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Thiamine, Magnesium and Plasma Lactate Abnormalities in Alcoholic Patients. (31574)

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Thiamine and magnesium deficiency as well as increased plasma lactate levels have been independently described in chronic alcoholics by several investigators(1-7). While previous attempts to measure thiamine levels have been at best cumbersome(8,9), a more practical assay by means of the transketolase reaction is now available(9). Based on the production of glucose resulting from *in vitro* incubation of thiamine pyrophosphate with a

red cell hemolysate, this method was first described in alcoholics(9,10) and subsequently confirmed in normal volunteers on restricted thiamine intake(8). This assay has proved to be an adequate index of functional thiamine levels and is applicable to clinical situations wherein marginal thiamine deficiency is suspected(8,11).

Although the role of magnesium in the thiamine complex is unclear, it is thought to be an integral factor in the binding of thiamine pyrophosphate to protein(12). While the clinical significance is uncertain, magnesium has frequently been described in alcoholic patients(3,5).

The relationship of plasma lactate to thiamine and magnesium abnormalities remains obscure although certain interrelationships are suggested. Elevated plasma lactate and decreased plasma lactate clearance have been demonstrated following chronic thiamine deprivation as well as following acute alcoholic ingestion(13,14,15). Furthermore the demonstration of an unexplaained lactate induced magnesium diuresis(16) and the increased excretion of magnesium and lactate following ethanol ingestion(13) suggests an association between alcohol ingestion and thiamine, magnesium, and plasma lactate abnormalities.

To determine their incidence and the relationships of thiamine, magnesium, and plasma lactate abnormalities, these studies were performed in a group of alcoholic patients.

Methods. In 41 alcoholic subjects with signs of intoxication or withdrawal symptoms all parameters were studied 24 to 48 hours after admission to an alcoholic ward. Thiamine activity alone or with magnesium levels was studied in an additional 29 patients. Patients with obvious hepatic disease on the basis of physical examination were excluded from this study.

Blood samples were drawn in a fasting state prior to the therapeutic use of vitamins. Thiamine activity was determined utilizing the transketolase reaction described by Brin(9). Serum and red cell magnesium was measured by atomic absorption spectrophotometry(17), and plasma lactate by the method of Barker and Summerson(18). Normal values in this laboratory for thiamine activity range from 0 to 15% increase over control values on addition of thiamine pyrophosphate to hemolyzed red cells. The normal serum magnesium is 1.92 $\pm$ .16 mg% and red cell magnesium is 4.10 $\pm$ .53 mg%. The normal plasma lactate is 14.6 $\pm$ 2.9 mg%(13). The normal values given and experimental results appearing elsewhere in the paper are expressed as the mean $\pm$ two standard deviations. After obtaining initial values, 34 of the patients received 50 mg of thiamine subcutaneously and were restudied in 24 hours.

Results. The incidence and degree of abnormality of the individual parameters studied are shown in Fig. 1. Of the 70 alcoholics studied elevations of transketolase activity greater than 15% indicative of thiamine deficiency occurred in 26 (37.1%). Abnormalities of serum magnesium concentration occurred in 17 of the 56 patients studied (30.3%) with 9 patients showing lower than normal serum magnesium concentration and 8 patients showing higher levels. The red cell magnesium concentration was abnormal in 12 of 42 subjects studied (28.6%) showing an increased content in 11 and a decrease in one. There was no correlation between changes in serum magnesium and red cell magnesium (Fig. 2) indicating serum magnesium deficiency occurs independently of reciprocal alteration in red cell magnesium. Plasma lactic acid content was found elevated in 14 of 41 patients (34.1%). Both plasma lactate and thiamine activity were within normal limits in 18 of the 41 subjects studied. In 7 patients elevation of lactate and thiamine deficiency were associated while 9 showed thiamine deficiency, but normal levels of lactate. Seven subjects, however, had increased lactate levels, although thiamine activity was normal. The relationship of thiamine activity to red cell magnesium concentration and to plasma lactate is analyzed in the scattergrams of Fig. 3 and 4. It is obvious that a significant correlation of thiamine with either is not present.

Patients with abnormal transketolase activity on admission showed a rapid and consistent response to 50 mg of thiamine given parenterally. Within 24 hours, previously elevated values had returned to normal.

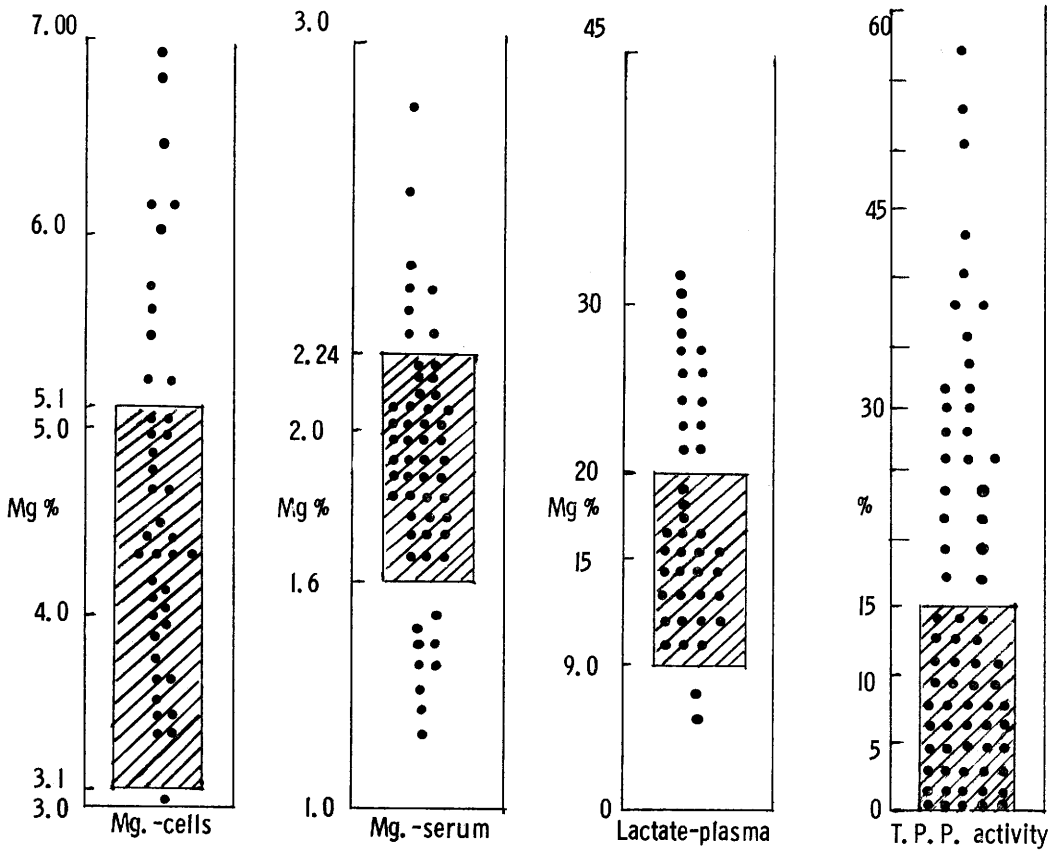


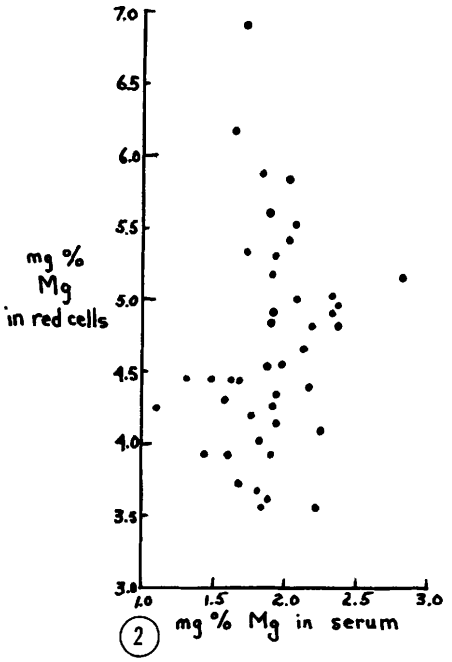
FIG. 1. Incidence and degree of abnormality in serum and red cell magnesium content, plasma lactate content, and transketolase activity in alcoholic patients. Striped areas indicate normal mean with 2 standard deviations.

Discussion. Evidence of thiamine deficiency as measured by the transketolase reaction in this group of alcoholic subjects was found in 37.1%. Approximately 25% of this group also showed abnormal plasma lactate elevations. Since abnormalities in lactate metabolism are known to be relatively insensitive indicators of thiamine deficiency (19) and the transketolase reaction an extremely sensitive one(8-10), these findings are consistent with sub-clinical thiamine deficiency. The presence of plasma lactate elevation when thiamine activity was within normal limits, as noted in 7 subjects, suggests that factors other than thiamine deficiency are responsible for the observed abnormalities in lactate concentration in this group.

The failure to demonstrate abnormal lactate elevation following lactate infusions in a similar group of subjects suggests that undetected hepatic disease is not responsible for the lactate elevations.

Although blood alcohol determinations were not performed, the period of hospitalization prior to study minimized the possibility that active alcohol metabolism was involved. Prior studies have indicated that factors other than blood level of alcohol are concerned in the abnormally elevated plasma lactate values found during acute alcoholic intoxication(13).

In the group showing initially abnormal transketolase activity, excluding the patient with unexplained excess lactate (42 mg%), the mean plasma lactate prior to therapy was 26 $\pm$ 9 mg%. Following the injection of 50 mg thiamine, the mean lactate in the same group was 16 $\pm$ 8 mg%. These findings indicate that the injection of thiamine and/or



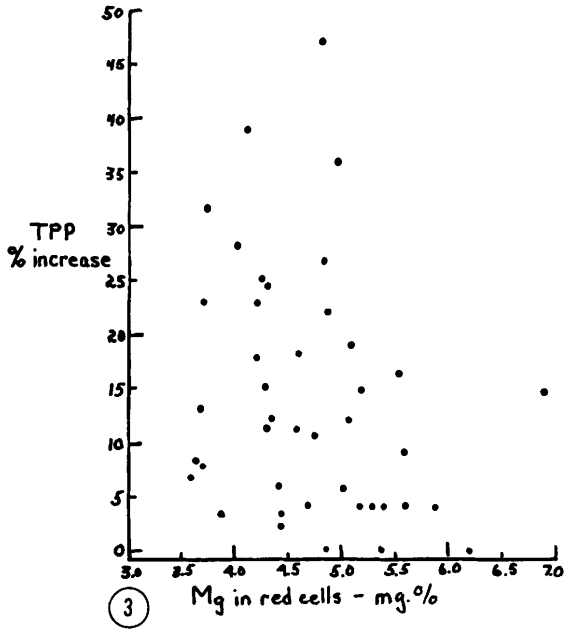


FIG. 2. Magnesium in serum and red blood cells of 42 alcoholic subjects.
FIG. 3. Independence of thiamine activity and cellular magnesium.

the associated 24-hour period of hospitalization tended to result in a parallel return towards normal of both transketolase activity and blood lactate. Similar changes in plasma lactate occurred after 24 hours in those without thiamine deficiency, indicating again the presence of other factors as determinants in the plasma lactate content.

As previously noted, there is poor correlation between red cell and serum magnesium content(20). The propensity to lowered serum magnesium concentration previously encountered in chronic alcoholics is again obvious. The failure to correlate decreased thiamine activity within the red cell, with the concentration of magnesium, indicates that magnesium deficiency is probably not a limiting factor in the thiamine pyrophosphate complex. Neuropathy as determined clinically occurred with equal frequency in those with normal thiamine activity and those with thiamine deficiency, contrary to the concept that the biochemical defect is generally apparent before the clinical defect(8,10). Better correlation might be expected with nerve conduction studies rather than clinical evaluation to determine marginal deficiencies(21).

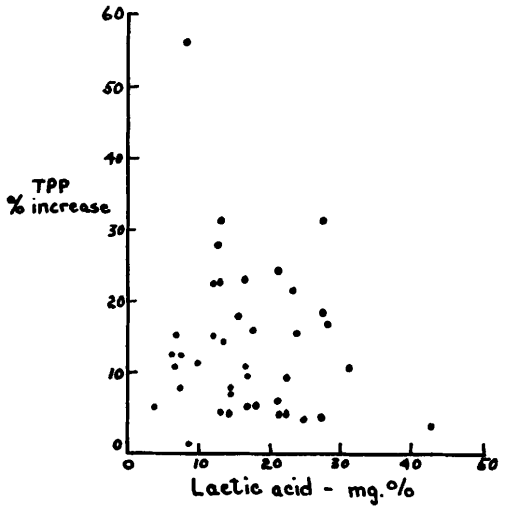


FIG. 4. Independence of thiamine activity and plasma lactate.

There was a definite tendency for thiamine deficiency to occur in an older age group, being present in 40% of those over the age of 40 and in only 22% of those under 40 years of age.

Summary. An evaluation of thiamine activity, magnesium levels, and plasma lactate

levels in chronic alcoholics demonstrated the expected common occurrence of deficiencies in each, but failed to show a correlation of these parameters in the individual alcoholic patients.

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Induction of Mitochondrial α-Glycerophosphate Dehydrogenase by Thyroid Hormone: Effect of Fasting and Refeeding.* (31575)

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Previous studies have shown that the induction of mitochondrial L-α-glycerophosphate dehydrogenase in rat liver (LM-GPDH) by triiodothyronine (T_3) may result from the acceleration of enzyme protein synthesis as judged by the fact that this induction is sensitive to inhibition by ethionine, puromycin, actinomcyin D, and 5-fluorouracil(1, 2). Starvation has been shown to suppress protein synthesis(3-5) and also to block the increase of basal metabolic rate and growth caused by T_3-administration(6). Therefore, the effect of fasting and refeeding on the induction of LM-GPDH by T_3-administration was investigated.

Materials and methods. The rats utilized, weighing between 200 and 280 g, obtained from Charles River Laboratories, were fed a control synthetic diet with the following composition: casein, 18%; dextrose, 72%; corn oil, 5%; salt-mixture (4%) and a vitamin-mixture (1%) which contained all of the known required vitamins and minerals(7). Rats were not used until they had eaten this diet for at least 5 days. The diets used in refeeding the animals after fasting contained different proportions of carbohydrate, protein and/or fat. Salt-mixture (5%) was always added to each diet used for refeeding but the vitamin-mixture was omitted owing to the brevity of the feeding period.

3,3',5-L-triiodothyronine sodium salt, ob-

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