been shown(17) that riboflavin can partially replace vit. B_{12} in the nutrition of rats receiving a diet containing thyroxine. Hartman *et al.*(18) also noted that riboflavin can replace vit. B_{12} in the rat and demonstrated that its activity is due to increased synthesis of vit. B_{12} by the intestinal flora. A similar utilization of lyxoflavin, which has been shown to have riboflavin activity under certain conditions, may account for the growth effects observed.

Wahlstrom and Johnson(15) recently reported that lyxoflavin stimulated the growth of baby pigs fed a low fat basal ration containing 0.01% protamone, although the pigs did quite well on the basal ration devoid of any known lyxoflavin. These authors point out that lyxoflavin may exert its effect in a manner similar to that of antibiotics or surfactants rather than as a new member of the vit. B complex. In view of our evidence that riboflavin exerts the same effect as lyxoflavin in promoting growth of chicks on a diet deficient is unknown factors, it is possible that riboflavin would also be active in the rat(6,7) or the pig(15) under conditions where lyxoflavin has been found to stimulate growth. It appears desirable to test riboflavin in any circumstances where lyxoflavin has activity before drawing any conclusions regarding unique functions for lyxoflavin.

Summary. Lyxoflavin has been shown to possess a limited ability to replace riboflavin in the nutrition of *L. casei* and the rat. In chicks, large doses of lyxoflavin produce small weight gains, which, however, can be matched by equal doses of riboflavin. The present evidence does not warrant the classification of lyxoflavin as a new vitamin.

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Effect of Citrovorum Factor upon Tyrosine Metabolism in Clinical Scurvy.* (19777)

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Administration of tyrosine to guinea pigs (1-3), monkeys(4), infants(5,6) or adult men(7) with ascorbic acid deficiency results in the urinary excretion of abnormal quantities of hydroxyphenyl compounds, which decrease

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TABLE I. Effect of Citrovorum Factor and Ascorbic Acid Upon l-Tyrosine Metabolism in a Scorbutic Man.

Days of study	Period of study	Buffy coat vit. C, mg %	Capillary fragility, 0-4+	Medication daily: l-Tyrosine, G p.o.	Medication daily: citrovorum factor, mg-i.m.	Medication daily: Ascorbic acid, G. p.o.	Urinary tyrosyl excretion, G/day
1-5	I	0	4+				.24
6							2.18
7-10	II		4+				6.45
11-15	III			10	6		8.34
16		0	4+				3.04
17-20	IV		0			1	.31
21-25	V	23.9	0				.19

promptly following ascorbic acid therapy. While pteroylglutamic acid (PGA) administered to scorbutic guinea pigs(3), and infants in large doses(6,8) has been reported to correct this hydroxyphenyluria, others have failed to demonstrate an effect of PGA in ascorbic acid-deficient infants(9), monkeys (4) or adult men(10). Recent investigations indicating that ascorbic acid augments the conversion of PGA to the citrovorum factor (CF)(11-14) suggest that CF might be involved in tyrosine metabolism. The present study was undertaken to determine the effect of CF upon the metabolism of tyrosine in an adult scorbutic man.

A 65-year-old bachelor was the subject of this study. On hospital admission he described a grossly inadequate dietary intake during the preceding year and the ingestion of little, if any, of the foods ordinarily providing ascorbic acid. Clinical evidences of scurvy included multiple petechial perifollicular hemorrhages and ecchymoses especially over the lower extremities, but also apparent on the forearms. There was an hyperkeratotic folliculosis over the abdominal wall and the thighs, and the hairs in these areas were brittle and crinkled. The gums were not hypertrophic. Ascorbic acid was not present in the buffy coat of peripheral venous blood. A tourniquet test was markedly positive. Bleeding time, coagulation time, prothrombin time, and platelet count were within normal limits. The hemoglobin was 12.5 g per 100 ml. All of the clinical manifestations of scurvy healed promptly after adequate therapy with ascorbic acid. Immediately upon hospitalization this patient was provided with an ascorbic acid deficient diet consisting of boiled milk, boiled rice, crackers, sugar, coffee, and water, which was continued throughout the study. The 24-hour urine volumes were collected in 10 ml of 1:5 mixture of toluol and glacial acetic acid. Suitable aliquots were stored in a refrigerator until analyzed for hydroxyphenyl compounds ("tyrosyl" derivatives) by the method of Medes(15), a modification of that of Folin and Ciocalteu(16). The tyrosyl derivatives measured by this method include tyrosine, p-hydroxyphenyl lactic acid, and p-hydroxyphenylpyruvic acid. Buffy coat ascorbic acid levels were done by the method of Butler and Cushman(17). An estimate of the number of hemorrhages occurring on a forearm after application of a blood pressure cuff to the upper arm at 100 mm Hg pressure for 10 minutes served as an index of capillary fragility.

Results. The results of this study are presented in Table I. During the initial 5 days of study while the patient ingested the diet described above, the daily urinary tyrosyl excretion ranged from 0.19 to 0.30 g daily. During the second 5-day period 10 g of l-tyrosine‡ was given orally and the tyrosyl excretion ranged from 2.18 to 7.55 g daily and averaged 5.60 g daily. Then 6 mg of CF§ was given intramuscularly daily for 5 days while the l-tyrosine was continued orally. Tyrosyl excretion ranged from 6.24 to 13.20 g daily and averaged 8.34 g daily. Tyrosine was

‡ Provided by Merck and Co., Rahway, N. J.

§ "Leucovorin", a synthetic material with citrovorum factor activity, was provided by Lederle Laboratories Division, American Cyanamid, Pearl River, N. Y.

continued during the fourth period of study, CF was discontinued, and 1 g ascorbic acid was given orally daily. Urinary tyrosyl excretion decreased promptly and progressively to values comparable to those observed during the initial study period, and ranged from 3.04 to .08 g daily. Tyrosine was discontinued and ascorbic acid continued during the final period, and tyrosyl values ranged from .11 g to .27 g daily.

Discussion. The patient with scurvy studied demonstrated an abnormality in tyrosine metabolism which was promptly reversed by ascorbic acid, in confirmation of previous observations in adult man(7). CF administered parenterally did not decrease urinary tyrosyl excretion. Thus, the results obtained in the man with scurvy studied were similar to those observed in the ascorbic acid deficient monkey, in whom a failure of CF to alter the metabolism of administered tyrosine has been noted(18).

A failure of CF to alleviate dietary ascorbic acid deficiency in guinea pigs has been reported(12). CF in the doses given did not alter capillary fragility in the patient reported here, or in an additional scorbutic patient in whom these observations were made before, during and after the intramuscular administration of 1 mg of CF daily for 10 days.

Summary and conclusions. 1. A patient with scurvy excreted large quantities of tyrosyl derivatives in the urine when given l-tyrosine orally during the scorbutic state. The tyrosyl excretion was not decreased by the intramuscular administration of 6 mg of citrovorum factor daily for 5 days, but was promptly corrected by 1 g of ascorbic acid administered orally daily. 2. Citrovorum factor in the doses indicated did not alter the abnormal capillary fragility of scurvy in 2 patients.

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