

8924 P

Successful Treatment of Human Pellagra with the "Filtrate Factor."

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György,¹ Elvehjem and Koehn,² and Lepkovsky and Jukes^{3, 4} have divided the vitamin B₂ complex into 3 components—flavins, the rat antiacrodynia (vitamin B₆) factor, and the filtrate or chick antidermatitis factor. Birch, György and Harris⁵ concluded that the human "P-P" factor and the canine anti-blacktongue factor are different, both from the rat vitamin B₆ and from lactoflavin, and that the canine anti-blacktongue factor may be identical with the "P-P" factor. They found that pellagra- and blacktongue-producing diets were rich in vitamin B₆. Maize was especially rich. Dogs fed on a purified diet supplemented with vitamin B₁ and lactoflavin could not be cured of blacktongue unless both maize (rat vitamin B₆) and liver extract were added to the diet. Dann⁶ likewise found that both yellow and white maize contained goodly amounts of vitamin B₆. Dann,⁶ and Spies and Chinn, as quoted by Birch, *et al.*,⁵ were unable to cure pellagrins with lactoflavin. The experimental evidence of Jukes and Lepkovsky⁷ indicates that the "filtrate factor" and the "P-P" factor may not be identical. In addition, Goldberger, *et al.*,⁸ have shown that the blacktongue preventative factor is absorbed from yeast by Fuller's earth. However, Koehn and Elvehjem,⁹ although unable to cure blacktongue with lactoflavin, found that liver extract, after treatment with alcohol and ether and Fuller's earth, not only contained the chick antidermatitis (filtrate) factor but would cure blacktongue.

On admission to the hospital the pellagrins treated in this study

¹ György, P., *Biochem. J.*, 1935, **29**, 741.

² Elvehjem, C. A., and Koehn, C. J., Jr., *J. Biol. Chem.*, 1935, **108**, 709.

³ Lepkovsky, S., and Jukes, T. H., *J. Biol. Chem.*, 1936, **114**, 109.

⁴ Lepkovsky, S., Jukes, T. H., and Krause, M. E., *J. Biol. Chem.*, 1936, **115**, 557.

⁵ Birch, T. W., György, P., and Harris, L. J., *Biochem. J.*, 1935, **29**, 2830.

⁶ Dann, W. J., *J. Nutrition*, 1936, **2**, 451.

⁷ Jukes, T. H., and Lepkovsky, S., *J. Biol. Chem.*, 1936, **114**, 117.

⁸ Goldberger, J., Wheeler, G. A., Lillie, R. D., and Rogers, L. M., *Pub. Health Rep., U. S. P. H. S.*, 1928, **43**, 657.

⁹ Koehn, C. J., Jr., and Elvehjem, C. A., *J. Nutrition*, 1936, **11**, 67.

were placed on a maize diet similar to the one described by Spies.¹⁰ During the 3 or more days of the control period their condition either remained stationary or became worse.

After remaining on the diet for 3 days, Patient No. 1 received 10 mg. of lactoflavin daily from December 8, 1935, to December 28, 1935. There was a definite improvement in the diarrhea, but the dermatitis and the stomatitis became more severe and dementia developed. The patient then received 6 vials (derived from 600 gm. of liver) of liver extract daily. This medication was followed by a rapid improvement in all symptoms.

Except for slight improvement in diarrhea, all symptoms of Patient No. 2 increased during the first 4 days on the Spies diet. She then received daily for 5 doses 20 mg. of lactoflavin. While on this therapy the diarrhea increased and the caloric intake dropped from a daily average of 1700 calories to 366 calories. The stomatitis and salivation were very severe, and nausea and vomiting and new patches of dermatitis developed. Following the daily administration of 6 vials of liver extract the improvement of all symptoms was very satisfactory.

The dermatitis and the stomatitis of Patient No. 3 became worse during the first 4 days on the diet. At noon of the fourth day the daily administration of 35 cc. (approximately 1 cc. per kilo) of the concentrate "K-50"⁴ of the filtrate factor (chick antidermatitis), free from the rat antidermatitis factor and lactoflavin, was begun. The improvement of this patient was quite dramatic. At the end of 10 days of this treatment the mouth was normal, there was no diarrhea, and of the dermatitis there remained only an increase in pigmentation of the skin over the involved parts. Exposure of the face and one hand to direct sunlight for one hour on the tenth day (July 6, 1936) failed to produce a recurrence of any symptoms.

Patient No. 4 had severe polyneuritis in addition to the dermatitis, stomatitis, and severe diarrhea. After 4 days on the Spies diet his general condition was very poor. Because of the predominance of the polyneuritic symptoms, he then received 20 cc. of concentrated vitamin B₁¹¹ daily intravenously. This product, as prepared by Stuart, is known to contain none of the vitamin B₂ complex.⁴ During the following 4 days the general condition improved and the caloric intake increased from 450 to about 1,000 calories per day, but the dermatitis, diarrhea, and stomatitis grew worse. Then 50 cc. of filtrate factor was administered daily. The diarrhea,

¹⁰ Spies, T. D., *J. Clin. Invest.*, 1934, **13**, 807.

¹¹ Stuart, E. H., Block, R. J., and Cowgill, G. R., *J. Biol. Chem.*, 1934, **105**, 463.

which had been very severe, rapidly improved, so that by the third day it had completely disappeared. Likewise, the dermatitis and stomatitis rapidly improved.

Pellagrins can be cured while on a maize diet by the administration of a liver filtrate which contains the chick antidermatitis factor but which is free from lactoflavin and rat vitamin B₆.

8925 P

Effect of Cortin upon Renal Excretion and Balance of Electrolytes in the Human Being.*

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Previous attempts to show a positive effect of cortin in normal subjects have met with little success. The present experiments demonstrate that large doses of this hormone produce a prompt effect on the kidney. Sodium, potassium and chloride excretion have been studied in 4 normal subjects and in 2 patients with Addison's disease. All were maintained on a constant diet and liquid intake. Hourly urine specimens were collected during the fasting state with the subject at rest. Cortin was injected intravenously each hour for 4 hours, a total of 80 cat units being injected in each subject. This was approximately 3 times the amount required to maintain a patient with severe Addison's disease for 24 hours. Sodium chloride (0.9%), heated cortin solution and a dilute adrenalin solution were used as control injections. The results are summarized in Table I.

Cortin injections were associated with a marked reduction (average 42%) in the excretion of sodium over a 5-hour period. In patients with Addison's disease similar injections of cortin caused reductions in sodium excretion ranging from 20 to 50% depending on the condition of the patient.

Potassium excretion was increased in the normal subject about 30% for the 5-hour period during which cortin was injected. In the case of one untreated patient there was no increase in potassium excretion during the 5-hour period. With the patients CB¹ and IB¹ the injection of cortin increased the excretion of potassium 66 and 170% respectively during the 5-hour period.

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