Urinary Tract Infections in Children: “The Muddy Waters”

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• 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

- **Bactiuria:** 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 Bactiuria:** Bacteria in the urine without clinical symptoms.
• 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 areus
- Staph saprophyticus
  - more common in adol/young women
- Candida
- You name it!
Clinical findings

- Quite variable
  - Depends on age
- Fever
  - If > 38.5°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
**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.)
• 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
• 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

No. of UTIs

0% 10% 20% 30% 40% 50% 60% 70%

1 2 3 4 5
• Evaluation: The sticky issue:
  – Who gets VCU 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
• 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
• 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.
• 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.
• 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:
      

  – **Blueberries/Blueberry Syrup:**

    - Blueberry, like its relative, the cranberry, also appears to prevent bacterial adhesion to the bladder and bacterial colonization by proanthocyanadin
    
• 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 then 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