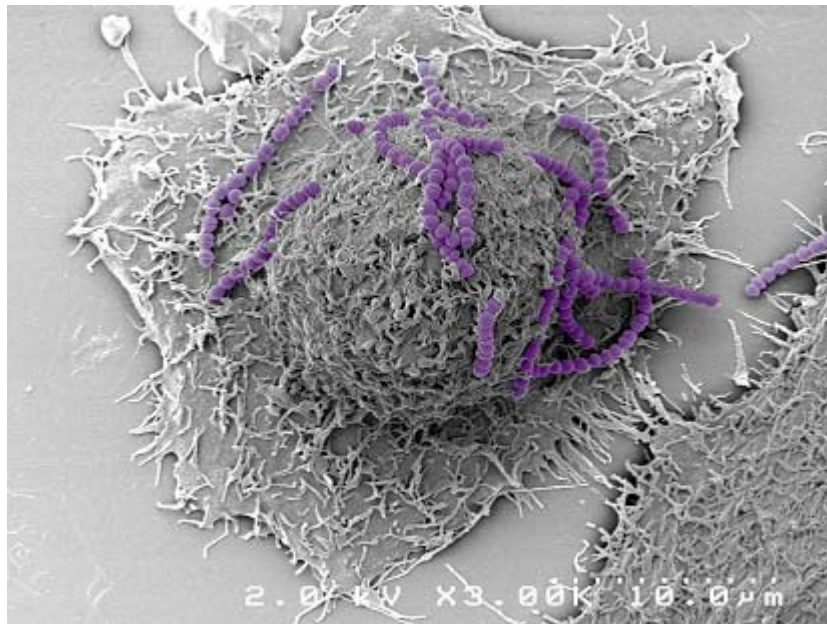




## **April 2004/March 2005 Annual Report**



**NATIONAL CENTRE FOR STREPTOCOCCUS  
PROVINCIAL LABORATORY FOR PUBLIC HEALTH  
(MICROBIOLOGY),  
EDMONTON, ALBERTA, CANADA**



## National Centre for Streptococcus - Canada

Reporting Period: April 1, 2004 to March 31, 2005.

### I.0 Introduction

#### I.1 Brief History and Overview

The NCS was established at the Provincial Laboratory for Public Health on April 1, 1992. It is a National Centre operated by the Provincial Laboratory for Public Health (Microbiology) Alberta for the National Microbiology Laboratory. The NCS provides streptococcal reference services for Canada. This includes M serotyping of Group A streptococci (GAS), serotyping of Group B streptococci (GBS), serotyping of *Streptococcus pneumoniae*, identification of catalase negative, gram positive cocci through biochemical and molecular methodology, molecular typing of *S. pneumoniae* and antimicrobial susceptibility trend analysis for GAS, GBS and *S. pneumoniae*.

The NCS is currently jointly funded by the National Microbiology Laboratory and the Provincial Laboratory for Public Health (Microbiology) Alberta.

The majority of data generated by the NCS is in the form of passive surveillance meaning that isolates are sent to the NCS by the provinces when the provinces indicate it is necessary for their programs. All isolates analyzed in the passive surveillance system are collected from sterile sites only and are considered invasive isolates. This data is contained within the NCS's annual reports as well as various publications put out by members of the NCS team.

The NCS also provides laboratory support for streptococcal outbreak investigation where invited. The majority of these investigations have involved GAS frequently in nursing home settings. These activities lead to our current participation in the National Invasive Group A Streptococcus Working Group. This group is currently developing a national case definition for invasive GAS and drafting guidelines for outbreak response.

In addition to the analysis of isolates submitted for passive surveillance, the NCS frequently participates in studies with researchers both in Canada and worldwide on a variety of streptococcal related issues. These may be initiated by either members of the NCS or by outside investigators. Services are provided on a cost recovery basis.

The NCS also acts as a repository for invasive, catalase negative gram-positive cocci for Canada. Access to this repository is granted to investigators provided the guidelines are adhered to for strain usage.

The following pages contain tables and graphs describing the results generated in this years reporting period.



## National Centre for Streptococcus - Canada

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### 2.0 Specimen volume

	<b>GAS sero-typing</b>	<b>GBS sero-typing</b>	<b><i>S. pneumoniae</i> serotyping</b>	<b>Species identification</b>	<b>TOTAL</b>	<b>Externally funded research</b>	<b>TOTAL excluding research</b>
<b>British Columbia</b>	138	0	240	8	386	0	386
<b>Alberta</b>	257	98	654	86	1095	292	803
<b>Saskatchewan</b>	56	16	112	0	184	10	174
<b>Manitoba</b>	16	3	178	3	200	18	182
<b>Ontario</b>	251	1	748	10	1010	633	377
<b>Quebec</b>	177	4	189	13	383	84	299
<b>New Brunswick</b>	64	0	0	7	71	0	71
<b>Nova Scotia</b>	0	0	16	0	16	16	0
<b>Newfoundland</b>	0	0	2	0	2	2	0
<b>Prince Edward Island</b>	1	0	2	1	4	0	4
<b>Yukon</b>	1	0	6	12	19	0	19
<b>Northwest Territories</b>	1	1	19	0	21	0	21
<b>Nunavut</b>	0	0	3	0	3	0	3
<b>International</b>	0	0	167	0	167	167	0
<b>TOTAL</b>	<b>962</b>	<b>123</b>	<b>2336</b>	<b>140</b>	<b>3561</b>	<b>1222</b>	<b>2339</b>

### 3.0 Laboratory Surveillance

All of the data presented in this section reflect passive surveillance only. The majority of all isolates tested at the NCS are recovered from normally sterile sites, and/or are associated with invasive disease. Occasionally non-invasive isolates are submitted due to atypical characteristics. Wherever possible, only one isolate was counted per patient, however specimen coding may have prevented interpretation of this information for some isolates.

All data from externally funded studies have been excluded from this report.



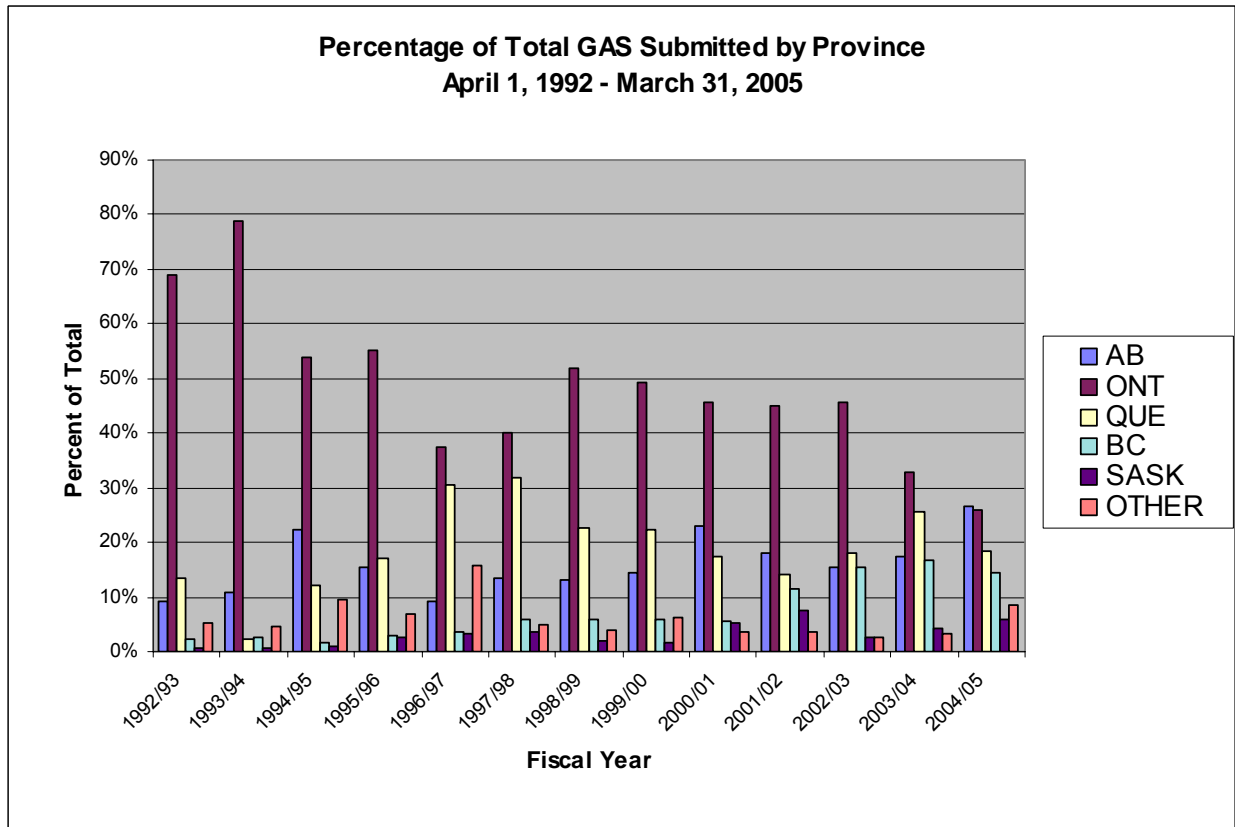
# National Centre for Streptococcus - Canada

Reporting Period: April 1, 2004 to March 31, 2005.

## Group A Streptococcus

Historically the majority of the GAS that were submitted to the NCS for serotyping have come from Alberta, Ontario and Quebec (Figure 1). Over the past four years we have observed an increase in GAS submitted from British Columbia and Saskatchewan. We believe that this increase represents enhanced surveillance, and may not necessarily reflect an increase in the incidence of invasive GAS disease in those provinces. GAS isolates submitted from these five provinces account for 91% (879 of 962) of the 2004/05 GAS collection.

Figure 1.





## National Centre for Streptococcus - Canada

Reporting Period: April 1, 2004 to March 31, 2005.

Table I presents M type distribution for the past year and comparative data for 2003/04 and 2002/03. Specific M types are known to be poorly antigenic, making it difficult to prepare the M antisera necessary for serological M type classification. Serotypes M28 and M77 fall into this category. These serotypes are more easily classified according to the AOF type, using antisera specific for the serum opacity factor produced by OF positive strains. The AOF type is, with few exceptions, consistent with the M type, and strains typed as 28 or 77 by either method have been listed together in this report.

Table I. Group A Streptococcus M type Distribution

M type	2004/05			2003/04			2002/03		
	# Cases	Rank	% of total	# Cases	Rank	% of total	# Cases	Rank	% of total
M1	166	1	20.3	277	1	30.9	295	1	29.7
AOF <sup>†</sup> 28	106	2	13.0	100	2	11.1	68	3	6.8
M12	51	3	6.2	65	3	7.3	89	2	9.0
M4	45	4	5.5	46	4	5.1	44	4	4.4
M/AOF <sup>†</sup> 77	33	5	4.0	33	5-6	3.7	43	5	4.3
M89	30	6-7	3.7	28	8	3.1	29	8-9	2.9
M5	30	6-7	3.7	25	9-10	2.8	28	10-11	2.8
M82	29	8	3.6	32	7	3.6	28	10-11	2.8
M61	27	9	3.3	1	NA	0.1	5	21	0.5
M75	24	10	2.9	15	15	1.7	17	17	1.7
M3	22	11	2.7	17	14	1.9	39	6	3.9
M11	21	12-13	2.6	23	11	2.6	38	7	3.8
M41	21	12-13	2.6	8	18	0.9	4	24	0.4
PT2967	20	14	2.4	25	9-10	2.8	27	12	2.7
M91	19	15	2.3	33	5-6	3.7	19	14-16	1.9
M nt*	54		6.6	47		5.2	58		5.8
Other	119		14.6	122		13.6	163		16.4
<b>Total</b>	<b>817</b>			<b>897</b>			<b>994</b>		

NA = not available

<sup>†</sup>AOF = Anti Opacity Factor

\*nt = not typable



## National Centre for Streptococcus - Canada

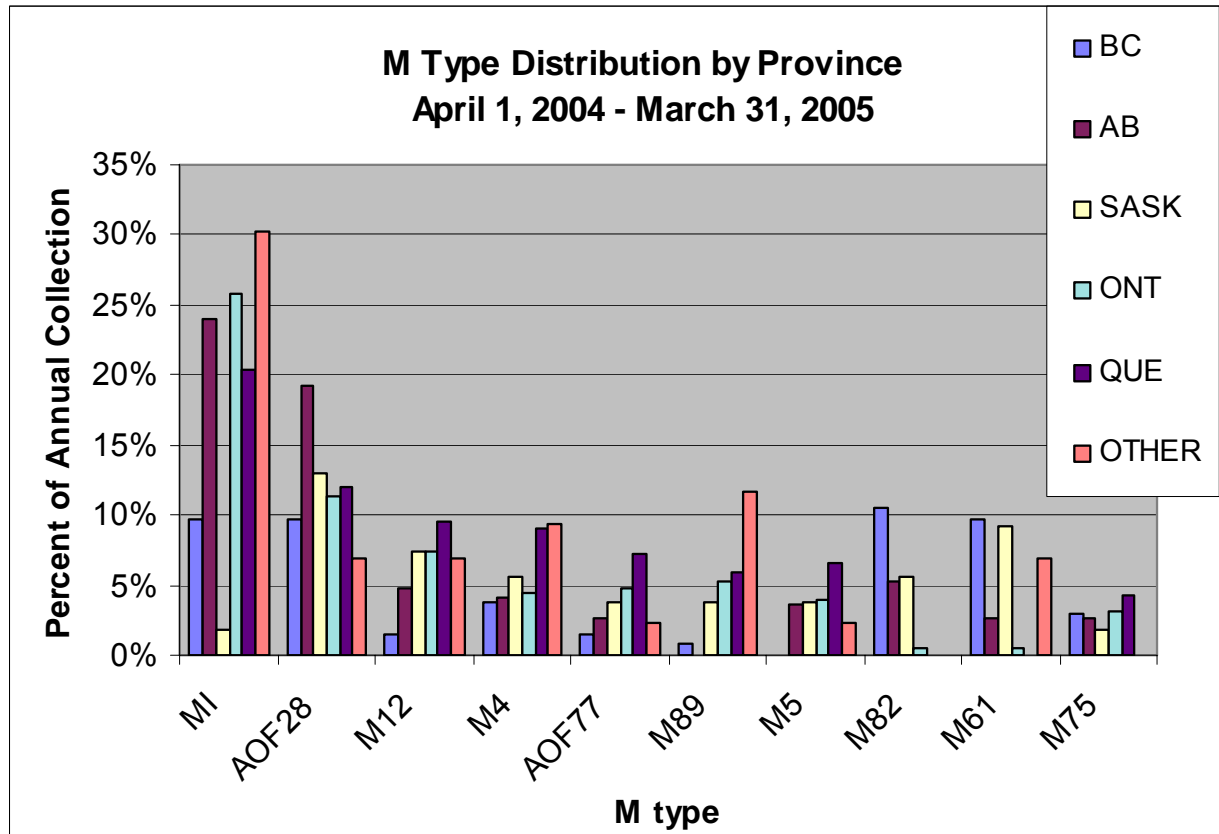
Reporting Period: April 1, 2004 to March 31, 2005.

With the exception of 2000/01 when M1 fell to second place, this M type has consistently been the most frequently encountered serotype since the NCS began reporting national GAS sero-prevalence in 1992. M1, AOF28, M12, M4 and M/AOF77 have ranked as the top five M types for the past three years. A marked increase was observed for M61 and M41 in 2004/05 over the previous two years. M61 was encountered most frequently from the province of British Columbia (13 of 27 isolates), while M41 was encountered most frequently from the province of Alberta (12 of 21 isolates)

The Provincial distribution of the top 10 ranking M types in the 2004/2005 collection, are presented in Figure 2. While M1 is frequently encountered in most regions represented here, the exception is Saskatchewan where this serotype accounts for only 2% (1 of 54) of the isolates received from that province.

Figure 2 shows the obvious geographic variation across Canada for some of the other M types. M89 is more commonly encountered in the East, while M82 and M61 are predominant in the Western regions.

Figure 2.



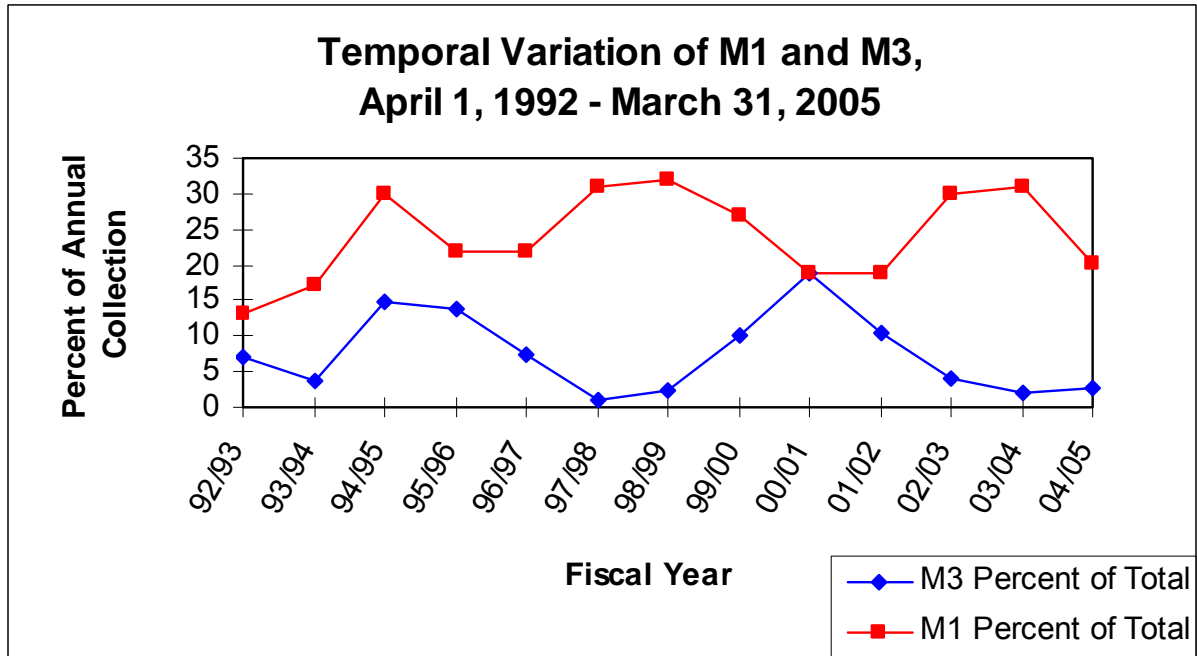


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The temporal variation of M1 over the past 13 years is compared with that of M3 in Figure 3. For the first four years of our surveillance, the ratio of these two types was relatively proportionate but in 1996/97, the prevalence of M3 began to decline followed by an increase in the prevalence of M1. During 2000/01 M3 was equally as important as M1 as a cause of invasive disease in Canada. The decline in M3 accompanied by an upswing in M1 between 2002 and 2004, and the decrease in prevalence of M1 for 2004/05 presents an interesting evolving pattern in seroprevalence variation for these M types.

Figure 3.





## National Centre for Streptococcus - Canada

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### GAS and Antibiotic Resistance

Antibiotic susceptibility of all GAS submitted for serotyping was determined by the disk diffusion method. Penicillin, erythromycin, clindamycin, chloramphenicol and vancomycin were routinely tested. Only data from Provinces submitting >50 isolates over the past year were analyzed in Table 2. Resistance to erythromycin was associated with MPT2967 (19 of 20 isolates – 95%), M92 (12 of 18 isolates – 67%), M58 (7 of 13 isolates – 54%), M11 (9 of 21 isolates – 42%), and M4 (12 of 45 isolates – 27%). The high proportion of erythromycin resistance in British Columbia correlates with the relatively high frequency of M58, M92 and MPT2967 observed for that province.

Table 2. Proportion (%) of Antibiotic Resistance by Region for Group A Streptococci; April 1/04 – March 31/05 (comparative data for April 1/03 - March 31/04)

Antibiotic	BC	AB	ON	QB	SASK	Other	Total
Erythromycin	22.6 (16.8)	7.3 (8.0)	9.7 (7.8)	11.4 (9.7)	5.6 (NA)	7.0 (7.7)	11.1 (9.8)
Clindamycin	2.3 (2.0)	0.5 (0.7)	2.2 (1.0)	3.6 (3.0)	1.9 (NA)	0 (0)	2.0 (1.6)
Chloramphenicol	0.8 (0)	0 (0)	0 (0)	0.6 (0)	0 (NA)	0 (0)	0.2 (0)
Penicillin	0 (0)	0 (0)	0 (0)	0 (0)	0 (NA)	0 (0)	0 (0)
Vancomycin	0 (0)	0 (0)	0 (0)	0 (0)	0 (NA)	0 (0)	0 (0)
<b>Total # isolates tested</b>	<b>133 (149)</b>	<b>192 (151)</b>	<b>228 (295)</b>	<b>167 (237)</b>	<b>54 (37)</b>	<b>43 (65)</b>	<b>817 (897)</b>

All erythromycin-resistant isolates were also screened for inducible resistance to clindamycin using the double disk test. Inducible resistance was detected in 68% (62 of 91) of the erythromycin-resistant isolates.



## National Centre for Streptococcus - Canada

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### Group B Streptococcus

The data presented in table 3 represents the number of cases of invasive disease for which isolates were submitted to the NCS for serotyping. These were primarily from the province of Alberta. Isolates from 89 of 112 cases received from April 1, 2004 – March 31, 2005, and 114 of 137 cases received from April 1, 2003 to March 31, 2004 were from that province. The data therefore may not be representative of national trends. Only one isolate per case was included in the analysis.

Table 3. Group B Streptococcus Serotype Distribution by Age for April 1, 2004 - March 31, 2005  
(Comparative data for April 1, 2003 - March 31, 2004)

Serotype	<3 mon	3 mon-20 yr	21-50 yr	>50 yrs	Age not specified	Total
III & III / R	11(9)	3(1)	3(4)	8(12)	0(0)	25(26)
V & V / R	3(2)	0(0)	2(13)	18(24)	0(0)	23(39)
II & II / c	5(2)	0(0)	7(3)	4(9)	0(0)	16(14)
Ia & Ia / c	4(4)	0(0)	6(8)	3(12)	0(0)	13(24)
Ib & Ib/ c	2(2)	0(1)	1(2)	9(9)	0(0)	12(14)
IV	0(0)	0(0)	2(1)	2(2)	0(0)	4(3)
VI	0(0)	0(0)	0(0)	0(1)	0(0)	0(1)
VII	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
VIII	0(0)	0(0)	0(0)	1(0)	0(0)	1(0)
Not typable*	1(0)	0(0)	5(5)	12(11)	0(0)	18(16)
<b>TOTAL</b>	<b>26(19)</b>	<b>3(2)</b>	<b>26(36)</b>	<b>57(80)</b>	<b>0(0)</b>	<b>112(137)</b>

\*Not typable = carbohydrate antigen not detected

Types III and V (with and without the R protein antigen) account for 43% of the disease represented by this sample. Isolates belonging to serotypes V, Ia, Ib, and II were associated with adult disease; 50 of 64 isolates (78%) belonging to these serotypes were recovered from patients  $\geq 21$  years of age. Nontypable isolates are most frequently encountered in older adults. Eleven of 26 isolates (42%) that caused invasive disease in the youngest age group (<3 months) belonged to serotype III and III/R.

Four isolates from cerebrospinal fluid were submitted. All were from children <3 months old; one belongs to serotype II and three belong to serotypes III and III/R.



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### GBS and Antibiotic Resistance

Antibiotic susceptibility of all GBS submitted for serotyping was determined by the disk diffusion method. Penicillin, erythromycin, clindamycin, chloramphenicol and vancomycin were routinely tested. Because the majority of the isolates were submitted from Alberta, data are presented for that province separately from the rest of Canada (TROC) in Table 4.

Overall, there was little change in the proportion of erythromycin resistance from that observed in 2003/04 with almost one quarter of all isolates showing resistance to this antibiotic. A slight increase was observed for isolates received from outside Alberta.

The proportion of clindamycin resistance has increased in Alberta over last year, but remained the same for isolates submitted from other provinces. All but one of the 26 erythromycin-resistant isolates were either cross-resistant to clindamycin, or showed inducible resistance to that drug.

There is no obvious association between serotype and resistance to either erythromycin or clindamycin; resistance was encountered in all of the most common serotypes and in nontypable isolates.

Readers are reminded that resistance rates for TROC should be interpreted with caution due to the small sample size.

Table 4. Proportion (%) of Antibiotic Resistance by Region for Group B Streptococci; April 1/04 – March 31/05 (comparative data for April 1/03 - March 31/04)

<b>Antibiotic</b>	<b>Alberta</b>	<b>TROC</b>	<b>Total</b>
Erythromycin	23.6 (25.4)	21.7 (17.4)	23.2 (24.1)
Clindamycin	14.6 (9.7)	8.7 (8.7)	13.4 (9.5)
Chloramphenicol	1.1 (0)	0 (0)	0.9 (0)
Penicillin	0 (0)	0 (0)	0 (0)
Vancomycin	0 (0)	0 (0)	0 (0)
<b>Total # isolates tested</b>	<b>89 (114)</b>	<b>23 (23)</b>	<b>112 (137)</b>



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Reporting Period: April 1, 2004 to March 31, 2005.

### Streptococcus pneumoniae

Analyses for April 1, 2000 to March 31, 2005 exclude data from isolates received from Laboratoire de Santé Publique du Québec (LSPQ), where serotyping for their provincial pneumococcal surveillance program is performed. Only isolates of less common serotypes are submitted to the National Centre for Streptococcus for factoring; data from these uncommon serotypes have been excluded in an effort to eliminate the resulting bias. Data specific for Quebec may be obtained by contacting the LSPQ directly.

Seroprevalence for pneumococcal isolates recovered from blood and CSF for the past five years is presented in Table 5. With the exception of types 6A and 8, these same serotypes have consistently been among the top 12 for the past 5 years with only slight changes in ranking. There has been an apparent increase in the prevalence of types 3, 6A and 8 over this time frame, the reason for which is unclear.

Table 5. Comparative Ranking of the Most Common Serotypes April 1, 2000- March 31, 2005

Serotype	2004-05	2003-04	2002-03	2001-02	2000-01
Type 14	1	1	1	1	1
Type 4	2	2	2	2	2
Type 6B	3	5	4	5	3
Type 9V	4	3-4	5	3	5
Type 3	5	3-4	8	6	11/12
Type 8	6	9	13	10	11/12
Type 6A	7	11	10	12	13
Type 23F	8	7	6	11	10
Type 19F	9	8	3	7	4
Type 18C	10	6	7	4	6
Type 22F	11	10	9	8	9
<b>Total cases</b>	<b>792</b>	<b>823</b>	<b>828</b>	<b>703</b>	<b>670</b>

All serotypes listed in table 5, except type 6A, are included in the currently available 23-valent vaccine. Overall, vaccine coverage can be expected for 89% (707 of 792) of the total cases represented in the 2004/05 collection, and 84% (666 of 792) if the expected cross-protection for serotype 6A is excluded. A comparison of vaccine coverage for the past five years is presented in Table 6.



## National Centre for Streptococcus - Canada

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Table 6. Vaccine coverage (23-valent) with and without type 6A ( cross-protection expected)

	2004-05	2003-04	2002-03	2001-02	2000-01
Percent coverage including serotype 6A	89	91	93	93	92
Percent coverage without serotype 6A	84	87	89	90	89

As in previous years, Alberta is disproportionately represented in this collection, presumably because of proximity and community awareness of national and provincial surveillance programs. Forty percent (316 of 792 isolates) of the 2004/05 sample was from Alberta. Because of this bias, Table 7 presents Alberta data separately from the rest of Canada (TROC).

With the exception of type 19A, the top twelve serotypes are the same for both Alberta and TROC. As in previous years, type 4 and type 14 continue to rank in the top three serotypes across Canada. Over the past two years, type 8 has become more prevalent in Alberta than in other provinces accounting for 9.5% versus 3.4% of the respective collections for 2004-05. Consistent with 2003-04, type 9V was encountered more frequently from TROC.

The number of nontypable isolates (5) received in 2004-05 is reduced from those received in 2003-04 (11), and interestingly, all but one of these 16 isolates was submitted from the same province. Consultation with the submitting laboratory indicates that these strains are not epidemiologically linked, and fingerprinting (PFGE) suggests that the strains are unrelated.



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Table 7. Serotype Distribution in Alberta compared with the rest of Canada (TROC) for 2004/05  
Rank and Percent of the total for 2004/05 (comparable data for 2003/04)

Serotype	Alberta		TROC	
	Rank	Percent of Total	Rank	Percent of Total
Type 4	1 (2)	10.1 (9.2)	4 (3)	7.6 (8.0)
Type 8	2 (5)	9.5 (6.4)	11 (11)	3.4 (3.0)
Type 14	3 (1)	7.3 (12.6)	1 (1)	12.4 (17.0)
Type 3	4-5 (4)	6.0 (6.4)	5 (4)	6.3 (7.3)
Type 6A	4-5 (14)	6.0 (2.5)	8 (10)	4.6 (4.1)
Type 6B	6-7 (3)	5.7 (8.1)	2 (5)	9.7 (5.8)
Type 9V	6-7 (7-8)	5.7 (4.7)	3 (2)	9.0 (9.2)
Type 22F	8 (13)	5.4 (3.0)	12 (9)	3.2 (4.7)
Type 18C	9 (6)	4.7 (5.9)	9 (8)	4.2 (5.2)
Type 19A	10-11 (17)	4.1 (1.4)	16 (12)	1.5 (2.6)
Type 23F	10-11 (7-8)	4.1 (4.7)	7 (6-7)	5.3 (5.6)
Type 19F	12 (9)	3.5 (4.5)	6 (6-7)	5.5 (5.6)
Other Types		27.9 (30.6)		26.3 (19.5)
Nontypable		0 (0)		1.0 (2.4)
<b>Total # cases</b>		<b>316 (358)</b>		<b>476 (465)</b>

The majority of the pneumococcal isolates that are submitted to the NCS for routine serotyping are from Western Canada. However, the number of isolates submitted from Ontario has gradually increased over the past three years. A comparison of the number of isolates submitted from the three western most provinces compared with those submitted from Ontario and the rest of Canada (TROC), excluding Quebec, is presented in Figure 4. Even with the increase in the number of isolates submitted from Ontario since 2002, it appears that only selected pneumococcal isolates from provinces east of Saskatchewan are submitted for serotyping.

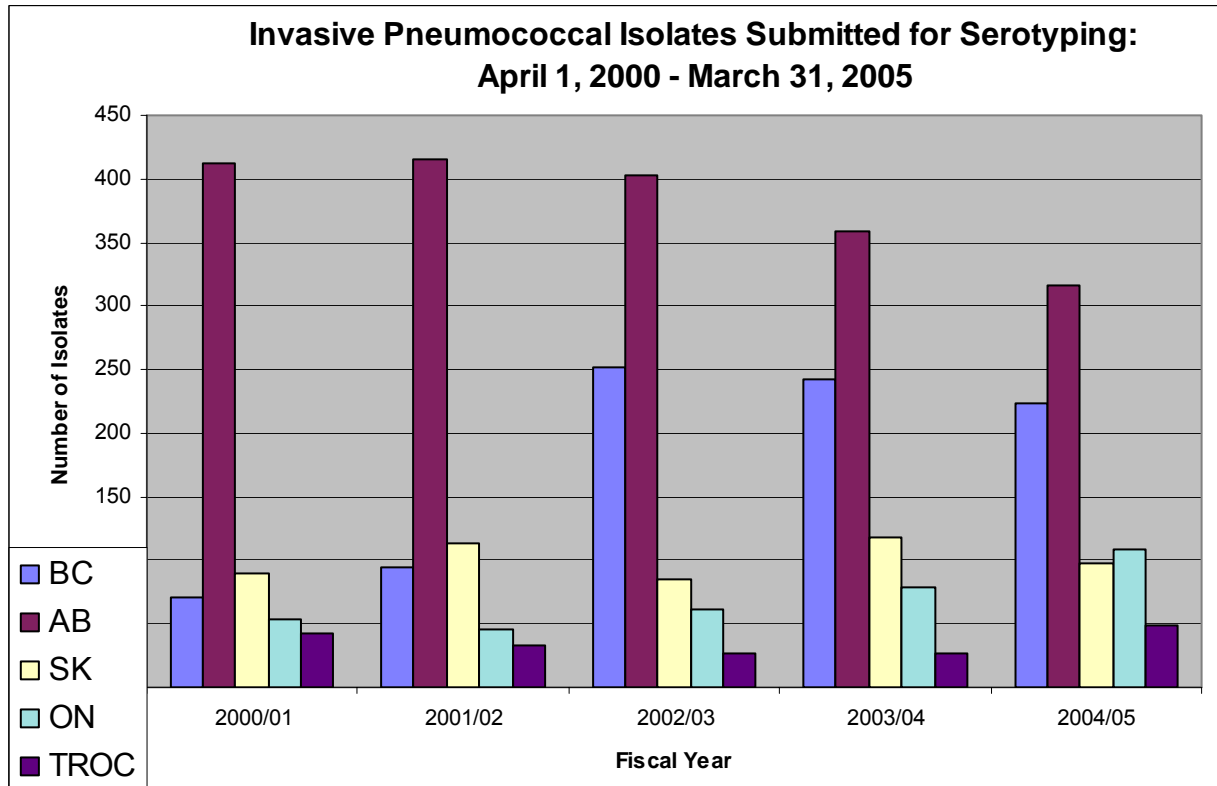
In August, 2002 Alberta added Prevnar™ to the childhood vaccination program for children under 2 years of age. The reduction in the number of pneumococcal isolates received over the past two years (between April 1, 2003 and March 31, 2005) was seen specifically in the under 5 age group (table 8) and it is tempting to attribute this to the implementation of this important public health intervention in Alberta and more recently in other provinces.



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Figure 4. Pneumococcal Isolates Submitted to the NCS. (Excludes Quebec)





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The serotypes that cause invasive disease in young children are known to be different from those causing disease in older patients. The data for April 1, 2004 – March 31, 2005 are presented in tables 8 and 9 sorted according to patient age. This analysis excludes 5 isolates for which the age was not provided. Comparative data for the previous year are also presented.

Table 8. Serotype Distribution for Children ( $\leq 16$  years) for April 1, 2004 - March 31, 2005  
(Comparative data for April 1, 2003 - March 31, 2004)

Serotype	$\leq 5$ years	6 - 16 years	Total $\leq 16$ years	
	# Cases	# Cases	# Cases	Rank
Type 14*	27 (54)	1 (2)	28 (56)	1 (1)
Type 6B*	22 (24)	2 (3)	24 (27)	2 (2)
Type 19F*	15 (22)	2 (0)	17 (22)	3 (3)
Type 18C*	13 (10)	2 (5)	15 (15)	4-5 (4-6)
Type 9V*	7 (13)	8 (2)	15 (15)	4-5 (4-6)
Type 19A	10 (5)	0 (0)	10 (5)	6 (11-12)
Type 6A	8 (10)	1 (0)	9 (10)	7 (7)
Type 4*	3 (6)	4 (1)	7 (7)	8 (9)
Type 23F*	4 (13)	2 (2)	6 (15)	9 (4-6)
Other Types	26 (33)	14 (16)	40 (49)	
<b>Total No. Cases</b>	<b>135 (190)</b>	<b>36 (31)</b>	<b>171 (221)</b>	

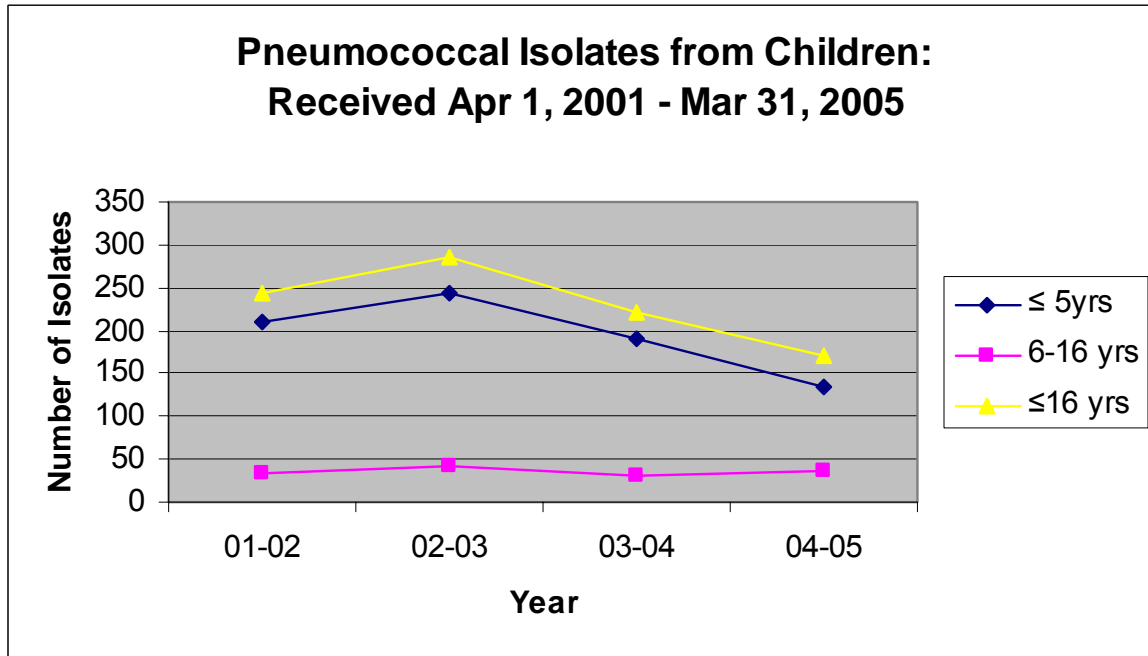
\* Serotypes included in the 7-valent conjugate vaccines

Sixty-seven percent (91 of 135) of the isolates submitted between April 1, 2004 and March 31, 2005 from children  $\leq 5$  years of age and 75% (142 of 190) of those from the same age group submitted between April 1, 2003 and March 31, 2004 belong to the seven serotypes which are included in the 7-valent conjugate vaccines. If the expected cross-protection against type 6A is included, coverage increases to 73% for 2004/05 and 80% for 2003/04.

In January, 2002, the National Advisory Committee on Immunization (NACI) published a statement recommending the use of this new vaccine for children less than 5 years of age, including infants. It was expected that its routine use would reduce the incidence of invasive disease in this age group. Our data suggest that this may be occurring. Over the past two years, we have received fewer invasive isolates from children  $\leq 5$  years than prior to the NACI statement (Figure 5). It is unlikely that this reduction is due to a change in interest by submitting agencies since the number of isolates received from the 6-16 year age group remained unchanged over this same time period, and the number of isolates received for the  $\geq 17$  year age group increased over the past three years (542 in 2002-03; 602 in 2003-04; 616 in 2004-05).

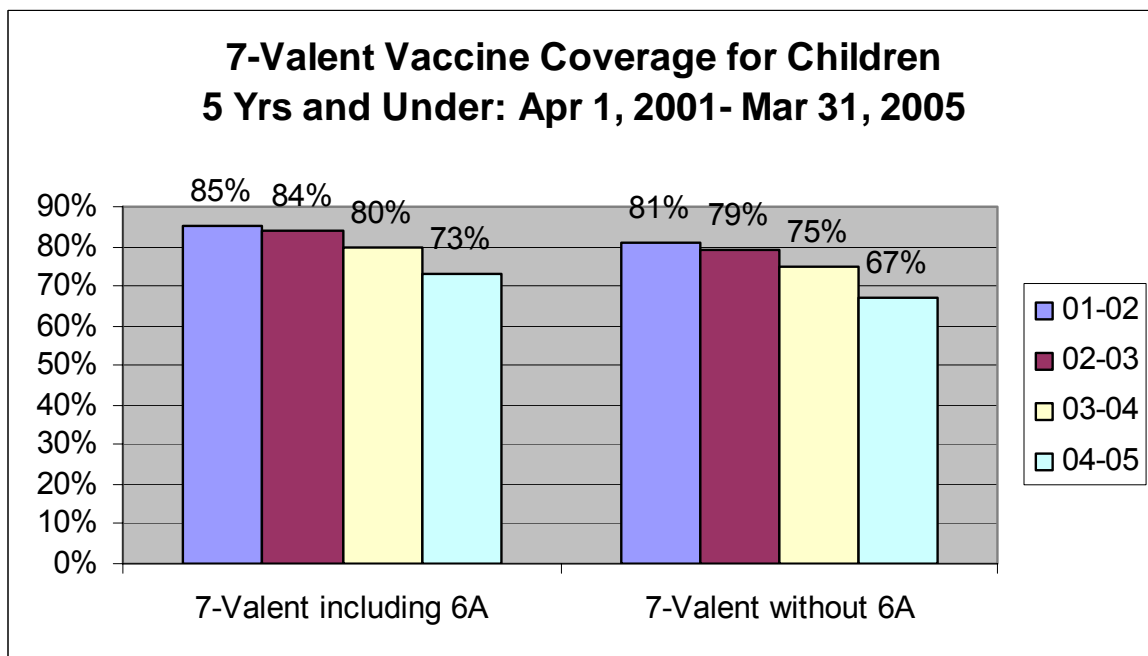


Figure 5. Invasive Pneumococcal Isolates from Children  $\leq 16$  yrs of Age



While our data support the expected reduction in invasive disease in young children, there is also a suggestion that there may be an increase in the proportion of disease caused by non-vaccine serotypes i.e. vaccine coverage may be reduced (Figure 6). Of the nine most prevalent serotypes listed in table 8, only type 19A is not covered by the conjugate vaccine (cross-coverage is expected for type 6A). It may be of concern that type 19A moved from eleventh to sixth in ranking over 2003/04, and that nine of the ten isolates received were from children of less than 2 years of age.

Figure 6. 7-Valent Conjugate Vaccine Coverage for Children  $\leq 5$  Years of Age





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Table 9. Serotype Distribution for Adults ( $\geq 17$  years) for April 1, 2004 – March 31, 2005  
(Comparative data for April 1, 2003 - March 31, 2004)

Serotype	17-64 years	$\geq 65$ years	Total $\geq 17$ years	
	# Cases	# Cases	# Cases	Rank
Type 4*	48 (53)	12 (10)	60 (63)	1 (2)
Type 14*	30 (42)	23 (26)	53 (68)	2 (1)
Type 3*	18 (28)	28 (26)	46 (54)	3-4 (3)
Type 9V*	26 (29)	20 (16)	46 (45)	3-4 (4)
Type 8*	36 (29)	8 (6)	44 (35)	5 (5)
Type 6B*	19 (16)	21 (13)	40 (29)	6 (7)
Type 23F*	12 (12)	20 (16)	32 (28)	7-8 (8-9)
Type 6A	14 (9)	18 (9)	32 (18)	7-8 (13)
Type 22F*	19 (13)	11 (15)	30 (28)	9 (8-9)
Type 1*	20 (16)	5 (1)	25 (17)	10 (14)
Type 19F*	10 (11)	10 (8)	20 (20 <sup>^</sup> )	11-12 (12)
Type 18C*	15 (19)	5 (11)	20 (30)	11-12 (6)
Type 9N*	12 (12)	5 (8)	17 (20)	13 (11)
Type 7F*	13 (18)	2 (4)	15 (22)	14 (10)
Type 11A*	7 (7)	6 (6)	13 (13)	15 (15)
Type 12F*	8 (9)	3 (1)	11 (10)	16 (17)
Type 19A	7 (11)	3 (8)	10 (12)	17 (16)
Other Types	64 (53)	38 (30)	102 (90)	
<b>Total No. Cases</b>	<b>378 (387)</b>	<b>238 (214)</b>	<b>616 (602<sup>^</sup>)</b>	

\* Serotypes included in the 23-valent vaccine

<sup>^</sup> Includes one adult case for which age was not available

Serotypes 3, 7F, 8, 9N, 11A and 12F were recovered from the adult population, but rarely from young ( $\leq 5$  yrs) children. The 23-valent vaccine (Pneumovax™) would provide coverage for 89% (546 of 616) of the invasive adult isolates submitted between April 1, 2004 and March 31, 2005 and 89% (536 of 602), of those submitted from April 1, 2003 – March 31, 2004 assuming cross-protection for types 6A and 6B.



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Similarly, the 23-valent vaccine, which is recommended for use in the  $\geq 65$  age group, would provide coverage for 87% (207 of 238) of the isolates recovered from those cases.

Thirty-three isolates from cerebrospinal fluid were submitted. These belonged to 19 different serotypes. Sixteen of the 33 cases had an accompanying blood isolate; the serotype of these isolates always matched the serotype of the CSF isolate. Four serotypes, 19F, 18C, 6B and 23F, accounted for 45% (15 of 33) of the cases.

Isolates that were received from cerebrospinal fluid were from patients of all age ranges; 15 (45%) were from patients  $\leq 16$  years of age including 7 from children  $\leq 2$  years; 5 of these cases were caused by serotypes included in the 7-valent conjugate vaccine. Of 18 isolates from the  $\geq 17$  year old age group, only 3 patients were  $\geq 65$ , the largest target group for the 23-valent conjugate vaccines. Overall 85% (28 of 33) of these isolates are covered by the 23-valent vaccine. Table 10 compares the serotype with the age range of the patients from whom pneumococci were isolated from CSF.

Table 10. Comparison of serotype & age range for pneumococci from CSF for Apr 1/04 - Mar 31/05.

Serotype	$\leq 2$ years	3-5 years	6-16 years	17-64 years	$\geq 65$ years	Total
Type 19F <sup>Δ+</sup>	2					5
Type 18C <sup>Δ+</sup>						4
Type 6B <sup>+</sup>				3		3
Type 23F <sup>Δ+</sup>						3
Type 3 <sup>Δ</sup>					2	2
Type 14 <sup>Δ+</sup>						2
Type 19A <sup>Δ</sup>						2
Type 8 <sup>Δ</sup>						
Type 9V <sup>Δ+</sup>						
Type 10A <sup>Δ</sup>						
Type 13						
Type 15C						
Type 16F <sup>Δ</sup>						
Type 17F <sup>Δ</sup>						
Type 20 <sup>Δ</sup>						
Type 23A						
Type 33F <sup>Δ</sup>						
Type 34						
Type 38						
<b>Total</b>	<b>7</b>	<b>5</b>	<b>3</b>	<b>15</b>	<b>3</b>	<b>33</b>

<sup>Δ</sup> Serotypes included in the 23-valent vaccine (Pneumovax™)

+ Serotypes included in the 7-valent conjugate vaccine (Prevnar™)



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### *Streptococcus pneumoniae* and Antibiotic Resistance

As of April 1, 2000 susceptibility testing of chloramphenicol, clindamycin, erythromycin, ofloxacin, trimethoprim-sulfamethoxazole and vancomycin was implemented for all invasive pneumococci submitted to the NCS for serotyping (excluding Quebec). In April, 2002, ofloxacin was replaced by levofloxacin as the representative quinolone in our testing panel. The minimum inhibitory concentration was determined by the Clinical and Laboratory Standards Institute (CLSI) recommended broth microdilution method.

Because isolates from Alberta account for almost half of this collection, antibiotic resistance data have been analyzed separately in Tables 11, 12 and 14. The proportion of intermediate and full resistance to seven antibiotics for Alberta compared with the rest of Canada (TROC) is presented in Table 11. These data are analyzed separately for children ( $\leq 16$  yrs) and adults ( $\geq 17$  yrs) in tables 12 and 15. The data presented in tables 12 and 15 exclude 5 isolates for which ages were not provided. As expected, all isolates were susceptible to vancomycin.

Table 11. Proportion (%) of Antibiotic Resistance by Region for Pneumococci;  
**Analysis for All Ages:** from April 1, 2004 - March 31, 2005  
 (Comparative data for April 1/03 - March 31/04)

Antibiotic	Interpretive Category	Alberta # of isolates = 316 (358)	TROC # of isolates = 476 (465)	Total for Canada # isolates = 792 (823)
Penicillin	Intermediate	7.9 (6.4)	7.6 (7.7)	7.7 (7.2)
	Resistant	1.3 (1.4)	4.6 (4.7)	3.3 (3.3)
	<b>Total</b>	<b>9.2 (7.8)</b>	<b>12.2 (12.5)</b>	<b>11.0 (10.5)</b>
Ceftriaxone	Intermediate	0 (0)	0.2 (0.4)	0.1 (0.2)
	Resistant	0 (0)	0.2 (0)	0.1 (0)
	<b>Total</b>	<b>0 (0)</b>	<b>0.4 (0.4)</b>	<b>0.2 (0.2)</b>
Chloramphenicol	Intermediate	0 (0)	0 (0)	0 (0)
	Resistant	0 (0.3)	0.8 (1.3)	0.5 (0.9)
	<b>Total</b>	<b>0 (0.3)</b>	<b>0.8 (1.3)</b>	<b>0.5 (0.9)</b>
Clindamycin	Intermediate	0.3 (0.3)	0 (0)	0.1 (0.1)
	Resistant	1.3 (2.8)	6.1 (2.2)	4.2 (2.4)
	<b>Total</b>	<b>1.6 (3.1)</b>	<b>6.1 (2.2)</b>	<b>4.3 (2.6)</b>
Erythromycin	Intermediate	0 (0)	0 (0)	0 (0)
	Resistant	7.9 (8.9)	13.9 (9.5)	11.5 (9.2)
	<b>Total</b>	<b>7.9 (8.9)</b>	<b>13.9 (9.5)</b>	<b>11.5 (9.2)</b>
Levofloxacin	Intermediate	0 (0)	0.2 (0)	0.1 (0)
	Resistant	0.3 (0.6)	1.3 (0)	0.9 (0.2)
	<b>Total</b>	<b>0.3 (0.6)</b>	<b>1.5 (0)</b>	<b>1.0 (0.2)</b>
Trimethoprim-Sulfamethoxazole	Intermediate	8.2 (9.8)	5.3 (5.8)	6.4 (7.5)
	Resistant	7.9 (6.7)	13.9 (13.8)	11.5 (10.7)
	<b>Total</b>	<b>16.1 (16.5)</b>	<b>19.1 (19.6)</b>	<b>17.9 (18.2)</b>



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Table 12. Proportion (%) of Antibiotic Resistance by Region for Pneumococci;  
**For children (≤16 yrs);** from April 1, 2004 – March 31, 2005  
 (comparative data for April 1/03 - March 31/04)

Antibiotic	Interpretive Category	Alberta # of isolates = 59 (78)	TROC # of isolates = 112 (143)	Total for Canada # isolates = 171 (221)
<b>Penicillin</b>	Intermediate Resistant	11.9 (7.7) 0 (0)	9.8 (7.0) 11.6 (7.7)	10.5 (7.2) 7.6 (5.0)
	<b>Total</b>	<b>11.9 (7.7)</b>	<b>21.4 (14.7)</b>	<b>18.1 (12.2)</b>
	<b>Ceftriaxone</b>	0(0) 0(0)	0 (1.4) 0.9 (0)	0 (0.9) 0.6 (0)
	<b>Total</b>	<b>0(0)</b>	<b>0.9 (1.4)</b>	<b>0.6 (0.9)</b>
<b>Chloramphenicol</b>	Intermediate Resistant	0(0) 0(0)	0(0) 0.9 (2.1)	0(0) 0.6 (1.4)
	<b>Total</b>	<b>0(0)</b>	<b>0.9 (2.1)</b>	<b>0.6 (1.4)</b>
	<b>Clindamycin</b>	Intermediate Resistant	0(0) 5.1 (1.3)	0(0) 11.6 (4.9)
<b>Total</b>		<b>5.1 (1.3)</b>	<b>11.6 (4.9)</b>	<b>9.4 (3.6)</b>
<b>Erythromycin</b>		Intermediate Resistant	0(0) 11.9 (7.7)	0(0) 21.4 (13.3)
	<b>Total</b>	<b>11.9 (7.7)</b>	<b>21.4 (13.3)</b>	<b>18.1 (11.3)</b>
	<b>Levofloxacin</b>	Intermediate Resistant	0(0) 0(0)	0(0) 0(0)
<b>Total</b>		<b>0(0)</b>	<b>0(0)</b>	<b>0(0)</b>
<b>Trimethoprim-Sulfamethoxazole</b>		Intermediate Resistant	8.5 (12.8) 6.8 (7.7)	8.9 (7.7) 21.4 (18.2)
	<b>Total</b>	<b>15.3 (20.5)</b>	<b>30.4 (25.9)</b>	<b>25.1 (24.0)</b>

In January, 2002, the NCCLS modified the interpretive standard for pneumococci when testing ceftriaxone, cefotaxime and cefepime (Document M100-S12). The MIC breakpoints for these drugs for pneumococci isolated from patients with meningitis are now interpreted differently from pneumococci isolated from non-meningitis cases. The new interpretation for all three antibiotics is provided in Table 13.

Table 13. Jan, 2002 NCCLS ceftriaxone, cefotaxime & cefepime interpretive standards for *S. pneumoniae*

	Susceptible MIC breakpoint	Intermediate MIC breakpoint	Resistant MIC breakpoint
<b>Meningitis</b>	≤0.5 µg/ml	1.0 µg/ml	≥2.0 µg/ml
<b>Nonmeningitis</b>	≤1.0 µg/ml	2.0 µg/ml	≥4.0 µg/ml

Because the interpretation of the ceftriaxone MIC is dependent upon whether or not the patient has meningitis, a breakdown of that MIC interpretation by specimen source is provided in Tables 14 and 16.



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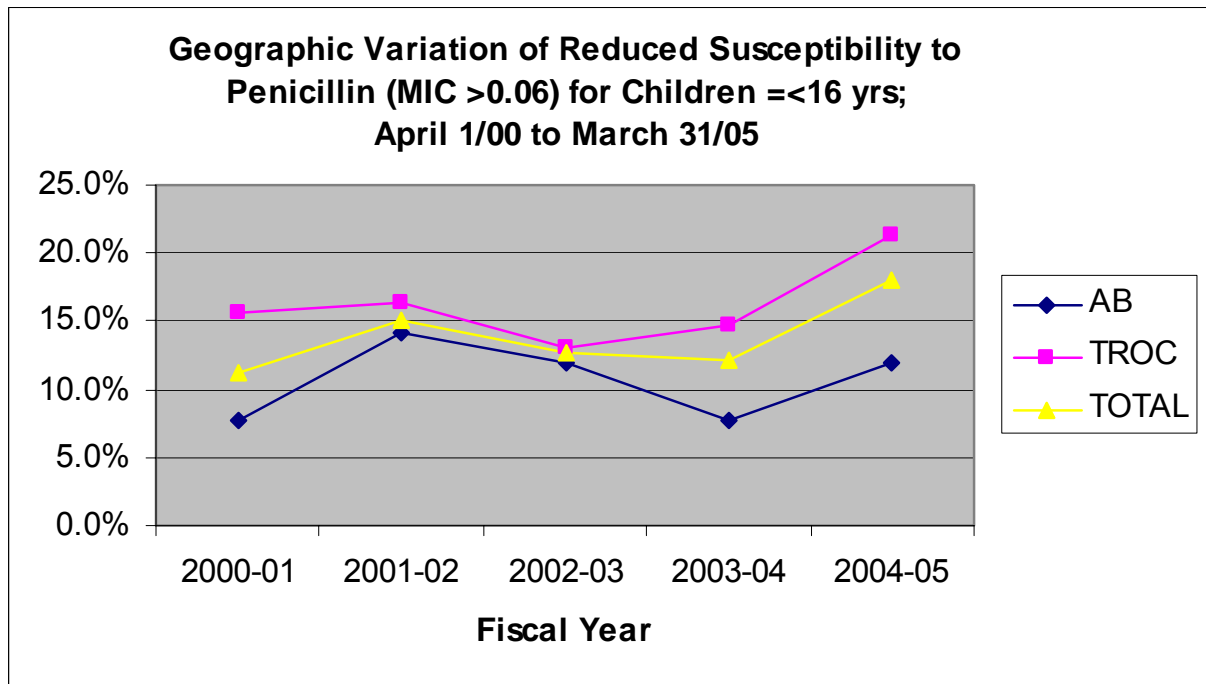
Reporting Period: April 1, 2004 to March 31, 2005.

Table 14. **Ceftriaxone interpretation** for pneumococci from **children ( $\leq 16$  yrs)** (April 1/04 - March 31/05) by specimen source according to NCCLS Document M100-S12, January, 2002

Specimen Source	ALBERTA			TROC			TOTAL		
	# Isolates	Inter-mediate	Resis-tant	# Isolates	Inter-mediate	Resis-tant	# Isolates	Inter-mediate	Resis-tant
Blood/nonmeningitis	51	0	0	105	0	0	156	0	0
CSF/meningitis	8	0	0	7	0	1	15	1	0
<b>Total</b>	<b>59</b>	<b>0</b>	<b>0</b>	<b>112</b>	<b>0</b>	<b>1</b>	<b>171</b>	<b>1</b>	<b>0</b>

During 04-05, our data show striking increases in resistance to penicillin, erythromycin and clindamycin in children across Canada. The proportion of resistance (includes intermediate and resistant categories) to these antibiotics over the past five years is presented in figures 7, 8 and 9.

Figure 7. Reduced Penicillin Susceptibility for Pneumococci Isolated from Children from Alberta and from the Rest of Canada (TROC), 2000-2005





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Figure 8. Erythromycin Resistance for Pneumococci Isolated from Children from Alberta and from the Rest of Canada (TROC), 2000-2005

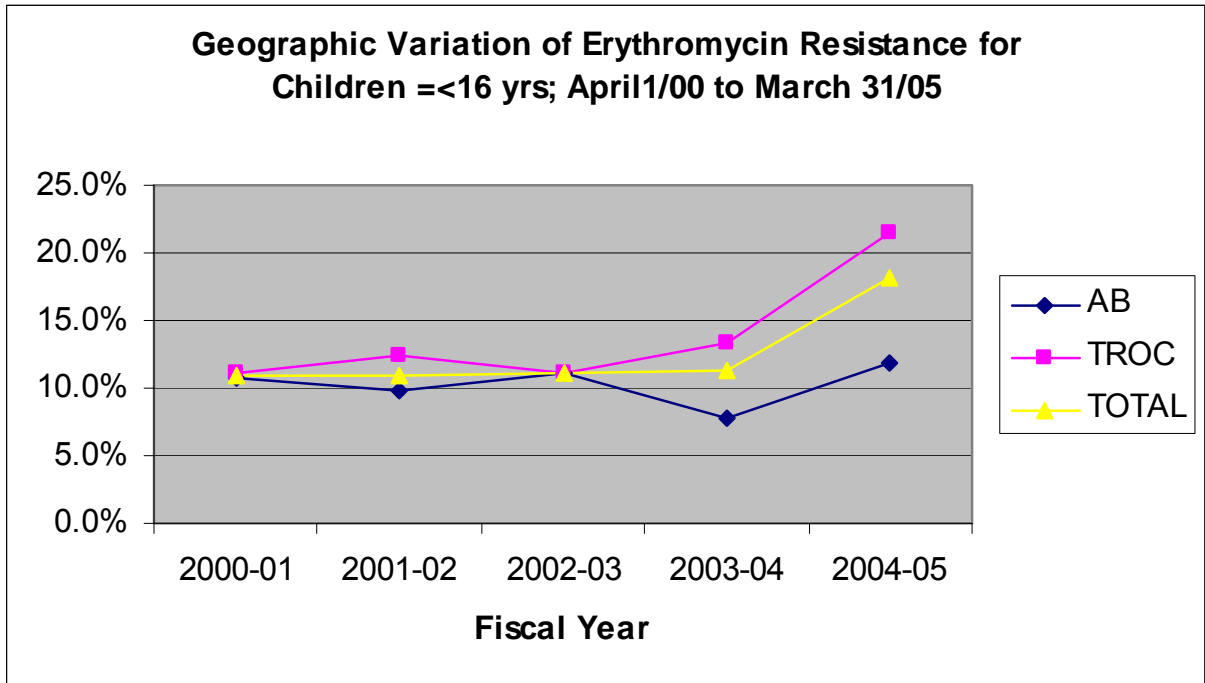
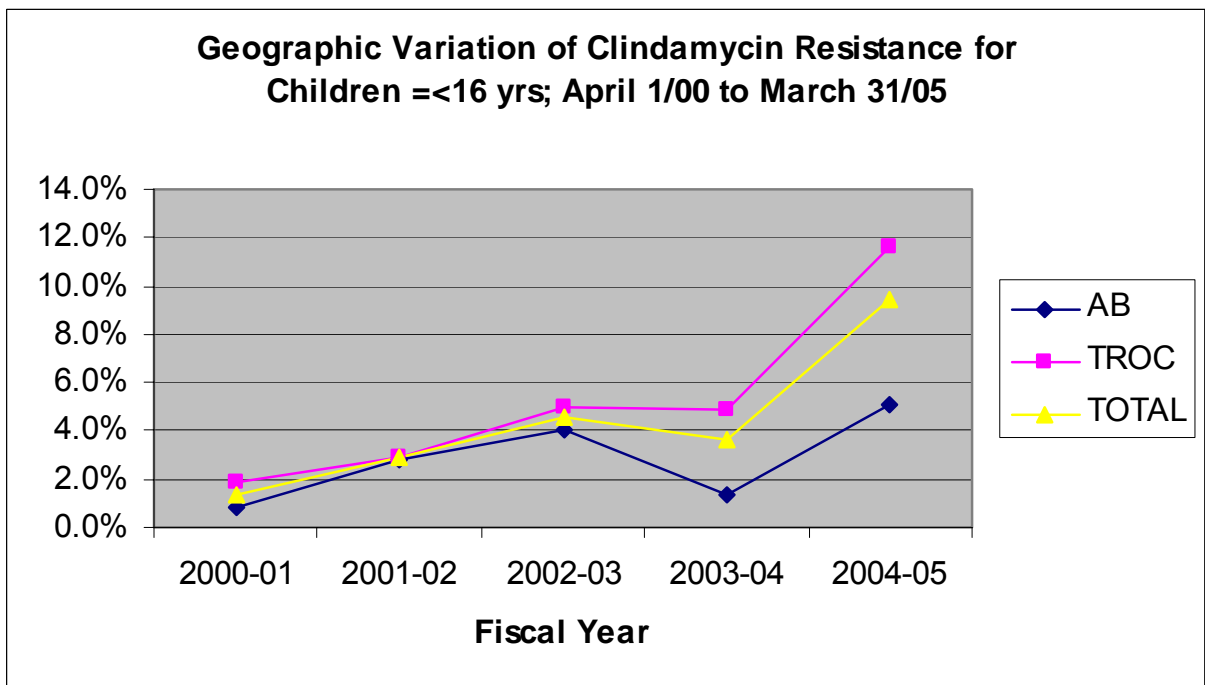


Figure 9. Clindamycin Resistance for Pneumococci Isolated from Children from Alberta and from the Rest of Canada (TROC), 2000-2005





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Table 15. Proportion (%) of Antibiotic Resistance by Region for Pneumococci;  
**For adults (≥17 yrs);** from April 1, 2004 – March 31, 2005  
 (comparative data for April 1/03 - March 31/04)

Antibiotic	Interpretive Category	Alberta # of isolates = 257 (280)	TROC # of isolates = 359 (322)	Total for Canada # isolates = 616 (602)
Penicillin	Intermediate	7.0 (6.1)	7.0 (8.1)	7.0 (7.1)
	Resistant	1.6 (1.8)	2.5 (3.4)	2.1 (2.7)
	<b>Total</b>	<b>8.6 (7.9)</b>	<b>9.5 (11.5)</b>	<b>9.1 (9.8)</b>
Ceftriaxone	Intermediate	0 (0)	0.3 (0)	0.2 (0)
	Resistant	0 (0)	0 (0)	0 (0)
	<b>Total</b>	<b>0 (0)</b>	<b>0.3 (0)</b>	<b>0.2 (0)</b>
Chloramphenicol	Intermediate	0 (0)	0 (0)	0 (0)
	Resistant	0 (0.4)	0.8 (0.9)	0.5 (0.7)
	<b>Total</b>	<b>0 (0.4)</b>	<b>0.8 (0.9)</b>	<b>0.5 (0.7)</b>
Clindamycin	Intermediate	0.4 (0.4)	0 (0)	0.2 (0.2)
	Resistant	0.4 (3.2)	4.5 (0.9)	2.8 (2.0)
	<b>Total</b>	<b>0.8 (3.6)</b>	<b>4.5 (0.9)</b>	<b>2.9 (2.2)</b>
Erythromycin	Intermediate	0 (0)	0 (0)	0 (0.0)
	Resistant	7.0 (9.3)	11.7 (7.8)	9.7 (8.5)
	<b>Total</b>	<b>7.0 (9.3)</b>	<b>11.7 (7.8)</b>	<b>9.7 (8.5)</b>
Levofloxacin	Intermediate	0 (0)	0.3 (0)	0.2 (0)
	Resistant	0.4 (0.7)	1.7 (0)	1.1 (0.3)
	<b>Total</b>	<b>0.4 (0.7)</b>	<b>2.0 (0)</b>	<b>1.3 (0.3)</b>
Trimethoprim-Sulfamethoxazole	Intermediate	8.2 (8.9)	4.2 (5.0)	5.8 (6.8)
	Resistant	8.2 (6.1)	11.7 (11.8)	10.2 (9.1)
	<b>Total</b>	<b>16.3 (15.0)</b>	<b>15.9 (16.8)</b>	<b>16.0 (15.9)</b>

Table 16. **Ceftriaxone interpretation** for pneumococci from **adults (≥17 yrs)** (April 1/04 - March 31/05)  
 by specimen source according to NCCLS Document M100-S12, January, 2002

Specimen Source	ALBERTA			TROC			TOTAL		
	# Isolates	Inter-mediate	Resis-tant	# Isolates	Inter-mediate	Resis-tant	# Isolates	Inter-mediate	Resis-tant
Blood/nonmeningitis	249	0	0	349	1	0	598	1	0
CSF/meningitis	8	0	0	10	0	0	18	0	0
<b>Total</b>	<b>257</b>	<b>0</b>	<b>0</b>	<b>359</b>	<b>1</b>	<b>0</b>	<b>616</b>	<b>1</b>	<b>0</b>



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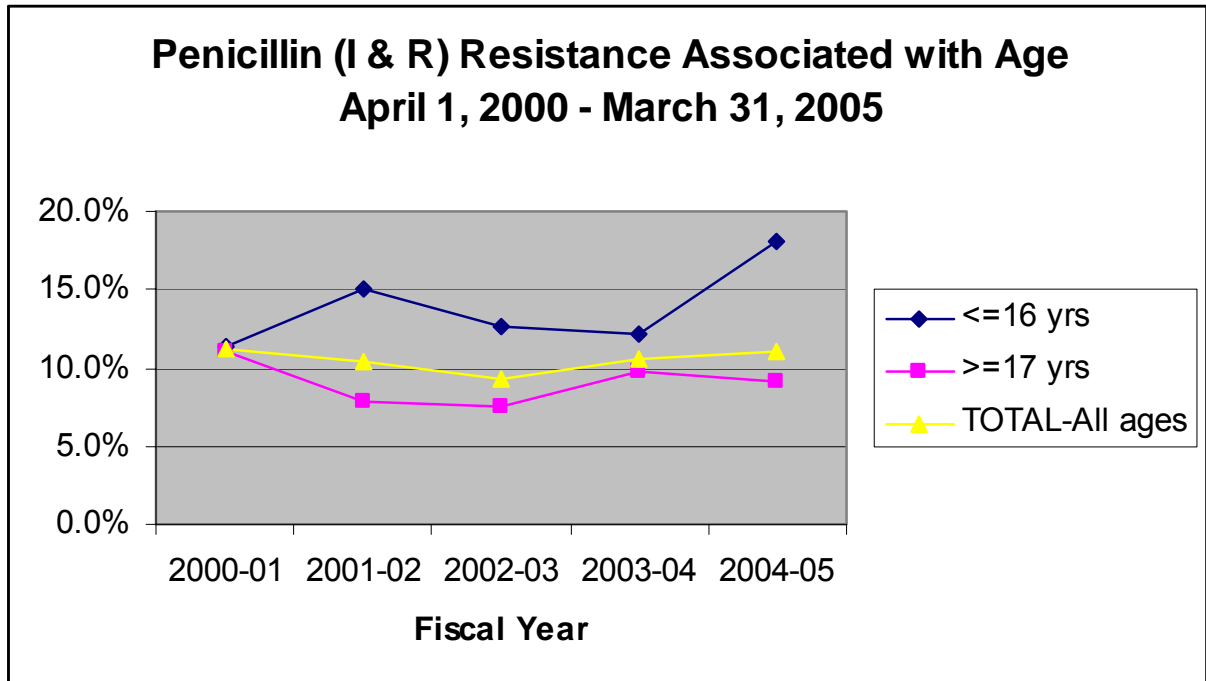
Unlike children, the overall resistance rates for adults have remained relatively stable over the past year, but there is evidence of some geographic variation. In Alberta, resistance to erythromycin and clindamycin decreased, however substantial increases for both antibiotics was observed for isolates submitted from the rest of Canada.

Similarly levofloxacin resistance was more commonly observed for pneumococci from other parts of Canada. In the previous fiscal year (2003-04) we did not receive any levofloxacin-resistant isolates from outside the province of Alberta, but over the past year (2004-05), 7 of the 8 isolates submitted were received from other parts of Canada. Levofloxacin resistance is still relatively uncommon (1.3%), at least for invasive pneumococci, and is unrelated to penicillin resistance (6 of 8 isolates were susceptible to penicillin). All isolates were recovered from adults, and belonged to five different serotypes.

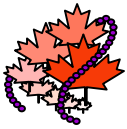
### General observations of antibiotic resistance for all ages

The age related differences in penicillin resistance observed especially over the past year are remarkable. Figure 10 compares these rates over the past five years.

Figure 10. Reduced Susceptibility to Penicillin for Adults and Children, 2000 - 2005



Reduced susceptibility to penicillin was detected in 87 isolates belonging to 10 different serotypes. Ninety-one percent of these (79 of 87) are covered by the 23-valent vaccine if one assumes cross-protection for serotype 6A. Thirty percent (26 of 87) of these strains are fully resistant to penicillin (MIC  $\geq 2.0$   $\mu\text{g/ml}$ ). Reduced susceptibility to penicillin may be expected for type 19A. Of 20 type 19A isolates tested in 04/05, 13 (65%) showed either intermediate (MIC 0.12-1.0  $\mu\text{g/ml}$ ) or full resistance. An increased likelihood of penicillin resistance is also associated with type 9V. Fifty-nine percent (36 of 61) of the type 9V isolates tested showed some level of resistance to penicillin; 20 were intermediate and 16 were resistant.

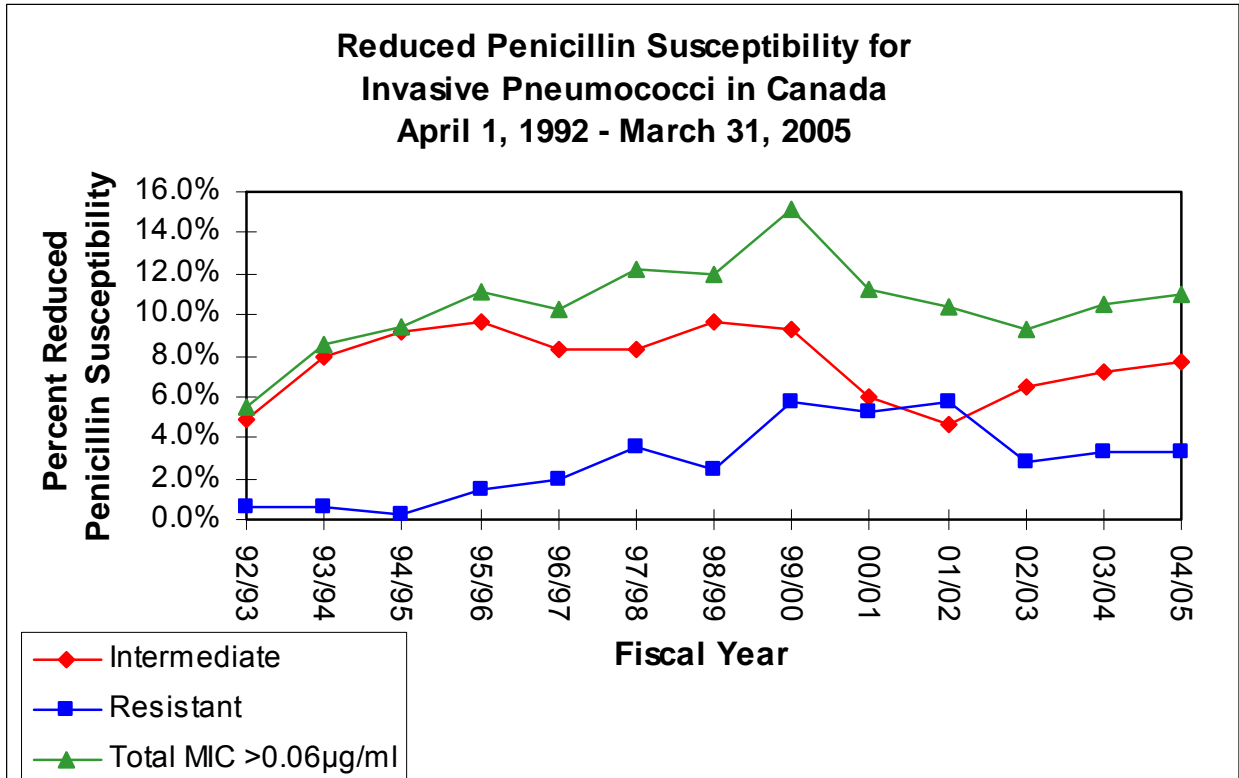


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The steadily decreasing rates of penicillin resistance that we have enjoyed since 2000 were halted in 2002-03 (Figure 11). Over the past two years the overall rates of resistance show slight increases, most of which can be attributed to isolates from children (Figure 10)

Figure 11. Reduced Penicillin Susceptibility in Canada; 1992 - 2005



As observed in previous years, resistance to erythromycin and to trimethoprim-sulfamethoxazole frequently occurred in the absence of reduced susceptibility to penicillin. Sixty percent (55 of 91) of the erythromycin-resistant pneumococci and 56% (79 of 142) of the trimethoprim-sulfamethoxazole intermediate or resistant pneumococci were susceptible to penicillin.

Erythromycin resistance was encountered most frequently for serotypes 19A (45%), 14 (38%), 12F (36%) and 6B (25%). All but 12F, are serotypes that are associated with invasive disease in children as well as adults. Erythromycin resistance occurred with (37%) and without (63%) cross-resistance to clindamycin. Inducible resistance to clindamycin was not observed.

There was one predominant resistance pattern observed for the erythromycin-resistant type 14 isolates; 77% (24 of 31) were susceptible to penicillin and clindamycin, and resistant only to erythromycin. This pattern was observed for isolates submitted from all Western provinces and from all ages. This may represent the proliferation of a new clone, and will require further investigation.

We have defined multiple resistance as intermediate or full resistance to three different classes of antibiotics. Thirty-nine of 792 isolates (4.9%) were multiply resistant; 33 (85%) of these had reduced susceptibility to penicillin. This compares to a multiple resistance rate of 3.9% in 2003-04. Multiple resistance was demonstrated in serotypes 6B (8 isolates), 19A (8 isolates), 9V (6 isolates), 14 (4 isolates), 23F (4 isolates), 19F (3 isolates), 6A (2 isolates), and one isolate each for types 9N, 15A, 20 and 23A.



## National Centre for Streptococcus - Canada

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### 4.0. Quality Indicators

#### 4.1 Description of Quality System and Laboratory Accreditation

The National Centre for Streptococcus operates as part of the Alberta Provincial Laboratory for Public Health. As such the Centre is fully accredited by the College of Physicians and Surgeons of Alberta (required) and by the College of American Pathologists (voluntary). Over the past two years the Provincial Laboratory, including the National Centre for Streptococcus, has been developing a comprehensive Quality System that guides all technical and administrative activities. We are currently in the process of implementing this System.

#### 4.2 Turn around times

Test	Average turn-around-time in days (April 1, 2004 – March 31, 2005)
Group A Serotyping	25 days
Group B Serotyping	9 days
<i>Streptococcus pneumoniae</i> serotyping	12 days
Identification of “ <i>Streptococcus</i> -like” organisms	21 days

#### 4.3 External Quality Assurance

*Streptococcus pneumoniae* Serotyping and Susceptibility testing - The NCS continues to participate in a collaborative Quality Control program involving the Laboratoire de Santé Publique du Québec and the Arctic Investigation Program laboratory in Anchorage, Alaska. This external quality assurance initiative supports the International Circumpolar Surveillance (ICS) program that now includes the northern regions of Canada, Alaska USA, Iceland, Greenland, Norway and Finland. In September, 2004, this program was expanded to include the Statens Serum Institut in Copenhagen, Denmark.

Over the past year four panels were distributed, one from each of the participating Centres. Correlation for serotyping data for all four labs was 90-100%. In total, 28 pneumococcal strains were distributed. The serotyping discrepancies resulted from three strains; one for which two different factors were reported (15B versus 15C), one that was nontypable and one for which antisera cross-reactivity was observed (25 versus 38). The four laboratories achieved 90-100% correlation with MIC values within +/- one log<sub>2</sub> dilution for nine antibiotics that are routinely tested. Some variation in reported MIC values was due to differences in methodology (Etest™ versus broth microdilution).

The NCS continues to serve as a resource for both education and Quality Assurance for the SIREVA Project in Latin America. Consistent with the model established in 1999, we have worked primarily with three Quality Control Centres (Mexico, Colombia and Brazil), for which we coordinate an external quality control program with semiannual distributions of pneumococci for serotyping and MIC testing. In 2005, the number of Quality Control Centres was reduced to two (Columbia and Brazil). Our role remains unchanged.



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In 2004, the NCS was asked to provide Quality Control support for the pneumococcal serotyping program that was implemented at the Mount Sinai Hospital in Toronto, Ontario. That centre forwards pneumococci for which they are unable to assign a serotype due to their limited antisera inventory, and also a random selection of typed strains for verification.

As a member of the World Health Organization Laboratory Working Group on Group A Streptococci, the NCS was invited to participate in an external quality assessment (EQA) activity targeted at the characterization of Group A streptococci. This 2004 EQA initiative was coordinated by the Central Public Health Laboratory, Colindale, England through the strep-EURO project, and involved the participation of 18 laboratories world-wide. Twenty strains of GAS were distributed for serotyping, and 14 strains were distributed for characterization by pulsed field gel electrophoresis (PFGE). The NCS successfully classified all 20 strains to the level for which antisera were available. (The addition of *emm* sequencing to our testing menu will enhance our ability to fully classify GAS in the near future.) The PFGE data were analyzed both for quality and for correct determination of relatedness. We are proud to report that, in addition to reporting the correct results for strain relatedness, the quality of the NCS gels was ranked first amongst the 13 laboratories that submitted PFGE typing results.

### 4.4 Others

Due to the specialized nature of the testing performed at the NCS, and the limited availability of External Proficiency Testing programs targeted at these assays, we supplement our External Quality Assurance program with internal Quality Assurance testing panels. This additional tool supports the regular assessment of our routine testing processes (group A serotyping, group B serotyping, *S. pneumoniae* serotyping and antibiotic susceptibility testing), and also provides the opportunity to assess the technical competency of all of our technologists on an annual basis.

### 5.0 Conclusion

We believe that NCS has performed well over the past year. We have been active in delivering mandated service work, outbreak investigation, Quality Assurance work, teaching and research and in disseminating our findings in the form of publications. In addition, new assays are being actively explored or initiated to provide as up to date a service as possible

At the recent Goals and Objectives Consensus Conference for Vaccine Preventable Diseases in Canada – 2005 (GOCC-VPD), June 13, 2005, Quebec City, Quebec, the point was made that provinces must submit *S. pneumoniae* isolates to the NCS for serotyping or how else will provinces know how effective vaccine programs such as the protein-conjugate vaccine program in children is working. The NCS fully supports this ideal. We would like to have the ability to serotype all invasive *S. pneumoniae* in Canada but due to current funding levels, this is not realistic. The NCS has begun to try and address this issue by exploring the implementation of new *S. pneumoniae* serotyping assays that maybe more cost effective, however, this will only cover a small portion of the anticipated increase in costs should these isolates be submitted in the increased numbers proposed.

In conclusion, the NCS has and continues to function well as a national reference laboratory, active in many areas including service work, outbreak investigation, research and education, actively collaborating with partners at local, national and international levels. We are proud of what we have accomplished and hope to continue to provide this reference service for Canada. The upcoming year presents many challenges that we are already addressing through the implementation of new assays and new personnel.