rats. Since lathyrus peas are grown extensively as a forage crop, this problem is important also in animal husbandry.

It is evident that the nutrition of the peoples of other continents than our own will become a matter of increasing concern to us in the years ahead. For this reason, it is desirable to understand the nutritive value of many foods not commonly used in America. The problems of lathyrism, favism, and related conditions, and diseases of nutrition associated with intoxicants, should be investigated. It is not unlikely that other disturbances due to similar toxic factors exist and may be important, particularly in periods of food shortage or among peoples whose nutrition is at a minimal level.

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REPLACEMENT OF VITAMINS OF THE B-GROUP BY AMINO ACIDS

Studies of the metabolism of microorganisms have often led to results of major significance for our understanding of metabolic events in animals. An excellent example of this has been the clarification of the mechanisms of tissue metabolism made possible, to a large extent, through studies of oxidation catalysts in yeast. Likewise a number of the vitamins of the B-group were first demonstrated as growth factors for microorganisms. Two different laboratories have described an interesting relation between some of the B-complex vitamins and certain amino acids. These findings may contribute to a fuller understanding of certain deficiency diseases.

A relation between pyridoxine and the amino acid, alanine, has been described by Snell and Guirard (*Proc. Nat. Acad. Sci.* **29**, *66 (1943)*). Their initial observation was the demonstration of the existence in natural products of a substance which is derived from pyridoxine, but which far surpasses pyridoxine as a growth factor for Streptococcus lactis R. This new growth factor has been called pseudopyridoxine. Other experiments showed that the growth promoting activity of pyridoxine was strikingly increased by autoclaving it with the culture medium. This enhanced growth effect was attributed to interaction between pyridoxine and the amino acids of the medium during the heating process, and led to studies of the effects of individual amino acids in promoting the activation of pyridoxine.

These studies revealed the surprising fact that large amounts of alanine can completely replace pyridoxine as a growth factor for this organism. Maximal growth effect of S. lactis R was obtained with 3 micrograms of pyridoxine per 10 ml. of medium or with 1 to 3 mg. of alanine per 100 ml. of medium. This effect of alanine was shown not to be due to contamination with pyridoxine since both synthetic dl-alanine or alanine treated with charcoal followed by recrystallization were equally effective. Moreover, the growth promoting action of alanine disappeared after treatment with nitrous acid, whereas the pyridoxine effect was not altered by nitrous acid.

Alanine supported continued heavy growth of the organism through repeated subcultures in the complete absence of pyridoxine. The authors seem justified, therefore, in concluding that alanine in high concentrations completely replaces pyridoxine as a growth factor. It would be interesting to know whether the organisms from subcultures grown with alanine instead of pyridoxine continue to contain pyridoxine. This knowledge would throw light on the question as to whether the alanine was used for the synthesis of pyridoxine, or whether

it caused the development of a new kind of metabolism in which pyridoxine was not needed.

The amino acid glycine inhibited growth of this organism, an inhibition which was removed by additional amounts of pyridoxine or alanine, but not by other vitamins or amino acids. The inhibitory effect of glycine was clearly noted when maximum growth of the organism was permitted by addition of 1 to 3 micrograms of pyridoxine, or of 1 mg. of alanine per 10 ml. of medium. If under these conditions 2 mg. of glycine were added, growth was suppressed to the level of the control (sample without additional pyridoxine). More than 30 mg. of glycine proved toxic for this organism. Beta-alanine, dl-serine, and dl-threonine also inhibited growth, but to a lesser extent. Similarly, inhibition produced by these amino acids could be counteracted by pyridoxine or alanine.

While alanine in high concentration can replace pyridoxine, the addition of excess pyridoxine does not permit growth in the absence of alanine. S. lactis R thus appears incapable of synthesizing alanine, a surprise considering the ease with which the organism can synthesize the structurally similar lactic acid. Glycine, serine, and threonine are also among the amino acids which are essential for the growth of this organism; they become inhibitory only when added in excessive amounts.

Another strain of lactic acid bacteria, S. lactis 125, responds in exactly the same manner to additions of pyridoxine, alanine, and glycine as S. lactis R. However, the strain Lactobacillus casei is not able to substitute pyridoxine for alanine as a growth factor.

The authors discuss the possible mechanism by which pyridoxine can be completely replaced by alanine for the growth of S. lactis R. They call attention to the fact that one half of the pyridoxine ring is actually made up of alanine which, therefore, might be the precursor of pyridoxine. The inhibition of growth of S. lactis R by glycine, serine, threonine, or beta-alanine and its removal by alpha-alanine was interpreted by Snell and Guirard as due to a metabolic interference of structurally similar compounds. The existence of such a competitive interference has been demonstrated by Woods (*Brit. J. Exp. Path.* **21,** *74 (1940)*) in the inhibition of the growth factor para-aminobenzoic acid by sulfonamides. The counteraction of glycine inhibition by alanine and pyridoxine may be due to the same mechanism, since these compounds replace one another. Snell and Guirard cite a number of authors who have observed toxic effects of glycine or serine when administered to animals. It is not known whether the toxicity of these compounds for animals can be alleviated by additional amounts of pyridoxine or of alanine.

The replacement of a vitamin of the B-group by an amino acid in the nutrition of a microorganism is apparently not an isolated phenomenon. Möller (*Angew. Chemie* **56,** *199 (1943)*) reports that Streptobact. plantarum which needs thiamin in minute amounts, is able to grow in the absence of this vitamin, provided l-tyrosine is added. Although tyrosine acted only when added in a thousand times higher concentrations than thiamin, the action was not due to impurities of thiamin in the tyrosine, since synthetic tyrosine had the same effect. Moreover, the growth of Staphylococcus aureus, which is extremely sensitive to stimulation by thiamin, was not stimulated by l-tyrosine.

A most important problem for the future will be to determine whether alanine and tyrosine serve as precursors for pyridoxine and thiamin, respectively. This possibility was discussed by Snell and Guirard in regard to the replacement of pyridoxine by alanine. The other possibility mentioned before is that subcultures growing in the absence of the B-vitamins actually do not need the factor due to a change of metabolism brought about by addition of the amino acid.