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CLINICAL CHARACTERISTICS OF CHILDREN WITH PNEUMOCOCCAL MENINGITIS

Abstract

The bacterium Streptococcus pneumoniae (also known as the pneumococcus) is a major cause of meningitis (inflammation of the lining of the brain) globally. It causes significant disability and death. In industrialised countries such as the UK, up to a third of survivors of pneumococcal meningitis may develop disabilities such as deafness, blindness, epilepsy and cerebral palsy.

There are almost 100 different strains of the pneumococcus. The UK and Ireland introduced a vaccine against the seven most common strains (PCV7) in their immunisation programmes in 2006 and 2008, respectively, and this vaccine was then replaced with one that protected against 13 strains (PCV13) in 2010. Both vaccines have led to rapid and sustained reductions in serious pneumococcal infections in children and adult as well, because of indirect (herd) protection. The overall reduction in pneumococcal disease, however, has been associated with a small and steady increase in disease due to strains that are not covered by the current vaccines. Currently nearly all invasive pneumococcal infections in children are caused by strains not covered by the existing vaccine.

Our study intends to measure how many children develop meningitis caused by pneumococcus, the strains of pneumococcus, the clinical severity, treatment given and outcomes one year later. This will provide important information for doctors treating children with meningitis, for public health specialists who monitor infectious disease and for those who are responsible for overseeing the vaccine programme.

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Background

Streptococcus pneumoniae is a major cause of bacterial meningitis globally,[1] with 10% to 40% dying of their infection.[1-3] Survivors of pneumococcal meningitis are more likely than any other causes of meningitis to suffer from neurological and other serious long-term complications.[4-6] In a recent meta-analysis including 48 studies, 32% had long-term complications, including hearing loss, seizures, brain injury and blindness.[7] The UK and the Republic of Ireland introduced a vaccine against the seven most common pneumococcal strain (serotypes (PCV7)) in the national childhood immunisation programme in 2006 and 2008, respectively; this vaccine was then replaced with one that protected against 13 serotypes (PCV13) in 2010.[8] Both vaccines have been associated with a rapid decline in pneumococcal disease, including meningitis caused by the vaccine serotypes.[9]The overall reduction, however, has been offset by a small increase in disease due to non-vaccine serotypes.[10] Currently, nearly all pneumococcal infections in children are caused by non-vaccine pneumococcal serotypes. Because these serotypes have only emerged after the pneumococcal vaccines were introduced, we have very little knowledge of the risk, clinical severity and outcomes of pneumococcal meningitis caused by these new and emerging serotypes.

Our aim is to understand the clinical severity, presenting features, acute management, clinical course and the outcomes after 12 months of such non-vaccine serotypes causing meningitis. We will compare our results with the national standard of care for children with serious infections. There are reports of extended hospitalisations for some children with pneumococcal meningitis because of prolonged inflammation after appropriate antibiotic treatment. A better understanding of the course of illness will guide clinical management, it will enable more accurate information to patients and their families on prognosis, and it will inform public health vaccine policy.

Coverage	United Kingdom and Republic of Ireland
Duration	January 2020 to January 2022 (25-months of surveillance) with a 1-year follow-up until January 2023
Research Questions	1. Estimate the incidence of childhood pneumococcal meningitis 2. Describe symptoms and signs at presentation. 3. Describe the investigations, management and treatment in hospital (including intensive care). 4. Describe the clinical course 5. Describe outcomes of pneumococcal meningitis.
Case definition	**Confirmed cases:** Children aged <16 years with CSF positive for pneumococcus by culture **AND/OR** PCR **Probable case:** CSF pleocytosis (abnormal increase in number of white blood cells in the CSF) **AND** pneumococcus identified in a sterile site other than the CSF i.e. blood, urine, synovial fluid, pleural space, deep intraoperatively accessed tissue, pus. **Possible cases:** No CSF specimen but abnormal temperature control (>38 oC or <36 oC), AND pneumococcus identified in sterile site other than CSF (blood, urine, synovial fluid, pleural space, deep intraoperatively accessed tissue or pus) AND clinical features indicative of meningitis (any combination of headache, stiff neck, vomiting, photophobia, confusion/delirium, unconscious, coma, seizures, bulging fontanelle, signs of meningism on examination).
Reporting instructions	Please report any child seen in the last month who meets the case definition in the UK or the Republic of Ireland regardless of country of birth.
Methods	Each paediatrician reporting a child who meets the above case definition of pneumococcal meningitis will be sent a clinical questionnaire by the study team. Throughout the study, all patient data will be dealt with in strict confidence, and the families of affected infants will not be contacted directly by the pneumococcal meningitis study team at any stage.
Ethics approval	London-Dulwich Research Ethics Committee (reference: 19/LO/0978); HRA Confidentiality Advisory Group (reference: 19/CAG/0073); and Public Benefit and Privacy Panel for Health and Social Care (reference: 1819-0357).
Support group	Meningitis Now (https://www.meningitisnow.org/) Meningitis Research Foundation (https://www.meningitis.org/)
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References

1. Johnson AP, Waight P, Andrews N, Pebody R, George RC, Miller E. Morbidity and mortality of pneumococcal meningitis and serotypes of causative strains prior to introduction of the 7-valent conjugant pneumococcal vaccine in England. J Infect. 2007;55(5):394-399.
2. Stanek RJ, Mufson MA. A 20-Year Epidemiological Study of Pneumococcal Meningitis. . Clin Infect Dis 6/1/1999. 1265;28(6):1265.
3. Oligbu G, Collins S, Sheppard CL, et al. Childhood Deaths Attributable to Invasive Pneumococcal Disease in England and Wales, 2006-2014. Clin Infect Dis. 2017;65(2):308-314.
4. Dery MA, Hasbun R. Changing epidemiology of bacterial meningitis. Curr Infect Dis Rep. 2007;9:301-307.
5. Neuman HB, Wald ER. Bacterial meningitis in childhood at the Children's Hospital of Pittsburgh: 1988-1998. Clin Pediatr (Phila). 2001;40(11):595-600.
6. Epstein FH, Quagliarello V, Scheld WM. Mechanisms of Disease: Bacterial meningitis: Pathogenesis, Pathophysiology, and Progress. N Engl J Med. 1992;327(12):864-872.
7. Jit M. The risk of sequelae due to pneumococcal meningitis in high-income countries: a systematic review and meta-analysis. J Infect. 2010;61(2):114-124.
8. Salisbury D, Ramsay M NK. Immunisation against Infectious Disease: The Green Book, Public Health England. Vol 297.; 2013. doi:10.1136/bmj.297.6660.1406.
9. Waight PA, Andrews NJ, Ladhani SN, Sheppard CL, Slack MPE, Miller E. Effect of the 13-valent pneumococcal conjugate vaccine on invasive pneumococcal disease in England and Wales 4 years after its introduction: An observational cohort study. Lancet Infect Dis. 2015;15(5):535-543.
10. Miller E, Andrews NJ, Waight PA, Slack MPE, George RC. Herd immunity and serotype replacement 4 years after seven-valent pneumococcal conjugate vaccination in England and Wales: An observational cohort study. Lancet Infect Dis. 2011;11(10):760-768.