Effects of Renal Pressor System During Hemorrhagic Hypotension.* (26322)

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During hemorrhagic shock, normal animals have larger amounts of circulating renin(1), better maintenance of blood pressure and longer survival periods(2) than nephrectomized animals; these observations have been considered as evidence for the participation of the renal pressor system. However, development of tachyphylaxis and decrease in plasma renin-substrate, source of the pressor agent angiotensin, led others(3,4) to doubt the efficiency of this emergency mechanism. Furthermore, it should be realized that some of these observations were based on determinations of the various components of the renal pressor system in blood for which there is yet no reliable or accurate method. In the present paper we measured pressor effects of kidneys and demonstrated that in rats with hemorrhagic hypotension renal pressor substances play a definite role in homeostatic regulation of blood pressure.

Methods. Normal kidneys were grafted onto bilaterally nephrectomized rats during hemorrhagic hypotension. A method of grafting without interruption of the renal circulation has been described(5). Femoral blood vessels of a nephrectomized recipient rat are first anastomosed with lumbar aorta and vena cava of a kidney donor; then perfusion of the left kidney with blood from the recipient is accomplished by transferring a clamp on aorta and vena cava from a position below to one above the left renal pedicle. Sprague-Dawley rats weighing around 200 g were matched according to weight and sex. The recipient was nephrectomized 18-24 hours prior to test, to increase its sensitivity to renal pressor substances. Following anesthesia with Amytal (9 mg/100 g of body weight), inguinal and neck areas were dissected for vascular anastomoses, tracheal cannulation and blood pressure recording. While the donor was anesthetized and prepared for transplantation, blood was withdrawn from the recipient through a femoral cannula to bring and maintain blood pressure at levels below 50 mm Hg. Then blood circulation was established between the recipient rat and the graft. Blood pressure was recorded on a smoked drum with a small bore mercury manometer. Pressure curves obtained were compared with those from nephrectomized animals which either received a renal graft or were made hypotensive by bleeding.

Results. A. Effects of renal grafts on nephrectomized rats (Fig. 1A). Grafting of a normal kidney caused regularly a pressor response consisting of an initial sharp rise of about 10 mm Hg followed by a slight gradual increase and/or a plateau which was maintained for periods of observation up to 3 hours. B. Effects of hemorrhage on nephrectomized rats (Fig. 1B). Sham operation for grafting was performed in 9 nephrectomized rats which were subsequently subjected to hemorrhagic hypotension. Amounts of blood necessary to cause sustained hypotension below 50 mm Hg ranged from 1.8 to 3.6 ml per 100 g of body weight. Blood was withdrawn slowly, first to reach a pressure around 40 mm Hg then smaller amounts were collected until pressure stabilized. Following this procedure there was usually a subsequent small rise in pressure of about 10 mm Hg then a plateau and finally terminal collapse. Death occurred between 15 and 110 minutes after the last bleeding. Survival periods following stabilization of pressure around 40 mm Hg were not closely related to a definite volume of blood. Thus in a 212 g rat removal of 6.4 ml of blood caused a fall in pressure from 110 to 40 mm Hg and death within 104 minutes while in another rat weighing 220 g five ml of blood caused a fall from 108 to 30 mm Hg and death within 48 minutes. C. Effects of renal grafts on shocked nephrecto-

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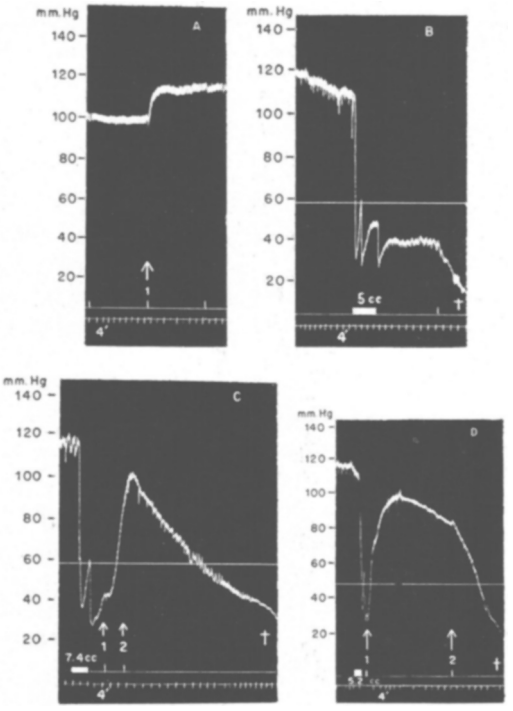

FIG. 1. Pressure responses in nephrectomized rats (A) to a renal graft, (B) to hemorrhage, (C) and (D) to renal grafts following hemorrhage. 1, grafting; 2, removal of graft.

mized rats. In 15 rats prepared as above, normal kidneys were grafted during established hypotension. There was an immediate and spectacular rise in pressure varying from 48 to 70 mm Hg towards levels existing prior to hemorrhage. This was followed by a prolonged plateau then a gradual and terminal fall. Survival periods varied between 26 and 108 minutes. Removal of the graft when the pressor response had reached its peak (Fig. 1C) or later on during the plateau (Fig. 1D) immediately caused a gradual and fatal circulatory collapse.

Discussion. It should be first emphasized that shock is a phenomenon difficult to standardize and that defense mechanisms are so varied and complex that a single factor may not have a significant influence on the evolution of the whole syndrome while having a definite beneficial effect on a particular function. The present experiments demonstrate clearly that the kidney restores blood pressure to near normal levels but has questionable effects on survival. The stimulus responsible for renin release is not anoxemia, but as suggested the low pressure acting on some renal baro-sensitive devices(6). Maintenance of blood pressure at a high level is only temporary. Its failure may be the result of an exhaustion of plasma renin-substrate or of loss of vascular reactivity(4,7).

Summary. Grafting of a normal kidney without interruption of renal circulation onto a nephrectomized rat during hemorrhagic hypotension causes a prompt return of blood pressure to near normal levels demonstrating that humoral renal mechanisms play a role in homeostatic regulation of blood pressure.

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