Emergence of penicillin-resistant Streptococcus pneumoniae in southern Ontario, 1993-94

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OBJECTIVE: To determine the prevalence of resistance of Streptococcus pneumoniae to penicillin and other antimicrobial agents in metropolitan Toronto.

DESIGN: Consecutive pneumococcal isolates from different patients were obtained from two private community-based laboratories and from patients assessed in the emergency department of a tertiary-care teaching hospital in Toronto, Ontario between June and December 1993, and between March and October 1994. In vitro susceptibility testing was done by broth microdilution in accordance with National Committee for Clinical Laboratory Standards guidelines.

RESULTS: Twenty (7.3±3.1%) of 274 pneumococcal isolates were resistant to penicillin; six (30%) isolates had high-level resistance (minimal inhibitory concentration [MIC] 2.0 µg/mL or greater); and 14 isolates had intermediate resistance (MIC 0.1 to 1.0 µg/mL). Penicillin-resistant strains were also frequently resistant to tetracycline (55%), cotrimoxazole (50%), erythromycin (40%) and cefuroxime (35%). Resistant strains comprised several serotypes: 19F (six isolates), 9V (three), 23F (three), and one each of 6A, 6B, 14, and 19A; four isolates were nontypeable.

CONCLUSIONS: There has been a recent emergence of penicillin-resistant S pneumoniae in southern Ontario. National and regional surveillance is warranted to determine the extent of the problem elsewhere in Canada.

(Pour résumé, voir page 158)

Key Words: Antibiotic resistance, Streptococcus pneumoniae
Émergence d’un *Streptococcus pneumoniae* pénicillino-résistant dans le Sud de l’Ontario, 1993-1994

**Objectif** : Déterminer la prévalence de la résistance de *Streptococcus pneumoniae* à la pénicilline et à d’autres antibiotiques dans le territoire métropolitain.

**Modèle** : Les isolats pneumococques consécutifs de différents patients ont été obtenus à partir de deux laboratoires privés et chez des patients évalués aux urgences d’un hôpital universitaire de soins tertiaires à Toronto, en Ontario, entre juin et décembre 1993 et entre mars et octobre 1994. Les épreuves de sensibilité in vitro ont été effectuées par microdilution sur bouillon de culture, conformément aux directives du National Committee for Clinical Laboratory Standards.

**Résultats** : Vingt (7.3±3.1 %) des 274 isolats pneumococques se sont révélés résistants à la pénicilline, six (30 %) des isolats présentaient une résistance forte (concentration minimale inhibitrice [CMI] 2.0 µg/mL ou plus) et 14 isolats présentaient une résistance intermédiaire (CMI, 0.1 à 1.0 µg/mL). Souvent, les souches pénicillino-résistantes étaient également résistantes à la tétracycline (55 %), au cotrimoxazole (50 %), à l’érythromycine (40 %) et au céfuroxime (35 %). Les souches résistantes comprenaient plusieurs sérotypes : 19F (6 isolats), 9V (3), 23F (3) et un de chacun des sérotypes suivants : 6A, 6B, 14 et 19A. Quatre isolats se sont révélés non typables.

**Conclusions** : On note une émergence récente de *S. pneumoniae* résistants à la pénicilline dans le Sud de l’Ontario. Une surveillance épidémiologique nationale et régionale s’impose afin de mesurer l’étendue du problème ailleurs au Canada.
(30%) of which had high-level resistance and 14 with intermediate resistance (Table 1). Fourteen resistant strains were eye, ear or sputum isolates from pediatric out-patients and six strains (two from sputum and one each from blood, cerebrospinal fluid, bronchoalveolar washings and the eye) were from adults seen in the emergency department. Penicillin-susceptible strains were generally susceptible to the other antimicrobial agents tested. However, penicillin-resistant \textit{S. pneumoniae} were also frequently resistant to ceftazidime (55%), tetracycline (55%), trimethoprim-sulfamethoxazole (50%), erythromycin (40%), cefuroxime (35%) and ceftriaxone (25%) (Table 1). Isolates were uniformly susceptible to only vancomycin and imipenem.

The penicillin-resistant pneumococci were serotyped as follows: 19F (six isolates), 9V (three), 23F (three), and one each of 6A, 6B, 14, 19A; four were nontypeable. The PFGE results of a representative sample of penicillin-resistant isolates are shown in Figure 1. Different serotypes had clearly distinguishable PFGE patterns. However, whereas all three serotype 9V isolates had identical patterns and a nontypeable strain shared an identical pattern with a serotype 23F isolate, the other 23F serotypes had distinct profiles and each of the 19F serotype isolates had a unique pattern.

**DISCUSSION**

The recent increase in the prevalence of penicillin-resistant \textit{S. pneumoniae} in the metropolitan Toronto region found in this survey is in marked contrast to results obtained in a 1988 study (10) of a similar community-based population when only eight of 551 (1.5%) penicillin-resistant strains were detected (P<0.0001). Furthermore, none of the previously identified pneumococcal isolates had demonstrated high-level penicillin resistance, whereas 30% of the resistant strains in this survey had high-level resistance.

The recent increase in prevalence is also reflected by notifications of invasive pneumococcal disease due to penicillin-resistant strains to the Ontario Pneumococcal Study Group (13) in 1993-94.

The results of serotyping and molecular typing by PFGE suggest that multiple clones of penicillin-resistant pneumococci are appearing simultaneously in the metropolitan Toronto region. Similar results have been suggested by a cross-Canada survey of penicillin-resistant isolates (14). Moreover, this preliminary experience with these typing methods suggests that for \textit{S. pneumoniae}, PFGE is more discriminatory than is serotyping; this observation would have to be confirmed by evaluating a larger number of isolates.

The emergence of penicillin-resistant \textit{S. pneumoniae} has major health care implications. Microbiology laboratories
must be able to detect rapidly and accurately penicillin resistance in pneumococcal isolates. Although drug-resistant strains of pneumococci now appear to be much more prevalent in several parts of Canada, regional variations may exist. 

If the results of this survey are confirmed elsewhere in Canada, empirical antimicrobial treatment of a variety of infectious diseases (including pneumonia, bronchitis, otitis media, sinusitis and meningitis) will have to be modified. Treatment options may be limited because penicillin-resistant strains are also frequently resistant to other beta-lactam antibiotics (15,16). Moreover, alternative antimicrobial agents for the treatment of pneumococcal infections may not be as effective as penicillin would be for susceptible strains (17,18). Because invasive infections due to resistant strains are associated with considerable morbidity and mortality, greater use of pneumococcal vaccine should be promoted, particularly for those at high risk for severe pneumococcal infections (19). Continuous surveillance of Streptococcus pneumoniae antimicrobial susceptibility is required to determine the extent of resistance to penicillin and alternative agents, so that appropriate therapy and control measures may be instituted.

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REFERENCES