observations, however, show that total results with these agents are different from those found with glycogen in this study.

Prior work with dextrans indicated that ability to release histamine from rabbit blood was dependent upon molecular size of the dextran(10). The same factor might apply to glycogen and its ability to release serotonin and histamine. The nature of end groups in the glycogen molecule, and alterations in its structure formed as a result of isolation and purification process, may also produce some of the properties in the polysaccharide needed to cause the effects found.

The distinct importance of platelets and leucocytes during anaphylaxis in the rabbit should be recognized. The role of these blood elements during allergic reactions in other animal species and in man could be of equal importance. In addition, the possibility that glycogen, or a polysaccharide-like material, may be involved in hypersensitivity processes needs further investigation.

Summary. When glycogen is incubated with normal rabbit blood, both serotonin and histamine are released from the platelets. EDTA inhibits this release. Intravenous injection of glycogen into rabbits produces a marked fall in whole blood concentration and a rise in lung content of serotonin and histamine. These results are secondary to trapping of platelets in the lung. In addition, both serotonin and histamine are released into the plasma. All of these changes are identical to those obtained when antigen is injected intravenously into a sensitized rabbit or when an antigen-antibody complex precipitate is injected intravenously into a normal rabbit.

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Sources of Excess Taurine Excreted in Rats Following Whole Body Irradiation.* (24853)

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Excessive urinary excretion of taurine has been observed in rat and man in the 24-hour period following exposure to whole-body x-irradiation(1-4). This taurine response appears to be an extremely sensitive and early indicator of radiation exposure, being detectable at doses as low as 35 r(4) and as early as 3 hours post-irradiation(2). Urinary taurine excretion increases semilogarithmically with roentgen dosage in the range between 0 and 250 r. Above this degree of radiation, taurine response does not increase(2). The magnitude of urinary excretion of taurine is a valuable index of survival in rats exposed to LD_{50} dose of x-ray(1). Since taurine is one of the major end products of SH oxidation

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(5), excessive excretion of taurine following irradiation might suggest an increase in rate of oxidation of this grouping. Barron *et al.* (6) have shown SH-containing enzymes especially sensitive to inactivation by x-irradiation, and various amino-SH compounds exert protective action against radiation death(7). These observations suggest that alterations in SH metabolism may play a role in cellular damage induced by x-irradiation. Thus determination of the source of additional urinary taurine excreted following exposure to whole-body x-irradiation may be of some importance in elucidation of metabolic changes occurring in the rat immediately following exposure to ionizing radiation. Taurine exists free in organs of many animals(9). On an absolute weight basis, striated muscle contains more than 75% of total body taurine of a rat(9,10). Taurine concentrations in rat organs remain remarkably constant following fasting, adrenalectomy, hypophysectomy, gonadectomy, estrogen treatment(9) and dietary procedures designed to deplete bodily stores of endogenous SH-compounds(11). On the other hand, urinary taurine levels are dependent upon diet, being decreased significantly by diets low in organic sulfur(14) and by concomitant administration of substances such as bromobenzene and cholic acid which divert cysteine into special metabolic pathways(13). The present work was designed to determine the source of urinary taurine excreted in response to whole-body irradiation.

Materials and methods. Isolation and determination of taurine from tissues and urine was done by the method of Awapara(8). Three to 4-month-old rats (Sprague-Dawley strain†), weighing 250-300 g were used and divided into 2 groups of 12 each. Group I was fed Rockland pellets and water *ad lib.* Group II was fasted 3 days and then maintained on protein-free, cholic acid-supplemented diet for 10 days prior to irradiation procedure. Protein-free diet was as used by Awapara(11)‡; cholic acid diet was prepared by incorporating 8.16 g of cholic acid into each kg of protein-free diet. The L-cystine diet contained 4.67 g/L-cystine/kg of protein-free diet. In each group, 6 rats were irradiated while the other 6 served as non-irradiated controls. Irradiation procedure was as follows: Twenty-four hours prior to irradiation all food, but not water, was removed from metabolic cages in which the rats were kept singly, and a "control" urine was collected from each rat during this 24-hour period. Then the rats were placed in irradiation cages of wire mesh. Each cage accommodated 3 rats in separate compartments. Radiation factors were: 250 Kv; 15 ma; 0.5 mm Cu and 1 mm Al filters: 50 cm T SD; 40 cm^2 field; 102 r mm to field. Three rats were irradiated at a time, each receiving 600r. Controls were handled similarly but not irradiated. Following irradiation all animals were returned immediately to metabolic cages and urine collected for a second 24 hour period. Rats in Group I, irradiated and non-irradiated, were sacrificed after 24 hours by stunning, and organ samples obtained immediately, weighed, frozen (dry ice), and stored at 4°C for subsequent analysis. Following completion of first part of the experiment, rats in Group II, which had served as non-irradiated controls, were removed from the protein-free-cholic acid diet and given a diet in which L-cystine replaced cholic acid as supplement to basic protein-free diet. These animals were maintained on the new diet for 10 days; then one-half of the group received 600r whole-body irradiation while the other half served as controls. Pre-irradiation control 24-hour urines and post-irradiation 24-hour urines were again collected.

Results. A. *Tissue taurine analyses.* Tissue concentrations of taurine prior to and following radiation are shown in Table I. Radiation did not cause significant alterations in taurine concentrations of tissues studied.

TABLE I. Tissue Levels of Taurine in Rats Exposed to X-radiation 24 Hr Prior to Analysis.

	μm taurine/g wet tissue			
Treatment	Ilio-psoas	Spleen	Thymus	Liver
Controls	13 ±.6†	7.7 ± 1.4	24 ± 2.1	.57 ± .1
Irrad.*	13 ±.8	7.2 ± 1.2	20 ± 1.8	.75 ±1

* As described under *Methods.*
† Means and stand. errors.

† Obtained from Holtzman Co., Madison, Wis.

‡ Obtained from Nutritional Biochemicals Co.

TABLE II. Effect of Radiation and Diet on Urinary Taurine Excretion.

Diet	No. of rats	Radiation dosage (r)	Control 24 hr urinary taurine excretion, mg/24 hr	2nd 24 hr taurine excretion, mg/24 hr	"P" values*
A. Normal (Rockland pellets)	6	0	36 ± 2†	41 ± 2	
B. *Idem*	6	600	36 ± 1	82 ± 2	<.01
C. Protein-free + cholic acid	6	0	5.58± .46	5.61± 1.20	
D. *Idem*	6	600	4.04± .31	11.01± 1.92	.02
E. Protein-free + L-cystine (following protein-free + cholic acid	3	0	12.2 ± 3.1	6.3 ± 1.9	
F. *Idem*	3	600	11.7 ± 4.4	16.9 ± 2.7	.1

* "P" values calculated for comparisons between irradiated and control animals with respect to increased urinary taurine.

† Means and stand. errors.

While tissue taurine concentrations do not decrease following irradiation, the net weight loss of these tissues is not great enough to account for the urinary taurine excretion(9,10). Apparently the source of taurine excreted following irradiation is not preformed tissue taurine, but rather excessive formation of taurine from precursors. Additional analyses of other organs were not necessary, since striated muscle alone has sufficient taurine content to account for the quantity excreted after irradiation(9). B. *Urinary taurine excretion.* I. *Rats on stock diet.* In irradiated rats maintained on a Rockland pellet diet, the second (*i.e.,* post-irradiation) 24 hour urines showed an increase of 46 ± 2 mg of taurine over the control 24-hour collection (Table II). In non-irradiated controls the second 24-hour urines showed an increase of 5 ± 3 mg of taurine over control 24-hour urines. The difference in increase between irradiated and controls is significant ("p" value <0.01).

II. *Rats on a protein-free cholic acid-containing diet for 10 days.* Irradiated animals in this group showed an increase, from control 24-hour collection to second 24-hour collection, of 6.97 ± 1.94 mg of taurine. Non-irradiated controls showed an increase of 0.03 ± 1.38 mg of taurine ("p" value = 0.02). Since the protein-free, cholic acid-containing diet reduced significantly the urinary taurine response to irradiation (Compare A and C, Table II), and since Awapara(11) has shown that this diet does not alter taurine content of tissues, it appears that lack of urinary taurine response in animals on this diet was due to relative absence of a requisite taurine precursor in the form of a sulfur-containing compound. In view of this, those non-irradiated animals which had been maintained on protein-free, cholic acid-containing diet were placed on protein-free, L-cystine-containing diet, to assess whether presence of sufficient amount of sulfur-containing amino acid would restore the urinary taurine response to irradiation. However, irradiated animals which had been transferred to the cystine-containing diet showed a questionably significant increase in taurine excretion (Table II, compare, Exp. E and F; "p" value = 0.1). These results may have several explanations: 1) These animals had previously been in negative N balance by maintenance on a protein-free, cholic acid-containing diet. The second protein-free diet contained only enough L-cystine to satisfy minimal nitrogen requirements and maintain the rats at constant weight. In this condition of relative protein deficiency, (each rat having lost about 30 g on the protein-free cholic acid-containing diet) dietary cystine may have been channeled into tissue protein and away from those metabolic pathways leading to taurine precursors. Thus, the normal marked urinary taurine response to irradiation was not seen. A corollary of this point might be that the period of L-cystine supplementation was too brief. 2) The possibility exists that methionine is the major source of taurine produced following irradiation. This would be predicated on the existence of as yet undescribed pathway from methionine to taurine. This possibility is indicated by the demonstration that intravenous injection of methionine

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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† Diuril and Daranide, supplied through courtesy of Merck, Sharp and Dohme Research Labs., Merck and Co., Inc.