Antibiotic resistance in children with *E coli* urinary tract infection

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It’s not an unusual presentation in primary care—an alert, responsive preschool child with a temperature of 39°C, unremarkable findings on examination, but with leucocytes and nitrites in the urine. Given a strong suspicion of a urinary tract infection, and with *Escherichia coli* being the most likely organism, empirical management with one of a small number of cheap and available antibiotics would follow.¹

In a linked paper, Bryce and colleagues (doi:10.1136/bmj.i939) present compelling evidence of the need to reconsider current approaches to community based management of paediatric urinary tract infection.² Their findings confront long established patterns of practice and are inextricably linked to the emerging global problem of antimicrobial resistance.³

Bryce’s team undertook a systematic review designed to identify the global prevalence of resistance to commonly recommended antibiotics in children with community acquired *E coli* urinary tract infection. They systematically reviewed 58 studies in 26 countries. Five of these studies allowed them to measure the association between previous prescription of antibiotics and subsequent *E coli* resistance in the same child. Drugs of interest included ampicillin, co-amoxiclav, co-trimoxazole, trimethoprim, ciprofloxacin, and nitrofurantoin. Ceftazidime was used as a marker for cephalosporin resistance.

For an antibiotic to be considered a first line empirical treatment for urinary tract infection, resistance should not exceed 20% in the most likely infecting strain.⁴ Bryce and colleagues show that this threshold has been reached for many first line antibiotics used for paediatric *E coli* urinary tract infection. Within countries in the OECD (Organisation for Economic Co-operation and Development), a half of all isolates were resistant to ampicillin, a third to co-trimoxazole, and a quarter to trimethoprim. Resistance was substantially greater in non-OECD countries. Data confirmed the group’s previous review⁵ suggesting that previous antibiotic use in primary care increased the subsequent risk of *E coli* resistance to that particular antibiotic.

Despite the clinical mixed inclusion criteria (a women aged 17 with symptoms of cystitis presents a very different clinical picture than a toddler with a fever of unknown origin), the findings have important implications for the management of paediatric urinary tract infection in primary care and for clinical decisions that have remained largely unchanged since the 1990s. The work of Bryce and colleagues makes the case for a change in guidelines for “first choice” antibiotics in this setting. The remarkable variability in *E coli* resistance among countries suggests that clinicians will need access to up to date data on patterns of resistance within their own and other jurisdictions.

The high prevalence of resistance in Middle Eastern countries, for example, is a particular challenge for management of refugee children from the current Syrian conflict. Primary care clinicians will probably need to get used to taking an “antibiotic history” before prescribing for common bacterial infections. A parent’s claim that “antibiotic x always works for my child” might need to be balanced with the notion that “if antibiotic x was used in the last six months, there’s a good chance that it’s not going to work as well if used again.”

Bryce and colleagues’ findings of profound resistance in children’s urine mirror dramatic increases in resistance to drugs commonly used to manage *Streptococcuspneumonia*, *Klebsiella pneumonia*, and *Staphylococcus aureus* infections.⁶ As is so often the case, the consequences have the greatest impact in the developing world.⁷

These patterns of antibiotic resistance bring into focus what several commentators have called a “tragedy of the commons.”⁸⁹ This economic concept describes a situation where rational decisions made by individuals can adversely affect the availability of a resource shared by, and benefiting, all.¹⁰ Every one can be seen as acting “rationally” with antibiotics; legislators promote availability when they allow antibiotics to be dispensed without prescription; doctors act to satisfy patients seeking relief from troubling symptoms; and farmers augment feed with antibiotics to increase food supply (in the United States over three quarters of all antibiotics are used in...
aquaculture or agriculture). The “tragedy” comes as the livestock producer, the legislator, the harried physician, and the anxious patient never feel the consequences of their decisions directly, yet their combined actions reduce the availability of effective antibiotics for everyone.

The World Health Organization’s 2014 global action plan on antimicrobial resistance outlines a strategy to deal with the effects of these multiple individual actions. The plan asks nations to adopt “whole of society” approaches to prevention (through public health and infection control measures), to enhance and better disseminate knowledge on antimicrobial resistance, and to develop an economic case for new investments in drugs, diagnostic tools, and vaccines.

Bryce and colleagues’ systematic review joins a host of recent studies, reports, and calls to action on this issue. Each adds evidence to justify change in how we protect a precious global resource. While I have no doubt that clinical practice guidelines will quickly be able to accommodate the findings, I am less confident that there is the will and commitment to deal with what the WHO has called “the post-antibiotic era.”

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