**Clinical evaluation of Streptococcus pneumoniae PCR in children with suspected septicaemia**

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Clinical evaluation of *Streptococcus pneumoniae* PCR in children with suspected septicaemia.

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Pneumococcal PCR in children with suspected sepsis.

Running Title

Pneumococcal PCR in suspected sepsis.

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Invasive infection with *Streptococcus pneumoniae* is the second commonest cause of meningitis and septicaemia in childhood, resulting in 10 to 15% of cases in the UK.\(^1,2\) Isolation of *Streptococcus pneumoniae* from a normally sterile site remains the gold standard for diagnosis. Blood culture sensitivity is low (around 45%) and decreases further when antibiotics have been administered (around 20%).\(^3\) Despite its accuracy and potential to detect pneumococcus in culture negative patients, the use of molecular testing for *Streptococcus pneumoniae* is not widespread and not yet recommended as part of routine investigations of suspected septicaemia.\(^1,2\)

We retrospectively tested 117 blood specimens for *Streptococcus pneumoniae lytA* using previously published PCR assays.\(^4\) These specimens were collected from children with suspected meningitis or septicaemia as part of an ethically approved study on the diagnostic accuracy of *Neisseria meningitidis* Loop Mediated Isothermal Assay.\(^5\)

Four of the 117 children tested had pneumococcal *lytA* detected by PCR. Only two of these had invasive pneumococcal disease confirmed by blood culture. The two children who were culture negative had clinical signs of septicaemia: A 10 month old boy with fever, vomiting and listlessness who required fluid resuscitation and admission to intensive care; A two year old girl with fever, cough, poor feeding, poor perfusion and focal chest signs.

Evaluating *lytA* PCR as a confirmatory test for pneumococcus is complicated because it appears to perform better than the gold standard traditional culture. The children included in this study were defined as ‘those whom the attending clinician suspected as having meningitis or septicaemia’. Review of the clinical details of the children in this study in combination with a positive *lytA* PCR make it likely that these children had invasive pneumococcal disease which conventional culture methods failed to
diagnose. Although our study was small and pneumococcal disease was rare these
data suggest that addition of lytA PCR to the routine investigations of children
presenting with signs of septicaemia and meningitis is likely to greatly improve
laboratory diagnosis of this serious infection. This is clinically a very desirable
outcome as treatment for invasive pneumococcal disease requires a longer course of
treatment than meningococcal disease\(^2\). We believe that reviewed National Institute
for Health and Care Excellence and other guidelines should consider recommending
this test to the panel of investigations of children with suspected meningitis or
septicaemia.

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   UK. London. Health Protection Agency Meningococcus and Haemophilus
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   ‘loop mediated isothermal amplification’ (LAMP) as a near-patient test for
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