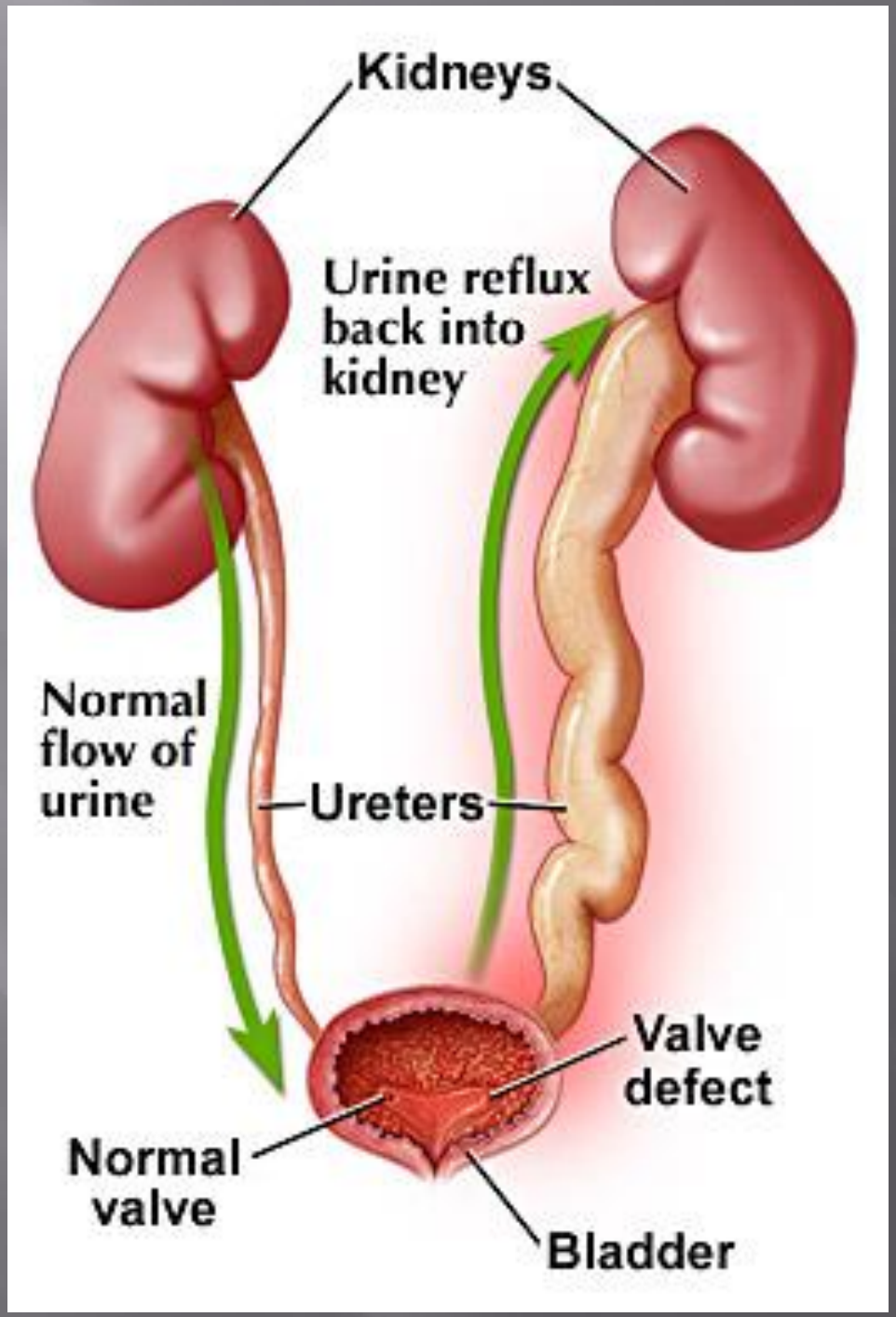
MANAGEMENT OF VESICOURETERAL REFLUX

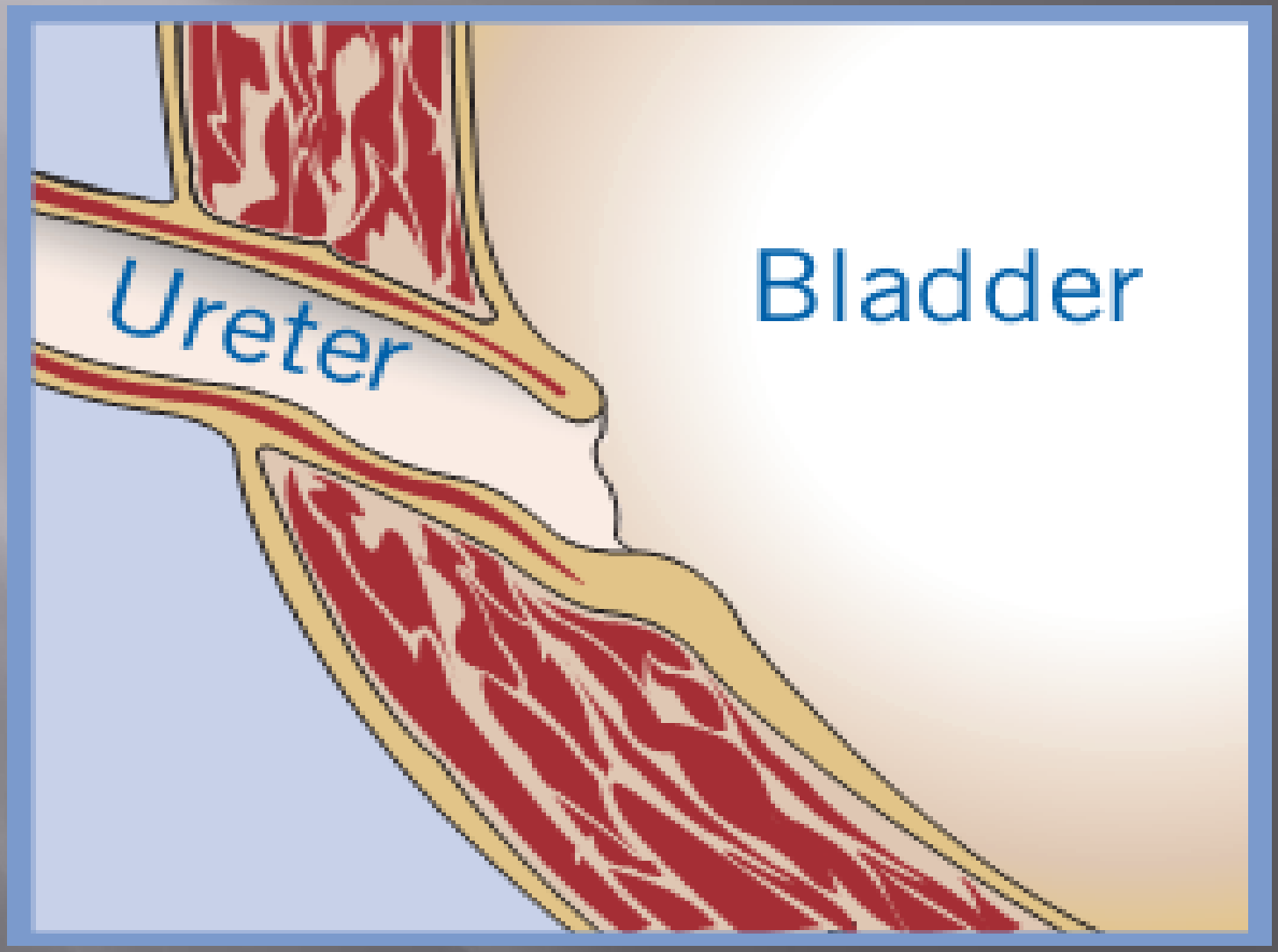
Department of Urology

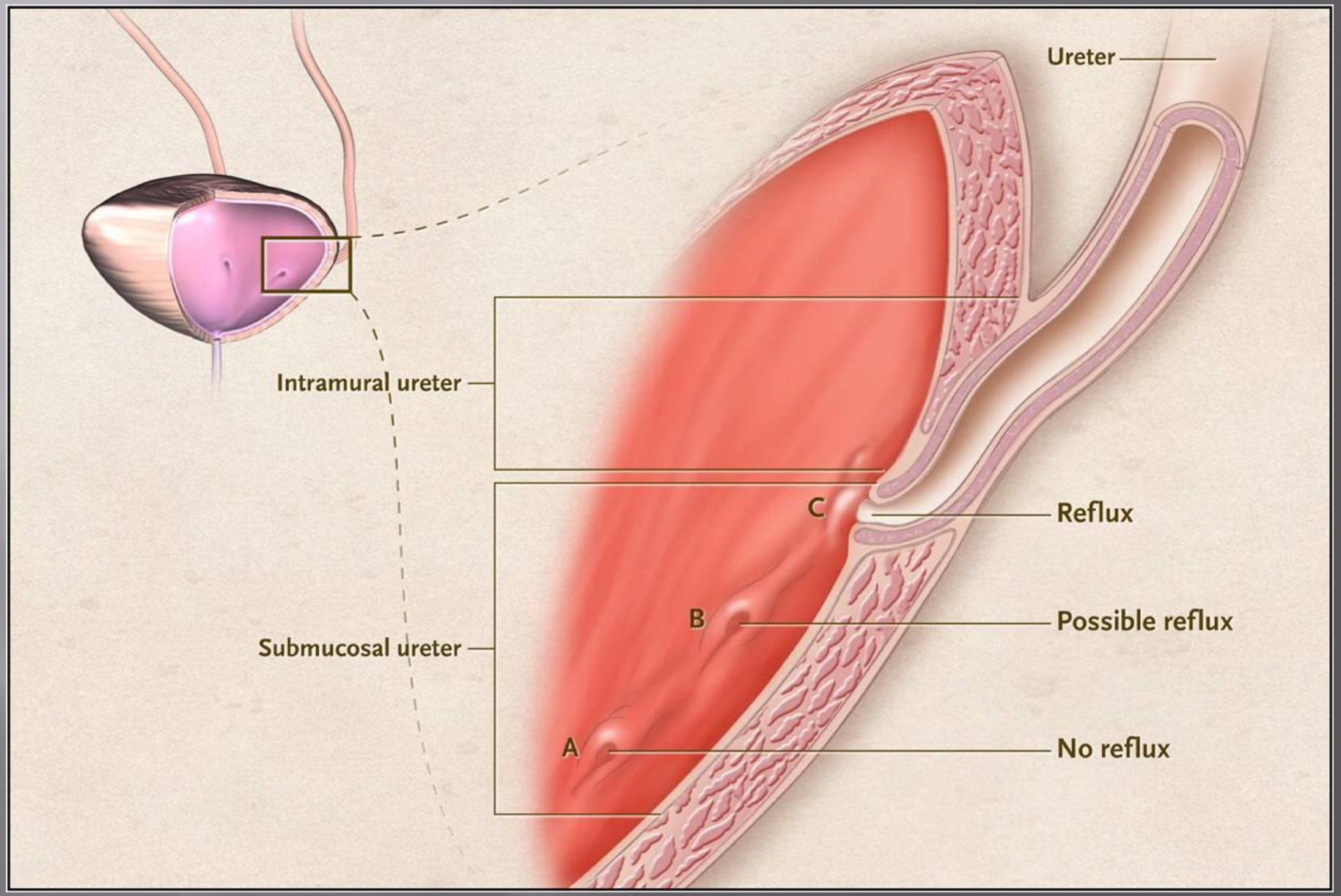

Kidneys
Urine reflux back into kidney
Normal flow of urine
Ureters
Valve defect
Normal valve
Bladder

EPIDEMIOLOGY

- 1% newborn
- 30 - 45% in children with UTIs
- Ethnicity, gender, age,
- Genetics (24,7% for siblings; 35,7% parents)

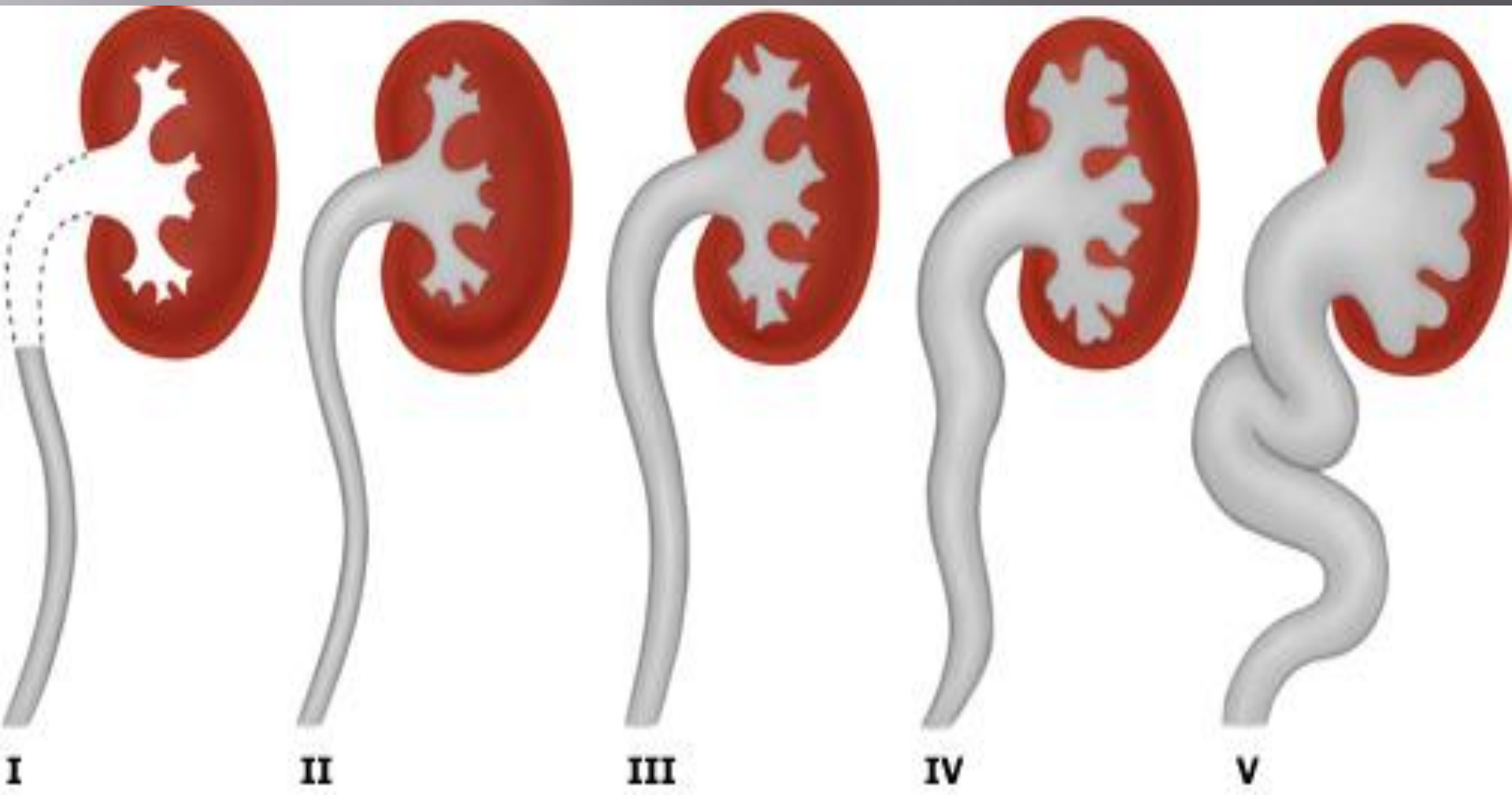
Primary VUR

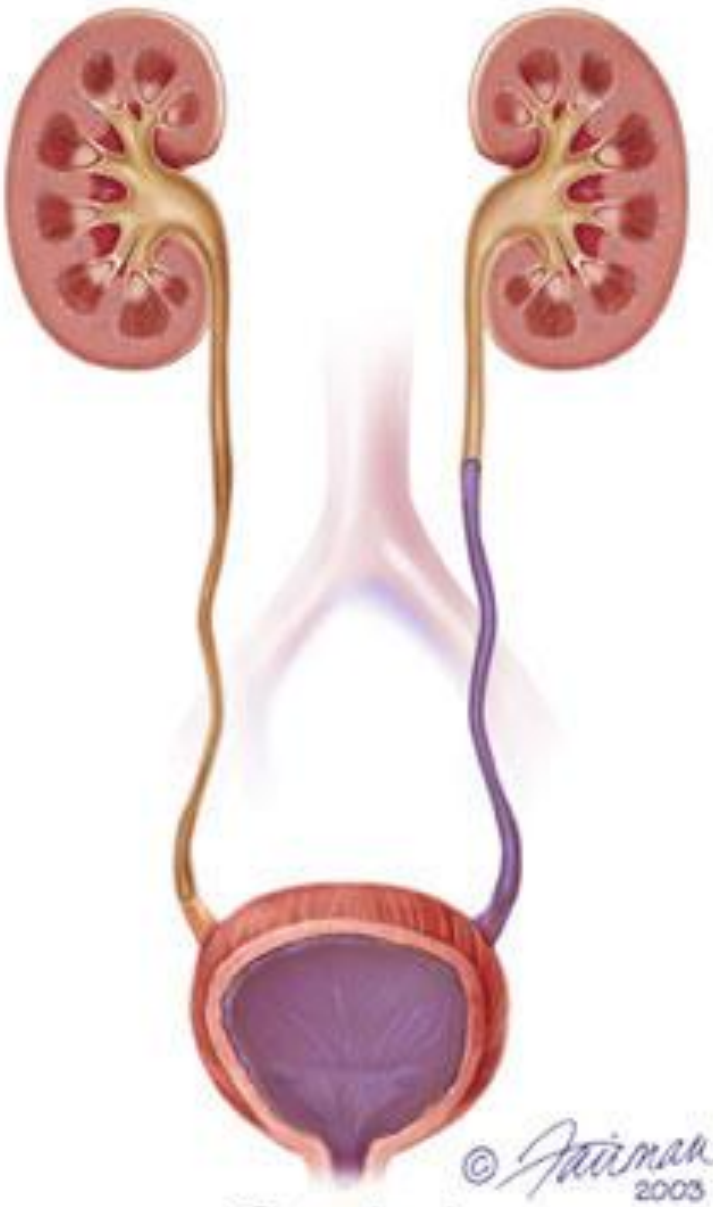



Ureter
Intramural ureter
Submucosal ureter
C
Reflux
B
Possible reflux
A
No reflux

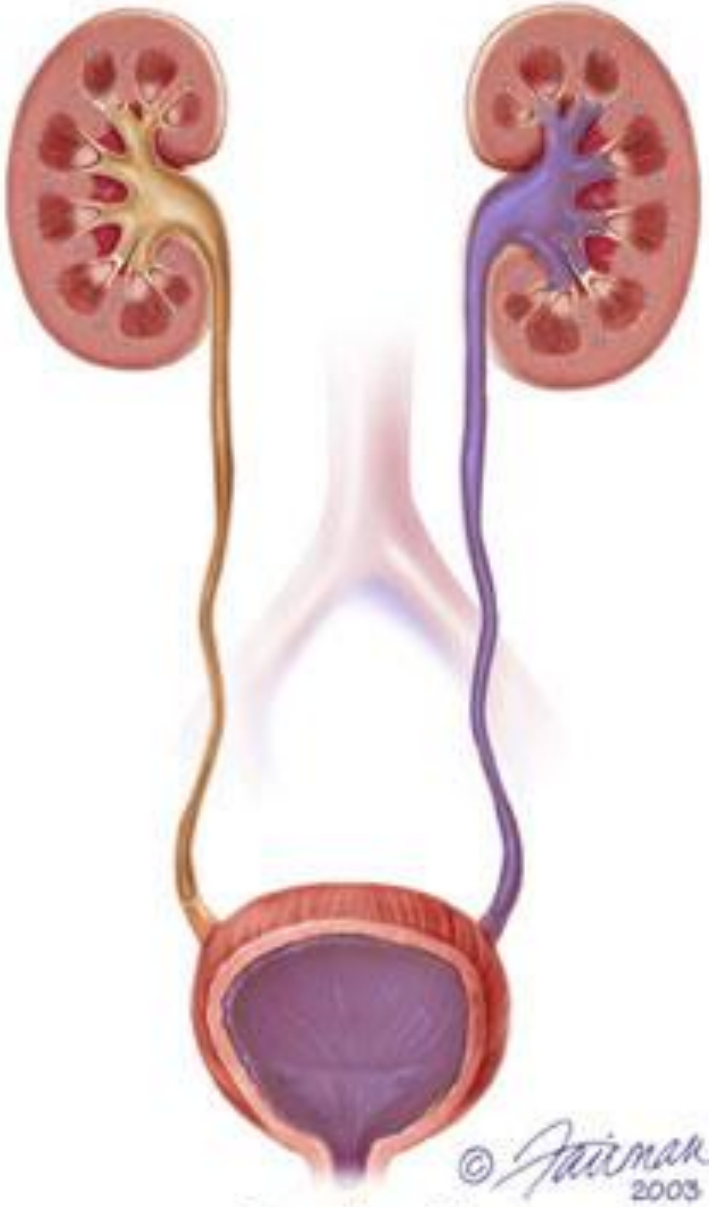
GRADING-IRSG

The International Reflux Study Group





Grade I



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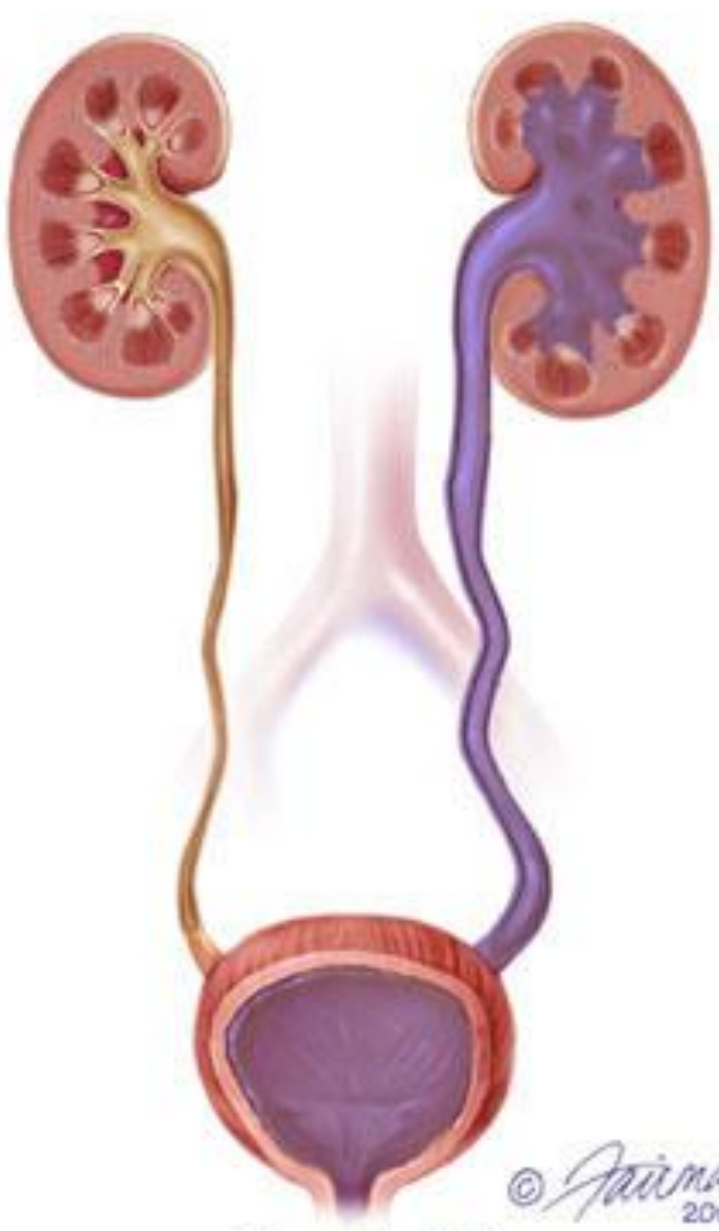
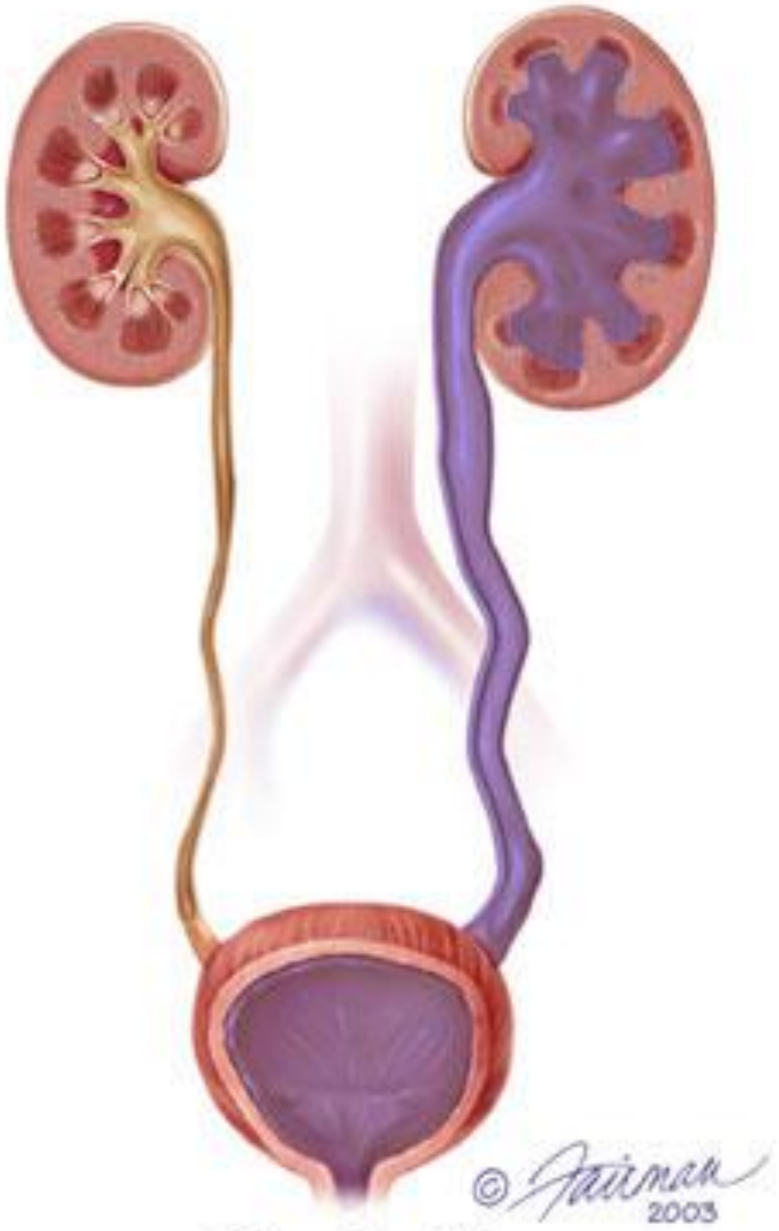
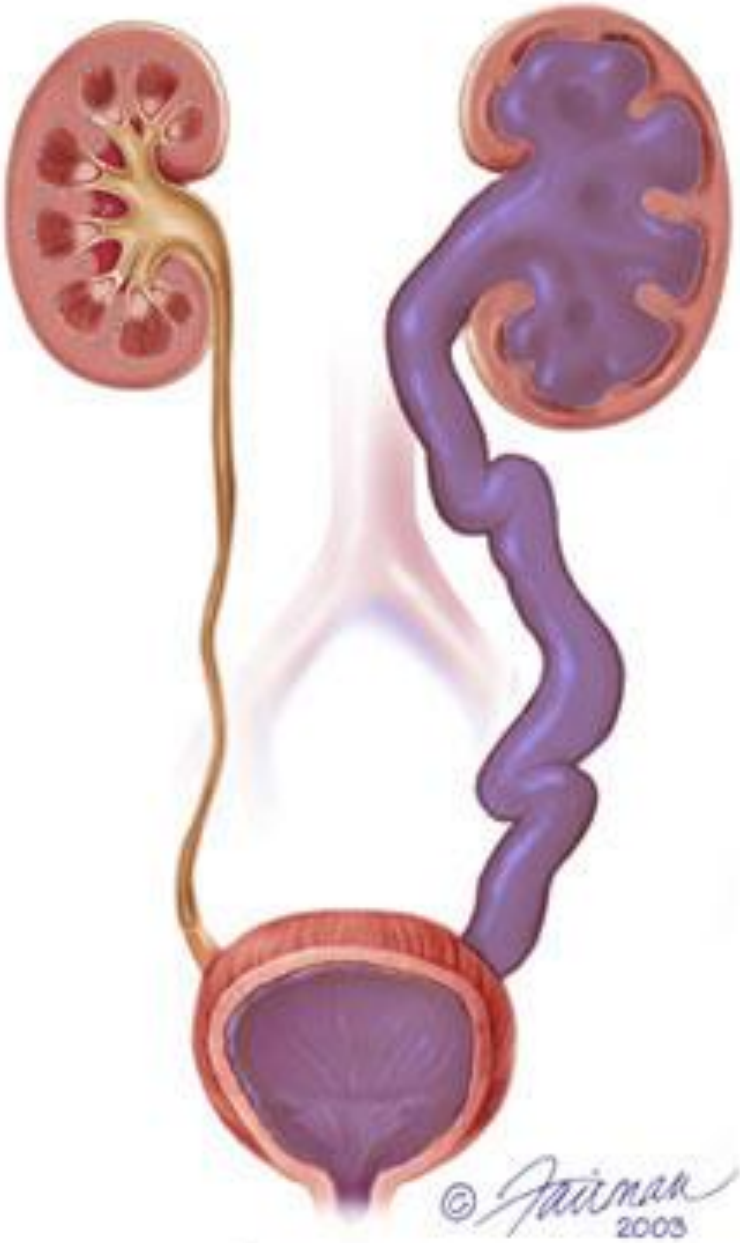


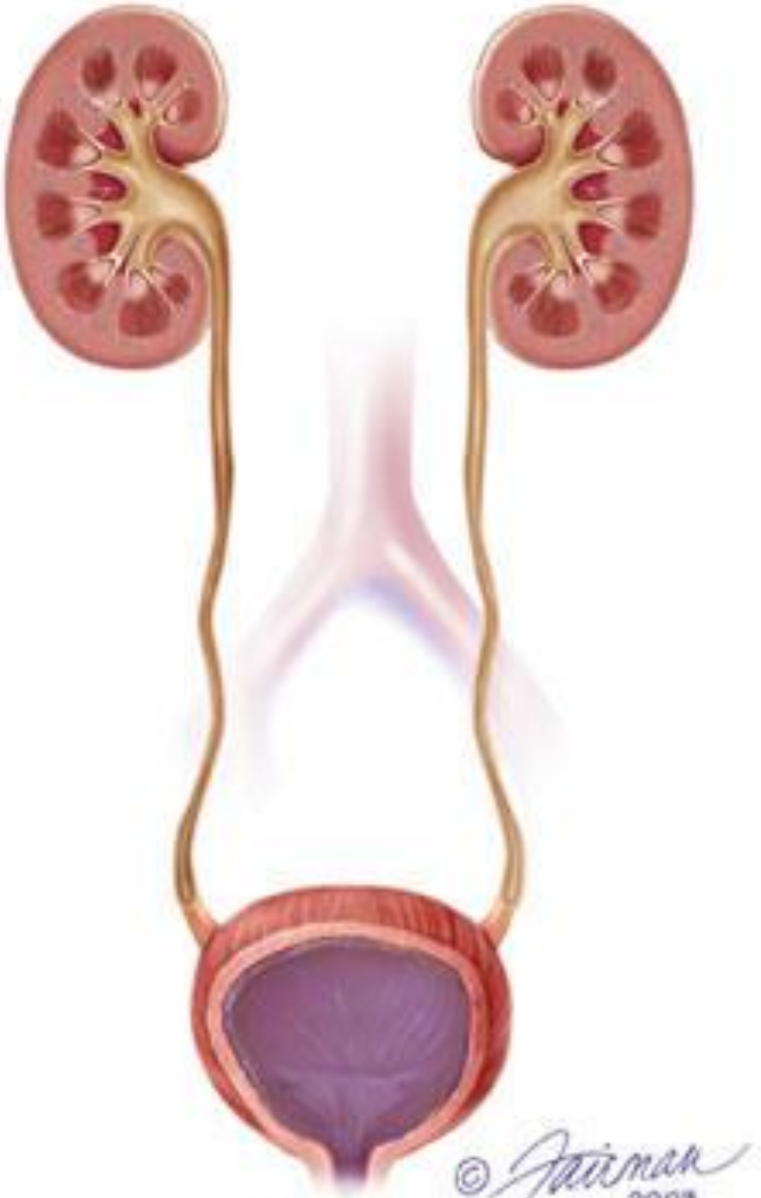
Grade III



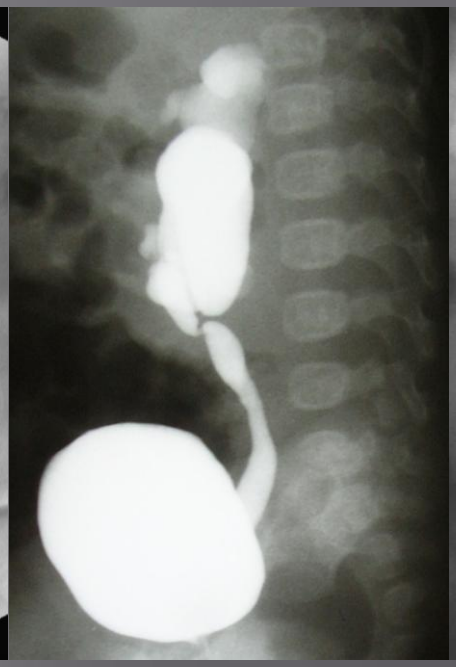
Grade IV

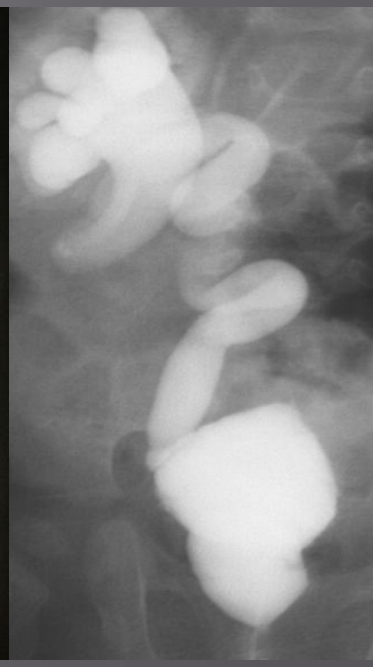


Grade V



Normal





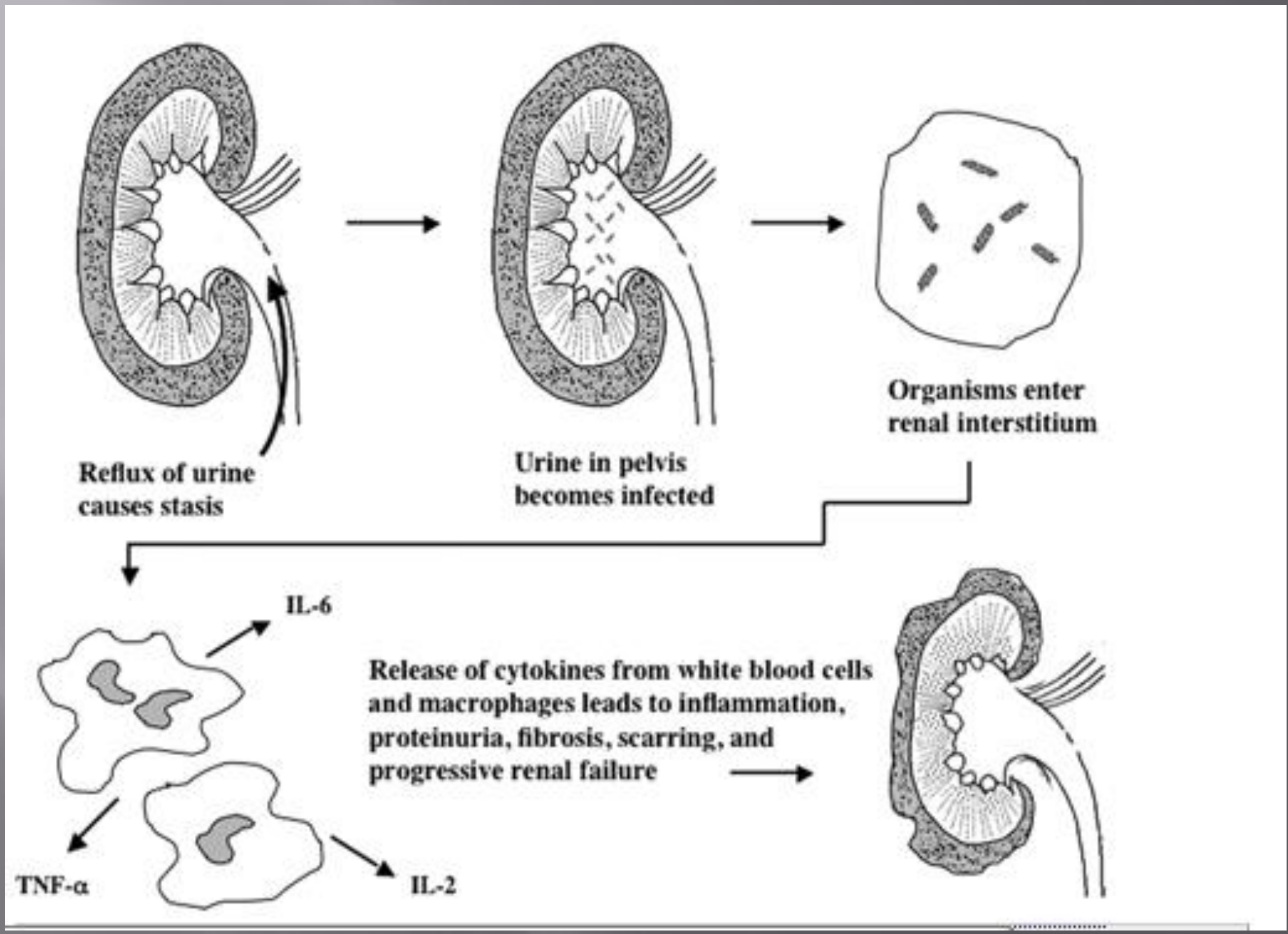
Grade I

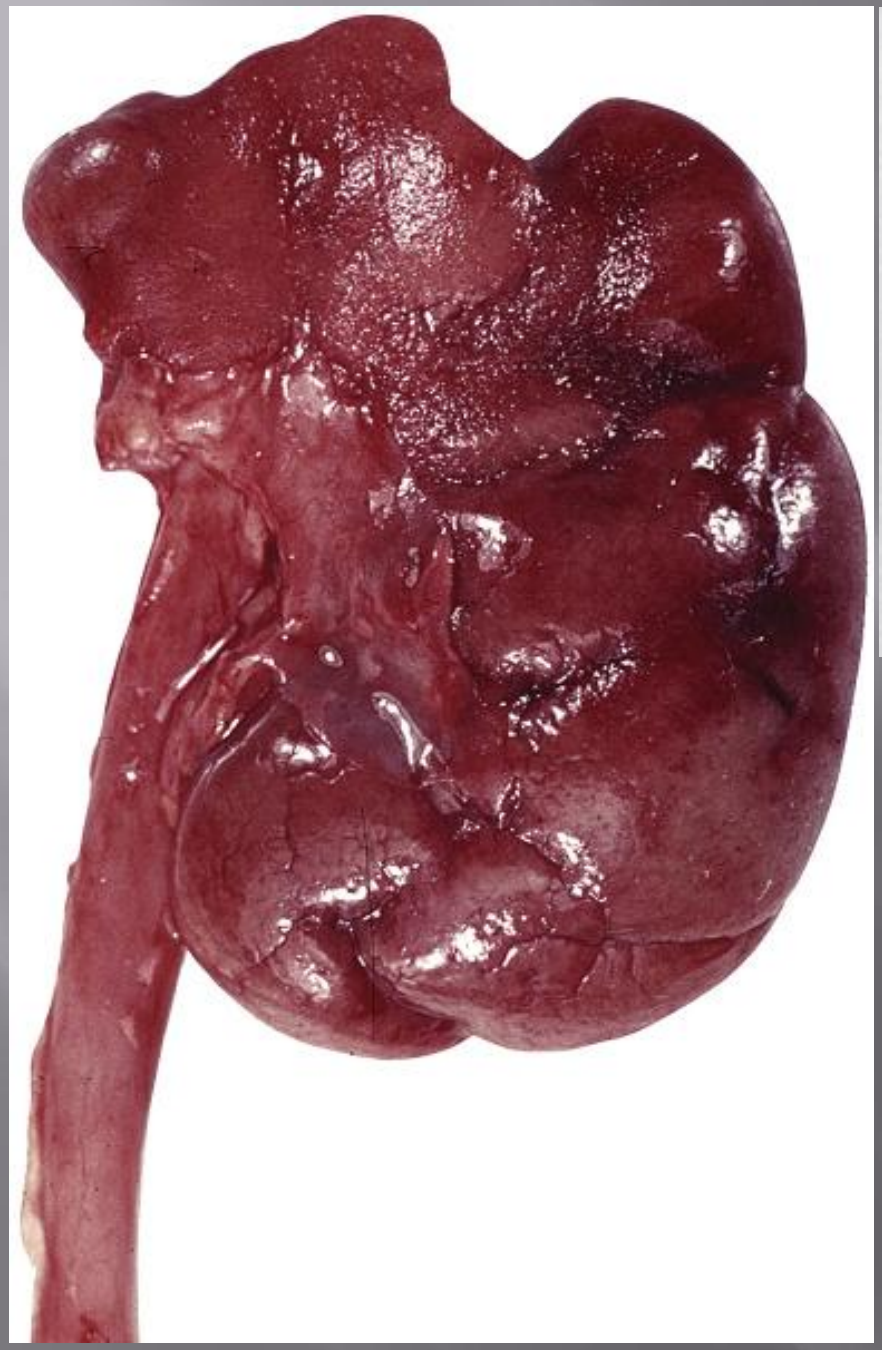
Grade II

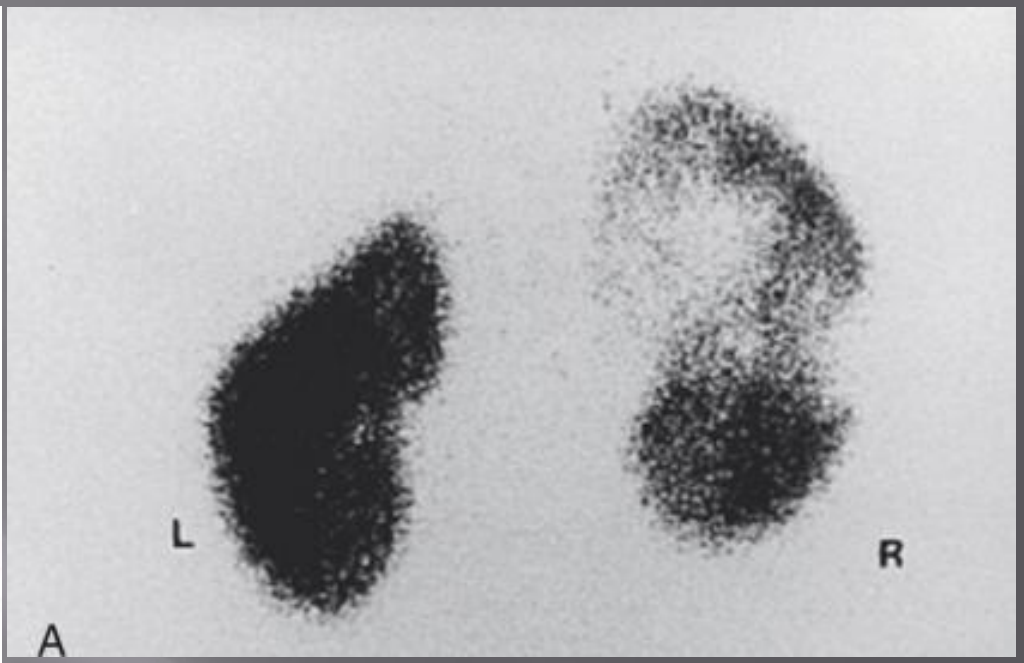
Grade III

Grade IV

Grade V


Reflux of urine causes stasis
Urine in pelvis becomes infected
Organisms enter renal interstitium
IL-6
TNF-α
IL-2
Release of cytokines from white blood cells and macrophages leads to inflammation, proteinuria, fibrosis, scarring, and progressive renal failure





Renal scaring: hypertension and chronic kidney disease

SPONTANEOUS RESOLUTION

Systematic Review of 26 studies of 1987 patients

Grades I and II: By 5 years of age, spontaneous resolution in 80% of patients.

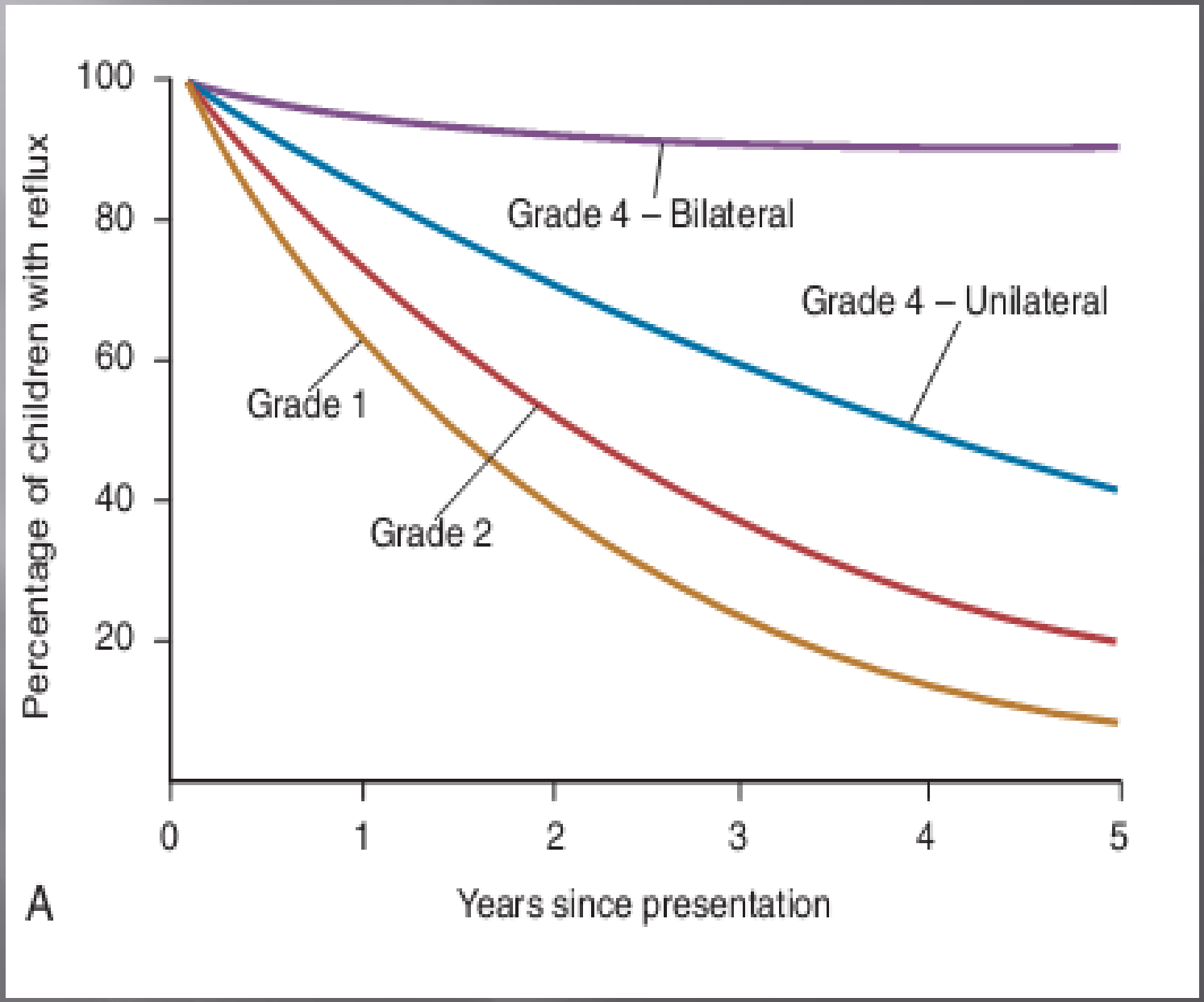
Grade III: Youngest group(1 - 2 yrs) with unilateral: 70% resolution
Oldest group (5 - 10 yrs) with bilateral: < 20% resolution.

Grade IV: 60% for unilateral
< 10% for bilateral reflux.

Grade V: Spontaneous resolution rarely occurred.

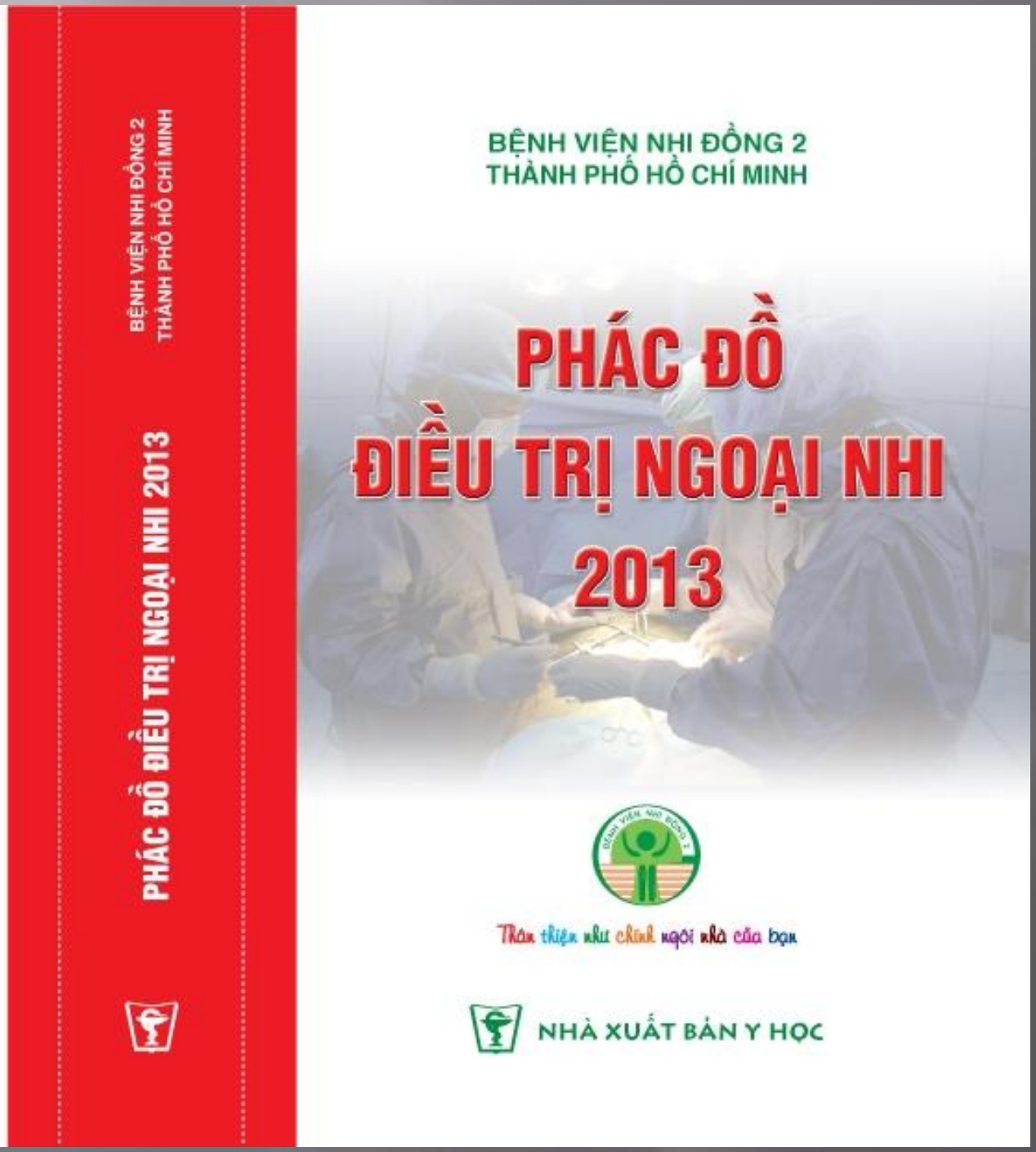
Elder JS, Peters CA, Arant BS Jr, et al. Pediatric Vesicoureteral Reflux Guidelines Panel summary report on the management of primary vesicoureteral reflux in children. J Urol 1997; 157:1846.(UP to date)

Spontaneous resolution



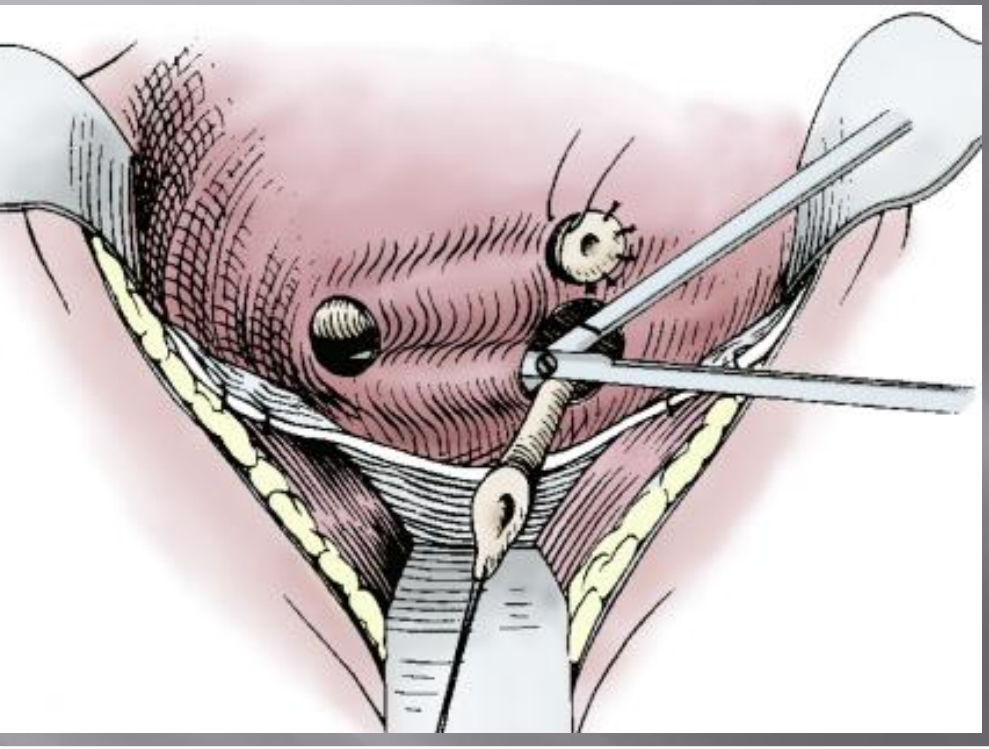
Therapeutic Interventions

- Long term antibiotic therapy
- Surgical treatment



- Medical therapy
- Surgical treatment

Open Surgical Reimplantation



- 95%-99% success rate

Kennelly MJ, Bloom DA, Ritchey ML, Panzl AC. Outcome analysis of bilateral Cohen cross-trigonal ureteroneocystostomy. Urology 1995; 46:393.

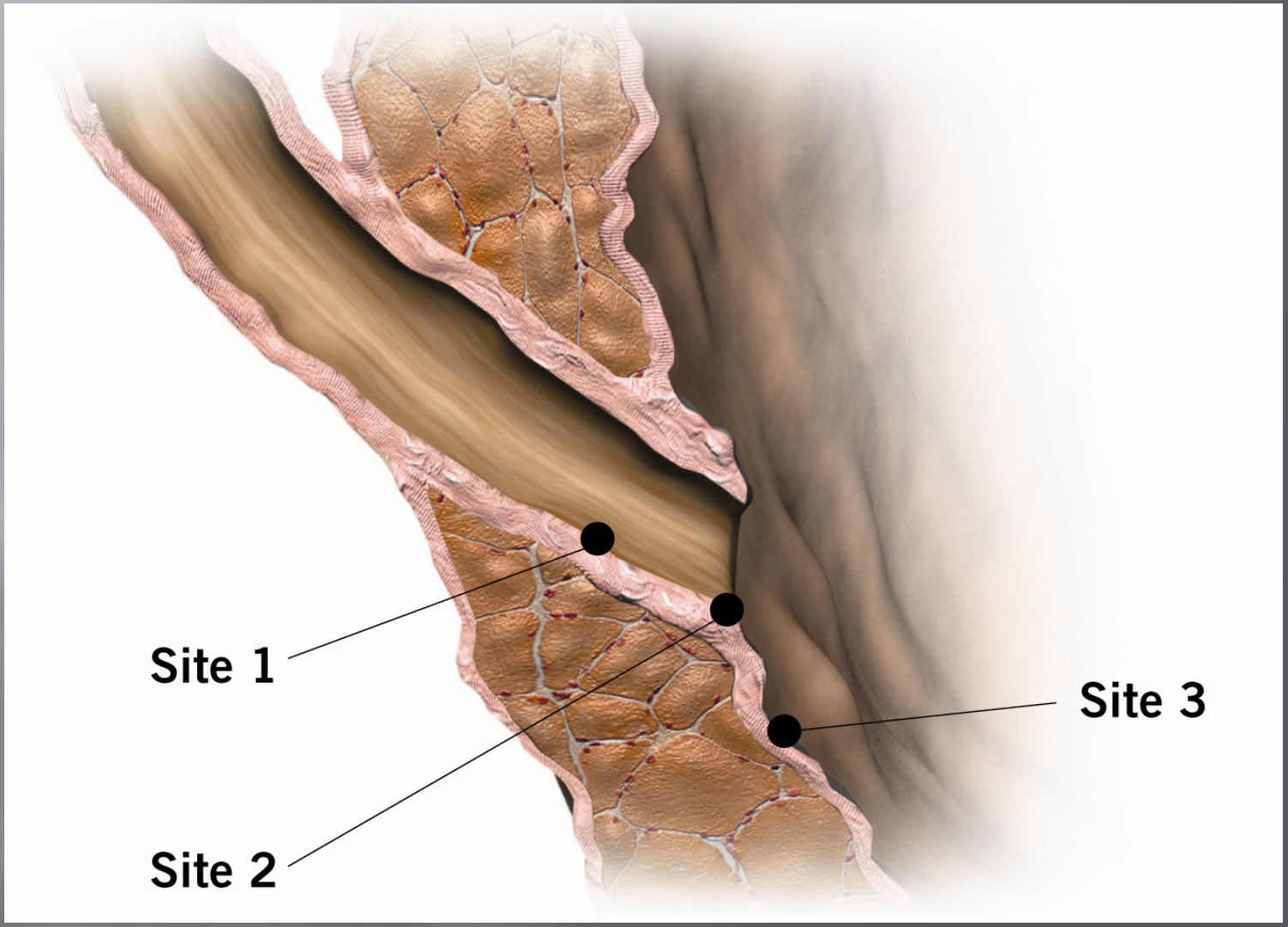
Ellsworth PI, Merguerian PA. Detrusorrhaphy for the repair of vesicoureteral reflux: comparison with the Leadbetter-Politano ureteroneocystostomy. J Pediatr Surg 1995; 30:600.

McLorie GA, Jayanthi VR, Kinahan TJ, et al. A modified extravesical technique for megaureter repair. Br J Urol 1994; 74:715.

Barrieras D, Lapointe S, Reddy PP, et al. Are postoperative studies justified after extravescial ureteral reimplantation? J Urol 2000; 164:1064.

Hubert KC, Kokorowski PJ, Huang L, et al. Clinical outcomes and long-term resolution in patients with persistent vesicoureteral reflux after open ureteral reimplantation. J Urol 2012; 188:1474.

Endoscopic Injection



Systematic Review of 7303 ureters from 89 reports:

Grade I: **89%** (95% CI, 69-90 percent)
Grade II: **83%** (95% CI, 76-90 percent)
Grade III: **71%** (95% CI, 64-79 percent)
Grade IV: **62%** (95% CI, 59-66 percent)
Grade V: **59%** (95% CI, 54-72 percent)

Routh JC, Inman BA, Reinberg Y. Dextranomer/hyaluronic acid for pediatric vesicoureteral reflux: systematic review. Pediatrics 2010; 125:1010.(Up To Date)

Complications of Endoscopic Correction

Contralateral VUR: Further studies are needed to verify whether this is a complication of the procedure or undetected preexisting reflux, and to determine its clinical significance.

Elmore JM, Kirsch AJ, Lyles RH, et al. New contralateral vesicoureteral reflux following dextranomer/hyaluronic Acid implantation: incidence and identification of a high risk group. J Urol 2006; 175:1097

Ureteral obstruction: Retrospective review of 745 patients with 1155 ureters , the incidence of postoperative ureteral obstruction was less than 1 percent.

Vandersteen DR, Routh JC, Kirsch AJ, et al. Postoperative ureteral obstruction after subureteral injection of dextranomer/hyaluronic Acid copolymer. J Urol 2006; 176:1593.

MEDICAL THERAPY

The PROBLEMS with Abx

- Resistance
- Compliance
- Side effects
- Cost

Antibiotic Prophylaxis

AUA/AAP Guidelines, 2010, state that all children with reflux should be on prophylaxis until resolution or surgical correction

Many studies challenging this and guidelines are under revision

The Birmingham Reflux Study

Medical and surgical management was prospectively compared in a randomized cohort of 104 patients with high-grade reflux (Birmingham Reflux Study Group, 1987) over a 5-year period.

The incidence of new scars was the same with either treatment modality.

Antibiotics VS No Treatment

Children were randomized to receive no treatment, daily antibiotic prophylaxis, or prophylaxis given on three days each week.

There was no significant difference in risk for UTI (29 children; RR 0.25; 95% CI 0.03 to 1.85) or renal parenychmal injury (29 children; RR 0.40; 95% CI 0.02 to 9.18) between children given no therapy and children given daily antibiotics.

Reddy PP, Evans MT, Hughes PA, et al. Antimicrobial prophylaxis in children with vesico-ureteral reflux: a randomised prospective study of continuous therapy vs intermittent therapy vs surveillance. Proceedings of AAP. Pediatrics Supplement, 1997.

Abx VS No Treatment (cont.)

Garin, et al (2006) randomized children with acute pyelolnephritis to abx prophylaxis versus no treatment. One year follow up.

113 had VUR grade 1-3

With abx (55 pts) 6 with cystitis, 7 with pyelonephritis, 5 renal scars

Without abx (58 pts): 9 with cystitis, 1 with pyelonephritis, 2 renal scars

Pediatrics 117(3):626-632. 2006

PEDIATRICS®

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DEDICATED TO THE HEALTH OF ALL CHILDREN™

ARTICLE

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

Giovanni Montini, MD[a], Luca Rigon, MD[a], Pietro Zucchetta, MD[b], Federica Fregonese, MD[c], Antonella Toffolo, MD[d], Daniela Gobber, MD[e], Diego Cecchin, MD[b], Luigi Pavanello, MD[f], Pier Paolo Molinari, MD[g], Francesca Maschio, MD[h], Sergio Zanchetta, MD[i], Walburga Cassar, MD[j],

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

www.pediatrics.org/cgi/doi/10.1542/peds.2007-3770

doi:10.1542/peds.2007-3770

This trial has been registered at 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
VCUG—voiding cystourethrography
IQR—interquartile range

Accepted for publication Mar 3, 2008

Address correspondence to Giovanni Montini, MD, Nephrology, Dialysis and Transplant Unit, Pediatric Department, Azienda Ospedaliera-University of Padova, Via Giustiniani, 3, 35128 Padova, Italy. E-mail: montini@pediatria.unipd.it

ARTICLE

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

Marco Pennesi, MD[a], Laura Travan, MD, PhD[a], Leopoldo Peratoner, MD[b], Andrea Bordugo, MD[b], Adriano Cattaneo, MD[c], Luca Ronfani, MD, PhD[d], Silvia Minisini, MD[a], Alessandro Ventura, MD[a], 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.

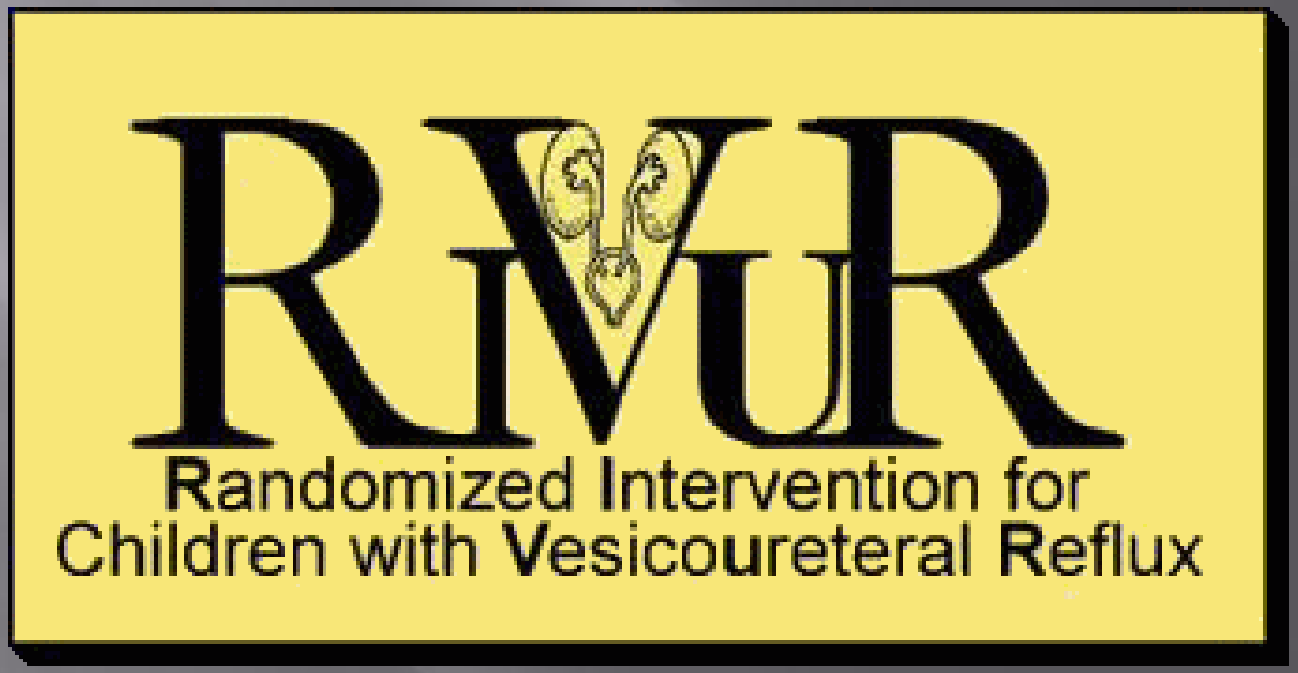
METHODS. One hundred patients with vesicoureteral reflux (grade II, III, or IV) diagnosed with cystourethrography after a first episode of acute pyelonephritis were randomly assigned to receive antibiotic prophylaxis with sulfamethoxazole/trimethoprim or not for 2 years. The main outcome of the study 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

Current research does not support nor refute the use of antimicrobial prophylaxis in patients with VUR

Well designed and conducted, randomized trials are necessary to settle this question- Randomized Intervention for Children with Vesicoureteral Reflux(RIVUR)



Journal of Pediatric Urology (2009) 5, 336–341

ELSEVIER

Journal of Pediatric urology

Controversies in the management of vesicoureteral reflux: The rationale for the RIVUR study☆

Ranjiv Mathews*, Myra Carpenter, Russell Chesney, Alejandro Hoberman, Ron Keren, Tej Mattoo, Marva Moxey-Mims, Lee Nyberg, Saul Greenfield

Division of Pediatric Urology, The Johns Hopkins School of Medicine, 600 North Wolfe St., Baltimore, MD 21287, USA

Received 11 March 2009; accepted 13 May 2009

RIVUR
Randomized Intervention for Children with Vesicoureteral Reflux

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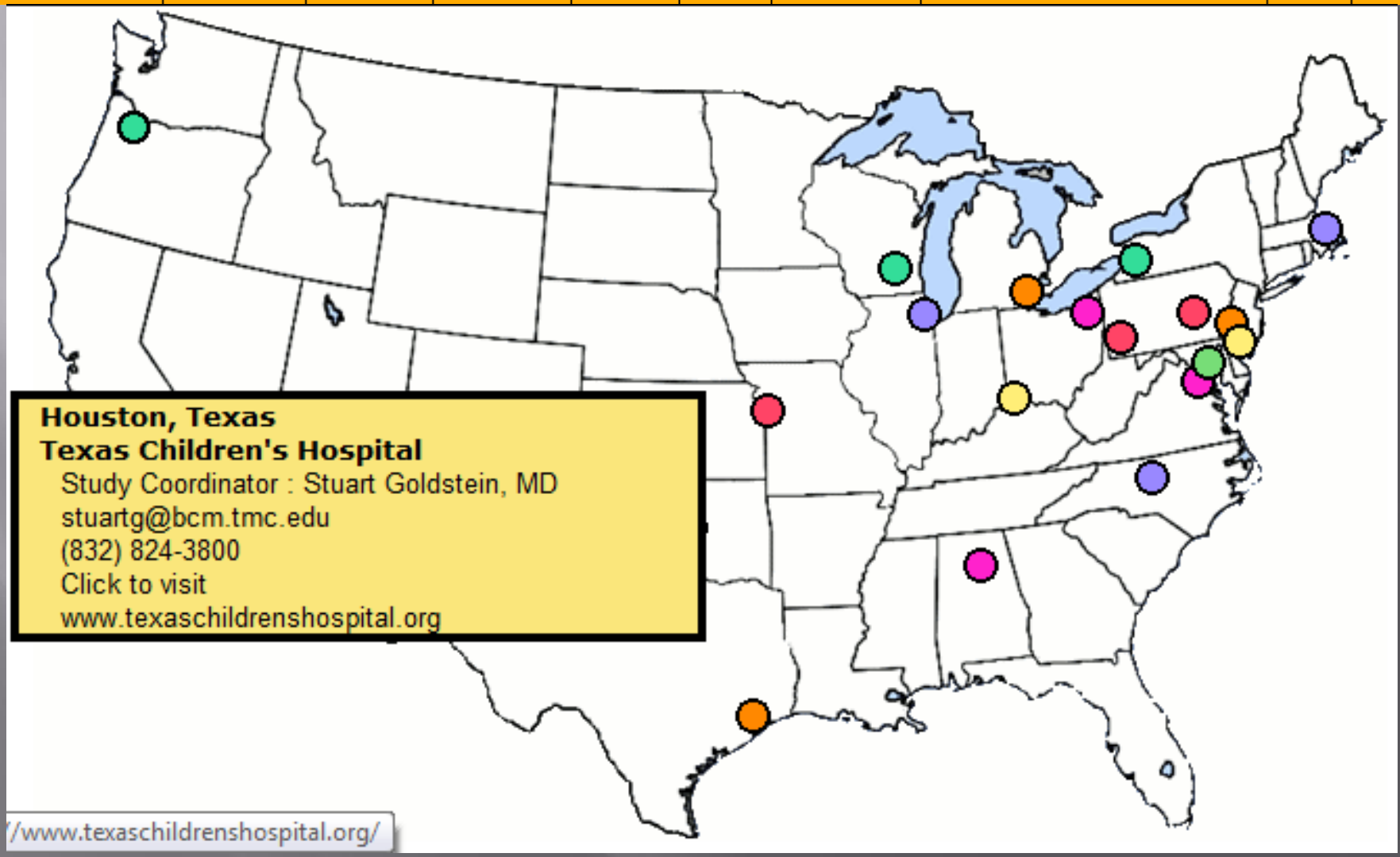

/www.texaschildrenshospital.org/

American Urology Association (AUA)-European Association of Urology (EAU) 2010

SURGERY :

Children who fail medical therapy or who have significant side effects from continuous prophylactic antibiotic coverage

Grade V reflux with scarring
Grade V reflux in children over six years of age

Thank you for listening!