Psychiatric Significance of the Plasma Concentrations of Magnesium and Vitamin B1 in Alcoholism and Delirium Tremens: Alcohol is a Biological Solvent

M.J.AJ.M. Hoes, M.D.[1]

Abstract

In the literature, a deficiency of magnesium or vitamin B1 in alcoholics is considered of etiologic importance in the development of delirium tremens or alcoholic encephalopathy (AE). As AE are comprised mnestic disorders, so severe as to lead to social invalidation, Korsakoff syndrome and dementia. Upon admission, the plasma concentrations of magnesium and vitamin B1 were determined in cases with alcoholism (56) or delirium tremens (43). Magnesium was as low in alcoholics as in delirium tremens cases (m-2 S.D.), vitamin B1 was in the alcoholics just below the 95 percent confidence level but very low in the delirium tremens group. The recovered cases had slightly subnormal plasma concentrations of magnesium (m-1a2 S.D.) and vitamin B1 upon admission, as did the AE cases admitted with alcoholism. Just the AE cases that were admitted with delirium tremens showed very low levels of magnesium (m-3 S.D.) and of vitamin B1 upon admission. It is concluded that a delirium tremens does not arise because of a magnesium deficiency, possibly in relation to a vitamin B1 deficiency. An AE is not caused by a pure magnesium deficiency, while a vitamin B1 deficiency is of some importance only in AE cases who were admitted with delirium. A combined deficiency of magnesium and vitamin B1 is not important to AE. AE can arise without any deficiency of magnesium or vitamin B1 in alcoholics.

[1]Dept. of Psychiatry, Radboud Hospital Theodoor Craanenlaan 4 6500 HB Nijmegen The Netherlands

Paper read at the AOP 10th Anniversary Symposion, New Orleans, 9th May 1981.

Introduction

Alcoholics often show deficiencies of essential nutrients such as minerals and vitamins. Such deficiencies are of pathophysiologic or etiologic importance for certain alcohol-related disabilities (Keller, 1977; Hoes, 1981-a,-b).

a. **Pathophysiologic:** a condition is that the deficiency and the disability are simultaneously present. In the alcohol withdrawal syndromes, delirium tremens or "tremulousness", this pathophysiologic significance is given to a deficiency of magnesium ions (McNichol, 1970; Mello and Mendelson, (1975) or of vitamin B1 (Bonjour, 1980).

b.Etiologic: the deficiency was present before the disability became apparent. A magnesium deficiency is considered etio-logically important in the occurrence of an alcoholic encephalopathy (AE). AE includes severe memory disorders with social complications, the Wernicke-Korsakoff syndrome and alcoholic dementia (Stendig-Lindberg, 1974). A vitamin B1 deficiency is considered etiologically important in the occurrence of Korsakoff syndrome (Victor et al., 1971) and possibly also of dementia (Haase, 1971).

There are, however, three reasons to reexamine the pathophysiologic or etiologic role of magnesium and vitamin B1 in alcohol-related disabilities. 1. Experimental magnesium or vitamin B1 deficiency in man does not cause any tremulousness, delirium tremens or encephalopathy (Hoes, 1979-a). 2. The neuropathology of experimental magnesium or vitamin B1 deficiencies in animals does not conform to that of dementia, whereas the neuropathologies of memory disorders, Wernicke-Korsakoff syndrome and dementia differ from each other (Hoes, 1980-d). 3. The metabolism of magnesium and that of thiamine are interdependent. Magnesium is required for the binding of thiamine to protein and is further activator of numerous enzymes, including thiamine-containing ones (Ebel and Gunther, 1980); thiamine promotes the mobilization of magnesium from bony tissue in a condition of magnesium deficiency (Itokowa et al., 1974). Further it has been reported that patients with Wernicke-Korsakoff syndrome based on hypomagnesaemia may be refractory to a vitamin B1 substitution therapy (Traviesa, 1974). This interdependence necessitates the simultaneous determination of magnesium and vitamin B1 plasma levels, before definitive conclusions may be drawn as to the specificity of findings.

In the following article the results of two published studies are combined (Hoes, 1979-a; 1980-d).

The magnesium and vitamin B1 plasma levels were determined upon admission of alcoholics (n=56) and delirium tremens patients (n=43). The pathophysiologic significance for delirium tremens or tremulousness is discussed. Further the etiologic significance of these plasma levels as determined upon admission is studied with regard to the existence of an AE upon discharge.

The Studies

The two studies (Hoes, 1979-a; 1980-d) included in total 56 alcoholics, admitted for withdrawal, and 43 patients who were admitted with a delirium tremens in a general hospital (Bethesda Hospital, Tiel). Immediately after admission venous blood samples were taken for determination of plasma levels of magnesium and vitamin B1. At the moment of blood sampling, the breath of none of the patients smelled of alcohol. The magnesium concentration was determined photometrically (m ± S.D.: 1.00 ±0.10 mmol/1; lab. Bethesda Hospital, Head of Dept. Dr. E. Kreutzer) and the vitamin B1 level microbiologically (75-225 nmol/1, 95 percent confidence range; TNO, Zeist). If it was likely that the patient had taken vitamin pills before his admission, the vitamin B1 level was not determined.

All patients were given an intramuscular injection of two ampoules of Parenterovite forte® a day for five days (aneurine HCI, 250mg, riboflavine 4 mg, pyridoxine 50 mg, ascorbic acid 500 mg, nicotinamide 160 mg, sodium pantothenate 5 mg); after that the vitamin therapy was changed to one tablet of Oralvite® t.i.d. (aneurine HCI 50 mg, riboflavine 5 mg, pyridoxine HCI 5 mg, nicotinamide 200 mg, d-calcium pantothenate 5 mg, ascorbic acid 100 mg). Furthermore 750 mg $MgSO_4$ (magnesium sulphate) was injected intravenously three times a day during the first three days. Upon discharge the patients were diagnosed as "AE" or as "recovered". In the first study the AE criteria were represented as "ADL" (the inability to perform one or more activities of daily living: taking a bath, getting dressed, eating, going to the toilet) (Hoes, 1979a) in the second study as memory disorders, Korsakoff syndrome or dementia (Hoes, 1980-d). For the classification criteria we refer to those studies.

Results

For as far as possible and desirable, the results of both studies were combined (Hoes 1981-a). The two groups upon discharge, recovered or AE, were further subdivided according to the diagnosis upon admission: alcoholism or delirium tremens, so that there are four subgroups upon discharge. There is no significant difference in sex or age distribution between the two groups upon admission or between the four subgroups upon discharge (Tables 1 and 2) (t-test). The plasma levels of vitamin B1 TABLE 1

SEX DISTRIBUTION OF THE PATIENTS STUDIED

PATIENT GROUP	SEX F	M
ADMISSION (N=99)		
alcoholism (56)	8	48
delirium tremens (43)	7	36
DISCHARGE (N=99)		
RECOVERED (N-81)		
alcoholism I49)	7	42
delirium tremens (32)	5	27
ENCEPHALOPATHY (N = 18)		
alcoholism (7)	0	7
delirium tremens (11)	2	11

There is no significant difference in sex distribution between the two groups upon admission or between the four subgroups upon discharge (t-test)

TABLE 2

AGE DISTRIBUTION OF THE PATIENTS STUDIED

PATIENT GROUP	AGE (Years) m	+ S.D.
ADMISSION (N=99)		
alcoholism (56)	46.6	14.1
delirium tremens (43)	49.2	11.6
DISCHARGE (N=99)		
RECOVERED (N=81)		
alcoholism (49)	46.5	14.4
delirium tremens (32)	46.3	10.8
ENCEPHALOPATHY (N = 18)		
alcoholism (7)	49.9	11.7
delirium tremens (11)	58.1	9.8

There is no significant difference in age distribution between the two groups upon admission or between the four subgroups upon discharge (t-test)

cannot be compared statistically with the reference values because the reference values are not distributed normally (positively skewed) and because TNO (organisation for Toegepast Natuurweten-schappelijk Onderzoek, applied scientific research) did not know the exact modus. Applicable to the two admission groups, however, (Table 3) is that the patients with

TABLE 3

VITAMIN B1 PLASMA LEVELS

PATIENT GROUP (nmol/1)	VITAMIN B1 m	± S.D.	
ADMISSION (N=99)			
alcoholism (56)	79.3	22.4	(49)
delirium tremens (43)	60.8	16.7	(26)
DISCHARGE (N=99)			
RECOVERED (N-81)			
alcoholism (49)	81.4	22.3	(41)
delirium tremens (32)	63.9	16.2	(21)
ENCEPHALOPATHY (N=18)			
alcoholism (7)	72.5	21.3	(06)
delirium tremens (11)	39.6	16.2	(11)
REFERENCE VALUES		75-225	

Upon admission the group of delirium tremens showed significantly ($p=0.01$) lower vitamin B1 levels than the group of alcoholics (t-test). Upon discharge the vitamin B1 level of the total AE group (52.4*23.3 nmol/1) is significantly lower ($p<0.0001$, t-test) than that of the total group of recovered patients (74.7±21.7 nmol/1). However, this difference is completely due to the contribution of the subgroup delirium tremens with AE. The vitamin B1 level of this AE subgroup with delirium tremens differs significantly ($p<0.01$) from that of the AE subgroup with alcoholism and even more significantly ($p<0.001$) from that of the total group of recovered patients. The vitamin B1 level of the AE subgroup with alcoholism does not differ significantly from that of the total group of recovered patients It-test).

delirium tremens show significantly lower vitamin B1 levels than the alcoholics (t-test; p=0.01). The average patient with delirium tremens shows values below the lower limit of 75 nmol/1 of the reference values. In the discharge groups the vitamin B1 plasma levels were lower in the AE group than in the group of recovered patients (p<0.0001; t-test). However, this difference is completely due to the subgroup of AE with delirium tremens (Table 4)

TABLE 4

MAGNESIUM PLASMA LEVELS

PATIENT GROUP (mmol/1)	MAGNESIUM m	± S.D.	
ADMISSION (N=99)			
alcoholism (56)	0 79 (54)	0.12	
delirium tremens (43)	0.72	0.17	(36)
DISCHARGE (N=99)			
RECOVERED (N=81)			
alcoholism (49)	0.78	0.15	(47)
delirium tremens (32)	0.72	0.16	(25)
ENCEPHALOPATHY (N=18)			
alcoholism (7)	0.84	0.16	(07)
delirium tremens (11)	0.76	0.19	(11)
REFERENCE VALUES	1.00	0.10	

The magnesium plasma levels of the two admission groups and the four discharge subgroups are equally reduced (pO.05) with regard to the reference values (t-test). There were no mutual differences between the two groups upon admission or between the four subgroups upon discharge.

The vitamin B1 values of this subgroup differ significantly from those of the

subgroup AE with alcoholism ($p<0.01$; t-test) or from those of the total group of recovered patients ($p<0.001$; t-test). The vitamin B1 values of the subgroup AE with alcoholism did not differ significantly from those of the total group of recovered patients (t-test). The AE subgroup with delirium tremens also shows lower vitamin B1 values than the lower limit of the reference values.

The magnesium plasma levels were reduced in the two admission and two discharge groups or four subgroups upon discharge, in comparison with the reference values (t-test, $p=0.05$ for all groups) and no mutual differences between the respective groups or subgroups were observed. In total, tremulousness occurred in 14 alcoholics. Their magnesium plasma levels did not differ significantly from those of the other alcoholics, in either of the two studies (t-test). The symptoms of tremulousness clearly improved upon an injection of magnesium; one to two hours later the symptoms recurred. In neither of the two studies was a correlation found between the magnesium and vitamin B1 values (Hoes, 1979-a; 1980-d).

Discussion

Women constitute 15 percent of the total group of patients and are evenly distributed over the two admission groups. So they suffer as much as men from delirium tremens. In the AE group there are no women with alcoholism as the diagnosis upon admission, but two women had delirium tremens as admission diagnosis. In the delirium group the man/woman ratio is the same as upon admission (1:5). The question remains whether the share of women with alcoholism will increase absolutely and relatively with regard to the current situation and to the number of men, or whether it will remain constant or decrease. The evolution of smoking habits, a sign of emancipation, gives rise to the worst fears (Hoes, 1980-c).

The magnesium plasma levels are evenly reduced in the patients with alcoholism and delirium tremens. We may conclude from this that both groups show the same lack of magnesium. But a few remarks have to be made about this. The magnesium plasma levels are in a dynamic equilibrium with the magnesium in the bones, from which magnesium is mobilized upon insufficient absorption in the gut, e.g. in deficient nutrition (less than 6 mg/kg/day according to Durlach et al., 1980).

The magnesium plasma level only begins to decrease when the total magnesium reserve has decreased by at least 1/3 (Bogert et al., 1973; Hoffman, 1970). This means a loss of 1/3 of 24 g = 8 g; the daily loss of magnesium in severely deficient nutrition is about 25 mg (Ebel and Gunther, 1980). Hence it takes about a month before the first signs are noted if a magnesium deficiency is provoked in man. This begins with fasciculations, muscle cramps, tremor, choreathetoid movements; afterwards irritability, depressiveness and aggressiveness occur; finally followed by disorientation, confusion and sometimes lethal convulsions. Therefore the clinical condition is not a measure of the exact quantification of the magnesium state (Katzman and Pappius, 1973; Yendt, 1972). Furthermore it should be considered that a pure magnesium deficiency is rarely observed; mostly deficiencies of other minerals and nutrients are also involved in the occurrence of the condition (Katzman and Pappius, 1973).

Another factor that must always be considered in alcoholics is the plasma level of alcohol. Alcohol reduces the plasma level of magnesium, and during 24 hours after the alcohol plasma level has reached zero the plasma level of magnesium increases; this increase starts as soon as the alcohol plasma level begins to decrease (Kramp et al., 1979). No smell of alcohol was observed on the breath of the studied patients upon admission. So the plasma levels of magnesium could still have been increasing. Considering the above, we may still conclude that no specific shortage of magnesium can be demonstrated in patients with delirium tremens, as reported in the literature (McNichol, 1970; Mello and Mendelson, 1975). The tremors and tremulousness of the delirium tremens patients and of the patients who developed tremulousness re-

sponded well to substitution of magnesium. However, the plasma levels of these patients did not differ significantly from those of the other alcoholics. Furthermore the favorable response does not confirm the existence of any deficiency. The clinical impression, though qualitative, is reliable, but magnesium ions have a curare-like effect on the neuromuscular transmission (Katzman and Pappius, 1973; Yendt, 1972). Suppression of signs of neuromuscular hypersensitivity is therefore a pharmacologic feature of magnesium ions and does not prove the existence of a magnesium deficiency at all. So a specific pathophysiologic role of a magnesium deficiency in delirium or tremulousness cannot be confirmed, either, although this has been reported in the literature (McNichol, 1970; Mello and Mendelson, 1975). The magnesium plasma levels of the four subgroups upon discharge do not differ from each other. Therefore a specific etiologic role of magnesium deficiency in the development of an alcoholic encephalopathy cannot be demonstrated, as has been suggested in the literature (Kramp et al., 1979; Stendig-Lindberg, 1974).

Vitamin B1 levels have been determined microbiologically. This is a reliable method but only the total vitamin content is established this way and not the active metabolite (Bonjour 1980). The vitamin B1 plasma levels are only reduced in patients with delirium tremens and not in alcoholics. This corresponds with a specific role attributed to a vitamin B1 deficiency in the occurrence of delirium tremens (Hemming-sen et al., 1979; Bonjour, 1980). Against a specific pathophysiologic role is the fact that an experimental vitamin B1 deficiency does not lead to delirium tremens. In experimental conditions a thiamine-poor diet results within a fortnight in symptoms such as fatigue, depressiveness, irritability, loss of concentration and interest. After three to four weeks symptoms such as further fatigue, loss of appetite, loss of weight, constipation, muscle cramps and diverse pains occur (Bogert et al., 1973). Thiamine has been called the "morale vitamin". The severity of a vitamin B1 deficiency in AE patients with delirium tremens suggests that they have almost exclusively consumed alcoholic beverages in the weeks prior to admission. In the discharge group vitamin B1 deficiency is only observed in the subgroup AE admitted with delirium tremens. Although it has been reported in the literature that the neuropathology of a Korsakoff syndrome (Victor et al., 1971), a dementia (Haase, 1971) or severe memory disorders (Lishman, 1978) may be based on a lack of vitamin B1, this has not been confirmed in the subgroup AE with alcoholism in this study, and in the subgroup AE with delirium tremens it is considered possible but not proven. In the subgroup AE with delirium tremens the pathophysiology of the delirium itself might have contributed to the development of the AE; but since there are also patients with delirium tremens and without AE at the end of the study, and since they show higher vitamin B1 plasma levels than the delirium patients with AE, the combination of a vitamin B1 deficiency and the pathophysiology of the delirium tremens must be held responsible for the occurrence of the AE (see also Hoes, 1979-b).

The existence of an AE in alcoholics cannot be explained by a higher age, a different sex distribution or a demonstrated deficiency of magnesium or vitamin B1, since all these factors appear to be negative. A combined effect of a marginal deficiency of magnesium and vitamin B1 is possible (Hoes 1981-b); it is, however, unlikely that this has been of any importance, because the same plasma levels of magnesium and vitamin B1 have been found in the group of alcoholics without AE but with complete recovery. In the group AE, the subgroup, severe memory disorders, Korsakoff syndrome and dementia were evenly distributed and these demonstrated no difference in magnesium or vitamin B1 levels (Hoes 1980-d). A last possible explanation for the occurrence of AE is another type of beverage or drinking pattern in these alcoholics. Alcohol and particularly its metabolite, acetaldehyde, are highly neurotoxic substances (Roebuck and Kessler, 1972; Hoes 1980-a). Beverages with a high alcohol content rather lead to high plasma levels of alcohol and its metabolite,

while also the drinking pattern plays a part. This neurotoxicity may certainly lead to the development of neuropathologic changes (Lishman, 1978). This brings the discussion in the last paragraph back to nutrition again.

An alcoholic has lost control of his drinking habits, he is preoccupied with drinking and the acquisition of it and this excessive drinking has a disastrous effect on his physical and social health (Chafetz and Demone, 1975). When he exceeds the limits of eight pints of beer or an equivalent amount of alcohol a day the diagnosis is almost certain. Pathognomonic are tremors, morning drinking and amnesia (Orford and Hawker, 1974). The patients are often capable of performing some activities. If such persons change their drinking pattern, type of beverage or their eating habits, the greatest attention should be paid to the patient because this change may forebode a delirium tremens and an AE.

Conclusions

1. It does make sense to determine the plasma levels of magnesium and vitamin B1 in patients with alcoholism or delirium tremens, because possible deficiencies may be traced and supplemented.
2. A magnesium deficiency does not play a specific part in the development or existence of an alcoholic encephalopathy or a delirium tremens.
3. A vitamin B1 deficiency possibly plays a part in the existence of a delirium tremens and presumably also in the occurrence of an alcoholic encephalopathy in exclusively delirium tremens patients.
4. A severe vitamin B1 deficiency in delirium tremens patients forebodes the occurrence of an alcoholic encephalopathy.
5. An interdependence of magnesium and vitamin B1 did not appear to be important for the development of a delirium tremens or the occurrence of an alcoholic encephalopathy.
6. Factors such as drinking pattern or type of beverage should be studied further with respect to delirium tremens.

Alcohol is a natural product of a fermentation process (Hoes, 1980-a). Excessive drinking of alcohol destroys the functioning and structure of all organs, liver, intestines, heart, bone marrow, hormonal apparatus, lymphatic system, nerves, muscles and brain (Lieber, 1977).

In the double sense of "biological", we may conclude therefore that alcohol essentially is a biological solvent.

Acknowledgement

All statistical calculations have been performed by Dr. N. Sijben, research psychologist, Dept. of Psychiatry Radboud Hospital, to whom the author is very grateful.

References

BOGERT, J.L.. BRIGGS, G.M. and CALLOWAY, D.H.: Nutrition and Physical Fitness. Saunders, Philadelphia, thiamin 117-127, magnesium 252-255,1973.

BONJOUR, J.P.: Vitamins and Alcoholism, Part IV: Thiamin. Internal. J. Vit. Nutr. Res. 50,321-338,1980.

CHAFETZ, M.E. and DEMONE, H.W.: Programs to Control Alcoholism. In: Arieti, S. (ed.) American Handbook of Psychiatry. Basic Books, New York, Vol. III,712-722,1975.

DURLACH, J., RAYSSIGUIER, Y. and LAGUITTON, A.: Le Besoin en Magnesium et son Apport dans la Ration. Med. et Nutr. 16, 15-21, 1980.

EBEL, H. and GUNTHER, T.: Magnesium Metabolism: A Review. J. Clin. Chem. Clin. Biochem. 18,257-270,1980.

HAASE, G.R.: Diseases Presenting as Dementia. In: Wells, Ch. E. (ed.) Dementia, Blackwell, Oxford, 163-219,1971.

HEMMINGSEN, R., KRAMP, P. and RAFAELSEN, O.J.: Delirium Tremens and Related Clinical States. Aetiology, pathophysiology and treatment. Acta Psychiat. Scand. 59,337-369,1979.

HOES, M.J.A.J.M.: The Significance of the Serum Levels of Vitamin B1 and Magnesium in Delirium Tremens and Alcoholism. J. Clin. Psychiat. 40,476479,1979-a.

HOES, M.J.A.J.M.: Misbruik van Psychoactieve Stoffen: Tolerantie en Afhankelijkheid. TGO/JDR 4, 506-512; 5, 572-578,1979-b.

HOES, M.J.A.J.M.: Biologisch-psychiatrische Aspecten van Afhankelijkheid van Alcohol. Tijdschr. Ale. Drugs Psychotrop. Stoff. 6, 11-21, 1980 a.

HOES, M.J.A.J.M.: De Klinisch psychiatrische Betekenis van de Plasma Concentrates van Vitamin B1 en Magnesium bij Opname van Patiemen met Alcoholisme of Delirium Tremens. In: Een Aantal Probleemsituaties in de Ambulante Psychiatrische Hulpverlening. Symposionverslag, Janssen Pharmaceutica 28 Februari, pp. 21 - 27,1980-b.

HOES, M.J.A.J.M.: Biologisch-psychiatrische Aspecten van de Afkanke-lijkheid van Tabak en Koffie. Tkjdschr. Ale. Drugs Psychotrop. Stoff. 6, 48-51,1980-c.

HOES, M.J.A.J.M.: Plasma Concentrates of Magnesium and Vitamin B1 in Alcoholism and Delirium Tremens: Pathogenic and prognostic implications. Acta Psychiat. Belg. 80, in press, 1980-d.

HOES, M.J.A.J.M.: Vitamine B1 en Magnesium bij Alcoholisten. Tijdschr. Ale. Drugs Psychotrop. Stoff. 7,65-70,1981 -a.

HOES, M.J.A.J.M.: Magnesiumsuppletie bij de Behandeling van Alco holisten, NTvG, 125,228-289,1981-b.

ITOKOWA, Y., TSENG, L. and FUUWARA, M.: Thiamine Metabolism in Magnesium-Deficient Rats. J. Nutr. Sci. Vitaminol. 21,249-255,1974.

KATZMAN, R. and PAPPIUS, H.M.: Brain Electrolytes and Fluid Metabolism. Williams and Wilkins, Baltimore, 265-278,1973.

KELLER, M.: A Lexicon of Disablements Related to Alcohol Consumption. In: Edwards, G., Gross, M.M., Keller, M. et al. (eds.) Alcohol-Related Disabilities, WHO Offset, Geneva, no. 32,2*61,1977.

KRAMP, P., HEMMINGSEN, R. and RAFAELSEN, O.J.: Magnesium Concentrations in Blood and Cerebrospinal Fluid during Delirium Tremens. Psycbiat. Res. 1,161-171,1979.

LIEBER, C.S.: Metabolic Aspects of Alcoholism. MTP Press, St. Leonards-gate, 1977.

LISHMAN, W.A.: Organic Psychiatry, Blackwell, Oxford, 1978.

McNICHOL, R.W.: The Treatment of Delirium Tremens and Related States. Ch. Thomas, Springfield, 46-71,1970.

MELLO, N.K. and MENDELSON. J.H.: Alcoholism, a Biobehavioral Disorder. In: Arieti, S. led.) American Handbook of Psychiatry Basic Books, New York, vol. IV, 375-403,1975.

ORFORD, J. and HAWKER, A.: Note on the Ordening of Onset of Symptoms of Alcohol Dependence. Psychol. Med.. 4,281 -288,1974.

ROEBUCK, J.B. and KESSLER, R.G.: The Etiology of Alcoholism. Ch. Thomas, Springfield, 1972.

STENDIG-LINDBERG, G.: Hypomagnesemia in Alcohol Encephalopathies. Acta Psychiat. Scand. 50,465-480,1974.

TRAVIESA, D.C.: Magnesium Deficiency: a Possible Cause of Thiamine Refractoriness in Wernicke-Korsakoff Encephalopathy. J. Neurol. Neurosurg. Psychiat. 37,959-962,1974.

VICTOR, M., ADAMS, R.D. and COLLINS, G.H.: The Wernicke-Korsakoff Syndrome. Davis, Philadelphia, 1971.

YENDT, E.R.: Disorders of Calcium, Phosphorus and Magnesium Metabolism. In: Maxwell, H.M., Kleeman, Ch. R. (eds.) Clinical Disorders in Fluid and Electrolyte Metabolism. McGraw-Hill, **New** York, **460-464,** 1972.