CREATINE, CREATININE AND TOTAL BODY POTASSIUM IN RELATION TO MUSCLE MASS IN CHILDREN

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The purpose of this paper is to report an investigation in children in which determinations of the 24-hourly creatine and creatinine excretion and the total body potassium measurements were correlated with attempts at estimation of total muscle mass by soft tissue radiography and by body measurements. Although studies on creatinine excretion in children have been done before, to the best of our knowledge, no one has investigated such a correlation.

Creatinine, the internal anhydride of creatine, is relatively evenly distributed in low concentration throughout the water of the body and regularly found in the urine. It has always been assumed that creatinine excretion is related to the muscle mass of both children and adults and there have been several studies to show that there is a constant relationship to body weight in lean individuals and to the expected weight in the obese (Muldowney, Crooks and Bluhm, 1957; Garn and Clark, 1955). Creatinuria is found regularly in children, diminishing quantitatively as the child grows older, but varying considerably from day to day (Beard, 1943). Catherwood and Stearns (1937) have shown that in infants and children there is a constant output of preformed creatinine from day to day and this increases as the child grows, presumably due to the increase in muscle mass.

Total body potassium increases with body growth until it reaches adult levels when growth terminates. Because the muscle of the body represents the largest active cellular mass, one assumes that the major fraction of body potassium is related to the total muscle. The value for total body potassium per kilogram varies widely from child to child, and we hoped to find close correlation between total body potassium and total muscle mass, thus enabling a better prediction of total expected body potassium to be made in cases where a loss of potassium was suspected.

Tanner (1955) has shown that as the child grows there is a constant increase in muscle as measured by his technique. This method, which we used, does not give an absolute figure for muscle mass but can only be used as an index which could be related to total body potassium. At the present time there is no method for calculating the absolute muscle weight in children.

Muldowney *et al.* (1957) used the Pace-Rathbun formula for calculating lean body mass (all tissues except fat) in normal adults.

They found a close correlation between total exchangeable potassium, creatinine excretion and lean body mass. We did not feel justified, however, in using a method traumatic to the child in order to calculate muscle mass.

There are certain limiting factors in dealing with infants which make it impossible to include them in the complete study, since the techniques used for the older children cannot be applied satisfactorily to the infant. It is difficult to collect urine from toddlers who will not tolerate the use of the ordinary collecting apparatus used for the infants, and who may still be incontinent. The principal study therefore includes all those children over the age of 6 years. A partial study of creatinine and total body potassium only was made in some infants.

Material and Methods

The children investigated were between 3 months and 13 years of age and were selected from in-patients who had no acute illness at the time. Febrile illnesses and diseases primarily affecting muscles, as well as certain metabolic diseases such as those involving the thyroid, alter the creatinine metabolism and therefore the excretion levels. All children with renal disease were excluded, but we did not consider that confinement to bed made any appreciable difference to our investigation. The conditions for which the children were admitted, and which were quiescent at the time, were asthma, gastro-enteritis, cirrhosis of the liver, chronic constipation, epilepsy, fibrocystic disease of the pancreas, bronchiectasis, psoriasis and eczema.

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As a preliminary, the method of Folin for the estimation of creatine and creatinine in the urine was checked carefully. It was found that Analar grade of picric acid was suitable without recrystallization. The standard creatinine solution was kept out of direct light and preservative, such as merthiolate, to prevent bacterial contamination, was added. If these precautions were not adhered to marked deterioration occurred in the standard, and straight line calibration curves could not be obtained. Strict temperature control when making the colorimetric reading is very important. A temperature of 20° C. gave the most satisfactory colour development using a 602 filter in an E.E.L. colorimeter, but the time for optimum colour development was 25 minutes and not 15 minutes.

The investigation was carried out in three parts. The first was the estimation of creatine and preformed creatinine in the 24-hour urine. The specimens were collected from 8 a.m. to 8 a.m. on two successive days or in some cases a few days apart. This was done to check the work of others who had shown that the preformed creatinine output was consistent for any given individual. It was found that no shorter period than 24 hours, such as four or eight hour collections, showed any constant result for creatinine (Best, Kuhl and Friedemann, 1952). To obtain the total creatinine value the urine was autoclaved with picric acid at 115°-120° C. for 20 minutes. The method for estimating the muscle mass was that used by Tanner (1955). Measurements were made of height and weight, shoulder and pelvic width, arm and thigh circumference and subcutaneous fat by skin-fold technique. Radiographs of upper arm, lower leg and thigh were also taken for soft tissue measurement.

Total exchangeable potassium was determined by W. W. Payne, by giving 1 microcurie of K⁴² per kg. by mouth and determining the specific activity of the urinary potassium 12 and 24 hours later, using a well-type scintillation counter. It is hoped to report this work in detail later.

Forty children were used for the first part of the investigation, and the results are given in Table 1. In only 13 children was a complete study made (Table 2) and their ages were from 6 to 11 years.

The figures in column 1 of Table 2 represent the total

TABLE 1
DAY TO DAY VARIATION IN PREFORMED CREATININE
IN 40 CHILDREN

Age (years)	Preformed Creatinine (mg./24 hrs)		Per cent Variation	Mean Creatinine Index
	First Period	Second Period		
3-12 mths	39.0	33.6	0.6	10.5
	43.6	45.2	1.8	
	56.7	68.1	9.1	
	126.3	128.5	0.9	
	136.8	133.5	1.1	
1-3	93.4	88.5	2.6	12.25
	100.0	116.3	7.5	
	118.2	111.5	2.09	
	119.1	120.1	0.4	
	248.5	258.4	2.05	
	251.0	262.5	2.2	
3-6	160.0	158.3	0.5	11.3
	214.2	244.0	6.0	
	224.2	264.4	8.2	
	265.2	277.5	2.2	
6-9	232.0	288.5	10.9	17.0
	332.0	378.3	6.5	
	338.4	313.0	3.9	
	361.8	332.2	4.2	
	340.0	307.5	4.0	
	390.5	443.7	6.3	
	394.4	410.5	1.9	
	420.4	439.6	2.1	
	426.4	487.2	4.4	
	453.0	488.8	3.8	
	466.2	450.2	1.7	
	472.0	419.1	5.4	
	577.1	560.6	1.4	
	690.1	699.2	1.4	
9-13	68.8	55.5	10.6	14.3
	290.0	344.0	8.5	
	293.0	324.0	5.0	
	575.0	560.0	3.4	
	585.0	522.5	5.6	
	592.8	617.1	2.0	
	594.5	569.4	2.1	
	604.2	608.3	0.06	
	613.6	400.5	1.0	
	636.5	632.9	0.2	
	869.0	814.0	3.2	

body potassium in mEq/litre/kg. body weight and are arranged in order of magnitude. The value for muscle was arrived at by taking the average of the three measurements of muscle from the soft tissue radiographs, i.e. thigh, lower leg, upper arm. This does not represent

TABLE 2
CREATINE, CREATININE AND TOTAL BODY POTASSIUM IN RELATION TO MUSCLE MASS
IN 13 CHILDREN AGED BETWEEN 6 AND 11

Potassium (mEq/litre/kg.)	Muscle Index	Muscle Corrected	Preformed Creatinine (kg./24 hrs)	Creatine (kg./24 hrs)	Height : Weight Ratio	Subcutaneous Fat
37.0	4.330	3.723	19.8	3.2	4.0	4.6
40.3	5.950	3.808	18.7	6.2	5.1	8.0
42.6	4.286	8.614	21.9	4.0	6.5	3.23
43.3	5.618	6.741	15.5	3.1	5.4	4.5
44.6	5.295	8.207	6.4	5.3	5.2	3.35
45.4	3.811	7.622	13.9	3.5	6.4	3.2
46.0	6.260	5.821	11.9	2.6	4.3	4.6
47.0	5.400	5.616	16.1	4.3	4.6	4.4
49.5	5.769	9.115	20.8	7.4	5.4	3.4
49.5	5.098	7.035	15.4	2.2	5.0	3.6
50.6	4.685	4.872	17.1	3.4	5.2	5.0
51.5	5.100	6.420	20.8	3.7	4.8	3.08
53.0	5.481	4.275	13.8	2.7	6.4	8.2

TABLE 3
WEIGHT AND AGE IN RELATION TO CREATININE INDEX

Age (years)	No. of Cases	Mean Creatinine Index	Range	Average Weight (kg.)	Mean Creatinine Index (Other Authors)	Mean Weight (kg.)
3-12 mths	5	10.5	6.5-13.5	7.1	12.5	7.4
1-3	6	12.25	10.5-14.0	10.2	12.4	—
3-6	4	11.3	8.6-14.0	17.0	20.4	18.9
6-9	14	17.0	15.6-18.4	23.5	24.9	29.4
9-13	11	14.3	12.2-16.4	34.5	24.4	37.2

an absolute figure for muscle mass, but only a relative one for comparison between different ages and sizes. A correction for height and weight and subcutaneous fat was applied to the muscle figure by taking the height : weight ratio and dividing this by the average of the measurements for subcutaneous fat. The result of this is to be found in the column headed 'Muscle Corrected'.

Results

From Table 1 it will be seen that the day-to-day variation in preformed creatinine is relatively small; the variation averages 3.5% in the 40 children studied. In Table 3 weight as well as age have been tabulated with the creatinine index. The output increases with age and weight but does not accord with the published values for normal children (Harding and Gaebler, 1922). There is, unfortunately, no complete set of figures of one investigation covering the age range which we have investigated.

It is clear from our figures that a child at complete rest who has recently suffered some acute illness does not have an entirely normal metabolism of creatinine as judged by the published work of other authors. The figures for creatine output are not included as there is no constancy, there being a marked variation from day to day and no close correlation with age and weight. This same lack of correlation was found for the total creatinine output. Table 3 shows that there is no correlation whatsoever between total body potassium and the 24-hour creatinine excretion or the muscle index, either alone or corrected for height, weight and subcutaneous fat.

This investigation was designed to find a single, clinically applicable method for estimating the expected total body potassium without having to resort to all the techniques used here. If our assumptions and methods are correct, then no correlation could be found between creatinine excretion, total exchangeable potassium and an index of muscle mass.

Summary

Duplicate 24-hour preformed creatinine and creatine excretion levels were estimated in 40 convalescent infants and children. The creatinine output for each individual was reasonably constant, but somewhat lower than the figures reported by other investigators for children over 3 years of age. The total creatinine and creatine outputs showed much greater variation, i.e. the creatine was more variable. In 13 children in addition, an attempt to estimate muscle mass was made by the following methods: measurement of weight, height, limb girth and fat thickness; measurement of muscle shadow in soft tissue radiographs; estimation of total exchangeable potassium using K^{42} . No correlation could be found between creatinine index, estimation of muscle mass from body measurements, estimation of muscle mass from soft tissue radiograph measurements and total exchangeable potassium.

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