The Use of Synthetic *L. Casei* Factor in the Treatment of Sprue[1,2]

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Vitamin M deficiency in the monkey (*5*) and the sprue syndrome in man present similar clinical pictures. The demonstration by Day and co-workers (*3*) that vitamin M deficiency in the monkey is cured promptly by the injection of highly purified *L. casei* factor has led us to test the efficacy of synthetic *L. casei* factor (Lederle) (*1*)[3] in the treatment of sprue. Liver and liver extracts have long been known to be of value in the treatment of this latter disease.

Three patients with sprue have been admitted to the Medical Service of Vanderbilt University Hospital since 24 September 1945. These cases have fulfilled all of the criteria necessary for such a diagnosis: viz., glossitis; diarrhea with increased fat content of the stools; marked loss of weight; pigmentation of the skin; macrocytic anemia; moderate leucopenia; impairment of absorption as indicated by a flat oral glucose tolerance curve with a normal intravenous tolerance curve, a flat vitamin A tolerance curve, and a very low serum carotene content; and a characteristic gastrointestinal pattern on X-ray examination. Free hydrochloric acid was present in the gastric juice of each. Sternal marrow of two of the patients was examined and found to be typical of that seen in untreated sprue and pernicious anemia.

After a preliminary period of observation these patients received daily intramuscular injections of 15 mg. of synthetic *L. casei* factor[4] as the sole therapeutic agent. In all three cases there has occurred prompt hematological and clinical improvement. The symptoms of glossitis have disappeared within three or four days, followed by rapid regeneration of the lingual papillae; there has been an improved sense of well being; the diarrhea has subsided; the appetite has improved, and there has followed an impressive gain in weight. The first man so treated has gained 26 pounds within the six-week period since the institution of therapy.

Maximum reticulocyte responses of 15.3 per cent and 43 per cent occurred respectively in the first two cases on the eighth and sixth days of treatment. The third case has 11 per cent reticulocytes on the sixth day of therapy (time of writing), having had less than 1 per cent prior to treatment. These responses have been accompanied by a great increase in the number of platelets and a rise in the white cell counts. There have also been increases of both red blood cells and hemoglobin concentration. Examinations of aspirated sternal marrow after treatment have shown the disappearance of the more primitive red blood cells and a return of the white cell series to normal proportions.

The striking and rapid response of these three patients leads us to suggest that this synthetic factor is identical with, or very closely allied to, the substance in liver extract which is effective in the treatment of sprue. Furthermore, it seems probable that vitamin M deficiency in the monkey is the experimental analogue of sprue in man. Inasmuch as that factor which relieves macrocytic anemia of pregnancy is so closely related to vitamin M (*2, 7*), it is suggested that this synthetic material may prove efficacious in the treatment of patients with this macrocytic anemia of pregnancy. A possible relationship of this *L. casei* factor to the erythrocyte maturating factor is suggested by the great similarity of the blood picture, the marrow, and the glossitis in sprue and pernicious anemia.

Spies, *et al.* (*6*) have reported that this synthetic factor is effective in the treatment of incompletely diagnosed macrocytic anemia. Goldsmith (*4*) has reported the successful treatment of a case of "nutritional macrocytic anemia" with "folic acid."

[1] Two of the cases discussed here were reported at the meeting of the Southern Medical Association, Cincinnati, 14 November 1945.

[2] A part of this study was supported by the Tennessee-Vanderbilt Nutrition Project, a cooperative undertaking of the International Health Division of the Rockefeller Foundation, the Nutrition Foundation, Inc., and the Tennessee Department of Public Health.

[3] We are indebted to Dr. Stanton M. Hardy, medical director of the Lederle Laboratories, Inc., for generous gifts of this synthetic *L. casei* factor.

[4] The crystalline material was dissolved in water by the addition of a minimal quantity of disodium phosphate, and the solution autoclaved at 10 pounds' pressure for 15 minutes.

References

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