with the vasopressor hormone of the neurohypophysis of oxen. In the quantitative determination of arginine vasopressin in an extract either type of assay could be employed. With the isolation of another naturally-occurring vasopressin which has a 1:6 murine vasopressor-canine antidiuretic ratio of doses, assays for antidiuretic hormone must take into account the source of the preparation, the species used for assay and the route of administration. The low potency of lysine vasopressin as an antidiuretic agent in the dog could be attributed to a difference in the response of another species. This explanation is untenable as a general statement because the vasopressor potency of lysine vasopressin, in comparison with the U.S.P. standard, is the same in the rat and dog.

Other investigations, some of which are still in progress, indicate that extracts of the neurohypophysis of man, the monkey, dog, rat, ox, sheep and camel, when assayed by intravenous methods, show a 1:1 ratio for vasopressor and antidiuretic potencies. The work described in this paper suggests that arginine vasopressin is the principal if not the only neurohypophyseal hormone responsible for these actions in the above mentioned species.

Summary. 1. The pharmacological effects of lysine and arginine vasopressins are the same with respect to their relative vasopressor, milk-ejecting and avian depressor potencies. 2. The ratio of pressor potency to antidiuretic potency is 1 for arginine vasopressin and 6 for lysine vasopressin when the antidiuretic potency is determined by intravenous injection in the hydrated, unanesthetized dog. On the other hand, this ratio of potencies is 1 for both vasopressins when the antidiuretic potency is determined by subcutaneous injection in the hydrated, unanesthetized rat. 3. Lysine vasopressin, compared with the U.S.P. standard or arginine vasopressin, is equally potent as an intravenous pressor agent in the dog and rat. Potency refers to *relative* potency; potency in units per mg is much higher for purified arginine vasopressin. 4. Lysine vasopressin is peculiar to the hog. The vasopressin of man, the macaque monkey, dog, rat, ox, sheep and camel appears, by pharmacological criteria, to be arginine vasopressin. These conclusions are tentative and must be confirmed by the isolation of the hormone from each species, other than the ox and hog, together with the demonstration of the amino acid composition of each vasopressin.

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Arterial Pressures in Tourniquet Shock. (22301)

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In this study arterial pressure was recorded during the entire period of tourniquet shock in the rat. The object was to correlate the pressure with the course and fatal outcome of the shock state.

Method. Our standard method for the production of shock in rats involves a high unilateral tourniquet applied to the left hind extremity for 5 hours. The technic was described previously(1). White male rats weighing about 250 g were used. Prior to removal of the tourniquet, the animals were anesthetized with 2% Nembutal, given intraperitoneally, and each received 0.2 cc liquid

heparin by vein. The right femoral artery was then cannulated (the carotid artery was used in a few instances) and connected to a mercury manometer. Practically all parts of the apparatus were treated with Monocote (Armour) to provide a non-wettable surface. Control readings were taken for several minutes before the tourniquet was released. Direct arterial pressures were obtained throughout the course of shock in 15 animals. In an occasional rat there was need for an extra dose of anesthesia during the period of observation.

Results. The arterial pressure curves were basically similar in all 15 rats with tourniquet shock. Fig. 1 illustrates 3 such curves in animals which died at 1½, 3, and 5 hours respectively after removal of the tourniquet. 1½ and 5 hour animals represented the shortest and longest survivals in the whole group. The mean survival time was 2 hours and 40 minutes.

The initial pressure in the various animals ranged from 104 to 130 mm, and there was no significant change during the control period. Almost immediately after tourniquet release, *i.e.* within a minute or so, there was an abrupt fall in pressure to levels of about 70 to 80 mm. This was probably due to reactive hyperemia in the injured limb as indicated by a bright pink flushing of the paw promptly after the tourniquet was removed. However, participation of nervous factors or possibly toxic material from the damaged extremity is difficult to exclude with certainty.

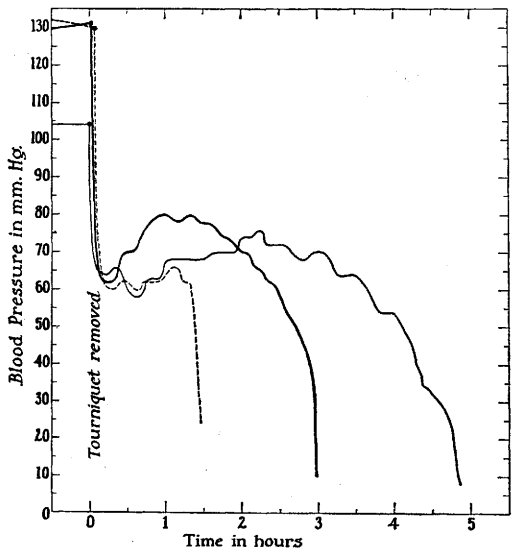

FIG. 1. Arterial pressures in tourniquet shock.

After the initial sharp drop, the arterial pressure showed a further mild decline for a short interval of about 10 to 15 minutes. Then over approximately the next one to 4 hours, depending on the duration of life, and continuing until shortly before death, there was sustained hypotension. During this time, which comprised most of the shock state, the pressure was maintained within a relatively narrow range of about 60 to 70 mm or 70 to 80 mm. That this occurred in spite of progressive shock with marked fluid loss in the injured limb amounting to about 5% of body weight(1) and reduction in effective circulating blood volume to about half the normal value(2), was presumably due to compensatory adjustments of the circulation such as vasoconstriction, increased cardiac action, etc. In fact the compensatory mechanism was probably responsible for the tendency of arterial pressure to rise slightly in some animals during the latter part of the shock state.

Terminally, over a period of a few to about 20 minutes, there was a collapse of the arterial pressure which was associated with death. This was the only interval during the entire course of shock when the pressure fell below 40 mm Hg. The most abrupt decline occurred in animals with the shortest survival time (Fig. 1).

The reason for the terminal drop in pressure was obscure. There was no clear indication that it resulted from impairment of cardiac action. No dilatation of the heart or pulmonary edema was found at autopsy. In fact examination failed to reveal any significant lesions beyond those observed in animals sacrificed prior to the terminal phase. It is unlikely, and at least not proven, that the cause was abrupt capillary stasis, either generalized or local. Through reduced blood flow and progressive anoxia in tourniquet shock, there is profound tissue injury with impairment of vital functions but exactly how this relates to sudden decline in arterial pressure and death is not clear.

Discussion. We are unaware of previous studies of arterial pressure curves in rats with tourniquet shock. Pressures generally resembling those in this study have been noted in dogs with tourniquet(3,4) or compression shock(5) and also in dogs with plasmapheresis(6).

The arterial pressures following release of a unilateral 5 hour tourniquet are of interest in connection with the problem of irreversibility. We have shown that this fulminant form of shock is not characterized by an irreversible stage. To the contrary it is reversible via fluid therapy, with or without replacement of the tourniquet, even up to the time of death (7,8). In addition, evidence is available that no bacterial factor is involved(9).

It might be said that this type of shock lacks irreversibility because it is not associated with drastic hypotension. Throughout most of tourniquet shock in our study the arterial pressure remained above 60 mm Hg. Blood pressure becomes especially pertinent when the tourniquet and hemorrhagic forms of shock are compared, since extremely low pressures, *i.e.* 30 to 45 mm Hg, maintained over a period of time, often form the basis of standard irreversible hemorrhagic shock(10, 11). Such technics, which involve loss of whole blood rather than plasma, presumably give more marked anoxia and tissue injury than occur in tourniquet shock and this might be a critical factor in the development of an irreversible state.

Regardless of the validity of this argument, there is no doubt that profound tissue injury can result from marked and rapid loss of plasma. In fact such injury in the tourniquet and related procedures is clearly out of proportion to the degree of hypotension. For example it was shown in dogs with compression shock that systemic blood flow was seriously impaired even when arterial pressures exceeded the 50 to 70 mm Hg range(5). In dogs with acute plasmapheresis cardiac output declined more rapidly than the blood pressure and the discrepancy was more marked with loss of plasma than with comparable hemorrhage(6). Our own view is that arterial pressure is not a reliable criterion of either the severity or outcome of tourniquet shock.

As indicated, the shock we produce by release of a unilateral 5 hour tourniquet is of acute type and, if untreated, causes death within a few to several hours. Nevertheless, proper therapy will save even moribund animals. Successful reversal of the shock state can be obtained in the last few minutes of life, when arterial pressure is declining abruptly and the levels are about 30 to 40 mm. Approximately 70% of rats recover with fluid therapy alone(8) and nearly 100% with fluid plus replacement of tourniquet(7). This indicates that in the rat tourniquet shock is basically a reversible form of shock.

Summary. Arterial pressure in rats with fatal tourniquet shock shows 3 main phases: (1) an abrupt fall immediately after tourniquet release, (2) sustained hypotension within a relatively narrow range during most of the shock state, and (3) a terminal more or less rapid decline associated with death. Only in the terminal period does profound hypotension intervene, with levels below 40 mm. Although arterial pressure is not a reliable index of the severity of tourniquet shock, the absence of drastic hypotension might help explain why this form of shock is not irreversible.

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