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Creatinine clearance following cimetidine for estimation of glomerular filtration rate

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Abstract. Simultaneous inulin (C_{in}) and creatinine clearance (C_{Cr}) studies were performed on 53 pediatric renal patients using a cimetidine protocol. Since cimetidine blocks the tubular secretion of creatinine, it was hypothesized that C_{Cr} measured following cimetidine would closely approximate the C_{in}. C_{in} was compared with C_{Cr} with the latter calculated from: (1) a 24-h urine collection, (2) plasma creatinine, height, and a proportionality constant, (3) the same plasma and urine specimens used for calculating C_{in}, and (4) from the plasma and urine specimens of the four 30-min clearance periods treated as a single 2-h clearance. The C_{in} was very closely approximated by the C_{Cr} calculated from the same specimens used for the C_{in} and by the 2-h clearance. The cimetidine protocol, with C_{Cr} derived from a 2-h urine collection obtained under supervision in the office or clinic, provides a convenient and inexpensive procedure for estimation of glomerular filtration rate in a clinical setting.

Key words: Inulin clearance – Creatinine clearance – Cimetidine – Glomerular filtration rate

Introduction

The level of glomerular filtration rate (GFR) is followed closely in seriously ill patients because of the importance of renal function in fluid balance and in the excretion of antibiotics and chemotherapeutic agents. In addition, GFR is the accepted parameter for monitoring renal function in urinary tract and kidney disorders, and for evaluating the effect of interventions. In clinical practice GFR is usually monitored using serum or plasma creatinine concentrations ([Cr]s or [Cr]p) or creatinine clearance (C_{Cr}), although numerous studies have documented the inaccuracy of these estimates [1–8]. The failure of C_{Cr} to closely approximate inulin clearance (C_{in}), the gold standard for GFR, is primarily a result of the tubular secretion of Cr. The disparity between C_{in} and C_{Cr} increases as GFR decreases.

A number of reports in adult patients and our studies in children have shown that C_{Cr} closely approximates GFR when the tubular secretion of Cr is inhibited by cimetidine [2, 9–19]. A variety of protocols have been employed in which cimetidine has been administered either as a single dose or over 1 to several days to inhibit the tubular secretion of Cr. The present report describes the results of the use of a cimetidine protocol for estimation of GFR in clinically stable pediatric renal patients. A relatively convenient and inexpensive procedure is described in which a 2-h C_{Cr} in patients pre-treated with cimetidine is shown to closely approximate C_{in}.

Patients and methods

Study patients

Children followed in the Children's Kidney Center at The Children's Mercy Hospital participated in this study. The sex, age, and diagnosis of the 53 children are shown in Table 1. The study protocol was approved by the University of Missouri at Kansas City Health Sciences Pediatric Institutional Review Board. Informed consent was obtained before a child was studied.

Cimetidine protocol

The cimetidine was administered orally using a modification of the regimen described by Hildbrands et al. [12]. This approach was followed since it allows for re-equilibration of Cr in the body subsequent to the rise in serum Cr concentration after administration of cimetidine. Patients with a C_{Cr} >75 ml/min per 1.73 m^2 (measured or calculated from [Cr]p) received a daily cimetidine dose of 20 mg/kg to a maximum of 1,600 mg. The daily dose was reduced to 80% for those with a C_{Cr} of 50–75 ml/min per 1.73 m^2, to 70% for a C_{Cr} of 30–50 ml/min per 1.73 m^2, to 60% for a C_{Cr} of 20–30 ml/min per 1.73 m^2, and to 50% for a C_{Cr} <20 ml/min per 1.73 m^2. Half of the daily dose of

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Table 1. Description of the study group

53 children	24 F, 29 M
Age	12.9 ± 3.9 years (4.6–20.6 years)
Diagnoses	
Reflux nephropathy	15
IgA nephropathy	7
Alport syndrome	3
Interstitial nephritis	3
Focal segmental glomerulosclerosis	5
Solitary kidney	5[b]
Henoch-Schönlein purpura nephritis	2
Neurogenic bladder	2
S/P kidney transplant	2
Hematuria	2
Posterior urethral valves	2
Other (1 each)[a]	5

F, Female; M, male; S/P, status post

[a] Ureteropelvic junction obstruction, membranoproliferative glomerulonephritis, hemolytic uremic syndrome, membranous nephropathy, urolithiasis

[b] One child had a solitary kidney and neurogenic bladder, but is listed only as a solitary kidney patient

cimetidine was administered at roughly 12-h intervals with a total of five doses. Typically, the first dose was administered at about 8:00 a.m. on Saturday and the last dose on the following Monday at about 8:00 a.m. The patients received the last dose of cimetidine in the infusion room of The Children's Kidney Center just prior to starting simultaneous C_{in} and C_{Cr} studies. During the 24 h preceding these studies, from Sunday morning until Monday morning, the children were on a diet free of meat, fish, and fowl (i.e., free of preformed Cr and Cr precursors). The children were asked to bring in a timed urine collection obtained during this period.

Clearance studies

Upon arrival at the Children's Kidney Center, the timed urine collection was completed if this was not done earlier, a heparin lock was inserted in one arm vein, and a baseline blood sample obtained for [Cr]p. An intravenous line was then inserted in the other arm and the priming dose of inulin (60 mg/kg) at a concentration of 100 mg/ml was infused over approximately 10 min. This dose was designed to bring the concentration of inulin to approximately 30 mg/dl in the extracellular fluid. Infusion of a sustaining inulin solution at a rate of 0.5 ml/min using a calibrated pump was then begun. The sustaining solution was prepared by adding the stock inulin (100 mg/ml) to half isotonic sodium chloride to yield a concentration estimated to deliver inulin at a rate equal to the rate of excretion of inulin. This was calculated using a plasma inulin of 30 mg/dl and the most recent C_{Cr}. Fluid intake during the clearance study consisted of water and other fluids free of caffeine, glucose, and fructose. During the 1st h, a fluid intake of 7.0–8.0 ml/kg was encouraged. After an hour, the patient was asked to void and the urine volume was measured. During the next and subsequent hours of the study, fluid intake was set to be approximately equal to the urine volume during the preceding hour.

The patients remained at rest in a recliner chair during the study, except for urine collections. Complete bladder emptying was urged, using a double voiding technique. Two of the children with neurogenic bladders used suprapubic pressure and Valsalva maneuvers to accomplish bladder emptying and 1, the child with a solitary kidney, used catheterization. After 2 h of equilibration, the patients emptied their urinary bladders as completely as possible and a blood sample was obtained. Four clearance periods of roughly 30 min each followed, with the time of each urine collection recorded accurately. A blood sample was obtained immediately after each timed urine specimen was collected.

Cr assay

Serum and urine Cr concentrations were measured using the Jaffe rate method. A Beckman Creatinine Analyzer was used during the first 18 months of the study (20 patients). Subsequently, serum and urine Cr concentrations were measured with a kinetic adaptation of the Jaffe method using a Gilford Impact 400E automated chemistry analyzer. All samples were analyzed three times. Control and assayed human serum (Sera Chem 1 and 2 and a 1:1 dilution of level 1, Fisher Scientific, Orangeburg, Calif., USA) were analyzed along with each plasma sample; urinary specimens were diluted 1:10 and assayed with urine controls (Lyphochek 1 and 2, Bio-Rad, Anaheim, Calif., USA). Over a 12-month period, reproducibility data for serum Cr were as follows: SeraChem 1 = 70.7 ± 1.8 μmol/l (0.80 ± 0.02 mg/dl), coefficient of variation (CV) = 2.5%; SeraChem 1, 1:1 dilution = 35.4 ± 0.9 μmol/l (0.40 ± 0.01 mg/dl) CV = 2.5%, SeraChem 2 = 541.0 μmol/l (6.10 ± 0.09 mg/dl), CV = 1.5%. The reproducibility for urine controls over 12 months was: Lyphochek 1 = 7,602.4 ± 88.4 μmol/l (86.0 ± 1.0 mg/dl), CV = 1.2%; Lyphochek 2 = 21,286.7 ± 159.1 μmol/l (240.8+1.8 mg/dl), CV = 0.7%.

Inulin assay

An automated enzymatic method was used for measuring plasma and urine inulin concentrations. Along with each urine sample hydrolyzed, a corresponding blank was analyzed using a reagent identical to the hydrolyzing reagent except for the omission of the inulinase. Inulin recovery and within-run variation were determined by measuring 11 replicate inulin-supplemented plasma and urine samples once weekly for 4 weeks [20]. The inulin concentrations in the supplemented plasma and urine were 30 mg/dl and 150 mg/dl, respectively. The average analytical recovery in plasma was 99.4% with a CV of 2.7%. The average recovery in urine was 98.4% with a CV of 1.7%. The reproducibility of plasma inulin determined using control specimens of 25 mg/dl and 40 mg/dl over 6 months (n = 24) showed a CV of 2.0% and 1.3%, respectively. The reproducibility study of a control urine specimen with an inulin concentration of 100 mg/dl over a 6-month period (n = 24) revealed a CV of 3.4% and the CV of a 150 mg/dl specimen over a 2-month period was 1.4% (n = 8).

Data analysis

Inulin clearance. Each subject had four clearance periods of approximately 30 min. The requirements for including a clearance period for estimation of C_{in} were that the plasma inulin immediately before and following a clearance interval varied by ≤1.0 mg/dl (an indication of constancy of the concentration of inulin in extracellular fluid) and that the rate of inulin excretion (mg/1.73 m^2 per min) varied by <10% between the clearance periods (indicating consistency of urine collection during the periods). Using the spontaneous voiding method for urine collection, a CV of about 10% is expected for the clearance periods within a single study [21]. Using the criteria described, C_{in} was derived from four clearance periods in 18 studies, three clearance periods in 22 instances, and two clearance periods in 13 instances. (All clearance data are presented as ml/min per 1.73 m^2.)

Creatinine clearance was calculated from four sets of data.

1. C_{Cr} with simultaneus [C_{cr} (cC_{in})]: C_{Cr} was calculated from [Cr]p and urinary Cr excretion rates using the plasma and urine samples obtained in each period accepted for measurement of C_{in}. The C_{in} and C_{Cr} were calculated using the mean plasma concentrations of inulin and Cr and the total urinary excretion of each substance divided by the total time of the clearance periods used.
2. Two-hour C_{Cr} (2-h C_{Cr}): C_{Cr} was calculated by treating the four 30-min clearance periods as a single clearance. The [Cr]p used was the mean of the five plasma samples measured for the clearance periods,

Table 2. Inulin clearance (C_{in}) compared with creatinine clearance (C_{Cr}) following cimetidine

Regression equations	r
C_{Cr} with simultaneous C_{in}[a]	
C_{in} = 0.93 [C_{Cr}(cC_{in})]+4.4	0.98
2-hC_{Cr}[b]	
C_{in} = 0.90 (C_{Cr}2-h)+6.4	0.96
24-hC_{Cr}[c]	
C_{in} = 0.85 (C_{Cr}24-h)+4.9	0.86
Calculated C_{Cr}[d]	
C_{in} = 0.89 (CalcC_{Cr})+7.7	0.90

[a] C_{Cr} with simultaneous C_{in} = C_{Cr} calculated from plasma Cr ([Cr]p) and urinary Cr using the same plasma and urine samples used for calculating C_{in}

[b] 2-hC_{Cr} = C_{Cr} calculated using the [Cr]p and urinary Cr excretion from all four clearance periods as one 2-h C_{Cr}

[c] 24-hC_{Cr} = C_{Cr} calculated from the baseline [Cr]p and the timed urine collection of the preceding 24-h

[d] Calculated C_{Cr} = C_{Cr} calculated from the baseline [Cr]p and height in cm (L) using the equation CalcC_{Cr} = kL/[Cr]p

and the urinary excretion rate of the Cr the sum of the four periods divided by the total time of those periods.

3. Twenty-four-hour C_{Cr} (24-hC_{Cr}): this calculation was based on the timed urine collection obtained during the 24 h preceding the C_{in} study with the child on a diet free of Cr and Cr precursors and the [Cr]p of the baseline blood specimen.

4. Calculated C_{Cr} (CalcC_{Cr}): CalcC_{Cr} = kL/[Cr]p, where L is height in centimeters and k is the proportionality constant [22]. The value for k was calculated for girls and boys with Tanner stage 3 or less sexual maturation and for boys Tanner stage 4 or greater using the equation k = (C_{in})[Cr]p/L. The values for k, a proportionality constant, were derived from data from our laboratory, since earlier studies showed differences from the values published by Schwartz [23]. As pointed out by Schwartz [24], it is necessary to determine k in one's own laboratory before applying it as a screening tool for estimation of C_{Cr}. The [Cr]p measured in the baseline blood specimen and height (L) measured at the time of the clearance studies were used. The k value derived from study of 38 girls and boys with sexual maturation of Tanner stage 3 or less was 0.50 ± 0.07 and that derived from 14 boys with sexual maturation Tanner stage 4 or greater was 0.60 ± 0.10. The data of 2 boys were omitted, 1 because of marked obesity and short stature and the other because the k value of 0.99 was an outlier.

Statistical methods. Each of the four data sets used for measurement of C_{Cr} following cimetidine were compared with C_{in} as follows:

(1) regression equations and correlation coefficients were obtained and regression lines plotted along with the line of identity (Table 2, Fig. 1, 2); (2) the means (±SD) for C_{in} and the measured and calculated C_{Cr} are shown in Table 3 along with the ratios of C_{Cr}/C_{in}, mean differences, and 95% confidence interval; (3) the C_{Cr} derived from the four data sets were compared with C_{in} by plotting the difference between the C_{in} and C_{Cr} against the C_{in}; the mean difference between the two clearance measurements and a value equal to the mean plus or minus twice the standard deviation (d ± 2 SD) were plotted as horizontal lines (as shown in Figs. 3a–d); the agreement between the two clearance methods is assessed by examining both the mean difference line and the distribution of data points in relation to ±2 SD from the mean over the range of clearance values; this is a modification of the graphical technique of Bland and Altman [25, 26] for assessment of agreement between two methods of measurement.

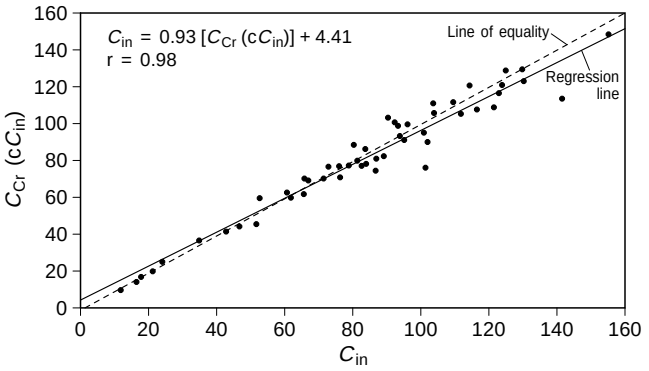

Fig. 1. The inulin clearance (C_{in}) versus the simultaneous creatinine clearance C_{Cr}(cC_{in}): the clearance was measured simultaneously using the same plasma and urine samples

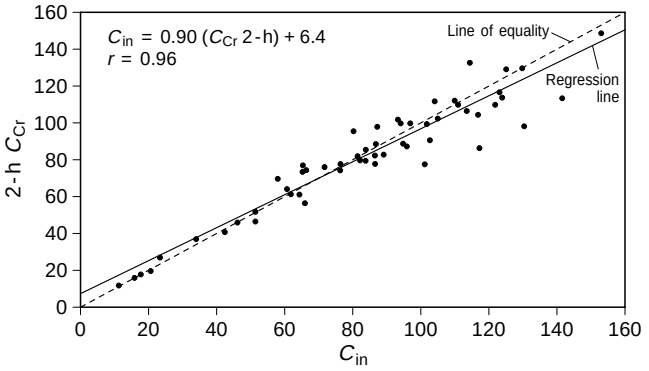

Fig. 2. The C_{in} versus 2-hC_{Cr}: the C_{Cr} claculated using the four 30-min clearance periods as a single 2-h clearance

Results

Table 2 shows the linear regression equations with the C_{in} as the independent variable and the four methods of measuring C_{Cr} as dependent variables. The correlation coefficients were 0.98 for the regression of C_{in} with C_{Cr}(cC_{in}), 0.96 for regression with 2-hC_{Cr}, 0.86 for regression with 24-hC_{Cr}, and 0.90 for regression with the CalcC_{Cr}. Figures 1 and 2 show the regression of C_{in} with C_{Cr}(cC_{in}) and 2-hC_{Cr}. Although the correlation coefficient measures the strength of a relationship between two variables, not agreement between them, when points lie close to the line of equality, as in Figs. 1 and 2, there is good agreement between two methods of measurement [26].

Table 3 shows that the mean differences between C_{in} and C_{Cr}(cCin) and 2-h C_{Cr} are similar at 1.1 ± 7.3 and 1.5 ± 9.4 ml/min per 1.73 m², respectively. The mean difference between C_{in} and CalcC_{Cr} is also small at 1.3 ml/min per 1.73 m², but the large SD of ±15.3 ml/min per 1.73 m² indicates that CalcC_{Cr} does not closely approximate the C_{in}. The 24-hC_{Cr} shows both a large mean difference and SD from the C_{in} (7.0 ± 17.8 ml/min per 1.73 m²). The ratios of C_{Cr}/C_{in} following cimetidine for the four methods of estimation of C_{Cr} are presented in Table 3. The ratio of C_{Cr}(cC_{in})/C$_{in}$ was 0.99 ± 0.08 and that of 2-h C_{Cr}/C_{in} 1.00 ± 0.10. The ratios of the CalcC_{Cr}/C_{in} and the 24-hC_{Cr}/

Table 3. C_{in} compared with C_{Cr} following cimetidine

Method	*n*	Clearance (ml/min per 1.73 m²)	Mean difference ($C_{in}-C_{Cr}$) (ml/min per 1.73 m²)	95% CI Paired *t*-test (ml/min per 1.73 m²)	C_{Cr}/C_{in} (ratio)
C_{in}	53	83.1 ± 33.6			
$C_{Cr}(cC_{in})$[a]	53	82.0 ± 32.1	1.1 ± 7.3	–0.9 to 3.1	0.99 ± 0.08
2-hC_{Cr}[b]	53	81.4 ± 31.6	1.5 ± 9.4	–1.1 to 4.1	1.00 ± 0.10
CalcC_{Cr}[c]	53	81.8 ± 33.5	1.3 ± 15.3	–2.9 to 5.5	1.01 ± 0.18
C_{in}	22	81.5 ± 33.1			
24-hC_{Cr}[d]	22	74.6 ± 33.1	7.0 ± 17.8	–9 to 14.9	0.95 ± 0.26

CI, Confidence interval

[a] $C_{Cr}(cC_{in})$ = C_{Cr} calculated using the [Cr]p and urinary Cr excretion using the same plasma and urine samples used for calculating C_{in}

[b] 2-hC_{Cr} = C_{Cr} calculated using the [Cr]p and urinary Cr excretion from all four clearance periods as one 2-hC_{Cr}

[c] CalcC_{Cr} = Cr calculated from the baseline [Cr]p and height in cm (L) using the equation CalcC_{Cr} = kL[Cr]p

[d] 24-hC_{Cr} = (22 subjects provided timed urine collections) calculated from the baseline [Cr]p and the timed urine collection of the preceding 24 h C_{Cr}

C_{in} were 1.01 ± 0.18 and 0.95 ± 0.26, respectively. The ratio of $C_{Cr}(cC_{in})$ and 2-hC_{Cr}/C_{in} are not significantly different from each other nor from 1.00.

Figure 3 compares the four different methods of estimating C_{in} from C_{Cr} following cimetidine using a modification of the graphical technique of Bland and Altman [25, 26]. Perusal of these graphs show that the $C_{Cr}(cC_{in})$ and the 2-hC_{Cr} give close approximations of C_{in} with relatively little scatter in the data points. This method of presentation of the comparison of the C_{in} with the clearance derived using Cr permits direct evaluation of the deviation of the predicted clearance over the entire range of GFR. The deviation of C_{Cr} from the reference standard, C_{in}, at a particular clearance level cannot be appreciated by consideration only of the mean difference for the entire range of values.

Discussion

Figure 1 shows the very close correlation between C_{in} and C_{Cr} employing the cimetidine protocol when the two clearances are measured simultaneously. The regression line for the C_{in} versus $C_{Cr}(cC_{in})$ is almost superimposed on the line of the identity. The ratio of C_{Cr}/C_{in} of 0.99 ± 0.08 (Table 2) and the relatively small deviation of the $C_{Cr}(cC_{in})$ from C_{in} (Fig. 3a) show that the inhibition of the tubular secretion of Cr with cimetidine results in C_{Cr} which closely approximates C_{in} with GFR ranging from 11 to 120 ml/min per 1.73 m². This being established, we addressed the question of the most accurate and suitable method of measurement of C_{Cr} following cimetidine for estimation GFR in a clinical setting.

Although there is good correlation of C_{in} with CalcC_{Cr} (r = 0.99), the calculated clearance is a poor predictor of C_{in}, as indicated by the large SD of the ratio of the CalcC_{Cr}/C_{in} (1.01 ± 0.18) and of the mean difference between the

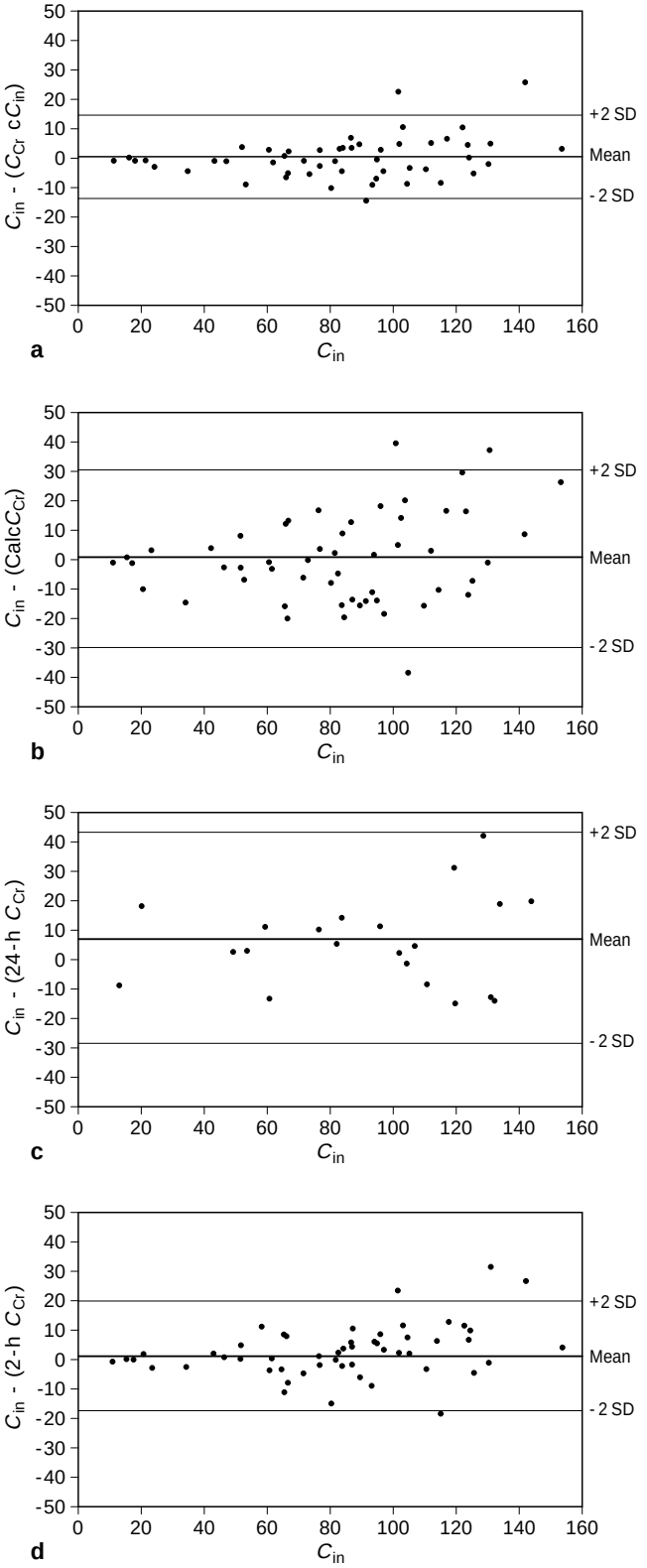

Fig. 3. Modified Bland-Altman graphical presentation. **a** The C_{in} versus $C_{Cr}(cC_{in})$. **b** The C_{in} versus CalcC_{Cr}. **c** The C_{in} versus 24-hC_{Cr}. C_{Cr} calculated from the baseline plasma Cr and the 24-h urine collection. **d** The C_{in} versus 2-hC_{Cr}. C_{Cr} calculated using the 2-h supervised urine collection

C_{in} and the CalcC_{Cr} (1.3 ± 15.3 ml/min per 1.73 m^2, Table 3). Perusal of the plot of the C_{in} versus C_{in} minus the CalcC_{Cr} shows that although the mean difference is only 1.3 ml/min per 1.73 m^2, the large SD of the mean difference results in deviations of the CalcC_{Cr} which are frequently larger than 10% of the GFR as measured by C_{in} (Fig. 3b).

Twenty-two of the children brought in timed urine collections obtained during the 24-h period while taking cimetidine and on a diet free of preformed Cr and Cr precursors. The mean urine collection time was 1,236 ± 212 min. The problems of obtaining accurate timed urine collections in all patients, but especially in pediatric patients, are well recognized. Although highly motivated parents with cooperative children often bring in accurate urine collections, the usual experience is that "24-h" urine collections obtained at home are inaccurate. Although there was good correlation between C_{in} and 24-hC_{Cr} (r = 0.86), the regression line deviated markedly from the line of identity. There was a large mean deviation of the C_{in} from the 24-hC_{Cr} (7.0 ± 17.8 ml/min per 1.73 m^2) and the ratio of the 24-hC_{Cr}/C_{in} was 0.95 ± 0.29 (Table 3). The plot of the C_{in} versus the C_{in} minus 24-hC_{Cr} shows that the 24-hC_{Cr} is seldom within 10% of the GFR as measured by C_{in} (Fig. 3c).

C_{Cr} measured using urine collection during all four of the clearance periods yielded values very close to C_{in}. The correlation coefficient of C_{in} versus 2-hC_{Cr} was 0.96 and the regression line was almost superimposed on the line of identity (Fig. 2). The 2-hC_{Cr} differs from the C_{Cr}(cC_{in}), since in the latter only the clearance periods used for C_{in} were used to derive the data from simultaneous C_{in} and C_{Cr}. The 2-hC_{Cr} was calculated from urine collection and plasma Cr from all four clearance periods. The plot in Fig. 3d shows that the 2-hC_{Cr} provides a good approximation of the C_{in} over the range of GFR studied. A CV of about 10% is expected between sequential collection periods during C_{in} studies [21]. As shown in Fig. 3d, the estimate of C_{in} from 2-hC_{Cr} does not usually deviate from the C_{in} by as much as 10%. The 2-hC_{Cr}, with the urine collection obtained during close supervision, appears to be the best choice for accurate estimation of GFR in the usual clinical setting. A single blood specimen is satisfactory for determination of serum Cr. In only a single instance did 1 of the 5 [Cr]p samples obtained during the 2-h clearance period vary from the mean by more than 5% (patient no. 43: the [Cr]p values were 0.81, 0.79, 0.77, 0.78, and 0.70 mg/dl). The value of 0.70 deviated from the mean value of 0.77 mg/dl by 9%.

The 2-hC_{Cr} closely approximates the C_{in}, with the value of the latter ranging from 10 to 125 ml/min per 1.73 m^2 (Fig. 3d). The protocol described in this report using a 2-h supervised urine collection should be useful for estimation of GFR in pediatric patients with stable renal function. In the usual outpatient clinic or office setting, the supervised 2-h urine collection may be obtained in conjunction with a scheduled visit and thus result in relatively little excess time in the facility. In our experience most families appear to have had little problem adhering to the 48-h period of cimetidine administration, although we had a number of instances in which meat, fish, or fowl were accidentally ingested at some point during the 24 h preceding the clearance studies. It is possible that a diet free of meat, fish, and fowl on the evening prior to and the morning of the clearance studies might suffice to prevent changes in urinary Cr excretion rate and [Cr]p as a result of intake of Cr and Cr precursors, but we have no data to support this.

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Nutrient intake and blood pressure in the dietary intervention study in children

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Delineating the role that diet plays in blood pressure levels in children is important for guiding dietary recommendations for the prevention of hypertension. The purpose of this study was to investigate relationships between dietary nutrients and blood pressure in children. Data were analyzed from 662 participants in the Dietary Intervention Study in Children who had elevated low-density lipoprotein cholesterol and were aged 8 to 11 years at baseline. Three 24-hour dietary recalls, systolic pressure, diastolic pressure, height, and weight were obtained at baseline, 1 year, and 3 years. Nutrients analyzed were the micronutrients calcium, magnesium, and potassium; the macronutrients protein, carbohydrates, total fat, saturated fat, polyunsaturated fat, and monounsaturated fat; dietary cholesterol; and total dietary fiber. Baseline and 3-year longitudinal relationships were examined through multivariate models on diastolic and systolic pressures separately, controlling for height, weight, sex, and total caloric intake. The following associations were found in longitudinal analyses: analyzing each nutrient separately, for systolic pressure, inverse associations with calcium ($P < 0.05$); magnesium, potassium and protein (all $P < 0.01$); and fiber ($P < 0.05$), and direct associations with total fat and monounsaturated fat (both $P < 0.05$); for diastolic pressure, inverse associations with calcium ($P < 0.01$); magnesium and potassium (both $P < 0.05$); protein ($P < 0.01$); and carbohydrates and fiber (both $P < 0.05$), and direct associations with polyunsaturated fat ($P < 0.01$) and monounsaturated fat ($P < 0.05$). Analyzing all nutrients simultaneously, for systolic pressure, direct association with total fat ($P < 0.01$); for diastolic pressure, inverse associations with calcium ($P < 0.01$) and fiber ($P < 0.05$), and direct association with total and monounsaturated fats (both $P < 0.05$). Results from this sample of children with elevated low-density lipoprotein cholesterol indicate that dietary calcium, fiber, and fat may be important determinants of blood pressure level in children.

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Neurogenic bladder dysfunction due to myelomeningocele – neonatal versus childhood treatment

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Purpose. We sought to determine whether the neonatal institution of treatment of neurogenic bladder dysfunction in myelomeningocele patients at high risk for urinary tract deterioration improves renal and bladder outcome.
Materials and methods. We reviewed the records of patients with bladder dysfunction believed to be at high risk for renal deterioration based on urodynamic studies. All patients were treated with clean intermittent catheterization. We compared rates of urinary infection, hydronephrosis, reflux, continence and surgical intervention in 46 patients in whom treatment was started in year 1 of life and 52 treated after age 4 years.
Results. Renal outcome was similar in both groups with persistent hydronephrosis in 6 of 46 patients (13%) and 7 of 52 (14%), respectively. However, significantly fewer bladder augmentation procedures were required in patients started on treatment during year 1 of life (5 of 46, 11% versus 14 of 52, 27%, $P < 0.05$).
Conclusions. In addition to any psychological benefit, early intervention with clean intermittent catheterization in children with neurogenic bladder dysfunction may help to prevent irreversible bladder dysfunction and limit the need for bladder augmentation.