

**Non-animal hyaluronic  
acid/dextranomer gel (Deflux<sup>®</sup>)  
endoscopic treatment  
in grade IV VUR Results  
after 15–25 years:  
durable and effective**

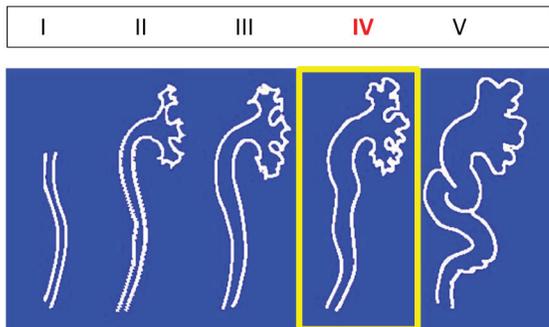
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## INTRODUCTION

- High-grade vesicoureteral reflux (VUR; Figure 1) is associated with a risk of febrile urinary tract infections (UTIs) and pyelonephritis.<sup>1,2</sup>
- Endoscopic injection is minimally invasive and offers the chance of curing VUR while enabling avoidance of ureteral reimplantation (open surgery).<sup>3,4</sup>
- Before availability of endoscopic treatment, all patients with pyelonephritis and grade IV VUR received antibiotic prophylaxis for  $\geq 1$  year. If dilating reflux persisted, these patients were treated by open surgery.
- We performed a long-term, observational study of children with grade IV VUR undergoing endoscopic injection of non-animal hyaluronic acid/dextranomer gel (Deflux®; Palette Life Sciences) and compared two 5-year treatment periods.<sup>5</sup>

Figure 1. Grades of vesicoureteral reflux.



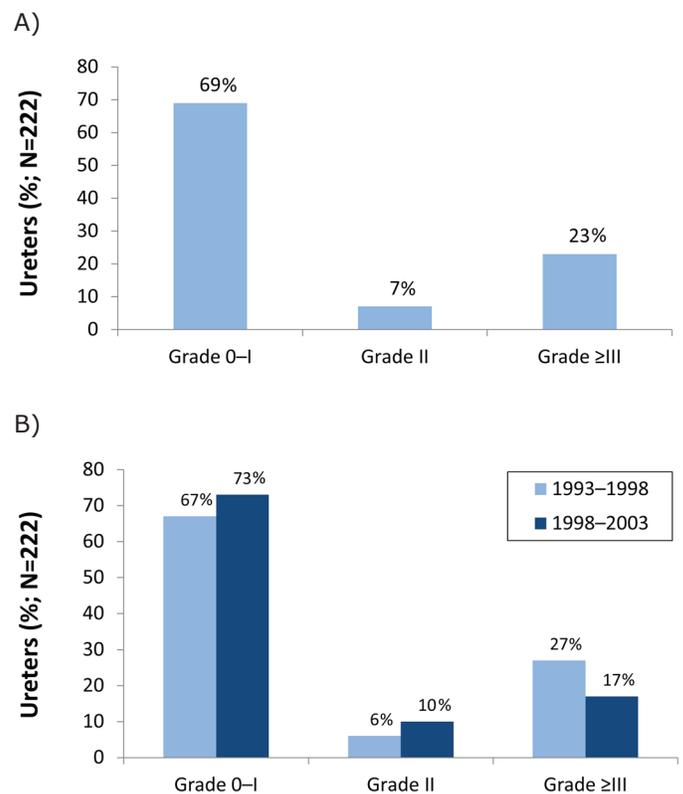
## METHODS

- Children with persisting grade III–V VUR and UTIs attending Uppsala University Hospital routinely received endoscopic treatment with Deflux.
- Inclusion criteria for this study were: children with grade IV VUR diagnosed by voiding cystourethrogram (VCUG); dilating VUR persisting for  $>1$  year; breakthrough febrile UTIs or poor compliance with antibiotic prophylaxis; and treatment with Deflux between 1993 and 2003.
- All study patients were diagnosed with VUR after pyelonephritis.
- Exclusion criteria were: endoscopic treatment with agents other than Deflux; neurogenic bladder dysfunction; previous ureteral surgery; bladder exstrophy and urethral valve.
- After endoscopic treatment, patients exhibiting grade  $\geq III$  VUR were offered repeat endoscopic treatment (maximum three procedures), or they could choose ureteral reimplantation (open surgery).
- In 2018 (15–25 years after endoscopic treatment), patients' charts from Uppsala University Hospital and local county hospitals were studied, and post-treatment VCUG results were analyzed.
  - For analyses of reflux grade after endoscopic treatment, any patients/ureters with missing data were excluded.

## RESULTS

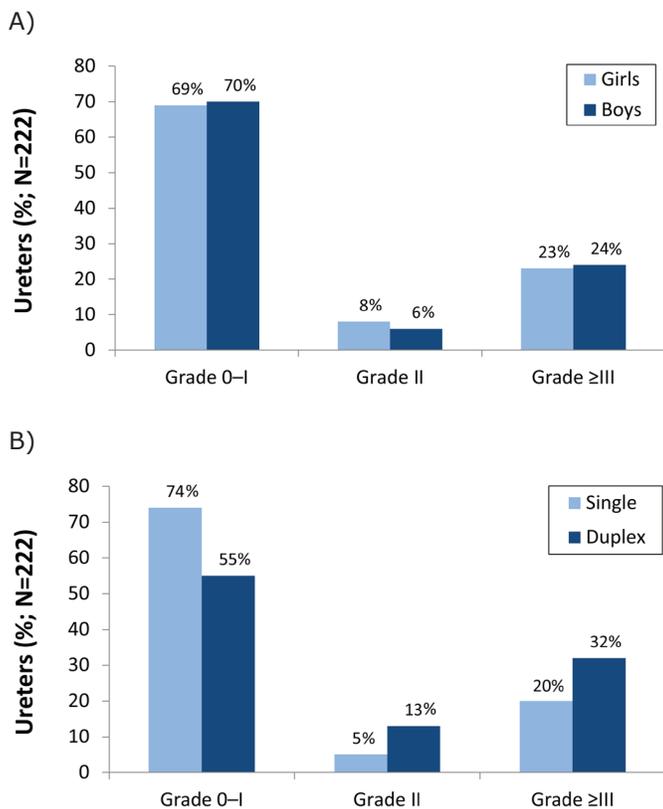
- Between 1 May 1993 and 30 April 2003, 185 patients (69 boys, 116 girls) were treated endoscopically and included in the current study; 237 ureters with grade IV VUR were treated.
- The mean number of endoscopic treatments per patient was 1.46 (1.50 during the first 5-year study period and 1.40 during the second period).
- The mean volume of Deflux injected was 0.73 mL/ureter – significantly higher during the second versus the first 5-year study period: (0.86 vs 0.64 mL;  $p < 0.0001$ ).
- According to the last VCUG, 69% of ureters showed positive response (VUR grade 0–I), 7% had VUR grade II and 23% had VUR grade  $\geq III$  (Figure 2).
- Minimal differences between boys and girls were observed in reflux grade at the last VCUG (Figure 3;  $p$ -value not significant).
- Single ureters showed significantly improved response compared with double ureters (Figure 3;  $p = 0.0225$ ).
- Similar patterns were observed when the results were analyzed 'by patient' instead of 'by ureter'.

Figure 2. Reflux grade at the last VCUG. Data are shown by ureter, for all patients (A), and for patients treated in the first versus the second 5-year time period of the study (B).\*



\*Ureters for which no VCUG test was performed after the last endoscopic treatment were excluded from the analyses

**Figure 3.** Reflux grade at the last VCUG. Data are shown by ureter, for girls versus boys (A), and for single versus double ureters (B).\*



\*Ureters for which no VCUG test was performed after the last endoscopic treatment were excluded from the analyses

- 46 patients (25%) – 29 females (25%) and 17 males (25%) – required ureteral reimplantation during follow-up.
  - Of these, 41 underwent surgery ‘early’ (mean 6 months after the last VCUG due to persistent grade III–V VUR).
- Five patients (3%) underwent surgery ‘late’, 6–10 years after the last VCUG:
  - one male and one female: recurrent VUR after treatment for lower UTI and bladder dysfunction
  - two females: obstructive refluxing megaureter at the time of Deflux treatment (now a contraindication)
  - one female: late obstruction and pyelonephritis 10 years after the last VCUG.
- In one male, calcification around the Deflux implantation site was observed during routine examination 2 years after endoscopic treatment; no intervention was required.
- There were no further long-term adverse events or complications. Thus, no safety issues were observed in 97% of the study population.

## DISCLOSURES

- Göran Läckgren: Speaker at teaching courses for Ferring AB, Sweden; Medical adviser and speaker at instructional courses for Palette Life Sciences, Inc.
- All other authors: None.

## KEY DIFFERENCES BETWEEN THE TWO 5-YEAR STUDY PERIODS

- The injection technique changed from the standard STING method during the first 5-year period, to injection directly into the ureteral mucosa at the orifice during the second period.
- There was a significant increase in the mean injection volume (34%;  $p < 0.0001$ ) during the second 5-year period of the study.
- Patients with obstructive refluxing megaureter, and those shown to have a narrow distal ureter, were no longer treated endoscopically during the second 5-year period.
- As a result of these changes, a trend towards an improved positive response rate (VUR grade 0–I) was observed during the second versus the first study time period (Figure 2).
- There was a significant decrease in the percentage of patients undergoing ureteral reimplantation during the second versus the first period (31% vs 16%;  $p = 0.0365$ ).
- The risk of adverse events remained low throughout the study.

## CONCLUSIONS

- Treatment with Deflux was shown to be durable and effective during a follow-up period of 15–25 years.
- Three-quarters of patients did not need ureteral reimplantation.
- Optimal placement and higher injection volumes were associated with a trend towards improved success.
- There was a low risk of late clinical recurrence (UTI, persistent VUR, or need for open surgery).
- Endoscopic injection of Deflux is a viable option for patients with grade IV VUR, including those with double ureters.

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