The anatomy of a fallible paradigm: Vesicoureteral reflux and the limits of surgical certainty

Ali Khatib, Andrew E. MacNeily
Department of Urologic Sciences, University of British Columbia, Vancouver, BC, Canada

Cite as: Khatib A, MacNeily AE. The anatomy of a fallible paradigm: Vesicoureteral reflux and the limits of surgical certainty. *Can Urol Assoc J* 2026 November 20; Epub ahead of print http://dx.doi.org/10.5489/cuaj.9982

Published online November 20, 2026

Corresponding author: Dr. Ali Khatib, Department of Urologic Sciences, University of British Columbia, Vancouver, BC, Canada; akhatib1@student.ubc.ca

***

INTRODUCTION

KEY MESSAGES

- Vesicoureteral reflux has evolved from a fixable anatomical defect to a heterogeneous, risk-stratified condition.
- The history of VUR demonstrates how a compelling biological theory shaped surgical practice for decades before being rigorously tested.
- Randomized trials clarified rather than resolved uncertainty, demonstrating that reducing recurrent urinary tract infections did not consistently prevent renal scarring.
- Modern VUR management relies on risk stratification, clinical judgment, and shared decision-making rather than routine intervention.

A paradox in pediatric surgery

The evolution of the treatment paradigm of vesicoureteral reflux (VUR) offers a clear example of how surgical practice can become so entrenched in assumption that it resists accumulating evidence for decades. It also reveals something deeper: the limits of what evidence alone can resolve. VUR is the retrograde flow of urine from the bladder into the ureters and kidneys during voiding, increasing the risk of urinary tract infections (UTIs). In some children, VUR with infection can lead to renal scarring and, in severe cases, long-term sequelae such as hypertension or chronic kidney disease (CKD). It is predominantly a pediatric presentation, occurring in approximately 1% of children (30-40% in those investigated following a UTI), with most low-grade cases resolving spontaneously with age.[1,2] For decades, VUR presented a paradox in pediatric surgery: a seemingly straightforward anatomical defect that appeared to justify corrective surgery to prevent renal complications, yet intervention did not consistently reduce those complications.

© 2026 Canadian Urological Association

The origins of a paradigm: Hutch and the case for correction

In the early 1950s, the American urologist John Hutch described VUR in paraplegic patients at a Veterans Administration hospital. He observed that it was persistently associated with progressive renal deterioration and accounted for most of the deaths among his patients. His conclusion, presented to the American Urological Association in 1951, was simple: reflux causes renal damage, and correcting the anatomy should prevent it. He therefore developed a surgical approach to restore the competence of the ureterovesical junction.[3] Although his evidence was anecdotal, the population highly selected, and the causal inference direct, the paradigm it generated would guide pediatric urology for decades. Hutch's premise was simple; correct the anatomy, prevent the damage.[1] The assumed pathophysiology was that reflux drives infected urine into the upper tract, leading to pyelonephritis, renal scarring, and long-term morbidity, including hypertension, proteinuria, and CKD.[1,2] On this basis, clinicians pursued increasingly effective interventions: open ureteral reimplantation, continuous antibiotic prophylaxis, and later minimally invasive endoscopic techniques.

However, the premise that correcting reflux prevents renal damage has not held up. Beginning in the 1990s, randomized trials and long-term follow-up studies have shown that, while interventions may reduce UTIs, they do not meaningfully alter the outcome that justified treatment: renal scarring.[4,5] On the other hand, the natural history of VUR has proven more favorable than initially believed, with many children faring well regardless of intervention.[6,7] Clinical practice has accordingly shifted toward risk stratification, selective treatment, and, in many cases, simple observation. In the case of VUR, evidence did not resolve uncertainty. It exposed it.[2]

Building the biological case: The "big bang" theory

VUR first entered clinical thinking with Hutch's observations in paraplegic patients with neurogenic bladder.[3] These findings linking reflux to renal damage were then generalized to otherwise healthy children presenting with UTIs, establishing a broader causal framework. Experimental work in the 1970s initially appeared to build on this framework. In porcine models, for example, Ransley and Risdon surgically induced reflux in piglets and introduced infected urine into the urinary tract. Renal scarring was seen to develop when infected urine was present, but not when it was sterile.[8] These findings offered a compelling biological mechanism linking reflux, infection, and permanent renal injury, and were widely accepted as confirmation of what became known as the "big bang theory" of reflux nephropathy, in which renal scarring was thought to result from acute episodes of infected reflux.[9]

Correlation mistaken for causation

Taken together, Hutch's work and Ransley and Risdon's studies produced a coherent and persuasive framework. However, each had important limitations: selected populations, uncertain timelines, and artificial experimental conditions. Hutch's observations were drawn from adult patients with neurogenic bladder, and Ransley and Risdon's porcine model relied on surgically

© 2026 Canadian Urological Association

induced reflux and deliberate infection, conditions far removed from typical pediatric presentations.[8] These were not secondary considerations but limitations of the evidence itself. Because the model was internally consistent and logically compelling, its gaps remained largely unexamined. Association came to be interpreted as causation, and reflux was treated as an intrinsically pathogenic process despite limited direct evidence.[10] The original model thus rested on correlation rather than causation, a distinction that took decades, and several well-powered trials, to fully interrogate.[10]

Consolidation of practice

By the latter half of the twentieth century, clinical management of VUR had consolidated around two parallel strategies. First was continuous antibiotic prophylaxis as first-line therapy aimed at preventing recurrent UTIs and, by extension, renal injury. The second was surgical correction through ureteral reimplantation in patients with breakthrough infections or more severe disease. Techniques such as Cohen's cross-trigonal reimplantation achieved success rates exceeding 90% and became standard.[1] For more than a decade, the dominant approach was initial prophylaxis, with surgery if conservative management failed. Intervention persisted not because outcomes confirmed it, but because the causal model underlying it was never meaningfully challenged.[10]

Evidence that failed to disrupt the model

Even early attempts to challenge this model failed to displace it. For example, in the 1980s, the International Reflux Study randomized children with higher-grade VUR to prophylaxis or surgery and found no meaningful difference in renal scarring.[7] Notably, the trial compared prophylaxis against surgery but included no observation arm, an omission that itself reflected the prevailing assumption that intervention was always warranted. Rather than undermining intervention, these findings were absorbed as validation of both approaches, and the paradigm remained intact. This reflects not only the structure of the evidence, but a deeper problem: confirmation bias, in which disconfirming findings were assimilated into the existing framework rather than used to challenge it. The approach to intervention was initially challenged by evidence that many cases of VUR resolve spontaneously. In 1976, Lenaghan and colleagues showed that lower-grade VUR could resolve spontaneously over time in a substantial proportion of patients.[11] Although this finding did not disrupt the prevailing model, lower grades were managed expectantly, while higher grades prompted treatment escalation. Observation did not replace intervention; it was incorporated into the existing framework. A true shift in clinical approach required a higher level of evidence.

The trials that changed the question

Randomized controlled trials (RCTs) in the late twentieth and early twenty-first centuries directly tested established interventions against the outcomes they were meant to prevent. What emerged was not refinement, but disruption. Early RCTs demonstrated that antibiotic prophylaxis did not significantly reduce recurrent infection or the development of new renal scars.[12,13] A large

© 2026 Canadian Urological Association

placebo-controlled trial clarified the pattern further: prophylaxis modestly reduced UTIs but had no effect on scarring.[14] The RIVUR trial, published in 2014, provided the most rigorous evaluation to date and reached the same conclusion.[5] The PREDICT trial showed that the same was true in higher-risk infants with severe reflux; UTIs decreased, scarring did not.[4] Notably, the PREDICT trial found that new renal defects occurred independently of infection, further challenging the presumed causal pathway. Across studies, a consistent conclusion emerged: interventions reduce infections, but they do not meaningfully change the outcome they were intended to prevent.[2,15] When the primary endpoint proves unmodifiable, the case for routine intervention becomes uncertain. Evidence has clarified what can be modified, but not what ultimately matters.

Why the evidence couldn't settle it

Part of the problem lies in the outcome itself. Renal scarring is relatively uncommon and difficult to measure reliably. Even in large trials, new scar formation occurs in only 8-10% of children, limiting statistical power.[5] Assessment is also subject to interobserver variability, as seen in the interpretation of renal scar imaging in the RIVUR trial.[2] These constraints do more than complicate interpretation; they make it harder for evidence to support definitive decisions. At the same time, VUR resists simplification because it is a heterogeneous disorder, not a single disease. Outcomes vary according to age, sex, reflux grade, bladder and bowel dysfunction, congenital renal abnormalities, and whether reflux is detected antenatally or following infection.[2] The distinction between congenital reflux nephropathy and acquired post-infectious scarring highlights this heterogeneity, with each differing in their natural history and response to intervention.[2]

From certainty to risk stratification

Risk stratification has refined management but has not resolved the fundamental question of which patients benefit from intervention. The consequence is not a failure of evidence, but a change in its function. Evidence no longer dictates a single course of action; it defines a range of acceptable options. Clinical guidelines reflect this shift. The American Urological Association, for example, stratifies management based on age, reflux grade, febrile UTI history, and bladder and bowel dysfunction, an approach that acknowledges the absence of a universally applicable strategy.[16] The guideline explicitly acknowledges the evidence cannot support firm standards in many scenarios, offering guidance rather than prescription. This reflects a broader transition in surgery: from selecting the correct treatment to navigating uncertainty between competing, imperfect choices. This is evident in how widely practice varies. That this framework does not resolve disagreement is evident across pediatric urology more broadly, where consensus on clinical care is often difficult to achieve. For example, a 2013 national survey of Canadian pediatric urologists and nephrologists found substantial variability in the management of antenatal hydronephrosis, with fewer than one in five clinicians adhering to a standardized

© 2026 Canadian Urological Association

protocol.[17] This variation does not reflect inconsistency, but rather a divergence grounded in interpretation.

DRAFT

© 2026 Canadian Urological Association

CONCLUSIONS

Judgment in the absence of certainty

The evolution of VUR management illustrates a broader truth of surgical decision-making: when pathophysiology is incompletely understood and outcomes are probabilistic, evidence can clarify uncertainty but cannot eliminate it. In such cases, the task is not to identify a single correct intervention but to choose among competing, imperfect options. VUR management therefore represents not a failure of progress but a transition to a more mature model of care, one in which uncertainty is not eliminated but deliberately navigated. Surgery is built on decisiveness and technical mastery, but VUR demands a different competency: the ability to make careful decisions in the absence of definitive answers. When evidence defines a range of acceptable options rather than a single course of action, that uncertainty places an ethical burden on the surgeon, one that is shared with patients and families.

Despite these uncertainties, several principles now guide contemporary VUR management. Treatment is increasingly individualized according to age, reflux grade, infection history, renal status, bladder function, and likelihood of spontaneous resolution rather than the presence of reflux alone.[18] Younger children, particularly those with lower-grade disease, often undergo initial conservative management, whereas continuous antibiotic prophylaxis remains appropriate in selected higher-risk patients and can reduce UTI recurrence without a proven reduction in renal scarring[4,5,18]. In symptomatic infants diagnosed during the first year of life, initial management commonly includes prophylaxis and surveillance, with intervention considered for breakthrough infections, persistent high-grade reflux, or renal abnormalities. In contrast, in toilet-trained children presenting with UTI with bladder and bowel dysfunction, identification and treatment of the underlying lower urinary tract dysfunction is a central component of management before considering antireflux intervention.[18] The lesson is not that better evidence will resolve this uncertainty, but that surgeons, and those who train them, must be prepared to navigate it through judgment and restraint in intervention, and ultimately to take responsibility for the decision to intervene or not.

© 2026 Canadian Urological Association

REFERENCES

1. Tullus K. Vesicoureteric reflux in children. *Lancet* 2015;385:371-9. https://doi.org/10.1016/S0140-6736(14)60383-4
2. Mattoo TK, Mohammad D. Primary vesicoureteral reflux and renal scarring. *Pediatr Clin North Am* 2022;69:1115-29. https://doi.org/10.1016/j.pcl.2022.07.007
3. Hutch JA. Vesico-ureteral reflux in the paraplegic: Cause and correction. *J Urol* 1952;68:457-69. https://doi.org/10.1016/S0022-5347(17)68223-5
4. Morello W, Baskin E, Jankauskiene A, et al. Antibiotic prophylaxis in infants with grade III, IV, or V vesicoureteral reflux. *N Engl J Med* 2023;389:987-97. https://doi.org/10.1056/NEJMoa2300161
5. The RIVUR Trial Investigators. Antimicrobial prophylaxis for children with vesicoureteral reflux. *N Engl J Med* 2014;370:2367-76. https://doi.org/10.1056/NEJMoa1401811
6. Smellie JM, Prescod NP, Shaw PJ, et al. Childhood reflux and urinary infection: A follow-up of 10-41 years in 226 adults. *Pediatr Nephrol* 1998;12:727-36. https://doi.org/10.1007/s004670050535
7. Jodal U, Smellie JM, Lax H, et al. Ten-year results of randomized treatment of children with severe vesicoureteral reflux: Final report of the International Reflux Study in Children. *Pediatr Nephrol* 2006;21:785-92. https://doi.org/10.1007/s00467-006-0063-0
8. Ransley PG, Risdon RA. The pathogenesis of reflux nephropathy. In: Brod J, Kühn K, eds. Contributions to nephrology. S. Karger AG; 1979:90-7. https://doi.org/10.1159/000402880
9. Decter RM. Update on vesicoureteral reflux: Pathogenesis, nephropathy, and management. *Rev Urol* 2001;3:172-8.
10. Zhang T, Wiygul J. Correlation not causation: Looking back at the history of VUR. *Urology* 2024;193:231-6. https://doi.org/10.1016/j.urology.2024.06.002
11. Lenaghan D, Whitaker JG, Jensen F, et al. The natural history of reflux and long-term effects of reflux on the kidney. *J Urol* 1976;115:728-30. https://doi.org/10.1016/S0022-5347(17)59352-0
12. Garin EH, Olavarria F, Garcia Nieto V, et al. Clinical significance of primary vesicoureteral reflux and urinary antibiotic prophylaxis after acute pyelonephritis: A multicenter, randomized, controlled study. *Pediatrics* 2006;117:626-32. https://doi.org/10.1542/peds.2005-1362
13. Pennesi M, Travan L, Peratoner L, et al. Is antibiotic prophylaxis in children with vesicoureteral reflux effective in preventing pyelonephritis and renal scars? A randomized, controlled trial. *Pediatrics* 2008;121:e1489-94. https://doi.org/10.1542/peds.2007-2652
14. Craig JC, Simpson JM, Williams GJ, et al. Antibiotic prophylaxis and recurrent urinary tract infection in children. *N Engl J Med* 2009;361:1748-59. https://doi.org/10.1056/NEJMoa0902295
15. Williams G, Hodson EM, Craig JC. Interventions for primary vesicoureteric reflux. *Cochrane Database Syst Rev* 2019. https://doi.org/10.1002/14651858.CD001532.pub5

© 2026 Canadian Urological Association

16. Peters C, Skoog SJ, Arant BS Jr. Management and screening of primary vesicoureteral reflux in children (2017). American Urological Association. Available at: https://www.auanet.org/guidelines-and-quality/guidelines/vesicoureteral-reflux-guideline.
17. Braga LHP, Ruzhynsky V, Pemberton J, et al. Evaluating practice patterns in postnatal management of antenatal hydronephrosis: A national survey of Canadian pediatric urologists and nephrologists. *Urology* 2014;83:909-14. https://doi.org/10.1016/j.urology.2013.10.054
18. European Association of Urology. Vesicoureteric reflux. In: EAU guidelines on paediatric urology. Available at: https://uroweb.org/guidelines/paediatric-urology/chapter/vesicoureteric-reflux. Accessed September 24, 2026.

DRAFT

© 2026 Canadian Urological Association