

*Urinary Tract Infections in
Children: “The Muddy Waters”*



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Disclosures




- No Disclosures

Objectives

- Review the “basics” of UTIs in Children
- Cover the “newer” guidelines/approaches
- Newer information “Muddy Waters”
 - Examine dogma
 - Genetic/predetermined factors
 - Outcomes
- What to do.
- CAM

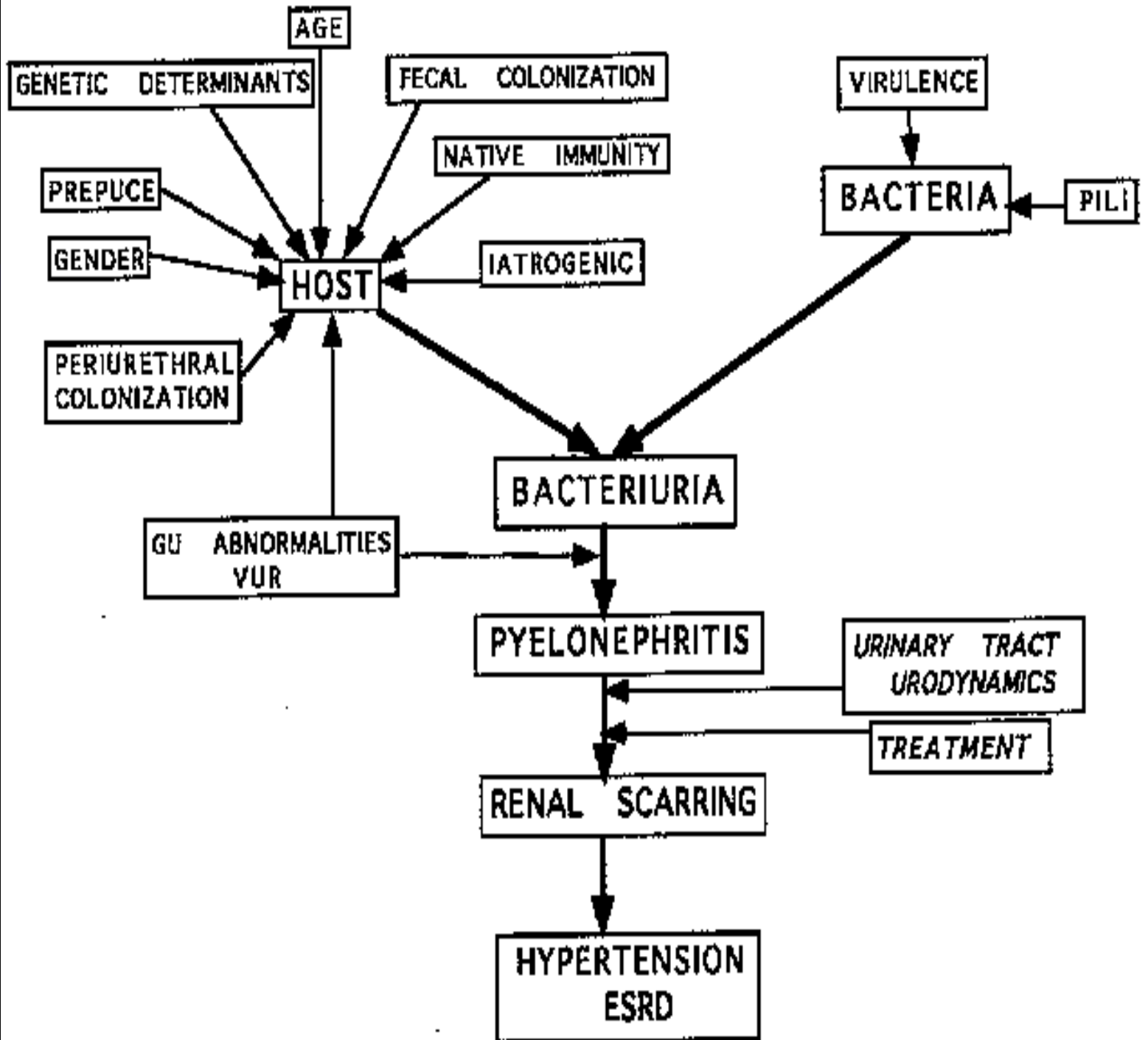
UTIs: Terminology

- Bacteriuria: Bacteria in the bladder urine.
- Acute Pyelonephritis: Symptomatic UTI with infections in the renal parenchyma.
- Acute Cystitis: Symptomatic UTI with infections in the bladder.
- Asymptomatic Bacteriuria: Bacteria in the urine without clinical symptoms.

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- Reflux nephropathy/Pyelonephritic renal scarring: Damage of the kidney(s) related to renal parenchymal infections, can be w/ or w/o VUR
 - Voiding cystourethrogram (VCUG): Bladder filled with contrast, when distended, voids and watch for reflux.
 - RNC: Same technique but with radionuclide.

UTIs: Prevalence and Risk Factors

- 5.3% infants w/fever in ER.
- Uncirced boys: 5-20X >circed
- Boys overall~1%, Girls as high as 8%
- Anatomic issues: What is normal incidence of VUR: few% vs 17%?



Microbiology (Anything!)

- E.Coli
 - P-fimbriated
- Proteus
- Pseudomonas
- Enterobacter
- Enterococci
- Klebsiella
- Neonates
 - E. Coli/Group B Streptococci
 - Hematogenous spread
- Staph aureus
- Staph saprophyticus
 - more common in adol/young women
- Candida
- You name it!

Clinical findings

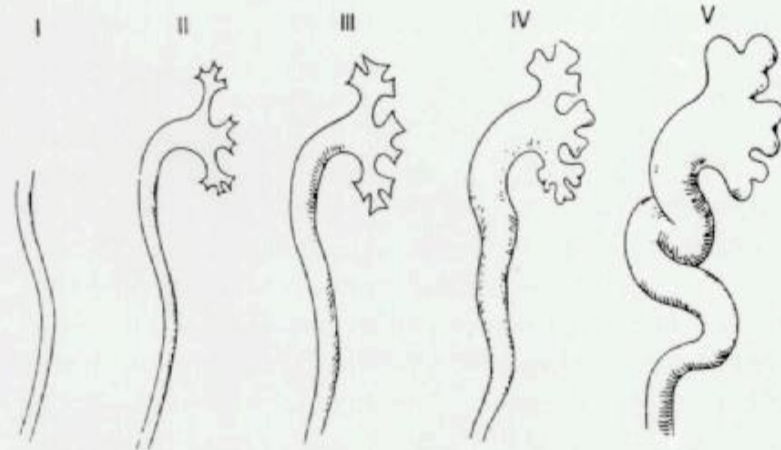
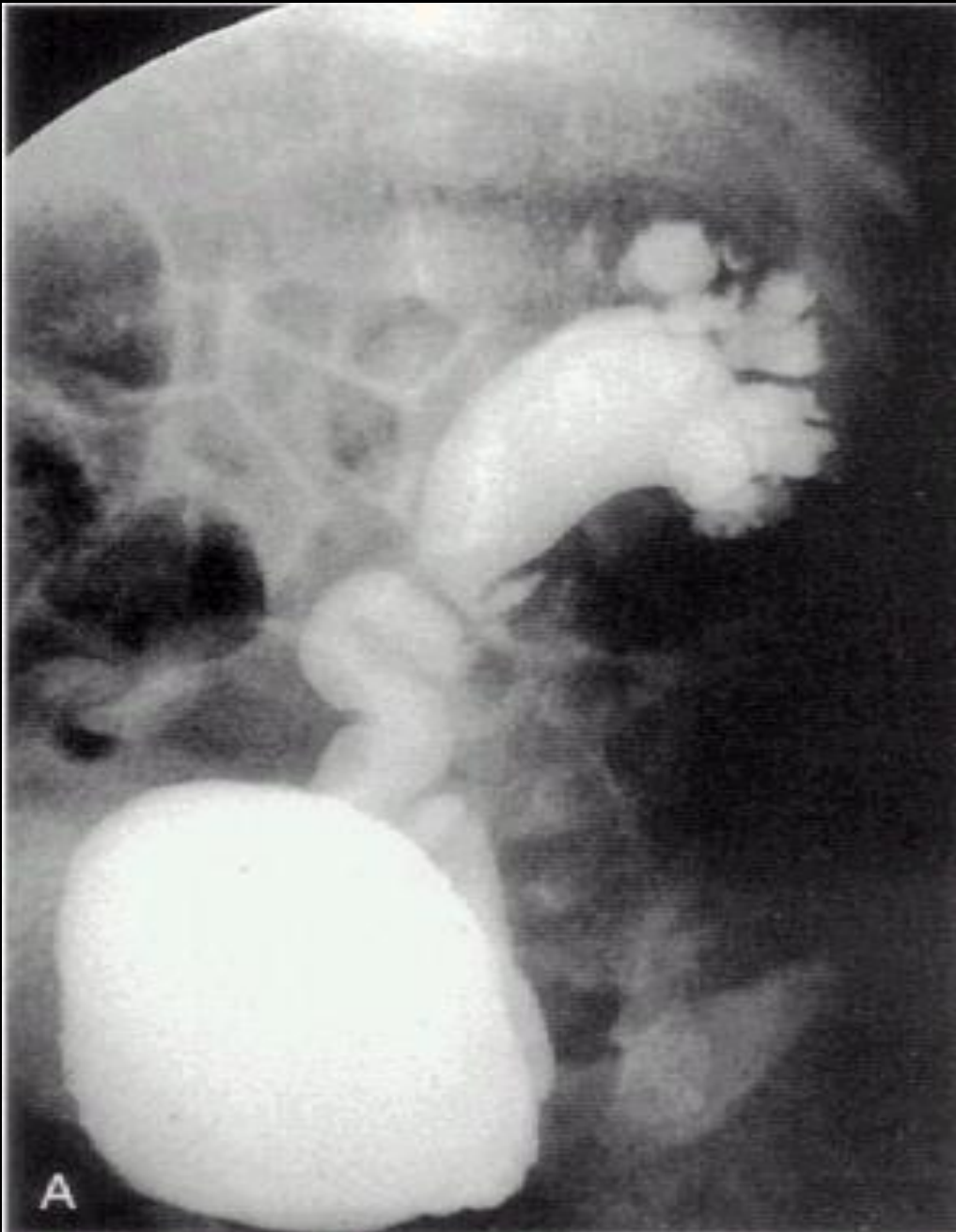
- Quite variable
 - Depends on age
- Fever
 - If $> 38.5^{\circ}\text{C}$, Consider upper tract- not definitive.
- Dysuria
- Flank pain/tenderness
- Vomiting
- In the newborn- anything
- Abdominal pain
- Anorexia
- Hematuria

Radiographic Procedures

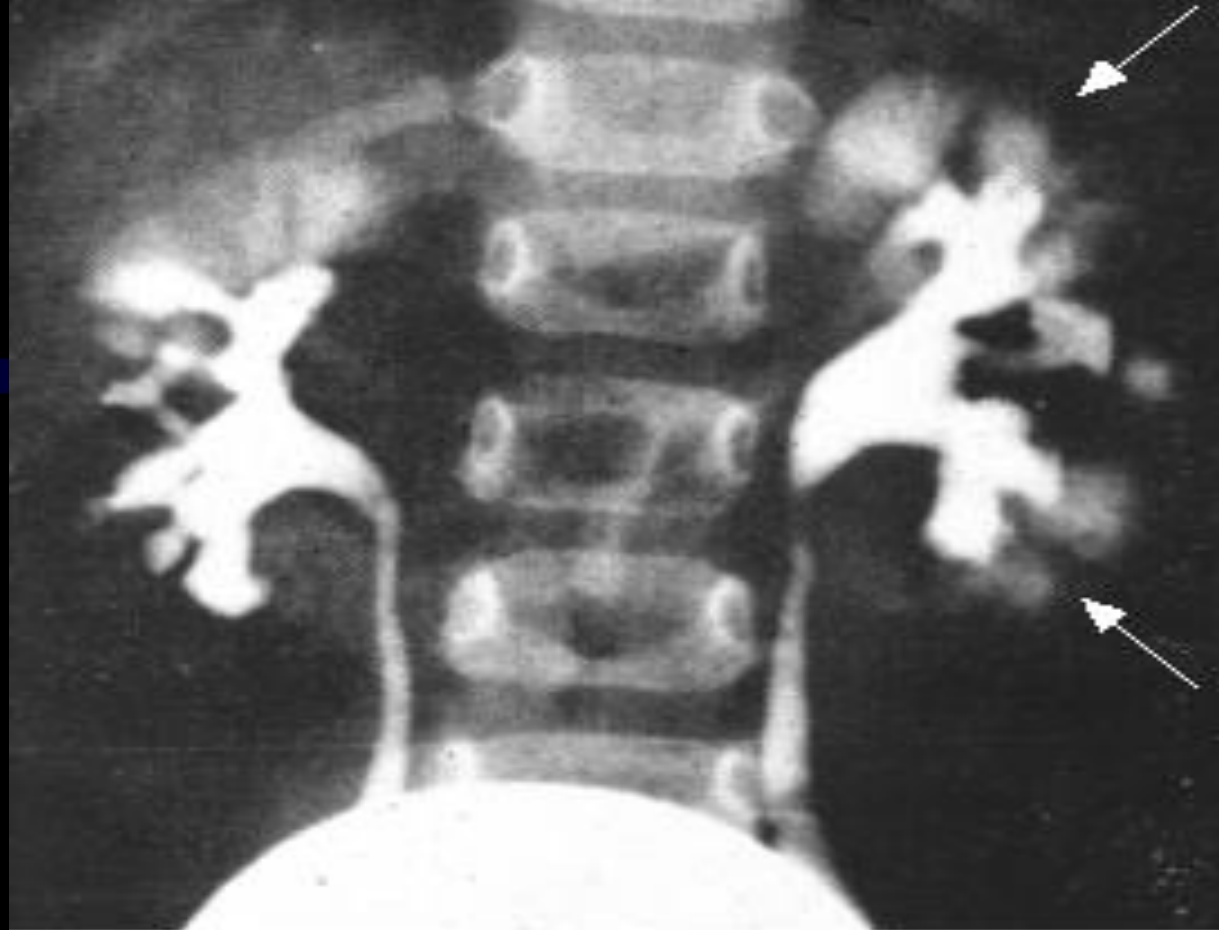


- Renal US
- VCUG/RNC
- DMSA scan/Other renal scans
- IVP: rarely used now

Vesicoureteral Reflux

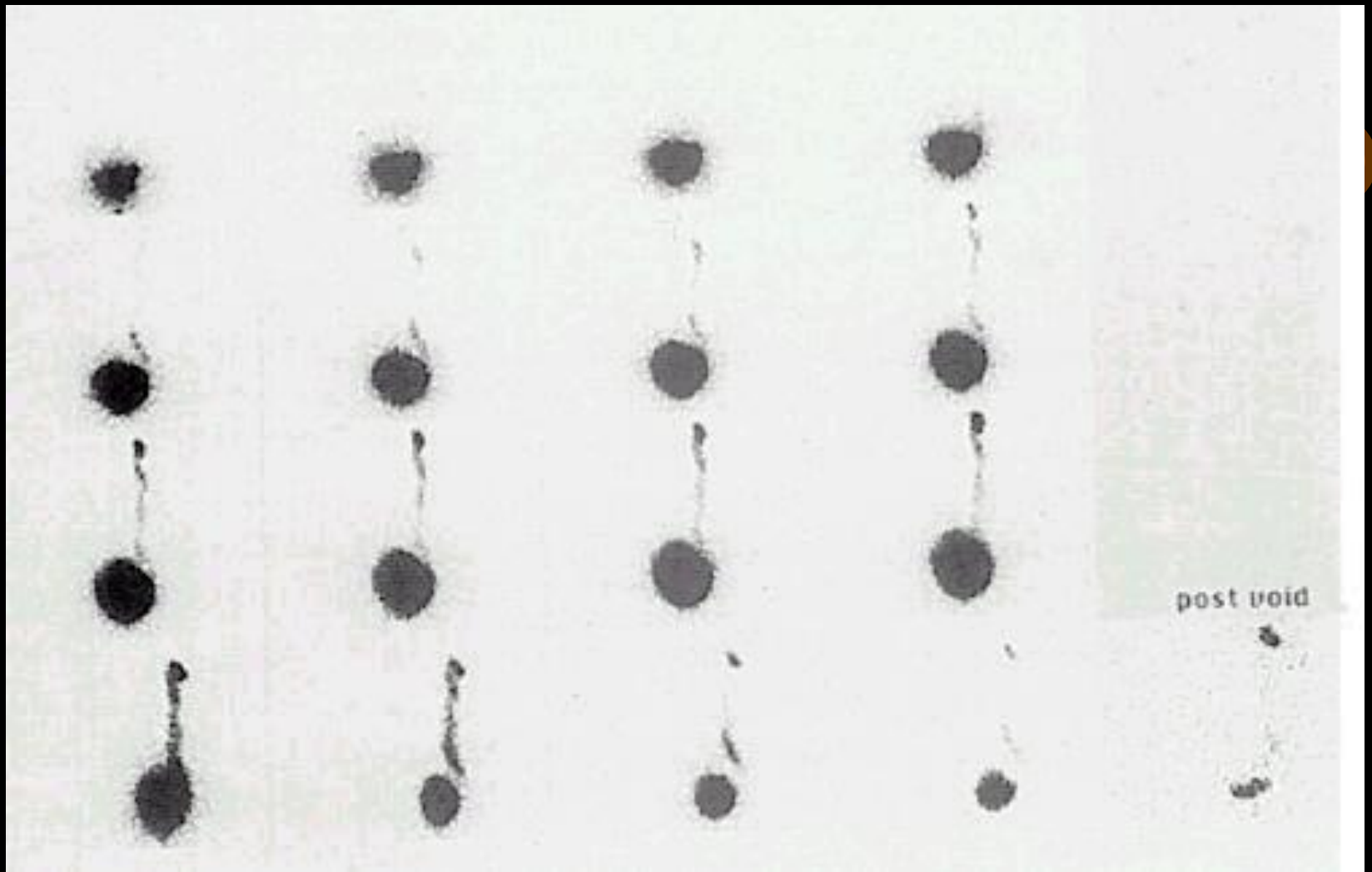


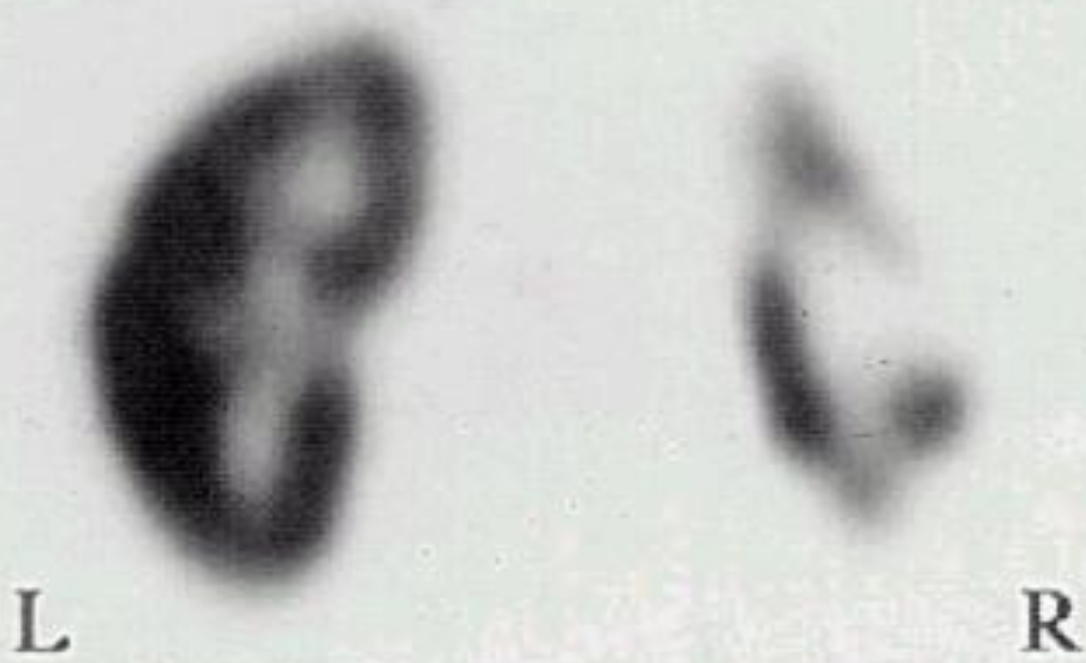
GRADES OF REFLUX




Intrarenal reflux Voiding cystourethrogram in a 4 year-old girl with recurrent urinary tract infections shows bilateral reflux into the renal pelvis and intrarenal reflux into the renal parenchyma (arrows). (From Amar, D, JAMA 1970; 213:293. By permission of the American Medical Association, copyright 1970.)








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- Why does it happen?
 - Shorter submucosal and intramural ureteral segment allows reflux. Need a 4:1 ratio of tunnel length to ureteral diameter to prevent reflux.
 - Changes on the ureteral orifice can be related to reflux.

Prior Recommendations

- Fairly Straight Forward
 - Any child <5-9 yo with UTI: Renal US and VCUG/RNC (RNC as follow up, or sometimes as initial in females)
 - If reflux, proph antibiotics
 - (1/4-1/2 full dose qd)
 - Given at night if dry
 - Repeat studies in 1 year.
 - Grade 1-2, medical txment, Grade 5, most likely surgery, 3-4 depended on break through UTIs

AAP 2011 : Guidelines for children 2mo-2yr

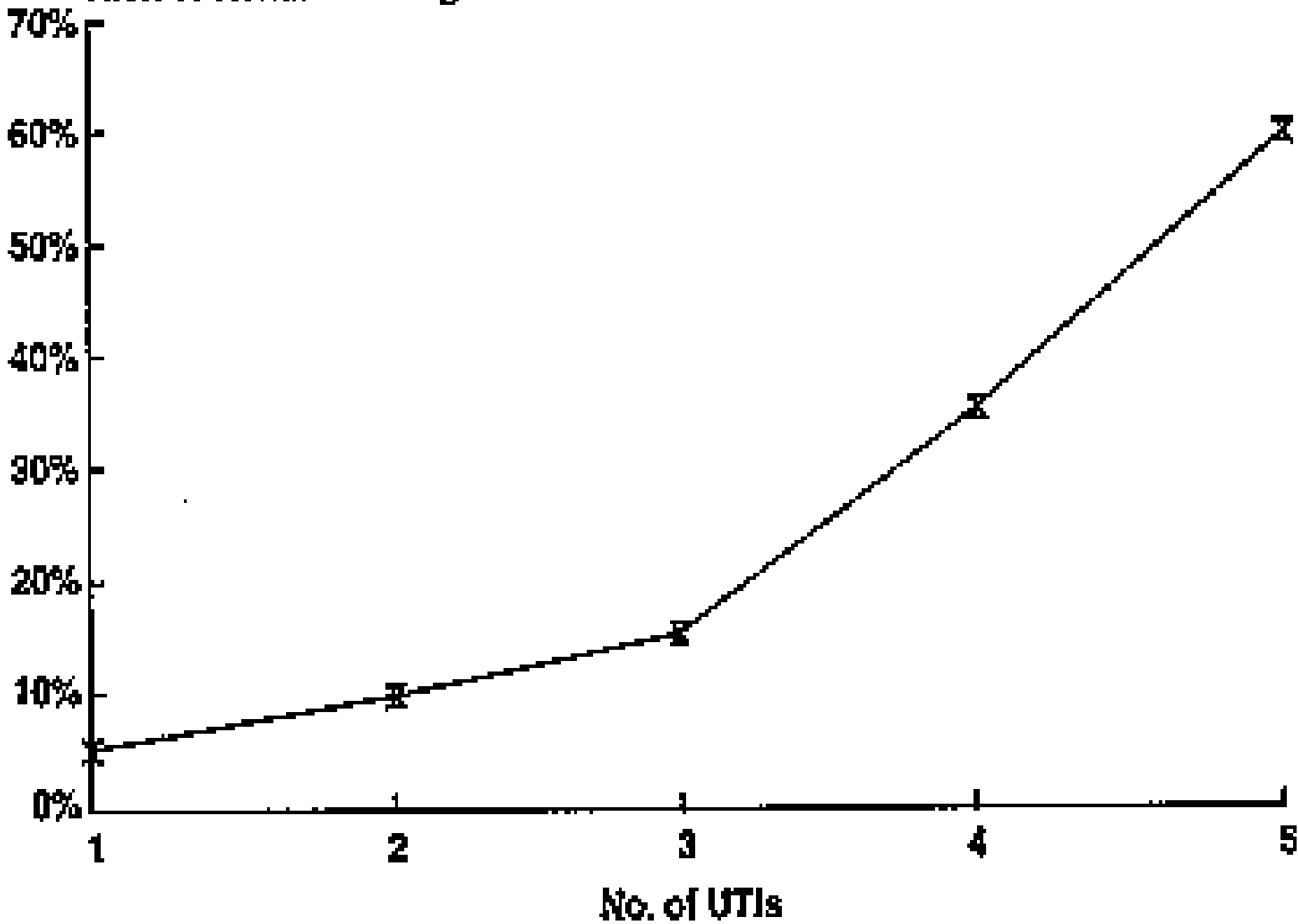
- Re-look from ~2000:
 - Basic beliefs
 - UTIs and reflux set up for parenchymal disease and therefore HTN and CRF
 - Higher risk in younger children IE<2yo
 - More infections, more scarring.
 - Obtain urine by cath or SP if highly suspicious

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- Primary changes over the years
 - Unclear efficacy of proph antibiotics
 - Hold on VCUG unless there is a change on US or recurrent infections

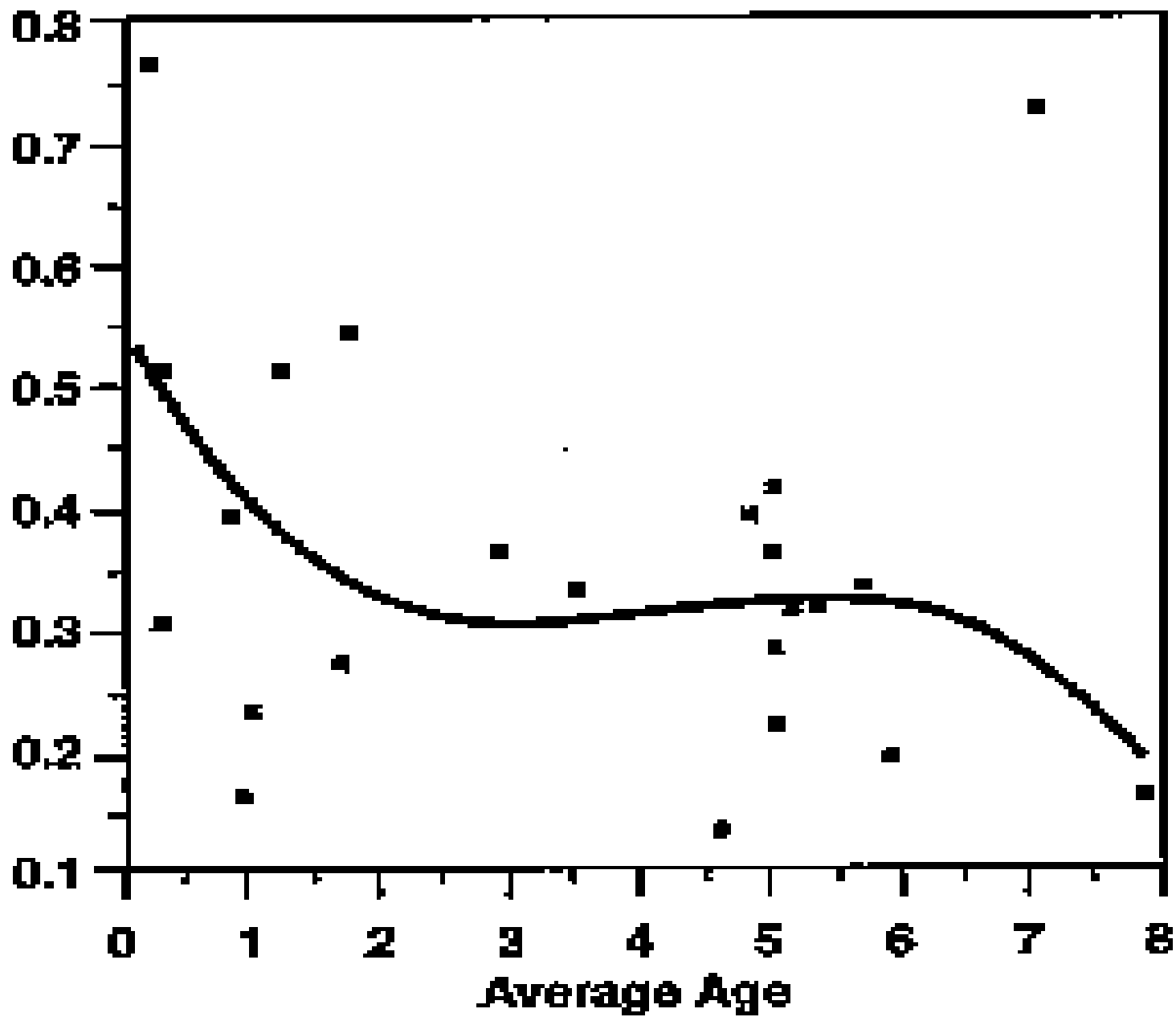
NICE guidelines 2007


- National Institute for Health and Care Excellence:
- United Kingdom
 - Essentially the following
 - Less VCUGs
 - Shorter duration antibiotics
 - More DMSA (Not sure why)

Risk of Renal Scarring



Prevalence of VUR



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- Evaluation: The sticky issue:
 - Who gets VCUG and US.
 - These protocols lead to multiple studies and reports in urologic journals disagreeing with the lack of evaluation.


Do we believe it?

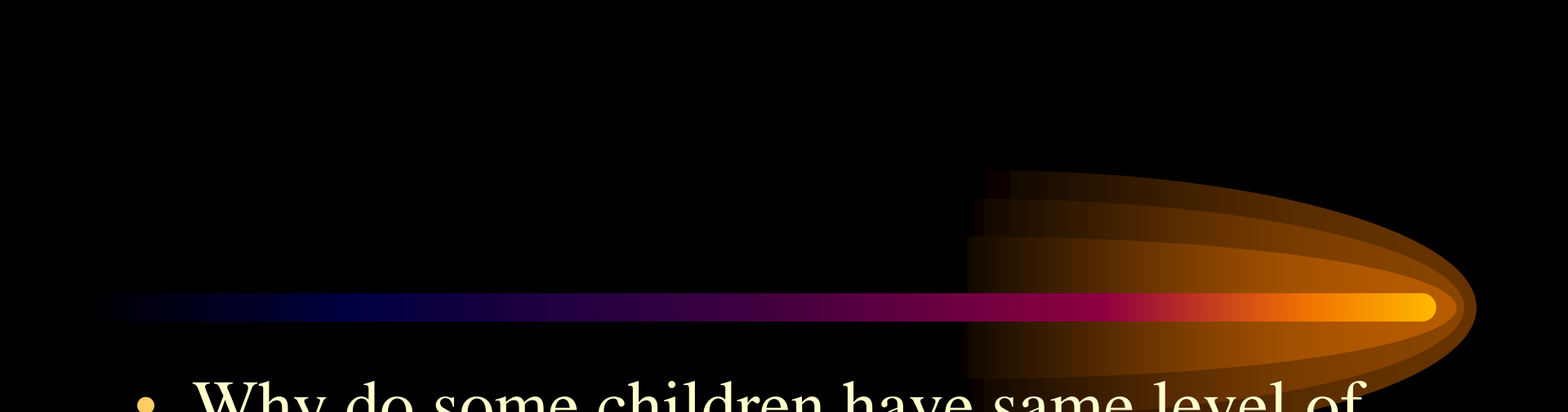
- Is HTN really a problem?
- Can we change the outcome?
 - Is it solely the infections?
 - Is it predetermined (IE dysplasia)
 - Is it related to ACE polymorphism?
 - Have we changed to outcome rate?




- Hypertension

- Prior reports: 20% of children with HTN related to renal scarring.
- Jacobson reported HTN in patients w/ renal scarring/ VUR as 23%. Patients followed into adulthood, initial eval with IVP: all had abnormal appearing collecting systems.
- 1993, Wolfish: Retrospect review of patients over a 17 year period for HTN and VUR

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- Wolfish cont.:
 - 35% with renal scars, no HTN (0%)
 - Suggested that dysplasia/hypoplasia was needed for HTN.
 - 1987 Savage: No direct correlation of PRA/Blood pressure or renal scarring.
 - Chronic Renal Failure (and all of its components): 5-10% of children with ESRD

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- Why do some children have same level of reflux and do well and some don't?
 - ? Predetermined by underlying dysplasia
 - 2000, Australia: Reviewed outcomes in pre and post treatment eras: no difference in outcome.

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- ACE polymorphism: RAS important in progressive renal damage both from flow and sclerosis standpoint.
 - ACE allele: Homozygous deletion of activity inhibitor with marked increase in scarring and associated complications.

Interventions

- Surgery Vs. Medical
 - No difference in outcome. (Reflux resolves ~10%/yr of patients who will resolve.
 - Therefore, 9-10 yo ~100% of those who will resolve.
 - Surgery may decrease incidence of UTIs but does not change the outcome. Will wait until child is older bigger >10kg as a general rule.

2 Studies

- Peds Neph 2006
 - >700 children
 - Followed 6-411 mo
 - 2-5% w/CRD
 - 3% w/ HTN
- Peds Neph 2006
 - International Reflux study
 - Reflux >3-4
 - ~300 patients
 - 5-10 yr course
 - No diff med vs surg
 - 1 pt CRD, 3 w/HTN

To Proph or not to Proph

- Recent articles:
- No improvement w/ proph, maybe worse outcome.
- May be helpful in high risk children.
- Needs to be individualized

Inpatient vs Outpatient?

- Previously: Most children w/ fever CVA tenderness=pyelo=admission.
- 1999 Hoberman Study
 - Young Children w/ Febrile UTI Treated with oral antibiotics or IM dose. No difference in outcome.
 - My rule: Admit if dehydrated or vomiting or complex urologic issues w/ complex bug.

CAM



- Much more commonly used/asked about particularly with newer info showing little value of our prior recs.
- Primary treatments
 - Probiotics: Peds Neph- better or same compared probiotics to antibiotics (100mill-6 billion colonies). More studies in adults to decrease infections.


- Cont

- Cranberry: Multiple studies, some + some –

- Mech: inhibition of adhesion of bacteria to uroepithelial cells by proanthocyanadin
 - Data Highly suggestive. Ex:
 - Howell AB, Vorsa N, Foo LY, et al. Inhibition of the Adherence of P-Fimbriated Escherichia coli to Uroepithelial-Cell Surfaces by Proanthocyanidin Extracts from Cranberries). [N Engl J Med 1998;339:1085-6.](#)

- Blueberrys/Blueberry Syrup:

- Blueberry, like its relative, the cranberry, also appears to prevent bacterial adhesion to the bladder and bacterial colonization by proanthocyanadin
 - Ofek I, Goldhar J, Zafriri D, et al. Anti-Escherichia coli adhesin activity of cranberry and blueberry juices. N Engl J Med 1991;324:1599.

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- Fluids
 - CONSTIPATION
 - Good voiding patterns.
 - Yogurt
 - No clear data I can find but more recently yogurts with increased cultures. No clear amount or survival of cultures.



- Cont

- Uva Ursi (bearberry): Cystinol

- Phenolic glycoside that is hydrolyzed to hydroquinone (Arbutin)
- Used for treatment and proph (adult study w/stat sig)
- Dosing not shown yet in kids (adult standard 250-500 mg up to tid) also can be infusion/tea.

Finally, Do the (my) numbers

- ~4% of children w/UTI's. ~280,000,000 Americans, ~30% Children=3,360,000 Children w/UTIs.
- ~10,000 Renal Tx per year, 1,000 <21 yo.
- 5% Related to VUR=50
- ~60,000 VCUGs for each one
- One review: 15,000 eval for each one who may be stopped from going on to ESRD

My Protocols

- Previously:
- Urine Cx
- Renal US
- VCUG



- Look at risks
 - Age, gender, severity/recurrence of infection, US findings
- Urine Cx and Renal US
- If + US
 - More likely to get VCUG
- If <2yo, febrile: probable VCUG
 - Relative low threshold <5yo
- Multiple infections or recurrent febrile >5yo, strong consideration
- Lower threshold for females given infection risk.

Treatment

- Proph
 - Children <2 yo w/ reflux and UTI's
 - Infections more often than q 2-3 months
 - Children 2-5 yo with higher grade reflux or infections.
 - >5 yo, clinical decision based on grade and UTI's
- Surgery: (**Deflux**, extravescico, standard reimplant)
 - Primarily for recurrent/break through UTI's
 - Lower threshold for Grade 5
- Studies
 - Generally every year when younger but may not repeat when older, no UTI's, lower grade, unilateral and no changes on US

Conclusion to all of this stuff!

- The diagnosis and treatment of the disease should not be worse than the disease itself.
- “The price of liberty is eternal vigilance.”
- Prevent or Decrease renal damage and its complications
- **MOST CRITICAL ISSUE: FOLLOW PATIENT AND TREAT UTI's AGGRESSIVELY**