Antimicrobial-resistant
Streptococcus pneumoniae

Penicillin-resistant Streptococcus pneumoniae is a relatively new phenomenon. It essentially did not exist in Canada in the 1980s when Dixon et al (1) published their results. In 1992, reduced susceptibility to penicillin, including both intermediate and resistant strains, was estimated by Applebaum (2) to be less than 5%. Loo et al in 1994 (3) and Simor et al in 1995 (4) identified rates of approximately 8%. The 1996 results of Simor et al (5) reported a rate of 12%.

The National Centre for Streptococcus (NCS), Edmonton, Alberta, is a voluntary passive reporting system that has been collecting data on penicillin-resistant pneumococci since April 1991. Table 1 reports the provincial and territorial distribution of isolates submitted to the NCS. Lovgren et al (6) reported that from 1992 to 1995 the overall reduced susceptibility rate for invasive isolates submitted to the NCS was approximately 8%. Throughout the four-year period, there was an upward trend in numbers of organisms with decreased susceptibility to penicillin; this trend was not statistically significant. However, the proportion of isolates with high level resistance did significantly increase during the four years (0.6% in 1992, 0.6% in 1993, 1.5% in 1994, and 5.8% in 1995). From April 1, 1996 to March 31, 1997, 10.2% (65 of 639) of invasive isolates across the country showed reduced penicillin susceptibility; in Alberta, the rate was 16.4% (Table 2).

A comparative ranking of the seroprevalence of serotypes by year has been completed by the NCS (Table 3). The most common serotype in the past three years was type 14. Serotype distribution among isolates with reduced susceptibility to penicillin from April 1, 1996 to March 31, 1997 is presented in Table 4. The serotypes most likely to be associated with reduced penicillin sensitivity include what is very likely a clonal 9V. Fortunately, the polysaccharide 23-valent and the proposed conjugate 7-valent vaccines cover from 59% to 86% of intermediately resistant isolates and 100% of the resistant isolates in the NCS 1992 to 1995 collection (Table 5).

Using an initial oxacillin disc screening test to select candidates for extended minimum inhibitory concentration (MIC) testing, the NCS detected that less than 4% of a year’s strains exhibited reduced susceptibility to third-generation cephalosporins in a 12-month period from April 1993 to March 1994. No vancomycin resistance has been detected to date. These results are consistent with Jette and Ringuette in 1994 (7). Simor et al in 1995 (4) detected a trimethoprim/sulfamethoxazole resistance rate of 18.5%; the NCS collection indicates a similar rate of 19.5%. Unfortunately, the oxacillin screen may miss as many as two-thirds of the trimethoprim/sulfamethoxazole resistant strains (6).

Studies of antibiotic resistance have mapped three general ways that organisms in a geographic area may become resistant. Antibiotic selective pressure may favour mutants in the local indigenous population, selecting for increased resistance. An exogenous organism possessing resistance may relocate to an area. Genes coding for resistance mechanisms may be passed from one organism to another; these organisms need not necessarily be other S pneumoniae.

All of these have been demonstrated for S pneumoniae, but the last is of special significance to the development of antibiotic resistance in pneumococci. The original experiments showing that DNA was the essential molecule for heredity were performed in S pneumoniae. They were possible because naked DNA (not just plasmid or transposons) can be incorporated by S pneumoniae, acted on and inherited. The mosaic
**TABLE 1**  
Provincial and territorial distribution of submitted *Streptococcus pneumoniae* isolates

| Province or territory | Total isolates | Isolates/100,000/year* |
|-----------------------|----------------|------------------------|
| Yukon/Northwest        | 35             | 9.72                   |
| Alberta               | 471            | 4.28                   |
| Manitoba              | 30             | 0.66                   |
| Ontario               | 282            | 0.64                   |
| British Columbia      | 66             | 0.44                   |
| Saskatchewan          | 18             | 0.44                   |
| New Brunswick         | 13             | 0.43                   |
| Quebec                | 51             | 0.17                   |
| Nova Scotia           | 9              | 0.24                   |
| Newfoundland          | 1              | 0.04                   |
| Prince Edward Island  | 0              | -                      |
| Total                 | 976            | 0.82                   |

*Average calculated per year from total organisms collected from 1992 to 1995

**TABLE 2**  
Penicillin resistance in invasive pneumococci (blood or cerebrospinal fluid [CSF]) from April 1, 1996 to March 31, 1997

|                      | Alberta | Other provinces | Total – all of Canada |
|----------------------|---------|-----------------|-----------------------|
| Blood and/or CSF isolates submitted | 171     | 468             | 639                   |
| Isolates with reduced penicillin susceptibility | 28      | 37              | 65                    |
| Penicillin resistance rate | 16.4%   | 7.9%            | 10.2%                 |

nature of the genes involved in penicillin resistance is strong evidence that this is an important mechanism for *S pneumoniae* to acquire new characteristics in the wild.

Similar promiscuity has been shown to operate for the capsular genes, where genetically similar or identical *S pneumoniae* can change their capsular type by acquiring the appropriate genes. This has significant implications not only for attempting to control antibiotic resistance with vaccines, which are targeted at the capsule, but also as a potential mechanism of vaccine escape for all *S pneumoniae*.

In Canada, there are both strengths and weaknesses with the current surveillance activities for *S pneumoniae*.

The strengths of Canada’s surveillance activities include the following.
- Canada has excellent laboratories at all levels capable of recognizing resistance.
- Canada has epidemiologists of the first rank to analyze and interpret data.
- Canada has a committed public health infrastructure with a proven track record of success of preventing disease, especially with respect to immunization.
- Canada has a highly trained and committed medical and academic establishment that have contributed greatly to the understanding of this organism, and its human and economic impact.

The weaknesses of Canada’s surveillance activities include the following.
- Insufficient numbers of organisms are characterized.
- The characterization that is now performed is unrepresentative with respect to the age groups affected and the geographic locations from which organisms are submitted.
- The population that is described by this information is poorly characterized.

a. Incidence and prevalence cannot be routinely calculated from the data currently being collected.
TABLE 5
Vaccine coverage and its relationship to reduced penicillin susceptibility

| Serotypes                      | Number (%) of isolates | Penicillin susceptibility |
|--------------------------------|-------------------------|--------------------------|
|                                | All ages | ≤5 years | Susceptible | Intermediate | Resistant |
| Covered by 23-valent vaccine   | 896 (92%) | 289 (95%) | 827 (92%) | 42 (86%) | 27 (100%) |
| Covered by 7-valent vaccine    | 638 (65%) | 273 (90%) | 582 (65%) | 29 (59%) | 27 (100%) |
| Not covered by either vaccine  | 80 (8%) | 14 (5%) | 73 (8%) | 7 (14%) | 0 |
| Total                          | 976 | 303 | 900 | 49 | 27 |

*Includes cross-protection expected for type 6A

b. Populations at increased risk can not be identified.

c. Accurate cost, benefit and effectiveness measures are difficult to acquire.

d. No standard basis for comparison exists now or is planned for in future.

- Communication and coordination among the primary stakeholders, public health units, hospitals, chronic care facilities, epidemiologists and laboratories are inconsistent.

- Communication and coordination between local, provincial, territorial and federal stakeholders are inconsistent.

- Canada lacks comprehensive, consistent, targeted ongoing surveillance.

In summary, the experience of the National Centre for Streptococcus is one of both good and bad news. The bad news is that penicillin resistance is here, and it is increasing. The good news is that vaccination may be an additional means of controlling the spread and effect of penicillin resistance. The best news is that the pneumococcal antibiotic resistance is not yet so pervasive that it is too late for Canadians to act.

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