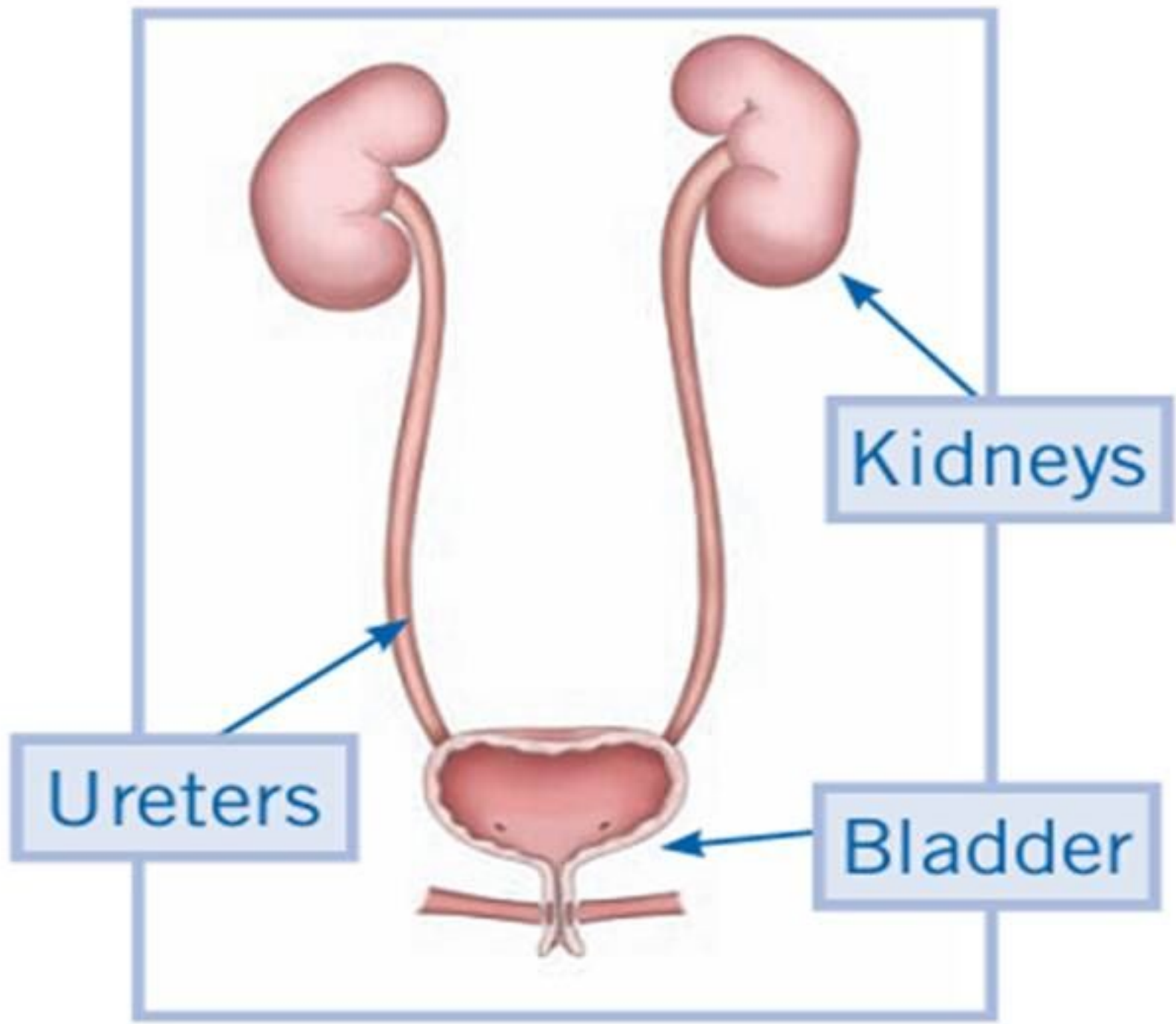




# MINIMALLY INVASIVE TREATMENT FOR VESICoureTERAL REFLUX

Pham Ngoc Thach, Le Tan Son



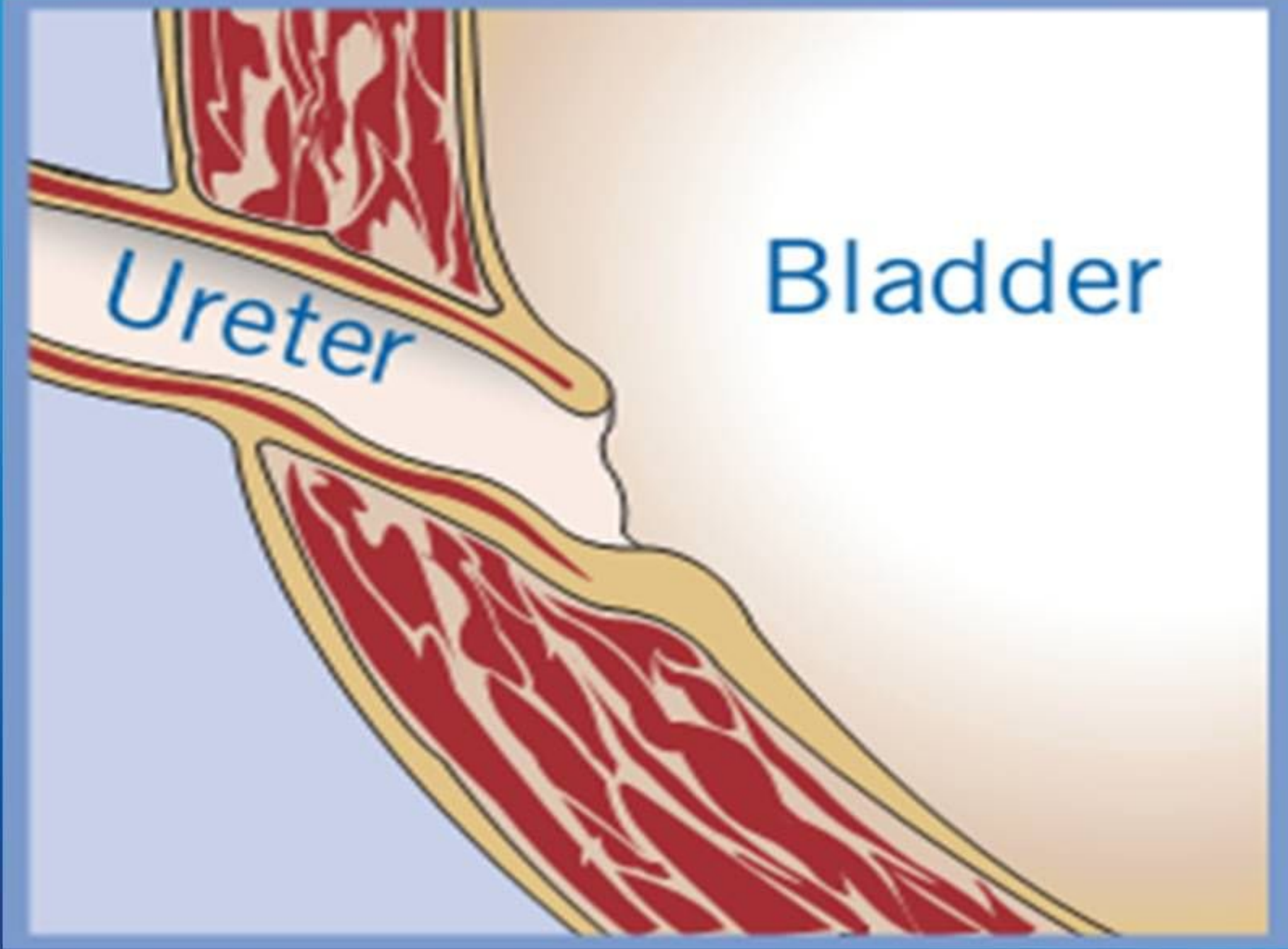
Kidneys

Ureters

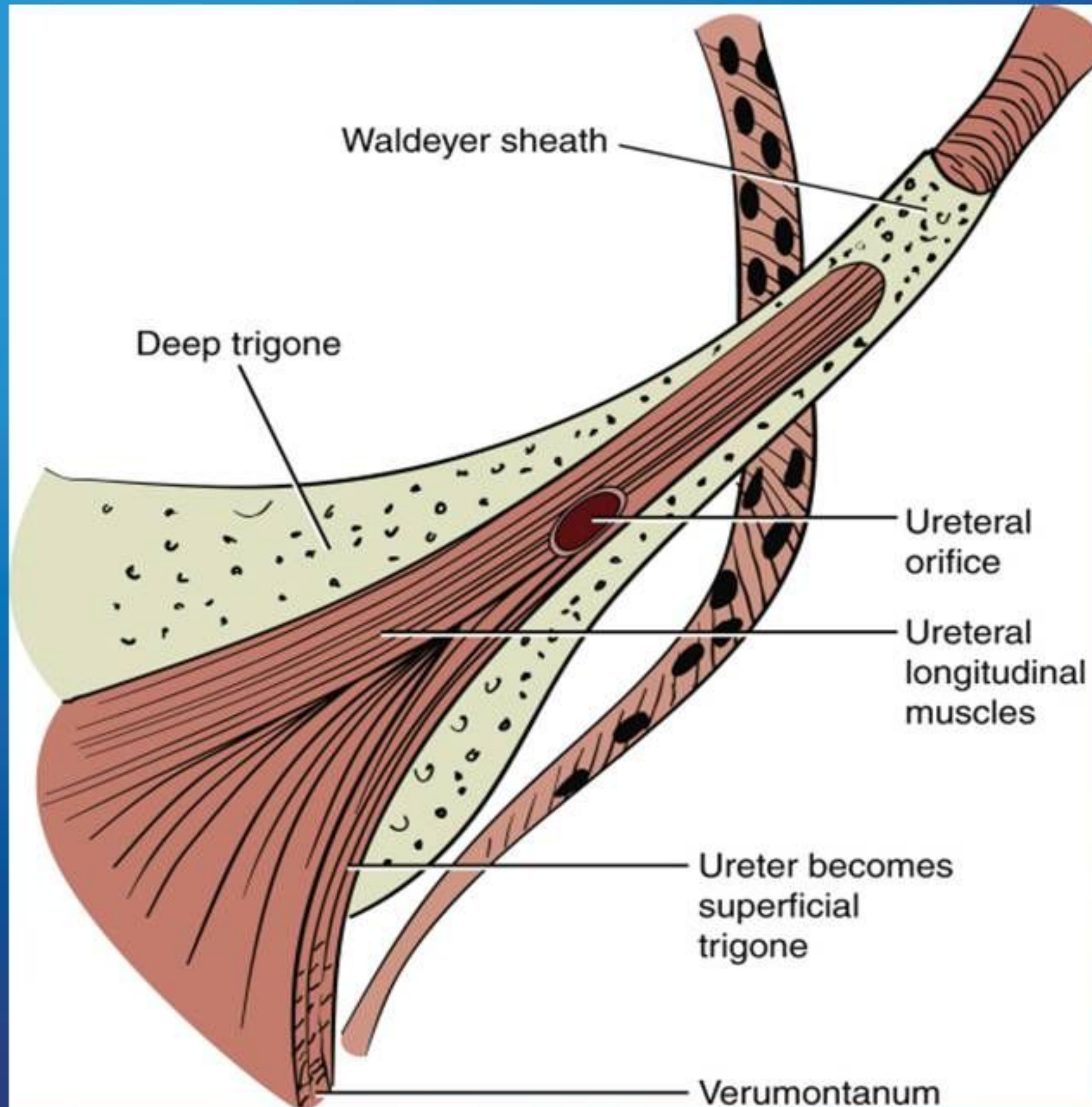
Bladder

Ureter

Bladder







Waldeyer sheath

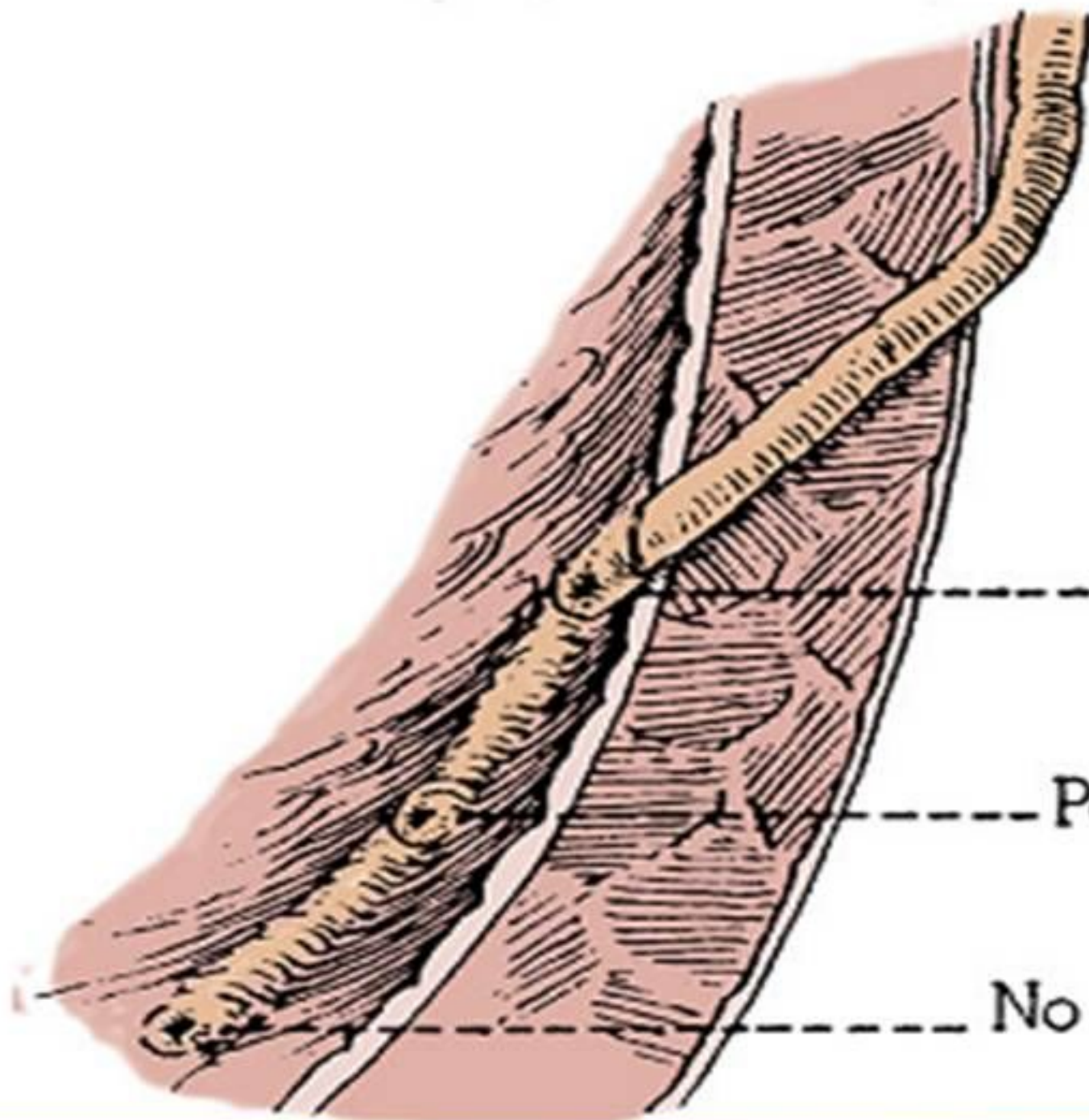
Deep trigone

Ureteral orifice

Ureteral longitudinal muscles

Ureter becomes superficial trigone

Verumontanum

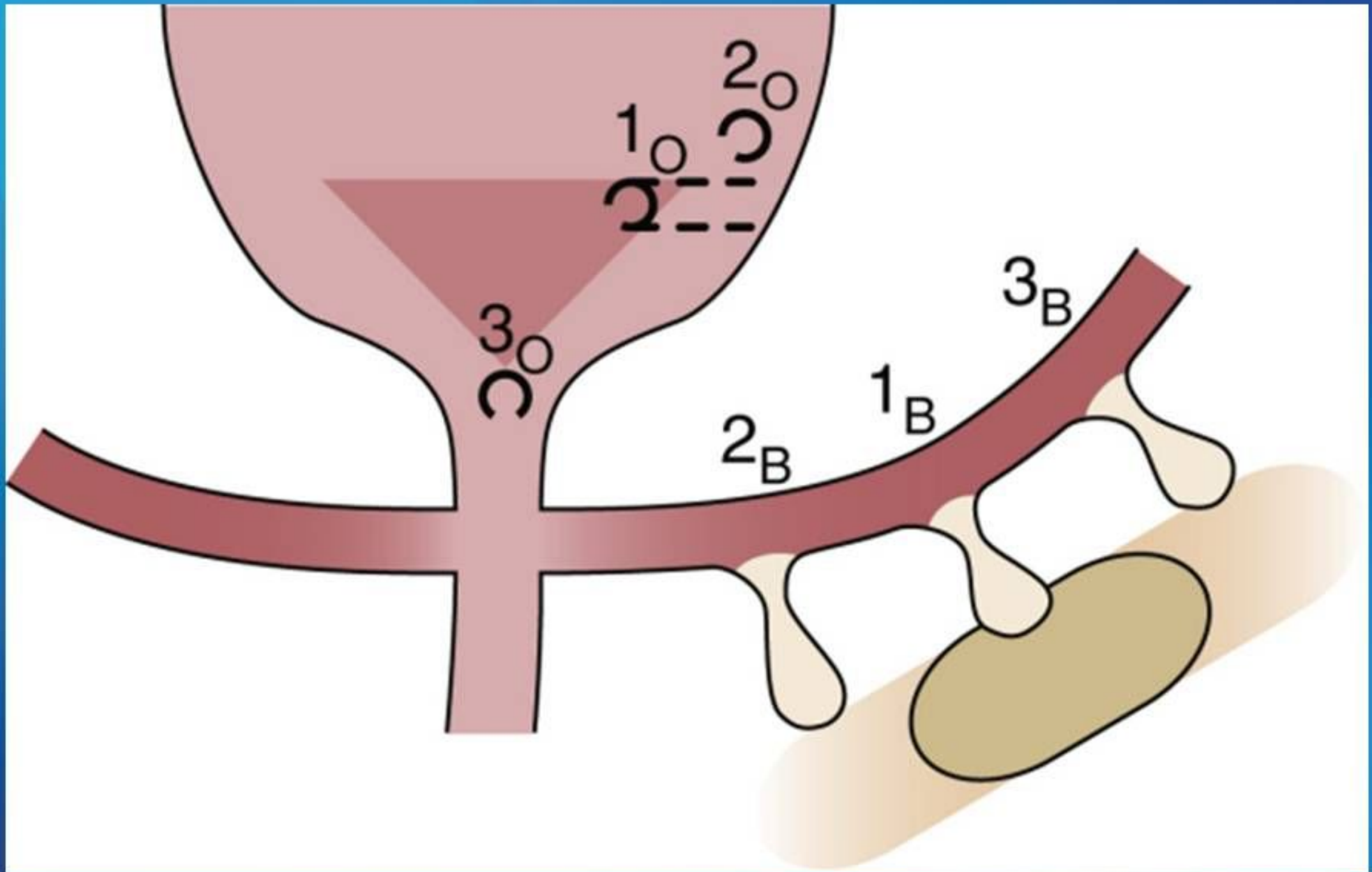


Reflux

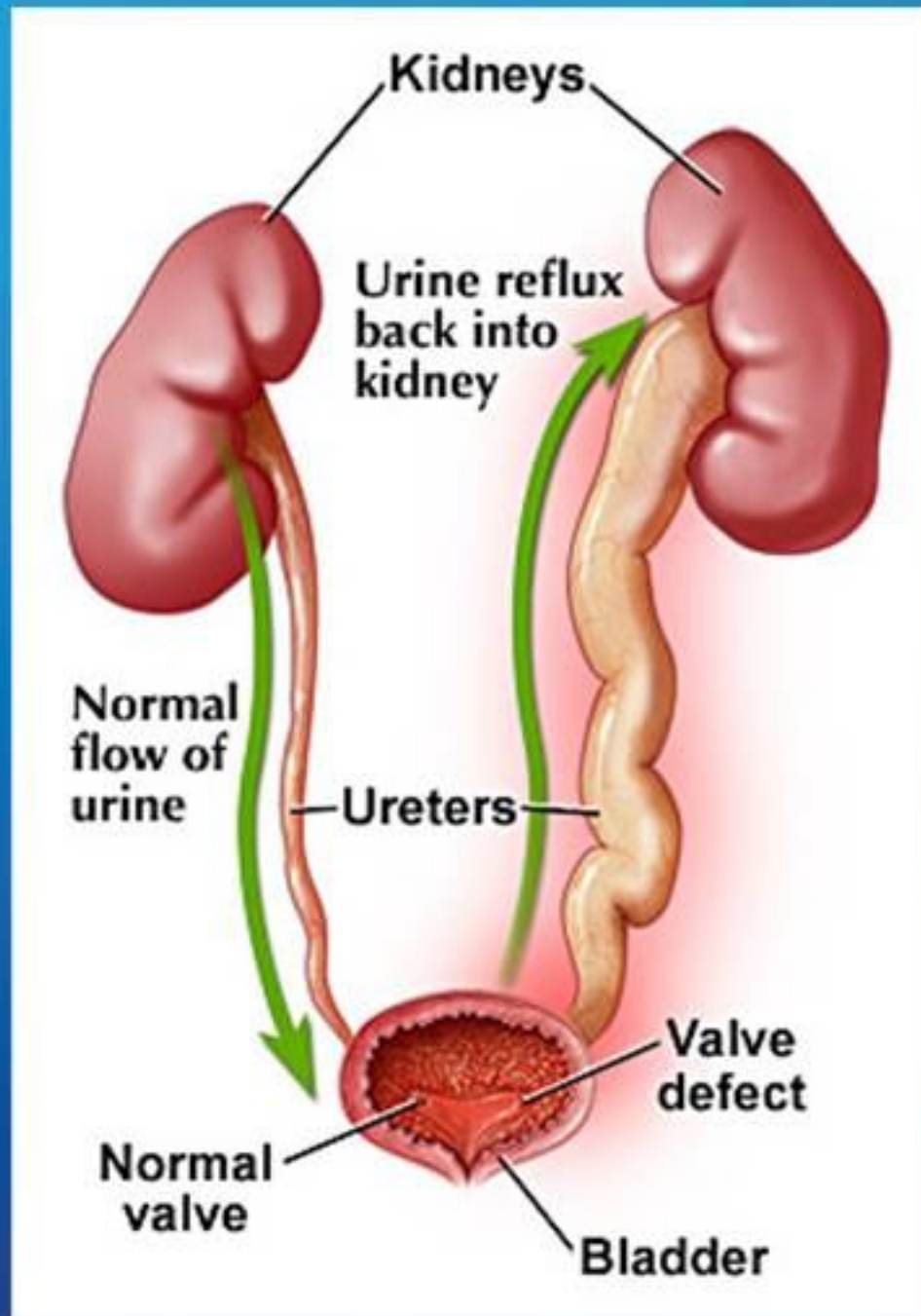
Possible reflux

No reflux





# What is VUR?



- VUR is a bladder valve defect that allows urine to reflux from the bladder through one or both ureters and up to the kidneys
- Febrile urinary tract infection (UTI) is the defining symptom

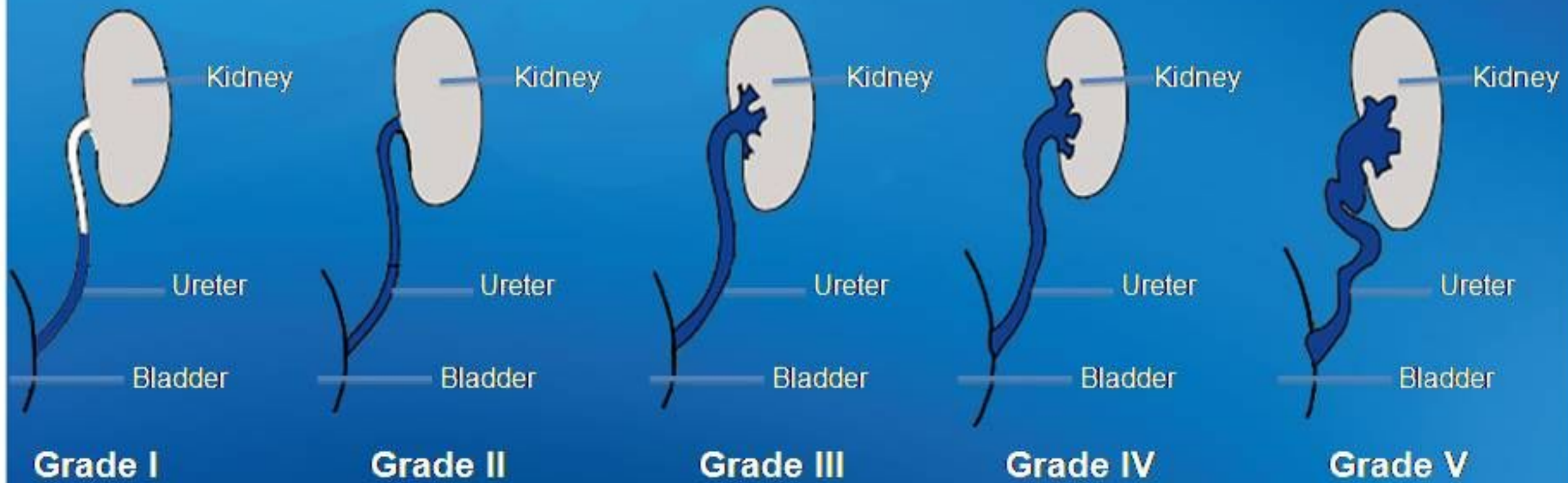


## VUR prevalence

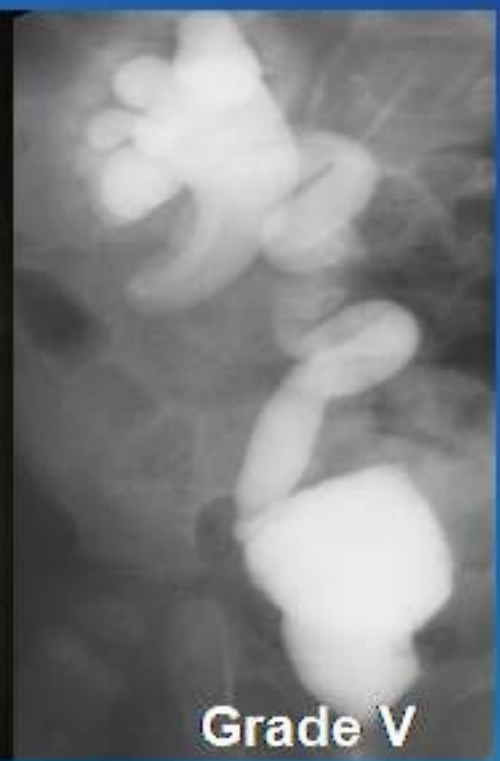
- 75%–80% of children diagnosed with VUR are girls
- Most children diagnosed with VUR are <4 years of age
- Affects approximately 1% of all children
- Found in 30%–40% of children with recurrent UTIs
- Some congenital anomalies of the upper urinary tract are associated with increased risk of VUR



# VUR grades



# VUR grades



Grade I

Grade II

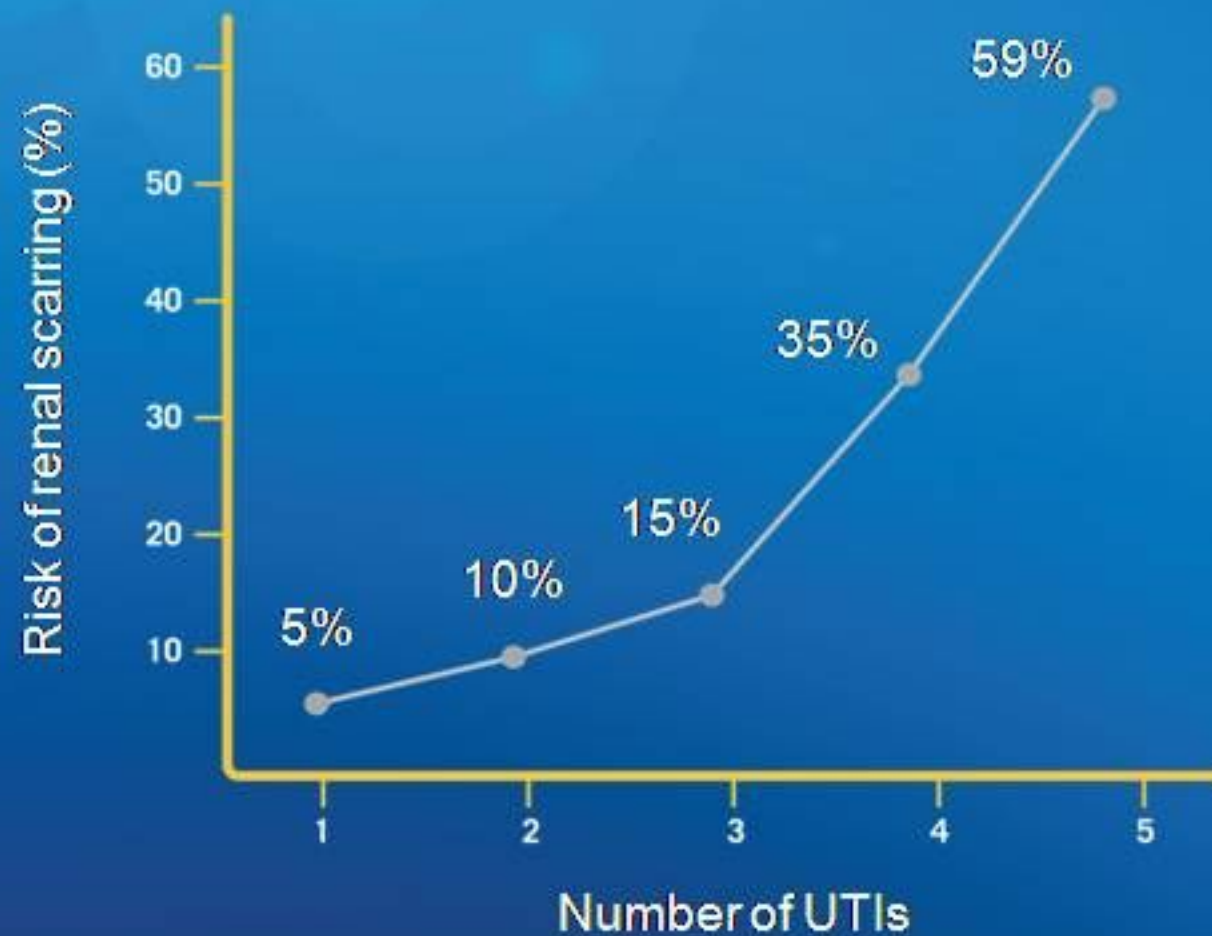
Grade III

Grade IV

Grade V

# VUR and renal scarring

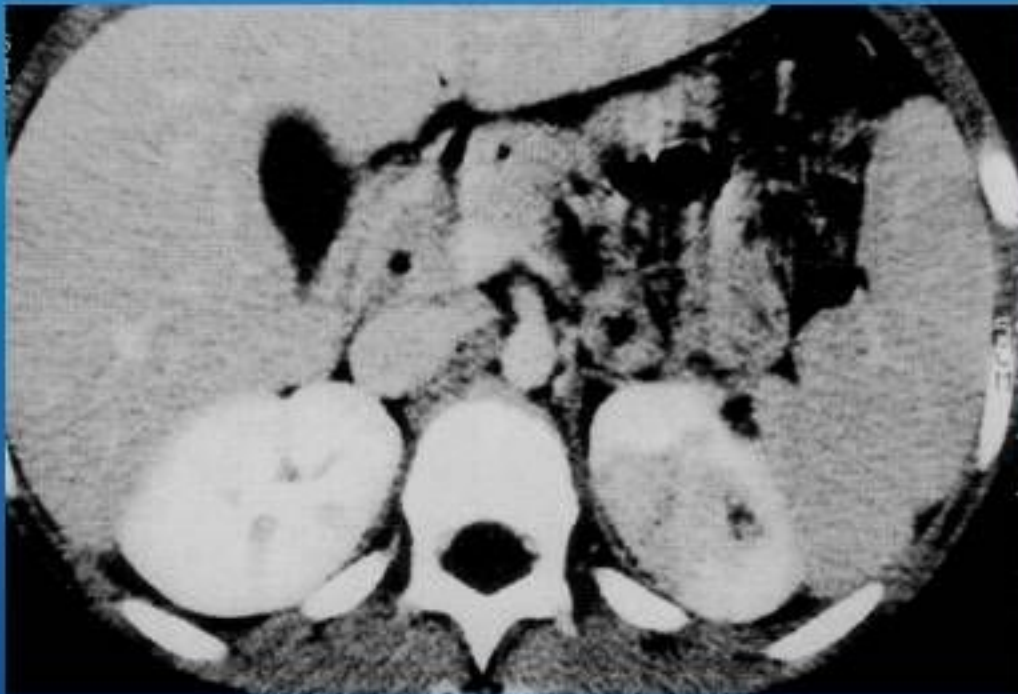
Renal damage usually occurs within the first 3-5 years of life<sup>1,2</sup>



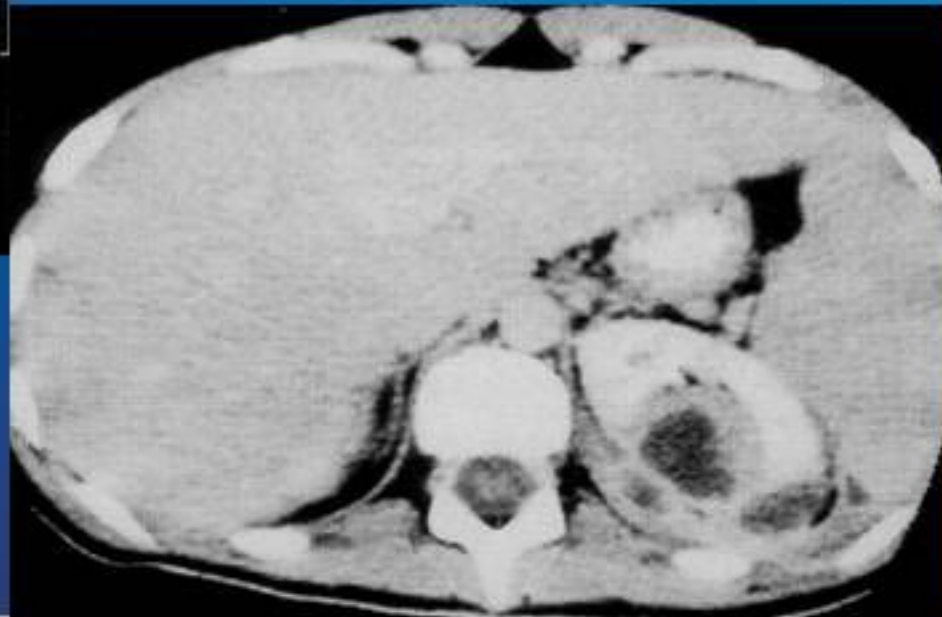




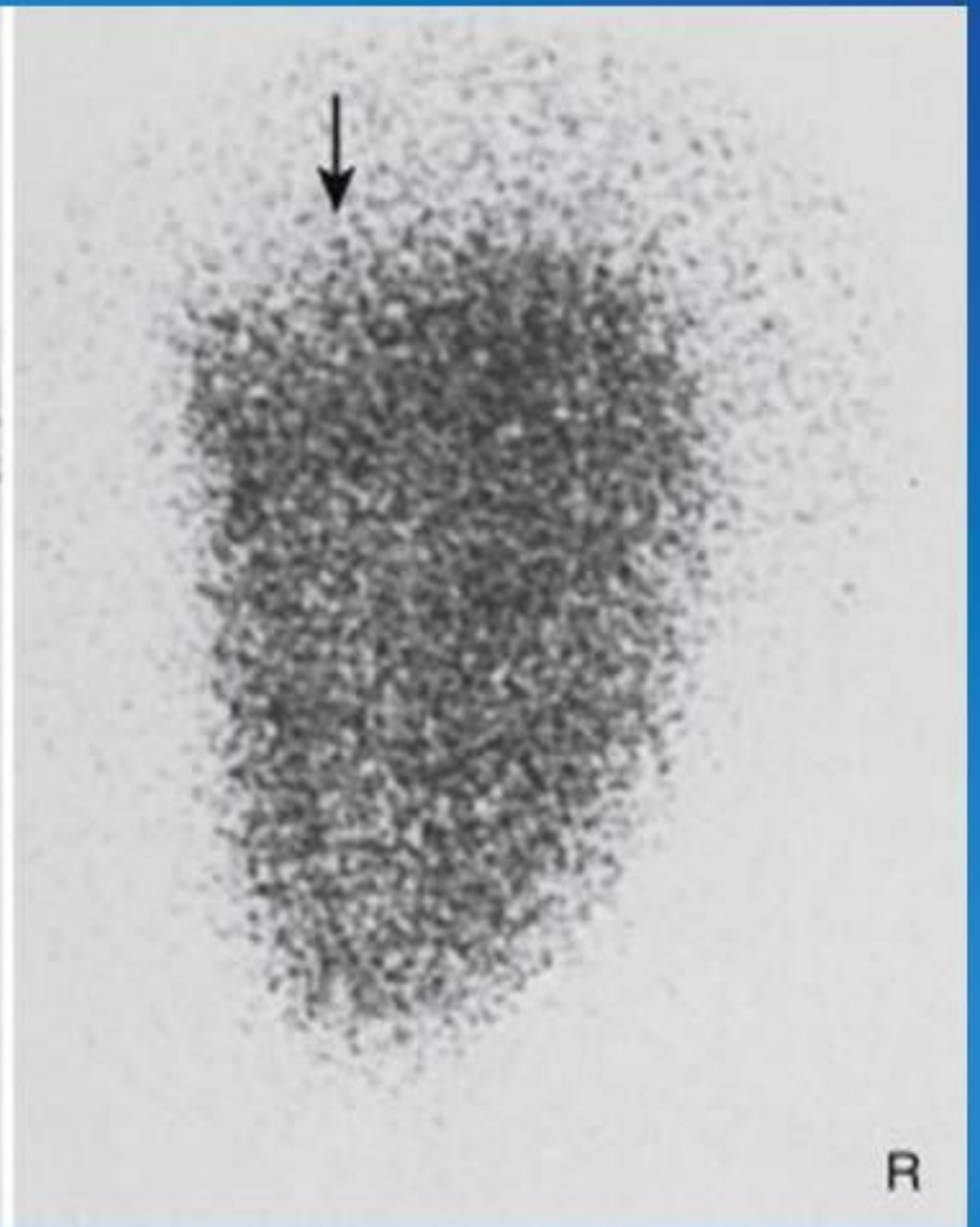
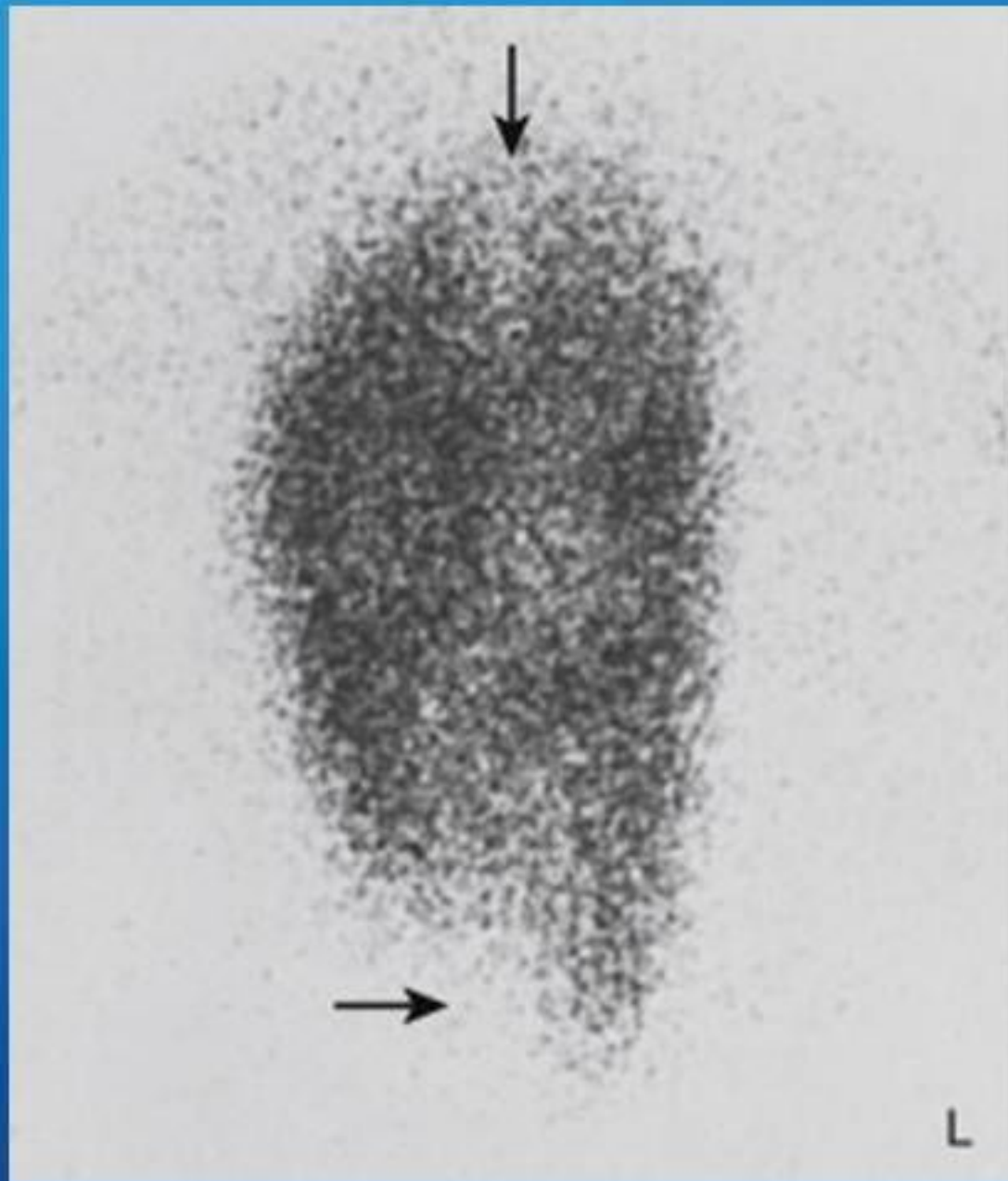
Acute pyelonephritis

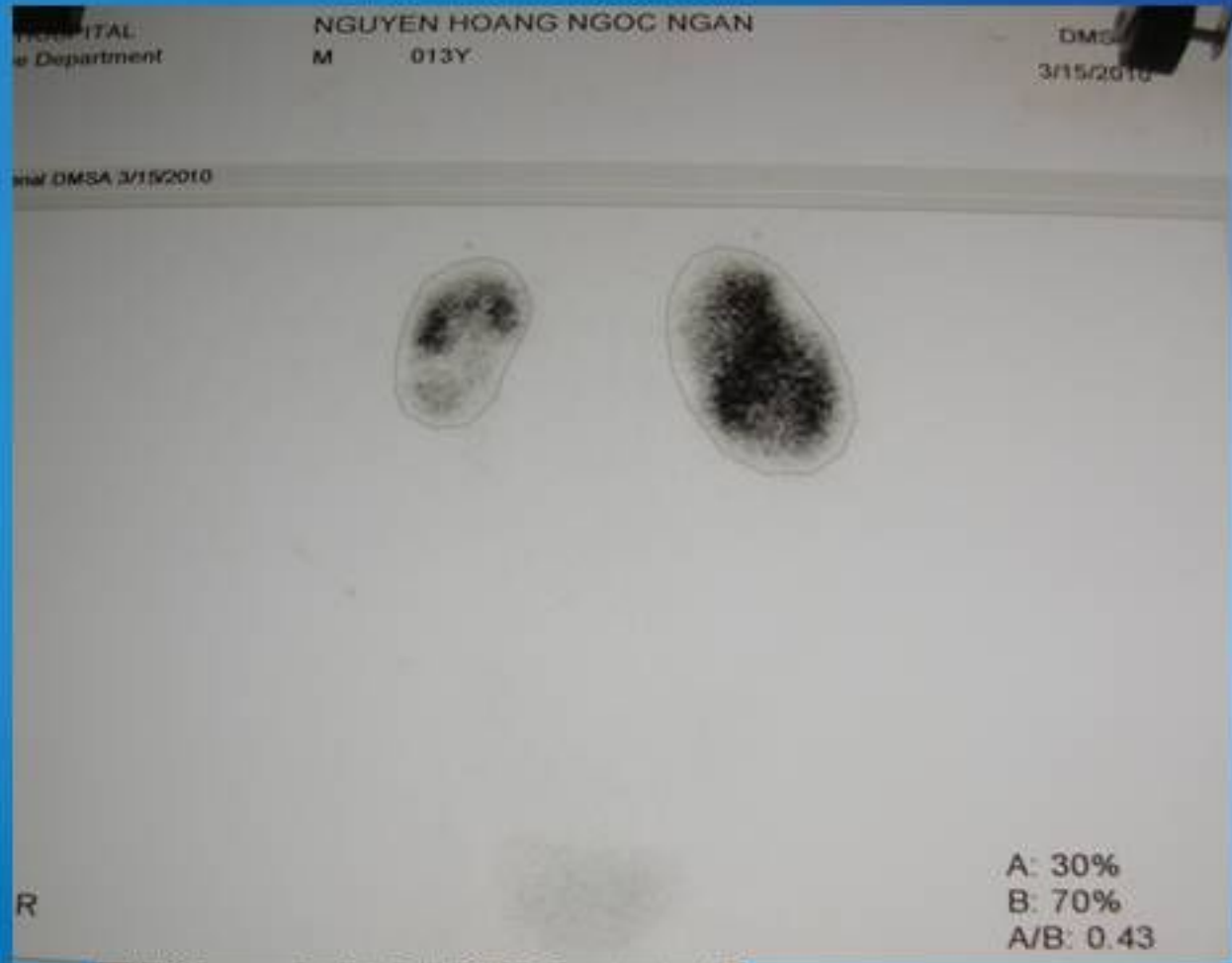


Acute nephritis

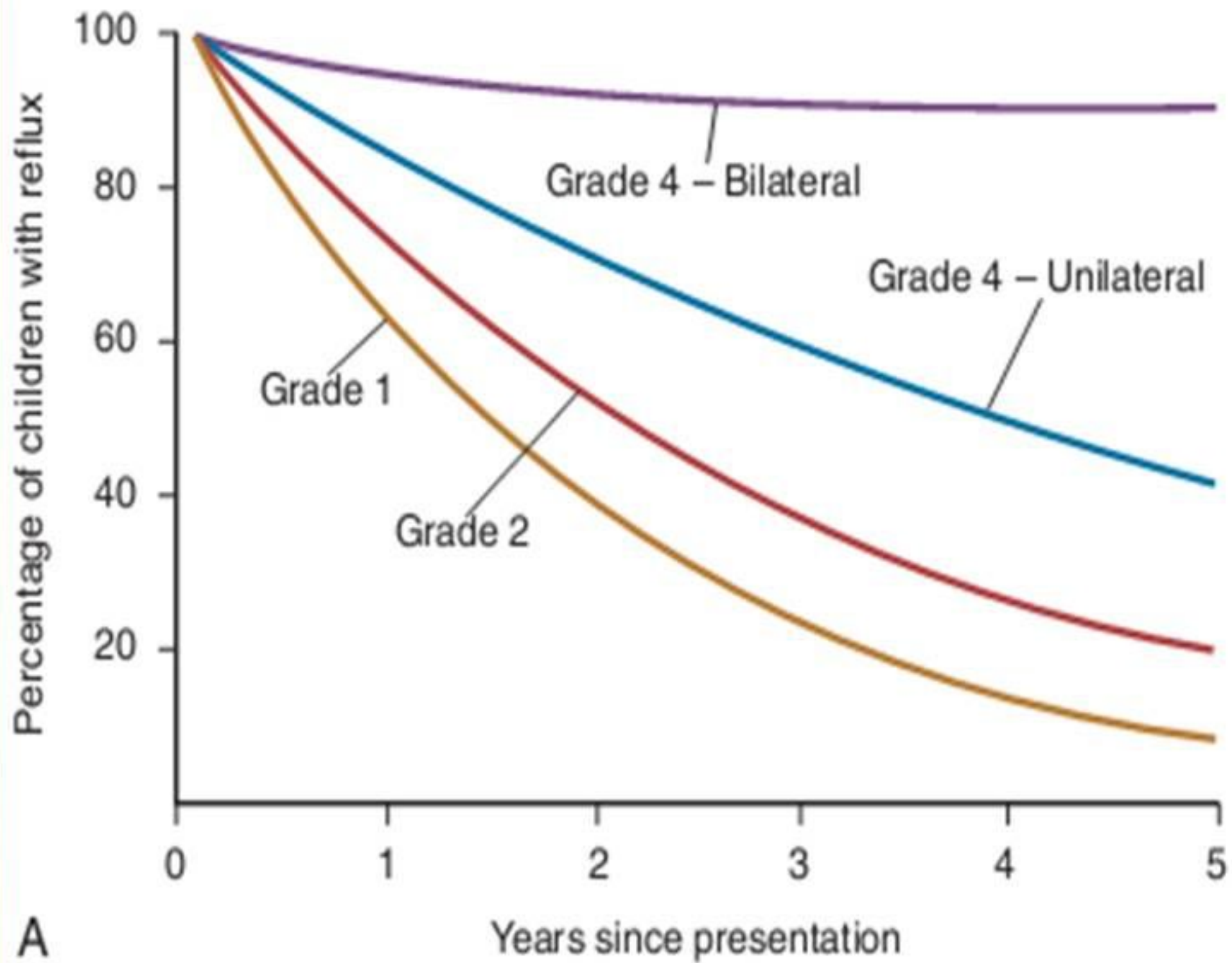


Renal abscess









A

# OPTIONS

- Long term antibiotic therapy
- Open surgery
- Endoscopic procedure

# Antibiotic therapy

- Approx. 70% success rate
- Even with preventative antibiotic treatment, about 1 in 10 children still develops urinary tract infections because the infections develop a resistance to the antibiotic

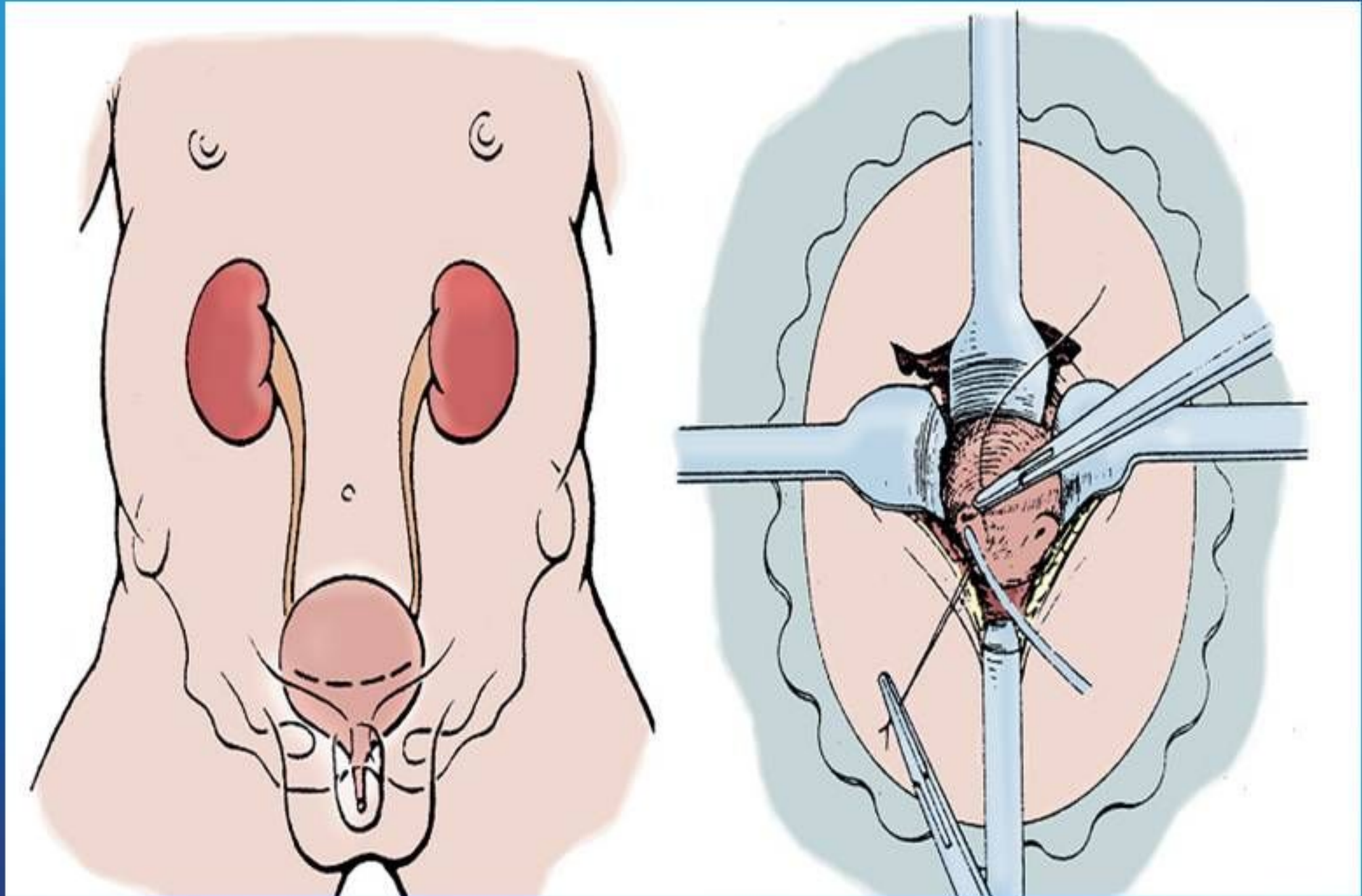


# Open surgery

- Approx. 95% success rate (more than 9 patients out of 10)

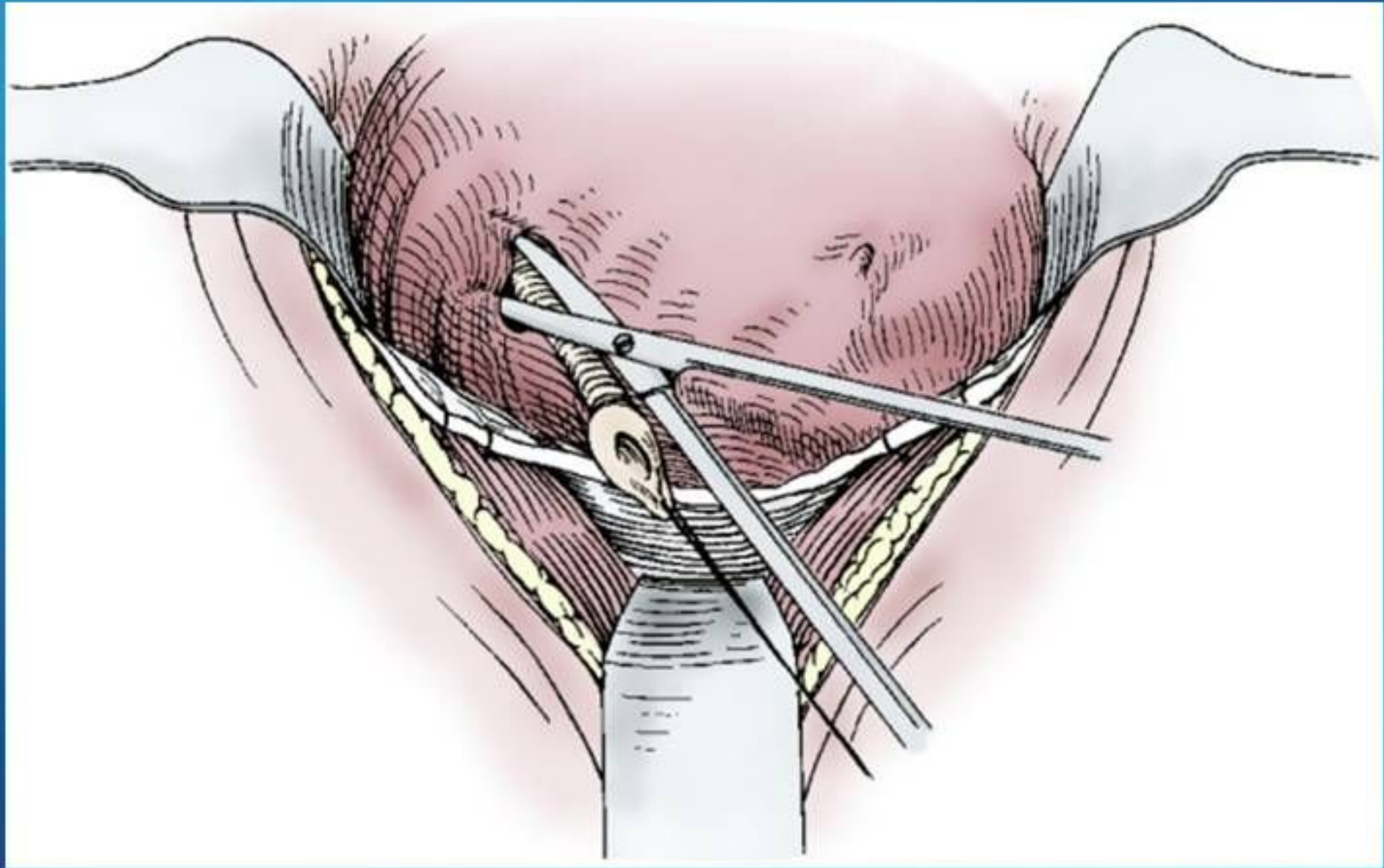
Open surgery  
Transtrigonal reimplantation-Cohen

# Open surgery(Transtrigonal reimplantation-Cohen)

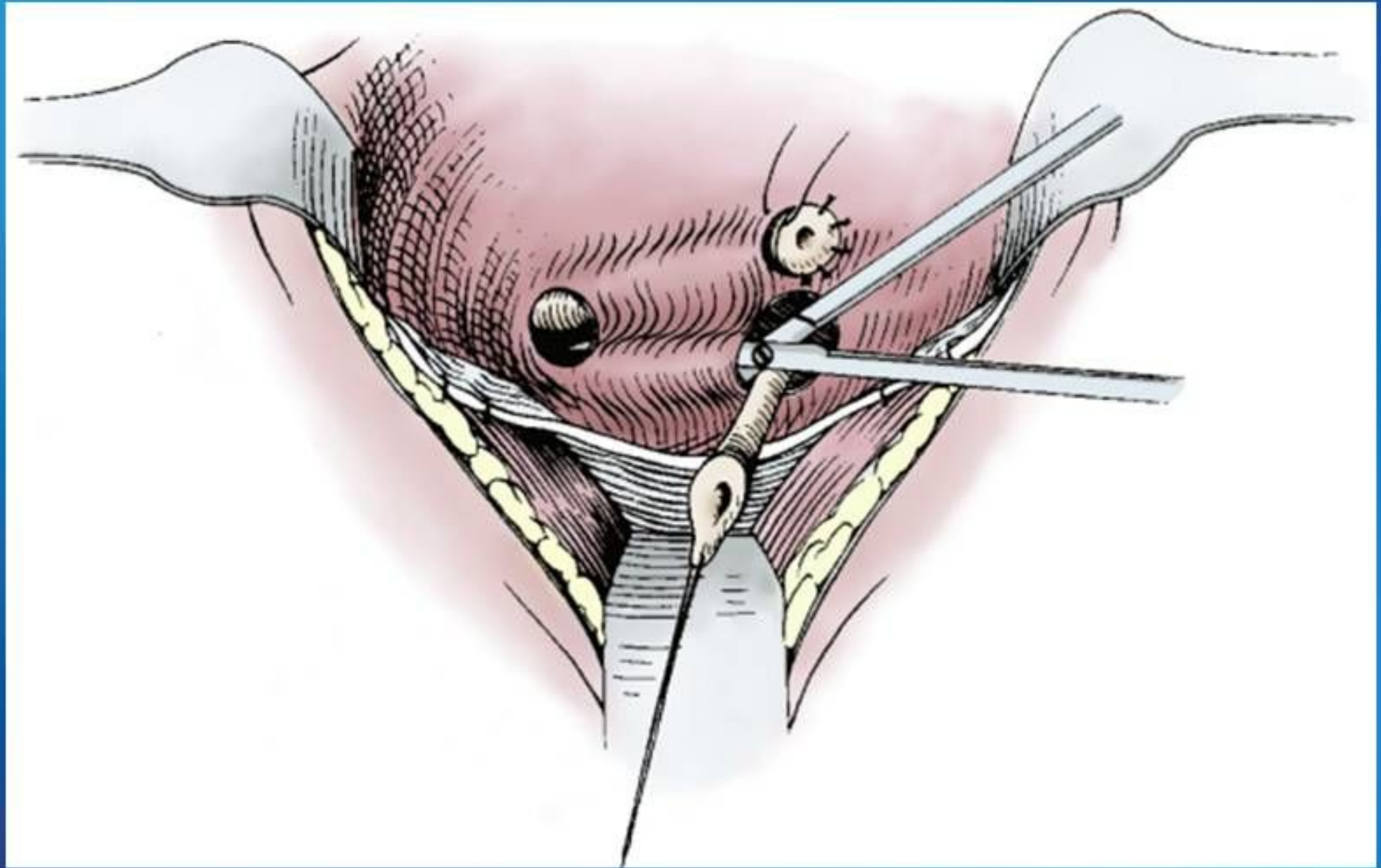




# Transtrigonal reimplantation

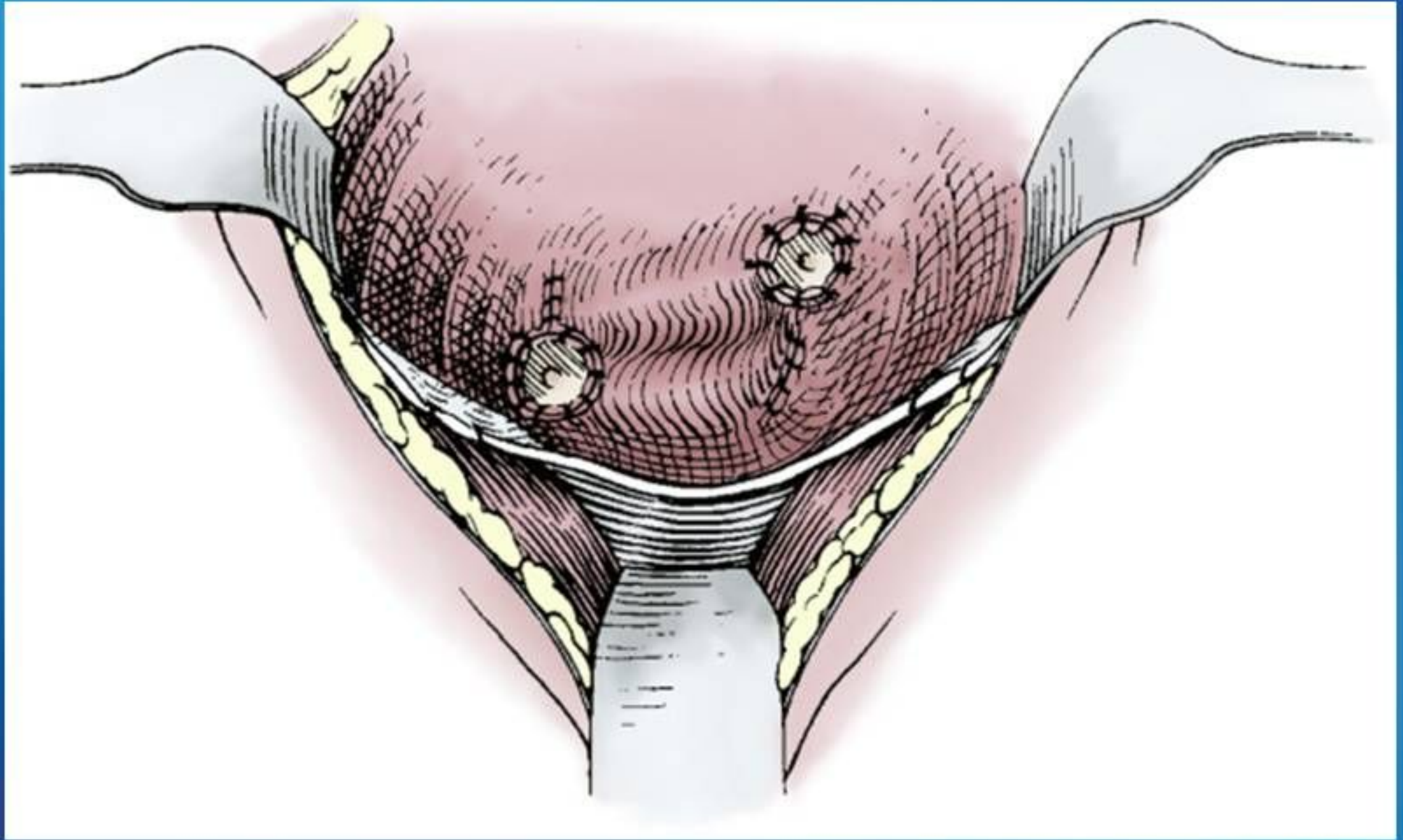


# Transtrigonal reimplantation





# Transtrigonal reimplantation

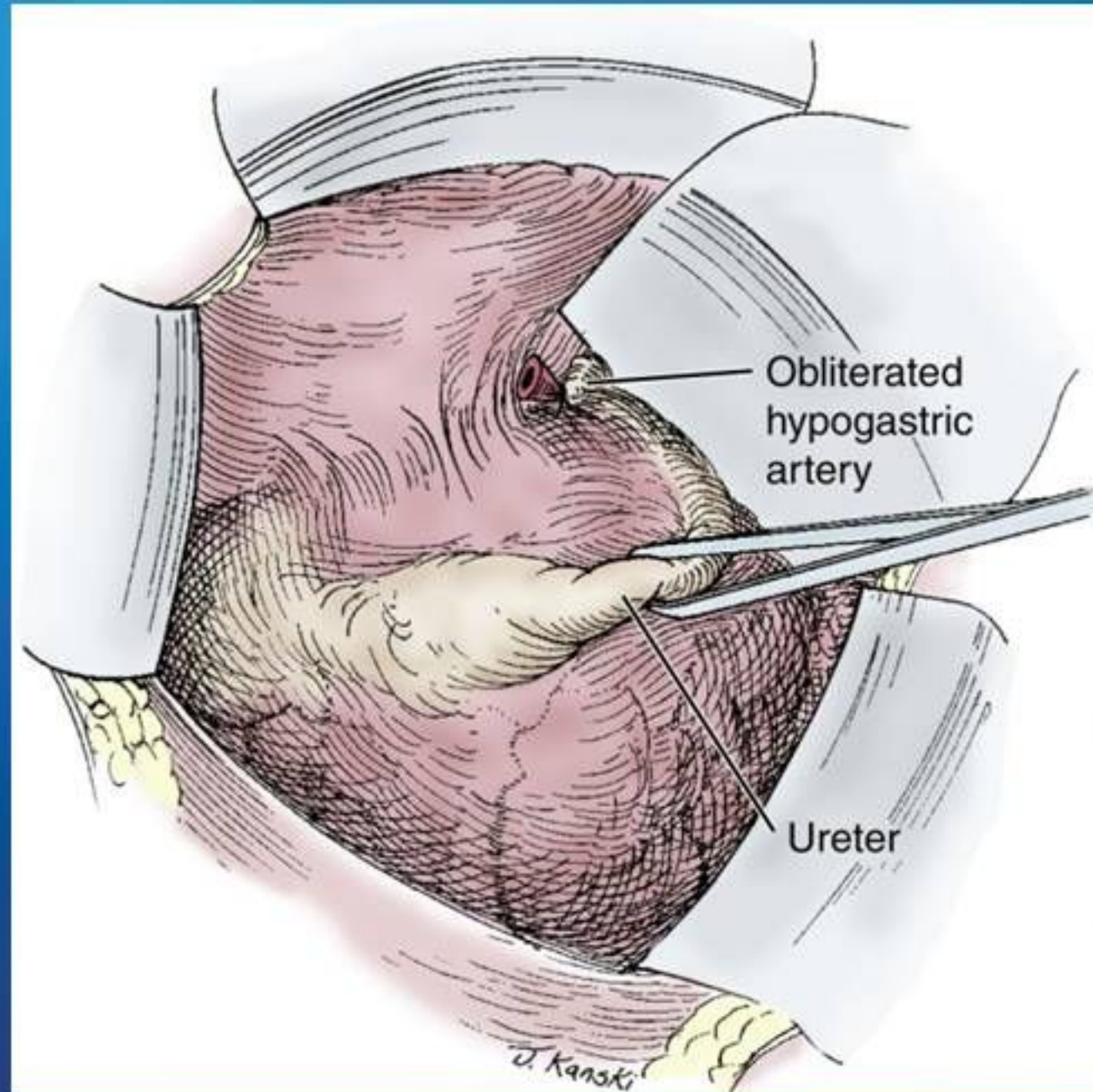




Open surgery

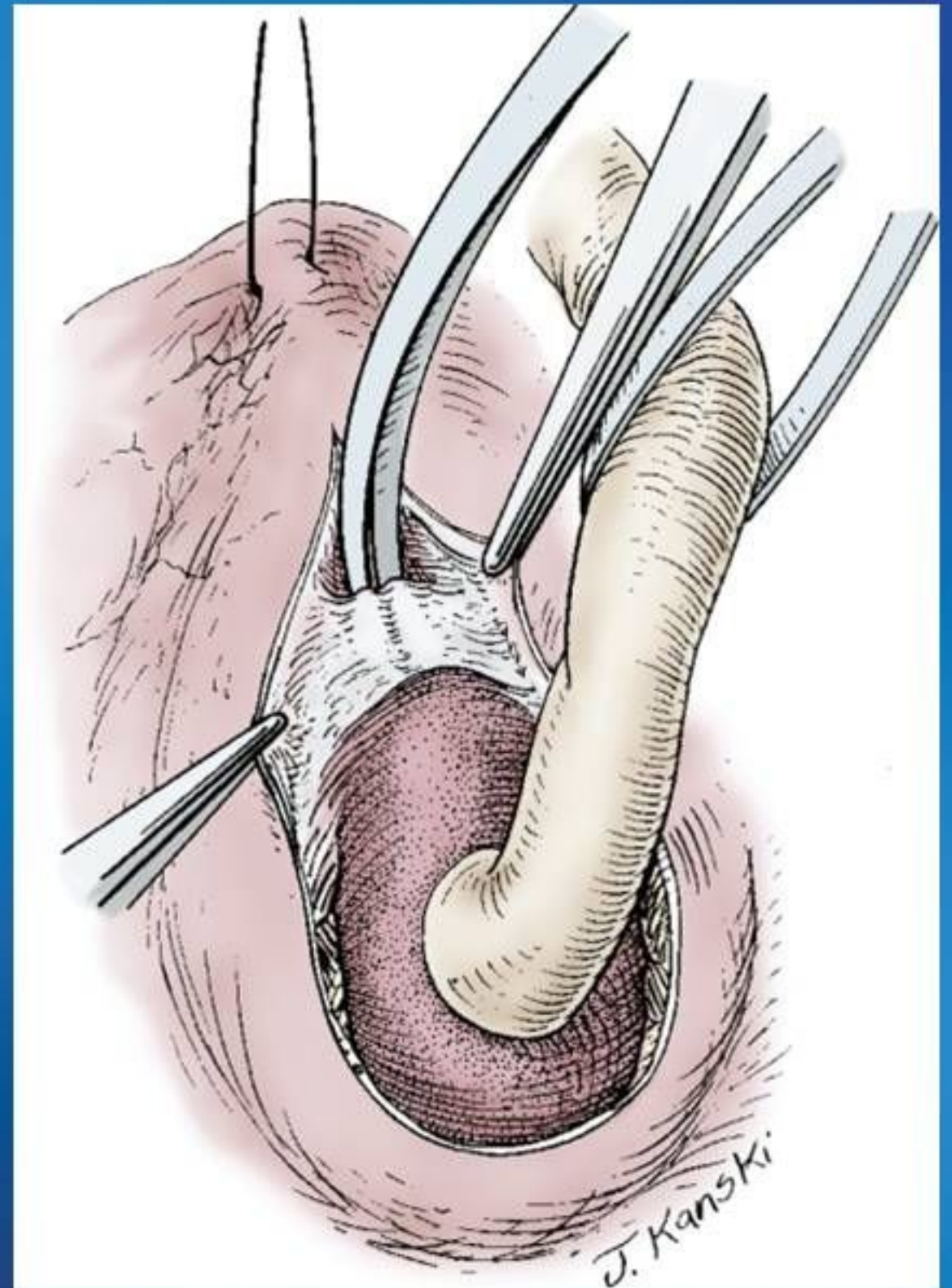
(Extravesical ureteral reimplantation  
Lich-Gregoire)

# Extravesical ureteral reimplantation



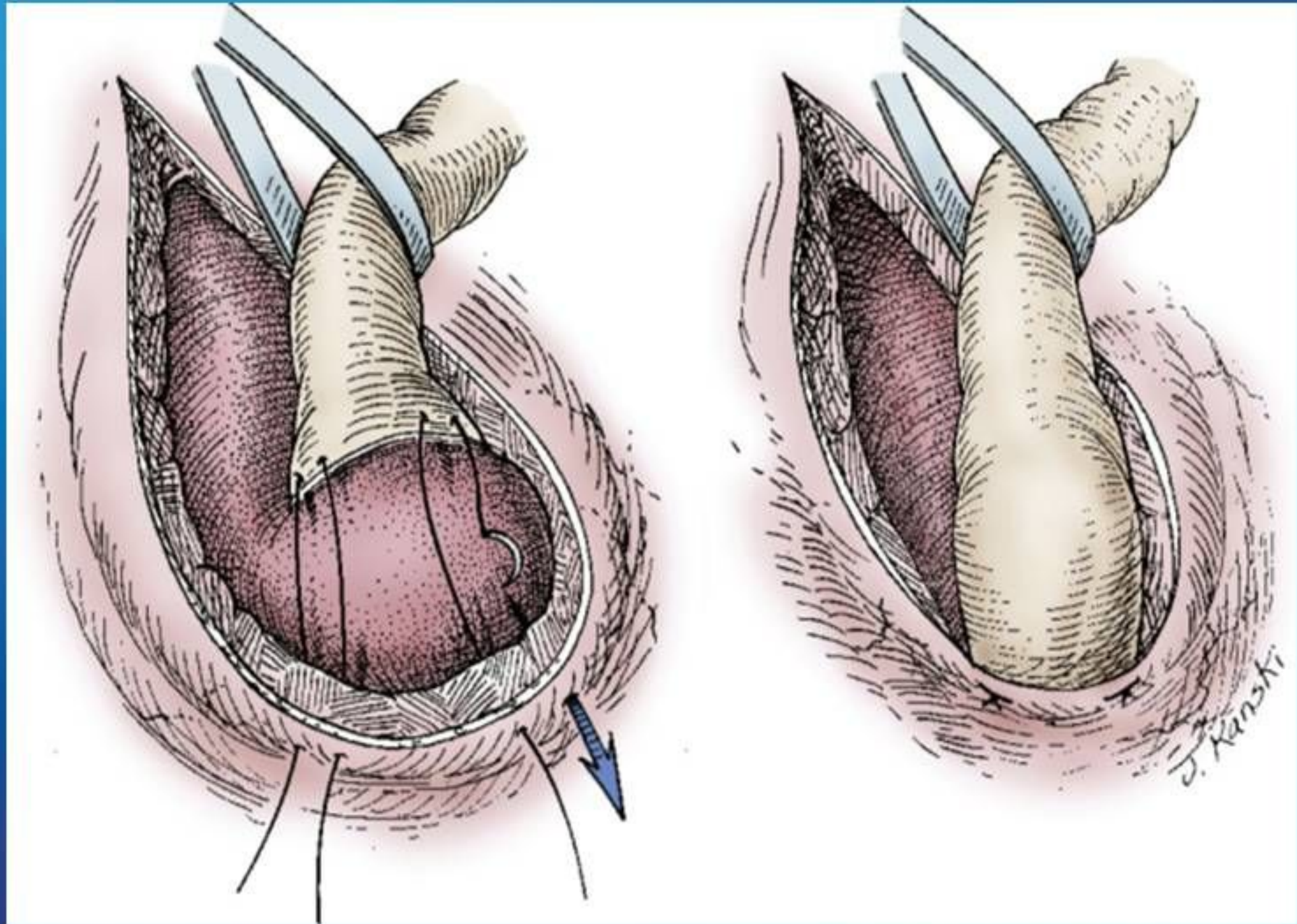


# Extravesical ureteral reimplantation



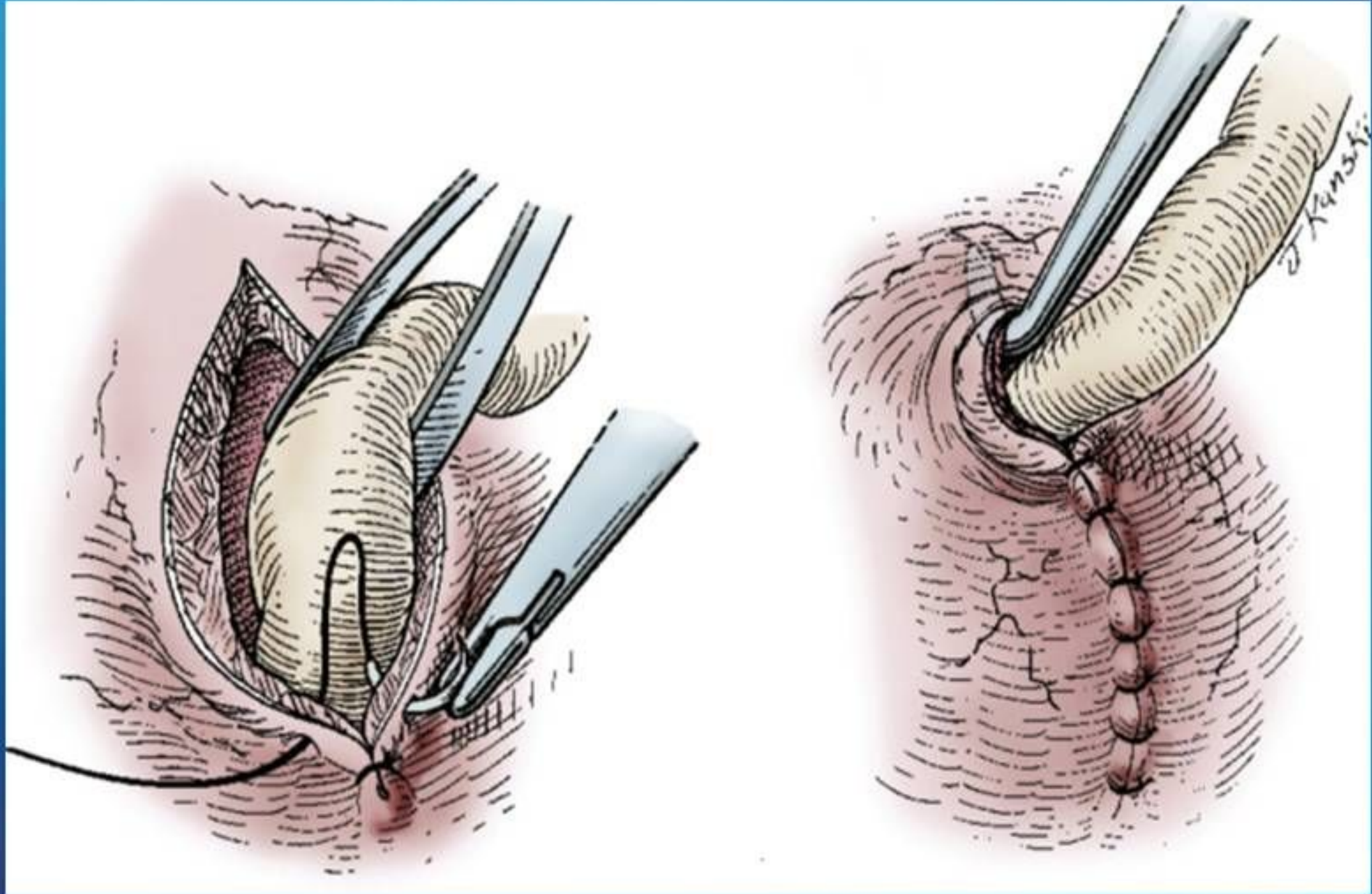


# Extravesical ureteral reimplantation

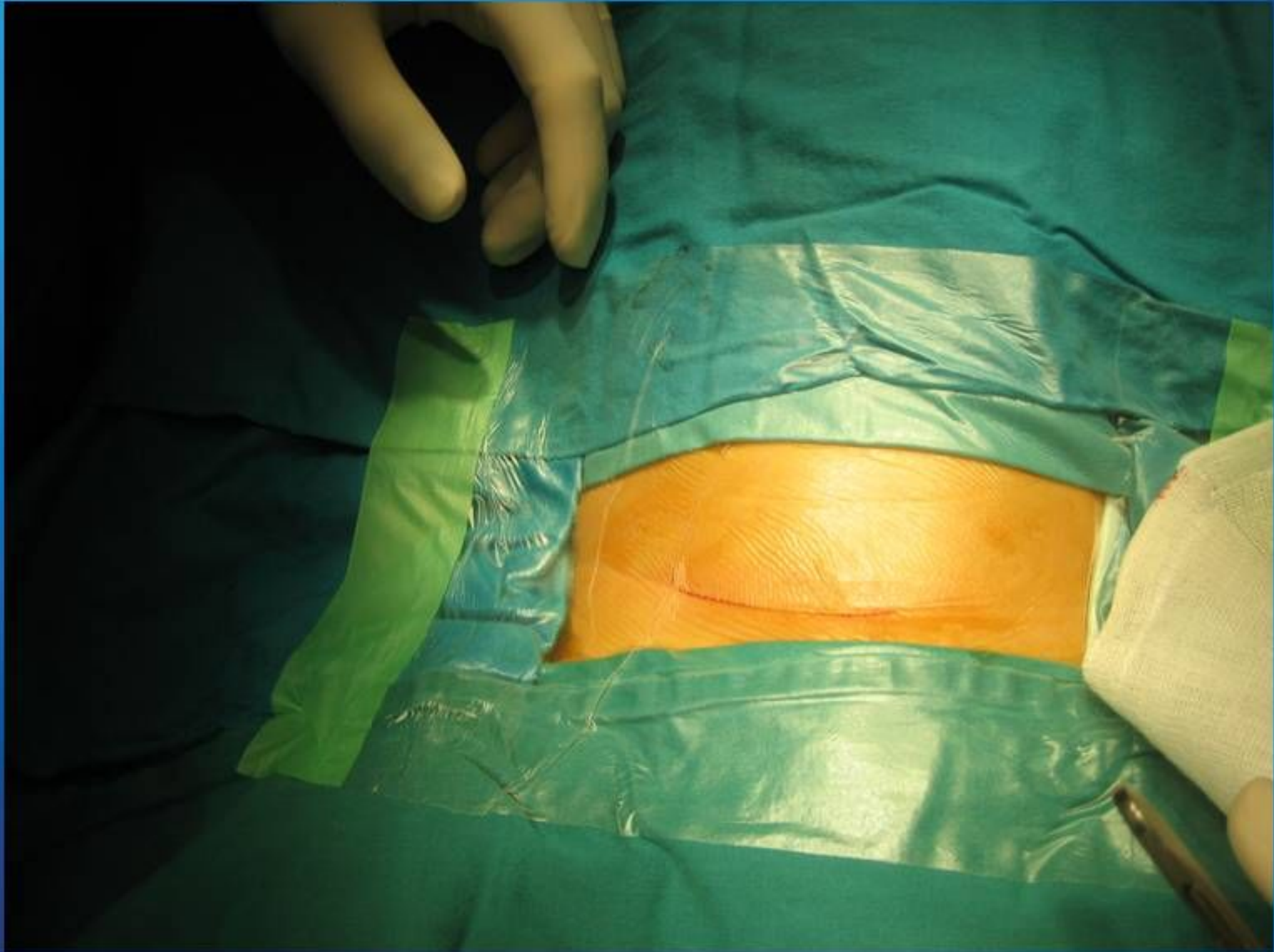




# Extravesical ureteral reimplantation



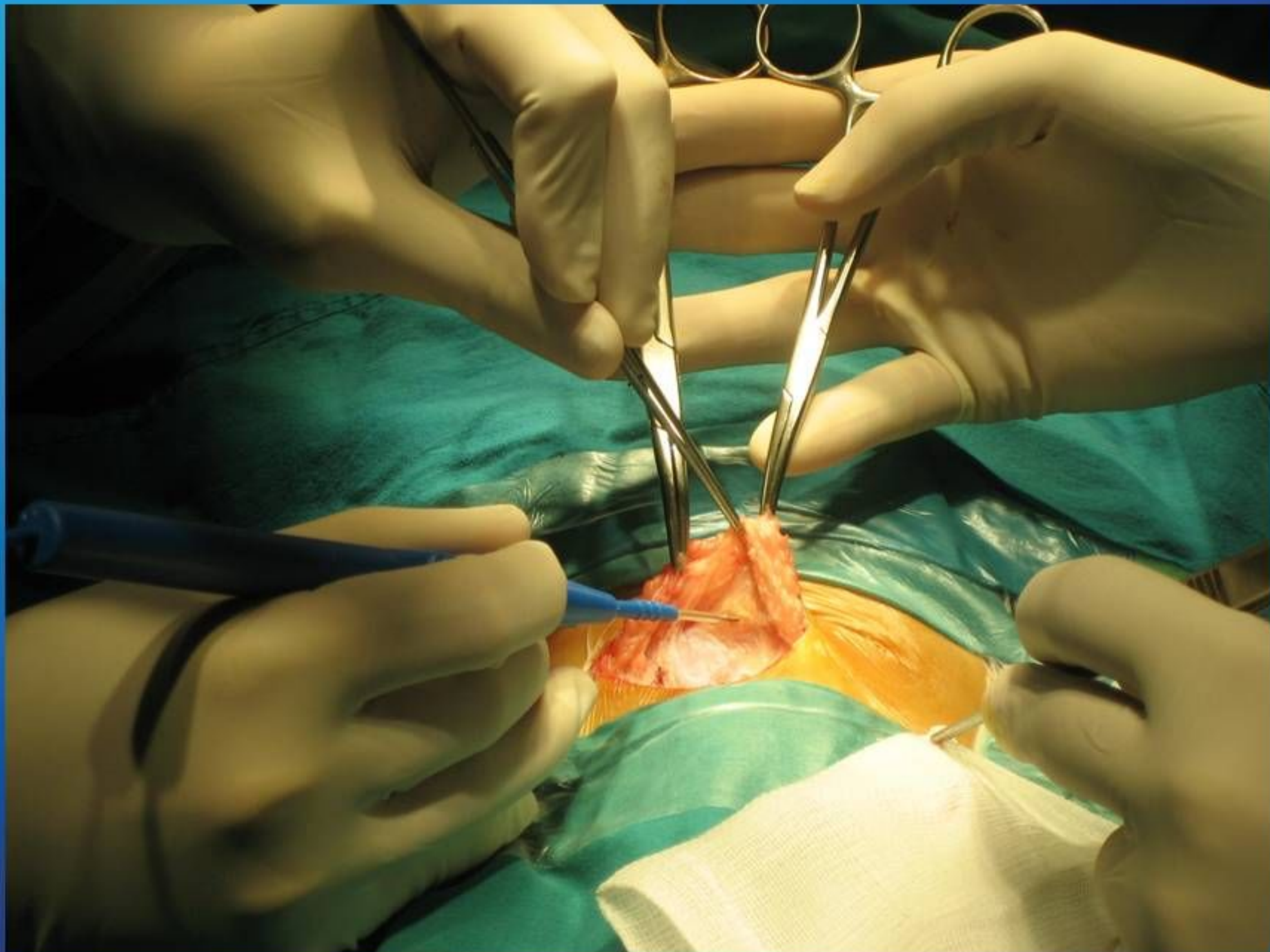
# Open surgery



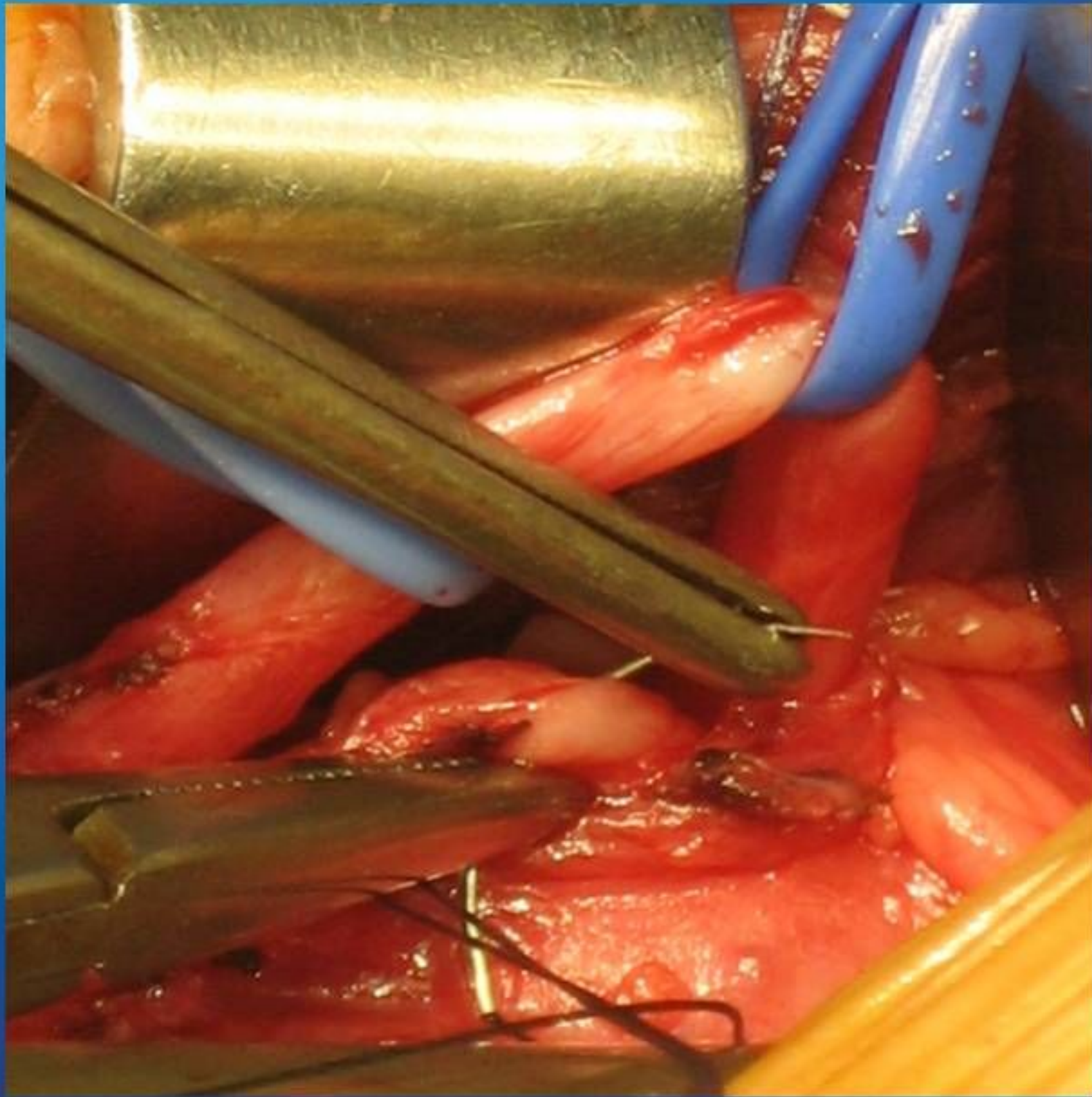




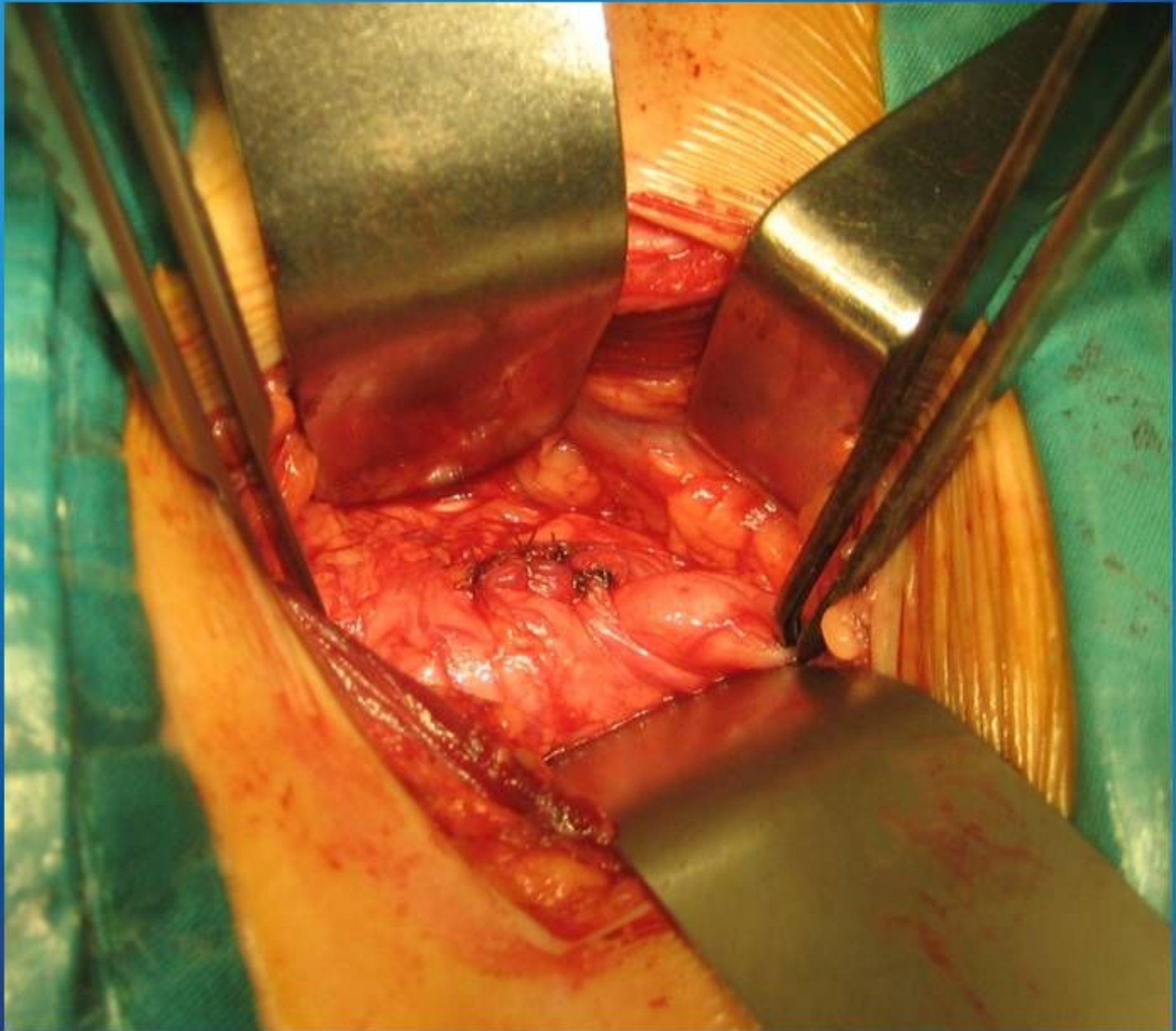












# Open surgery





# A minimally invasive endoscopic injection

- Approx. 80% success rate (8 patients out of 10)



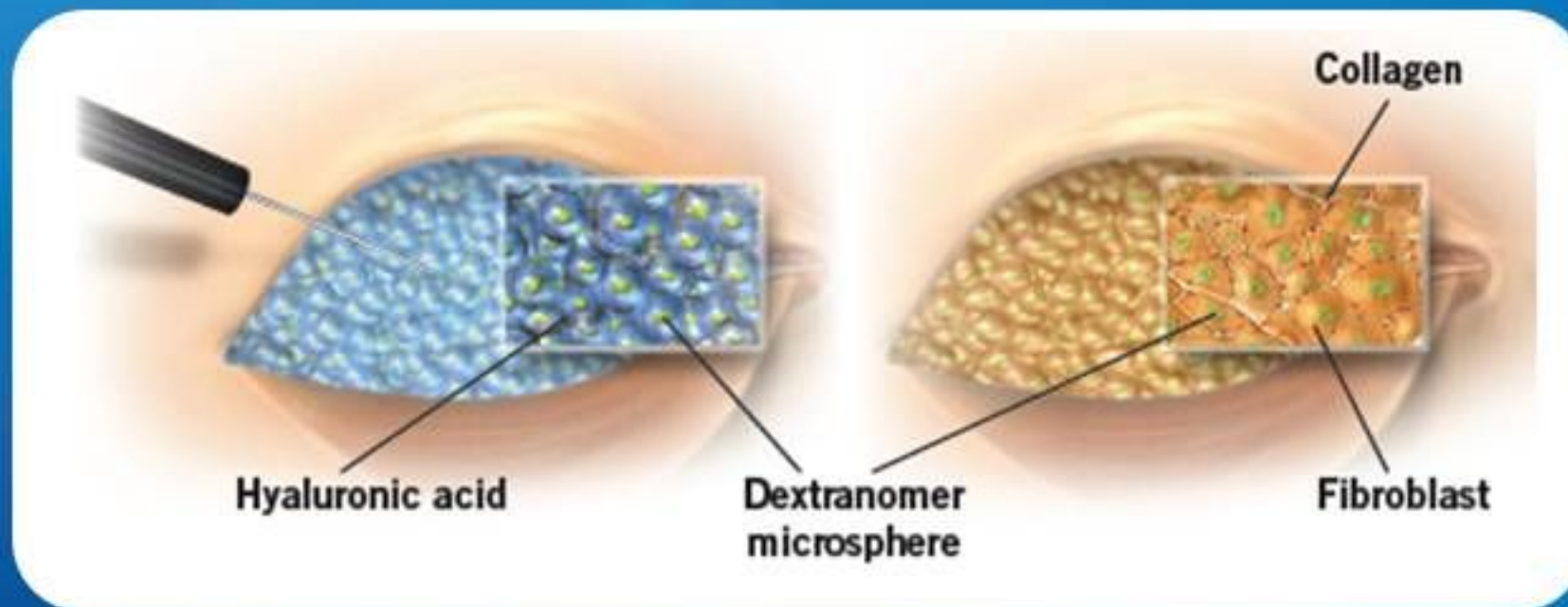
## A minimally invasive endoscopic injection

- Deflux is injected in or around the ureteral opening to create a valve function and stop urine from flowing back up the ureter

# Made from biocompatible material

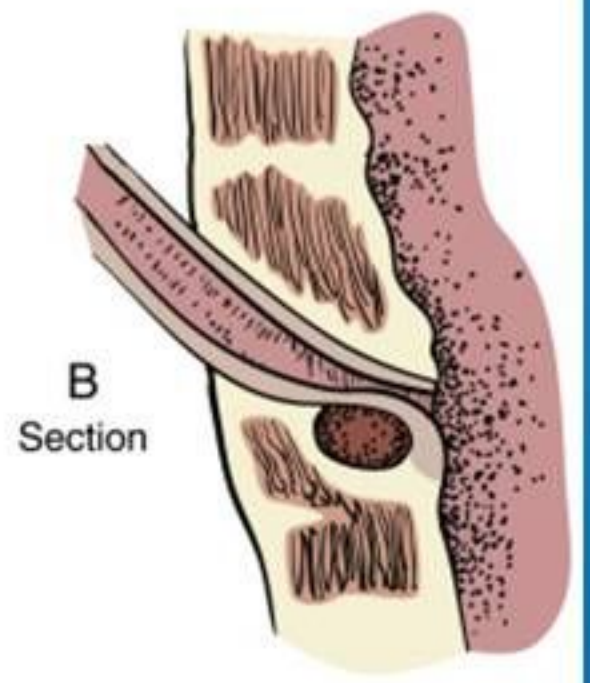
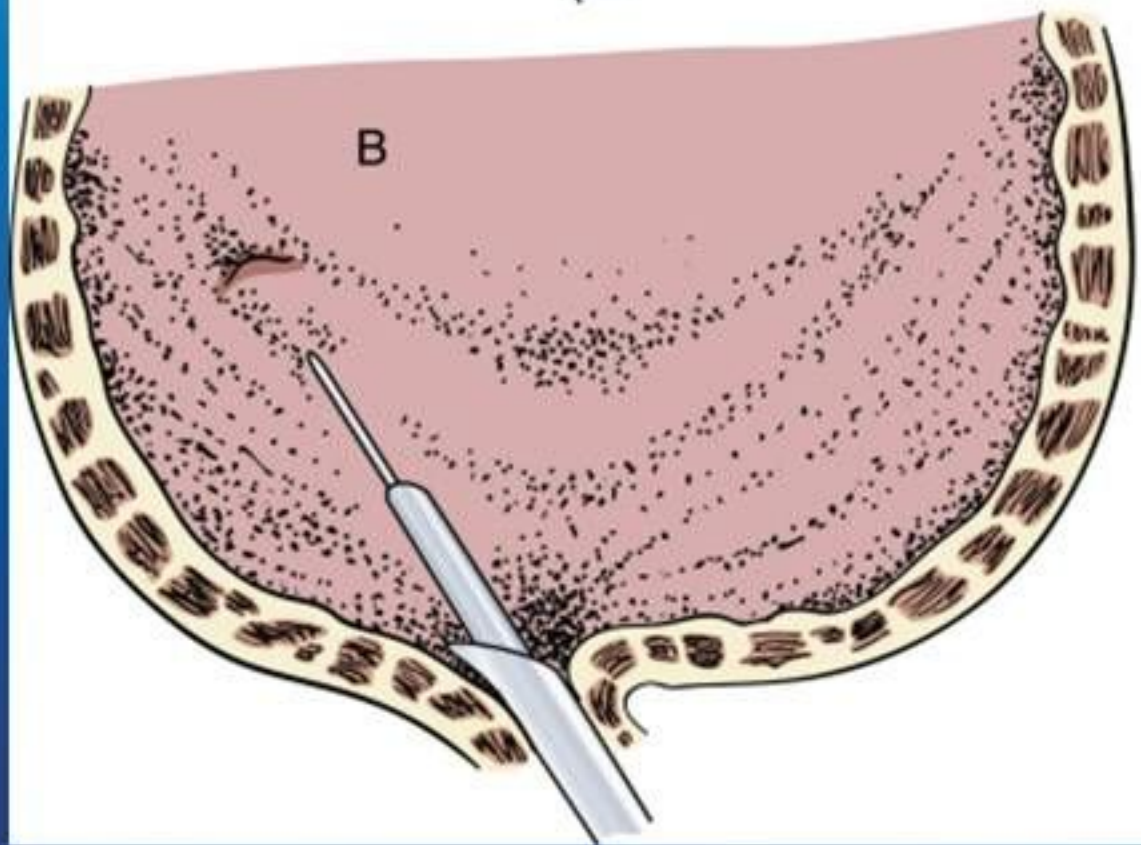
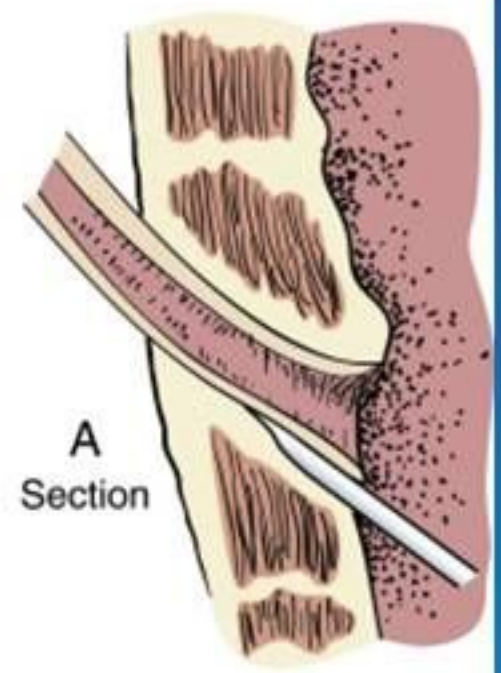
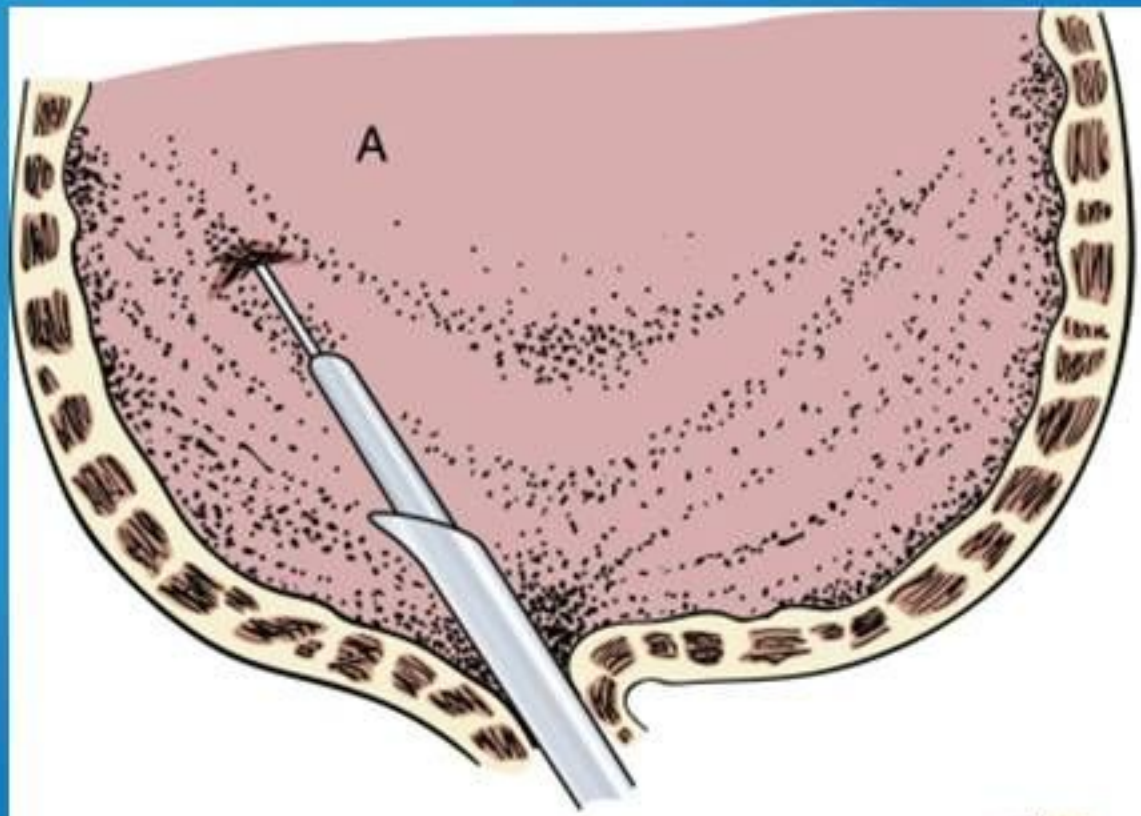
Easily injectable, viscous gel made from 2 polysaccharides<sup>1,2</sup>

- Non-animal stabilized hyaluronic acid (NASHA™)
- Dextranomer microspheres (80–250  $\mu\text{m}$ )

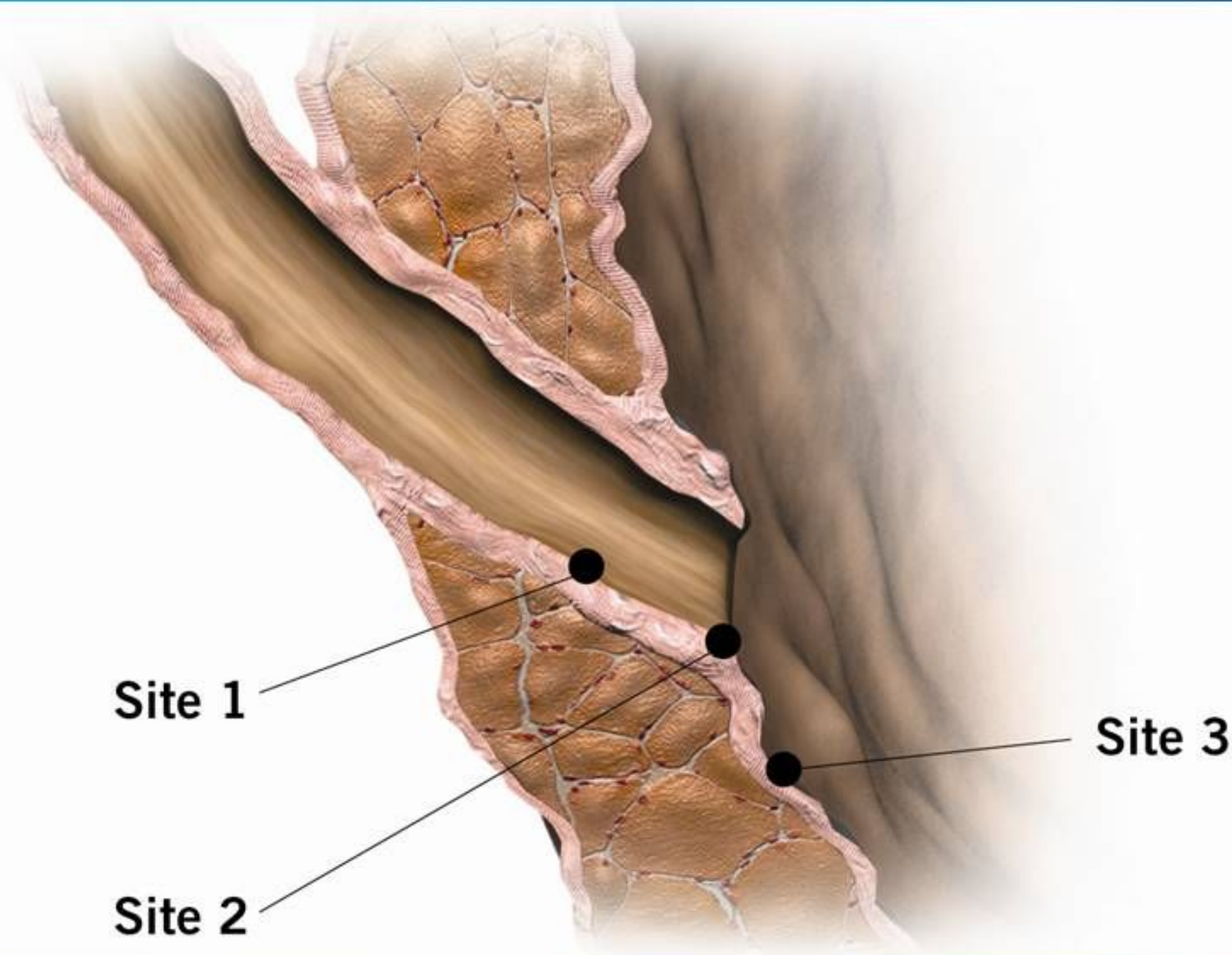


Implant is stable, long term, remains in position, and does not disappear over time<sup>2,3</sup>





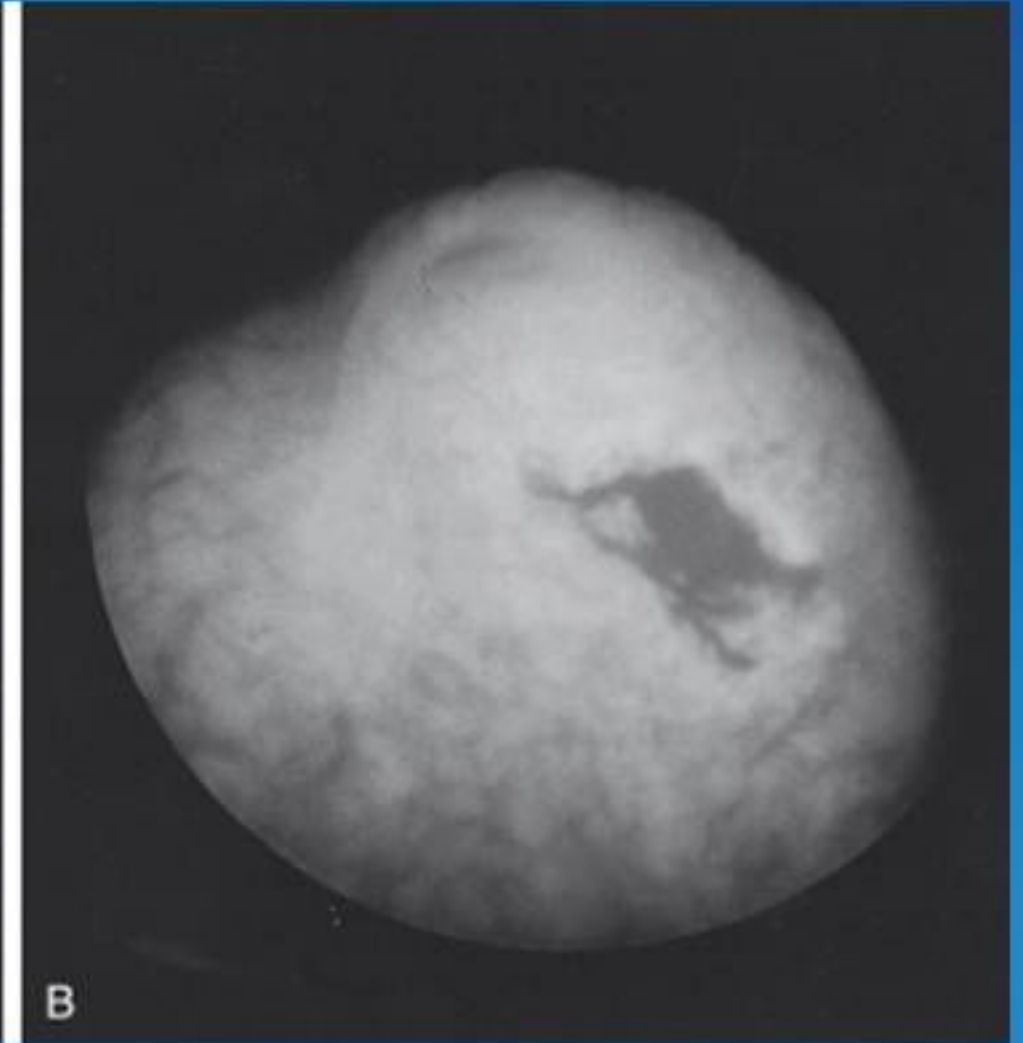
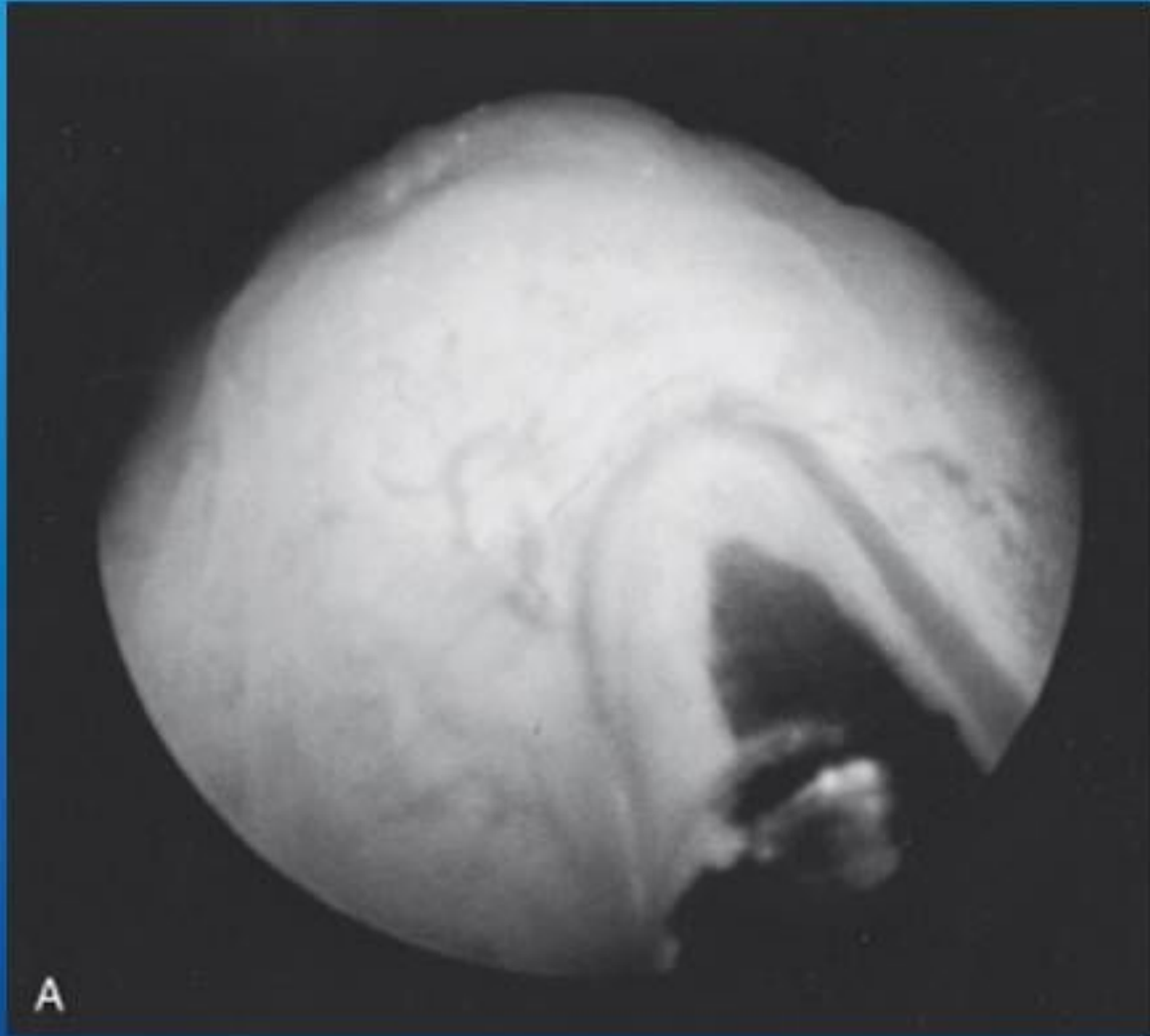




**Site 1**

**Site 2**

**Site 3**

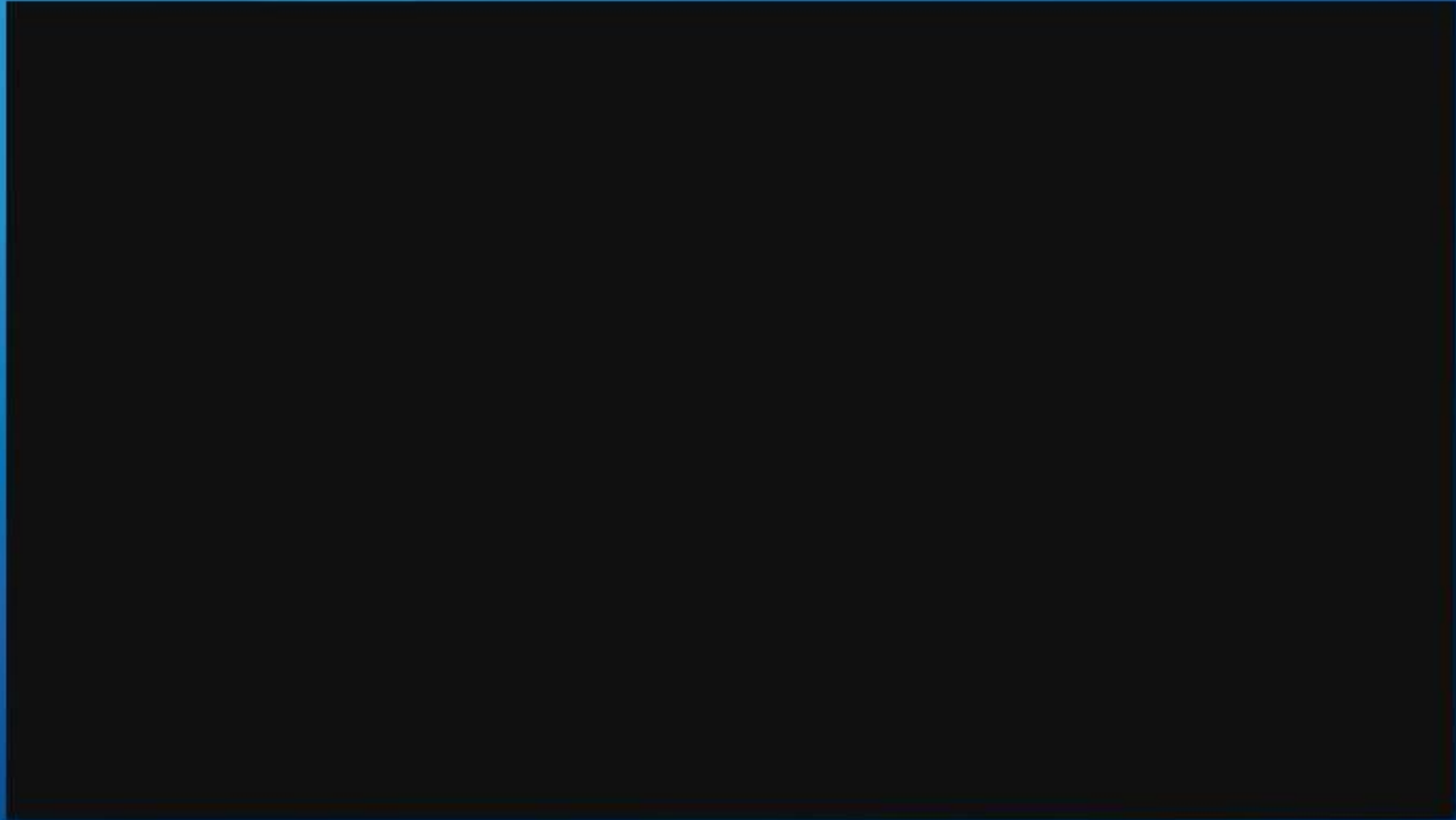


Mountain range

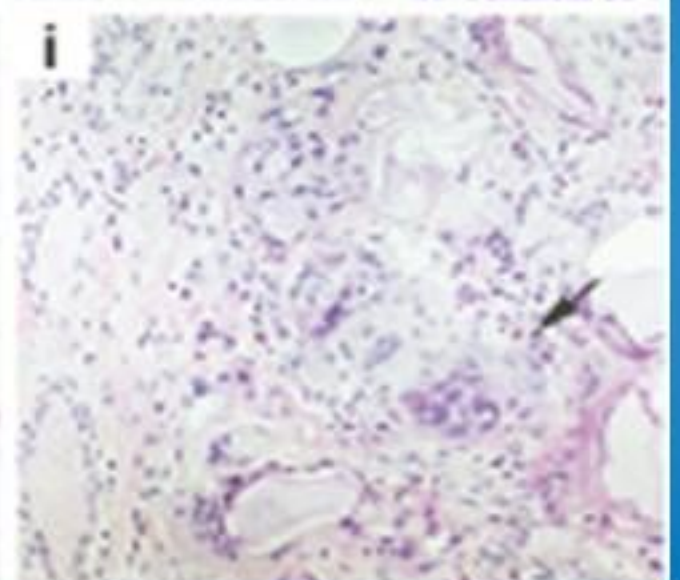
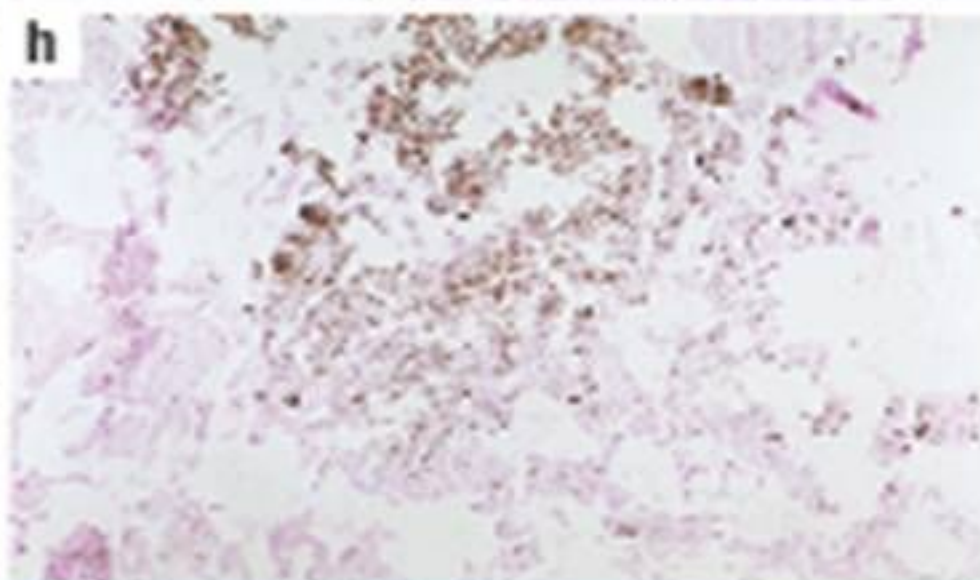
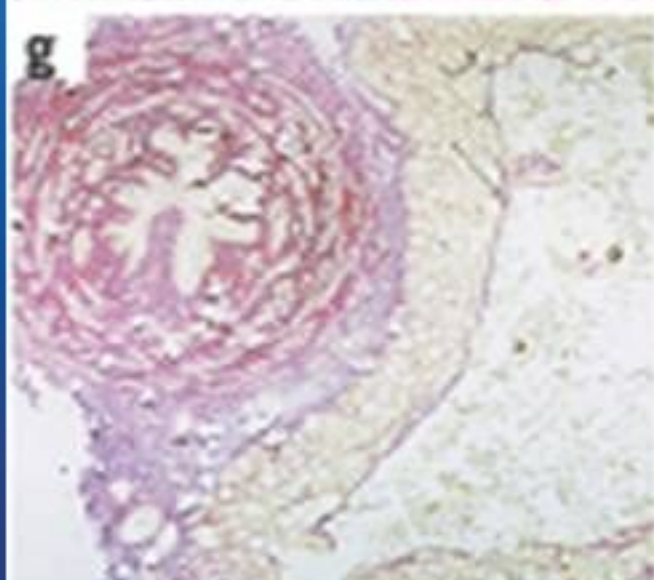
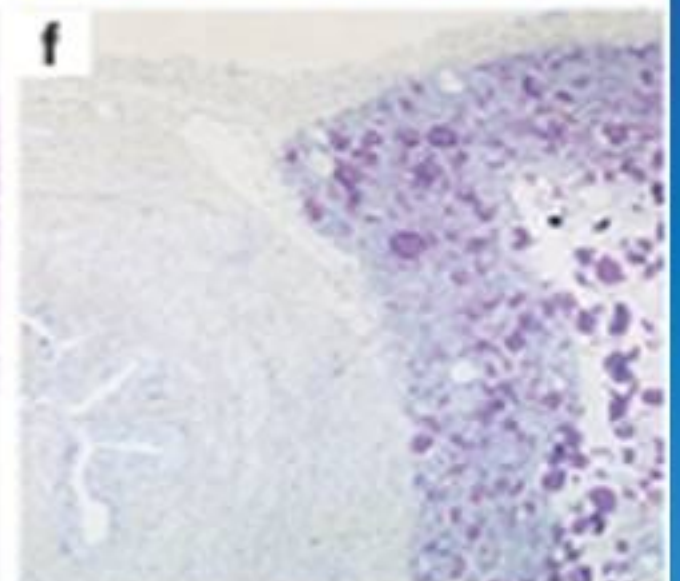
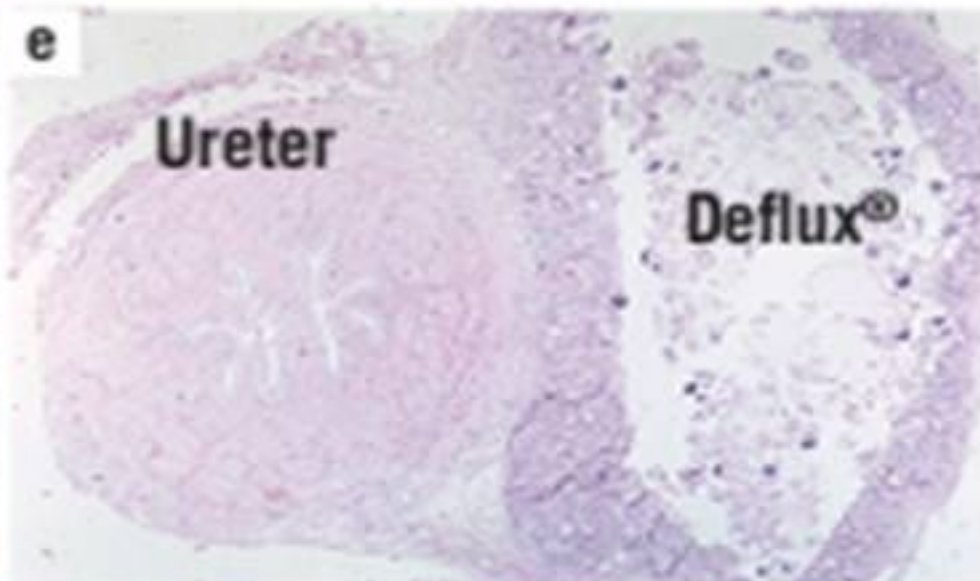
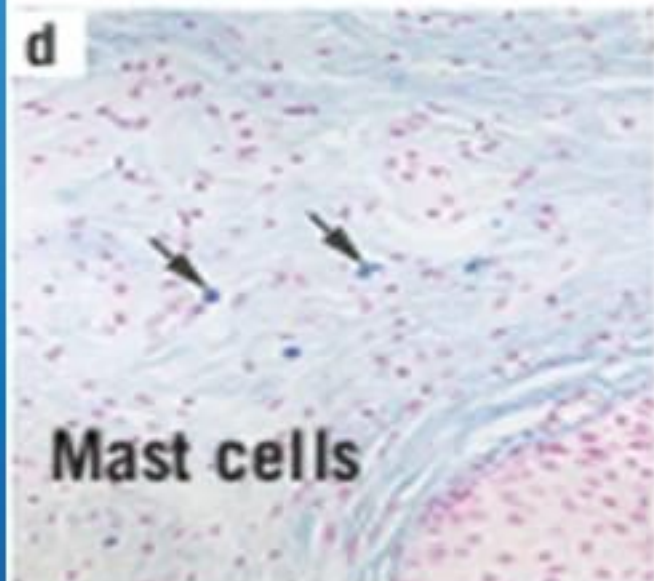
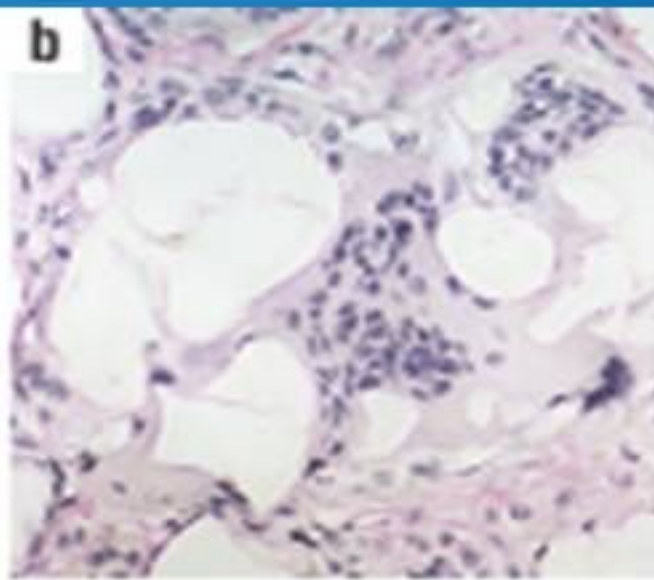
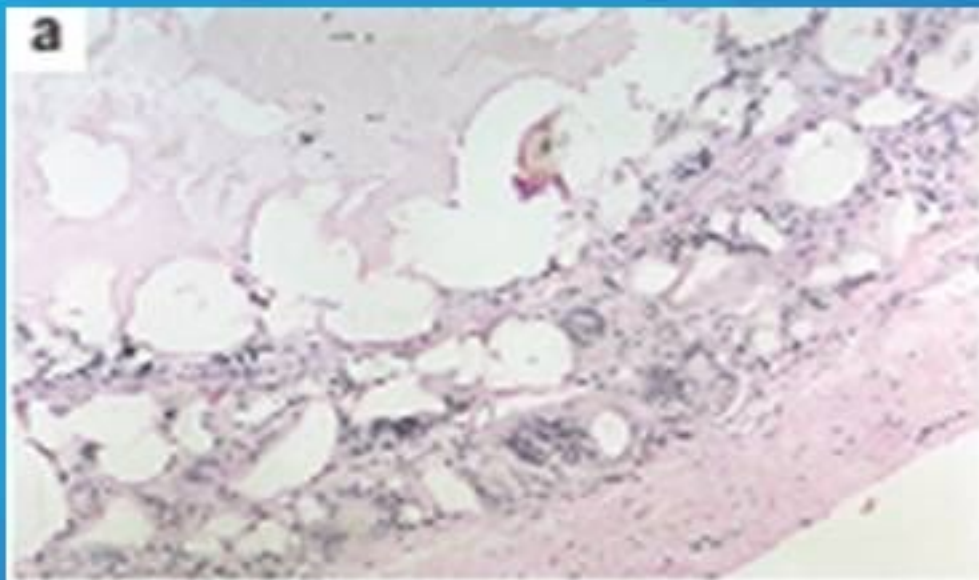














## OBSERVATION

Deflux<sup>®</sup> gel shows no evidence of allergic reaction

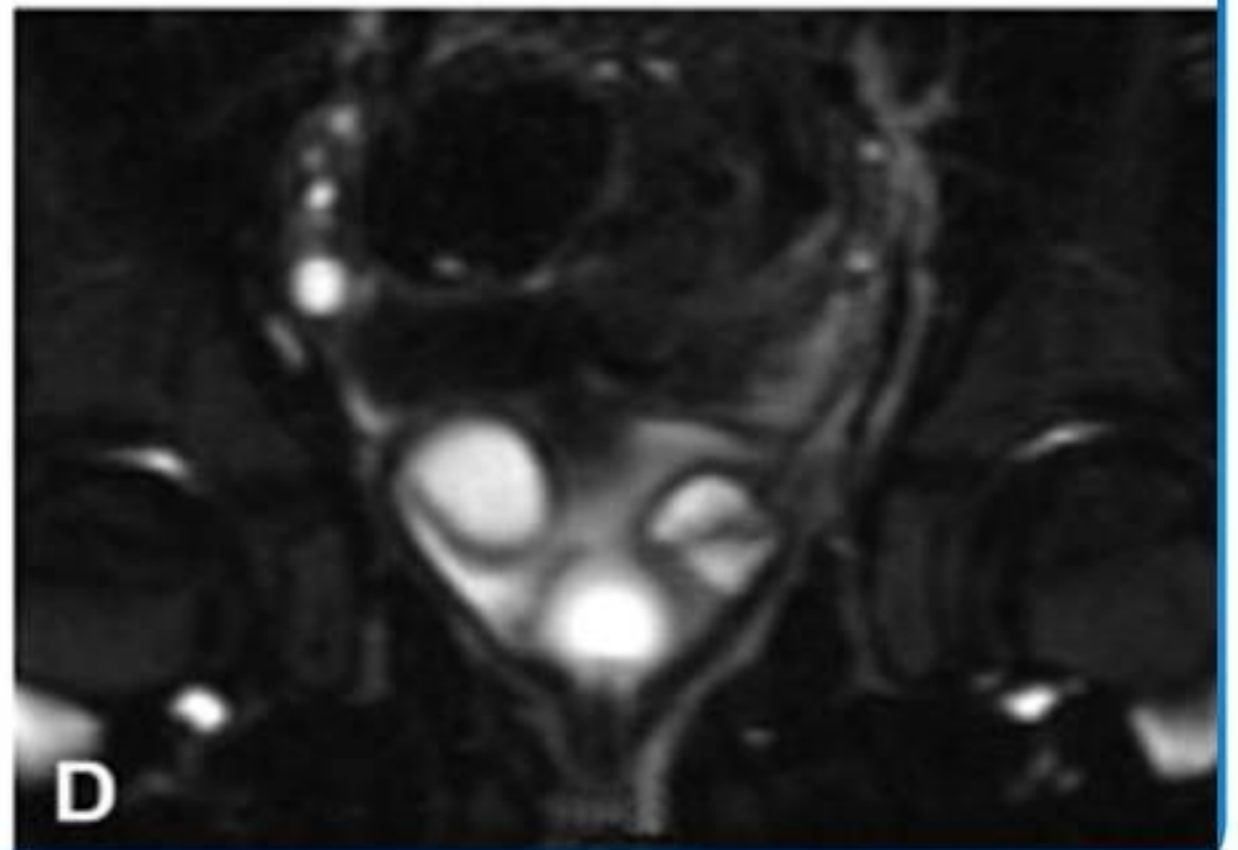
A mild inflammatory reaction following Deflux gel injection occurs as expected

The tissues surrounding the implant show no evidence of major changes in structure

## EVIDENCE

- Injection of Deflux gel into the bladder of pigs did not cause the lymph nodes to enlarge, indicating lack of an immune response.<sup>4</sup>
- In the early stages (2–6 weeks) after Deflux gel injection into pigs and rats, cell types indicative of a mild inflammatory response are present (macrophages, lymphocytes and giant cells).<sup>4</sup> Giant cells have been observed at the site of the implant both in animal studies and in patients with VUR injected with Deflux gel.<sup>2,4</sup> These indicate a foreign body type inflammatory reaction. Such an inflammatory response is to be expected and is a natural reaction provoked by injection of any substance into the body.
- In rats undergoing abdominal injection of Deflux gel, no changes in the organs were observed.<sup>4</sup> Fibrosis in the area of the Deflux gel implant was observed in 13 patients with VUR examined following ureteral reimplantation. However, the incidence of fibrosis was similar to control patients, suggesting that it is a result of the condition and not of the treatment.<sup>2</sup>



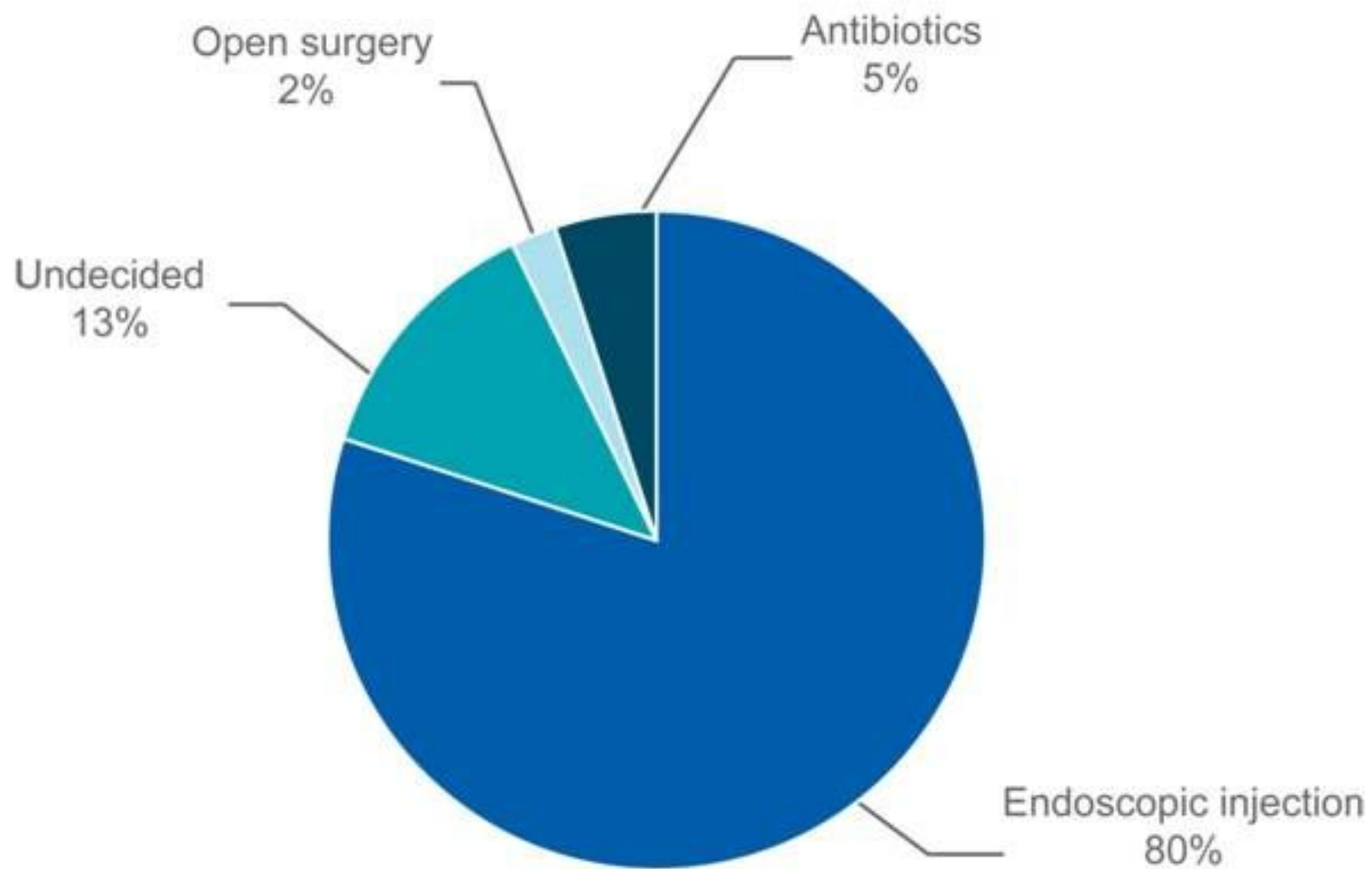


## Deflux gel—A minimally invasive endoscopic procedure

- Outpatient procedure takes approximately 15 minutes<sup>1</sup>
- Requires short-acting general anesthesia<sup>2</sup>
- Made from materials that have been in medical use for over a decade<sup>3</sup>
- More than 50,000 children have been treated<sup>3</sup>
- Dextranomer microspheres stay at the implant site<sup>1,4,5</sup>
- Does not migrate from the injection site<sup>1,4,5</sup>



# Parent preferred<sup>1</sup>



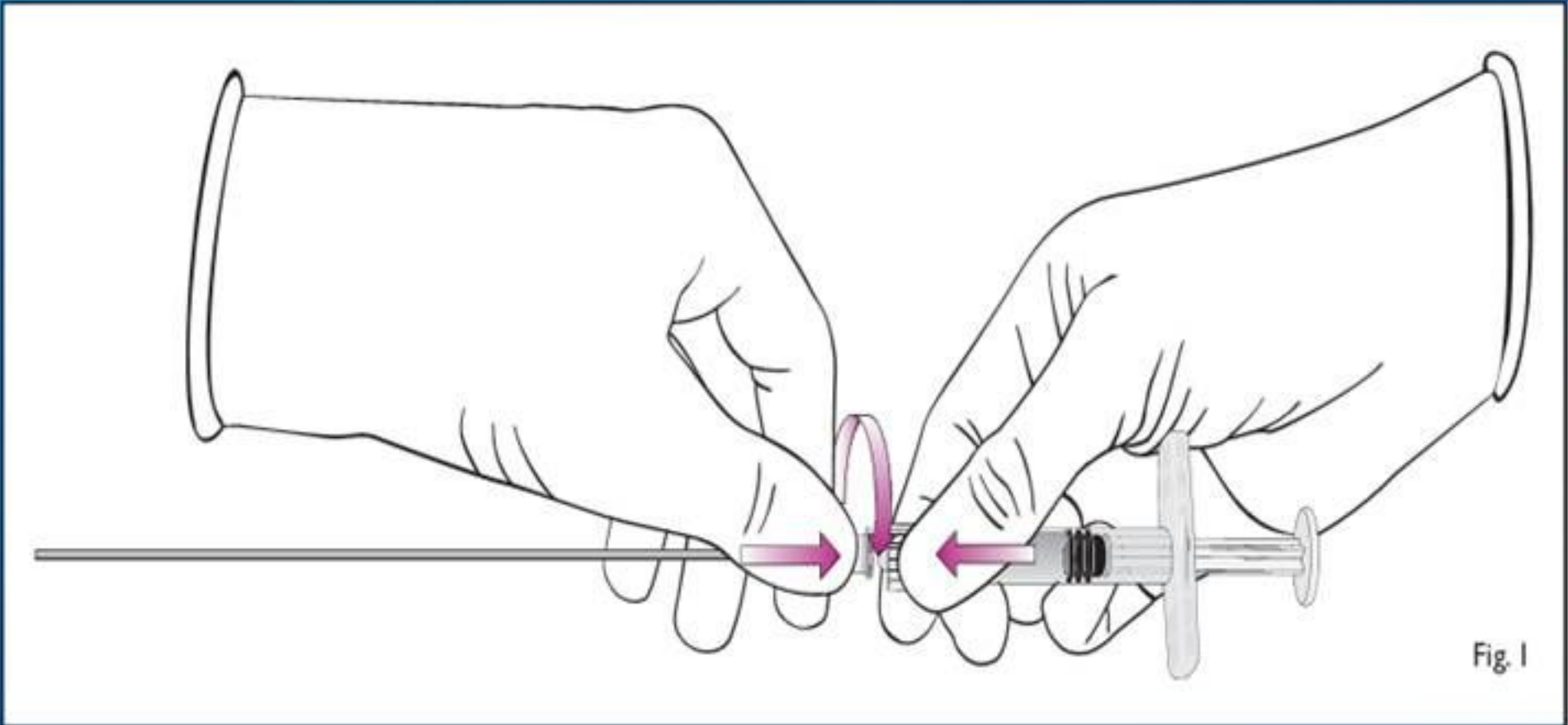


Fig. 1



# RESEARCH

Journal of Pediatric Urology (2008) 4, 221–228

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**Pediatric**  
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EDUCATIONAL ARTICLE

## Endoscopic treatment of vesicoureteral reflux using dextranomer hyaluronic acid copolymer

Joseph A. Moliterno, Hal C. Scherz, Andrew J. Kirsch\*

*Children's Healthcare of Atlanta, Emory University School of Medicine, Atlanta, GA, USA*

Received 24 August 2007; accepted 26 November 2007  
Available online 5 March 2008

# RESEARCH

Journal of Pediatric Urology (2010) 6, 15–22



Journal of  
**Pediatric  
urology**

## The clinical utility and safety of the endoscopic treatment of vesicoureteral reflux in patients with duplex ureters

T.W. Hensle<sup>a,b,\*</sup>, E.A. Reiley<sup>c</sup>, C. Ritch<sup>b</sup>, A. Murphy<sup>b</sup>

<sup>a</sup> Children's Hospital of New York, 3959 Broadway, 219N, New York, NY 10032, USA

<sup>b</sup> Columbia University, College of Physicians and Surgeons, Department of Urology, 161 Fort Washington Avenue, New York, NY 10032, USA

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Received 24 February 2009; accepted 28 May 2009  
Available online 21 July 2009



# RESEARCH

Journal of Pediatric Urology (2008) 4, 341–344



ELSEVIER

Journal of  
**Pediatric  
urology**

## Endoscopic Deflux<sup>®</sup> injection for pediatric transplant reflux: A feasible alternative to open ureteral reimplant

Mark A. Williams<sup>a,\*</sup>, Dana W. Giel<sup>a</sup>, M. Colleen Hastings<sup>b</sup>

<sup>a</sup> Department of Urology, Division of Pediatric Urology (MW and DG), University of Tennessee, Memphis, TN, USA

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# RESEARCH



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## **Incidence of Urinary Tract Infections in Children After Successful Ureteral Reimplantation Versus Endoscopic Dextranomer/Hyaluronic Acid Implantation**

James M. Elmore, Andrew J. Kirsch, Erik A. Heiss,  
Alexander Gächrist and Hal C. Scherr



# Incidence of Urinary Tract Infections in Children After Successful Ureteral Reimplantation Versus Endoscopic Dextranomer/Hyaluronic Acid Implantation

James M. Elmore, Andrew J. Kirsch,\* Erik A. Heiss, Alienor Gilchrist and Hal C. Scherz

*From Children's Healthcare of Atlanta and Emory University School of Medicine, Atlanta, Georgia*

**Purpose:** Endoscopic implantation of dextranomer/hyaluronic acid has proved to be an effective minimally invasive technique for correcting vesicoureteral reflux in children. There is some evidence suggesting that in addition to being less invasive, successful dextranomer/hyaluronic acid implantation compared to successful antireflux surgery is associated with fewer febrile and nonfebrile urinary tract infections. We review the clinical outcomes of 2 groups of children cured of reflux with open surgery and dextranomer/hyaluronic acid implantation to determine if a difference in clinical outcomes exists.

**Materials and Methods:** We reviewed the charts of 43 patients who underwent dextranomer/hyaluronic acid implantation and 33 who underwent open surgery for vesicoureteral reflux. Data collected included age, gender, preoperative and postoperative grades of reflux, and urinalysis and urine culture results. Urinary tract infection was defined as any culture that grew more than  $10^5$  colonies of a single organism, with symptoms typical of cystitis (urgency, frequency, dysuria). A febrile urinary tract infection was defined as an infection accompanied by a temperature greater than 101.5F. Any hospitalizations for febrile episodes were also recorded.

**Results:** The incidence of urinary tract infection after successful open surgery (38%) was significantly higher than that observed following successful dextranomer/hyaluronic acid treatment (15%,  $p = 0.03$ ). Febrile urinary tract infections occurred in 24% of the children who underwent open surgery and in 5% of those who underwent dextranomer/hyaluronic acid implantation ( $p = 0.02$ ). Hospital readmissions occurred only in the group undergoing open surgery.

**Conclusions:** Children successfully cured of vesicoureteral reflux with dextranomer/hyaluronic acid implantation have a lower incidence of febrile and nonfebrile urinary tract infections compared to those cured with open surgery. These findings suggest that dextranomer/hyaluronic acid implantation, when successful, may result in more favorable clinical outcomes.

*Key Words: dextranomer-hyaluronic acid copolymer, vesico-ureteral reflux, urologic surgical procedures, endoscopy*

RESEARCH

# PEDIATRICS<sup>®</sup>

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# Clinical Significance of Primary Vesicoureteral Reflux and Urinary Antibiotic Prophylaxis After Acute Pyelonephritis: A Multicenter, Randomized, Controlled Study

Eduardo H. Garin, MD<sup>a</sup>, Fernando Olavarria, MD<sup>b</sup>, Victor Garcia Nieto, MD<sup>c</sup>, Blanca Valenciano, MD<sup>d</sup>, Alfonso Campos, MD<sup>e</sup>, Linda Young, PhD<sup>a</sup>

<sup>a</sup>Department of Pediatrics, University of South Florida, Tampa, Florida; <sup>b</sup>Universidad Austral, Valdivia, Chile; <sup>c</sup>Hospital Nuestra Señora de la Candelaria, Tenerife, Spain;

<sup>d</sup>Hospital Las Palmas, Gran Canaria, Spain; <sup>e</sup>Department of Pediatrics, University of Florida, Gainesville, Florida

The authors have indicated they have no financial relationships relevant to this article to disclose.

## ABSTRACT

**OBJECTIVES.** To evaluate the role of primary vesicoureteral reflux (VUR) in increasing the frequency and severity of urinary tract infections (UTIs) and renal parenchymal damage among patients with acute pyelonephritis and to determine whether urinary antibiotic prophylaxis reduces the frequency and/or severity of UTIs and/or prevents renal parenchymal damage among patients with mild/moderate VUR.

**METHODS.** Patients 3 months to 18 years of age with acute pyelonephritis, with or without VUR, were assigned randomly to receive urinary antibiotic prophylaxis or not. Patients were monitored every 3 months for 1 year. Dimercaptosuccinic acid renal scans were repeated at 6 months or if there was a recurrence of febrile UTI. Urinalysis and urine culture were performed at each clinic visit. Renal ultrasound scans and voiding cystourethrograms were repeated at the end of 1 year of follow-up monitoring.

**RESULTS.** Of the 236 patients enrolled in the study, 218 completed the 1-year follow-up monitoring. Groups were similar with respect to age, gender, and reflux grade distribution for those with VUR. No statistically significant differences were found among the groups with respect to rate of recurrent UTI, type of recurrence, rate of subsequent pyelonephritis, and development of renal parenchymal scars.

**CONCLUSIONS.** After 1 year of follow-up monitoring, mild/moderate VUR does not increase the incidence of UTI, pyelonephritis, or renal scarring after acute pyelonephritis. Moreover, a role for urinary antibiotic prophylaxis in preventing the recurrence of infection and the development of renal scars is not supported by this study.



ARTICLE

## Is Antibiotic Prophylaxis in Children With Vesicoureteral Reflux Effective in Preventing Pyelonephritis and Renal Scars? A Randomized, Controlled Trial

Marco Pennesi, MD<sup>a</sup>, Laura Travan, MD, PhD<sup>a</sup>, Leopoldo Peratoner, MD<sup>b</sup>, Andrea Bordugo, MD<sup>b</sup>, Adriano Cattaneo, MD<sup>c</sup>, Luca Ronfani, MD, PhD<sup>d</sup>, Silvia Minisini, MD<sup>a</sup>, Alessandro Ventura, MD<sup>a</sup>, for the North East Italy Prophylaxis in VUR study group

### ABSTRACT

**OBJECTIVES.** There has been intense discussion on the effectiveness of continuous antibiotic prophylaxis for children with vesicoureteral reflux, and randomized, controlled trials are still needed to determine the effectiveness of long-term antibiotics for the prevention of acute pyelonephritis. In this multicenter, open-label, randomized, controlled trial, we tested the effectiveness of antibiotic prophylaxis in preventing recurrence of pyelonephritis and avoiding new scars in a sample of children who were younger than 30 months and vesicoureteral reflux.

**METHODS.** One hundred patients with vesicoureteral reflux (grade II, III, or IV) diagnosed with cystourethrography after a first episode of acute pyelonephritis were randomly assigned to receive antibiotic prophylaxis with sulfamethoxazole/trimethoprim or not for 2 years. The main outcome of the study was the recurrence of pyelonephritis during a follow-up period of 4 years. During follow-up, the patients were evaluated through repeated cystourethrographies, renal ultrasounds, and dimercaptosuccinic acid scans.

**RESULTS.** The baseline characteristics in the 2 study groups were similar. There were no differences in the risk for having at least 1 pyelonephritis episode between the intervention and control groups. At the end of follow-up, the presence of renal scars was the same in children with and without antibiotic prophylaxis.

**CONCLUSIONS.** Continuous antibiotic prophylaxis was ineffective in reducing the rate of pyelonephritis recurrence and the incidence of renal damage in children who were younger than 30 months and had vesicoureteral reflux grades II through IV. *Pediatrics* 2008;121:e1489–e1494



# Prophylaxis After First Febrile Urinary Tract Infection in Children? A Multicenter, Randomized, Controlled, Noninferiority Trial

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## ABSTRACT

**OBJECTIVES.** Febrile urinary tract infections are common in children and associated with the risk for renal scarring and long-term complications. Antimicrobial prophylaxis has been used to reduce the risk for recurrence. We performed a study to determine whether no prophylaxis is similar to antimicrobial prophylaxis for 12 months in reducing the recurrence of febrile urinary tract infections in children after a first febrile urinary tract infection.

**METHODS.** The study was a controlled, randomized, open-label, 2-armed, noninferiority trial comparing no prophylaxis with prophylaxis (co-trimoxazole 15 mg/kg per day or co-amoxiclav 15 mg/kg per day) for 12 months. A total of 338 children who were aged 2 months to <7 years and had a first episode of febrile urinary tract infection were enrolled: 309 with a confirmed pyelonephritis on a technetium 99m dimercaptosuccinic acid scan with or without reflux and 27 with a clinical pyelonephritis and reflux. The primary end point was recurrence rate of febrile urinary tract infections during 12 months. Secondary end point was the rate of renal scarring produced by recurrent urinary tract infections on technetium 99m dimercaptosuccinic acid scan after 12 months.

**RESULTS.** Intention-to-treat analysis showed no significant differences in the primary outcome between no prophylaxis and prophylaxis: 12 (9.45%) of 127 vs 15 (7.11%) of 211. In the subgroup of children with reflux, the recurrence of febrile urinary tract infections was 9 (19.6%) of 46 on no prophylaxis and 10 (12.1%) of 82 on prophylaxis. No significant difference was found in the secondary outcome: 2 (1.9%) of 108 on no prophylaxis versus 2 (1.1%) of 187 on prophylaxis. Bivariate analysis and Cox proportional hazard model showed that grade III reflux was a risk factor for recurrent febrile urinary tract infections. Whereas increasing age was protective, use of no prophylaxis was not a risk factor.

**CONCLUSIONS.** For children with or without primary nonsevere reflux, prophylaxis does not reduce the rate of recurrent febrile urinary tract infections after the first episode. *Pediatrics* 2008;122:1064–1071

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This trial has been registered at [www.clinicaltrials.gov](http://www.clinicaltrials.gov) (identifier NCT00156546).

### Key Words

urinary tract infection, antibiotic prophylaxis, renal scar, DMSA scan

### Abbreviations

UTI—urinary tract infection

RR—relative risk

CI—confidence interval

VUR—vesicoureteral reflux

ITT—intention-to-treat

DMSA—dimercaptosuccinic acid

VCIU—voiding cystourethrography

IQR—interquartile range

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# Case report



- Girl, 12 years old, UTIs
- VUR Right side, grade II







**THANKS FOR WATCHING!!**

In the Management of Children  
With Grade II-IV Vesicoureteral Reflux (VUR)

**Stop Febrile UTIs  
in Their Tracts**