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CLINICAL COMMENTARY

Encourage varicella vaccination, except for the immunocompromised

For many parents, vaccination decisions are made based on school district requirements. Varicella zoster vaccine is an exception to that rule. Parents can choose to immunize their child at 12 months or wait and let nature take its course—hopefully before the child starts kindergarten. The major concern with the vaccine has been its long-term efficacy. Although no one knows for sure how long immunity is sustained, studies show that detectable antibodies are present for up to 20 years.

As a parent and physician, my decision to vaccinate my daughter was made after I witnessed an 8-year-old boy in the emergency room with respiratory distress secondary to complications from chickenpox. This experience reinforced for me that chickenpox is a life-threatening disease. The effects of chickenpox include scarring as well as time away from work for parents. I therefore encourage varicella vaccination for my patients, with the only exception being those who are immunocompromised, for whom we have no data.

To the question of whether we should we vaccinate children to prevent chickenpox, I give a resounding "yes."

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Do antibiotics prevent recurrent UTI in children with anatomic abnormalities?

EVIDENCE-BASED ANSWER

Evidence is insufficient to recommend for or against antibiotic prophylaxis to prevent recurrent urinary tract infections (UTI) in children with anatomic abnormalities. Guidelines acknowledge this lack of evidence, but still recommend using prophylactic antibiotics in children with vesicoureteral reflux (strength of recommendation: **B**, based on poor-quality or inconclusive cohort and randomized controlled studies).[1–3] No controlled, prospective studies have examined the effectiveness of prophylactic antibiotics to prevent UTI recurrence or renal scarring.

EVIDENCE SUMMARY

Recommendations about antibiotic prophylaxis are based on several premises. Reflux predisposes children to acute pyelonephritis; reflux plus infection leads to reflux nephropathy and ultimately to renal scarring. In theory, if antibiotics could be initiated at the appropriate time and be maintained until reflux resolves, we could successfully prevent infection and scarring.[4]

A recent systematic review evaluated the use of antibiotics to prevent UTI in children.[5] This review of 5 randomized controlled trials included a total of 463 children between the ages of 2 months to 16 years. Three out of 5 trials evaluated the effectiveness of antibiotic treatment for 2 to 6 months to prevent subsequent off-treatment recurrence. The 2 smaller trials (n=71) evaluated the use of low-dose long-term antibiotics to prevent UTI.

There was a clinically, but not statistically, significant trend towards reduced risk of UTI during long-term antibiotic treatment (risk reduction [RR]=0.31; 95% confidence interval [CI]=0.10–1.00); however, no sustained benefit was seen once antibiotics were stopped

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(RR=0.79; 95% CI, 0.61–1.02). There were many problems with the methodological quality of these trials, including significant heterogeneity. The researchers concluded that well-designed randomized controlled trails are still needed to evaluate this commonly used intervention in the pediatric population.[4] Benefits for long-term prophylaxis are even less clear in children with low-grade reflux (I–II).[5] Furthermore, no randomized controlled trials assess whether prophylaxis prevents the development of new renal scars in children.[6]

In addition, a recent systematic review of studies done in children with normal urinary tracts, as well in children with neurogenic bladders, found that the available evidence is of low quality. Only 6 out of 31 potential studies fulfilled the inclusion criteria. These were small (mean sample size was 28), and the quality scores of all 6 trials were low, indicating that the evidence may be unreliable.[7]

Two of 3 studies done in children with normal urinary tracts demonstrated statistically significant higher rates of UTI recurrence in control groups compared with treatment groups receiving 6 to 10 months of either nitrofurantoin or cotrimoxazole (RR=24–31). The third study showed no difference between groups.

One of 2 trials in children with neurogenic bladder demonstrated higher recurrence rates of 2.9 per 10 patient years for patients receiving antibiotics compared with 1.5 in the untreated group. The other study showed lower recurrence rates of 17.1 for patients receiving antibiotics, compared with 33 in the untreated group.[7] Neither of these findings were statistically significant.

A different meta-analysis of 15 controlled clinical trials in children with neurogenic bladder due to spinal cord dysfunction. This analysis showed that antibiotic prophylaxis was associated with a reduction in asymptomatic bacteruria among children with acute spinal cord injury ($P<.05$), but there was no significant reduction in symptomatic infections. Prophylaxis resulted in an approximately twofold increase in antimicrobial-resistant bacteria. The researchers concluded that although a clinically important effect has not been excluded, the regular use of antimicrobial prophylaxis for most patients who have neurogenic bladder caused by spinal cord dysfunction is not supported at this time.[8]

No controlled prospective studies examine the effectiveness of antibiotics to prevent UTI

Poor compliance may be an issue with long-term prophylaxis and may represent patient or parent practice.[9] One study found that in children taking low-dose trimethoprim, 97% of the parents reported giving antibiotics on daily basis, but in 31% of subjects, trimethoprim was not detectable in the urine.[6] Risk of prophylaxis includes nausea, vomiting, and rash in 8% to 10% of patients; development of resistant organisms; and change in indigenous microflora.[6] One study of resistance found that children who received antibiotics for more than 4 weeks in the previous 6 months were more likely to have resistant *Escherichia coli* isolates than children who had not received prolonged antibiotic treatment (odds ratio [OR]=13.9; 95% CI, 8.2–23.5). Children with abnormalities of the genitourinary tract were approximately 4 times more likely to have resistant isolates of *E coli* than children without abnormalities of the genitourinary tract (OR=3.9; 95% CI, 2.7–5.7).[11]

RECOMMENDATIONS FROM OTHERS

The American Academy of Pediatrics, American Urological Association, and the Swedish Medical Research Council guidelines recommend prophylaxis for children with reflux (**Table**), but they all acknowledge that the recommendations are not supported by well-designed randomized controlled trials.[1–3] No guidelines are available for children with neurogenic bladder and recurrent urinary tract infections.[7]

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TABLE

Oral antibiotics for prophylaxis of urinary tract infections in children

Antimicrobial	Prophylaxis dosage
Trimethoprim/sulfamethoxazole (TMP/SMX) (Bactrim, Septra)	2 mg of TMP, 10 mg of SMX per kg as single bedtime *or* 5 mg of TMP, 25 mg of SMX per kg twice per week
Nitrofurantoin (Macrodantin)	1–2 mg/kg as single daily dose
Cephalexin (Keflex)	10 mg/kg as single daily dose
Amoxicillin	10 mg/kg as single daily dose
Sulfisoxazole (Gantrisin Pedatric)	10–20 mg/kg divided every 12 h

Modified with permission from AAP 1999;[3] Allen et al1999.[10]

CLINICAL COMMENTARY:

UTI prevention most successful when the child exhibits efficiency of voiding

The relative benefit of antibiotic prophylaxis in prevention of UTI in children with anatomic abnormalities like vesicoureteral reflux could best be determined if all other risk factors for UTI were controlled. Unfortunately, these other factors are often more significant in promoting UTI than is reflux, and they are also more difficult to quantify. Voiding dysfunction and constipation can both increase bladder storage pressures and postvoid residual urine volumes, and as such greatly predispose children for UTI. Furthermore, a distended colon provides an abundant reservoir of pathogens with an array of uropathogenic virulence factors.

Published reports have failed to detect significant benefit for antibiotic prophylaxis in part because the children studied possess varying risks for UTI. Prevention of UTI is most successful when the child exhibits efficiency of voiding and elimination. Clinical practice in pediatric urology advocates use of antibiotic prophylaxis in children with vesicoureteral reflux. Reflux should be suspected in children with hydroureter, multicystic renal dysplasia, ureteral duplication, and ureterocele.

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