

Ulf Jodal · Jean M. Smellie · Hildegard Lax ·  
Peter F. Hoyer

## Ten-year results of randomized treatment of children with severe vesicoureteral reflux. Final report of the International Reflux Study in Children

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**Abstract** For the comparison of long-term outcome of the management of medical or surgical treatment of children with severe vesicoureteral reflux (VUR), children aged <11 years with non-obstructive grade III/IV reflux, previous urinary tract infection (UTI) and glomerular filtration rate (GFR)  $\geq 70$  ml/min per  $1.73 \text{ m}^2$  body surface area were recruited, and 306 were randomly allocated to receive antimicrobial prophylaxis or ureteral reimplantation. Primary endpoints were new renal scars and renal growth. Follow up, originally planned for 5 years, was extended to 10 years for 252 children, 223 of whom had follow-up imaging. Up to 5 years, 40 new urographic scars (medical 19, surgical 21) were seen. Between 5 years and 10 years, only two further scars were observed. Renal growth and UTI recurrence rate were similar, except that medically

treated patients had more febrile infections. There was no difference in somatic growth, radionuclide imaging or renal function. A GFR  $< 70$  ml/min per  $1.73 \text{ m}^2$  was found in only one patient. Three patients developed hypertension requiring treatment. We conclude that, with close supervision and prompt treatment of recurrences, children entering the study with GFR  $\geq 70$  ml/min per  $1.73 \text{ m}^2$  progressed remarkably well under either medical or surgical management, emphasizing the importance of continued supervision and the entry level of renal function.

**Keywords** Urinary tract infection · Urography · Renal scar · Renal function · Hypertension · Kidney growth · DMSA scan

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U. Jodal (✉)  
The Pediatric Uro-Nephrologic Centre,  
The Queen Silvia Children's Hospital,  
Göteborg University,  
416 85 Gothenburg, Sweden  
e-mail: ulf.jodal@pediat.gu.se  
Tel.: +46-31-343-4664  
Fax: +46-31-199-365

J. M. Smellie  
The Department of Paediatrics,  
University College London Hospitals,  
London, UK

H. Lax  
Institute for Medical Informatics,  
Biometry and Epidemiology, Medical Faculty,  
University of Essen,  
Essen, Germany

P. F. Hoyer  
Clinic of Paediatric Nephrology,  
University Children's Hospital,  
Essen, Germany

## Introduction

In the 1970s and early 1980s there were widely divergent opinions as to the optimal management of treatment for infants and children with severe primary vesicoureteral reflux (VUR). The International Reflux Study in Children (IRSC) was set up to compare the outcome of medical or surgical treatment of children, managed according to a strict protocol, who had grade III or IV non-obstructive VUR and a history of at least one symptomatic urinary tract infection (UTI) [1, 2]. The primary endpoint was the development of new renal scars and impairment of renal growth. Recurrence of UTI, renal function, the development of hypertension, somatic growth and the progress of reflux in medically treated children were also documented. Clinicians in 8 European university centres and 16 academic centres in the USA agreed to co-operate. It was estimated that 125 patients in each treatment group would be required to demonstrate an expected difference of at least 20%, and 200 in each treatment group to demonstrate a difference of 10% in the acquisition rate of new renal scars [1, 3]. The recruitment period was from January 1980 to February 1985, with an intended follow up period of 5 years [3].

The entry characteristics, protocol, management and 5-year follow-up results of the 438 patients originally randomly allocated have been reported [3–11]. Extended follow up beyond the originally scheduled 5 years was proposed in the 306 patients of the European limb and was possible in 252 patients. The randomization and stratification remained evenly distributed between the original group of 306 patients and the 252 followed during the second 5-year period (Table 1). Some 10-year results have already been reported in detail [12–15]. This paper presents the overall results of the study and of the 252 patients who completed the 10-year clinical follow up. Also included are the results concerning renal function and hypertension and

the 5–10 year findings of nuclear imaging and of recurrence of UTI, which have not been previously reported.

## Methods and patients

Infants and children under 11 years of age, with grade III or IV reflux (only grade IV for infants under 1 year of age) according to the reflux grading system developed for the study [2], with or without renal scarring were recruited [3]. The reflux had been detected on investigation of acute UTI that, in 90% of the children, had been diagnosed as acute pyelonephritis because of a temperature  $\geq 38.5^\circ\text{C}$ ; 68% had experienced at least two episodes of acute pyelonephritis before entry [4]. All had normal blood pressure (hypertension controlled for at least 6 months in three), and glomerular filtration rate (GFR)  $\geq 70$  ml/min per  $1.73\text{ m}^2$ . Those with outflow obstruction, other renal malformation, overt bladder dysfunction or previous urinary tract surgery were excluded.

After the patients had undergone a confirmatory second voiding cysto-urethrogram (VCU) within 2–6 months, in accordance with the protocol for the European limb of the study, the VUR in 80 of the 401 patients recruited in Europe had improved such that they no longer qualified and were followed on a medical regimen in a 'sideline' group [3]. After written parental consent had been obtained, 321 were randomly allocated by a computer program at the coordinating centre in Essen, Germany, to medical or surgical management. The computer program was optimized for dynamic allocation, making allowances for relevant stratification factors, which included university centre, age at entry, gender, grade of VUR, unilateral or bilateral reflux, and renal scarring. After random allocation, 15 children (medical three, surgical 12) did not follow the treatment allocation, mainly because of parental preference. Thus, 306 children, of whom 72 were infants

**Table 1** Children's characteristics at entry into the study, for all patients ( $n=306$ ) and for those completing 10 years of follow up ( $n=252$ ) according to treatment group. There were no significant differences between the groups

Characteristic	Entered into the study		Completed 10 years	
	Medical ( $n=155$ )	Surgical ( $n=151$ )	Medical ( $n=125$ )	Surgical ( $n=127$ )
Gender				
Girls	118	115	92	99
Boys	37	36	33	28
Kidney status				
Unscarred kidneys	76	81	64	64
Unilateral scarring	52	51	40	47
Bilateral scarring	27	19	21	16
VUR grades of the two kidneys				
0/III	8	6	6	5
0/IV	28	27	22	21
<III/III	11	8	9	5
III/III	12	11	8	9
<III/IV	25	16	19	15
III/IV	38	40	33	33
IV/IV	33	43	28	39
Maximum reflux grade III	31	25	23	19
Maximum reflux grade IV	124	126	102	108

under 1 year of age, were treated according to their random allocation, 155 children medically and 151 surgically [5].

At entry, clinical history, height, weight and blood pressure were recorded, and investigations included urinalysis and culture, urography (IVU),  $^{99}\text{Tc}$ -dimercaptosuccinic acid (DMSA) studies and contrast VCU using standardized techniques [3]. GFR was measured using  $^{51}\text{Cr}$ -chromium-edetic acid (EDTA) [16], and serum creatinine determinations were carried out in a single central laboratory using the Jaffé method [3]. The serum creatinine values were used to estimate clearance according to the formula of Schwartz et al. [17].

Ureteral reimplantation was performed according to the individual surgeon's choice, mainly Leadbetter–Politano ( $n=83$ , 55%) or Cohen ( $n=38$ , 25%) techniques, with VCU 6 months postoperatively and antimicrobial prophylaxis discontinued when no VUR was seen [6, 9]. The medically treated group received continuous low-dose antibacterial prophylaxis with co-trimoxazole, trimethoprim or nitrofurantoin [4] until the VUR had resolved or improved to grade I. If the kidneys were unscarred, prophylaxis was usually discontinued at the age of 8 years [15]. The importance of prompt treatment of symptomatic recurrence of UTI was emphasized to local physicians. In both groups, attention to fluid intake, avoidance of constipation, frequent voiding, and double micturition at bedtime were encouraged, although compliance was not controlled.

During the first 5 years, urine was cultured monthly or if suggestive symptoms developed, when parents were advised to contact their local physician. There was also a 3-monthly clinical check when blood pressure was measured by standard sphygmomanometry or by Doppler device, and presented as centiles in relation to height [18]. VCU (radiological or radionuclide) was scheduled at 6, 18, 30, 42 and 54 months, and at 6, 8 and 10 years until two consecutive findings without VUR were obtained [14]. Serial IVUs were done at 6, 18 and 54 months, according to protocol, and DMSA scans at the same intervals. Between 5 years and 10 years, supervision was less intense with regular reports on clinical progress, repeat urinalysis and culture at 6, 8 and 10 years and also imaging and renal function studies at 10 years after entry. All radiological and radionuclide imaging assessments of morphology and serial measurements of renal size were made by a team of experienced examiners blind to the treatment group.

Urographic renal scarring was defined according to Hodson [19] as a deformed calyx with reduced overlying parenchyma. New scarring was defined as scarring in an area of renal parenchyma that had previously been normal. Renal scars were typed as described by Smellie et al. [20]: type A, one or two scars; type B, affecting more than two areas but with some normal parenchyma remaining; type C, generalized irregular parenchymal reduction; type D, small end-stage kidney.

Renal size was measured planimetrically on tracings of serial urograms. The standard deviation score for each kidney was determined by relating the measured parenchymal area to the vertebral height from L1 through L3

[21]. Total renal growth was evaluated using the mean of the areas of the right and the left kidney.

The detailed method of DMSA studies has been published [11]. The images were classified as normal or abnormal and according to a classification where type 1 and 2 corresponded to rather slight defects in kidneys of normal shape, type 3 to a small kidney of normal shape without focal impairment of uptake and a split function of <45% of total function, type 4 corresponded to gross defects, 4a in a normal size kidney and 4b in a small kidney. Deterioration on serial examination was defined as the appearance of a new defect or an increase in the extent of an existing defect.

During the first 5 years, annual investigator meetings were held to assess the quality of data collection and submission to the coordinating centre, but analysis of the 5-year, and later 10-year, results was deferred until the follow-up period had been completed. Quality and progress was supervised by the External Monitoring Committee.

Of the 306 patients originally treated, four were lost to follow up during the first 6 months and 302 continuing for up to 5 years. Of these, 276 had been cared for in the 5 larger centres. During the second 5-year period, 16 medical patients were excluded who had undergone surgery at 5 years by prior arrangement and 34 patients did not agree to continued follow up, so that 252 completed follow up for 10 years.

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## Ethics

The study protocol was approved in accordance with the standards in the Declaration of Helsinki by the local ethics committees of each participating hospital and by the External Monitoring Committee of the Study. Two centres that had originally enlisted had to withdraw, because they were unable to obtain ethics consent for the study.

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## Statistical methods

The computer software used for analysis was SAS for PC, version 8 (SAS Institute, Cary, N.C., USA). For details of the statistical methods, see references [13, 14]. A life-table analysis and a Gehan–Wilcoxon generalized rank test was performed to compare both groups as to the primary outcome of renal scars. Because of successful stratified randomization, it was not necessary to take any co-variable into account. The predefined level of statistical significance was  $2\alpha=0.05$ . Empirically found *P* values are given descriptively, without further adjustment for multiple testing.

## Results

### Five-year results

The 5-year results of the 306 children randomly allocated in the European limb showed no overall statistical difference in outcome between the medical and surgical treatment groups in acquisition of urographic new scars [5], changes in images or differential function on DMSA studies [11], renal growth or function [13], or rate of recurrence of UTI [4]. However, there were some differences, such as the higher proportion of children in the medical group (21%) who had febrile UTI (presumed acute pyelonephritis) than in the surgical group (11%) ( $P<0.01$ ). Furthermore, new scars in the surgical group were seen in 18 of 20 patients and in the medical group in 11 of 19 patients at 6 months; this difference, however, was not statistically significant ( $P=0.57$ , log-rank test).

Few side effects of prophylaxis were recorded, none of them serious. Postoperative unilateral obstruction occurred in ten children, five of them under 2 years of age, requiring further surgery in seven [6]. Six of these children with obstruction developed a new renal scar. VUR persisted postoperatively in another 16 patients at 6 months, but, at 5 years, only three of these had reflux with dilatation, and no further reimplantation was performed.

### Ten-year results

Of the 252 children (medical 125, surgical 127) who continued clinical follow up for 10 years, 223 (medical 113, surgical 110) had an IVU at 10 years. DMSA studies were also done at 10 years in 223 patients. The image quality was satisfactory for analysis in 216 (medical 109, surgical 107). The entry characteristics of the 252 followed clinically and the 223 who had imaging at 10 years were similarly distributed between the two treatment groups, making selection bias by different motivation to protocol adherence unlikely (Table 1).

### Urographic renal scarring

Urographic renal scarring was present at entry in 149 (49 %) of the 306 children originally treated and in 113 (51%) of the 223 who were followed up with IVU for 10 years (Table 1). The proportion of scarring was not related to age or gender [3]. Renal status at entry was similar in the two treatment groups. Bilateral scarring at entry was slightly more common in the medical group (medical 26, surgical 19, among 302 followed for more than 6 months, and medical 19, surgical 15, among 223 followed radiologically for 10 years).

During the first 5 years of the study, a total of 40 patients acquired new scars (medical 19, surgical 21). In one child a new scar had developed during the first 5 years, but, because of a late submission of the result, this was not included in the 5-year report. Of these children, 28 were

among the 223 followed radiologically for 10 years (14 medical, 14 surgical). At 10 years, new scars had been identified in a further two patients, making a total of 42 patients with identified new scars (20 medical, 22 surgical). In 25 children these new scars were seen in kidneys that were unscarred on IVU at entry [15].

The younger the patients at entry, the higher was the frequency of new scars, <2 years 20%, 2 to 4 years 10% and  $\geq 5$  years 5% ( $P<0.05$ ). New scars were identified under the age of 5 years in 31 of the 42 children, 15 in the medical and 16 in the surgical group.

### Renal growth

There was no significant difference overall in mean renal growth between patients treated medically or those treated surgically after a 5-year or 10-year follow up [13]. During the study, among the 223 followed for 10 years, the mean size of the right and the left kidneys on serial measurement remained within 1 standard deviation score in 75 (66%) of 113 patients in the medical group and in 80 (73%) of 110 patients in the surgical group. A decreasing mean standard deviation score of the right and left kidney was seen in five medical and seven surgical patients, but the final score was below  $-2$  standard deviations in only three medical and one surgical patient. There was, in fact, actual growth of the total renal parenchymal area in all of the 223 patients.

### DMSA studies

The published comparison of the DMSA scan findings during the first 5 years in 287 patients (medical 147, surgical 140) with satisfactory serial images showed no significant difference in either image or differential function between those treated medically or surgically [11]. There was a corresponding image defect on the DMSA scan in 75 (77%) of the 98 with urographic scarring in the medical group and 70 (77%) of the 91 children with scarred kidneys on IVU in the surgical group, in whom a satisfactory DMSA study was available at entry. In all the patients with a unilateral urographic scar of type B, C, or D there was  $>5\%$  reduction in function of that kidney ( $>10\%$  difference in function between the kidneys). In 46 patients among the original 306 who had bilateral urographic scars, there were corresponding defects of isotope uptake in 41.

In 216 children who had satisfactory serial DMSA study results at 10 years, there was no significant overall difference in image changes seen after 5 years between those treated medically ( $n=109$ ) or surgically ( $n=107$ ). There was some deterioration of image in 13 medical and 9 surgical patients (13 and nine kidneys, respectively; difference not significant,  $P>0.11$ ). This deterioration of image was in 19 of the 22 seen among the 79 children entering the study under 2 years of age. However, there was a change to gross defect (type 4 images) from a less



extensive defect in no medically treated patients and in only two surgically treated patients.

### Renal function

The GFR was measured by EDTA clearance [16] and estimated by the Schwartz formula [17]. At entry and at 5 years, the mean GFR was similar in the two treatment groups (Table 2). At 10 years the GFR was evaluated by either or both methods in 133 patients, and the results were similar in medically and surgically treated patients. Among the 112 patients with formula clearance available, there were 46 with unilateral and 17 with bilateral scarring. In only one of these, a clearance under the minimal entry level of 70 ml/min per 1.73 m<sup>2</sup> was reported, at 67 ml/min per 1.73 m<sup>2</sup>. This was a boy who had the first UTI at the age of 2 weeks and was entered in the study after a recurrence at 18 months of age with bilateral reflux grade IV and bilateral renal scarring type B. His development was retarded, and it was only at 4 to 5 years of age that he clearly had severe dysfunctional voiding, normally a contraindication to inclusion. He developed new scars in both kidneys, which progressed to type C. Treatment of hypertension was started 5 years after entry (see below).

### Urinary tract infection

The pattern of symptomatic recurrences during the first 5 years in the 252 patients who completed the 10-year clinical follow up was similar to that reported in the 306 children originally treated [4]. There was, however, a different pattern for girls and boys, as well as for medically and surgically treated patients (Table 3). Overall, girls had symptomatic recurrences more frequently than boys. Febrile recurrence (pyelonephritis) occurred more often among children in the medically managed group than in the surgically managed group, over the 10 year period, in 32 of 127 versus 17 of 125, respectively ( $P<0.03$ ). Episodes of pyelonephritis occurring after the patient had been taken off antibacterial prophylaxis were seen in 15 of 32 medical patients and 15 of 17 surgical patients.

The overall number of girls with symptomatic recurrence of UTI was similar in the two treatment groups, but febrile recurrence was seen more often in the medically treated girls (in 26 of 94 compared to 15 of 97,  $P=0.052$ ).

Two episodes of febrile recurrence were seen in six girls in the medical group and two in the surgical group. Another two girls in the medical group experienced three febrile recurrences. There were nine girls in the medical group and three in the surgical group who had no recurrence during the first 5 years but had a febrile UTI during the second 5-year period.

Of the 12 boys with recurrence, eight had a febrile UTI. There were two boys in the medical group and one in the surgical group that had two febrile recurrences. During the second 5-year period there was one boy in the medical group who, for the first time, had a febrile recurrence.

### Hypertension

Hypertension was defined as systolic or diastolic blood pressure records of over the 95th centile on at least two occasions [18]. Three patients (medical two, surgical one) entered the study on antihypertensive treatment. In two, treatment was discontinued during the first 5 years without relapse; the third continued treatment throughout the 10 years of observation.

A further three children were deemed to require treatment for hypertension, all in the medical treatment group. A male patient who received treatment for only 3 months acquired unilateral renal damage type B during the study. Two patients started treatment 5 years and 6 years after entry and continued until the end of the study. One was the boy described above, with a GFR of 67 ml/min per 1.73 m<sup>2</sup>, who had bilateral renal damage type B that progressed to bilateral type C. The other was a girl with normal kidneys at entry who developed unilateral damage type B.

### Reflux progress in patients treated medically

There was progressive reduction in severity of reflux during the first 5 years [7]. This improvement continued during the second period of observation (Table 4) [14]. At 10 years, among the 102 patients undergoing VCU, VUR with dilatation was seen in 27, 22 with grade IV and 5 with grade III, and VUR without dilatation also in 27. Absence of VUR (in 47%) was significantly associated with grade III vs grade IV reflux ( $P=0.007$ ), unilateral vs bilateral reflux ( $P=0.0002$ ), and age  $\geq 5$  years vs age  $< 5$

**Table 2** Glomerular filtration rate (ml/min per 1.73 m<sup>2</sup>) measured by EDTA clearance and estimated by the formula of Schwartz et al. [17]

Treatment	Entry		Five years		Ten years	
	No.	Mean (SD)	No.	Mean (SD)	No.	Mean (SD)
<b>Medical</b>						
EDTA clearance	136	114 (24)	148	120 (24)	38	115 (27)
Formula clearance	132	106 (29)	144	115 (20)	60	121 (23)
<b>Surgical</b>						
EDTA clearance	133	115 (27)	141	119 (26)	31	119 (16)
Formula clearance	126	105 (21)	141	117 (18)	52	123 (33)

**Table 3** Number of children with symptomatic recurrence of UTI according to gender, treatment modality and time period in the 252 patients who completed a 10-year clinical follow up. Data for children with febrile infection are shown in parentheses. Febrile recurrences occurred more often in children treated medically than surgically ( $P<0.03$ )

Period	Girls		Boys	
	Medical ( $n=94$ )	Surgical ( $n=97$ )	Medical ( $n=33$ )	Surgical ( $n=28$ )
	Girls with recurrence		Boys with recurrence	
0–5 years	25 (17)	34 (12)	5 (5)	2 (2)
5–10 years	26 (15)	21 (5)	5 (3)	3 (1)
Total 0–10 years <sup>a</sup>	40 (26)	46 (15)	8 (6)	4 (2)

<sup>a</sup>Some children with recurrence in the first period had a further recurrence in the second period

years at entry ( $P=0.001$ ). The resolution of VUR was not affected by renal scarring at entry or gender. Reflux was seen intermittently during follow up in 24 children, and, of those, only four had reflux with dilatation at 10 years.

Among the 80 children assigned at entry to the 'sideline group' with medical management, 75 were followed for 5 years and 47 up to 10 years. Of these, 15 (32%) had reflux with dilatation at 5 years and seven (15%) at 10 years [14].

### Body growth

Data on body height and weight for the 10-year study period were available for 236 patients (medical 118, surgical 118). At 10 years, there was no significant difference in height or weight between the two treatment groups [12]. Furthermore, this result was not influenced by grade of VUR, renal parenchymal scars or UTI.

## Discussion

VUR has consistently been found in 30–40 % of all young children investigated for febrile UTI and has a natural tendency to improve or cease with time. Reflux with dilatation represents only a small proportion [20, 22]. It was thus considered necessary to set up a multicentre study to enter sufficient children with grades III or IV VUR to obtain a statistically significant result. Grade V reflux is generally regarded as part of a widespread malformation of the renal tract, and such children were not included. It had already been demonstrated by the early 1980s, when the IRSC was initiated, that lesser grades of reflux are likely to resolve spontaneously and that when the urinary tract was

**Table 4** Maximum grade of vesicoureteral reflux in each patient at entry and at 5 years and 10 years in 102 medically managed patients followed for up to 10 years

Maximum grade of reflux	Number at entry	Number at 5 years	Number at 10 years
IV	83	51	22
III	19	6	5
Total with dilating reflux	102	57	27

kept free from infection during this period of resolution, new renal scars were rarely observed [1].

In the 302 children (153 medical, 149 surgical) who completed at least 6 months and up to 5 years of follow up, and also among the 223 who continued radiological follow up to 10 years (113 medical, 110 surgical), there was no significant difference between the treatment groups in the overall number who developed new urographic renal scars, the main end point, impairment of renal growth or function, deterioration of DMSA image or differential function, or recurrence of symptomatic UTI. The only difference observed was that over the 10-year period a higher proportion of children in the medically treated group had a febrile recurrence of UTI, 32 of 127, compared with 17 of 125 in the surgically treated group ( $P<0.03$ ), but this was not accompanied by deterioration of kidney growth or loss of renal function. In this study, febrile UTI appeared to be a less serious event at a recurrence than at the first diagnosed UTI. This may be explained, at least partly, by the increased awareness of a recurrence and its implications by both the families and their doctors, resulting in a more rapid start of treatment. Furthermore, Szlyk et al. found a relatively low risk of renal damage at a recurrence by showing that only five (15%) of 34 children with VUR and febrile breakthrough UTI had renal inflammatory changes on acute DMSA scan [23].

Many of the reports of large series of children, in whom VUR was corrected surgically, some demonstrating over 95% success rates, included the more common, milder, grades less prone to complications [24]. It is among the less common children with severe reflux with dilatation of the upper urinary tract that surgical complications are more likely to occur. In this study, six of the new scars that developed in the surgical group were associated with postoperative obstruction, three in boys under 2 years of age [6].

Approximately half of the children had renal scarring at entry, a common finding among children with severe reflux [20], though it is not possible to know what proportion was congenital or acquired. In 31% of those with scarring it was bilateral. Renal scarring was of the more extensive types B, C or D in 94 (63 %) of 149 children entering the study with scarred kidneys. Nevertheless, in only one patient, the GFR deteriorated to below the minimal entry value of 70 ml/min per 1.73 m<sup>2</sup>. No patient developed hypertension during the first 5 years, while three patients in the medical group were

deemed to need treatment during the 5–10 year follow-up period. These favourable findings are in contrast to the result of a randomized treatment trial of 52 children with bilateral renal scarring and bilateral severe VUR, including grade V, and with an entry GFR of >20 ml/min per 1.73 m<sup>2</sup> [25]. In the latter study there was no difference after 10 years between the groups treated medically and surgically, but four children (two medical, two surgical) developed end stage renal disease, and seven developed hypertension that required treatment. This emphasizes the importance of renal function at entry.

The IRSC was set up to compare two methods of treatment, medical or surgical, and not to study the pathogenesis of acquired renal scars or the efficacy of prophylaxis. The timing of imaging was set by protocol and not in relation to any recurrence of UTI. Without serial imaging from birth it is not possible to distinguish between congenital dysplastic or hypoplastic kidneys and those with acquired scars. So far, this is more of a theoretical than practical clinical interest, since it is not known if there is a different long-term risk in those with congenital, as compared to acquired, renal damage. Based on DMSA scintigraphy alone, it can be difficult to determine if an uptake defect represents acute inflammatory changes or permanent scarring [26, 27]. Transient uptake defects have been observed on scans up to 5 months after renal infection [28]. Thus, to verify permanent renal damage, one needs to perform a DMSA scan at least 6 months after the acute infection. On the other hand, the progressive structural changes of scarring may not be fully evident for some time [29]. In this study, by the demonstration of such structural change in serial IVUs, it was possible to identify development of new scars in the previously unscarred kidneys of 25 children among the 42 patients who developed new scars, and progression of the scarring in 63 of the 149 children with renal scarring at entry [5]. A further 22 children who entered the study with scarred kidneys were known to have had radiologically normal kidneys on earlier IVUs.

It would be of considerable interest to extend the follow-up period of this group for a further decade. This is clearly not feasible in a multi-centred, multi-national study. Methods of investigation and management change, but future studies can be planned, using some of the information from the IRSC as a basis.

To conclude, in this study of children with severe reflux entering with good renal function, a regimen of closely monitored care over the long-term, and collaboration between consultants and primary care providers, there was no evidence over 10 years of any significant difference in outcome between the two treatment methods in relation to acquisition of new renal scars, or to renal growth or function.

A decision on the appropriate treatment of an individual child should rest on the available local expertise and on anticipated compliance [10]. When medical factors do not clearly favour either medical or surgical management, family preferences should be respected. It is expected that most children will do well in the long term, but for the

small number with extensive kidney damage, especially when bilateral, monitoring should include blood pressure and excretory function assessment.

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