tion. This more rapid (3 day) determination of neutralizing effect is particularly valuable with the adenovirus group due to their tendency to readily "break-through" the neutralizing effect of antiserums.

Summary. A colorimetric assay method for measuring neutralizing antibodies against adenovirus in HeLa cell tissue culture in plastic panel cups is described. Advantage is taken of the fact that adenovirus growth in HeLa cell cultures lowers the pH of the medium below that of uninfected cultures. The reaction is standardized so that in 3 days the phenol red indicator has turned yellow by unneutralized virus while the indicator has turned only to red orange by the metabolism of the HeLa cells when the virus antigen is neutralized. It has been shown that this colorimetric test gives titers in paired serums from human adenovirus infections with antigen types 1 through 10 which are similar or slightly higher than those obtained with a test tube method depending for reading on microscopic observation of cytopathogenesis. This method has also been found suitable for typing adenoviruses.

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Dibenamine Blockade of Epinephrine and Glucagon Hyperkalemias.* (22938)

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Although the liver is the major source(2,3) of increased plasma potassium which follows intravenous injection of epinephrine(1), the mechanism by which hepatic release of potassium occurs is still unknown(4). The hyperkalemic response to epinephrine has not been correlated definitively with either vasopressor or hyperglycemic response to epinephrine (2,5,6,7). Nonetheless, some findings suggest an association between potassium and

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glucose release from the liver. Thus, Verzar and Somogyi(8) observed that epinephrine did not elevate plasma potassium or glucose in adrenalectomized cats which showed marked evidence of adrenal insufficiency, but when adrenalectomized cats were maintained on desoxycorticosterone, epinephrine produced essentially normal elevations in plasma potassium and glucose. Recently, it was found that glucagon, which appears to mimic the glycogenolytic action of epinephrine on the liver but to act only on that organ, produces hyperkalemia as well as hyperglycemia (9). Some reports on ability of adrenergic blocking agents to antagonized hyperkalemic response to epinephrine suggest an independence of the hyperglycemic and hyperkalemic responses. The fact that ergot derivatives antagonize the hyperkalemic(1,3,10) is in keeping with their antagonism toward the hyperglycemic and most other responses to epinephrine. This action may indicate that these alkaloids prevent access of epinephrine to the reactive sites ("receptors") in the liver cell. On the other hand, the ability of dibenamine to blockade the hyperkalemic response to epinephrine in cats(11) and in dogs (10) is unexpected in view of the extremely weak antagonism of dibenamine against epinephrine hyperglycemia in cats(12). From these reports one could not safely conclude that dibenamine selectively blockaded potassium release from the liver without blockading glucose release since none of the investigators had studied both responses.

In the present report we have attempted to supplement previous work by determining the epinephrine-induced changes in plasma potassium and glucose in the cat before and after administration of dibenamine. Since we confirmed the findings of other investigators, that dibenamine has little effect on epinephrine hyperglycemia but has remarkable ability to prevent epinephrine hyperkalemia, we have investigated the ability of dibenamine to blockade glucagon hyperkalemia. The latter study was important for determining selectivity and mode of action of dibenamine since the glycogenolytic effect of glucagon appears identical with that of epinephrine(13) except for the fact that the cell "receptors" for glucagon and epinephrine differ(14,15).

Methods. The experiments were performed upon cats anesthetized with Dial. The methods used were the same as those reported previously(9), except for analysis for plasma potassium which was done on Baird Associates Flame Photometer with an internal lithium standard. Epinephrine bitartrate (10 μg/kg) and glucagon (50 μg/kg) in volumes of approximately 0.1 ml were injected rapidly into the femoral vein. Dibenamine dissolved in 50% ethyl alcohol and diluted appropriately with 0.9% sodium chloride solution so that a total dose of 15 mg/kg in a volume of about 15 ml was administered in 15 minutes by continuous infusion. One hour was allowed after completion of the infusion of dibenamine before testing of either glucagon or epinephrine. Arterial blood samples were taken before and 1, 10, and 30 minutes after administration of the hyperkalemic agent. Since maximal increases in plasma potassium occur 1 minute after and maximal increases in plasma glucose occur 10 minutes after administration of either epinephrine or glucagon, only these two values will be included in this report.

Results. Observations summarized in Fig. 1 indicate that dibenamine suppresses selectively the hyperkalemic responses to epinephrine and glucagon, but that dibenamine does not markedly depress the hyperglycemic responses to epinephrine or glucagon. The results with epinephrine confirm in the same animals results previously reported on independent studies of the blockade by dibenamine of epinephrine hyperkalemia in the cat (11) and in the dog(10) and the very small effect of dibenamine on epinephrine hyperglycemia in the cat(12).

The effect of dibenamine on hepatic release of potassium cannot be the result of a blockade of epinephrine receptors in the liver. Dibenamine did not influence the ability of epinephrine to activate the glycogenolytic system of the liver. For this glycogenolytic effect epinephrine must first combine with the receptors but this step is circumvented in

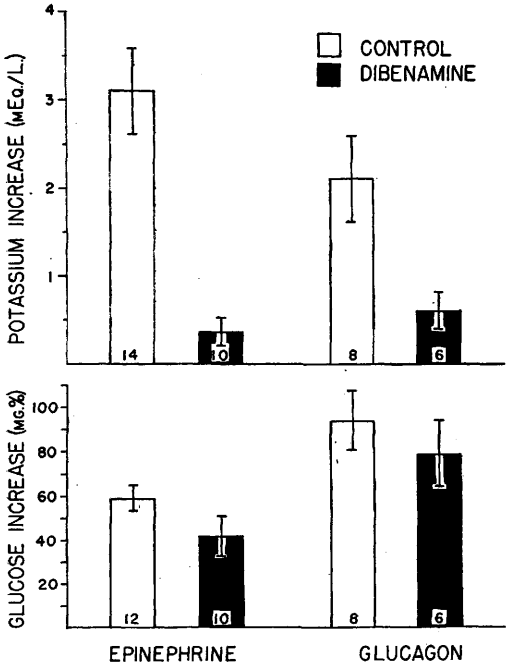

FIG. 1. Effects of epinephrine and glucagon on plasma potassium (1 min after injection) and on plasma glucose (10 min after injection) in control and in dibenamine-treated cats. Heights of columns indicate averages of the number of experiments designated at bottom of each column and vertical bars show standard error of mean.

the action of glucagon(15). Thus, it is possible to blockade the glycogenolytic effect of glucagon without interfering with the glycogenolytic effect of epinephrine(14), and *vice versa*(15).

Blockade of the hyperkalemic response to glucagon by dibenamine, as in the experiments with epinephrine, was not accompanied by a marked reduction in hyperglycemic response to glucagon. This result suggests that the blockade of the hyperkalemic responses to epinephrine and to glucagon is not a specific adrenergic blocking action of dibenamine. It would appear more probable that this action of dibenamine is some new action of dibenamine more specifically directed toward potassium metabolism. Of interest in this connection is the observation by Huggins *et al.*(16) that dibenamine increased the volume of distribution of intravenously administered potassium. Our analyses of the potassium content of liver water indicate that in cats and rats dibenamine increases liver potassium, so that the dibenamine action cannot be attributed to depletion of hepatic potassium.

Summary. In cats the hyperkalemic response to epinephrine or to glucagon was blockaded by dibenamine, but dibenamine had little effect on the hyperglycemic response to epinephrine or to glucagon. The results suggest a selective action of dibenamine on potassium metabolism in the liver.

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