dimethylamino-hexose-reductone, dimethylamino-hexose-reductone, and anhydro-piperidino-hexose-reductone in mice were 300, 400, and 900 mg/kg respectively, while for the morpholino and piperidino-hexose-reductones they were greater than 1200 mg/kg. Single intraperitoneal injections and single oral doses of dimethylamino-hexose-reductone in both mice and rats, as well as long-term feeding of dimethylamino and piperidino-hexose-reductones in rats produced typical symptoms of hyperexcitability, elevation and nodding of the head, and whirling.

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Effect of Colchicine on Taurine Excretion.*† (26434)

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Many of the characteristic biological effects of colchicine parallel those produced by X-rays. Since Kay and Entenman(1) have demonstrated that X-irradiation markedly increases excretion of taurine by the rat, the effect of colchicine on taurine excretion in the rat was studied.

Materials and methods. Male Wistar rats weighing 200-300 g were used, each rat serving as its own control. During the control period urine was collected for at least 2 successive days of 21 hours each, 3 hours of each full control day being allotted to feeding the animals. Food was withheld during the treatment period but water was given *ad libitum* throughout. After the control period the rats were administered colchicine intraperitoneally in doses ranging from 0.8 to 6.4 mg/kg, and urine was collected for various periods up to 36 hours after colchicine administration. Values for taurine output are expressed as a percentage of each animal's taurine output during the control period. For assay of taurine in urine and tissues a modification of the method of Pentz *et al.*(2) was used. In this method extraction of the chloroform-soluble dinitrophenyl (DNP)-derivatives of Dowex-50-treated samples of the urine or tissues leaves DNP-taurine in the aqueous phase. Taurine content is then determined by comparing the absorption of the sample at 355 mμ in a Bausch & Lomb Spectrophotometer with that produced by standard taurine solutions under the same conditions. Paper chromatograms of the DNP-derivatives from urine and tissues in 3 solvent systems showed one component, the mobility of which was the same as authentic DNP-taurine.

Results and discussion. When urine samples were collected over the periods of 0-3, 3-6, 6-14, and 14-36 hours after colchicine administration, it was found that increased taurine excretion begins in the first 3 hours but does not continue beyond 14 hours after treatment. The data also suggest that the peak rate of excretion occurs sometime between 6 and 14 hours following colchicine.

In the control periods preceding treatment taurine excretion averaged 2 micromoles/hr/

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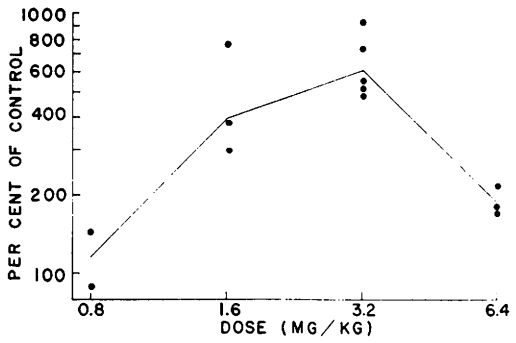

FIG. 1. Taurine output in first 14 hr after various doses of colchicine. Each point represents 1 animal.

rat, or 5.25 mg/21 hr rat. Rats given 0.8 mg/kg did not excrete increased amounts of taurine but those given 1.6 and 3.2 mg/kg colchicine excreted approximately 4 and 6 times as much taurine, respectively, as they did during their control period (Fig. 1). However, in animals given 6.4 mg/kg colchicine taurine excretion increased to only twice the control values, indicating that this dose was less effective than the 2 lower doses of 1.6 and 3.2 mg/kg. In this respect colchicine differs from X-rays, since Kay, Early and Entenman(3) reported that X-irradiation produced equal and maximal effects in all doses from 250 to 25,000 r. The relative ineffectiveness of such a high dose of colchicine (6.4 mg/kg) in promoting taurine excretion is not readily attributed to kidney failure, since taurine blood levels did not increase significantly 4 hours after either 1.6, 3.2, 6.4 and 12.8 mg/kg colchicine.

Several substances of physiological interest which may be liberated following X-irradiation were investigated to determine whether they might increase taurine excretion in rats. Intramuscular administration of 5 I.U. of vasopressin tannate in oil did not increase urinary taurine excretion significantly. Beta-aminoisobutyric acid and beta-alanine, 2 beta amino acids reported to increase taurine excretion in mice(4), appeared to be relatively ineffective when given intraperitoneally in doses as high as 40 millimoles/kg.

The question as to whether the extra urinary taurine comes from preformed tissue taurine was investigated by determining taurine levels in heart, small intestine and brain at 3, 6, 12, and 24 hours after administration of 1.6 mg/kg of colchicine, a dose which increases taurine excretion about 4 times that of controls. At none of these time intervals was there a significant change in taurine levels nor did significant changes occur in these tissues when they were investigated 24 hours after administering 1.6, 3.2, and 6.4 mg/kg of colchicine. In a separate experiment taurine levels in skin were determined 4 hours after 3.2 mg/kg of colchicine. Taurine in the skin of the paws (618 μg/g), abdomen (460 μg/g) and dorsum (478 μg/g), on the basis of wet weight of the skin, did not change significantly from control levels. Thus, preformed tissue taurine does not appear to be the source of the extra taurine excreted by rats following colchicine administration. Stern and Stim(5) conclude that preformed tissue taurine was probably not the source of the extra urinary taurine excreted after X-irradiation, since taurine levels in muscle, spleen, thymus and liver did not change 24 hours after a dose of 600 r.

Summary. Colchicine in doses of 1.6, 3.2 and 6.4 mg/kg increases urinary taurine excretion in rats, but doses of 6.4 mg/kg are less effective than the two lower doses. Preformed tissue taurine does not appear to be the source of the extra urinary taurine excreted after colchicine administration.

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