**Editorial**

# Judicious use of antibiotics in paediatric infections: issues and challenges

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Soon after the introduction of antibiotics just over half a century ago, clinical failures due to antibiotic resistance were witnessed. Despite efforts to stem this, the tide of bacteria resistance continues to evolve. The widespread use of antimicrobials, whether appropriate or inappropriate, has driven the emergence and spread of resistant organisms[1]. The association of resistance with the use of antibiotics has been documented in both inpatient[2] and outpatient[3] settings. For example, it has been shown that recent antibiotic use increases the risk of nasopharyngeal carriage of penicillin-resistant pneumococcus[3,4]. There is also evidence to show that among patients with invasive pneumococcal disease, recent antibiotic use is a risk factor for infection with multiple drug-resistant strains[5,6]. This process can be reversed through judicious use of antibiotics[7].

Data from the National Center for Health Statistics in the United States indicate that approximately three-quarters of all outpatient antibiotics have been prescribed for otitis media, sinusitis, bronchitis, pharyngitis and non-specific upper respiratory tract infections (URTI), with prescription rates being highest in children[8]. Most childhood URTI are caused by viruses and only less then 5% are complicated by secondary bacterial infections[9]. The use of antibiotics neither shortens the length of URTI nor prevents the development of bacterial pneumonia[10]. Despite this knowledge, in a survey examining antibiotic prescribing for different respiratory infections in preschool children in Canada, Wang et al found that antibiotics were prescribed to 49% of children with URTI, 18% with nasopharyngitis, and 24% with influenza[11]. This practice often extended to paediatric inpatient care. In this issue of the Singapore Medical Journal (SMJ), Shankar et al, in their study of prescribing patterns among paediatric inpatients in a teaching hospital in Nepal, found antibiotics being used for viral infections or without definite indications in 85 of 356 patients surveyed[12].

Factors that contribute to inappropriate antibiotic use in paediatric URTI are many and varied, including patient, parental and physician factors. Also in this issue of the SMJ, Chan et al found large deficiencies in the parental knowledge of childhood URTI in a primary healthcare setting[13]. The majority (>65%) believe that antibiotics will be helpful in alleviating symptoms, and 28% requested for antibiotics of which 93% received as requested[13]. Baucher et al, in a survey of 915 paediatricians, found that 48% of paediatricians reported frequent parental pressure to prescribe antibiotics when not clinically indicated and that they occasionally or more frequently comply with these requests[14]. 78% felt that educating parents would be the single most important programme for reducing inappropriate oral antibiotic use and 54% indicated that parental pressure, in contrast to concerns about legal liability (12%) or need to be efficient in practice (19%), contributed most to inappropriate use of oral antibiotics[14]. Vinson et al, in a study of 1,398 patients found that physician perception of parental expectations for antibiotics was associated with a diagnosis of bronchitis and prescription of antibiotics[15]. However, there is no association found between a prescription for antibiotics and patient satisfaction[16]. Patient satisfaction often relates to physician-parent-patient interactions.

Strategies to improve antibiotic use in the community include education of both healthcare professionals and the public. Many national bodies have, to this end, published guidelines for judicious use of antibiotics in common paediatric respiratory infections[17-21] and the approach to management of infants and children with fever[22]. The Centers for Disease Control/American Academy of Paediatrics (CDC/AAP) have detailed in their publications, guidelines on the use of antimicrobials in the management of the common cold, otits media, sinusitis and pharyngitis[17-20]. However, diagnostic uncertainty, e.g. difficulty differentiating bacterial

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from viral infection[23], acute otitis media from otitis media with effusion, bacteria sinusitis from prolonged URTI, as well as experience with treatment failures with first line antibiotics[24,25], have led to difficulty in compliance with prescribed guidelines. Most pharyngitis are of viral aetiology and diagnosis of group A Streptococcus (GAS), the leading bacterial cause of bacterial pharyngitis, should be based on the results of appropriate laboratory tests in conjunction with clinical and epidemiological findings[20]. To date, no GAS resistance to β-lactam antibiotics has been identified and penicillin/amoxicillin remains the drug of choice for treatment of GAS pharyngitis.

However, beginning in the late 1970s, clinical failure rates with penicillin therapy began to increase steadily over time, and is now reported to be approximately 30%. The leading hypothesis to explain this widening gap relates to two major concepts: the co-pathogen hypothesis and the alteration of normal ecology hypothesis detailed in a review by Pichichero et al[25]. It has been suggested that co-colonising, β-lactamase-producing normal bacteria flora of the throat or β-lactamase producing bacteria (BLPB) present in the core of the tonsil, can produce enough β-lactamases to shield GAS or other organisms from β-lactam antibiotics[26]. Studies conducted in various regions of the world have shown that over three-quarters of patients undergoing elective tonsillectomy because of recurrent tonsillitis harboured aerobic and anaerobic BLPB[26]. In this issue of the SMJ, Loganathan et al had similar findings in his study of bacteriology in recurrent tonsillitis in children, with the most common bacteria found being *Staphylococcus aureus, Haemophilus influenza* and GAS[27]. In these situations, cephalosporins may have a role to play with better eradication of bacteria and shorter course of therapy needed.

Adding to the conundrum is the difficulty of distinguishing the presence of bacteria infection in younger children and infants due to their relative inability to demonstrate clinical evidence of illness. In one study of 747 infants with fever, two-thirds of those with bacterial diseases appeared well to the examining-attending paediatrician[28]. Many investigators have focused their effects on identification of clinical or laboratory factors that would identify a subset of children and infants with bacteria infection. Factors commonly considered include clinical observation scores, height and duration of fever, age of child, total white counts, absolute neutrophil counts, band-to-neutrophil ratio, and inflammatory markers, e.g. interleukin 6, C-reactive protein, procalcitonin and erythrocyte sedimentation rate. In our own local study, published in this issue of the SMJ, Goh et al in a retrospective review of 86 children aged three to 36 months, found that duration of fever ≤ three days and total white count of <16,000/mm$^3$ had an excellent negative predictive value for serious bacterial infection[29]. Empirical antibiotics would often be used in these children in an attempt to treat possible serious bacteria infection, occult bacteraemia, and to prevent serious sequelae. In deciding among various management strategies, the physician must weigh the risks and benefits of each approach, including unnecessary hospitalisation and the use of antibiotics with increased bacteria resistance, resource utilisation, emotional distress versus possible prevention of severe illness.

In the era of increasing antibiotic resistance, optimal treatment of paediatric infections continues to be a challenge. There are many issues to be considered. Judicious use of antibiotics by all clinicians is imperative to stem the tide of increasing bacteria resistance. SMJ

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