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Effect of Yeast and Nicotinic Acid on Porphyrinuria.*

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It has been shown by Beckh, Ellinger and Spies[1] that pellagrins have increased amounts of coproporphyrin I or III in their urine which disappear following the successful treatment of the pellagra by means of large amounts of yeast or liver extract. Since nicotinic acid had been shown to be effective in curing the mucous membrane lesions of pellagra,[2] it seemed desirable to determine whether or not it would decrease the porphyrinuria of pellagra and other diseases.

Specimens of urine were obtained from 4 groups of people (Table I). Group I included a patient with gonorrheal arthritis who had sulphanilamide treatment, a patient with diabetic coma, one with catarrhal jaundice, and one with alcoholic cirrhosis and ascites. Group II included 2 patients, one with barbital intoxication, and one with hypertensive heart disease, congestive heart failure, and an enlarged, tender liver. Group III included 2 cases of pellagra, one very severe, and the other mild. In Group IV were 6 normal persons who ate large quantities of a well-balanced diet.

The studies were conducted in such a manner that the source of the specimen of urine for analysis was unknown to the person examining it. Whenever positive tests were obtained, repeated observations were performed, usually by more than one examiner. After increased porphyrinuria had been demonstrated repeatedly, yeast or nicotinic acid was administered and the urine collected and examined as before. As indicated in the table, nicotinic acid, in doses of 500 mg., was administered to the persons in Group I and Group III, and yeast, in 50 gm. amounts, was given to the 2 patients in Group II. After the yeast or nicotinic acid had been given, and the test for porphyrinuria had become negative, the yeast or nicotinic acid was discontinued without any other changes. Subsequent urine

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1 Beckh, Walter, Ellinger, Philipp, and Spies, Tom D., *Quar. J. Med.*, New Series, 1937, **6**, 305.

2 Spies, Tom D., Cooper, Clark, and Blankenhorn, M. A., *The Use of Nicotinic Acid in the Treatment of Human Pellagra*, read before the Central Society for Clinical Research in Chicago, Illinois, November 5, 1937.

TABLE I.
Summary of Data.

Case		Clinical Diagnosis	Days 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
											Group I																
1	C.M.	Gonococcal arthritis	+	+	+	+↑	—	—	—	—	+	+↑	—	—	—	—	+	+↑	—								
2	C.S.	Diabetic coma	+	+	+	+↑	—	—	—	+	+↑	—	—														
3	R.M.	Catarrhal jaundice	+↑	—	—	+	+↑	—	—	—																	
4	C.R.	Alcoholic cirrhosis with ascites	+		+	+	+		+	+		+	+	+	+	+	+	+↑	—	—	—	—	—	—	+↑	—	—
											Group II																
5	F.B.	Barbital intoxication	+↑	—	—								—	—	—												
6	M.B.	Hypertensive heart disease with congestive failure	+	↑	+	—	—↑	↑	—↑	—↑	—↑	—↑	—↑	—↑	—												
											Group III																
7	G.S.	Pellagra	+↑	+↑	↑	↑	+↑	↑	↑	↑	+↑	↑	—↑	—↑													
8	P.L.	Mild pellagra	+↑	—																							

\+ = Positive test for porphyrinuria.
— = Negative test for porphyrinuria.
↑ = 500 mg. nicotinic acid in Groups I and III.
↑ = 50 gm. Brewers' Yeast (Harris) in Group II.

samples were examined. The method used for testing the urine was the same as that described by Beckh, Ellinger and Spies[1] for the estimation of ether-soluble porphyrin in small amounts in the urine.

As shown in the table, all persons with increased porphyrinuria gave a negative test for porphyrinuria following the administration of either nicotinic acid or yeast. The test for porphyrinuria became negative in 7 of the patients within 24 hours after the administration of either nicotinic acid or yeast. In the case of severe pellagra the porphyrinuria steadily decreased from the time the nicotinic acid was administered, but the test remained positive for several days. In the case of mild pellagra the test became negative over night following the administration of nicotinic acid. The urine specimens from the 6 persons who ate large amounts of a well-balanced diet always gave negative tests for porphyrinuria.

The present study confirms the observations of Beckh, Ellinger and Spies[1] that pellagrins have increased porphyrinuria. In addition these studies show that the administration of yeast was followed by the disappearance of porphyrin in the urine of a case of barbital intoxication and of another case with cardiac decompensation. Also, it has been shown in these studies that nicotinic acid likewise remits porphyrinuria in pellagra and in certain other diseases. Since there is a similarity between the clinical symptoms of pellagra and those of acute porphyrinuria, the presence of an excessive amount of porphyrin in the body of pellagrins might explain some of the clinical symptoms. If the increased porphyrin of the urine of pellagrins proves to be coproporphyrin I, we must consider the possibility of a complete new synthesis of porphyrin as suggested by Fischer and Duesberg.[3] If, on the other hand, it is coproporphyrin III, we may assume a connection with an abnormal hemoglobin metabolism. In the functionally impaired liver bilirubin eventually may be broken down into coproporphyrin III. It seems to the authors that the latter explanation is the most probable one, and it is consistent with the observation[1] that patients dying from pellagra frequently show anatomical changes in the liver. We must admit, however, that there are many discrepancies between anatomical and functional liver changes.

Summary and Conclusions. 1. These studies confirm the previous observations of Beckh, Ellinger and Spies[1] that porphyrinuria is a frequent finding in pellagra and disappears following the adminis-

[3] Fischer, H., and Duesberg, R., *Arch. f. exp. Path. u. Pharm.*, Berlin, 1932, **166**, 95.

tration of yeast. 2. The present study shows that nicotinic acid, a substance which has been shown to be curative for the mucous membrane lesions of pellagra, likewise produces a decrease of porphyrinuria in pellagrins. 3. In addition, the present study shows that the porphyrinuria associated with a number of diseases other than pellagra likewise is promptly decreased following the administration of either yeast or nicotinic acid.

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Intravenous Benzedrine Sulfate as an Antagonist to Intravenous Soluble Amytal.

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During our previous investigations of the stimulating action of benzedrine sulfate on the central nervous system[1, 2, 3] the possibility suggested itself of employing this drug to counteract the narcosis produced by barbiturates. Alles[4] observed that benzedrine intravenously had considerable effect in waking animals from barbital anesthesia. In man, Myerson, *et al.*,[5] reported that benzedrine sulfate subcutaneously did not affect the depth, although it definitely shortened the duration of soluble amytal narcosis; and stated that hypertension produced by benzedrine sulfate subcutaneously could be reduced by soluble amytal intravenously, and also that hypotension produced by soluble amytal intravenously could be elevated by benzedrine sulfate subcutaneously. In rats, rabbits and guinea pigs unprotected by barbiturates the minimum lethal dose subcutaneously or intravenously has been reported by all observers[4, 6, 7] to be at least 25 mg. per kg. body weight. On the basis of these determinations it was felt that the dosage herein employed was entirely safe.

In the present study we decided to employ both soluble amytal and

[1] Davidoff, E., *Psychiat. Quart.*, 1936, **10**, 652.

[2] Davidoff, E., and Reifenstein, E. C., Jr., *J. A. M. A.*, May 22, 1937, **108**, 1770.

[3] Davidoff, E., and Reifenstein, E. C., Jr., *J. Lab. and Clin. Med.*, to be published.

[4] Alles, G. A., *J. Pharm. and Exp. Therap.*, 1933, **47**, 339.

[5] Myerson, A., Loman, J., and Dameshek, W., *Am. J. M. Sci.*, 1936, **192**, 560.

[6] Hartung, W. H., and Munch, J. C., *J. Am. Chem. Soc.*, 1931, **53**, 1875.

[7] Ehrich, W. E., and Krumbhaar, F. B., *Ann. Int. Med.*, 1937, **10**, 1874.