sulfoxide preceding or accompanying cholic acid ingestion produces an increase in taurine excreted as taurocholic acid(12). It is possible that methionine is converted in part to methionine sulfoxide by irradiation. 3) Although there is no definite evidence that cholic acid feeding produces liver damage and thus may interfere with production of taurine from its precursors, this possibility is not excluded and would explain the data obtained.

Summary. 1. X-irradiation does not alter concentration of taurine in muscle, spleen, thymus or liver tissue of rats exposed to x-radiation 24 hrs. prior to study. However, during this period, there is a marked increase in urinary excretion of taurine. Thus preformed tissue taurine does not appear to be the source of excess taurine excreted following irradiation. 2. Rats maintained on a diet designed to cause a depletion of sulfhydryl compounds (cholic acid feeding) have a significantly reduced urinary taurine response to whole-body irradiation. 3. When rats maintained on sulfhydryl-depleting diet were given subsequently an L-cystine supplemented diet, the lowered urinary taurine response to irradiation was not restored to normal.

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Vascular Reactivity as Influenced by Acetazolamide, Dichlorophenamide and Mercaptomerin.* (24854)

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Chlorothiazide (Diuril)† has been reported to exert an antihypertensive effect(1). However, a mechanism for this effect has not been clearly demonstrated. Previous studies have shown that chlorothiazide decreases arterial pressure responses to injections of norepinephrine, epinephrine and isopropyl-norepinephrine in the dog(2). Since it has been observed that renal effects of chlorothiazide on water and electrolyte excretion bear a similarity to the mercurial diuretics(3) and that mercurials may have an antihypertensive action(4), it was of interest to test the effects of a mercurial diuretic on vascular reactivity. In addition, the effect on vascular reactivity of acetazolamide (Diamox) and dichlorophenamide (Daranide),† diuretics which inhibit carbonic anhydrase, was determined.

Methods. Fifty-three experiments were performed on adult mongrel dogs anesthetized with sodium pentobarbital (30-35 mg/kg) and vagotomized. Arterial blood pressures were taken with a mercury manometer and recorded on a smoked drum. The experimental procedure followed in obtaining the controls and administering the drug was similar to that described previously(2). Acetazolamide, 10 mg/kg was administered in a priming dose intravenously, followed by continuous infusion of 10 mg/kg for 30 minutes. Dichloro-

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TABLE I. Effect of Acetazolamide, Dichlorophenamide, and Mercaptomerin on Vascular Reactivity.

Dose (μg/kg)	Control: No. of animals	Control: Before infusion (mm Hg)	Control: After infusion (mm Hg)	Control: Change	Drug: No. of animals	Drug: Before infusion (mm Hg)	Drug: After infusion (mm Hg)	Drug: Change	Level of significance*
Effect of acetazolamide on vascular reactivity									
A. Pressor responses to norepinephrine									
.05	9	17.3	16.7	− .6	9	15.2	9.0	−6.8	<.05
.10	9	24.1	22.7	−1.4	9	16.6	11.4	−5.2	"
B. Depressor responses to isopropylnorepinephrine									
.05	7	9.8	9.7	− .1	9	22.1	9.9	−12.2	<.01
Effect of dichlorophenamide on vascular reactivity									
A. Pressor responses to norepinephrine									
.05	9	17.3	16.7	− .6	8	13.1	9.8	−3.3	>.05
.10	9	24.1	22.7	−1.4	8	16.1	12.7	−3.4	"
B. Depressor responses to isopropylnorepinephrine									
.05	7	9.8	9.7	− .1	8	19.2	10.4	−8.8	<.01
Effect of mercaptomerin on vascular reactivity									
A. Pressor responses to norepinephrine									
.05	7	14.5	13.6	− .9	13	16.5	11.4	−5.1	<.001
.10	7	18.3	17.1	−1.2	13	22.3	15.9	−6.4	"
B. Depressor responses to isopropylnorepinephrine									
.05	7	9.8	9.7	− .1	8	16.1	10.2	−5.9	<.05

* Considered significant if $P < .05$.

phenamide, 20 mg/kg was given as a priming dose and 20 mg/kg infused for a 30 minute period. Mercaptomerin (Thiomerin), 2.5 mg/kg was given intravenously as a priming dose followed by continuous infusion for 30 minutes in a dose of 3.0 mg/kg. Responses in all animals were determined immediately after infusion of the diuretic with the exception of mercaptomerin; these responses were obtained 30 minutes after cessation of the infusion since no changes were noted in preliminary experiments until diuresis began with this compound. Base pressures during evaluation of the responses following each diuretic differed less than 10 mm Hg from control levels. Animals treated identically to the experimental groups with the exception that no diuretic agent was present in the glucose solutions served as controls.

Results. The results obtained are illustrated in Table I. Acetazolamide infusion decreased pressor response to norepinephrine and depressor response to isopropylnorepinephrine. These changes occurred in all animals tested and were significant. In contrast to acetazolamide, dichlorophenamide did not decrease vascular reactivity in response to norepinephrine though decreasing depressor response to isopropylnorepinephrine.

Mercaptomerin infusion reduced pressor responses to norepinephrine and depressor responses to isopropylnorepinephrine in every experiment.

Determinations of plasma sodium concentrations before and after administration of the 3 diuretics did not show significant changes. Preliminary experiments in which urinary excretion of sodium and potassium were measured indicated that acetazolamide and dichlorophamide produced increases in these electrolytes comparable to that observed with chlorothiazide. Excretion of sodium and potassium 30 minutes following cessation of mercaptomerin infusion likewise caused an increased electrolyte excretion paralleling that noted with chlorothiazide.

Discussion. The results obtained indicate that the ability of chlorothiazide to decrease vascular reactivity as measured by its ability to decrease responses to injected norepinephrine and isopropylnorepinephrine is not unique for this diuretic. The results support the concept that increased sodium excretion plays a dominant role in the diminished vascu-

lar reactivity since the common property of all the agents studied is the capacity to increase electrolyte excretion, primarily sodium. The failure of dichlorophenamide to alter pressor response to norepinephrine remains obscure.

The similarity of the changes in responses resulting from the several diuretics raises a question whether a singular intrinsic antipressor action is associated with chlorothiazide. Although the mechanism is not known, it is conceivable that the antihypertensive action of chlorothiazide may be due to: a) a direct effect upon peripheral vascular smooth muscle to alter its state of contraction, or b) a shift in sodium and potassium across the cell membrane resulting in a change in tonus of the vascular system, or c) its diuretic and saluretic action to alter plasma volume and electrolyte balance. Evidence available at the present time would suggest that the diuretic and saluretic action plays the most important role. Independent of changes in volume, excretion of large amounts of sodium may play a role in the antihypertensive properties of a diuretic, since low sodium diets will decrease blood pressure and increase the effectiveness of ganglion blocking drugs in hypertensive patients(5). Recently it has been reported that both chlorothiazide and mercurial diuretics appear to have an antihypertensive action that may be potentiated by a decrease in body sodium(4). In addition, an increase in electrolyte excretion associated with a diminished plasma volume has been observed to decrease the dosage of ganglionic blocking agents required in hypertensive patients(6). Results obtained in this study lend support to changes in electrolyte excretion as being a dominant factor. In each case, no change in response was noted until an interval of time had elapsed when diuresis was established. The possibility that a simultaneous decrease in plasma volume may have been an important factor can not be ruled out since measurements of this parameter were not made.

Summary. The effects on the vascular responses to norepinephrine and isopropylnorepinephrine induced by 3 diuretic agents, acetazolamide, dichlorophenamide and mercaptomerin were determined. Acetazolamide and mercaptomerin diminished vascular responses to these catechol amines similarly to the decrease previously reported with chlorothiazide administration. It is considered probable that the effect on vascular reactivity resulting from these agents is due to augmentation of sodium excretion.

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Interactions of Human Sera and Spinal Fluids with Human Brain Antigen and Antibrain Rabbit Serum. (24855)

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Investigations concerning both immunological differentiation of body organs (*e.g.*, 1,2) and possible existence of "autoantibodies" to human organs have been reported(3,4,5,6). Gadjusek(7) searched for "autoimmune" antibodies in sera of patients with various diseases and found positive complement fixation reactions in 3% tested with liver antigens and