Keep the old, in with the new: The changing face of pleural effusions

Pleural effusion (PE) is a collection of fluid in the pleural space and is a common complication of pneumonia in children. Despite advances in prevention and management, pneumonia remains a leading cause of morbidity and mortality, accounting for 15% of deaths in children under 5 years worldwide.[1] Developing countries are disproportionately affected as more than 95% of all global cases of clinical pneumonia occur in developing countries, particularly in sub-Saharan Africa.[2,3] In this context, improvements in the incidence and severity of pneumonia in children have been achieved due to strategies such as reducing paediatric HIV and immunisation with conjugate vaccines. However, these successes are threatened by a lack of diagnostic infrastructure, human resources, and funding.

The introduction of the 7-valent pneumococcal conjugate vaccine (PCV7) in 2009 and PCV13 in 2011 catalysed a reduction of 89% and 57% of the respective serotype-related invasive pneumococcal disease incidence in South African children as early as 2012.[4] At the same time, a meta-analysis of pragmatic studies worldwide similarly demonstrated a reduction of 31% and 17% of clinically and radiologically confirmed pneumonia and hospitalisation rates, respectively.[5] Furthermore, and as expected, an investigation of the 8 years after the introduction of PCV at a Cape Town tertiary paediatric hospital highlighted sustained effectiveness and halving of *Streptococcus pneumoniae*-related PE.[6]

In this issue of the *AJTCCM*, Golden *et al.*[7] published data from a 3-year review of children presenting with PE in Cape Town. Of interest is that the incidence of PE has declined to 5.6 per 1 000 children with pneumonia, and the proportion of those with *S. pneumoniae* infection has declined significantly, with *S. pneumoniae* accounting only for 8% of PE.[7] *Staphylococcus aureus (S. aureus)* has emerged as the predominant bacterial cause of PEs, and all of these were cloxacillin sensitive. They also found that pulmonary tuberculosis (TB) accounted for almost 40% of PEs. This is a high number but considering the high incidence of TB in Cape Town (~500/100 000), it highlights the importance of investigating and excluding TB as a potential cause of PE.

A fifth of children in the study had unclassified PE (no organism was identified on microscopy, culture or sensitivity). In contrast to previous culture-based studies, PCR testing afforded a higher sensitivity for detecting *S. pneumoniae*. However, in the study by Golden *et al.*,[7] molecular testing was limited due to a lack of funding. A study conducted in a developed country on the epidemiology of PE before the introduction of PCV13 found that molecular diagnostic testing significantly increased the identification of pathogens in 84% of samples from 63 paediatric patients with PE compared with only 35% of samples using conventional culture methods ($p<0.001$).[8] Secondly, dual infections involving *S. pneumoniae* in patients with cultures positive for a single pathogen were noticed. Thirdly, *S. pneumoniae* was the most common cause of culture-negative PE. Lastly, but perhaps most importantly, the study also highlighted the potential for bias when relying on culture alone for epidemiological studies, as *S. aureus* was most likely isolated in culture compared with *S. pneumoniae* and bacterial pathogens commonly susceptible to penicillins were identified by PCR. So, a future study using PCR and serotyping in the reported cohort in Cape Town may assist in increasing the yield and improve organism identification for better targeted treatment.

What is probably of more practical guidance for treating clinicians is the characterisation of the clinical presentation and laboratory results of participants with PE. As expected, TB should be suspected in those with chronic cough and weight loss and in children who are older at presentation. Infants with higher serum inflammatory markers at presentation and higher pleural fluid protein and adenosine deaminase (ADA) were more likely to have bacterial infection and should include *S. aureus* cover.

Molecular diagnostics are informing understanding of the changing epidemiology in PE in countries implementing their use. Future studies should attempt to characterise the role of PCR in epidemiological studies to improve our understanding of the spectrum of pathogens in a high TB setting.

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