ARTICLE

Renal Function 16 to 26 Years After the First Urinary Tract Infection in Childhood

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Objective: To evaluate renal function in a population-based cohort with urographic renal scarring after childhood urinary tract infection (UTI).

Design: Follow-up investigation 16 to 26 years after the first recognized UTI.

Setting: Outpatient university clinic for children with UTI serving the local area.

Patients: From the original cohort of 1221 consecutive children with first UTI diagnosed during 1970 to 1979, 57 (41 females and 16 males; mean age, 24.5 years) of 68 with nonobstructive renal scarring participated as well as 51 (38 females and 13 males; mean age, 24.9 years) matched subjects without scarring.

Main Outcome Measure: Glomerular filtration rate (GFR) measured by chromium 51–EDTA clearance, expressed as milliliters per minute per 1.73 square meters.

Results: Median GFR was 99 in both those with and without renal scarring. In patients with unilateral scarring, the total GFR remained unchanged over the years whereas the individual GFR of the scarred kidneys declined significantly from 46 to 39. In 7 patients with bilateral scarring, the GFR declined from 94 to 84 ($P = .14$); compared with those with unilateral scarring, the GFR was significantly lower at follow-up ($P = .007$). Median urinary albumin-creatinine ratio was 1.2 and 0.6 mg/mmol in those with scarring and those without, respectively ($P = .30$).

Conclusions: The GFR 2 decades after the first recognized UTI in childhood was well preserved. However, a significant reduction of individual renal GFR in the unilaterally scarred kidneys indicates that further follow-up is required. Although there were few patients with bilateral scarring, a more serious prognosis can be expected among them.

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Editor's Note: The results of this study are encouraging. However, because there is evidence that individual affected organ dysfunction exists, later follow-up might have different results. Keep the study flowing.

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URINARY TRACT infection (UTI) is one of the most common bacterial infections during childhood, and the frequency of urographic renal scarring, detected after pyelonephritis, is 5% to 10%.[1,2] Risk factors for scarring are obstructive malformations, vesicoureteral reflux (VUR),[3] number of pyelonephritic attacks,[4] and delay of treatment of acute infections.[5,6]

In the long term, patients with pyelonephritic scarring are at risk for hypertension[7] and deteriorating renal function.[8] There is also risk for complications during pregnancy.[9] However, the true frequency of such complications is not completely known. Divergent results in the literature can be explained by factors such as differences in selection criteria, follow-up time, and extent of renal damage.

We present herein the renal function in a population-based group of patients with renal scarring and a matched group without renal scarring, 2 decades after their first known symptomatic UTI in childhood.

RESULTS

STUDY GROUP WITH UROGRAPHIC SCARRING IN CHILDHOOD

Of the 68 patients with renal scarring, 57 (84%) (41 females and 16 males) participated in the follow-up investigation (50 with unilateral lesions and 7 with bilateral lesions). The median time after the first recognized UTI was 22 (range, 16-26)

PATIENTS AND METHODS

PATIENTS

During 1970 to 1979, 1221 children (989 girls and 232 boys) were registered at the single children's hospital in Göteborg, Sweden, with their first known symptomatic UTI.[10] They were aged 0 to 15 years, residents of the city, and attended a special UTI clinic with regular checkups according to a standardized protocol. All children younger than 2 years and all with febrile infections were recommended to undergo imaging of the urinary tract (during the 1970s, urography and voiding cystourethrography) after the first infection. Children with nonfebrile infections were investigated if other signs suggested renal involvement or if recurrent infections appeared. Initially during the 10-year period all children were followed up for 3 years. However, from 1975 on, those with a single UTI without fever or other signs of renal involvement[11] were followed up for only 3 months.

In 652 children the index infection was febrile and 545 (84%) of them were investigated by urography. This investigation was also performed in 37% (208/569) of those with a nonfebrile index UTI. Of 753 children investigated by urography, 21 had obstructive malformation and they were excluded from further analyses.

Nonobstructive renal scarring was ultimately found in 74 children—21 boys with a median age of 0.25 years and 53 girls with a median age of 2.8 years at first recognized UTI.[12] Ten of these 74 patients had bilateral scarring. Three children underwent nephrectomy and 3 underwent heminephrectomy, including 1 with bilateral scarring, and were therefore excluded from the study. The intention was to observe all children with renal scarring until 16 years of age. However, follow-up was discontinued in 17 of the 68 remaining patients (15 families moved from the area and 2 were lost). To evaluate renal function, patients with renal scarring were compared with individuals from the original cohort of children who had normal kidneys at urography. The comparison group was selected individual for individual by minimizing the maximal *t* values between the scarring and the comparison group over the variables sex, age, calendar year, and characteristics of first UTI (febrile/nonfebrile).

The follow-up investigation was performed from 1995 to 1997 at the children's hospital. The total group of 68 patients (18 males and 50 females) with renal scarring who were not operated on, and the matched group without scarring were searched for through the Swedish Central Registry of Inhabitants. They were contacted by letter and thereafter informed consent was obtained by telephone. The study was approved by the Ethics Committee of the Medical Faculty of Göteborg University.

DEFINITIONS

A diagnosis of UTI required significant bacteriuria, ie, more than 10^5 colony-forming units per milliliter of a single species in 1 midstream or 2 bag urine samples, or any growth of bacteria in urine obtained by suprapubic bladder aspiration. A child with a temperature of 38.5°C or higher was considered to have febrile infection.

Renal scarring on urography was defined as a reduction of parenchymal thickness with corresponding caliceal deformation.[13] Primary scarring was defined as damage identified on the first urogram. This group also included kidneys with isolated caliceal deformity or isolated parenchymal thinning that later developed into classic renal scarring according to Hodson.[13] Acquired scarring was defined as damage developing in a previously normal kidney. Isolated parenchymal thinning was defined as reduction of the parenchyma to more than 2.5 SDs below the normal mean.[14,15]

A technetium Tc 99m succimer (DMSA) scan was considered abnormal when focal or generalized uptake defects were noticed or if the relative uptake of DMSA in 1 of the kidneys was less than 45% of the total glomerular filtration rate (GFR). The relative uptake was calculated in the posterior view after background subtraction.[16]

Vesicoureteral reflux was classified into 5 grades according to an international grading system.[17] When referring to VUR observed during childhood, the maximum grade of the damaged kidney was used.

FOLLOW-UP INVESTIGATIONS

Renal Function

The GFR was determined using a multisample plasma clearance method with chromium 51–labeled EDTA (^{51}Cr-EDTA), expressed as milliliters per minute per 1.73 square meters.[18] Split renal function and identification of renal damage was determined by DMSA scan with posterior, anterior, and posterior oblique views. Individual kidney GFR was estimated by multiplying the total GFR by the percentage side function using the posterior view. In patients with bilateral scarring, the kidneys with the lowest function were chosen to analyze the correlation between individual clearance of the scarred kidneys and grade of VUR.

The results of the follow-up investigation were compared with those of the last ^{51}Cr-EDTA investigations performed during childhood, registered in 50 children at a median age of 15 (mean, 14; range, 5-17) years. Split renal function at that time was determined by probe renography with iodohippurate sodium I 131 (^{131}I-hippuran).[19]

Albumin Excretion

In samples of first morning urine, albumin was measured by an immunochemical assay and creatinine was determined according to the method of Jaffé. Urine albumin excretion was expressed as the quotient of albumin (milligrams per liter) and creatinine (millimoles per liter).[20,21] An albumin-creatinine ratio greater than 2.0 mg/mmol was considered abnormal.

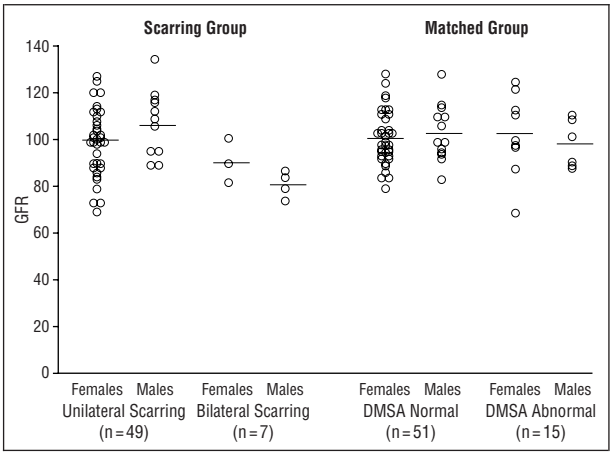
Identification of Renal Damage

DMSA scanning was performed in all patients as well as in all subjects in the matched group. Urography was repeated at the follow-up only in those not found to have DMSA scan lesions corresponding to the scarring on the previous urogram. In the matched group, a new urogram was obtained if DMSA scan results were abnormal. Evaluation of the renal status was done without knowledge of clinical data.

Continued on next page

STATISTICAL METHODS

The computer software used for data analyses was SAS for PC, release 6.12 (SAS Institute, Cary, NC). The Mann-Whitney test was used for comparisons between groups. Changes over time and tests between scarred and contralateral unscarred kidneys within the same patient were analyzed with the Wilcoxon signed rank test. Correlation between VUR grade and individual GFR of the corresponding kidney was analyzed with the Spearman correlation coefficient (r_s).



Distribution of glomerular filtration rate (GFR) (expressed as milliliters per minute per 1.73 square meters) of all individuals participating in the follow-up investigation, except 1 male patient with unilateral scarring in whom estimation failed. The horizontal lines represent the mean values in each subgroup. DMSA indicates technetium Tc 99m succimer scan.

years. Median age at investigation was 24.6 (mean, 24.5; range, 16.5-33.8) years. Of the 11 patients not participating, 5 had moved abroad and could not be traced (4 with unilateral scarring and 1 with bilateral scarring) and 6 declined participation (5 with unilateral scarring and 1 with bilateral scarring). Determination of GFR was unsuccessful in 1 individual because of technical problems.

Of the 57 patients, 53 had uptake lesions on DMSA scans, all corresponding to previous urographic findings. Four patients had normal DMSA scan results but unchanged findings on repeated urography: symmetrical bilateral scarring of mild degree in 1 patient, a scarred duplex kidney in 1 patient, and minimal unilateral scarring in 2 patients. No patients had evidence of new scarring in a previously unscarred kidney.

In 43 (77%) of 56 cases investigated by voiding cystourethrography, VUR to the scarred kidney was found during childhood; in 13 (23%) no VUR was found. Vesicoureteral reflux was maximally grade I in 5 (9%), grade II in 14 (25%), grade III in 13 (23%), grade IV in 9 (16%), and grade V in 2 (4%).

MATCHED GROUP WITHOUT UROGRAPHIC SCARRING IN CHILDHOOD

A total of 66 matched subjects participated in the follow-up investigation; 15 were found to have uptake defects on DMSA scanning and are therefore presented as a separate group (adults with defects on DMSA scan).

The distributions of the matching variables for the 51 subjects with normal DMSA scan results and the 57 patients with renal scarring were nearly the same: 75% vs 72% females, 92% vs 91% with febrile first UTI, and 53% vs 54% presenting during the first half of the period 1970 to 1979. Mean age at first UTI was 2.8 years in both groups.

Adults With Defects on DMSA Scan

In 8 of 15 subjects, minor uptake lesions or split renal function discrepancy (42%-44% side function) was found on DMSA scan but the repeated urogram was normal. The remaining 7 patients showed abnormalities on DMSA scans and urography. Four males had parenchymal thinning without caliceal deformation; the relative uptake of DMSA was 43% in 2 kidneys and 44% and 46% in 1 each. Three female patients had classic urographic scarring; 2 had unilateral damage with side function of 39% and 45%, respectively, and 1 had bilateral damage. Follow-up at the children's hospital had been discontinued in these 3 females, and the last urographic examination had been performed at the age of 4 years in 2 of them and at 11 years in 1.

During childhood VUR was shown in 7 (47%) of 15 subjects: 8 (53%) had no VUR, 2 (13%) had grade I, 3 (20%) had grade II, and 2 (13%) had grade III. One of the 3 female patients with urographic scarring had VUR (grade II).

Adults With Normal DMSA Scan

Fifty-one of the 66 matched subjects had normal kidneys on DMSA scan. In this group, VUR had been shown in 22 subjects (43%) during childhood: 29 (57%) had no VUR, 2 (4%) had grade I, 17 (33%) had grade II, and 3 (6%) had grade III.

RENAL FUNCTION

GFR Results

The **Figure** shows the GFR of all patients and subjects in the follow-up investigation. There were no significant sex differences within the subgroups.

The median GFR in the 56 patients with renal scarring was 99 (mean, 99; range, 69-134) compared with 99 (mean, 101; range, 79-128) in the 51 subjects with normal DMSA scan findings at follow-up.

Unilateral Scarring

The median GFR at follow-up was 101 (mean, 101; range, 69-134). Comparison with a previous investigation performed at a median age of 15 years in 43 patients showed

Table 1. GFR Determined by Chromium 51–EDTA Clearance at the Last Investigation in Childhood vs the Follow-up Investigation*

Subjects	No.	GFR, Median (Mean, Range)			P
		In Childhood†	At Follow-up‡	Difference	
Study group with urographic scarring in childhood					
Unilateral scarring	43	103 (104, 83 to 127)	101 (101, 69 to 134)	2 (3, –21 to 36)	.11
Bilateral scarring	7	94 (95, 75 to 123)	84 (85, 74 to 101)	8 (10, –13 to 33)	.16
Matched group without scarring in childhood					
Adults with DMSA scan defects	15	Not done	100 (101, 69 to 125)	. . .	. . .
Adults with normal DMSA scan	51	Not done	99 (101, 79 to 128)	. . .	. . .

*GFR indicates glomerular filtration rate, given in units of milliliters per minute per 1.73 square meters; DMSA, technetium Tc 99m succimer.
†Median age, 15 years (range, 5-17 years).
‡Median age, 24.5 years (range, 16.5-33.8 years).

no significant change (median of 103 compared with 101 at follow-up; **Table 1**).

Bilateral Scarring

There was a decline of GFR from the last investigation in childhood until follow-up (median GFRs, 94 and 84, respectively), but the difference was not significant (Table 1). Compared with those with unilateral scarring, the median GFR was significantly ($P = .007$) lower at the follow-up investigation; at the childhood investigation significance was not reached ($P = .06$).

GFR <80

Eight individuals had a GFR of less than 80—6 patients in the scarring group and 2 subjects in the matched group. In the first group, 2 male patients had bilateral (GFRs, 74 and 79) and 4 female patients had unilateral scarring (GFRs 69, 73, 73, and 79). These 6 children presented with a febrile UTI before age 6½ years and VUR was demonstrated in 4 of them (maximally grade I in 1, grade III in 2, and grade V in 1). Recurrent febrile UTI was documented in 4 of 6 during childhood—a single recurrence in 2 patients, and 2 and 4 recurrences in 1 each. No one in this group had febrile recurrences recognized during adulthood.

In the matched group, a female patient with bilateral scarring had a GFR of 69. She presented with a febrile UTI at 2½ years of age and had a febrile recurrence at 4 years of age but after that she was lost from follow-up. No scarring or VUR was demonstrated at radiological investigation 1 month after the second infection. A second febrile recurrence was registered at another hospital when she was 6 years old. During the present study, urography that had been performed at the age of 10 years showed bilateral renal damage. Another female patient with normal DMSA scan results at follow-up had a GFR of 79. She presented at age 1 year with a febrile UTI but had no recurrence or VUR.

Individual Kidney Function

The distribution of individual GFR in damaged kidneys at the follow-up investigation is shown in **Table 2**; in 31 patients individual GFR was less than 40 in 1 of the kidneys. In **Table 3** current individual kidney GFR in the group with unilateral scarring is compared with function during childhood. In the scarred kidneys the reduction from a median GFR of 46 in childhood to 39 at follow-up was significant. In the contralateral unscarred kidneys, the clearance remained stable (GFRs, 60 and 61, respectively). The difference between scarred and unscarred kidneys was significant ($P<.001$) both at last childhood and at follow-up investigation. The individual GFR in the unscarred kidneys (median, 61; mean, 62) of those with unilateral scarring was significantly higher than in the kidneys with the highest function of the matched group with normal DMSA scan results (median, 53; mean, 53) ($P<.001$).

Table 2. Distribution of Individual GFR of Scarred Kidneys in 56 Patients With Renal Scarring*

Individual GFR	No. of Kidneys	
	Unilateral Scarring	Bilateral Scarring
10-19	4	0
20-29	6	2
30-39	15	4
≥40	24	8
Total No.	**49**	**14**

*Glomerular filtration rate (GFR) determination failed in 1 patient. GFR is given in units of milliliters per minute per 1.73 square meters.

In the scarring group, a negative correlation was found between individual GFR of scarred kidneys and VUR grade to the corresponding kidney ($P = .047$, $r_s = –0.27$). The mean GFR of 14 kidneys with nonrefluxing ureters, of 17 kidneys with grade I to II refluxing ureters, and of 24 kidneys with grade III to V refluxing ureters was 41, 39, and 35, respectively.

Primary vs Acquired Scarring

In Table 3 the scarred kidneys of patients with unilateral damage have also been subdivided into primary and acquired scarring. The reduction in individual kidney GFR was significant in both subgroups ($P = .002$ and $P = .04$, respectively). However, the difference in individual kidney GFR between the subgroups was not significant, neither at childhood nor at follow-up investigation.

Table 3. Individual GFR in Patients With Unilateral Scarring at the Last Investigation in Childhood vs Follow-up Investigation*

Kidneys	No.	GFR, Median (Mean, Range)			P
		In Childhood	At Follow-up	Difference	
Scarred	43	46 (43, 16 to 62)†	39 (39, 18 to 66)‡	4 (4, –8 to 18)	<.001
Unscarred	43	60 (61, 46 to 99)†	61 (62, 39 to 94)‡	–2 (–1, –18 to 18)	.24
Primary scarring	18	41 (41, 16 to 62)	37 (35, 18 to 66)	7 (6, –5 to 17)	.002
Acquired scarring	25	46 (44, 28 to 61)	40 (41, 25 to 56)	3 (3, –8 to 18)	.04

*GFR indicates glomerular filtration rate, given in units of milliliters per minute per 1.73 square meters.
†Median difference (mean, range): 13 (18, –5 to 83); P<.001.
‡Median difference (mean, range): 20 (23, –7 to 76); P<.001.

In the patients with bilateral scarring, all males (n = 4) had primary and all females (n = 3) had acquired scarring.

Albumin Excretion

Samples of first morning urine were obtained from 55 patients in the scarring group and 51 matched individuals with normal DMSA scans. One patient in each group had bacteriuria and these patients were therefore excluded. Median albumin-creatinine ratio was 1.2 (mean, 0.6; range, 0.2-32) mg/mmol and 0.6 (mean, 0.5; range, 0.2-2.3) mg/mmol, respectively ($P = .30$). Pronounced albuminuria (32 mg/mmol) was found in 1 male patient with bilateral scarring and a GFR of 84. Minimal albuminuria (2.4 and 2.3 mg/mmol, respectively) was found in a male patient with unilateral scarring and a female patient without scarring, both with normal GFRs.

COMMENT

Most children with febrile UTI in Göteborg are diagnosed at the children's hospital.[22] A study of the files of all pediatric outpatient units in the area for the years 1979 to 1981 showed that only 14% of the cases with first recognized febrile UTI were identified outside the hospital.[23] In the present study, 84% of the 68 patients with urographic scarring participated in the follow-up investigation 22 years after the first known UTI in childhood.

The most widely used method for detection of renal scarring today is the DMSA scan. Therefore, this technique was used at the follow-up investigation in contrast to the 1970s when urography was the method of choice. The DMSA scans were evaluated as normal in 4 of 57 patients with childhood urographic scarring. In 2 of them a repeated urogram showed symmetrical bilateral scarring and a scarred duplex kidney, respectively, which are known causes of misinterpretation of the DMSA scan.[16] Split renal function was assessed by ^{131}I-hippuran renography during the 1970s as compared with DMSA scan at the follow-up investigation. It has been shown, however, that the correlation between relative uptake, determined by these two methods, is good.[24]

Some patients with renal scarring probably escaped detection in childhood. This is illustrated by the findings in the matched group of subjects with normal urograms in childhood. Of 66 participating in the follow-up investigation, 15 had uptake defects or individual renal function less than 45% of the total GFR on the DMSA scan. However, 12 had minor lesions and only 3 girls had classic scarring on a new urogram. The latter 3 had all discontinued follow-up at the children's hospital and the last urography was performed at 4, 4, and 11 years of age, respectively. None of the patients had acquired a scar in a previously unscarred kidney after completed checkups during childhood. Thus, the risk of developing late renal scarring is small, which has been shown previously.[25] That minor lesions on DMSA scan would be seen among the subjects in the matched group was expected since this technique is more sensitive for detection of damage than urography.[26,27]

In the patients with renal scarring, the renal function was well preserved; the median GFR was 99. There was in fact no difference between the 56 patients and the matched group of 51 subjects with normal DMSA scans. Only 6 of 56 patients had GFRs of less than 80 and the reduction of function was small, with values in the range of 69 to 79. Thus, the long-term outcome concerning total renal function in patients with pyelonephritic scarring was favorable 22 years after the first recognized UTI. The GFR remained stable from the last childhood investigation in patients with unilateral scarring, although there was a significant decline in individual function of the scarred kidneys from a GFR of 46 to a GFR of 39. This decline was correlated to the VUR grade observed during childhood. The individual function of the unscarred kidneys in the patients with unilateral scarring was significantly higher than in the matched group with normal DMSA scans as an indication of compensatory hypertrophy. It is important to observe these patients for longer periods to determine whether progressive deterioration of function will occur. For those with bilateral scarring, there was a decline in GFR from 94 to 84. The number of patients was small (n = 7) and the difference did not reach statistical significance.

We found that 54% (40/74) of the patients with scarring had acquired scarring, ie, there was at least 1 urogram without signs of renal damage.[12] The GFR in kidneys with primary scarring was not different from that of those with acquired scarring. In this context it is important to notice that our definition of "primary" does not necessarily mean congenital.

In the literature there is considerable variation in the frequency of chronic renal insufficiency and terminal renal failure in patients with pyelonephritic scarring.[8,25,28-34] Several factors must be taken into consider-

ation when interpreting these different results. The most important of these factors are patient selection, prospective or retrospective study design, extent of scarring, and follow-up time.

Jacobson et al[8] investigated 30 (26 females) patients 27 years after the detection of nonobstructive pyelonephritic scarring. Three patients had developed end-stage renal failure and the remaining had significantly lower GFRs (mean, 90) than 13 healthy control subjects. Their patients were selected retrospectively through the department of pediatric radiology, where urograms from the period 1951 to 1967 were reviewed. The mean age at detection of scarring was 6 years, at which time most kidneys were severely damaged.[35] They were not followed up. At reinvestigation, progression of scarring had occurred in one third of the kidneys. In a prospective study by Martinell et al,[34] more favorable results were demonstrated. A group of 54 female patients with renal scarring, of whom 19 had severe scarring, were followed up continuously from their first known UTI in childhood. They had rapid access to medical care for treatment of recurrent UTI, both during childhood and adulthood. After 15 years of follow-up, the GFR was significantly lower (96) in those with severe scarring compared with controls, but there was no difference between those with moderate scarring and controls. The GFR was less than 80 in 4 patients with severe scarring but not less than 70 in any patient. Consequently, close supervision seems important for minimizing deterioration of renal function in patients with renal scarring. This is also in accordance with our results, where almost all patients were followed up at least up to 16 years of age.

In a recent follow-up report by Smellie et al,[25] 226 patients (189 females and 37 males) were reinvestigated at a mean age of 27 years. They were followed up prospectively, from a mean age of 5 years, throughout childhood because of recurrent UTI and VUR. Radiological renal scarring was found in 85 patients before the age of 10 years and none developed new scars thereafter. During childhood low-dose antibacterial prophylaxis was given to all with scarring or persistent VUR, but during adulthood checkups were rare. At follow-up investigation, renal function measured by plasma creatinine level was impaired in 9 (11%) of those with scarring, all but 1 of whom had bilateral scarring. Two patients underwent transplantation and 1 had died because of malignant hypertension. In the scarring group, markedly raised albumin excretion was found in 3% and microalbuminuria in 13%. At a further follow-up by postal questionnaire at a median age of 35 years, there were no additional patients with impaired renal function or end-stage renal disease. Although these patients were originally referred, ie, selected, they were under close supervision during the rest of their childhood, and in contrast to the study by Jacobson et al,[35] no significant radiological deterioration was seen in those who had repeated urography. This is in accordance with a report by Berg[36] showing that reduction in renal function occurred early after pyelonephritis and that further reduction was slow in children followed up continuously. On the other hand, the patients described by Smellie et al[25] differed from ours in that they were of an older age at detection and that scarring was present at the initial investigation in all but 1 patient. This is further support for the importance of early detection for prevention of deterioration of renal function in children with renal scarring.

Bailey et al[32] also reported on a group followed up from early childhood: 17 patients (8 boys) with gross VUR and renal scarring, diagnosed in infancy during 1952 to 1970, were followed up for 24 years. Two (2 males) of the 4 patients with bilateral scarring had renal insufficiency, but in the others the GFR was not less than 70. At the same center, 24 patients with end-stage reflux nephropathy, in the same age span and during the same period, entered the renal replacement program. In contrast, the latter group presented later and were not regularly followed up. Thus, also in this study the benefit of early detection and continuous follow-up was suggested.

Several reports on adults with pyelonephritic scarring have been presented, although the accuracy of GFR estimation was low in most of them.[28-31,33] Impaired renal function was found in 18% to 38%. In general, renal scarring was extensive and it was shown that bilateral scarring is a risk factor for declining renal function. However, some authors pointed out that patients with unilateral scarring are also at risk of decreasing function, presumably secondary to hypertensive vascular damage.[28,31] In studies with this type of design, females presenting with UTI are the dominant group while the smaller group of males frequently presents with features of renal damage, such as hypertension, proteinuria, or symptoms of renal failure.[30,33] Thus, reports of studies in adults have shown that patients with renal failure as a consequence of pyelonephritic scarring are not a neglectable group. Most were not under medical supervision until progressive deterioration of renal function was inevitable and bilateral scarring was frequent but not a prerequisite for impairment of renal function. In our study there were only 7 patients (12%) with bilateral scarring. Although not significant, their median GFR decreased from 94 to 84 during the 10-year period between 15 and 25 years of age. However, none had progressive renal deterioration, neither those with bilateral nor those with unilateral scarring.

In our study, pronounced albuminuria was found in only 1 male who had bilateral scarring and a GFR of 84. A negative correlation between GFR and urinary albumin excretion in patients with pyelonephritic scarring has been described previously.[37] Proteinuria, as an indication of glomerular lesions, has been reported to be a constant finding in such patients with progressive deterioration of renal function.[38] Consequently, the low frequency of albuminuria in our study, where no one had a GFR less than 69, was not surprising.

Although nonobstructive renal scarring is still a global major cause of end-stage renal disease in children,[39] the frequency has decreased during the past decades in some countries with modern medical care.[40] In Sweden there has not been registered any child during the last decade,[41] and in adulthood the incidence of end-stage renal failure as a consequence of pyelonephritic scarring is relatively low—6% to 7%—according to the Swedish Registry of Uremia. In a recent national survey, a high

detection rate of UTI in children was shown not only in Göteborg but in the whole of Sweden.[42] We suggest that the high frequency of preserved renal function in patients with scarring presented herein is a consequence of special attention to UTI and adequate checkups during childhood.

In conclusion, high awareness of UTI in infants and young children and close supervision of those with renal scarring seem important to minimize deteriorating renal function in such patients in the long term.

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