about one killing dose of histamine (ergamine acid phosphate) that is, 200 mg. per kilo of body weight. All the rats in both groups died within a few hours.

No protective effect against histamine poisoning was observed in suprarenalectomized animals repeatedly injected with an excess of ascorbic acid. It is probable that the altered natural resistance of suprarenalectomized rats is in no part due to a loss of ascorbic acid, nor can it be modified by an excess availability of the same.

Conclusion. It is suggested that the removal of the large store of ascorbic acid found in the cortex of the suprarenal gland is in no way responsible for the depression in resistance following suprarenalectomy.†

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Is Heparin an Antiprothrombin?

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Heparin while not itself an antithrombin will react with an unknown substance in the plasma to form a strong antithrombin.[1] Obviously it is essential to eliminate or correct for this antithrombic reaction in any experiment designed to determine whether heparin can also act as an antiprothrombin. A simple means to accomplish this has been found. Eagle[2] has shown that by passing carbon dioxide through plasma diluted with distilled water, prothrombin with some fibrinogen and a small amount of other constituents are precipitated. This precipitate when dissolved and neutralized is readily converted to thrombin by the addition of calcium. If heparin is an antiprothrombin it should prevent this conversion. The details of the experiment and the results are as follows:

Ten cc. of oxalated human plasma were diluted with 100 cc. cold distilled water and carbon dioxide bubbled through for 10 minutes. The precipitate was removed by centrifugation, dissolved in 8 cc. of normal saline, neutralized to pH 7.0, diluted to 9 cc., and divided

† This is not, however, inconsistent with the evidence that vitamin C may play an important rôle in the natural resistance of certain animal species to infection. (See review on vitamin C and resistance by D. Perla and J. Marmorston, in press.)

1 Howell, W. H., and Holt, E., *Am. J. Physiol.*, 1918, **47**, 328.

2 Eagle, H., *J. Gen. Physiol.*, 1935, **18**, 531.

into 2 equal portions. To the first were added 0.5 cc. heparin solution containing 5 mg. and 0.2 cc. of 0.1M calcium chloride, to the second, which served as control, 0.5 cc. saline and 0.2 cc. calcium chloride. A clot formed in both but appeared somewhat later in the solution containing heparin. After the removal of the fibrin, both were tested for their thrombic activity. 0.2 cc. of fibrinogen solution was mixed with 0.1 cc. of the thrombin solution and the clotting time determined. The reaction was carried out at a temperature of 39°-40°C. With this procedure, the coagulating potency of progressive dilutions of both thrombin preparations were determined. The results were:

	Clotting Time in Seconds				
Concentration of Thrombin	1	1/5	1/10	1/20	1/40
Thrombin Solution I (Heparin)	3	7.5	13	20	36
" " II (Control)	3	7.5	14	24	39

The fibrinogen was prepared from rabbit plasma. It was twice precipitated with half saturated sodium chloride and once with ammonium sulfate (quarter saturation). The heparin was prepared from beef lung by the method of Charles and Scott.[3] It had the same potency as the commercial product of Hynson, Westcott, and Dunning.

The results show that as much thrombin is formed in the presence of a large excess of heparin as in the control containing none. In this experiment heparin has no anticoagulating action, because neither the prothrombin preparation nor the fibrinogen contain the constituent with which heparin reacts to form an antithrombin. Since heparin does not appear to influence the conversion of prothrombin to thrombin, one must seriously question the commonly held view that it is an antiprothrombin. The author[4] has furthermore presented data to show that thromboplastin does not neutralize heparin. Experimental evidence suggests that heparin is neither an antithrombin nor antiprothrombin, but an antithrombogen, *i. e.*, an agent which reacts with a constituent in the plasma to form a true antithrombin.

[3] Charles, A. F., and Scott, D. A., *Trans. Roy. Soc. Canada*, 1934, **28**, Sec. V, 55.

[4] Quick, A. J., *Am. J. Physiol.*, 1936, **115**, 317.