

Effect of Nicotinic Acid on Increased Porphyrinuria Occurring in Seven Painters.

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Recently, Spies, Gross and Sasaki¹ demonstrated that the increased porphyrinuria occurring in pellagra and certain other diseases decreases rapidly following the administration of nicotinic acid. In view of these observations, it seemed important to determine the effect of this substance on increased porphyrinuria due to some other cause. Previous work² has shown that lead poisoning may be accompanied by increased porphyrinuria. Since many paints contain lead, it seemed likely that men who had been painters for a number of years might have increased porphyrinuria. Seven painters, who had been exposed to lead for a period of at least 15 years were, therefore, selected for study.

A group of 45 medical students served as controls for the degree of porphyrinuria one might expect in normal adult males. Samples of urine from each member of this control group were collected on the same day and were tested for increased porphyrinuria.* A sample was reported positive only if the color was definitely pink; no color or traces of color were considered to be negative tests for increased porphyrinuria. Of the 45 samples of urine, 22 showed no color, ten showed only a trace of color, and 13 showed a definite pink color. Since subsequent tests on the urine from this latter group showed no color or only traces of color, with the exception of one case, the authors believe that the ingestion of alcohol and dietary irregularities might account for the slightly increased porphyrinuria noted in the initial test.

¹ Spies, T. D., Gross, E. S., and Sasaki, Y., *Proc. Soc. Exp. Biol. and Med.*, 1938, **38**, 178.

² Mason, V. R., Courville, C., and Ziskind, E., *Medicine*, 1933, **12**, 355.

* The method of Beckh, Ellinger and Spies³ was used for the determination of porphyrin in the urine. This method may be described briefly as follows: 10 cc. of urine were acidified with glacial acetic acid to pH 4 (about 6 drops) and then extracted in a separatory funnel with 10-15 cc. of ether. The ether extract was washed twice with 10-15 cc. of distilled water. After the second washing, the entire aqueous portion was discarded. To the ether extract was added $\frac{1}{6}$ its volume of 25% hydrochloric acid. With thorough mixing, the ether soluble porphyrin enters the acid layer where it produces colors ranging from pink to purple, according to the concentration of porphyrin present.

³ Beckh, W., Ellinger, P., and Spies, T. D., *Quart. J. Med.*, 1937, **6**, 305.

After the amount of porphyrin occurring in the urine of these control subjects had been determined, the following studies were made on the 7 painters. Throughout the entire period of study the urine of each painter was tested daily for porphyrin. The first 3 days served as a control period. During the next 9 days, nicotinic acid (2 doses of 200 mg. each, dissolved in 200 cc. of water, and administered at 11:30 A. M. and 4:00 P. M.) was given on the days indicated in Table I. Each painter received a total amount of 2.4 gm. of nicotinic acid. The daily tests for porphyrinuria were continued for 14 days after the administration of nicotinic acid had been discontinued, in order to determine whether the porphyrinuria would return to the amount observed in the initial control period.

Except for a transitory flushing and feeling of warmth, which were obtained in all cases but in varying degrees in different persons, no subjective effects were noted with the oral ingestion of nicotinic acid in the amount administered in this study. The effect of the first dose was, however, more intense than were subsequent doses. This abnormal dilatation of the peripheral vessels reached a maximum about one-half hour after the oral administration of the nicotinic acid and disappeared in the following 2 hours. This effect has been noted by several investigators^{4, 5, 6} and is not interpreted by the authors as being harmful.

During the 3-day control period, all of the painters consistently showed a strongly positive test for porphyrin in the urine, although there were variations among the individuals of the group. The day after the administration of nicotinic acid was begun, reductions in the amount of color produced were noted in all cases. After the 9-day period of nicotinic acid medication, the urines of all 7 painters gave no color or only traces of color. The administration of nicotinic acid was then discontinued. Within the next 14 days the amount of color gradually increased to the intensity observed during the initial control period.

In order to be certain that the presence of nicotinic acid in the urine was not giving false negative tests for increased porphyrinuria, varying quantities of nicotinic acid were added to samples of urine containing an increased amount of porphyrin. In no case was the intensity of the color altered by the addition of nicotinic acid. It was also found that urine obtained from an individual who had

⁴ Spies, T. D., Cooper, C., and Blankenhorn, M. A., read before the Central Society for Clinical Research in Chicago, Illinois, November 5, 1937.

⁵ Smith, D. T., Ruffin, J. M., and Smith, S. G., *J. A. M. A.*, 1937, **109**, 2054.

⁶ Fouts, P. J., Helmer, O. M., Lepkovsky, S., and Jukes, T. H., *Proc. Soc. Exp. Biol. and Med.*, 1937, **37**, 405.

ingested large quantities of nicotinic acid did not obscure the test for porphyrins when it was added to urine with an increased quantity of porphyrin.

Twelve control subjects showed a transitory increased porphyrinuria, which, however, was not as great as that found in 7 painters before the administration of nicotinic acid.

The results summarized in Table I show that even in cases of long standing increased porphyrinuria such as that resulting from exposure to lead for periods of at least 15 years, nicotinic acid in the amounts given readily reduced the degree of porphyrinuria. This finding supports the observation of Spies, Gross and Sasaki¹ that the porphyrinuria present in pellagra and certain other diseases decreased rapidly following the administration of nicotinic acid. Since the porphyrinuria was reduced to its minimal quantities only after a number of days, rather than immediately after the nicotinic acid was administered, it seems that this substance does not mask the porphyrinuria but plays a rôle in the metabolism of porphyrin.

Summary and Conclusions. 1. The urine of 7 painters showed increased porphyrinuria as compared with the amount present in the urine of 45 control subjects. 2. In every instance this increased porphyrinuria decreased following the administration of nicotinic acid. 3. These studies suggest that nicotinic acid may play a rôle in the metabolism of porphyrins.

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A Complement-binding Antigen in Extracts of the Brown-Pearce Carcinoma of Rabbits.

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Previous studies¹ have shown that a complement-binding antigen is present in extracts of virus-induced rabbit papillomas, and that this antigen is closely associated with the virus causing the growths, if not identical with it.² In the present work it has been learned that extracts of a transplantable epithelioma of rabbits³ also contain

¹ Kidd, John G., *PROC. SOC. EXP. BIOL. AND MED.*, 1937, **35**, 612.

² Kidd, John G., *PROC. SOC. EXP. BIOL. AND MED.*, 1938, **37**, 657.

³ Brown, W. H., and Pearce, L., *J. Exp. Med.*, 1923, **37**, 601.