that a direct action of epinephrine on the adrenal cortex is problematic.

Summary. 1. The repetitive daily administration of epinephrine in the dog results in a progressively diminished eosinopenic response.

2. During the state of epinephrine resistance, there is neither a depletion of endogenous ACTH nor an exhaustion of the adrenal cortex.

3. Adaptation of the organism to epinephrine stress with decreased tissue utilization of corticoids seems to most satisfactorily explain the phenomenon of epinephrine resistance at the present time.

4. Demonstration of resistance to epinephrine speaks against epinephrine as the only physiological stimulus for the continuous secretion of ACTH.

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Inhibition of Vascularization of the Rabbit Cornea by Local Application of Cortisone.* (17822)

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It has become apparent that one of the most striking properties of cortisone is its selective depression of certain mesenchymal cells, as evidenced experimentally in the effect on mouse lymphosarcoma(1) and on wound healing(2). Presumably, the antirheumatic effect of cortisone is likewise due to the selective suppression of cells of mesenchymal origin, involved in an as yet undetermined mechanism in the production of rheumatic diseases. It was thought of interest to investigate whether capillary endothelial cells were among those influenced by cortisone. The vascularization of the cornea appeared to be most suitable for the study of this effect, especially since cortisone might be expected to exert its action on capillary growth when applied locally. Such local application would allow use of the fellow eye as a control. The vascular responses to corneal injury are well known, having been investigated thoroughly by several authors (3,4).

As will be shown by the data here presented, the subconjunctival injection of cortisone did indeed inhibit the growth of capillaries into a chemical burn of the cornea to a high degree.

Method. Three groups containing 6 albino rabbits each were used. The first group sustained corneal burns with 0.2 N alkali, and the second and third groups received burns with 0.5 N alkali. The control eyes in the first and second groups were given no subconjunctival injection, while the third group's control eyes received a suspension of cholesterol in the same medium as the cortisone suspension. The experiments were carried out in the following manner: under topical nupercaine anesthesia, an injection of 0.03 cc NaOH in the concentrations mentioned above was made into the superficial corneal layers half way between the apex of the cornea and the superior limbus with a 30 gauge needle. This was done on both eyes of all animals. A burn about 3 mm in diameter resulted when the weaker solution

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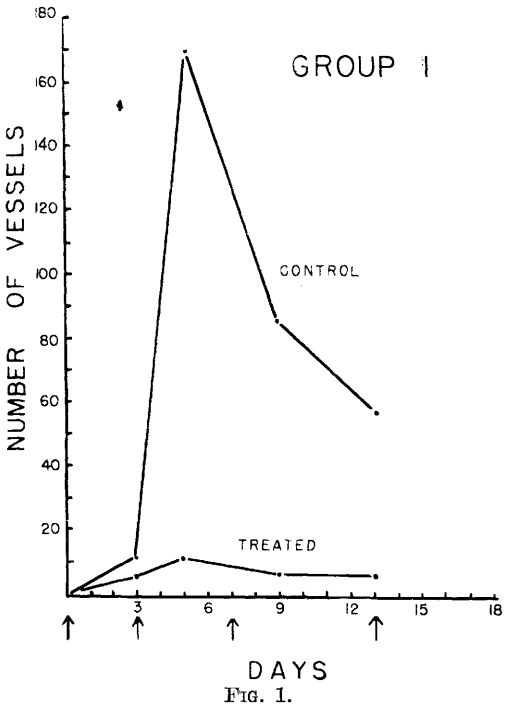

FIG. 1.

Comparison of number of corneal vessels in 6 control (right) and 6 treated (left) eyes following intracorneal injection of 0.2N NaOH. The arrows indicate injection of 0.05 ml (1.25 mg) of cortisone acetate.

was used. In one eye of each animal a saline suspension of cortisone acetate (Merck) containing 1.25 mg in 0.05 cc was injected subconjunctivally at the point nearest the burn. The control eyes of the third group received a similar injection of cholesterol. Penicillin ointment was used in the conjunctival sacs on the operative day. Reinjections of cortisone were done on the third and seventh days in Group I, and on the third, sixth, and tenth days in Group III. Cholesterol injections of the control eyes in Group III were carried out at the same time cortisone was reinjected. In Group II on the seventh day cortisone was injected subconjunctivally in the control eyes. All eyes were examined daily with a loupe during the florid phase, and at longer intervals thereafter as the activity subsided.

Results. The results are expressed as the number of vessels invading the cornea. In the graph, it should be noted that the peaks occurred at the same time, and that disappearance of vessels was rapid on the control side (Fig. 1). The graph for Group II shows simultaneous peaks on the fourth day, but the treated eyes, receiving no new cortisone when the original injection was exhausted, reached a new peak on the seventh day. At this point cortisone was injected in the control eyes, but not in the treated, and a precipitous decline in the number of vessels in the control eyes occurred. Whether this can be credited to cortisone is doubtful, in view of a similar decline in the number of vessels in control eyes of Group I in the absence of cortisone influence (Fig. 2). Group III shows a retardation of new vessel formation due to the severity of the burns. Otherwise, the shape of the graph is in conformity with that on the previous group (Fig. 3).

The length of the newly-formed vessels, while greater on the control than on the treated side in all groups, did not seem significantly different.

Slit lamp examination of treated and con-

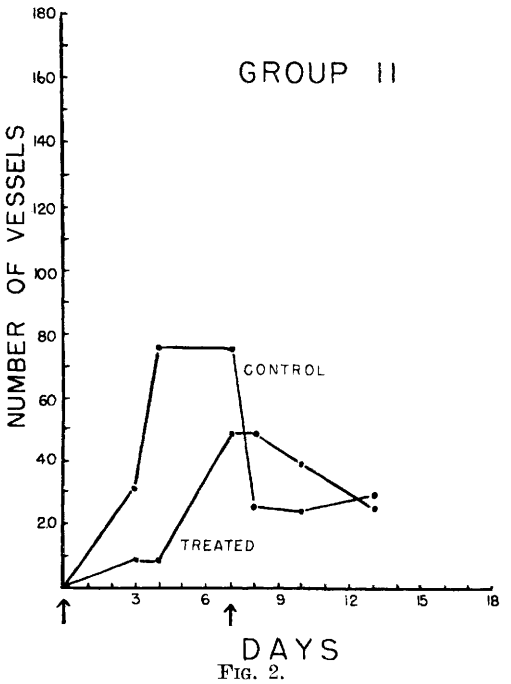

FIG. 2.

Both eyes treated as in Fig. 1, except that 0.5N NaOH was injected. The treated eyes were injected with cortisone only on the first day. The control eyes were injected with cortisone on the seventh day.

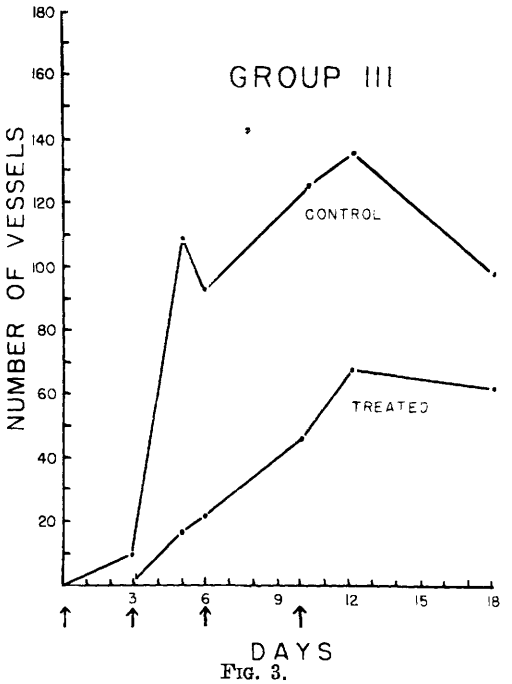

FIG. 3.
Same as Fig. 1, except that 0.5N NaOH was used.

trol eyes showed all the vessels to be superficial, and revealed no gross difference in caliber or branching.

Discussion. The experiments reported here appear to demonstrate the depression of capillary growth by the local application of cortisone. The mechanism of this action is unknown. Two possible mechanisms suggest themselves as the mode of action of cortisone: (1) the blocking of the chemotactic influence on the limbus capillaries exerted by the injured corneal tissue, and (2) the prevention of the response of the endothelial cells to a chemotactic stimulus by inhibition of processes essential for capillary proliferation. Vascularization of the cornea has been suggested to be initiated by the enzymatic hydrolysis of the mucopolysaccharide of the ground substance of the cornea(5). Cortisone has been claimed to be an inhibitor of the action of hyaluronidase both on dermal spreading in animals(6) and in man(7) and on the permeability of the synovial membrane(8). Corneal vascularization appears to be especially suited to submit these hypotheses to experimental proof.

Summary. The subconjunctival injection of cortisone inhibits markedly the vascularization of the cornea caused by intracorneal injection of alkali.

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Antihistamine Therapy in Experimental Shock.* (17823)

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Among the theories proposed to explain the cause of secondary shock there have been many suggestions that histamine, "H substance" and similar agents, released by injured tissue, account for the shock symptoms. Repeated injections of histamine have been reported by Dale and Laidlaw(1) to induce fluid loss and cardiovascular changes typical of secondary shock. In shock from burns and occlusion tourniquets loss of fluid from the blood has been considered an important contributing factor to cardiovascular failure. The possibility that such fluid shifts might be reduced by the use of antihistamine

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