

Abstract

Background: The Canadian Bacterial Surveillance Network (CBSN) has been monitoring trends in antimicrobial resistance in pneumococcal isolates in Canada since 1993.

Methods: CBSN is a collaborative network of Canadian microbiology laboratories that systematically sample pneumococci for reference broth microdilution susceptibility testing performed to CLSI standards. Non-meningeal breakpoints were used for interpretation of amoxicillin and ceftriaxone resistance. Meningeal breakpoints were used for penicillin. All sterile site isolates collected between 2000-2010 have been serotyped. Publicly-funded infant PCV7 vaccine programs were introduced in Canada between 2002 and 2005.

Results: Of the 9587 SPN isolates from sterile sites collected between 2000 and 2010, 2071 (22%) were from children (age<15 years). Among paediatric isolates, the proportion of PCV7 serotypes (ST) decreased from 83.9% to 3.3%, while isolates of PCV10/not7 increased from 0.8% to 21.5%, PCV13/not10 from 8.3% to 39.7% and non-conjugate vaccine (NPCV) serotypes from 7.0% to 35.5%. Erythromycin resistance increased from 11.2% to 39.2% and penicillin resistance from 13.1% to 21.0%. No levofloxacin resistance was identified in isolates from children. Among isolates in adults, 93.2% were from blood, 2.3% from CSF, 2.0% from pleural fluid, and 3.2% from other sterile sites; 44.7% were from adults ≥65 years of age. Trends in serotypes and antimicrobial resistance in adults are shown in the Table 1.

Results

From 2000 to 2010, 9587 SPN isolates from sterile sites were collected, including 8860 (92.4%) from blood, 276 (2.9%) from CSF, 167 (1.7%) from pleural fluid, and 284 (2.9%) from other sterile sites. All isolates underwent susceptibility testing and serotyping. Paediatric cases (<15yrs) represented 21.8% of cases, adult (15-64 yrs) cases 43.2%, and older adults (>=65yrs) 35.0%. Overall, 60.6% of isolates were from Ontario, 18.1% from the Prairies/Northwest Territories, 8.9% from Atlantic provinces, 6.9% from Quebec, and 5.4% from British Columbia/Yukon.

In 2009/2010, the most common serotypes in paediatric and adult IPD were 19A (30.6%, 15.7%, respectively), 7F (15.5%, 13.3%), 22F (6.9%,6.8%), and 3 (5.8%, 8.7%). Serotype 19A was the most common in samples from blood (18.5%), CSF (14.7%), and other sterile sites (15.5%). Serotype 31 was most common from pleural fluid (17.4%).

From 2000 to 2010, among paediatric isolates, the percent of PCV7 serotypes decreased (83.9% to 3.3%) while the percent of PCV10/not7 serotypes increased from 0.8% to 21.5%, and the percent of PCV13/not10 serotypes increased from 8.3% to 39.7%. The percent of NPCV serotypes also increased from 7.0% to 35.5%. Similar trends were seen in adult isolates although the decrease in the proportion of PCV7 serotypes has been slower (Figure 2).

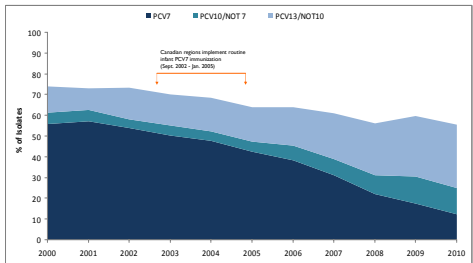


Figure 2. Percent of serotypes covered by the PCV7, PCV10/NOT7, and PCV13/NOT10 vaccines; Canadian isolates collected from adult sterile sites, 2000-2010.

For adult isolates sampled, the overall percent of erythromycin resistance increased from 9.2% in 2000 to 25.4% in 2010. Resistance to penicillin (meningeal) increased from 6.6% in 2000 to 10.7% in 2010. A slight increase in the percent resistant to amoxicillin was observed, from 0% in 2000 to 1.7% in 2010. Levofloxacin resistance remained unchanged from 2000 to 2010 (1.2% to 0.8%) (Figure 3).

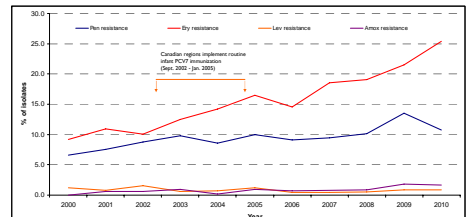


Figure 3. Percent of isolates resistant to erythromycin, amoxicillin, penicillin (meningeal), and levofloxacin; Canadian isolates collected from adult sterile sites, 2000-2010.

Results (cont)

The proportion of PCV7, PCV13/not10, and NPCV serotypes resistant to erythromycin have been increasing since 2000. Erythromycin resistance remains rare in PCV10/not7 serotype isolates. For penicillin resistance, serotypes in the PCV7 and PCV13/not10 group showed an upward trend; in comparison, serotypes in the PCV10/not7, and NPCV groups did not change. The proportion of PCV7 serotypes that are levofloxacin resistant increased in recent years, while there was no noticeable trend in other serotype groups (Figure 4).

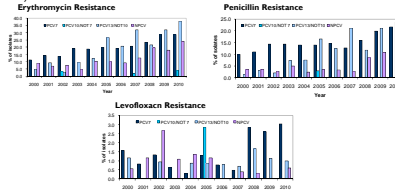


Figure 4. Percent of isolates resistant to erythromycin, penicillin, and levofloxacin by PCV groups; Canadian isolates collected from adult sterile sites, 2000-2010.

In 2009/2010, paediatric isolates were more likely to be resistant to erythromycin (p=0.009), penicillin (p=0.005), TMP-SMX (p=0.002) and amoxicillin (p<0.001) than adult isolates (Figure 5). No fluoroquinolone resistance has been seen in paediatric isolates since 2006.

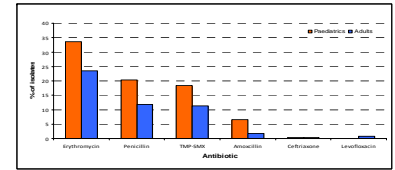


Figure 5. Percent of paediatric and adult sterile site isolates resistant to erythromycin, penicillin (meningeal), trimethoprim-sulfamethoxazole (TMP-SMX), amoxicillin, ceftriaxone, and levofloxacin from across Canada, 2009/2010.

Resistance varied across different serotypes (Figure 6). In 2009/2010, serotypes 15A (65.6%) and 33A (64.1%) were most likely to be erythromycin resistant (compared to 25.3% overall). Serotypes 15A (50.0%) and 35B (44.4%) were most likely to be penicillin resistant (13.4% overall). Levofloxacin resistance was most likely in serotypes 14 (11.1%) and 6B (4.8%) (0.7% overall). Serotype 19A (12.2%) and 19F (10.5%) were most likely to be resistant to amoxicillin (2.5% overall).

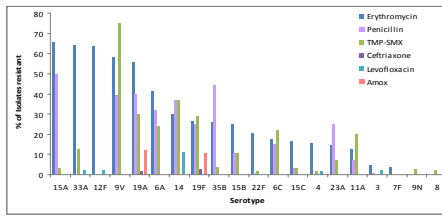


Figure 6. Percent of sterile site isolates resistant to erythromycin, penicillin (meningeal), TMP-SMX, ceftriaxone, levofloxacin, and amoxicillin by serotype, Canadian isolates, 2009-2010. *Includes the 20 most commonly observed serotypes of 2009-2010 isolates.

In 2009/2010, 19A was over represented among erythromycin, amoxicillin, and penicillin resistant isolates in both adults and children. In children < 5 years old, 19A represented 23.3% of erythromycin resistant isolates (vs. 10.9% overall), 62.5% of amoxicillin resistant isolates, and 24.2% of penicillin resistant isolates. Similar trends were seen in adults.

Results (cont)

Although levofloxacin resistance is generally stable, since 2000, levofloxacin resistance has increased in serotypes 14 (from 1.9% to 16.7% in 2010) and 6B (from 1.9% to 9.1% in 2009) for adult IPD isolates. In the same period, erythromycin resistance increased from 0.0% to 69.2% in serotype 33A and 0.0% to 53.3% in 15A. Penicillin resistance increased from 0% to 29.3% in serotype 19A but remained relatively stable in serotype 19F (Figure 7).

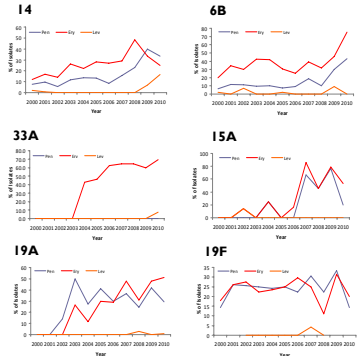


Figure 7. Trends in antibiotic resistance by serotypes most likely to be resistant to erythromycin (33A/15A), penicillin (19A/19F), and levofloxacin (14/6B) in 2009/2010. Canadian isolates collected from adult sterile sites, 2000-2010.

The percent of isolates with multi-drug resistance (R to >2 of penicillin/amoxicillin/ceftriaxone, erythromycin, TMP-SMX, tetracycline, fluoroquinolones) has increased from 2.3 % in 2000, to 5.7% in 2005 and 8.9% in 2010 (p<0.001).

In 2010, the distribution of MDR isolates was PCV13/notPCV10 6.2%, PCV7 20.3%, NPCV 13.5%, and PCV10/notPCV7 0%. MDR isolates are most prevalent in serotypes 19A(56.8%), 6A(9.4%), 9V(5.4%), and 14(4.0%).

Conclusions

Erythromycin resistance has been increasing in all groups; penicillin resistance in PCV7 and PCV13/notPCV10 groups; and fluoroquinolone resistance in PCV7 serotypes 14 and 6B.

Resistance varied across different serotypes; 15A and 33A were most likely to be resistant to erythromycin; 19A and 19F were most likely to be resistant to penicillin and 14 and 6B most likely to be resistant to levofloxacin.

In 2009/2010, 19A comprised 18.2% of all isolates and is over represented among resistant isolates (40.4% of erythromycin R, 87.5% of penicillin R, and 44.2.1% of amoxicillin R).

Most MDR isolates are now in PCV13/not10 group.

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Methods

Since 1993, CBSN has collected all SPN sterile site isolates from participating Canadian hospitals and private microbiology labs (Figure 1). In total, 186 labs have participated with 40 labs submitting for the entire period.

Only one isolate per patient episode is included.

Isolates are shipped to the central lab at Mount Sinai Hospital where they are confirmed as SPN and frozen.

Broth microdilution susceptibility testing is performed and interpreted using CLSI standards. Non-meningeal breakpoints were used for amoxicillin and ceftriaxone susceptibilities. Meningeal breakpoints were used for penicillin. Serotypes were determined using latex pneumococcal antisera (Statens Serum Institut, DK) and Quellung reaction as required.



Figure 1. Canadian regions represented in the Canadian Bacterial Surveillance Network.