The Effect of Steroids on Mortality in Experimental Traumatic Shock.* (27303)

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The increased use of adrenal cortical compounds and the relationship of these compounds to blood pressure has prompted many investigators to determine the effect of these compounds on shock. There is evidence to indicate the glucocorticoids reduce the mortality of hemorrhagic shock(1,5). However, other experiments have reported failure of cortisone and hydrocortisone to increase survival rates in hemorrhagic shock(2,3). The purpose of this experiment has been to determine the effect, if any, of various glucocorticoids on traumatic non-hemorrhagic shock.

Materials and methods. A modified "drum shock" preparation of Noble and Collip(4) was adopted using white female rats weighing 240-280 g. One unanesthetized animal was placed in each drum after the legs had been taped together to prevent jumping. The galvanized iron drum measured 15″ in diameter, 8″ in depth and contained one 3″ triangular baffle located at the periphery. The drum was rotated at 60 rpm and 74°F for 40 minutes, causing the animal to be carried up by the baffle and dropped approximately 2400 times.

At the conclusion of the trauma the animals were removed from the drum and placed in one of the following 6 groups: (1) untreated controls; (2) hydrocortisone, 0.5 mg; (3) 5 cc of physiologic saline; (4) 6α-methylprednisolone, 0.05 mg; (5) prednisolone, 0.1 mg; and (6) 2 alpha methyl-9-alpha fluorohydrocortisone 0.025 mg. The steroids were diluted to 5 cc with physiologic saline and all injections made intraperitoneally immediately after removal from the drum. The tapes were then removed from the legs and the animals observed for 6 hours. The number of deaths within this period following inoculation of the drugs was compared to the number in the control and saline series, except that all animals dying from hemorrhage (as determined by autopsy) were excluded from the series.

Results. Approximately 60% of the 78 animals in each group survived the trauma and showed the following: marked tachypnea and tachychardia, lethargy but response to stimulation, weakness and moderately bloody diarrhea. Animals which recovered usually appeared improved within an hour and those which expired within 6 hours were autopsied. The following findings were evident: Moderate vascular engorgement of the abdominal muscles, moderate hyperemia, edema and increased prominence of vessels in the intestines, especially the small bowel which contained serosanguinous fluid. Distention of the stomach and cecum were frequently observed. The lungs appeared normal or moderately congested but there was no evidence of pulmonary edema. The spleen and liver were slightly enlarged. Kidneys and adrenals appeared normal. The brain appeared hyperemic and subdural hematomas represented the most frequent hemorrhage. Seventeen (6.6%) of the 254 animals surviving drum trauma died within the 6-hour period, and at autopsy had evidence of gross hemorrhage; accordingly they were excluded from the series.

Discussion. It is apparent from the above results that in non-hemorrhagic traumatic shock 3 of the 4 steroids have exhibited a beneficial effect on mortality rates. Bruns

TABLE I.

Group	Treated	Died in 6 hr	Mortality %
1. Control	45	33	73
2. Hydrocortisone	39	10	26 ($p < .001$)
3. Saline	36	25	70
4. 6α-Methylprednisolone	37	12	32 ($p < .001$)
5. Prednisolone	40	12	30 ($p < .001$)
6. 2-Alpha methyl-9-alpha fluorohydrocortisone	40	19	48 ($p < .001$)

* Supported in part by a grant from The Upjohn Co.

and Connally(5), in a similar experiment evaluating the effect of steroids, showed that glucocorticoids are more effective than mineral corticoids in hemorrhagic shock, presumably augmenting the responsiveness of vessels to vasopressor drugs.

The site of action of the trauma in this experiment would appear to be largely confined to the abdomen, both by autopsy and microscopic examinations of the abdominal organs. This fact has been substantiated by Noble and Collip(4) and by Chambers, Zweibach and Lowenstein(6) who had shown that taping the abdomen or evisceration will reduce mortality. It appears that death is attributable to shock produced by trauma to the viscera. It has been postulated that a toxic substance(7,8) is absorbed and produced from the anoxic traumatized tissues and that this toxin may be the cause of shock.

The mechanism by which glucocorticoids reduce the mortality rate is not known although extensive investigations have been made. Hume and Nelson(9) have shown that operative trauma and hemorrhage produce an increase in output of 17 hydroxycorticoids and that the increase is maintained during hypotension. Further studies also suggest that in severe hypotension (below 35 mm Hg) the decreased level of corticoids may be the result of a decreased adrenal minute flow. Other experiments(10) have revealed that in severe hemorrhagic shock the adrenal blood flow remained only 15% of pre-shock levels while the output of the corticosteroids remained at 60-100% of normal levels. Fritz (11) showed that adrenalectomized rats did not exhibit the pressor response to norepinephrine and concluded that the 11 oxygenated steroids are necessary to "prime" blood vessels to constrict in response to pressor agents. In further experiments, responsiveness of one vessel was restored by topical application of adrenal cortical extracts.

Summary. We have performed an experiment using a modified Noble-Collip drum to evaluate the effect of various steroids on traumatic non-hemorrhagic shock. Our results indicate that certain glucocorticoids including hydrocortisone, prednisolone and 6α-methylprednisolone will significantly reduce the mortality of the animals subjected to the trauma.

We hereby express appreciation for technical assistance rendered by Mrs. Marija, A. Petravicius.

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Received December 22, 1961. P.S.E.B.M., 1962, v109.

Effect of Cyanide and Fluoride on *in vitro* Incorporation of H^3-Cholesterol into Rabbit Artery. (27304)

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The earliest lesions of rabbit intima appear within a few days after feeding large amounts of cholesterol and consist of groups of 10-50 fat-filled fibrocytes and a few histocytes lying

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