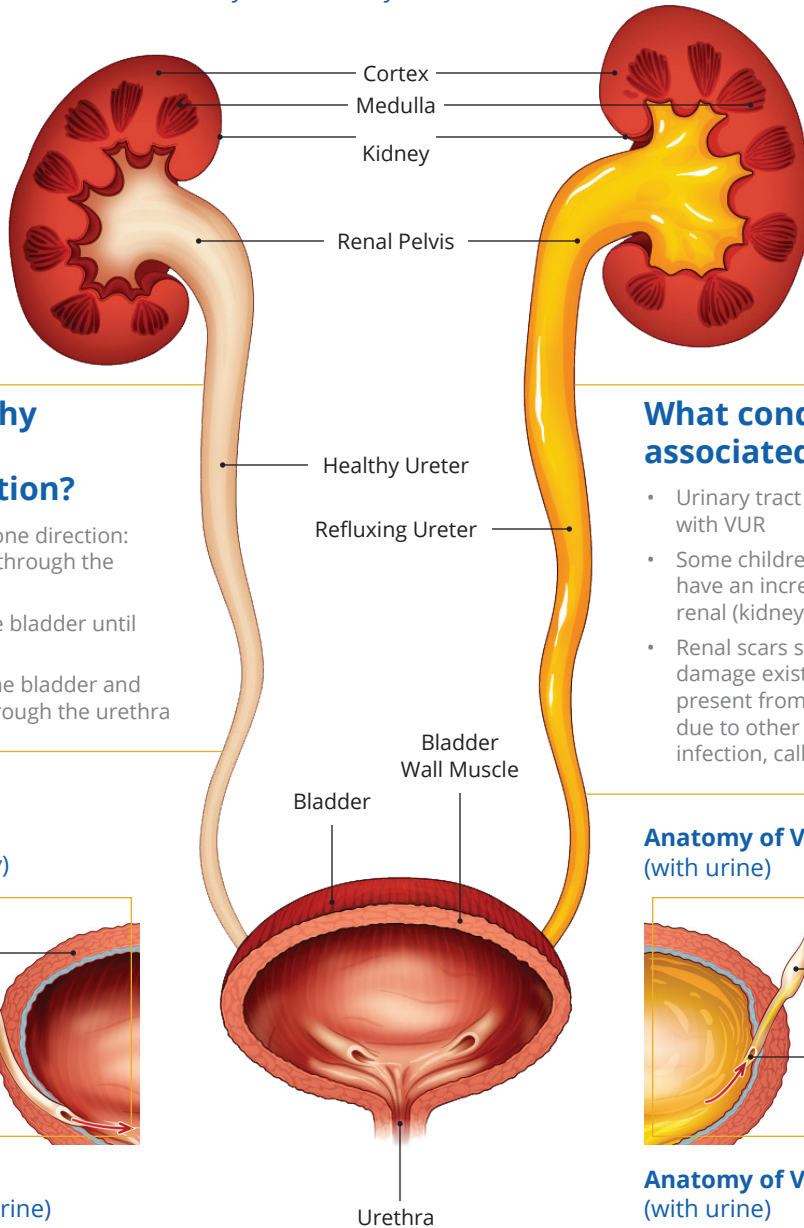


Understanding Vesicoureteral Reflux (VUR)

What is VUR?

VUR occurs when the ureter opening located at the joining of the ureter and the bladder does not close properly. This causes urine to flow back up (reflux) from the bladder to the ureters and eventually to the kidneys.



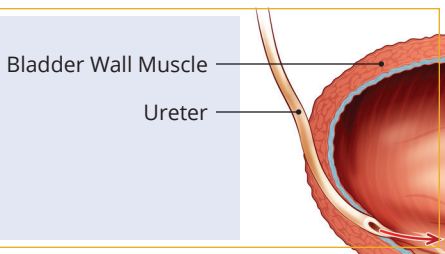
How does a healthy kidney, ureter and bladder function?

- Urine normally flows in one direction: down from the kidneys, through the ureters, to the bladder
- The urine is stored in the bladder until urination occurs
- Urine is released from the bladder and flows out of the body through the urethra

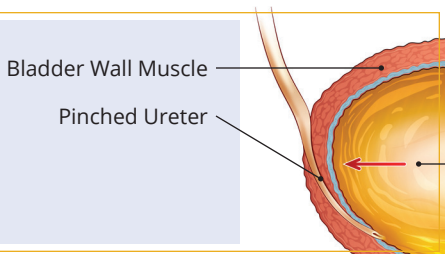
What conditions are associated with VUR?

- Urinary tract infection (UTI) is associated with VUR
- Some children with VUR and febrile UTI have an increased risk of developing renal (kidney) scars
- Renal scars suggest that areas of renal damage exist, which may have been present from birth, or may have occurred due to other causes such as a kidney infection, called pyelonephritis

Healthy Bladder (empty)

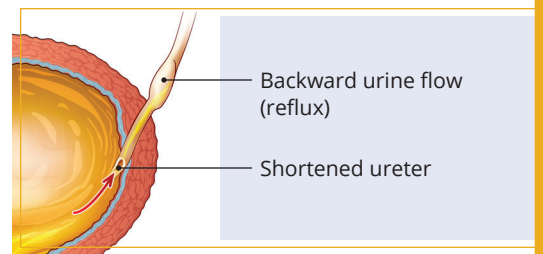


Healthy Bladder (with urine)

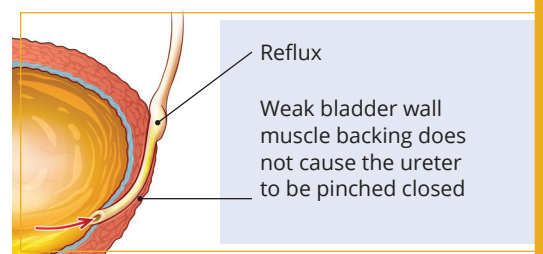


Pressure from a full bladder causes the ureter opening to be pinched closed like a straw

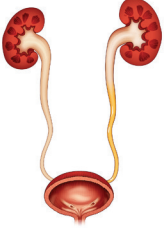
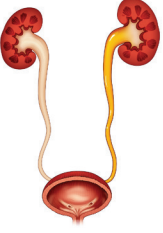
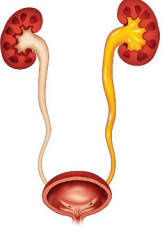
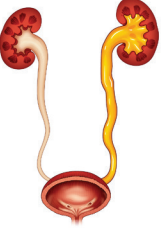
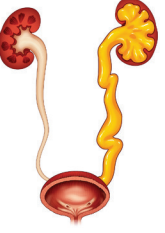
Anatomy of VUR - Shortened Ureter (with urine)



Anatomy of VUR - Weak Bladder Wall (with urine)



Grades of VUR¹

| Grade 1 | Grade 2 | Grade 3 | Grade 4 | Grade 5 |
|-------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|  |  |  |  |  |
| The mildest form of VUR. Urine enters the ureter but does not travel all the way up to the kidney. The ureters look normal in size. | Urine travels all the way up the ureter and enters the part of the kidney where urine is collected before it drains to the ureter (renal pelvis). The ureters and renal pelvis appear normal in size. | Similar to grade 2, except the ureters and/or the renal pelvis appear abnormal in size or shape. | Similar to grade 3, except the ureter is grossly enlarged. | The most severe form of VUR. Similar to grade 4, except the ureter is also twisted and curved. The renal pelvis is also enlarged and its normal structural details are no longer detectable. |

What is Deflux™ Injectable Gel?

Deflux is a gel made from two naturally occurring sugars, hyaluronic acid and dextranomer, and is indicated for the treatment of children with VUR grades 2-4. A pediatric urologist injects Deflux in or around the ureter opening (where the ureter joins the bladder). Deflux has been used safely and effectively for over 20 years, showing up to 93% success rates after one treatment.²

Will VUR resolve on its own?

The percent chance of reflux resolution after specified number of years (95% confidence interval)^{3*}

| RISK CATEGORY age in months; number of patients on which estimates are based | 1 YEAR | 2 YEARS | 3 YEARS | 4 YEARS | 5 YEARS |
|------------------------------------------------------------------------------------|----------------------------|----------------------------|----------------------------|----------------------------|----------------------------|
| Grade 1[†] N=15 | 39.3 (24.6-51.1) | 63.1 (43.2-76.1) | 77.6 (57.2-88.3) | 86.4 (67.7-94.3) | 91.8 (75.7-97.2) |
| Grade 2[†] N=250 | 28 (24.1-31.7) | 48.1 (42.3-53.4) | 62.7 (56.2-68.1) | 73.1 (66.8-78.2) | 80.6 (74.8-85.1) |
| Grade 3, unilateral, age 0-24 N=27 | 21.4 (10.8-30.8) | 38.2 (20.4-52.1) | 51.5 (29-66.8) | 61.9 (36.6-77.1) | 70 (43.5-84.1) |
| Grade 3, unilateral, age 25-60 N=27 | 13.4 (4.6-21.4) | 25 (8.9-38.3) | 35.1 (13.1-51.5) | 43.8 (17.1-61.9) | 51.3 (20.9-70.1) |
| Grade 3, unilateral, age 61-120 N=15 | 10.8 (3.5-17.5) | 20.5 (6.9-32) | 29.1 (10.2-43.9) | 36.7 (13.4-53.8) | 43.6 (16.5-61.9) |
| Grade 3, bilateral, age 0-24 N=62 | 12.7 (7-18.1) | 23.8 (13.5-32.9) | 33.5 (19.5-45) | 41.9 (25.1-55) | 49.3 (30.3-63.1) |
| Grade 3, bilateral, age 25-60 N=53 | 7 (3.1-10.8) | 13.5 (6.1-20.4) | 19.6 (9-28.9) | 25.2 (11.8-36.6) | 30.5 (14.6-43.4) |
| Grade 3, bilateral, age 61-120 N=14 | 2.6 (0.7-4.5) | 5.2 (1.4-8.8) | 7.7 (2.1-13) | 10.1 (2.8-16.9) | 12.5 (3.5-20.7) |
| Grade 4, unilateral[‡] N=28 | 16.1 (8.5-23.1) | 29.7 (16.4-40.8) | 41 (23.5-54.5) | 50.5 (30-65) | 58.5 (36-73.1) |
| Grade 4, bilateral[‡] N=96 | 4.5 (1-7.9) | 6.4 (2-15.1) | 7.8 (3-21.8) | 8.9 (4-28) | 9.9 (4.9-33.7) |

* The yearly rate of reflux resolution remains constant for each group

[†] No difference shown by age or laterality (unilateral/bilateral); therefore, these categories were combined

[‡] Estimates only apply to the time of diagnosis and are not age specific.

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- Elder JS, Peters CA, Arant BS, et al. AUA pediatric vesicoureteral reflux clinical guidelines panel: The management of primary vesicoureteral reflux in children. *American Urological Association Education and Research, Inc.* 1997.

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Important information about Deflux

Deflux™ injectable gel is indicated for treatment of children with vesicoureteral reflux (VUR) grades II-IV. As with any medical procedure, individual results may vary. The following adverse events were associated with the use of Deflux gel from spontaneous post-marketing surveillance reporting or from clinical studies (occurring >2%) and include but are not limited to: ureteral obstruction with or without hydronephrosis (some cases requiring temporary placement of a ureteric stent, and rare cases of ureteral re-implant procedures), hematuria, urgency, frequency, pyelonephritis, foreign body reaction, calcification, pyrexia, hypertonic bladder, bladder irritation, Henoch-Schonlein purpura, delayed ureteral obstruction; impact on renal function; newly detected contralateral VUR; and pelvic, lateral or flank pain. More information on indications, contraindications, warnings and instructions for use can be found in the Instructions For Use at <https://www.deflux.com/important-safety-information/>.

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