Coproporphyrin Studies in Children. I. Urinary Coproporphyrin Excretion in Normal Children.* (20794)

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As a result of studies by Watson and associates(1), urinary coproporphyrin excretion has been found to be abnormal in many clinical conditions. In children, it is elevated, not only in congenital porphyria(2-4), but also in liver disease(5-7), lead poisoning (8-10), poliomyelitis(11), and blood dyscracias(12). Many of the disturbances of blood formation and hemoglobin synthesis seen characteristically in this age group will probably ultimately be found to be related to change in coproporphyrin metabolism(13). Schwartz and coworkers(14) have presented an improved method for measuring urinary coproporphyrins. By modifications including: (a) maintenance of a neutral or alkaline urine during the period of collection, (b) conversion and measurement of coproporphyrin precursor, (c) more efficient extraction, and (d) more efficient fluorimetry, a 3-fold increase of the average 24-hour value has been obtained by the new method as compared with the former "long method"(15). Zieve and his coworkers(16) have found that the mean coproporphyrin excretion for a group of 685 normal men was 189 $\pm$ 59 μg per day. There appeared to be a sequential increase in average coproporphyrin excretion as the customary alcohol intake increased in these men.

The purpose of the present report is to define the limits of 24-hour urinary coproporphyrin excretion in normal children as determined by the improved procedure. Subsequent reports will show the changes of urinary coproporphyrin excretion in various diseases in children.

Methods and materials. The main group of subjects studied consisted of 94 normal boys aged 6 to 16. All were residents in a summer camp for boys during the month of July. All were pronounced healthy by physical examination at the time of study and none had any history of serious illnesses in the past. All of the urines were collected over the same 24-hour period while the subjects were on the same diet and pursuing approximately the same amount of activity. None of the subjects consumed alcohol. Two other groups of subjects were studied in essentially the same manner: (1) normal adults, and (2) normal children under 6 years of age. The latter group was made up of healthy children of counsellors and physicians who were not campers. These two groups were included to provide a composite picture of the urinary coproporphyrin excretion in all age groups. The urinary coproporphyrin was determined by the method of Schwartz *et al.*(14). The urines were collected in colorless bottles containing 5 g of sodium carbonate and they were stored at 4°C. With this method of storage, the coproporphyrin content remained unchanged as long as 3 months after the collection and initial determination. Duplicate 5 ml aliquots were taken from the 24-hour urine samples and used for determination. The coproporphyrin in the test samples was determined fluorimetrically with a Calectron fluorimeter† employing a photomultiplier tube and with the Corning No. 5543 as the primary filter and Corning No. 2418 as the secondary filter. Values were determined from a standard curve obtained from a series of coproporphyrin solutions of known concentration.‡

Results. The urinary coproporphyrin excretion in children on the basis of age is shown in Fig. 1. Similar data plotted on the basis of body weight are shown in Fig. 2, and for surface area in Fig. 3.

The data are divided into groups and sum-

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† Manufactured by Calectron, Inc., St. Paul, Minn.

‡ Kindly supplied by Samuel S. Schwartz, M.D.

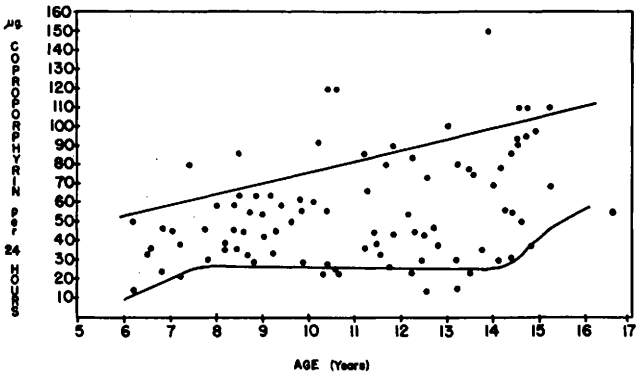

FIG. 1. Urinary coproporphyrin excretion in normal boys based upon age. The black line above represents one S.D. above the mean and the black line below represents one S.D. below the mean.

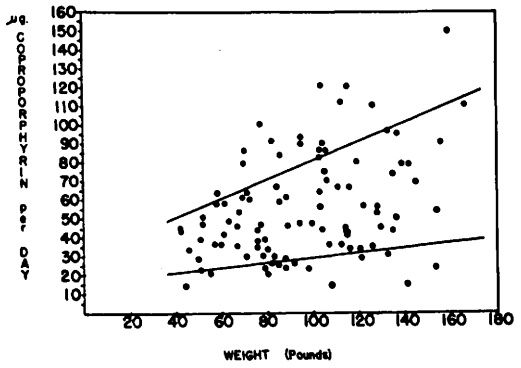

FIG. 2. Urinary coproporphyrin excretion in normal boys based upon body wt. The black line above represents one S.D. above the mean and the black line below represents one S.D. below the mean.

marized in Table I.

Discussion. From data on coproporphyrin excretion on successive days in a number of normal adults, Strait(17) has noted that there exists a simple relationship between the weight of the subject and the mean value of coproporphyrin excretion. He felt that the total urinary coproporphyrin excretion reflects primarily an endogenous metabolic function and that the coproporphyrin excretion fits more closely the relationship of body weight to blood volume than the relationship of body weight to surface area, the well known basal metabolic rate function. In studies with a small group of children, he found that their coproporphyrin excretion also depended on weight, but did not fit the extrapolated linear relationship described for the adults. Instead, the weight-coproporphyrin function for children may require an exponent of the weight somewhat greater than unity for the extrapolated fit.

Although the urine collections were not made over a number of days in each indi-

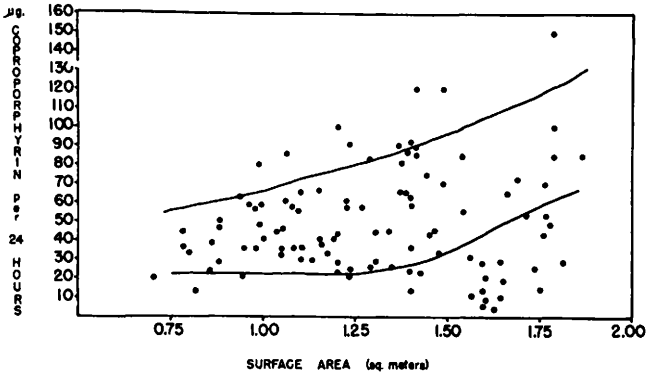

FIG. 3. Urinary coproporphyrin excretion in normal boys based upon body surface. The black line above represents one S.D. above the mean and the black line below represents one S.D. below the mean.

TABLE I (A). Mean Coproporphyrin Excretion of Boys 6 to 16 Years Based upon Age.

Years	No.	Mean copro. excr., μg/24 hr	S.D.
<6 yr*	4	41.7	14.9
6 to 7 " 11 mo	14	38.4	16.5
8 " 9 " 11 "	24	50.6	18.6
10 " 11 " 11 "	20	56.3	30.2
12 " 13 " 11 "	20	56.2	31.5
14 " 15 " 11 "	16	75.2	27.0
Adults*	9	145.5	63.6

* The under 6 years and adult group are included to show composite picture of coproporphyrin excretion at all ages.

TABLE I (B). Mean Coproporphyrin Excretion of Boys Aged 6 to 16 Based upon Body Weight.

Wt, lb	No.	Mean copro. excr., μg/24 hr	S.D.
41- 60	12	38.5	17.9
61- 80	22	47.4	19.5
81-100	17	48.5	23.6
101-120	22	62.8	29.4
121-170	21	66.2	32.8

TABLE I (C). Mean Coproporphyrin Excretion of Boys Aged 6 to 16 Based upon Body Surface Area.

Body surface, sq. meter	No.	Mean copro. excr., μg/24 hr	S.D.
.75-1.0	16	41.8	16.1
1.01-1.25	25	26.4	16.1
1.26-1.50	28	61.1	29.1
1.51-1.75	17	54.4	26.4
1.76-2.0	8	92.4	28.6

vidual as recommended by Strait, the data in general appear to confirm his concepts. Examining first the changes of coproporphyrin excretion on the basis of age, one is impressed by the moderate rise prior to the age of 6 and 7, the levelling off during the next 6 years, and the rapid rise during puberty and adolescence. This closely parallels the changes in body weight in normal boys and is confirmed by the steady rise of coproporphyrin when correlated with body weight as shown in Table I(B). Surface area did not appear to correlate as satisfactorily as weight. It would appear on the basis of these data that the best criterion for defining abnormal urinary coproporphyrin excretion in children would be in cases where the 24-hour collection is twice the standard deviation above the mean for the group the individual belongs to by weight.

Summary. 1. The urinary coproporphyrin excretion on 24-hour urine collections has been determined on a group of normal healthy boys aged 6 to 16 by the new improved method. 2. The urinary coproporphyrin level correlates closer with body weight than with age or surface area. 3. The urine coproporphyrin excretion in children is probably abnormal if the determination in a 24-hour collection is twice the standard deviation above the mean for the group the individual belongs to by weight.

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1. Watson, C. J., and Larson, E. A., *Phys. Rev.*, 1947, v27, 478.

2. Dunsky, J., Freeman, S., and Gibson, S., *Am. J. Dis. Ch.*, 1947, v74, 305.

3. Dobriner, K., Strain, W. H., Guild, H., and Localio, S. A., *J. Clin. Invest.*, 1938, v17, 761.

4. Rimington, C., *Nature*, London, 1937, v140, 105.

5. Watson, C. J., Hawkinson, V., Capps, R. B., and Rappaport, E. M., *J. Clin. Invest.*, 1949, v28, 621.

6. Watson, C. J., Sutherland, D., and Hawkinson, V., *J. Lab. and Clin. Med.*, 1951, v37, 8.

7. Sutherland, D. A., and Bollier, M., *Gastroenterology*, 1952, v20, 39.

8. Watson, C. J., *J. Clin. Invest.*, 1936, v15, 332.

9. Schmid, R., Hanson, B., and Schwartz, S., PROC. SOC. EXP. BIOL. AND MED., 1952, v79, 459.

10. Schwartz, S., Keprios, M., and Schmid, R., *ibid.*, 1952, v79, 463.

11. Watson, C. J., Schulze, W., Hawkinson, V., and Baker, A. B., *ibid.*, 1947, v64, 73.

12. Watson, C. J., *J. Lab. and Clin. Med.*, 1951, v37, 29.

13. ———, *The relation of porphyrins to erythropoiesis.* New York: Science Press Printing Co., 1940.

14. Schwartz, S., Zieve, L., and Watson, C. J., *J. Lab. and Clin. Med.*, 1951, v37, 843.

15. Schwartz, S., Hawkinson, V., Cohen, S., and Watson, C. J., *J. Biol. Chem.*, 1947, v168, 133.

16. Zieve, L., Hill, E., Schwartz, S., and Watson, C. J., *J. Lab. and Clin. Med.*, 1953, v41, 663.

17. Strait, L. A., Bierman, H. R., Eddy, B., Hrenoff, M., and Eiler, J. J., *J. Appl. Physiol.*, 1952, v9, 699.

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