in subjects L.M. and L.W. Serum triglyceride levels fell significantly in subject P.G.

No significant change in serum lipids occurred in the hypercholesterolemic subject M.W., whose diet was not constant.

Alpha lipoprotein cholesterol and phospholipids diminished, absolutely as well as relatively, in all but subject P.G. in whom no change occurred. Beta and lower density lipoprotein lipids showed no consistent patterns of response. The β lipoprotein lipids in subject M.W. with hyperbetalipoproteinemia did not diminish nor did the $d<1.019$ g/ml lipoprotein lipids in the mildly hyperlipemic subject L.M.

Δ^1-Testololactone did not affect libido in the hypogonadal man nor lead to changes in breasts, vagina or hair growth in the women. No decrease in the elevated urinary gonadotropin excretion occurred in the oophorectomized subject.

Discussion. Androgens such as testosterone propionate and methyltestosterone characteristically enhance protein anabolism and diminish α lipoprotein concentrations. Beta lipoprotein concentrations usually increase (6,7), although this response is somewhat variable. Recent studies of 17-methylandrostano(2,3-c)pyrazole suggested an association of lipoprotein effects with protein anabolic properties, since both were apparent with doses too small to elicit an overt androgenic response(8).

Although large doses of Δ^1-testololactone produced only slight decreases in α lipoprotein lipids, these changes are characteristic of testosterone. The lack of protein anabolic or clinically manifest androgenic response suggests that dissociation of anabolic and androgenic effects from serum lipoprotein effects may have been achieved.

Summary. Δ^1-Testololactone administration caused no protein anabolic or androgenic effects in 4 subjects. Serum cholesterol and phospholipid levels fell, however, as did α lipoprotein lipids in three. The α lipoprotein effect is typical of testosterone and suggests a separation of lipoprotein from androgenic-anabolic properties in a testosterone derivative

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Effect of Hydrocortisone on Blood Pooling Due to Cobra Venom.* (27475)

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Clinical(1-4), and some experimental(5,6) evidence suggests that steroids are of value, in treatment of envenomation, but the mechanism of this beneficial effect is not known. Experiments reported below were undertaken to determine if hydrocortisone changes the rate of pooling of blood in the perfused ani-

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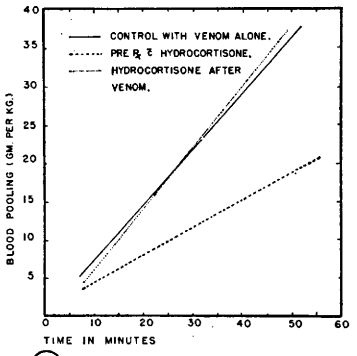
mal and in the perfused isolated hind limb of the dog injected with venom of *Naja naja*. Pre-treatment with hydrocortisone was shown to decrease rate at which blood is pooled in the perfused animal but not in the isolated hind limb unless the limb donor animal had received the steroid prior to removal of the hind limb for study. This latter observation suggests that the action of hydrocortisone is not directly upon the blood vessel but an additional factor is required.

Materials and methods. Adult mongrel dogs of either sex weighing from 10 to 15 kg anesthetized with sodium pentobarbital (25 mg/kg) were utilized. Experiments were of 2 types. In the first group the animal was ventilated by a mechanical respirator, the thorax opened and the animal was prepared for total cardiopulmonary bypass using a DeWall type plastic bag oxygenator and sigmamotor pump. Venous blood was withdrawn by catheters in both inferior and superior venae cavae and oxygenated blood returned by another catheter placed in the femoral artery. The oxygenator was suspended from a scale and primed with fresh heparinized blood obtained from healthy donor dogs. Total cardiopulmonary bypass was instituted. After blood pressure had stabilized and there was no significant gain or loss of weight by the suspended plastic oxygenator, 2 mg of venom of *Naja naja*/kg body weight was introduced into the catheter leading to the arterial return. Changes in blood pressure were monitored by means of strain gauge and Sanborn direct writing recorder through a catheter inserted into the opposite femoral artery. Changes in weight of the oxygenator indicated uptake or loss of blood by the animal. Observations were continued over a period 50 to 70 minutes after the venom had been given. Three animals were given only venom; another 3 received 35 mg of hydrocortisone/kg 30 minutes before anesthesia and start of the experiment, and 3 animals received the steroid 30 minutes after venom had been administered.

In the second experiment the hind limbs of large anesthetized mongrel dogs were excised. The last structures to be cut were the femoral artery and vein after the remainder of the limb had been carefully severed with particular attention to hemostasis. The femoral artery was cannulated and the severed end of the femoral vein was allowed to drain freely into a reservoir. The limb was suspended from a scale recording with an accuracy of ± 1 g and was perfused with donor heparinized canine blood utilizing a bubble oxygenator and sigmamotor pump. Venous return from the femoral vein collected into the reservoir and was carried by gravity to the intake of the bubble oxygenator. The limb was deprived of its blood supply only transiently while the necessary cannulations were made. Perfusion of the limb was begun and a steady state achieved wherein no significant gain or weight loss of either the suspended oxygenator or the hanging limb was observed. In 3 experiments the hind limb was simply perfused with blood and changes in pressure and weight recorded. In 3 animals 0.02 mg venom of *Naja naja*/ml of perfusing blood was introduced into the arterial cannula and changes in pressure and weight recorded. Three other dogs received 35 mg of hydrocortisone/kg body weight, 30 minutes prior to beginning operation for excision of the limb and in 3 experiments hydrocortisone 35 mg/kg body weight (of the limb donor) was added to the perfusing blood 30 minutes prior to introduction of venom. In all experiments arterial pressure and weight of oxygenator and hind limb were observed for 60-100 minutes after venom was introduced and in the case of controls, for a total period of 2 hours. The perfusing volumes varied from 1000 to 1500 ml.

Results. The intravascular introduction of venom of *Naja naja* during total body perfusion resulted in a rapid fall in arterial pressure and rapid loss of blood from the oxygenator into the animal. It was necessary to stop the perfusion after relatively short periods of time because of the rapidity of the uptake of blood into the animal depleting the reserve in the oxygenator making further perfusion impossible. The rate of uptake of blood by the perfused animal and the effect of hydrocortisone is shown in Fig. 1. Each curve is constructed from data obtained from three experiments and was derived by regres-



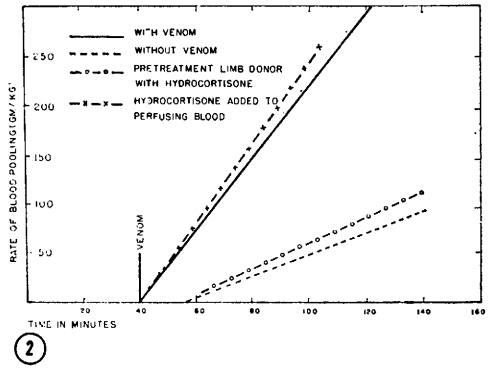


FIG. 1. Effect of hydrocortisone on venom induced blood pooling in dogs perfused by pump oxygenator.

FIG. 2. Effect of hydrocortisone on venom induced blood pooling in isolated canine hind limb.

sion method. The rate of pooling of blood by animals decreased when hydrocortisone was given prior to venom injection. When hydrocortisone was given after injection of venom there was no significant difference in the rate of uptake of blood as compared with control animals.

Injection of venom into perfusing blood caused fall in arterial pressure and rapid gain in weight of the isolated hind limb. There is no decrease in the rate of blood pooling when hydrocortisone is added to the perfusing blood prior to venom administration. However when hydrocortisone was given to the limb donor prior to excision of the limb the rate of the blood pooling caused by venom in the isolated limb is decreased considerably. No change in precipitous fall in arterial pressure caused by venom was noted. These changes are demonstrated in Fig. 2. Each of the curves therein depicted is drawn from mean values of three experiments.

Discussion. Intravascular introduction of venom of *Naja naja* results in rapid decrease in peripheral vascular resistance with fall in arterial blood pressure and pooling of blood. Large doses of hydrocortisone prolong survival of animals receiving lethal doses of venom of *Naja naja* and long term survivors can be obtained(6). At least part of the beneficial effect noted when hydrocortisone is utilized appears to arise from decrease rate at which blood is pooled in the animal. Whether this pooling is intravascular or results from extravasation is not determined by these experiments. Examination of animals dying after *Naja naja* envenomation shows edema and hemorrhage of tissues indicating pooling is at least partially extravascular. Whatever the mechanism of action of hydrocortisone it appears that it is not directly upon the blood vessel but intermediate mechanism is necessary. This factor is not supplied in whole blood but participation of some noncirculating tissue of the animal's body is required. Further experiments along this line are in progress.

Summary. Hydrocortisone reduces the rate at which blood is pooled following injection of cobra venom. It appears that the action of this substance is not directly upon the vessel itself but an intermediate mechanism is required.

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