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Effect of Mercurials on Thiamine Excretion in Patients with Congestive Heart Failure. (20347)

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(Introduced by Ernest Spiegel.)

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Much interest attaches to the question of thiamine excretion following mercurial diuresis. There are some references to thiamine losses due to diuretics used in the treatment of congestive heart failure; however, this question has not been systematically investigated. The opinion is held generally that the water-soluble vitamins are lost in greater quantities in the urine as the urinary volume increases. Actually, little is known of the mechanisms available in the kidney for regulation of thiamine excretion, or of the manner in which these mechanisms are affected by the action of mercurials upon the renal tubules.

The present study was undertaken to determine the effect of mercurials upon daily output of thiamine in the urine in patients under treatment for congestive heart failure. This work was conducted in conjunction with another study made upon a separate group of patients and control subjects to ascertain the status of thiamine nutrition in patients with chronic heart disease. The statistical analysis of the results obtained in this group of patients appeared to indicate that thiamine deficiency in association with chronic cardiac failure is more than a coincidence(1). The present group of patients was not included in that study because they had received supplemental vit. B complex in conjunction with their cardiac therapy prior to observations recorded in this communication.

Methods and materials. Patients under treatment for congestive heart failure were selected from the medical service of Temple University Hospital. In each instance the patient presented signs and symptoms of cardiac decompensation: orthopnea, edema, marked congestion of the lungs, engorgement of the liver. The causes leading to heart failure were hypertensive heart disease in 5 patients, arteriosclerotic heart disease in 3 patients, mitral stenosis in one patient, and amyloidosis in one patient. The cardiac failure was refractory to treatment with digitalis, mercurial diuretics, salt poor diet and vitamin supplements. Five of the 10 patients studied have succumbed to their disease since initiation of these studies. The food taken by each patient indicated a relatively low protein and caloric intake in most instances. No specific signs or symptoms of thiamine deficiency were elicited, possibly due to the reduced caloric intake as well as vitamin supplementation in the past. Vitamins and mercurials were discontinued for 5 days prior to initiation of the study. The urine was collected on the wards for 24-hour periods. During the period of observation, the patient was given a balanced diet providing approximately 1800-2000 calories and 1.0 to 1.2 mg of thiamine daily. The calculations were based on tables compiled by Bowes and Church(2). Urine collections during the first 3 days for each patient represented the control period. A mercurial diuretic, Thiomerin or Mercuhydrin, 2 cc, was given intramuscularly on the morning of the fourth day. The 24-hour urine collections continued during the day of mercurial injection, the day following, and for one or 2 more days of mercurial injections and days following. The urine was collected for an additional

TABLE I. Mean Urinary Thiamine Excretion and Urine Volumes for 9 Patients on Constant Thiamine Intake during Control Periods and following Administration of Mercurial Diuretics.

	Control day			Day of mercurial			Day following mercurial		
Patients	Thiamine content, μg	Urine, cc	Thiamine, μg/cc	Thiamine, μg	Urine, cc	Thiamine, μg/cc	Thiamine, μg	Urine, cc	Thiamine, μg/cc
C. M.	280.7	500	.561	759.4	1120	.678	208.1	720	.289
E. R.	86.9	1260	.069	282.1	1800	.157	84.6	1800	.047
S. G.	54.1	1095	.049	293.8	1555	.189	517.1	1190	.435
F. B.	247.4	370	.669	366.5	740	.495	903.3	2700	.335
M. M.	156.4	1290	.121	574.8	990	.581	764.4	1250	.612
S. S.	91.1	858	.106	375.8	1467	.256	344.6	1220	.282
V. M.	61.0	700	.087	103.5	1000	.104	185.8	1250	.149
J. M.	24.3	450	.054	543.2	1400	.388	130.0	1450	.090
L. M.	211.8	1102	.192	329.3	2290	.144	636.6	2430	.262
Mean	134.9	847	.212	403.2†	1374†	.332	419.4†	1557*	.278

* Significantly greater than control at <.02 probability.
† " " " " " <.01 "

control day between the mercurial injections and at the end of the study. The collected urine was measured quantitatively and then a 200 cc aliquot was acidified and kept refrigerated until analyzed for the thiamine content by the method described previously(1). The total thiamine excretion was recorded as well as the amount per cc of urine.

Results. The object of the initial analysis of data (Table I) accumulated was to evaluate the relationship between the absolute thiamine content and the volume of urine excreted by the individual patients. The Spearman coefficient of rank correlation was determined for thiamine content versus the urine volume. Rank correlation appeared sufficient to observe whether or not larger volumes of urine were associated with larger amounts of thiamine in the urine. None of the coefficients differed significantly from zero and hence could have been caused by chance alone even though there is no relationship between ranks in the variables considered. There is no evidence to indicate that high volume of urine is associated with high absolute amounts of thiamine.

	Spearman coefficients of rank correlation (p) = rho		
	Control	Day of mercurial	Day after mercurial
Absolute amt of thiamine vs vol of urine	—.06	—.35	+.20
Thiamine/cc of urine vs vol of urine	—.23	—.55	—.33

In Table I will be found a summary of the urine volume and the mean urinary thiamine excretion data in 9 patients during control and mercurial therapy periods. The 10th patient was not included in the table because of an inadequate number of control determinations. It is clear from the data that the concentration of thiamine in the urine increased from the control day to the day of the mercurial. It was shown previously that, among individuals, higher urine volumes were associated with somewhat lower concentrations of thiamine. Therefore it would appear that the effect of mercurial is to increase the concentration of and absolute amounts of thiamine in the urine.

Discussion. The use of mercurials is generally admitted to be the most effective means of controlling edema in the treatment of congestive heart failure. The effect of these agents upon electrolyte excretion has been adequately studied. However, there have not been sufficient accounts to provide the basis for quantitative treatment of the influence of mercurials upon vitamin excretion. The report of Williams and Bissel(3) dealing with thiamine excretion in various clinical states included 2 patients with congestive heart failure. A pronounced diuresis of thiamine occurred in each patient following mercurial administration after thiamine loading(3). Their observations tended to indicate that the increased thiamine elimination was not due to the increased urine volume. One patient studied in the present series received an intra-

muscular injection of 10 mg of thiamine after which a mercurial was given. During the next 24 hours, 13.2 mg of thiamine was eliminated. The results obtained in the present series demonstrate that the levels of thiamine excretion following the administration of mercurials are significantly increased over the levels observed on control days.

The urinary thiamine content compared with urine volumes among the individual patients fail to show higher levels of the vitamin with larger volumes of urine. Certain patients with low urine output had a higher level of thiamine excretion than those with greater urine output. These data seem to indicate that the mercurial-induced thiamine excretion is not a function of the increased urine volume. Although the mechanism of mercurial-induced thiamine excretion is obscure at present, the most likely explanation for these results is the depression of renal tubular reabsorption of thiamine.

In support of the impairment of renal tubular mechanisms for thiamine reabsorption by mercurials is the evidence that the vitamin, when administered to patients deficient in vit. B_1, is retained within the cells by conversion to diphosphothiamine(3). The excretion of thiamine after a loading dose administered to B_1-deficient patients is reduced. This deficiency, reflected in the kidneys, would promote an increased rate of conversion of thiamine derived from tubular urine into diphosphothiamine by the phosphorylating systems of the tubular cells. The levels of thiamine excretion would be reduced, thus preventing losses of the vitamin from the body. Thiamine reclaimed by the tubules would be shunted into the blood(3). In normal subjects, thiamine loading doses are rapidly excreted in the urine because of adequate concentration of the vitamin within the tubular cells as well as the other tissues.

The absence of manifestations of thiamine deficiency in patients receiving mercurials over long periods may be related to an inadequate caloric intake. Furthermore, the patients described in this report had received vitamin supplementation which may have replaced the losses produced by the action of the diuretic. The usual finding in chronic heart failure of muscle atrophy and weight loss was present in each of our patients. This has been attributed to the inability to maintain adequate nutrition due to anorexia, impaired absorption and utilization of ingested foods, and the effect of chronic disease upon cellular metabolism. It is apparent that the oral administration of thiamine and other essential food factors is not capable of correcting the nutritional abnormalities found in these patients.

Summary. The effect of mercurials on output of thiamine in the urine was investigated in 9 patients with congestive heart failure. The statistical analysis of the accumulated data indicates that the levels of thiamine excretion following mercurial administration are significantly increased over the levels observed on control days. The data seem to indicate that the mercurial-induced thiamine excretion is not due to the increased diuresis; it is suggested that it may be related to the depressed tubular absorption of the thiamine.

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