse was 48, but she was still very pale. By 2:30 p.m. the blood pressure was 120 mm. systolic and 80 mm. diastolic and the pulse was 74. Pituitrin therapy was again instituted at 2 a.m. on February 14, 1948, without further difficulty.

Discussion

Circulatory collapse after procedures such as those reported go unrecognized because the onset is usually after the patient has returned to the ward. Although the patients respond after the anesthetic has been discontinued, they remain under the influence of pentothal for some time. The maximum action of pituitrin develops thirty to forty-five minutes after intramuscular injection and may coincide with residual pentothal depression. Shock unaccompanied by trauma or acute hemorrhage may be justifiably attributed to medication. The clinical picture presented is identical with that of pituitrin shock produced by larger doses, as seen by Adelman and Lennon (4) and experimentally by Kolls and Geiling (9). In view of the absence of shock with subsequent doses of pituitrin it may be that the pentothal potentiates the pituitrin and that the two drugs should not be used simultaneously. If the condition should present itself the corrective treatment consists of oxygenating the patient and administering epinephrine or ephedrine to counteract specifically the coronary constriction (7). To avoid its development, pitocin, the oxytocic factor, or ergonovine would seem to be a more suitable drug than pituitrin for the desired effect.

Summary and Conclusion

Two cases of circulatory collapse following administration of 10 units (1 cc.) of pituitrin in the presence of pentothal anesthesia are
reported. A discussion of the mechanism of production of shock with the accentuating factor of hypoxia and direct myocardial depression from the barbiturate is given to substantiate our opinion that pentothal and pituitrin should not be given simultaneously. In obstetric and gynecologic surgery, where pentothal anesthesia has found great favor, substitutes for pituitrin must be used to avoid shock.

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