Short reports

Serotype 6C invasive pneumococcal disease in Indigenous people in North Queensland

Jeffrey N Hanna, Jan L Humphreys, Amy Jennison, Megan Penny, Helen V Smith

A previously unrecognised serotype of *Streptococcus* pneumoniae, designated as serotype 6C, was first described in 2007.¹ Although classical serological procedures (i.e. Quellung reactions) do not distinguish this serotype from closely-related serotype 6A, it is now recognised that 6A and 6C are quite distinct and separate serotypes.^{1,2}

The seven-valent pneumococcal conjugate vaccine (7vPCV) includes serotype 6B. No invasive pneumococcal disease (IPD) caused by this serotype has occurred in Indigenous people in north Queensland since 7vPCV was made freely available to Indigenous children in the latter part of 2001.³ Although 7vPCV does not include serotype 6A, the experience in the United States of America (USA) indicates that the serotype 6B antigen included in 7vPCV provides cross-protection against serotype 6A IPD in children.^{4,5} However, these studies were undertaken before serotype 6C was first recognised, and therefore serotype 6C cases may have been inadvertently included in what were then considered to have been serotype 6A IPD.

More recent studies, using methods to discriminate serotypes 6A and 6C, have revealed that although 7vPCV does indeed provide some cross-protection against serotype 6A, it does not provide protection against serotype 6C IPD.^{6,7} Moreover, in the USA, the incidence of serotype 6C IPD has increased in recent years, with a concomitant increase in the proportion of serotype 6C to 6A cases of IPD.^{6,8} This is probably a consequence of the widespread use of 7vPCV, as it is not only ineffective in preventing serotype 6C IPD, but it also appears to enable serotype 6C replacement carriage within the nasopharynx of young children.⁷ The latter, in turn, increases the potential for transmission of serotype 6C pneumococci via respiratory droplets.

Although the number of cases was small, it initially seemed that serotype 6A had apparently become a 'prominent' cause of IPD in young Indigenous children in north Queensland following the introduction of 7vPCV.³ However, because the Quellung reaction had been used to identify the infecting serotypes, there was no ability to distinguish any serotype 6C IPD that may have occurred and inadvertently identified as serotype 6A cases. To determine the relevance that serotype 6C may have had since 7vPCV was introduced, all invasive serotype 6A pneumococci isolated in Queensland from 1997 to mid-2009 were re-examined using molecular methods.² From mid-2009 all serogroup 6 IPD isolates were routinely examined for serotype 6C using new specific antisera from Statens Serum Institut, Denmark and were also confirmed using the molecular methods.

Upon retesting, five of the IPD isolates from Indigenous people in north Queensland which were initially designated by the Quellung reaction as serotype 6A were correctly identified as serotype 6C. Three of these were in young Indigenous children included in the earlier report.³ The earliest recognised invasive serotype 6C in an Indigenous person in north Queensland was isolated from an adult in August 2003; the earliest from an Indigenous child < 5 years of age was isolated in July 2004. A further 2 cases of serotype 6C IPD were identified through routine testing after mid-2009 (Table 1).

While the earlier results showed there were 6 serotype 6A cases in Indigenous children following the introduction of $7vPCV_{v}^{3}$ it is now apparent that half (3) of these were serotype 6C cases (Table 2). There is now no evidence that serotype 6A has become a more prominent cause of IPD in young Indigenous children in recent years; indeed it would seem that it is serotype 6C that has become more prominent.

A new 13-valent PCV includes serotype 6A but not 6C,⁹ so that even with this vaccine, serotype 6C could become an even more prominent cause of IPD.

Table 1: Serogroup C invasive pneumococcaldisease occurring in Indigenous people innorth Queensland, 1999 to 2009

| Serotype | 1999– 2001 | 2002– 2004 | 2005– 2007 | 2008– 2009 |
|----------|---------------|---------------|---------------|---------------|
| 6A | 2 | 3 | 2 | 0 |
| 6B | 7 | 0 | 0 | 0 |
| 6C | 0 | 2 | 2 | 3 |

| | Serotype | 1999–2001 | 2002–2004 | 2005–2007 |
|---|----------|-----------|-----------|-----------|
| Prior to testing for serotype 6C ³ | 6A | 1 | 3 | 3 |
| Upon testing for serotype 6C | 6A | 1 | 2 | 1 |
| | 6C | 0 | 1 | 2 |

Table 2: Serotype 6A and 6C invasive pneumococcal disease occurring in Indigenous children less than 5 years of age in north Queensland, 1999 to 2007

Addendum

In 2010 (up to the end of May), there have been 3 cases of serotype 6C, but no serotype 6A cases of IPD in Indigenous people in north Queensland.

Author details

Jeffrey N Hanna, Public Health Physician¹ Jan L Humphreys, Public Health Nursing Officer² Amy Jennison, Senior Scientist³ Megan Penny, Scientist³ Helen V Smith, Supervising Scientist³

- 1. Cairns Public Health Unit, Tropical Regional Services, Division of the Chief Health Officer, Queensland Health, Cairns Queensland
- 2. Townsville Public Health Unit, Tropical Regional Services, Division of the Chief Health Officer, Queensland Health, Townsville Queensland
- 3. Public Health Microbiology, Queensland Health Forensic and Scientific Services, Coopers Plains Queensland

Corresponding author: Dr J Hanna, Cairns Public Health Unit, PO Box 1103, CAIRNS QLD 4870. Telephone: +61 7 4050 3600. Facsimile: +61 7 4019 6459. Email: Jeffrey_hanna@ health.qld.gov.au

References

- Park IH, Pritchard DG, Cartee R, Brandao A, Brandileone MC, Nahm MH. Discovery of a new capsular serotype (6C) within serogroup 6 of Streptococcus pneumoniae. J Clin Microbiol 2007;45(4):1225–1233.
- Park IH, Park S, Hollingshead SK, Nahm MH. Genetic basis for the new pneumococcal serotype, 6C. Infect Immun 2007;75(9):4482–4489.

- Hanna JN, Humphreys JL, Murphy DM. Invasive pneumococcal disease in Indigenous people in north Queensland: an update, 2005–2007. Med J Aust 2008;189(1):43–46.
- Whitney CG, Pilishvili T, Farley MM, Schaffner W, Craig AS, Lynfield R, et al. Effectiveness of seven-valent pneumococcal conjugate vaccine against invasive pneumococcal disease: a matched case-control study. *Lancet* 2006;368(9546):1495–1502.
- Hicks LA, Harrison LH, Flannery B, Hadler JL, Schaffner W, Craig AS, et al. Incidence of pneumococcal disease due to non-pneumococcal conjugate vaccine (PCV7) serotypes in the United States during the era of widespread PCV7 vaccination, 1998–2004. J Infect Dis 2007;196(9):1346–1354.
- Park IH, Moore MR, Treanor JJ, Pelton SI, Pilishvili T, Beall B, et al. Differential effects of pneumococcal vaccines against serotypes 6A and 6C. J Infect Dis 2008;198(12):1818–1822.
- Nahm MH, Lin J, Finkelstein JA, Pelton SI. Increase in the prevalence of the newly discovered pneumococcal serotype 6C in the nasopharynx after introduction of the pneumococcal conjugate vaccine. J Infect Dis 2009;199(3):320–325.
- da Gloria Caravalho M, Pimenta FC, Gertz RE Jr, Joshi HH, Trujillo AA, Keys LE, et al. PCR-based quantitation and clonal diversity of the current prevalent invasive serogroup 6 pneumococcal serotype, 6C, in the United States in 1999 and 2006 to 2007. J Clin Microbiol 2009;47(3):554–559.
- Centers for Disease Control and Prevention. Licensure of a 13-valent pneumococcal conjugate vaccine (PCV13) and recommendations for use among children – Advisory Committee on Immunization Practices (ACIP), 2010. MMWR Morb Mortal Wkly Rep 2010;59(9):258–261.