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Urea and nitrogen excretion in pediatric peritoneal dialysis patients

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Background. Adequate nutrition is critical to the care of children with end-stage renal disease, and failure to reach the target dietary intake is associated with growth failure. Prospective studies of urea and nitrogen output in adults have led to the derivation of quantitative relationships, which allow assessment of dietary protein intake when only urea appearance is known. Such a clinically useful relationship has not been defined in children receiving chronic peritoneal dialysis (PD).

Methods. We studied 18 pediatric PD patients (ages 0.8 to 14.3 years) on 132 occasions and determined norms of urea nitrogen appearance (UNA), total nitrogen appearance (TNA), and nonurea nitrogen appearance (NUNA). We stratified data on UNA, TNA, NUNA, nonprotein nitrogen appearance, and the protein equivalent of nitrogen appearance by age groups (0 to 5, 6 to 10, and 11 to 15 years of age) and demonstrated significant differences. In addition, dietary protein and energy intake were measured in the outpatient setting with food scales and dietitian interviews, and the results were stratified by age, presence of residual renal function, and recombinant human growth hormone (rhGH) therapy.

Results. UNA (3.05 ± 1.38 g/day, 103 ± 42 mg/kg/day) and TNA (4.67 ± 1.86 g/day, 159 ± 52 mg/kg/day) varied significantly between different age groups. NUNA in pediatric subjects (56 ± 24 mg/kg/day) was significantly greater than previously published adult norms. A linear relationship was defined between UNA and TNA that was specific to pediatric PD patients [TNA (g/day) = 1.26(UNA) + 0.83]. When the relationship was scaled to body mass, the *y* intercept was significantly different in the youngest subjects [TNA = 1.03 (UNA) + 0.02 (weight in kg) + 0.56 (for subjects age 0 to 5) or 0.98 (for subjects age 11 to 15 or 6 to 10), $r^2 = 0.91$]. Dietary protein intake was significantly greater in subjects receiving rhGH therapy, although nitrogen excretion was unchanged.

Conclusions. Markers of protein metabolism in pediatric PD patients are age dependent and differ from adult values. An age-specific relationship between TNA and UNA is defined for pediatric subjects; it does not vary with rhGH or the presence of residual renal function.

Key words: peritoneal dialysis, chronic renal failure, nutrition, pediatric infant, child, adolescent renal failure, nitrogen, urea, protein metabolism, recombinant human growth hormone.

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The effect of nutritional status on the long-term outcome of patients with ESRD is well established [1, 2]. Indeed, undernutrition contributes importantly to growth failure in children with renal disease [3–8]. Deficient anabolism and statural growth are common in these patients and may prove irremediable after a prolonged period of dialysis. Thus, great effort is devoted to ensuring delivery of targeted dietary protein and calorie intake in children receiving maintenance dialysis treatments; these efforts include intensive dietary counseling and nasogastric feedings [9, 10]. An enhanced dose of dialysis (as Kt/V_{urea}) may improve protein and energy intake as well [11, 12].

In stable peritoneal dialysis (PD) patients, adherence to dietary protein instructions may be determined by measuring total nitrogen appearance (TNA) at steady state in dialysate and urine. While steady-state TNA is the standard for indirect assessment of dietary protein intake, usually only urea nitrogen appearance (UNA) is readily available. This has led to the derivation of quantitative relationships between total nitrogen and UNA [13–19] for adult patients with chronic renal insufficiency (CRI) and those receiving PD. Previous studies in pediatric patients have focused on the use of UNA as in indicator of dietary protein intake [20, 21], while only preliminary data exist to establish a relationship between UNA and TNA (abstract; Edefonti, *J Am Soc Nephrol* 6:576, 1995). Nitrogen balance studies performed on children receiving chronic PD have often been of limited size and duration, resulting in incomplete stabilization of nitrogen intake, and have not provided sufficient data to utilize urea nitrogen and TNA interchangeably [22–24]. Thus, we sought to determine a predictable relationship between urea nitrogen and total nitrogen excretion to facilitate nutritional assessment in this patient population, which is at greatest risk for undernutrition and growth failure.

In this study, repeated measurements of urea nitrogen and total nitrogen excretion in stable pediatric PD patients were obtained, allowing usual dietary intake in the outpatient setting. We have defined norms of urea and nitrogen excretion for children across a wide range of

Table 1. Patient demographics

Category	
Number of males/females	10/8
Subjects/studies age 0–5	7/25
Subjects/studies age 6–10	3/22
Subject/studies age 11–15	8/85
Caucasian/African American/Hispanic	10/3/5
Age *years*: mean ± SD (range)	7.8 ± 4.9 (0.8–13.9)
Duration of ESRD *years*: mean ± SD (range)	1.7 ± 2 (0.1–6.0)
Mean serum albumin ± SD	3.0 ± 0.6
Subjects/studies with residual kidney function (>200 mL urine/day)	11/30
Subjects/studies treated with recombinant human growth hormone	10/55
Mean weekly total Kt/V_{urea}	2.19 ± 0.37

ages (9 months to 14 years), stratified them by age and have adjusted for body size. Furthermore, the results in subjects with and without residual renal function and recombinant human growth hormone (rhGH) therapy were compared. This large data set was used to define the relationship between urea nitrogen and total nitrogen excretion for chronic PD patients of different age groups, and normalized it to weight. Finally, we compared this relationship in pediatric PD patients with the results of prior studies in adults.

METHODS

Subjects

Eighteen stable chronic PD outpatients, ages 9 months to 14.3 years, were studied over 132 separate 24-hour periods (mean 7.3 studies per patient, range 1 to 16). The mean interval between studies was 38 days (range 5 to 154). Table 1 shows data for the study population and for age subgroups 0 to 5, 6 to 10, and 11 to 15 years. All subjects over six years of age attended school full time. The nutritional status of subjects was assessed by clinical history, dietary history, interval growth and weight gain, and measurement of serum albumin. Formal anthropometric measurements were performed quarterly by the same dietitian. Subjects considered undernourished, those with declining serum albumin, and those with the nephrotic syndrome were excluded. Patients with intercurrent illness (including peritonitis) or hospitalization were excluded from the study for at least three months before repeat measurements were obtained.

Concomitant therapy

Patients received the usual therapy to prevent the metabolic complications of end-stage renal disease (ESRD), including calcium carbonate, calcitriol, erythropoietin, sodium bicarbonate, antihypertensives, multivitamins, and iron. Eleven patients were treated with rhGH during part or all of the study. No subjects were studied during the first month of therapy with rhGH.

Dialysis techniques

Chronic ambulatory PD (CAPD) and chronic cycling PD (CCPD) were performed by patients and parents. The dialysis prescription and choice of modality were based on kinetic modeling of dialysis delivery (target $Kt/V_{urea} > 2.0$) and adequacy of ultrafiltration. Kt/V_{urea} (including dialysis + residual renal function) was determined by direct measurement of 24-hour dialysate and urine collections and serum urea [25] and was performed at least quarterly. The accuracy of Kt/V_{urea} was assessed by ensuring the completeness of collection and the consistent performance of daily PD prescription by nurse and physician interview, review of stored data on the automated PD cycler compared with prescribed PD volume, and occasional home visits.

Diet records

Parents and patients were instructed in measuring and recording food intake by an experienced pediatric renal dietitian. Food scales accurate to 0.1 g were provided to improve the reliability of outpatient diet records; patients and parents were instructed in their use. Three-day diet logs were completed at home by the subjects or parents prior to office visits, which were timed to coincide with urine and dialysate collections. Either the subjects or parents were interviewed by a dietitian to validate the diet records. Diet records were analyzed for protein and calorie content by dietary technicians using the computer program Food Processor for Windows 6.0 (ESHA Research, Salem, OR, USA).

Diet prescriptions

Dietary prescriptions were based on accepted age-appropriate guidelines [26]: 102 kcal/kg and 2 to 2.5 g protein/kg for ages 1 to 3 years, 90 kcal/kg and 2 to 2.5 g protein/kg for ages 4 to 6 years, 70 kcal/kg and 2 to 2.5 g protein/kg for ages 7 to 10 years, and 40 to 55 kcal/kg and 1.5 g protein/kg for ages 11 to 18 years. Actual dietary intakes often varied widely from this regimen. Three subjects had their diets supplemented by nasogastric feedings.

Dialysate and urine collections

Spent dialysate and urine were collected over a 24-hour period prior to office visits. Total volume was determined by weight (accuracy ± 10 g; Scale-tronix 4800; Wheaton, IL, USA) and then aliquoted for determination of total nitrogen (Kjeldahl), urea nitrogen (urease rate conductivity), and protein (modified biuret). The reliability of dialysate and urine collections was assessed by a PD nurse interview with subjects and their parents, and by a review of the automated cycler program.

Calculations

Both UNA and TNA were measured in 24-hour pooled collections of dialysate and urine. Serum urea nitrogen

Table 2. Comparison of nitrogen appearance in the entire study group

	UNA *g/day*	UNA *mg/kg/day*	TNA *g/day*	TNA *mg/kg/day*	NUNA *g/day*	NUNA *mg/kg/day*
All subjects	3.05 ± 1.38	103 ± 42	4.67 ± 1.86	159 ± 52	1.62 ± 0.74	56 ± 24
	3.17, 0.27–7.37	94, 29–265[j]	5.01, 0.63–9.64	150, 67–328[j]	1.56, 0.31–3.79	53, 10–208[l]
Age 0–5 years	1.43 ± 1.01	106 ± 57	2.29 ± 1.24	174 ± 68	0.86 ± 0.44	68 ± 33
	1.25, 0.27–4.51[f,i]	83, 29–265[e,g,j]	2.16, 0.63–5.58[f,i]	153, 67–328[d,g,j]	0.85, 0.31–2.22[f,i]	64, 33–208[d,h,l]
Age 6–10	3.43 ± 1.00	132 ± 27	5.02 ± 1.28	195 ± 33	1.59 ± 0.54	62 ± 23
	3.46, 1.74–4.99[c,g]	126, 91–175[b,i,j]	5.47, 2.80–7.17[c,g]	189, 139–256[a,i,k]	1.57, 0.59–2.85[c,g]	56, 33–145[a,g,l]
Age 11–15 years	3.43 ± 1.21	95 ± 36	5.29 ± 1.56	145 ± 45	1.86 ± 0.72	50 ± 18
	3.41, 0.89–7.37[c,d]	88, 42–208[a,f,j]	5.45, 1.76–9.64[c,d]	139, 74–121[a,f,j]	1.78, 0.40–3.79[c,d]	49, 10–124[b,d,l]

(*continued*)

was measured only at the end of each collection. Body surface area was calculated as

$$BSA = 0.0235(Ht)^{0.42246} \cdot (Wt)^{0.51456}$$

according to Gehan and George [27]; this formula has been validated previously in children. Nonurea nitrogen appearance (NUNA) was calculated by subtracting urea nitrogen from total nitrogen in dialysate and urine. Nonprotein nitrogen appearance (NPNA) was calculated by subtracting protein content of dialysate and urine from TNA. This calculated value allows an assessment of nitrogen excretion without the potentially confounding effects of dialysate and urinary protein losses. When steady-state nitrogen balance is assumed, dietary protein intake can be estimated as the protein equivalent of nitrogen appearance (PNA) = 6.25 × TNA or even more precisely as the protein equivalent of nonprotein nitrogen appearance (PNPNA) = 6.25 × NPNA. These formulae were normalized to body weight.

Statistical methods

Data are reported as mean ± SD of the sample, median, and range. A comparison of data on nitrogen appearance (Table 2) for the entire patient group with previously published data for adults receiving chronic PD was made by Mann–Whitney nonparametric test; comparisons within different age subgroups were made by Kruskal–Wallis nonparametric analysis of variance. Comparisons of dietary intake, serum albumin, and delivered dialysis dose (Table 3) were also by Mann–Whitney test and Kruskal–Wallis nonparametric analysis of variance (ANOVA) for multiple subgroups. The relationship between TNA and UNA was derived by linear regression, while models incorporating weight and age were obtained by ANOVA using SAS statistical software. $P < 0.05$ was considered significant.

RESULTS

Characteristics of the study patients are presented in Table 1. In age, ethnicity, and duration of ESRD, the subjects were similar to our entire population of chronic PD patients. Mean serum albumin was low, but typical of our chronic PD patients. Ten subjects had residual kidney function (>200 mL/day) during some of the time of the study, reflected in 30 collections. Many subjects lost residual function over months of observation. Eleven subjects were treated with rhGH during part or all of their study period for a total of 55 collections during rhGH therapy. Mean delivered dialysis dose by Kt/V_{urea} was >2.1.

The results of UNA, TNA, NUNA, PNA, NPNA, and PNPNA for 132 dialysate and urine collections (in those patients with residual urine output) are shown in Table 2, expressed both as absolute daily excretion and normalized to body weight. Data are shown for the entire study group and are then stratified by age group. Our subjects are also compared with adults previously reported by Bergström et al [18]; adult values have been divided by reported patient weight to permit comparison with pediatric subjects. While absolute UNA and TNA (g/day) in children are lower than values reported for adults, once normalized to body weight (mg/kg/day), UNA and TNA for the entire pediatric study population did not differ significantly from adult values. However, a comparison of each pediatric age subgroup with Bergström et al's data did yield significant differences in TNA and NPNA for some groups (Table 2). In addition, the presence of residual kidney function in children was associated with higher TNA [172 ± 44, 173 (range 67 to 271) vs. 155 ± 53, 144 (74 to 328) mg/kg/day, $P = 0.02$ by Mann–Whitney] and UNA [112 ± 35, 111(29 to 193) vs. 101 ± 43, 88 (40 to 265) mg/kg/day, $P = 0.02$], while therapy with rhGH did not affect TNA or UNA.

Nonurea nitrogen appearance in children [56 ± 24, 51 (10 to 208) mg/kg/day] was greater than that previously reported by Maroni, Steinman, and Mitch for adults [31 ± 12, 31 (10 to 59) mg/kg/day, $P < 0.001$] and also varied by age as shown in Table 2 [14]. NUNA in the youngest subjects was significantly greater than that seen in the subjects ages [11–15]. In subjects who still had residual renal function, NUNA was not different from that seen in subjects without continued urine output. However, NUNA was significantly greater in subjects

Table 2. *Continued*

	PNA *g/day*	NPNA *g/day*	NPNA *mg/kg/day*	PNPNA *g/day*	PNPNA *g/kg/day*
All subjects	29.25 ± 11.63	4.05 ± 1.71	137 ± 49	25.28 ± 10.70	0.85 ± 0.30
	31.30, 3.93–60.24	4.2, 0.44–8.78	127, 43–306[j]	26.26, 2.73–54.87	0.79, 0.27–1.91
Age 0–5 years	14.31 ± 7.75	1.88 ± 1.11	144 ± 68	11.75 ± 6.92	0.90 ± 0.42
	13.48, 3.93–34.88[f,i]	1.70, 0.44–4.82[f,i]	124, 43–306[e,g,j]	10.6, 2.73–30.12[f,i]	0.76, 0.27–1.91[e,g]
Age 6–10	31.39 ± 8.01	4.45 ± 1.19	172 ± 30	27.8 ± 7.41	1.08 ± 0.19
	34.19, 17.48–44.82[c,g]	4.69, 2.46–6.48[c,g]	169, 127–231[b,i,j]	29.31, 15.37–40.50[c,g]	1.06, 0.79–1.45[b,i]
Age 11–15 years	33.08 ± 9.76	4.58 ± 1.46	126 ± 41	8.629 ± 9.14	0.78 ± 0.25
	34.07, 11.02–60.24[c,d]	4.65, 1.52–8.78[c,d]	119, 68–250[a,f,k]	29.04, 9.50–54.87[c,d]	0.74, 0.42–1.56[a,f]

Data are shown as mean ± SD, median and range.
Comparison with ages 0–5: [a]P = not significant; [b]$P < 0.05$; [c]$P < 0.001$, by nonparametric ANOVA, Kruskal-Wallis test
Comparison with ages 6–10: [d]P = not significant; [e]$P < 0.05$; [f]$P < 0.001$
Comparison with ages 11–15: [g]P = not significant; [h]$P < 0.05$; [i]$P < 0.001$
Comparison to data of Bergström et al [18], [j]P = not significant, [k]$P < 0.05$
Comparison to data of Maroni et al [14], 31 mg/kg/day, [l]$P < 0.001$

Table 3. Comparisons of dietary intake, serum albumin and dialysis dose

Age	Energy intake *kcal/kg/day*	Energy intake *kcal/kg IBW/day*	Protein intake *g/kg/day*	Protein intake *g/kg IBW/day*	Serum albumin *g/dL*	Measured total Kt/V_{urea}
0–5 years	84 ± 36	86 ± 33	2.55 ± 1.19	2.62 ± 1.14	3.0 ± 0.6	2.35 ± 0.82
	69, 45–154[d,i]	74, 50–154[f,i]	2.30, 0.91–4.84[d,h]	2.56, 0.99–4.84[d,g]	2.9, 1.9–4.0[f,g]	2.15, 1.37–4.26[d,g]
6–10 years	56 ± 14	52 ± 17	2.06 ± 0.45	1.88 ± 0.46	3.8 ± 0.3	2.57 ± 0.52
	56, 35–82[a,g]	53, 31–82[c,g]	2.21, 1.31–2.78[a,g]	1.81, 1.14–2.78[a,g]	3.9, 2.8–4.6[c,i]	2.67, 1.81–3.51[a,i]
11–15 years	46 ± 20	51 ± 20	1.77 ± 0.8	1.98 ± 0.75	3.2 ± 0.6	2.08 ± 0.49
	44, 12–102[c,d]	45, 22–113[c,d]	1.69, 0.54–4.06[b,d]	1.79, 0.68–4.30[a,d]	3.25, 1.7–4.4[a,f]	2.00, 1.13–3.50[a,f]

Data shown as mean ± SD, median and range.
Comparison with ages 0–5: [a]P = not significant; [b]$P < 0.05$; [c]$P < 0.01$, by nonparametric ANOVA, Kruskal-Wallis test
Comparison with ages 6–10: [d]P = not significant; [e]$P < 0.05$; [f]$P < 0.01$
Comparison with ages 11–15: [g]P = not significant; [h]$P < 0.05$; [i]$P < 0.01$

treated with rhGH than in subjects not so treated [59 ± 14, 59 (34 to 95) vs. 54 ± 28, 48 (10 to 208) mg/kg/day, $P = 0.0016$]. On average, 64 ± 11% of total nitrogen output and 75 ± 10% of nonprotein nitrogen are excreted as urea in this pediatric population.

Self-reported, measured dietary intake of energy and protein is shown in Table 3 and is stratified by age. Results are normalized to actual body weight and ideal body weight (IBW) to correct for subjects who were significantly underweight or overweight. Energy intake was greater in the youngest subjects (age 0 to 5) than in the oldest age group (11 to 15, $P < 0.01$). Protein intake was greater in the youngest subjects when compared with the oldest subjects ($P < 0.05$), but that difference became insignificant when weight was corrected to IBW. Measured dialysis delivery (Kt/V_{urea}) and serum albumin were greater in the subjects aged 6 to 10 than in those aged 11 to 15; however, dietary protein intake was not different. Protein and energy intakes were significantly greater in subjects treated with rhGH when compared with subjects who did not receive the therapy [2.15 ± 0.77, 2.21 (0.82 to 4.16) vs. 1.60 ± 0.86, 1.66 (0.54 to 4.84) g/kg/day and 57 ± 20, 53 (25 to 131) vs. 46 ± 30, 40 (12 to 154) kcal/kg/day, $P < 0.001$]. This difference was maintained even when dietary intake was scaled to IBW.

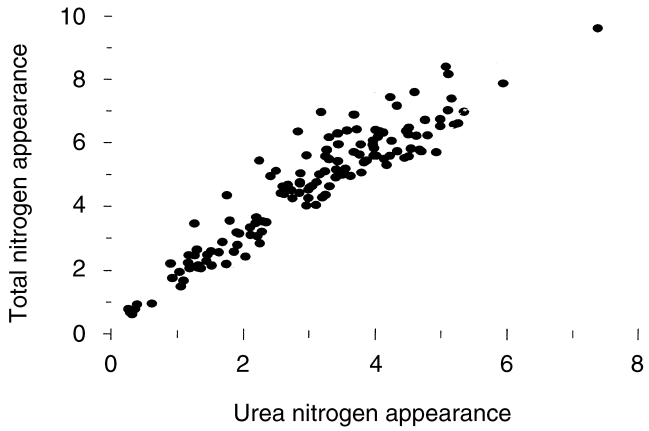

Fig. 1. Relationship of the total nitrogen appearance (TNA; g/day) and urea nitrogen appearance (UNA; g/day) is TNA = 1.26 (UNA) + 0.83.

The relationship of UNA and TNA is demonstrated in Figure 1. TNA was closely correlated with UNA in 132 paired measurements with TNA (g/day) = 1.26 (UNA) + 0.83, with $r^2 = 0.88$ and $P < 0.0001$. The relationship between UNA and TNA was compared to two previously published adult series in Figure 2. The

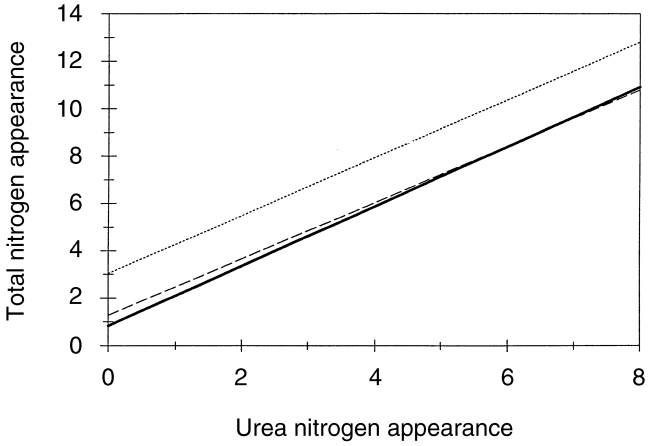

Fig. 2. Comparison of relationship of TNA and UNA in pediatric subjects with published formulae for adults. Symbols are: (——) pediatric data set; (- - -) Kopple et al [16]; (· · ·) Bergström et al [18].

relationship defined in our subjects was similar to those obtained by Kopple, Gao, and Qing [16] and Bergström et al [18]. In each case, the slope of the defined lines fell within the 95% CI of our data, but the intercept was significantly different. Furthermore, the relationship between TNA and UNA did not vary significantly with the use of rhGH or the presence of residual kidney function in our study population.

In our pediatric study population, TNA could be even more precisely predicted from UNA when normalized to body weight [TNA = 1.07 (UNA) + 0.023 (weight in kg) + 0.67, $r^2 = 0.90$ and $P < 0.0001$]. This relationship could be further refined by incorporating age into the analysis, which allowed us to define age-specific constants [TNA = 1.03 (UNA) + 0.02 (weight) + 0.56 (for subjects age 0 to 5) or 0.98 (for subjects age 11 to 15 or 6 to 10), $r^2 = 0.91$]. The constant for subjects age 0 to 5 (0.56) was significantly different from that for the older subjects (0.98) by the Bonferroni (Dunn) *t*-test.

The dietary protein intake (DPI) of stable pediatric patients can be estimated from the PNA. From UNA, PNA for this population can be calculated as follows: PNA (g/day) = 6.69 (UNA) + 0.14 (wt) + 4.19.

Nonprotein nitrogen appearance may be a more useful measure of nitrogen output and allow a more meaningful estimate of protein intake, since it avoids the confounding effect of dialysate and urine protein losses. As expected, NPNA also closely correlated with UNA (with NPNA = 1.18 (UNA) + 0.45, $r^2 = 0.90$, $P < 0.0001$). When normalized to body mass, the relationship became NPNA = 1.04 (UNA) + 0.018 (weight) + 0.33, $r^2 = 0.92$ and $P < 0.0001$. The relationship between NPNA and UNA did not vary significantly with the use of rhGH or the presence of residual kidney function.

DISCUSSION

In this study, we sought to define a relationship between measures of nitrogen excretion (UNA, TNA, and NPNA) in pediatric PD patients. Furthermore, our large data set and wide age range allowed us to compare markers of protein metabolism between different age groups and published adult values. Significant differences in UNA, TNA, NUNA, PNA, NPNA, and PNPNA were demonstrated that define norms of nitrogen excretion for these age groups. Differences noted between UNA and TNA in our subjects and previously reported values from adult studies should be interpreted cautiously, as dietary intakes appear to have differed importantly and there are methodologic differences in study design and sample collection.

Nonurea nitrogen excretion in children receiving PD was significantly greater than that reported by Maroni, Steinman, and Mitch and varied with age and with rhGH therapy [14]. This result is all the more striking in that we did not account for fecal nitrogen as Maroni, Steinman, and Mitch did; we expect that the difference would have been even greater had fecal nitrogen been included. The larger NUNA in young children (and even more so in those receiving rhGH) when compared with Maroni, Steinman, and Mitch's adult subjects may represent a developmental alteration in urea metabolism, which is unique to growing children.

When the effects of rhGH and residual kidney function were assessed on markers of protein metabolism, we found that subjects with residual renal function excreted more nitrogen, whether measured as UNA or TNA. NUNA was not affected by residual urine output. It is possible the increased nitrogen excretion reflects a slightly higher nitrogen intake in those subjects with residual renal function, although the difference in DPI was not detected by diet history. This would be consistent with data from Caravaca, Arrobas, and Dominguez [28]. Growth hormone therapy did not change total nitrogen excretion, although a larger amount was excreted as nonurea nitrogen.

When normalized to body mass, children in our study ate more protein than adults in previously published series [16, 18]. Subjects attained their age-specific goal for dietary protein intake, but the younger subjects were often below their goal for dietary energy intake despite the use of supplemental nasogastric feeding. Subjects ages 6 to 10 had the highest Kt/V_{urea} and serum albumin values. However, this could not be directly related to improved dietary intake of protein; the DPI for this age group was not significantly different from the other subjects, and all children had adequate DPI and Kt/V_{urea}.

Subjects treated with growth hormone had significantly greater DPI, although no greater nitrogen excretion. This implied difference in dietary nitrogen utiliza-

tion suggests an anabolic state from rhGH therapy, but the current study design does not permit a firm conclusion.

One hundred thirty-two simultaneous measurements of nitrogen and urea allowed us to conclude that urea nitrogen excretion in dialysate and urine can be used to predict dialysate and urine total nitrogen excretion in pediatric patients in clinical situations where actual measurement of nitrogen is impractical. We have defined a reliable relationship between UNA and TNA and body mass in this population. Furthermore, we have stratified our results by subject age and demonstrated that the constant (*y* intercept) of the equation relating UNA and TNA is age dependent, implying a fixed difference in nitrogen excretion in subjects age five and under. The relationship does not vary with residual renal function or rhGH therapy.

The relationship defined between UNA and TNA was compared with those defined by Kopple et al [16] and Bergström et al [18] in adult subjects. In each case, the slope of the relationship fell within the 95% confidence interval of our data, but the *y* intercept (constant) was significantly different. When our data were adjusted for body mass (allowing for the wide range of body habitus typical of pediatric populations), we again found that the *y* intercept was age dependent and was significantly different for children aged five or less. We hypothesize that among chronic PD patients, there are fixed nitrogen losses that vary with patient age across the spectrum from infancy to adulthood.

Nonetheless, the similarity in the slope of the relationship of UNA and TNA across the full spectrum of age is reassuring, providing evidence of the constancy of markers of protein metabolism. Based on this similarity, one can be more confident in applying principles of dietary assessment from nitrogen appearance, which have been derived in adults with ESRD, to pediatric patients as well. There are significant methodologic differences between our study and those of Kopple et al [16] and Bergström et al [18]. Our pediatric subjects could not be confined to the clinical research center for 24.8 ± 9.5 days, as in the former study, or 8 to 17 days, as in the latter. Thus, formal nitrogen balance studies could not be performed, and while dietary guidance and instructions were given regularly, subjects ingested their usual diet during all dialysate and urine collection periods. As such, our study provides a more realistic assessment of typical nitrogen excretion, yet we are limited in our ability to correlate nitrogen excretion with actual protein ingested.

The assumption that nitrogen appearance is an accurate reflection of nitrogen intake depends on subjects remaining in approximate nitrogen balance; in stable outpatients, net daily accretion of nitrogen is relatively small compared with dietary protein intake and total nitrogen output. This assumption is invalid in highly catabolic patients (for example in septic acute renal failure) in whom nitrogen appearance may exceed protein intake, and likewise may be invalid in the setting of rapid anabolism where nitrogen accretion may represent a greater fraction of dietary nitrogen intake. We have assumed that even in growing children, daily nitrogen accretion is small enough so that over a 24-hour observation period, it will not invalidate an assumption regarding urea and TNA. The effect of anabolism may be more significant in our subjects treated with rhGH, even though they were all studied after they had stabilized on therapy for at least one month.

In summary, we have defined a relationship between nitrogen output and urea nitrogen excretion in children receiving chronic PD that differs importantly from that defined for adults. This should prove useful for future studies of kinetic modeling and adequacy of pediatric PD. As well, it may provide a clinically useful tool to allow an estimation of dietary protein intake; with it, one should be able to identify and address inadequate dietary intake early, rather than waiting for the insidious development of malnutrition or growth failure.

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APPENDIX

Formulae for calculations

TNA (g/day) = dialysate nitrogen (g/day) + urine nitrogen (g/day)
UNA (g/day) = dialysate urea (g/day) + urine urea (g/day)
For anuric patients, urine nitrogen and urine urea = 0
NUNA (g/day) = TNA − UNA
NPNA (g/day) = TNA − [dialysate protein (g/day + urine protein (g/day)]/6.25
For anuric patients urine protein = 0
PNA (g/day) = 6.25(TNA)
PNPNA (g/day) = 6.25(NPNA)
PNPNA (g/kg/day) = 6.25(NPNA)/weight in kg

Representative calculation

A three-year-old (11.2 kg) male with ESRD secondary to obstructive uropathy who maintains urine output through chronic PD grows slowly over several months. Dietary protein prescription is 2 to 2.5 g/kg/day, while dietary records from home suggest protein intake of 40 to 50 g/day.

Dialysate urea = 0.91 g/day
Urine urea = 0.6 g/day

UNA = 1.51 g/day
Dialysate nitrogen = 1.43 g/day
Urine nitrogen = 0.73 g/day
Estimated TNA [1.03(1.51) + 0.02(11.2) + 0.56] = 2.34 g/day
Measured TNA = 2.16 g/day
PNA from estimated TNA = 14.6 g/day
PNA from measured TNA = 13.5 g/day
Dialysate protein = 1.72 g/day
Urine protein = 0.02 g/day
NPNA = 1.88 g/day
PNPNA = 11.8 g/day

Results of dialysate and urine collection reveal a likely etiology for growth failure. Although parents report a large dietary intake, total nitrogen excretion and urea excretion data suggest inadequate protein ingestion. Both measured and estimated PNA suggest dietary protein intake only slightly greater than 1 g/kg/day. PNPNA suggests even lower intake when the confounding effects of dialysate and urinary protein losses are removed. Dietary supplementation may be required to improve intake. These calculations are insufficiently precise for nitrogen balance studies, but provide an approximation that can be utilized in clinical settings.

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