Resolve reflux: follow the Swedes

The long-awaited results of a landmark trial in pediatric urology have been published. A series of five papers in the July issue of *the Journal of Urology* provide welcome guidance to clinicians wishing to take a better-informed approach to decision-making for their patients with dilating vesicoureteral reflux (VUR).

A lack of high-quality studies has led to individual biases—of both clinicians and parents—factoring heavily in choice of management strategy for children with VUR. Ten years ago, a team based in Sweden began recruiting patients for an ambitious trial comparing the efficacy of surveillance, antibiotic prophylaxis, and endoscopic treatment.

In the first of their papers, Sverker Hansson and colleagues describe the challenges of conducting a prospective, randomized trial of VUR management protocols. Recruitment at 23 centers was slower than anticipated; 203 children were eventually recruited, rather than the 330 originally desired. Participation was restricted to those aged between 1 and 2 years with grade III–IV VUR.

After 24 months of follow-up, endoscopic injection of dextranomer/hyaluronic acid copolymer emerged as the approach most likely to result in downgrading or resolution of reflux (in 71% of patients, compared with 39% and 47% for prophylaxis and surveillance, respectively). Recurrence of dilating VUR was noted, however, in one-fifth of children who were treated endoscopically.

Adverse events are also more likely to occur following this invasive procedure; six were reported in the 64-strong Swedish endoscopic cohort. “I [also] worry about the long-term consequences of chronic granulomatous inflammation in patients treated with ... copolymer injection”, states George Steinhardt in an Editorial Comment that accompanies the Swedish trial publications.

With regard to the two other primary end points of the Swedish trial—recurrent febrile urinary tract infection, and kidney damage assessed using serial dimercaptosuccinic acid scintigraphy—distinct differences between boys and girls became evident as data accumulated. “We found a very low risk of recurrent infections and renal damage in boys over 1 year of age ($n = 75$), implying that they should not need prophylaxis or surgical treatment”, reports senior author Hansson.

By contrast, marked variations in response to the three management strategies were noted in the female cohort ($n = 128$). Hansson summarizes: “in girls, recurrent infections were significantly reduced in both the prophylaxis group (19%) and in the endoscopic group (23%) compared to [the] surveillance [group] (57%). The risk of new renal damage was related to febrile recurrences, and was not seen in the prophylaxis group, while it [did occur] in the endoscopic ($n = 5$) and surveillance ($n = 8$) groups.”

“This study supports my current practice of recommending prophylactic antibiotics in female infants until successful toilet training, but not in boys after age 1 year”, comments Steinhardt, from the Helen DeVos Children’s Hospital in Michigan, USA. Clinicians with outstanding questions despite the commendable efforts of the Swedish team might find answers in the ongoing, 600-strong Randomized Intervention for Children with Vesicoureteral Reflux (RIVUR) trial in which prophylaxis and placebo are being compared.

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Original articles Brandström, P. *et al.* The Swedish Reflux Trial in Children: I–V. *J. Urol.* **184**, 274–304 (2010)