Sero-epidemiology of Pneumococcal Pneumonia and Invasive Pneumococcal Disease in Adults in Ontario, Canada, 2000-2010

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Abstract

OBJECTIVES: To assess the changing sero-epidemiology of pneumococcal disease in adults.

METHODS: TIBDN has conducted population-based surveillance for invasive pneumococcal disease (IPD) and lab-confirmed non-bacteremic pneumococcal pneumonia (NBPP) since 2002. Serotyping and broth microdilution susceptibility testing to CLSI standards is performed. PCV7 was licensed in 2001. Publicly-funded infant PCV7 began in 2005.

RESULTS: From 2002 to 2010, 3828 cases of adult IPD/NBPP were identified. In adults >65y, the IPD rate decreased from 34.3 to 26.5/100000/y (2002-2010). The IPD rate due to serotypes (STs) included in PCV7 decreased from 19.1 to 3.3/100000/y; that due to serotypes in PCV13/not PCV7 increased from 5.3 to 11.5/100000/y, and that due to non-conjugate vaccine (NPCV) serotypes increased from 9.9 to 11.7/100000/y. The rate of IPD for adults 15-64y was 5.3 and 4.8/100000/y in 2002 and 2010. The rate of IPD due to PCV7 serotypes decreased from 3.1 to 0.5/100000/y, that due to PCV13/nonPCV7 serotypes increased from 1.0 to 2.2/100000/y, and that due to NPCV serotypes increased from 1.2 to 2.0/100000/y. Changes in serotype distribution are greater than changes in incidence (see Table 1 below).

Percent (%) of disease due to serotypes of:	IPD			NBPP			Other respiratory isolates		
	2002	2006	2010	2002	2006	2010	2002	2006	2010
PCV7	56.7	34.4	10.1	43.3	30.4	6.1	45.3	30.1	15.9
PCV10, not PCV7	2.6	3.6	16.5	0	0	3	0.9	0.6	2.7
PCV13, not PCV7/10	14.6	22.7	32.1	23.3	30.4	42.4	17	23.3	21.2
Non-conjugate vaccine	26.2	39.3	41.4	33.3	39.3	48.5	36.8	46	60.3

Serotypes in PCV10 but not PCV7 are more common in IPD than NBPP and were rare until 2008, when serotype 7F emerged. Among NPCV serotypes, disease due to serotypes 12F, 22F, and 31 has been decreasing, and disease due to serotypes 11A, 23A, 33A, and 8 has been increasing. PCV7 serotype isolates were more resistant (R) to penicillin/cephalosporins, erythromycin, and levofloxacin; however, increasing resistance overall means combined resistance to erythromycin has increased, resistance to penicillin/cephalosporins is stable. Resistance to levofloxacin has decreased.

CONCLUSIONS:
Infant PCV7 has dramatically reduced the incidence of adult IPD and NBPP due to PCV7 serotypes; however, overall disease rates have decreased only 25%. PCV13/nonPCV7 strains now comprise nearly 50% of adult IPD and NBPP.

Methods

From 1995 to 2010, prospective, population-based surveillance for invasive pneumococcal disease (defined as illness associated with a sterile site isolate of *S. pneumoniae*) was conducted in metropolitan Toronto and Peel region. From 2002 to 2010, all respiratory site isolates from hospital laboratories were also collected.

Serotype is determined using latex pneumococcal antisera (Statens Serum Institute, DK) and the Quellung reaction. Antimicrobial susceptibility testing is performed by broth microdilution to CLSI standards. Population data are obtained from Statistics Canada. Demographic and clinical data are collected from review of health records and interviews with patients and attending physicians.

Nonbacteremic pneumococcal pneumonia (NBPP) was defined using a modified version of the Musher criteria (Medicine 79:210-21, 2000): clinical presentation suggestive of pneumonia, infiltrate on plain chest radiography; microscopic examination of a Gram-stained sputum with white blood cells≥epithelial cells and predominance of Gram-positive cocci, culture of sputum yielding *S. pneumoniae* and no other likely bacterial pathogens; and blood cultures either negative or not done.

Results

From 2000 to 2010, 3894 cases of adult (≥15y) IPD and 508 cases of non-bacteremic pneumococcal pneumonia (NBPP) were identified. There were 3590 other isolates of pneumococci identified from respiratory specimens. Older adults (≥65y) comprised 47% of cases.

In 2009/10, serotypes 19A, 7F, and 3 were the most common in adult IPD. Serotypes 19A, 3, and 23B were the most common in adult NBPP and 3, 11A, and 19A in other respiratory isolates (Table 2). The most common NPCV13 serotypes were 22F, 11A and 8 in IPD, 23B and 11A in NBPP, and 11A and 23A in other respiratory isolates.

From 2002/03 to 2009/10, the proportion of disease attributed to PCV7 serotypes decreased in all case/isolate types (Table 1). The percent of isolates from PCV13/nonPCV7 serotypes increased from 19% to 46% in IPD, from 25% to 31% in NBPP and from 19% to 26% in other respiratory isolates.

Table 2: Serotype distribution of isolates covered by PCV13 in adult IPD and NBPP cases and other respiratory-site isolates [2002, 2006 and 2010].

	Serotype	IPD 2002	IPD 2006	IPD 2010	NBPP 2002	NBPP 2006	NBPP 2010	Other Respiratory 2002	Other Respiratory 2006	Other Respiratory 2010
PCV13 (%) PCV10 (%) PCV7 (%)	4	7.3	8.0	0.7	0.0	5.4	0.0	2.4	0.6	0.8
	6B	5.8	5.3	1.7	10.0	5.4	0.0	9.9	5.2	2.7
	9V	6.6	6.1	1.9	3.3	1.8	0.0	1.9	1.9	1.1
	14	15.6	5.8	1.7	3.3	0.0	0.0	3.8	1.6	0.8
	18C	3.6	3.1	1.0	0.0	3.6	0.0	2.4	2.7	1.9
	19F	7.3	3.6	2.4	23.3	7.1	6.1	12.3	12.9	7.4
	23F	10.6	2.5	0.7	3.3	7.1	0.0	12.7	5.2	1.3
	1	0.0	0.3	0.5	0.0	0.0	0.0	0.0	0.0	0.0
	5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	7F	2.6	3.3	16.0	0.0	0.0	3.0	0.9	0.6	2.7
	3	10.6	10.5	9.1	20.0	23.2	18.2	6.6	11.8	11.6
	6A	2.2	6.1	4.1	3.3	5.4	6.1	7.6	7.4	4.0
	19A	1.8	6.1	18.9	0.0	1.8	18.2	2.8	4.1	5.6
	NPCV13 (%)	26.2	39.3	41.4	33.3	39.3	48.5	36.8	46.0	60.3

From 2002 to 2010, the IPD rate in adults decreased from 9.5 to 8.0/100000/y (Figure 1). In older adults (≥65y) the rate decreased (34.3 to 26.5/100000/y), while the rate in adults 15-64y remained constant (5.3 in 2002 and 4.8/100000/y in 2010).

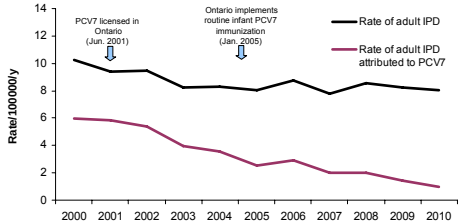

Figure 1: Rate of adult (≥15 years) IPD and adult IPD due to PCV7 serotypes in Toronto/Peel, 2000 - 2010.

From 2002 to 2010, in older adults (≥65y), IPD due to serotypes included in PCV7 decreased from 19.1 to 3.3/100000/y, that due to PCV13/nonPCV7 serotypes increased from 5.3 to 11.5/100000/y, and that due to NPCV serotypes increased from 9.9 to 11.7/100000/y.

In adults 15-64y, the rate of IPD due to PCV7 serotypes decreased from 3.1 to 0.5/100000/y, IPD due to PCV13/nonPCV7 serotypes increased from 1.0 to 2.2/100000/y, and that due to NPCV serotypes increased from 1.2 to 2.0/100000/y.

Results (con't)

From 2000 to 2010, 47 NPCV serotypes were represented in IPD isolates. Only serotypes 8, 22F and 6C represented >5% of any year's IPD isolates. Serotype 6C was differentiated from 6A starting in July 2010 and represented 8.8% of July-Dec 2010 adult IPD isolates.

Among NPCV serotypes, adult IPD due to serotypes 12F, 22F, and 31 has been decreasing, and disease due to serotypes 11A, 23A, 33A, 15A and 8 has been increasing.

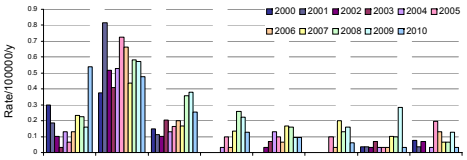

Figure 2: Rates of adult IPD due to NPCV13 serotypes which represent more than 5% of isolates in 2010 or have been associated with more than a 2 fold increase in incidence since 2004 [where n>20].

In 2010, PCV13/nonPCV7 strains comprised 48% of adult IPD, 45% of adult NBPP and 24% of other respiratory isolates (Figure 3). No isolates of serotype 1 or 5 were identified. Serotype 7F is more common in IPD than NBPP or other respiratory isolates, while serotype 3 is more likely in NBPP than IPD or other respiratory isolates.

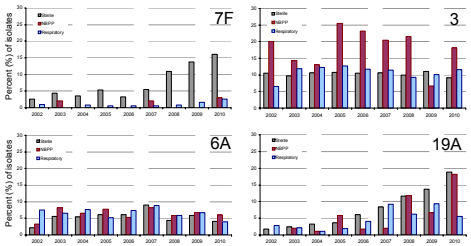

Figure 3: Percent of isolates of serotypes included in the PCV13 vaccine and not PCV7 vaccine (no isolates of serotype 5 or 1) by type of case, 2002-2010.

In 2009/10, isolates from NBPP were more likely to be penicillin resistant (p=0.13) and levofloxacin resistant (p=0.21) than isolates from sterile sites or other respiratory cases (Figure 4).

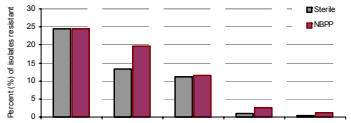

Figure 4: Percent of adult NBPP and sterile site isolates resistant to erythromycin, trimethoprim-sulfamethoxazole (TMP-SMX), penicillin, levofloxacin, and ceftriaxone in 2009/10 (CLSI breakpoints, non-mening used cxt, mening used for pen).

Results (con't)

Changes in antibiotic resistance are serogroup specific (Figure 5).

Penicillin resistance has increased in isolates included in PCV7 and PCV13/nonPCV10, but remained virtually nil in PCV10/non7 and NPCV isolates. Serotype 19A comprised 29% of pen R isolates in 2010.

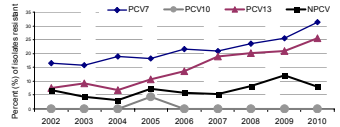

Figure 5a: Percent penicillin resistant by vaccine group, all adult isolates, 2002-2010 (CLSI mening breakpoints).

Resistance to respiratory fluoroquinolones has remained stable and low in all serotypes (overall resistance to levofloxacin in 2010 1.1%).

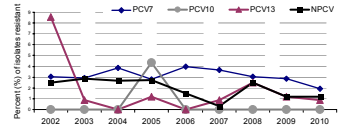

Figure 5b: Percent levofloxacin resistant by vaccine group, all adult isolates, 2002-2010 (CLSI breakpoints).

Erythromycin resistance has increased steadily in all serotypes, although serotype 19A was over represented (27% of ery R isolates in 2010).

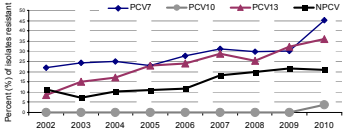

Figure 5c: Percent erythromycin resistant by vaccine group, all adult isolates, 2002-2010 (CLSI breakpoints).

Conclusions

- Infant PCV7 has reduced the incidence of adult IPD and NBPP due to PCV7 serotypes 10 fold; however, overall disease incidence has decreased by only 25%.
- Among adults, serotype 19F is more common among respiratory than IPD isolates, 19A is more common in NBPP and IPD than in other respiratory isolates, serotype 3 is associated with NBPP rather than IPD or other respiratory isolates, and serotype 7F is associated with IPD.
- The evolution of antimicrobial resistance is different in different serotypes. Serotype 19A was over represented among resistant isolates (29% of pen R and 27% of ery R isolates in 2010). Almost all pen R is due to PCV13 strains; however, ery R is emerging among NPCV strains.

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