

been reported in a number of papers²⁻⁶ to produce the same effect. Van Landingham *et al.*⁶ found that feeding thyroprotein reduced the ascorbic acid content of milk approximately one-third. The present report deals with the effect of feeding thyroprotein upon the content of vitamin A, thiamin, riboflavin and niacin in milk.

Two pure bred Guernsey cows and 2 pure bred Holstein cows were fed a grain mixture supplemented with alfalfa hay. The amount of feed was kept constant for each cow during the entire experimental period of 12 weeks. At the start of the experiment the cows were fed the regular ration, for 3 weeks, then for 6 weeks the regular ration plus 15 g iodinated casein* daily, and for the remaining 3 weeks the regular ration again.

Thiamin was determined by the method of Hodson,⁷ niacin by the method of Krehl, Strong and Elvehjem,⁸ and riboflavin by the method of Hand⁹ modified according to Mc-

Laren, Cover and Pearson.¹⁰ Vitamin A and carotene were determined by the method of Berl and Peterson.¹¹

The average results obtained with the 2 Guernsey cows are given graphically in Fig 1. As in previous reports²⁻⁶ the feeding of thyroprotein caused a rise in milk production which lessened during the latter part of the period of thyroprotein feeding. In addition the concentration (γ /ml) of niacin and thiamin in the milk was increased while that of riboflavin was decreased. It is interesting that the maximum concentration of niacin and thiamin and the minimum concentration of riboflavin were reached at the peak of the milk production. The rise in thiamin content was comparatively very small and not significant. On the 12th week it was only slightly less than the peak value. The rise in niacin was comparatively large and highly significant. Curves showing the effect of the thyroprotein on the concentration of vitamin A and carotene in the milk are not included in Fig. 1 since no significant changes were observed. The results obtained with the Holstein cows closely approximated those with the Guernseys.

² Reineke, E. P., *J. Dairy Sci.*, 1942, **25**, 201.

³ Reineke, E. P., *J. Dairy Sci.*, 1943, **26**, 750.

⁴ Reineke, E. P., and Turner, C. W., *J. Dairy Sci.*, 1942, **25**, 393.

⁵ Reese, R. P., *J. Dairy Sci.*, 1944, **27**, 545.

⁶ Van Landingham, A. H., Henderson, H. O., and Weakley, C. E., Jr., *J. Dairy Sci.*, 1944, **27**, 385.

* Acknowledgment is made to W. R. Graham, Jr., Cerophyll Laboratories, Inc., for the generous supplies of iodinated casein.

⁷ Hodson, A. Z., *Food Research*, 1945, **10**, 351.

⁸ Krehl, W. A., Strong, F. M., and Elvehjem,

C. A., *Ind. Eng. Chem., Anal. Ed.*, 1943, **15**, 471.

⁹ Hand, D. B., *Ind. Eng. Chem., Anal. Ed.*, 1939, **11**, 306.

¹⁰ McLaren, B., Cover, S., and Pearson, P. B., *Arch. Biochem.*, 1944, **4**, 1.

¹¹ Berl, S., and Peterson, W. H., *J. Nutr.*, 1943, **26**, 527.

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Plasma Tocopherol Levels in Sprue.*

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(Introduced by C. S. Robinson.)

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The steatorrhea of sprue is accompanied by low levels of vitamin A and carotene in

the blood plasma,^{1,2} by hypoprothrombinemia were through the Tennessee-Vanderbilt Nutrition Project.

* This work was supported by grants from Distillation Products, Inc., the Nutrition Foundation, the International Health Division of The Rockefeller Foundation, and by the Tennessee State Department of Public Health. The latter 3 grants

¹ Ingelfinger, F. J., *New Eng. J. Med.*, 1943, **228**, 180.

² Cayer, D., Ruffin, J. M., and Perlzweig, W. A., *Am. J. Med. Sci.*, 1945, **210**, 200.

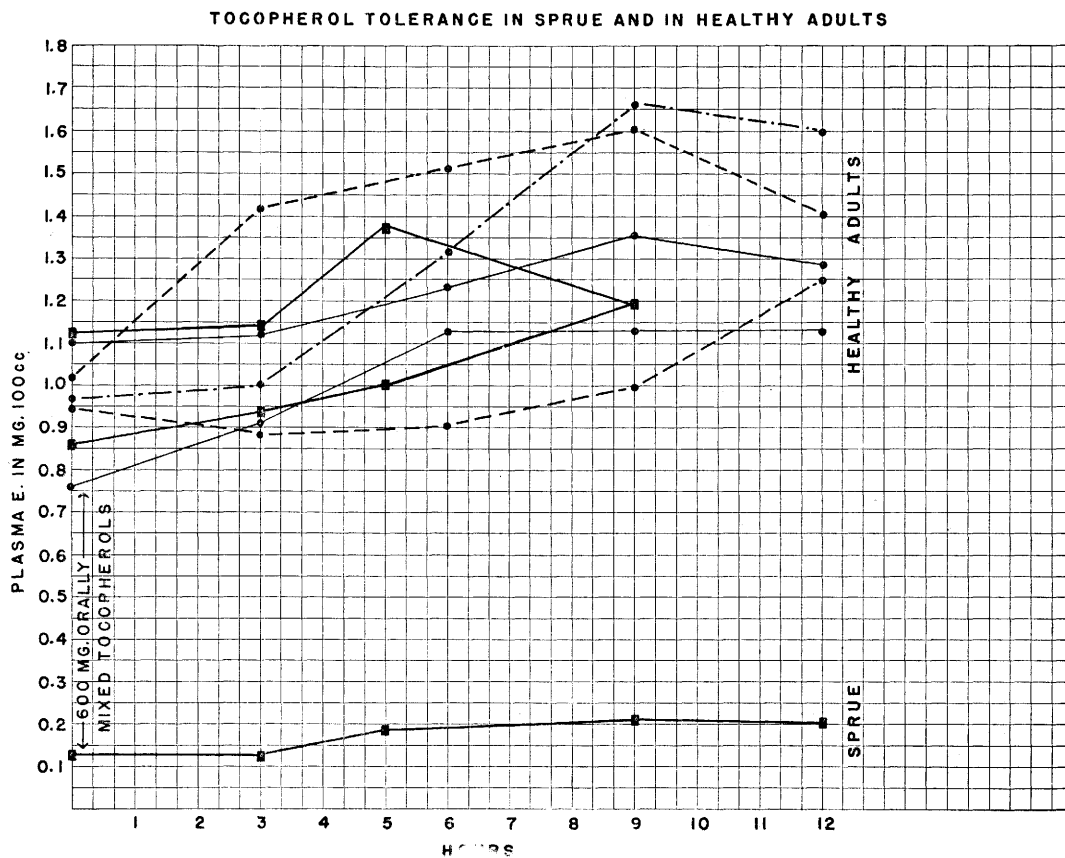


Fig. 1.

of vitamin K deficiency,^{3,4,1} by a flattening of the glucose tolerance curve, and by deranged calcium metabolism⁵ perhaps in part due to vitamin D deficiency. Studies on rats with bile fistulas indicate that the absorption of fat-soluble vitamin E is dependent upon the presence of normal fat absorption.⁶ The plasma tocopherol level in sprue does not appear to have been investigated, but Minot⁷ found a relatively low value in a child with celiac disease.

We have recently studied the plasma

tocopherol levels^{8,9} in 20 patients with sprue in relapse or remission. The lowest values have occurred in those patients who were in relapse or early remission. In one of these patients (J.D.) the tocopherol level gradually decreased to a very low value as the patient underwent a relapse following the withholding of pteroylglutamic acid (PGA) therapy, and is again increasing after reinstitution of therapy with PGA. During relapse a maximum rise in serum concentration of tocopherols of 0.09 mg per 100 cc was noted after an oral dose of 600 mg of mixed tocopherols, in contrast to the mean maximal rise of 0.37 mg in 7 healthy adults after a similar dose. These changes are depicted

³ Fanconi, *Deut. Med. Wochensh.*, 1938, **64**, 1565.

⁴ Butt, H. R., and Snell, A. M., *Vitamin K*, Philadelphia, 1941, 101.

⁵ Bennett, T. I., Hunter, D., and Vaughan, J. M., *Quart. J. Med.*, 1932, **1**, 603.

⁶ Greaves, J. D., and Schmidt, C. L. A., *Proc. Soc. Exp. Biol. and Med.*, 1937, **37**, 40.

⁷ Minot, A. S., *J. Lab. Clin. Med.*, 1944, **29**, 772.

⁸ Quaife, M. L., and Harris, P. L., *J. Biol. Chem.*, 1944, **156**, 499.

⁹ Quaife, M. L., and Biehler, R., *J. Biol. Chem.*, 1945, **159**, 663.

TABLE I.
Plasma Tocopherol Levels in Sprue in Relapse and Early Remission Following Therapy with Pteroylglutamic Acid (PGA).

Case	Date	Plasma tocopherol, mg/100 cc	Remarks
J.D.	5-1-46	0.76	Clinical remission after PGA therapy.
	6-19-46	0.30	Clinical and hematologic relapse.
	7-13-46	0.14	" " " "
	7-16-46	0.12	" " " "
	7-25-46	—	Therapy with PGA reinstituted.
	9-4-46	0.34	Clinical remission after PGA therapy.
W.O.	4-27-46	0.25	In relapse.
	5-6-46	—	Therapy instituted with PGA.
	5-16-46	0.43	Remission.
	7-13-46	0.43	"
P.B.	6-5-46	0.32	Clinical remission following therapy with
	7-16-46	0.36	PGA from November, 1945.

in Fig. 1. In another patient (W.O.) there was a slight increase in plasma tocopherol concentration following the administration of pteroylglutamic acid. The concentration of serum carotene has tended to parallel the tocopherol levels in these cases. Low values of serum vitamin E have also been found in an infant with cystic fibrosis of the pancreas and in some patients having liver disease, either hepatitis or cirrhosis.

The mean value of plasma tocopherol in 10 apparently healthy adults was 1.06 ± 0.06 mg per 100 cc. These results are in agreement with those of other workers.^{7,8} In 140 determinations on patients having either pernicious anemia or acromegaly, and in pregnancy, we have not encountered any value of plasma tocopherol below 0.62 mg per 100 cc.

In 17 patients with sprue in remission following a long period of treatment with liver extract, the tocopherol levels were found to be essentially normal, the mean value being 0.97 ± 0.08 mg per 100 cc.

The possible significance of these low values during a relapse of sprue is underscored by the reports^{10,11} that muscle tissue at autopsy from patients with sprue showed pigment resembling that seen in vitamin E deficient animals. Furthermore, experimental

studies reveal that sulfa-treated rats become deficient in vitamin M and sometimes manifest tocopherol deficiency.¹² It seems probable that a deficiency of some members of the vitamin M complex may affect the absorption or utilization of fat-soluble vitamins. In seeking evidences of tocopherol deficiency in man it may be fruitful to study carefully active cases of steatorrhea.

Summary. Three patients with sprue in relapse or early remission were found to exhibit very low plasma tocopherol levels. The rise in plasma concentration of tocopherols following an oral dose of 600 mg was less in a patient with sprue in relapse than in 7 healthy subjects. The average concentration of plasma tocopherols was essentially normal in 17 sprue patients treated with liver extract for long periods. These findings are of interest in view of the recognized occurrence of deficiencies of other fat-soluble vitamins in sprue.

¹⁰ Pappenheimer, A. M., and Victor, J., *Am. J. Path.*, 1946, **22**, 395.

¹¹ Adlersberg, D., and Schein, J. T., reported at the San Francisco Meeting of the American Medical Assn., Section on Gastroenterology, July 3, 1946.

¹² Daft, F. S., Endicott, K. M., Ashburn, L. L., and Sebrell, W. H., *Proc. Soc. Exp. Biol. and Med.*, 1943, **53**, 130.