Anthropometry-based reference values for 24-h urinary creatinine excretion during growth and their use in endocrine and nutritional research[1–3]

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ABSTRACT

Background: Urinary creatinine reference values that take anthropometric data into account, which is mandatory during growth, are not available for healthy white children.

Objective: We sought to establish anthropometry-based reference values for 24-h urinary creatinine excretion in healthy white children aged 3–18 y.

Design: Anthropometric variables and 24-h urinary creatinine excretion rates were determined cross-sectionally (225 boys and 229 girls). Age and sex dependency of 24-h creatinine excretion (crude and related to individual anthropometric variables) were assessed to derive appropriate creatinine reference values. The applicability of these creatinine reference values for estimation of daily excretion of certain analytes was assessed in 40 additional children.

Results: Sex-specific, body-weight-related creatinine reference values were derived for the following age groups: 3, 4–5, 6–8, 9–13, and 14–18 y. The 5th percentile exceeded 0.1 $mmol \cdot kg^{-1} \cdot d^{-1}$ in all age groups >3 y. The use of these creatinine reference values for estimating average 24-h excretion rates of certain analytes (determined as the ratio of analyte to creatinine in spot urine samples) yielded reasonable estimates of mean 24-h urinary excretion rates actually analyzed (spot and 24-h urine samples from the same children). Ideal 24-h creatinine excretion values for height were also derived for a potential determination of the creatinine height index.

Conclusions: Established anthropometry-based creatinine reference values are recommended as a convenient, simple tool to *1*) identify severe 24-h urine collection errors, *2*) calculate average 24-h excretion rates of certain analytes (from respective ratios of analyte to creatinine) determined in spot urine samples, and *3*) assess somatic protein status by determining the creatinine height index. *Am J Clin Nutr* 2002;75:561–9.

KEY WORDS Analyte-to-creatinine ratio, body height, body surface area, body weight, calcium, children, cortisol, creatinine height index, dehydroepiandrosterone sulfate, deoxypyridinoline cross-links, protein status, spot urine, 24-h urine collection

INTRODUCTION

Most of the creatinine excreted in urine is derived from the intracellular creatinine precursors creatine and phosphocreatine by nonenzymatic processes (ie, dehydration and hydrolysis) occurring in muscle. Therefore, measurement of urinary creatinine excretion serves as a simple biochemical tool for evaluating total-body skeletal muscle mass or body composition (1–4). In addition, urinary creatinine output is frequently used to check roughly the completeness of urine collection (5–8) or to estimate the excretion rates of certain analytes from the respective ratios of analyte to creatinine (5, 9, 10). Although normal ranges of 24-h urinary creatinine excretion are well documented in adults (11–14), only a few articles have been published during the past decades that present reference values of 24-h urinary creatinine excretion (creatinine reference values) in children and adolescents (15–18). Despite the fact that anthropometric characteristics and sex are major determinants of urinary creatinine excretion, only one of the studies involving children and adolescents presented sex-specific creatinine data in relation with anthropometric predictors (18). However, this study was conducted in Indian children who clearly had lower values for height, weight, body mass index, protein intake, and urinary creatinine output than do healthy white children of comparable age, so that these creatinine data are inappropriate as creatinine reference values for children of developed countries.

Therefore, the aim of the present study was to establish anthropometry-based age- and sex-specific reference values of the urinary 24-h creatinine excretion of healthy white children. In addition, our intention was to check the applicability of these creatinine reference values for the estimation of 24-h excretion rates of nutritionally and endocrinologically relevant urine analytes quantified in spontaneous urine samples.

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SUBJECTS AND METHODS

Subjects

The study group comprised 494 healthy children and adolescents (245 boys and 249 girls aged 3–18 y) participating in the DONALD (Dortmund Nutritional and Anthropometric Longitudinally Designed) Study, an ongoing observational study investigating the interrelations between nutrition, growth, metabolic changes, and endocrine changes during childhood and adolescence. The study was approved by the institutional review board of the Research Institute of Child Nutrition, Dortmund, Germany, and parental consent and children's assent were obtained before entry into the study. Once a year the subjects were medically examined, anthropometric measurements were taken, and a 24-h urine sample was collected. To ensure compliance in the 24-h urine collection, the children and their parents were carefully instructed in the collection procedure and also received written directions. Children were asked to void their bladders upon rising in the morning; this micturition was completely discarded and the time was registered (start of collection). All the urine passed for the next 24 h was collected, including the complete sample produced upon rising the next morning (19). All micturitions were stored immediately in preservative-free, Extran-cleaned (Extran, MA03; Merck, Darmstadt, Germany), 1-L plastic containers at temperatures <–12°C before transfer to the research institute where samples were stored at ≤–20°C until analyzed. A dietitian, who visited the families at home and brought the urine samples back to the institute, explicitly asked parents about their child's compliance and discussed the completeness of the urine collection in detail with the family (20). Samples reported to contain incomplete micturitions were not included in the study. In general, urine was collected along with a weighed 24-h diet record. Dietary intakes were estimated from this record with the use of an in-house computer database of foods that was primarily based on the food-composition tables of Souci et al (21).

From the total number of 494 children, 40 subjects (10 boys and 10 girls aged 6–7 y and 10 boys and 10 girls aged 11–13 y) were assigned to a test group to specifically check the applicability of the established creatinine reference values. Apart from the 24-h urine sample, the children of the test group additionally collected a spontaneously voided urine sample within a few days before or after the respective 24-h collection. The data set of the remaining 454 children was used to establish 24-h urinary creatinine reference values. For performing a true cross-sectional study, a random sample—with each child occurring only once—was selected from the overall number of available 24-h urine specimens (n = 1454) collected from these 454 children.

Anthropometry and quantification of urinary analytes

Standardized anthropometric measurements (22) were performed (on the right side of the body) by experienced, well-trained anthropometrists. Body weight was measured to the nearest 0.1 kg and height to the nearest 0.1 cm by use of an electronic scale (Seca 753 E; Seca Weighing and Measuring Systems, Hamburg, Germany) and a digital telescopic wall-mounted stadiometer (Harpenden; Holtain Ltd, Crymych, United Kingdom), respectively. Skinfold thickness was measured to the nearest 0.1 mm at the triceps, biceps, subscapular, and suprailiac sites by using a Holtain skinfold caliper (Holtain Ltd). Standardization exercises, regularly performed, yielded interobserver CVs (23) <0.1% for height and ≈12% (range: 10.5–14.9%) for skinfold-thickness measurements. The stages of pubertal development were determined by a physician by use of the grading system defined by Tanner (24) for pubic hair. Fat-free mass was determined by use of the skinfold thickness equations of Brook (25) and Slaughter et al (26) for children (3–8 y) and adolescents (≥9 y), respectively.

Urinary creatinine concentrations were measured by use of a kinetic Jaffé procedure (27) with a Beckman-2 creatinine analyzer (Beckman Instruments, Inc, Fullerton, CA) according to the manufacturer's instructions. Calcium was measured by flame atomic absorption spectrometry by using a Perkin Elmer 1100 Spectrometer (Perkin Elmer, Überlingen, Germany) that had a detection limit of 0.01 mmol/L and an intra- and interassay precision of <5%. Quantification of free deoxypyridinoline cross-links was performed with a specific competitive enzyme immunoassay with the use of a monoclonal antideoxypyridinoline antibody (Metra Biosystems, Mountain View, CA). Urinary steroids were measured by radioimmunoassay by using tritiated steroids (Amersham Pharmacia Biotech, Freiburg, Germany) and specific antibodies that were raised and characterized, as described elsewhere (28). The dehydroepiandrosterone sulfate (DHEAS) radioimmunoassay was performed directly in diluted urine samples. Before radioimmunoassay, cortisol was extracted from the urine with dichloromethane and was chromatographically purified by using Celite columns (Celite columns 545 AW; Sigma-Aldrich Chemie GmbH, Steinheim, Germany) (29). For the steroids measured, the intra- and interassay CVs were <10%.

Statistical analysis

Pearson correlation coefficients, multiple regression analysis, analysis of covariance (ANCOVA), two-way analysis of variance (ANOVA), and unpaired t tests (significance: P = 0.05) were applied for statistical analysis (SPSS version 9.0; SPSS Inc, Chicago). All tests were two-tailed. Data are presented as means ± SDs unless otherwise indicated. Urinary creatinine excretion for height (mmol/d) was smoothed according to the method of the running median by using triplets of data in the middle and pairs of data at the end.

RESULTS

The subjects' baseline anthropometric characteristics and dietary intakes of energy and animal protein are shown in **Table 1**. As expected, a strong age dependency was seen for absolute daily creatinine excretion from age 3 y onward (**Figure 1**A). When urinary creatinine output was adjusted for anthropometric characteristics by relating creatinine excretion to body surface area (Figure 1B), to body weight (Figure 1C), or to fat-free mass (data not shown), a significant age dependency in creatinine excretion was seen for all 3 adjustment variables. Because age dependency was reduced to a larger degree by relating creatinine to body weight (r = 0.45) than to fat-free mass (r = 0.49) or body surface area (r = 0.73), we calculated the individual ratios of creatinine to body weight to control for body-composition changes during growth. ANCOVA showed that sex (F = 12.1, P < 0.001) and the covariate age (F = 119.6, P < 0.0001) significantly improved the proportion of explained variation in urinary creatinine output related to body weight. By using two-way ANOVA, an adequate control of the influence of age on the ratio of creatinine to body weight could be achieved by establishing the following 5 age groups: 3, 4–5, 6–8, 9–13, and 14–18 y. Within these age groups no significant increase was found for the ratio

TABLE 1
Baseline nutritional and anthropometric characteristics of the study population grouped according to age and sex[1]

Sex and age group (y)	Intake		Body weight	Body height	BMI
	Energy	Animal protein			
	kJ/d	*g/d*	*kg*	*cm*	*kg/m²*
Boys					
3 (*n* = 23)	5050 ± 703	23.3 ± 7.2	15.4 ± 1.5	99.0 ± 3.6	15.7 ± 1.3
4–5 (*n* = 62)	5904 ± 1435	27.0 ± 10.8	18.5 ± 2.2	108.3 ± 5.2	15.7 ± 0.9
6–8 (*n* = 53)	7033 ± 1481	35.9 ± 13.2	25.0 ± 3.9	125.5 ± 7.2	15.8 ± 1.3
9–13 (*n* = 59)	8556 ± 2033	40.2 ± 16.4	36.7 ± 7.9	143.3 ± 8.9	17.7 ± 2.2
14–18 (*n* = 28)	10929 ± 2598	56.9 ± 21.4	64.5 ± 13.6	174.8 ± 10.8	20.9 ± 2.6
Girls					
3 (n = 31)	4586 ± 674	21.9 ± 6.1	14.5 ± 1.6	95.6 ± 3.1	15.8 ± 1.1
4–5 (*n* = 59)	5025 ± 1314	23.2 ± 10.3	18.3 ± 2.7	108.4 ± 6.0	15.5 ± 1.4
6–8 (*n* = 63)	6025 ± 1280	28.4 ± 10.1	24.8 ± 4.9	123.7 ± 7.2	16.1 ± 2.0
9–13 (*n* = 54)	7418 ± 2050	36.3 ± 16.4	37.3 ± 9.4	145.8 ± 10.9	17.3 ± 2.5
14–18 (*n* = 22)	7996 ± 2489	44.7 ± 19.1	59.7 ± 8.3	167.6 ± 4.7	21.2 ± 2.6

[1] $\bar{x}$ ± SD.

of creatinine to body weight from the respective youngest to the respective oldest age (*F* values of two-way ANOVA for age ranged between 0.13 and 0.64), whereas the sex difference remained largely stable (*F* values: 2.4–3.3). The corresponding sex-specific reference values for body weight–related 24-h urinary creatinine excretion during growth are shown in **Table 2**. From 3 to 14–18 y of age, the ratio of mean creatinine to body weight increased by 50% in boys and 43% in girls.

The curved relation between 24-h urinary creatinine excretion and height in the subjects is shown in **Figure 2**A. After logarithmic transformation of creatinine, the relation was linear and height alone explained 87% of the overall variability (Figure 2B). Inclusion of sex as a further predictor (multiple regression with sex as the dummy variable) increased the R^2 by only ≈0.3% (new total R^2 = 0.873). Stage of sexual maturation did not show any further influence on log creatinine after adjustment for height and sex (ANCOVA).

The ratios of analyte to creatinine, determined for calcium, DHEAS, deoxypyridinoline, and cortisol in spontaneous urine samples of the subgroups of children aged 6–7 y and 11–13 y, are shown in **Table 3**. Ratios were significantly different between the 2 age groups for calcium and DHEAS only. Mean estimated daily excretion rates of the analytes [(analyte/creatinine$_{spontaneous}$) × body weight$_{individual}$ × (creatinine/body weight$_{reference}$)] were comparable with the analyzed 24-h excretion rates for calcium, deoxypyridinoline, and DHEAS, but not for cortisol (**Figure 3**). Highly significant increases in 24-h urinary output with increasing age were seen for deoxypyridinoline and DHEAS, with both analyzed and estimated data.

When the measurement of daily creatinine excretion is used for the biochemical evaluation of the nutritional status of adults and children, the individual 24-h creatinine excretion should be preferentially expressed as a percentage of the 24-h creatinine excretion of well-nourished individuals of the same height (30–32). Therefore, the current data on 24-h urinary creatinine excretion are given according to definite height groups, either as empirical or smoothed mean values, in **Table 4**. It is discernible that, for example, in boys ≥95.0–99.9 cm, daily creatinine excretion approximately doubled after an average height gain of 25 cm and tripled after an increase in height of only ≈45 cm. The ideal 24-h creatinine excretion for height derived from the present well-characterized sample of healthy children and adolescents ingesting self-selected diets is shown in **Table 5**.

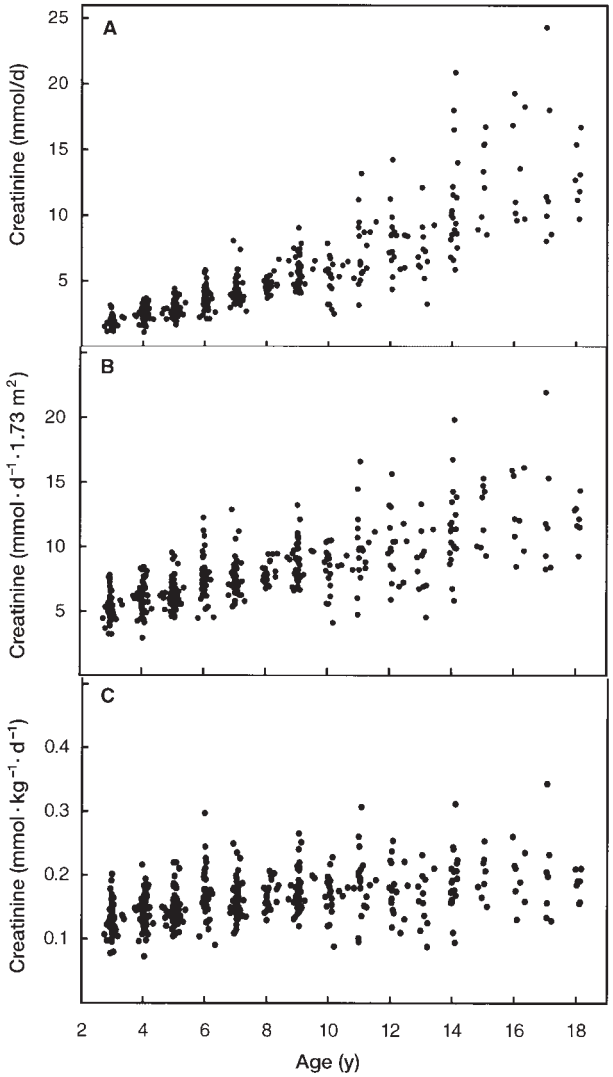

FIGURE 1. Twenty-four–hour urinary creatinine excretion in children aged 3–8 y (*n* = 454). A, absolute excretion rates (*r* = 0.86, *P* < 0.01); B, body-surface-area-related excretion rates (*r* = 0.73, *P* < 0.001); C, body-weight-related excretion rates (*r* = 0.45, *P* < 0.001).

TABLE 2
Twenty-four–hour urinary creatinine excretion related to body weight in healthy children and adolescents grouped according to sex and age

	Creatinine excretion				
	3 y	4–5 y	6–8 y	9–13 y	14–18 y
			$mmol \cdot kg^{-1} \cdot d^{-1}$		
Boys					
Value	0.134 ± 0.023[1]	0.151 ± 0.026	0.172 ± 0.026	0.182 ± 0.036	0.201 ± 0.043
Median	0.131	0.150	0.171	0.183	0.206
5th percentile	0.096	0.106	0.134	0.100	0.117
95th percentile	0.189	0.214	0.226	0.245	0.294
Girls					
Value	0.127 ± 0.026	0.142 ± 0.025	0.160 ± 0.031	0.171 ± 0.036	0.182 ± 0.028
Median	0.128	0.139	0.158	0.167	0.185
5th percentile	0.079	0.109	0.110	0.117	0.129
95th percentile	0.182	0.187	0.235	0.244	0.238

[1] $\bar{x}$ ± SD; *n* values given in Table 1.

DISCUSSION

According to sample collection guidelines published for trace elements, for example, measurements of creatinine and urine density are mandatory, irrespective of whether spot or 24-h urine samples are collected (33). In principle, urinary creatinine measurements are used to *1*) check roughly the completeness of 24-h urine collections, *2*) calculate average 24-h excretion rates of certain analytes determined in spot urine samples, and *3*) assess nutritional or somatic protein status. However, appropriate creatinine reference values that also consider anthropometric data, accounting for which is mandatory, especially during growth, are not available for healthy white children. In the present study, we

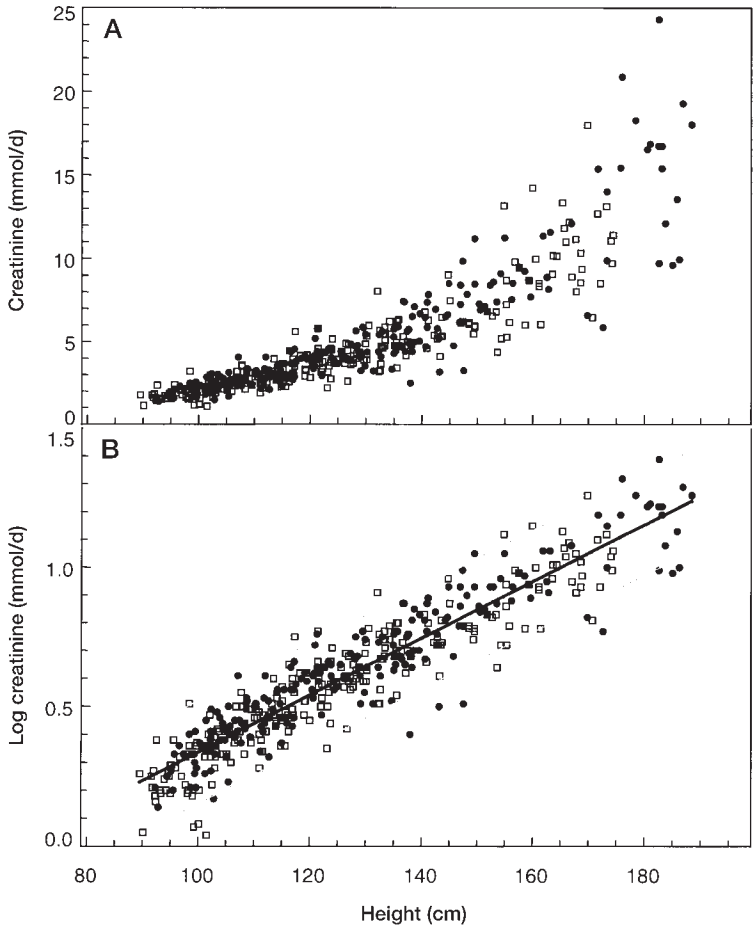

FIGURE 2. Twenty-four–hour urinary creatinine excretion in children. *n* = 225 boys (●) and 229 girls (□), plotted against height. A, original creatinine excretion rates; B, $\log_{10}$-transformed creatinine excretion rates shown with 95% CIs around the prediction line (boys and girls combined; $y = 0.0102x - 0.6854$; $R^2 = 0.87$, $P < 0.0001$).

TABLE 3
Ratios of analyte to creatinine analyzed in spontaneous urine samples of children aged 6–7 and 11–13 y[1]

Ratio	Age groups	
	6–7 y (n = 20)	11–13 y (n = 20)
Calcium:creatinine (mmol/mmol)	0.272 ± 0.21	0.158 ± 0.11[2]
DHEAS:creatinine (μmol/mmol)	0.104 ± 0.09	0.426 ± 0.21[3]
Deoxypyridinoline:creatinine (nmol/mmol)	20.27 ± 5.10	17.74 ± 5.16
Cortisol:creatinine (nmol/mmol)	14.92 ± 13.41	8.67 ± 8.62

[1] $\bar{x}$ ± SD. DHEAS, dehydroepiandrosterone sulfate.
[2,3] Significantly different from 6–7 y age group: [2] $P < 0.05$, [3] $P < 0.001$.

show for the first time anthropometry-based reference values for urinary creatinine excretion established in a large sample of healthy white children. In accord with the fact that creatinine is a crude measure of muscle mass, the adjustment of daily creatinine output to indexes of individual body composition reduced a large portion of the variability in creatinine seen with increasing age. To minimize age dependency, adjustment for body weight proved to be superior to adjustments for body surface area and fat-free mass. In addition, body weight is a routine anthropometric variable that can be simply and precisely measured. Therefore, in the present study, specific creatinine reference values are given as 24-h urinary creatinine output normalized to individual body weight. From the age of 3 y to the oldest age group of 14–18 y, mean ratios of creatinine to body weight increased 1.4-fold and 1.5-fold in girls and boys, respectively. This was probably due to an increase in the proportion of skeletal muscle mass to body weight (34).

Check on compliance of 24-h urine collection

Although measurements of urinary creatinine output are frequently used to check compliance of 24-h urine collections (5–8), clear criteria to categorize samples are presented sporadically. In studies reporting compliance criteria (6, 8), longitudinal checks were performed on intraindividual variation of urinary creatinine output. However, for cross-sectional investigations, no reasonable tool was available to help identify incomplete 24-h urine samples. As is discernible from the creatinine reference values shown in Table 2, in all age groups of both sexes—except for the 3-y-old boys and girls—the 5th percentiles exceeded 0.1 mmol·kg^{-1}·d^{-1}. Because the final numbers of children left in the specific age- and sex-stratified subgroups were moderately high and furthermore varied markedly, the respective 5th and 95th percentiles can be considered as rough estimates for lower and upper creatinine reference limits. Consequently, no deduction of clear-cut limits definitely identifying under- and over-collected 24-h urine samples is possible for individual subgroups. On the other hand, it appears reasonable to conclude from the overall data that daily creatinine excretion rates that fall below 0.1 mmol·kg^{-1}·d^{-1} in healthy white children are highly suspect to be incomplete. But this does not mean that the decision to exclude urine samples from a study should be made exclusively on the basis of the proposed cutoff rate of 0.1 mmol·kg^{-1}·d^{-1}; the use of a second criterion would be preferable. For example, a psychologically skillful repetition of questioning the child's compliance during the collection period could be considered in addition to a second 24-h urine collection if no previous 24-h urine collection is available for comparison. Unlike some investigators, eg, Bingham et al (35), who argue that creatinine excretion is too variable to use for the detection of undercollection in single 24-h urine specimens, we suggest that at least extreme collection errors can be detected by determining the body weight-related daily creatinine excretion rates.

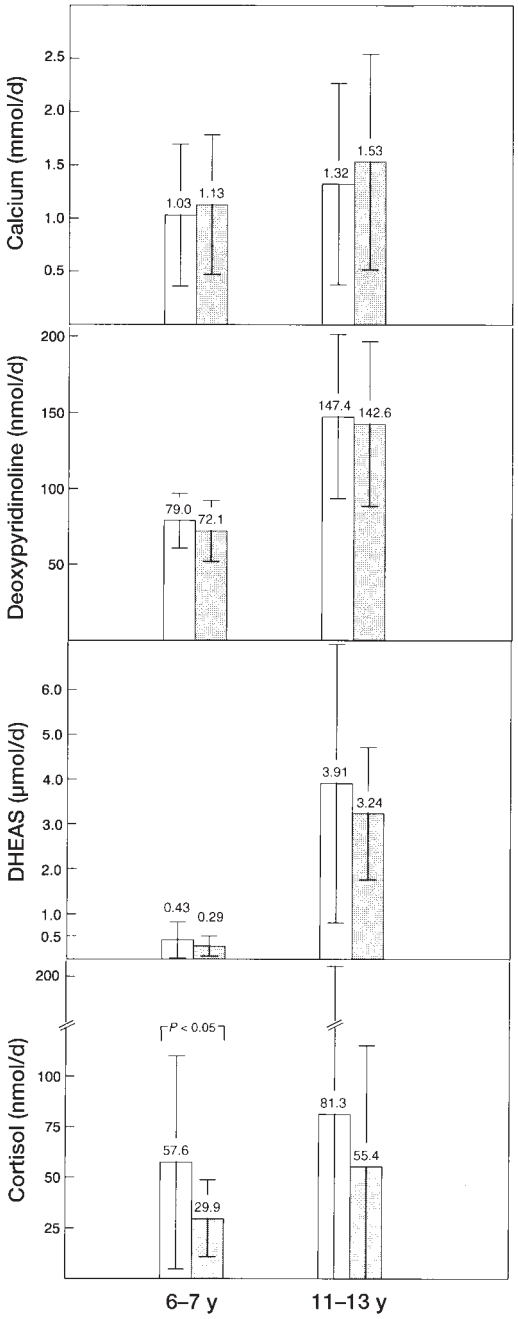

FIGURE 3. Mean (±SD) estimated (□) and analyzed (▨) 24-h urinary excretion rates of analytes determined in spot urine samples and 24-h specimens. Estimates were obtained by multiplying the respective ratio of analyte to creatinine by the age-corresponding, body-weight-related creatinine reference values from Table 2 and by individual body weights. For cortisol, a significant difference was seen between estimated and analyzed values in the 6–7-y age group ($P < 0.05$, paired t test). The increases for deoxypyridinoline and dehydroepiandrosterone sulfate (DHEAS) between 6–7 y olds (n = 20) and 11–13 y olds (n = 20) were significant ($P < 0.001$) for both estimated and analyzed daily excretion rates.

TABLE 4
Twenty-four–hour urinary creatinine excretion according to definite height groups

Height group (cm)	Height[1]	Body weight[2]	Creatinine[2]	Smoothed creatinine[1,3]
	cm	*kg*	*mmol/d*	*mmol/d*
Boys (n = 225)				
90.0–94.9 (n = 3)	93.2	14.0 ± 1.5	1.59 ± 0.19	1.59
95.0–99.9 (n = 14)	98.1	15.3 ± 1.5	2.02 ± 0.31	2.02
100.0–104.9 (n = 23)	102.5	16.5 ± 1.0	2.39 ± 0.38	2.39
105.0–109.9 (n = 22)	107.4	17.7 ± 1.3	2.77 ± 0.51	2.77
110.0–114.9 (n = 18)	112.4	19.8 ± 1.3	3.01 ± 0.49	3.01
115.0–119.9 (n = 15)	116.9	21.7 ± 1.8	3.49 ± 0.68	3.49
120.0–124.9 (n = 19)	122.1	23.2 ± 1.6	4.10 ± 0.64	4.10
125.0–129.9 (n = 15)	128.1	26.9 ± 1.6	4.58 ± 0.83	4.47
130.0–134.9 (n = 8)	132.6	26.9 ± 2.5	4.47 ± 0.92	4.47
135.0–139.9 (n = 24)	137.1	31.6 ± 4.3	5.36 ± 1.14	5.36
140.0–144.9 (n = 12)	142.4	34.5 ± 2.7	6.26 ± 1.44	6.26
145.0–149.9 (n = 11)	147.6	40.5 ± 4.8	8.24 ± 3.14	8.11
150.0–154.9 (n = 9)	152.4	43.5 ± 4.0	8.11 ± 1.43	8.11
155.0–159.9 (n = 6)	157.9	47.6 ± 5.6	8.55 ± 0.79	8.55
160.0–164.9 (n = 4)	162.6	50.1 ± 3.7	10.00 ± 1.73	9.35
165.0–169.9 (n = 2)	168.4	56.2 ± 5.4	9.35 ± 3.90	9.35
170.0–174.9 (n = 4)	172.7	63.4 ± 3.6	11.29 ± 4.29	11.29
175.0–179.9 (n = 3)	176.7	68.5 ± 8.5	18.19 ± 2.72	16.05
180.0–184.9 (n = 8)	182.4	73.5 ± 8.6	16.05 ± 4.23	16.05
185.0–189.9 (n = 5)	186.4	75.4 ± 9.6	14.09 ± 4.46	15.07
Girls (n = 228)[4]				
90.0–94.9 (n = 13)	92.8	13.2 ± 0.9	1.68 ± 0.29	1.68
95.0–99.9 (n = 18)	97.5	15.2 ± 1.3	1.97 ± 0.46	1.97
100.0–104.9 (n = 18)	102.6	16.2 ± 1.8	2.13 ± 0.49	2.13
105.0–109.9 (n = 17)	107.1	17.7 ± 1.1	2.64 ± 0.50	2.64
110.0–114.9 (n = 21)	112.5	19.2 ± 1.8	2.83 ± 0.44	2.83
115.0–119.9 (n = 20)	117.0	21.5 ± 2.8	3.45 ± 0.76	3.45
120.0–124.9 (n = 19)	122.8	24.8 ± 3.7	3.85 ± 0.87	3.85
125.0–129.9 (n = 16)	127.6	26.1 ± 2.6	4.10 ± 0.58	4.10
130.0–134.9 (n = 17)	132.4	28.6 ± 2.4	5.04 ± 1.22	5.01
135.0–139.9 (n = 9)	136.3	30.5 ± 2.7	5.01 ± 0.92	5.01
140.0–144.9 (n = 11)	142.6	34.3 ± 5.2	5.84 ± 1.32	5.84
145.0–149.9 (n = 8)	148.1	40.2 ± 7.7	6.18 ± 0.58	6.18
150.0–154.9 (n = 6)	153.4	40.8 ± 4.5	7.16 ± 3.11	7.16
155.0–159.9 (n = 9)	157.1	46.3 ± 7.7	8.41 ± 2.72	8.41
160.0–164.9 (n = 8)	162.4	53.1 ± 4.3	8.94 ± 1.36	8.94
165.0–169.9 (n = 11)	167.4	61.3 ± 7.4	11.17 ± 2.80	10.44
170.0–174.9 (n = 7)	172.9	60.5 ± 10.5	10.44 ± 2.36	11.07

[1] $\bar{x}$.
[2] $\bar{x}$ ± SD.
[3] Smoothed by running median.
[4] The data of one girl (height < 90 cm) were not considered.

Estimation of 24-h urinary excretion rates

As a matter of routine, several analytes determined in spot urine samples are normalized to urinary creatinine (36, 37). In addition, the ratios of certain analytes to urinary creatinine have been used to estimate 24-h excretion rates by multiplying these ratios with sex- and age-specific creatinine reference values. The analytes for which this procedure has been successfully applied in adults are iodine (9, 38), albumin (5), porphyrin (10), and mercury (10). Our current findings clearly show that this procedure can also be applied to DHEAS, deoxypyridinoline, and calcium, resulting in reliable estimates of the actual average 24-h excretion rates of these analytes in children. However, as expected, it was not possible to obtain a useful estimate of daily urinary output for cortisol. Obviously, the effect of the circadian rhythm and the spontaneous increments in cortisol secretion are so important that a reasonable estimation of 24-h cortisol excretion is not possible. However, as shown previously, measurement of the midnight-to-morning urinary cortisol-to-creatinine increment is an accurate, noninvasive method for assessing the hypothalamic-pituitary-adrenal axis (39). In principle, 2 points should be considered when daily excretion rates of certain analytes are estimated from their respective ratios to creatinine. First, the use of appropriate and reliable reference values for urinary 24-h creatinine excretion is essential, and second, the obtained output values do indeed characterize reasonably the precise mean 24-h excretion value of groups, but not of an individual. This is probably due to day-to-day variation in the respective analytes measured and the frequently described day-to-day variation in urinary 24-h creatinine (4, 40).

TABLE 5
Ideal 24-h urinary creatinine excretion for height of healthy white children consuming self-selected diets[1]

Height (cm)	Creatinine excretion	
	Boys	Girls
	mmol/d	
90	1.3	1.5
92	1.5	1.6
94	1.7	1.8
96	1.8	1.9
98	2.0	2.0
100	2.2	2.1
102	2.4	2.1
104	2.5	2.3
106	2.7	2.5
108	2.8	2.7
110	2.9	2.7
112	3.0	2.8
114	3.2	3.0
116	3.4	3.3
118	3.6	3.5
120	3.9	3.7
122	4.1	3.8
124	4.2	3.9
126	4.2	4.0
128	4.3	4.1
130	4.4	4.4
132	4.5	4.6
134	4.8	4.8
136	5.1	5.0
138	5.5	5.2
140	5.9	5.5
142	6.2	5.8
144	6.6	5.9
146	6.9	6.1
148	7.3	6.2
150	7.7	6.5
152	8.0	6.9
154	8.2	7.4
156	8.4	8.0
158	8.6	8.5
160	8.7	8.7
162	8.9	8.9
164	9.0	9.4
166	9.2	10.0
168	9.3	10.5
170	10.1	10.6
172	11.0	10.8
174	11.9	
176	12.9	
178	13.9	
180	14.9	
182	15.9	
184	16.8	
186	17.8	

[1] Ideal 24-h urinary creatinine for height is defined to represent standard values of daily creatinine excretion for given heights of an appropriately defined reference population. Ideal creatinine can be used to calculate the creatinine height index (CHI) for individuals (eg, undernourished subjects; 30). CHI (%) = (measured 24-h urinary creatinine × 100)/(ideal 24-h urinary creatinine for height). These ideal values were derived by linear interpolation of the smoothed mean creatinine excretion values from Table 4 for given 2-cm increments in mean height.

Assessment of somatic protein status: use of ideal creatinine excretion as a standard

It is known that urinary creatinine excretion is not only a biochemical reflection of total muscle mass but is also affected by several factors, such as strenuous exercise, diet, infection, fever, trauma, and renal function (30). Despite this limitation, many investigators have suggested that urinary creatinine output for a given height is a convenient measure for the assessment of somatic protein status (30–32, 41–43) because, on one hand, creatinine is a sufficiently reliable estimate of fat-free mass and muscle mass and, on the other hand, height (as a major determinant of fat-free mass and muscle mass) is not affected by fluid and adipose tissue imbalances. Especially, the so-called creatinine height index has been recommended for evaluating the degree of protein depletion and repletion in potentially malnourished children (30, 31, 41). The creatinine height index (expressed as a percentage) is defined as the individual 24-h urinary creatinine output of a patient divided by the ideal 24-h urinary creatinine excretion for a given height (in a reference population) multiplied by 100. A creatinine height index of 60–80% of the standard (ie, in comparison with the ideal) has been suggested to represent a moderate deficit in body muscle mass, whereas a value of <60% indicates a severe deficit of body muscle mass (30). However, ideal creatinine excretion data for height (to be used as the standard), with both creatinine and height obtained from the same, well-defined, healthy children have not been published yet. The hitherto available ideal creatinine excretion rates of healthy children were estimated on the basis of normal height, weight, and separate creatinine excretion data from different literature sources (41). In the same article, urinary 24-h creatinine excretion was presented for a height range of 50–129 cm. The values (tabulated for boys and girls, combined) ranged from 0.31 mmol/d (height: 50 cm) to >1.76 mmol/d (height: 90 cm) and 3.18 mmol/d (height: 111 cm) to 5.45 mmol/d (height: 129 cm) (41) and thus were consistently higher than our ideal creatinine excretion values listed in Table 5. This discrepancy may, at least in part, be because the literature values were calculated from heterogeneous data published >40 y ago.

The current ideal 24-h creatinine excretion rates for height (Table 5) are the first data derived from a large set of well-characterized anthropometric and urinary creatinine data determined in the same children. According to Gibson (30), the creatinine height index calculated with such ideal 24-h creatinine excretion data should allow for monitoring the effects of long-term nutritional intervention on the repletion of lean body mass. Until now, the creatinine height index was most frequently used to assess the degree of muscle mass depletion in children with the marasmic form of protein-energy malnutrition (30, 41). In such subjects, there will be a decrease in the creatinine height index resulting from the loss of lean body mass. This serves to maintain serum protein concentrations (30, 41). However, the interpretive values for creatinine height index (eg, values <60%, which suggest severe deficit of muscle mass) should be used with caution and also need to be validated (30).

Animal protein intake is an important nutritional confounder when assessing somatic protein status through urinary creatinine. Cooked meat, but also heat-treated milk, contains a considerable amount of creatinine (19), which is promptly excreted in urine after ingestion (1). Thus, healthy children with an especially low or high intake of animal protein must be expected to have correspondingly lower or higher creatinine excretion rates

than what the mean anthropometry-based values showed in the present study. We estimated previously that a change of ≈1 g·kg body weight^{-1}·d^{-1} of animal protein intake could account for a change of ≈9% in daily urinary creatinine output related to body weight (19).

Another important aspect of the current study is that during normal human growth, absolute daily creatinine excretion is similar in both sexes if creatinine is expressed in relation to height. This is especially evident in Figure 2 and Table 5 and is probably due to the fact that girls mature earlier than boys. For example, girls participating in the DONALD study attained their peak height velocity at a mean age of 14.5 y, whereas boys reached it at a mean age of ≈16.5 y (44), which implies that most endocrine variables relevant to skeletal muscle anabolism reach their respective optimum with a delay of ≈2 y in boys. This difference of 2 y in chronologic age corresponds to an average height difference of nearly 14 cm between boys and girls (44). Again, the difference in mean height is also discernible between sexes in the respective highest height groups of the present study (Table 4). Thus, it is obvious that during the time period in which the male-to-female height difference occurs, boys also attain greater muscle mass and creatinine excretion.

Considered together, the results of the present study suggest that the currently established anthropometry-based creatinine reference values for healthy, well-nourished white children can be used as a convenient, simple tool to *1*) identify at least severe 24-h urine collection errors, *2*) calculate average 24-h excretion rates of certain analytes determined in spot urine samples, and *3*) assess the relative degree of protein depletion in children. Whether the current creatinine reference values can also be applied unrestrictedly to healthy white children with markedly different body composition and dietary intakes needs to be tested in future studies.

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