The Impact of Routine Immunization Using Meningococcal C Conjugate Vaccine on Invasive Meningococcal Disease in British Columbia

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ABSTRACT

Objectives: 1) To examine trends in serogroup-specific invasive meningococcal disease (IMD) incidence associated with the protein-polysaccharide conjugate C vaccine (MCC) program in BC; 2) To assess for evidence of capsule switching and serogroup replacement; 3) To discuss whether recent data support modification of the current MCC program to include the quadrivalent protein-polysaccharide conjugate vaccine (MCV-4).

Methods: Information on IMD cases since 1998 were extracted from surveillance databases. Annual IMD incidence rates and corresponding three-year moving averages were calculated. Data management was performed using Microsoft® Office Excel 2003. Time trends were analyzed using chi-square test for linear trend.

Results: For 2003-2006, no significant trends were found in rates of serogroup-specific or total IMD in the overall BC population. Among children <18 years, average annual incidence of serogroup-C IMD has declined with a downward trend (p=0.05). Median age of serogroup-C IMD increased from 16 years (2003) to 42 years (2006). No significant change in incidence rates of pediatric IMD from any non-C serogroup was detected.

Discussion: We document a decreasing trend of pediatric serogroup-C IMD and an increase in median age of serogroup-C IMD cases since 2003, most likely explained by protection from immunization. While the proportion of serogroup-Y IMD has increased, incidence rates of non-C vaccine-preventable IMD have not increased in BC. While incorporation of MCV-4 in routine childhood immunization is desirable to address the few residual cases of non-C vaccine-preventable IMD, it would take several decades to appreciate a benefit from a modified childhood program.

Key words: Meningococcal infections; meningococcal vaccines; incidence

La traduction du résumé se trouve à la fin de l'article.

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In Canada, *Neisseria meningitidis* is the leading cause of bacterial meningitis in children 5-19 years of age.[1] In 2003, British Columbia (BC) initiated a routine protein-polysaccharide conjugate C vaccine (MCC) program for infants and adolescents.[2] The objectives of this study were to explore the trends in serogroup-specific invasive meningococcal disease (IMD) incidence associated with the MCC immunization program in BC, and to explore for evidence of capsule switching and serogroup replacement.[3,4] Given the recent availability of a quadrivalent protein-polysaccharide conjugate vaccine (MCV-4), our discussion will consider whether recent data support modification of the current MCC program to include MCV-4.

METHODS

In BC, IMD cases are reported to BC Centre for Disease Control (BCCDC) through the integrated Public Health Information System and an enhanced surveillance database which captures additional epidemiology and laboratory data (serotyping and subtyping of *N. meningitidis* isolates were performed at BCCDC Laboratory Services and National Microbiology Laboratory). Information on IMD cases reported since 1998 were extracted from these two sources. Total and serogroup-specific IMD annual incidence rates were calculated. Median age of each serogroup-specific IMD was also calculated. Denominator was obtained from an estimation of BC annual population using Population Extrapolation for Organization Planning with Less Error (run-cycle 31, BC STATS). Due to small number of pediatric (<18 years) IMD events, we calculated pediatric rates using a three-year moving average to smooth out short-term fluctuations. Data management was performed using Microsoft® Office Excel 2003. Time trends were analyzed using chi-square test for linear trend with StatCalc (EpiInfo6). A statistically significant ($p \leq 0.05$) upward trend in any non-C IMD after the introduction of MCC immunization program would be considered as evidence for possible capsule switching or serogroup replacement.

RESULTS

Since initiation of routine MCC immunization in July 2003, annual IMD inci-

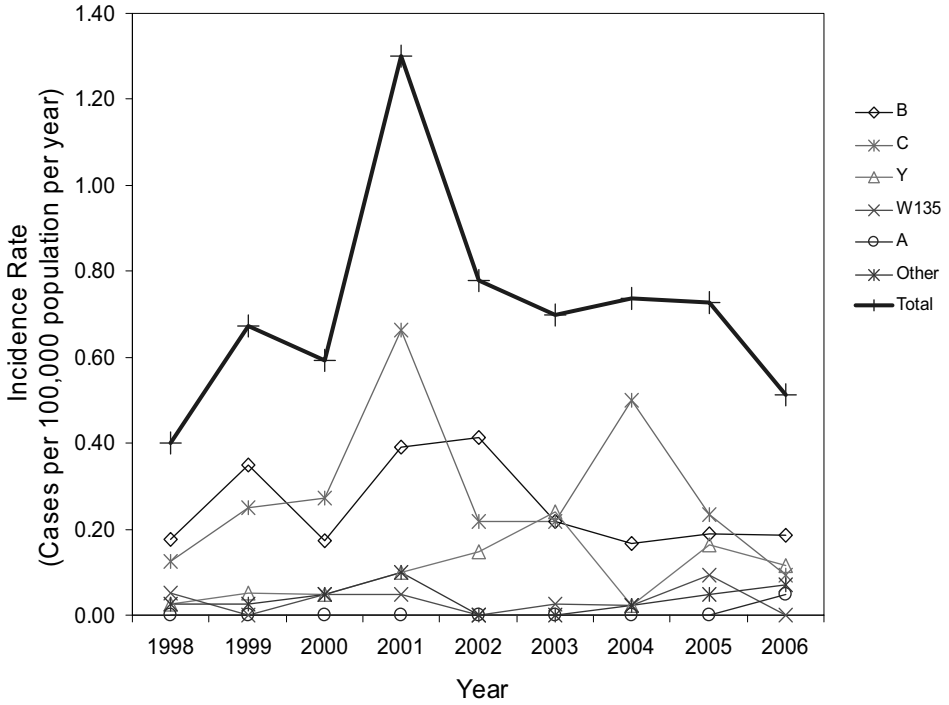

Figure 1. Annual incidence of invasive meningococcal disease, by serogroup and year, British Columbia, 1998-2006

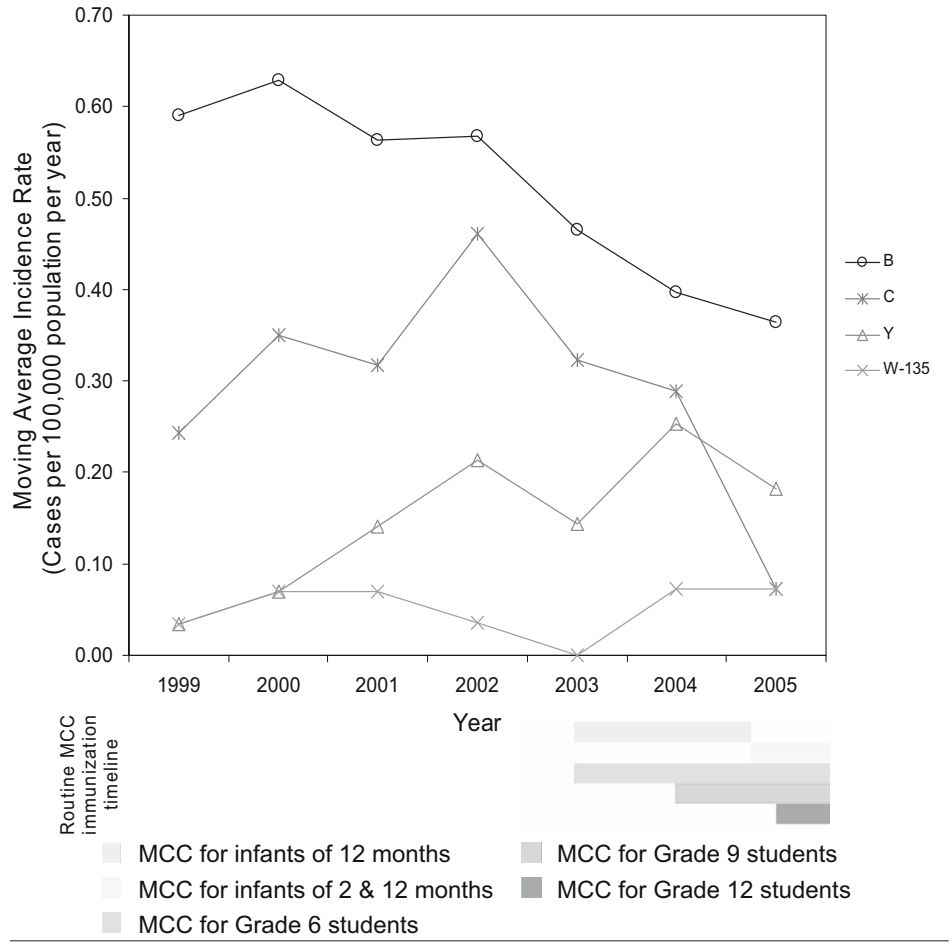

Figure 2. Three-year moving average incidence of invasive meningococcal disease in children <18 years and corresponding routine MCC immunization timeline, British Columbia, 1998-2006

dence from all serogroups in BC population has remained below the 2002 rate (see Figure 1). A peak in IMD incidence from serogroup-C occurred in 2004. During 2003-2006, no significant trends were found in rates of serogroup-specific or total IMD in the overall BC population ($p>0.05$ for all tests).

Among children <18 years, there were 6, 1 and 1 serogroup-C cases in 2003, 2004 and 2005 respectively (1 case in 2003 was an eligible infant who was not vaccinated). No serogroup-C cases were reported in 2006. Average annual incidence of serogroup-C IMD has declined from 0.32/100,000 in 2003 to 0.07/100,000 in 2005 in this age group with a significant downward trend ($p=0.05$) (see Figure 2). Median age of serogroup-C IMD also increased from 16 years (2003) to 42 years (2006).

There were 2 and 5 pediatric serogroup-Y IMD cases for 2003 and 2005 respectively (median age 15 years, range 3 to 17 years). No pediatric serogroup Y IMD was reported during 2004 and 2006. Similarly, two pediatric serogroup W-135 IMD cases (0.75 and 4 years) were reported in 2005. For 2003-2006, no significant changes in incidence rates of pediatric IMD from any non-C serogroup was detected.

DISCUSSION

BC has embraced the MCC program with coverage of 88.7%, 93.0%, and 79.8% among 2 year olds, Grade 6 and Grade 12 students, respectively.[5-7] Despite the high coverage and in contrast to Quebec's experience with MCC,[8] we did not detect a declining incidence of IMD serogroup-C disease in the general population following introduction of MCC. Two reasons for this include a selective BC program (infants and adolescents) as opposed to the broader Quebec program (2 months to 20 year olds) and occurrence of a 2004 Vancouver outbreak of C:2A:P1.5 IMD among men who have sex with men (not initially covered by the MCC program).

Our analysis documents a decreasing trend of pediatric serogroup-C IMD and an increase in median age of serogroup-C IMD cases since 2003. This is most likely explained by protection from childhood MCC immunization.

In accordance with the experience in England and Wales,[9] we find no appreciable upward trend in incidence of other serogroups in the general population as well as among the targeted age groups since introduction of routine MCC immunization. We conclude that currently there is no evidence for capsule switching or serogroup replacement due to the MCC immunization program in BC.

While incorporation of MCV-4 in routine childhood immunization is desirable to address the few residual cases of non-C vaccine-preventable IMD, it should be noted that most cases of Y and W-135 disease in BC affect older individuals, therefore it would take several decades to appreciate a benefit from a modified childhood program.[10] While the proportion of serogroup-Y IMD has increased,[11,12] incidence rates of Y or other non-C vaccine-preventable IMD have not increased in BC.

Major limitations of this study are 1) short timeline since implementation of the MCC program and 2) small annual IMD case count. Given these factors, continuing the enhanced surveillance of IMD is important to assessing the possibility of capsule switching or serogroup replacement as well as determining MCC vaccine effectiveness over time.

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RÉSUMÉ

Objectifs : 1) Examiner l'incidence de l'infection invasive meningocoque (IIM) associée à des sérogroupes spécifiques en relation avec l'utilisation du vaccin conjugué contre le méningocoque C (VCM-C) en Colombie-Britannique ; 2) Évaluer s'il y a eu un changement dans la capsule et une substitution de sérogroupe ; 3) Évaluer si ces données récentes indiquent la nécessité de modifier le programme de vaccination utilisant le VCM-C pour inclure le vaccin quadrivalent conjugué (VCM-4).

Méthodes : Recherche d'information sur les cas de IIM remontant à 1998 à partir de données de surveillance. Les taux d'incidence annuels et des moyennes mobiles sur 3 ans ont été calculés. La gestion des données a été effectuée sur Microsoft Office Excel 2003. Le test du χ^2 a été utilisé pour évaluer la linéarité des tendances dans le temps.

Résultats : De 2003 à 2006, aucun changement significatif n'a été observé tant au niveau de la IIM associée à des sérogroupes spécifique tant au niveau de la IIM totale dans la population globale de la Colombie-Britannique. Chez les sujets âgés de moins de 18 ans, le taux d'incidence annuel de la IIM du sérogroupe C a démontré une tendance à la baisse (p=0,05). L'âge médian des sujets atteints de la IIM du sérogroupe C est passé de 16 ans en 2003 à 42 ans en 2006. Aucun changement significatif dans le taux d'incidence de la IIM pédiatrique d'un sérogroupe autre que le sérogroupe C n'a été détecté.

Discussion : Nous avons documenté une tendance à la baisse de la IIM pédiatrique du sérogroupe C depuis 2003. Ces tendances pourraient être expliquées par la protection acquise lors de l'immunisation. Alors que le pourcentage de IIM du sérogroupe Y a augmenté, le taux d'incidence de la IIM autre que du sérogroupe C évitable par la vaccination n'a pas augmenté en Colombie-Britannique. Alors qu'il serait désirable d'introduire le vaccin CMC-4 dans le programme d'immunisation routinière de la petite enfance pour prévenir le peu de cas résiduels de la IIM non-C qui peuvent être prévenus par la vaccination, plusieurs décennies seraient nécessaires pour atteindre le bénéfice d'un tel programme.

Mots clés : infections méningococciques; vaccins contre la méningococcie; incidence