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THE RELEVANCE OF COMMUNITY-ACQUIRED PNEUMONIA IN YOUNG CHILDREN

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Annotation: Community-acquired pneumonia (CAP) is the leading cause of mortality in children under 5 years of age globally. To improve the management of CAP, we must distinguish CAP from other common pediatric conditions and develop better diagnostic methods to detect the causative organism, so as to best direct appropriate resources in both industrialized and developing countries. Here, we review the diagnostic modalities available for identifying viruses and bacteria in the upper and lower respiratory tract of children, with a discussion of their utility and limitations in diagnosing CAP in children.
Keywords: CAP, method, diagnosis, treatment, children.

INTRODUCTION

Community-acquired pneumonia (CAP) remains an important cause of morbidity and mortality in both industrialized and developing countries. Of all the children who died before their fifth birthday in 2013, pneumonia was the single most important disease, accounting for 14.9% (n = 935,000) of cases (1). However, despite being among the three most common infectious causes of death worldwide, pneumonia, diarrhea, and measles showed the greatest reductions between 2000 and 2013, suggesting that inroads are being made in preventing, recognizing, and treating these conditions. Improvements in access to health care, vaccination programs, living conditions, and nutrition are key to further reducing CAP mortality, and failure to do so is likely to disproportionately affect children in developing countries and directly influence their CAP incidence.

MATERIALS AND METHODS

Traditionally, medical practitioners, having formulated a differential diagnosis from a constellation of clinical signs and symptoms, will utilize diagnostic tests to determine illness etiology. However, the diagnostic challenge of childhood CAP lies in the broad range of presenting features and the absence of an accepted gold standard diagnostic test. Furthermore, the diverse age range within pediatric practice adds to this challenge differences in immune development and vaccination status and reliance on caregivers for detailed patient histories. In addition, many diagnostic methods are initially validated in adult populations, which can make interpretation in the pediatric setting more difficult.

RESULTS AND DISCUSSION

The definition of CAP varies between different sources; on a pathological level, pneumonia is considered infection of the lung parenchyma, i.e., lower respiratory tract (LRT) infection by microorganisms (1). CAP is defined clinically as “the presence of signs and symptoms of pneumonia in a previously healthy child due to an infection which has been acquired outside hospital” by both the British Thoracic Society (BTS) and the Infectious Diseases Society of America (IDSA), acknowledging that in resource-poor settings, chest X-rays (CXR) are not always available to aid diagnosis.

Children can present with CAP at different stages of illness and with clinical features that are difficult to discriminate from other common pediatric diagnoses. Symptoms of CAP, including fever, cough, dyspnea, wheeze, chest or abdominal pain, lethargy, vomiting, and headache, can also be indicators of sepsis, congenital heart disease, profound anemia, malaria, or acute asthma (2), as can the typical examination findings of tachypnea, tachycardia, hypoxia, respiratory distress (grunting, nasal flaring, recession, and abdominal breathing), and crackles or

wheeze on auscultation. The extent to which these signs are present with CAP is highly variable, which adds to the diagnostic complexity.

CAP can be caused by viruses, bacteria, or both. These causative agents are indistinguishable on the basis of clinical features alone; the diagnostic difficulty is primarily due to the inability to isolate the causative organism from the lower respiratory tract, as few young children have productive sputum or positive blood sample cultures (1). Older children and adults can produce sputum for examination under microscopy and culture. This is much more difficult in younger children, who typically do not expectorate.

Clinical virology diagnosis has been revolutionized over the past 2 decades with the introduction of nucleic acid-based detection. The majority of respiratory tract infections in children are viral in origin, and both the BTS and IDSA guidelines for management of childhood CAP recommend viral testing of nasopharyngeal secretions and/or nasal swabs by PCR or immunofluorescence (2). PCR has been demonstrated to have greater sensitivity than virus isolation in cell culture, shell vial culture, and immunofluorescence testing and is now the mainstay of respiratory virus detection in industrialized countries (5). While rapid antigen detection testing (RADT) for respiratory syncytial virus (RSV) and influenza virus is still in conventional use due to its low cost and fast results, this technique has relatively poor sensitivity in comparison to that of nucleic acid-based detection methods.

Thus, multiplex PCR, enabling the detection of numerous pathogens simultaneously without additional time or sampling, is used extensively. The results of multiplex PCR assays are rapid and typically available within 1 to 6 h, and as the availability of this technology grows, competition is decreasing prices, making the technology more affordable, which is essential for implementation in the developing world setting. Indeed, some laboratories are developing custom kits with performance comparable to that of commercial ones at a much-reduced cost. It is worth noting, however, that despite this, multiplex PCR is an expensive technology, and while publications often cite the use of over 20 targets, the selection of multiplex kits is based on a range of factors, including local expertise, funding structures, and the panel of pathogens detected, which has the disadvantage of leading to variations in practice between hospital centers.

CONCLUSION

To assess current research directions for molecular testing in childhood CAP, we performed a comprehensive search of all active clinical trials registered in the United Kingdom, European, WHO, and U.S. clinical trial databases. This strategy identified 11 current trials involving molecular testing for childhood CAP, which are summarized in Table 4. Due for completion by the end of 2019, these studies include POC testing and clinical applicability trials for directing patient therapy/management. The results of these and future trials may answer some of the questions surrounding the clinical application of molecular testing in microbial diagnosis and help inform clinical practices regarding their role in the diagnosis and management of childhood CAP. With the current significant limitations of diagnostics in CAP, the advent of new technologies and the prospect of rapid POC testing are very exciting. For the clinician, the ability to rapidly diagnose CAP and to distinguish at diagnosis the specific etiological agent, whether bacterial, viral, or both, would prove invaluable in directing the appropriate use of antibiotics and is likely to transform the way we deliver care to these children in future.

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