Protection Against *Naja naja* Venom in Dogs by Hydrocortisone.* (26985)

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Although utilized clinically in therapy of ophidism, the value of steroid treatment has not been clearly defined. Experiments recorded here were designed to determine if steroid treatment would favorably alter the outcome following administration of venom of the cobra, *Naja naja*, in lethal dosage to dogs. Results indicate that when this substance is given in massive doses at frequently repeated intervals, survival of some animals can be obtained.

Method. Adult mongrel dogs of either sex were anesthetized with sodium pentobarbital (15 mg/kg). Arterial blood pressure was measured by means of a pressure transducer and Sandborn recorder utilizing a plastic catheter in the femoral artery. A large bore plastic tube was passed into the trachea of the animal and respiration maintained by a mechanical respirator utilizing room air. The calculated dose of dried venom of *Naja naja* reconstituted with 1-2 ml of normal saline was administered intravenously. Treated animals received hydrocortisone intravenously and no other medication or therapy was utilized. Hydrocortisone was given before venom injection or following it and was repeated when systemic arterial pressure began to fall. Animals were treated until blood pressure appeared to be stabilized or proved refractory to further injections of the steroid. After periods of 4 to 12 hours of observation and treatment, the arterial cannula was removed from the femoral artery of survivors and the artery ligated. Artificial respiration was terminated and the animals were returned to their cages. Survivors were classified as those animals living at least 10 days beyond the experiment.

Results. Sixteen control animals received from 1 to 3 mg of cobra venom/kg body weight intravenously. Immediately following venom administration there was a precipitous fall in arterial blood pressure followed by its recovery to near normal levels. Thereafter arterial pressure fell slowly until a preterminal phase was reached where a precipitous drop occurred just before death. Duration of survival of animals is shown in Table I. All animals died. Three animals receiving 1, 1.25, and 1.5 mg of venom/kg body weight lived 8, 12 and 16 hours respectively. All others died within 4 hours of time of venom injection.

Table II shows that pretreatment alone with 15-30 mg hydrocortisone/kg did not result in survival of any animals. However, pretreatment followed by additional hydrocortisone administration in similar massive doses after envenomation resulted in survival of all 3 animals so treated. When hydrocortisone was administered only after venom injection survival of 3 of the animals receiving 2 to 2.5 mg of venom/kg body weight occurred (Table III). Although they eventually died, life was prolonged in at least 3 other dogs.

Discussion. Several authors have recorded favorable clinical impressions in treatment of

TABLE I. Length of Survival of Dogs Following Intravenous Injection of Venom of *Naja naja*

Animal	Wt (kg)	Venom mg/kg	Period of Survival
1	12.3	1	8 hr.
2	9.5	1.5	47 min.
3	6.8	1.25	12 hr.
4	10	1.5	99 min.
5	8.6	1.5	16 hr.
6	12.3	1.65	160 min.
7	10	2	115 "
8	10	2.25	51 "
9	11.8	2	71 "
10	10.5	2.30	42 "
11	7.2	2.30	51 "
12	9.1	3	60 "
13	7.6	3	42 "
14	10.5	2.5	240 "
15	9.1	3	180 "
16	8.6	3	125 "

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bites by copperheads, vipers, and cobras with steroid.(1-5) Experimental data are more in conflict. No significant effect of cortisone on mortality rates following injection of a lethal dose of *Crotalus adamanteus* venom could be shown by Allam and associates(6). However, Deichman and associates(7) found hydrocortisone to protect some of the dogs studied from "two approximate lethal doses" of *Crotalus adamanteus* venom when the steroid was given intravenously immediately or 2 to 4 hours after the venom. Schottler(8) reported that ACTH, cortisone or hydrocortisone afforded no protection for mice injected with

TABLE II. Treatment of Experimental *Naja naja* Envenomation in Dogs with Hydrocortisone.

Dog	Wt (kg)	Venom mg/kg	Hydrocortisone mg/kg	Time given	Period Survival
17	9.1	2	30	Pretreated (45 minutes)	4 hr
18	8.2	3	30	idem	22 min.
19	7.2	3		Pretreated with hydrocortisone 15 mg/kg a day × 5 days	125 "
20	8.2	2	30 15	Pretreated (30 min) 4 hr after venom	Survival
21	7.6	2	15 30	Pretreated (60 min) 30 min after venom	"
22	7.2	2	30 20 15	Pretreated (30 min) 3 hr after venom 7 hr after venom	"

TABLE III. Treatment of Experimental *Naja naja* Envenomation in Dogs with Hydrocortisone.

Dog	Wt (kg)	Venom mg/kg	Hydrocortisone mg/kg	Time given	Period Survival
23	11.4	3	30 15 15	20 min after venom 4 hr after initial dose 4 hr " 2nd dose	5 hr 10 min
24	11.8	2	30 15 15	30 min after venom 4 hr after venom 8 hr " "	Survival
25	9.1	2	30 15	1 hr " " 5 " " "	"
26	7.2	3	40 20	45 min after venom 4 hr " first dose	5 hr 15 min
27	6.3	3	40 40 40	45 min after venom 4 hr " initial dose 4 " " 2nd dose	26 hr
28	9.1	3	40 40 40 30	20 min after venom 4 hr " initial dose 4 hr " 2nd dose 12 hr " venom	20 hr
29	10.5	2.5	40 30	30 min after venom 4 hr " initial dose	5 hr 30 min
30	8.1	2.5	40 30 20 20	30 min after venom 4 hr " initial dose 4 hr " 2nd dose 4 hr " 3rd dose	Survival
31	9.1	2.5	40	25 min after venom	3 hr 30 min
32	9.1	2.5	40 30 30	40 " " " 4 hr " initial dose 4 " " 2nd dose	12 hr
33	10.5	2	40	30 min after venom	3 "

LD_{50} of *Crotalus terrificus* or *Bothrops jararaca* venom. Russell and Emery(9) found methylprednisone and hydrocortisone did not suppress the lethal activity of *Ancistrodon contortrix* venom in mice with the possible exception that hydrocortisone in dosage of 100 mg/kg body weight afforded some protection. Ganatra and associates(10) stated that hydrocortisone in dosage of 2 mg/20 g body weight significantly reduced the mortality rate of mice injected with 2 LD_{50} of viper venom as compared to antivenin. These authors commented that the doses of hydrocortisone used in this experiment were very large. There are no previously reported experiments wherein the effect of hydrocortisone on experimental cobra envenomation has been studied.

The mechanism of the lethal effects of venoms and bacterial endotoxin appear in many respects to be similar(11). Lillehei and MacLean(12) found pretreatment with hydrocortisone in massive doses protected the majority of dogs tested against endotoxin in lethal dosage. In the experiments reported here, doses of hydrocortisone utilized were much greater than those usually employed clinically. Repetition of hydrocortisone administration whenever systemic blood pressure began to fall appeared necessary for survival of animals. In preliminary experiments not recorded here, when smaller amounts of cortisone or hydrocortisone were utilized, no apparent benefit was obtained and all animals died. As in the experiments with endotoxin (12), it appears that massive doses of the substance are necessary if animals are to survive.

Summary. Hydrocortisone in large doses reduces the lethality of *Naja naja* venom for dogs.

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Multiplication and Cytopathogenicity of Mouse Hepatitis Virus in Mouse Cell Cultures.* (26986)

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Since 1951, several investigators have reported isolation of 8 viral agents which produce a focal hepatic necrosis in mice(1-8). Spontaneous disease was induced by none with the exception of the virus of Gledhill and Andrewes(1). The remainder became manifest only in mice inoculated with tissue suspensions in attempts to pass other agents. A number of differences between certain of these agents have been demonstrated which suggest the group is heterogeneous. Never-

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