10348

Studies of Blood Volume in Ergotamine Tartrate Poisoning in Rats.

J. Q. GRIFFITH, JR.,* B. I. COMROE AND C. J. ZINN.

From the Robinette Foundation, the Medical Clinic and the Endocrine Section of the Hospital of the University of Pennsylvania.

McGrath[1] described gangrene of the tail in rats given ergotamine tartrate in toxic dosage. He quoted Polak[2] as having demonstrated that lumbar sympathectomy rendered the rat more susceptible to such gangrene. Rubin and Rapoport,[3] studying vascular hypertension in rats poisoned by ergotamine tartrate noted gangrene of the tail in most of their animals. None of these authors reported blood volume findings.

Albino rats were used in the present study. Blood volume was measured by the dye method of Griffith and Campbell.[4] The normal value by this method ranges between 4.0 and 5.3 cc per 100 g body weight, averaging 4.3 cc. Systolic blood pressure was measured under ether anesthesia by the indirect method of Griffith.[5] The normal blood pressure by this method does not exceed 150 mm of mercury. Ergotamine tartrate† was given subcutaneously in doses varying from 1.5 to 3.0 mg per 100 g body weight.

Six normal rats given 1.5 mg per 100 g body weight of ergotamine tartrate had normal blood volumes on the 5th and again on the 12th days. None developed gangrene of the tail. Blood pressure was not measured.

Blood volume measurements were made on 18 animals approximately 2 weeks after bilateral lumbar sympathectomy. The range was from 4.1 to 6.0 cc per 100 g, averaging 4.9. Seven of the 18 animals were above and 11 were within normal limits. Thus there is a tendency toward increased blood volume 2 weeks after bilateral lumbar sympathectomy.

Twenty sympathectomized animals and 21 normal animals were

---

* Atwater Kent Fellow in Medicine.

1 McGrath, E. J. G., *Arch. Int. Med.*, 1935, **55**, 942.

2 Polak, E. (quoted by McGrath), *Casop. lek. cesk.*, 1924, **63**, 1409.

3 Rubin, M. L., and Rapoport, M., *Arch. Int. Med.*, 1937, **59**, 714.

4 Griffith, J. Q., Jr., and Campbell, R., PROC. SOC. EXP. BIOL. AND MED., 1937, **36**, 38.

5 Griffith, J. Q., Jr., PROC. SOC. EXP. BIOL. AND MED., 1934, **32**, 394.

† The ergotamine tartrate was supplied through the courtesy of the Sandoz Chemical Works.

given 2.5 mg of ergotamine tartrate per 100 g body weight. Five of the normal animals and 12 of the sympathectomized animals developed gangrene of the tail. Blood volume was measured in 20 of the normal animals on the twelfth day following the injection. This was normal or slightly increased in 11 animals, and definitely reduced in 9 animals, ranging from 2.8 to 3.9 cc. All 5 animals with gangrene of the tail had lowered blood volume. Blood volume was again measured in the 8 survivors of this group on the 19th day after ergotamine tartrate. This was either normal (1 animal) or elevated (7 animals), the latter including one animal with healed gangrene. Blood volume measured on the eleventh day after the injection in 18 of the sympathectomized animals, was normal in 7 animals and reduced (2.7 to 3.9 cc) in 11 animals. All surviving animals with gangrene of the tail (10 animals) had lowered blood volume. On the 19th day after injection the 5 survivors, 4 of which had healed gangrene of the tail, had normal (2 animals) or elevated (3 animals) blood volume. Thus Polak's[2] observation that lumbar sympathectomy predisposes to gangrene of the tail was confirmed. In addition, it was found that this gangrene was regularly associated with diminished blood volume, which returned to normal or above after healing occurred.

Blood pressure was measured on the eleventh or twelfth day after injection of 2.5 mg of ergotamine tartrate per 100 g body weight in 9 normal and 8 sympathectomized animals, and again on 4 of the survivors on the 19th day. On the eleventh or twelfth day 7 were hypertensive, with blood pressures ranging from 150 to 240 mm of mercury, while 11 had normal pressures. Blood volume was normal or somewhat elevated in 7 animals, all of which had normal blood pressure. Blood volume was reduced in 10 animals, 3 of which had normal and 7 elevated blood pressures. No animal was hypertensive with normal or elevated blood volume. On the 19th day, the 4 animals which had previously had the highest blood pressures now had normal pressures and normal or slightly increased blood volume. Thus, hypertension was found to be regularly associated with diminished blood volume, which returned to normal or above when the blood pressure fell to normal.

Twelve normal animals were given 3.0 mg of ergotamine tartrate per 100 g body weight; 1 or 2 animals were used for blood pressure and blood volume measurements daily. The experiment was discontinued by the eighth day because of the death or poor condition of the animals, but it was found that the hypertension and the diminished blood volume appeared by the 6th day.

In 8 animals with diminished blood volume the rate of disappearance of the dye from the blood stream was followed. It was found to be normal. The finding of the diminished blood volume was, therefore, not an error due to delayed mixing of injected dye.

The primary vascular effect of ergotamine tartrate poisoning may be thought to be a generalized vascular spasm. This results in a diminished blood volume, which may occur alone or in association with either gangrene of the tail or vascular hypertension, or both. The localized vascular dilatation which follows bilateral lumbar sympathectomy tends to raise general blood volume. It also makes the tail more susceptible to the gangrene of ergotamine tartrate poisoning.

10349

Observations on the Mode of Action of Sulfanilamide *in vitro*.

CAROLINE A. CHANDLER AND CHARLES A. JANEWAY.* (Introduced by Hans Zinsser.)

From the Department of Obstetrics and the Department of Bacteriology and Immunology, Harvard Medical School, Boston.

The bacteriostatic effect of sulfanilamide *in vitro* has been demonstrated by many workers and there is little doubt that it plays an important part in the action of the drug *in vivo*. The experiments reported in this paper were designed to analyze some of the factors that play a rôle in this bacteriostatic action.

Methods. For the sake of uniformity, a single strain was used throughout. This strain, obtained through the courtesy of Dr. Rebecca Lancefield, was a group A, type 6, mucoid, hemolytic streptococcus, designated S 43. Unless otherwise stated, the medium used was neopeptone-water[1] to which horse serum was added to a final concentration of 25%. The concentration of sulfanilamide† was 10 mg %. Bactericidal and phagocytic experiments were performed according to the technics described by Ward[2] and Ward and Lyons.[1] Defibrinated human blood containing no antibody to this particular strain was employed. In the phagocytic

* Work done under tenure of the Edward Hickling Bradford Fellowship.

1 Ward, H. K., and Lyons, C., *J. Exp. Med.*, 1935, **61**, 515.

† Sulfanilamide obtained through the courtesy of the Research Department of the Winthrop Chemical Co.

2 Ward, H. K., *J. Exp. Med.*, 1930, **51**, 675.