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# National Surveillance of Antimicrobial Susceptibilities of *Neisseria gonorrhoeae* Summary Report 2005-2008

Streptococcus and STI Unit  
Bacteriology and Enteric Diseases Program  
National Microbiology Laboratory  
Public Health Agency of Canada



Public Health  
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Canada

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## Executive Summary

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- Gonorrhea is a major public health concern in Canada and rates of gonorrhea have been rising since 1997.
- Effective antibiotic treatment is a vital part of gonococcal infection control and the impact of antimicrobial resistance in *Neisseria gonorrhoeae* is of foremost concern. Over time, *N. gonorrhoeae* has acquired resistance to many antibiotics such as penicillin, tetracycline, erythromycin and ciprofloxacin.
- In Canada, ciprofloxacin resistance in *N. gonorrhoeae* has increased to a level where ciprofloxacin is no longer an option for first-line treatment. The number of ciprofloxacin resistant *N. gonorrhoeae* isolates out of all isolates tested increased from 59 in 2000 (1.3%) to 858 in 2008 (22.0%).
- The current Canadian treatment guidelines recommend a single dose treatment of 125 mg of intramuscular ceftriaxone or a single dose of 400 mg of oral cefixime for the treatment of gonorrhea. Oral cephalosporin treatment failures and in vitro reduced susceptibilities have been reported from Asia and Australia. A WHO/CDC Global Consultation on the strategic response to the emergence of cephalosporin resistance in *N. gonorrhoeae* took place in April 2010.
- In Canada, the MICs of the 3rd generation cephalosporins have been increasing over time. There has been a shift in the mode of the MICs of both ceftriaxone and cefixime from 0.016 µg/ml in 2000 to 0.032 µg/ml in 2008. Three isolates (one each in 2004, 2007 and 2008) were identified with a cefixime MIC equal to 0.5 µg/ml, classified as reduced-susceptibility.
- Between 2000 and 2008, there was an increasing prevalence of isolates that were classified as Chromosomal Mediated Resistant *Neisseria gonorrhoeae*, while the plasmid-mediated resistant strains all had a declining trend.
- One of the challenges faced by the laboratories that perform surveillance of antimicrobial resistance of *N. gonorrhoeae* is the shift from the use of cultures (required for antimicrobial susceptibility testing) to the Nucleic Acid Amplification Test (NAAT) for the diagnosis of gonorrhea.
- In 2010, a sentinel surveillance system for *N. gonorrhoeae* is being initiated in Canada to collect integrated epidemiological and laboratory information. The objectives of surveillance would be to determine the prevalence and trends of antimicrobial resistance in *N. gonorrhoeae* in order to develop population-level evidence-based public health interventions; to characterize both antimicrobial susceptible and resistant strains of gonorrhea in order to understand the spread of strains in Canada and to inform Canadian STI management guidelines.

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## Introduction

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*Neisseria gonorrhoeae*, the causative agent of gonorrhea is the second most commonly reported bacterial sexually transmitted infection in Canada with 12,723 cases reported in 2008 (1). The national rate of gonorrhea is on the rise and has increased by 156.3% from a rate of 14.9 per 100,000 in 1997 to 38.2 per 100,000 in 2008 (1) (Figure 1). The treatment and control of gonorrhea is complicated by the ability of *N. gonorrhoeae* to evolve and develop resistance to many of the antibiotics used to treat it including penicillins, tetracyclines, macrolides and quinolones (2,3). A further challenge is the shift from the use of culture to Nucleic Acid Amplification Test (NAAT) for the diagnosis of gonorrhea, limiting the availability of cultures which are required for antimicrobial susceptibility testing. The National Microbiology Laboratory (NML) has been monitoring the antimicrobial susceptibilities of *N. gonorrhoeae* since 1985 and these results contribute to the Canadian Guidelines on Sexually Transmitted Infections for treatment of gonorrhea.

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## Methods

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*N. gonorrhoeae* strains were submitted to the NML from sexually transmitted infection clinics and provincial public health laboratories for antimicrobial susceptibility testing (Table 1).

**Table 1. Number of *Neisseria gonorrhoeae* isolates tested from each province, 2000-2008**

Province	2000	2001	2002	2003	2004	2005	2006	2007	2008	Total
British Columbia	161	101	207	115	146	117	86	95	104	1132
Alberta	52	36	26	34	57	50	96	189	55	595
Saskatchewan	7	5	36	17	42	49	39	34	1	230
Manitoba	35	35	39	45	26	54	53	2	3	292
Ontario	680	805	482	437	442	452	855	705	539	5397
Québec	221	181	177	138	137	179	392	391	230	2046
New Brunswick	2	1	1	1	2	2	2	8	5	24
Nova Scotia	43	69	192	4	1	1	0	0	0	310
Newfoundland	3	0	3	9	0	1	9	14	10	49
Prince Edward Island	0	0	0	0	2	0	0	0	0	2
Yukon Territories	2	1	0	0	0	0	0	0	0	3
Total isolates tested at NML	1206	1234	1163	800	855	905	1532	1438	947	10080
Total isolates resistant to at least one antibiotic	1092	1100	926	703	802	850	1472	1395	929	9269
Total number of isolates tested in each province	4458	4591	4465	4235	4018	3619	4201	4275	3907	37769
Total cases reported in Canada	6189	6756	7365	8241	9317	9199	11334	11873	12723	82997

Isolates are submitted to NML when the provincial laboratories identify resistance to at least one antibiotic or if the provincial laboratories do not do any antimicrobial susceptibility testing. Submission of isolates is voluntary and not standardized across the country. The overall interpretation of the results is difficult due to the limitations related to the isolates available for testing. Therefore, the total number of isolates cultured in each jurisdiction was used as the denominator to calculate resistance proportion. To standardize the susceptibility testing between laboratories, proficiency surveys are conducted two times a year. Minimum inhibitory concentration, MIC (the minimum concentration of antibiotic which will inhibit the growth of the organism) was performed using agar dilution and interpretations were based on the criteria of the Clinical Laboratory Standards Institute (Table 2). Resistance characterization definitions are provided in Table 3. All isolates were also characterized by auxotyping, plasmid profiles analysis, production of  $\beta$ -lactamase and presence of *tetM* determinant.

**Table 2. *Neisseria gonorrhoeae* Antimicrobial Resistance Criteria**

MIC Interpretative standards used to determine the ranges of the antibiotic concentrations in media for testing *N. gonorrhoeae* as recommended by the Clinical and Laboratory Standards Institute (4) except for erythromycin (5) and azithromycin (6, 7).

Antibiotic	MIC Interpretive Standard (mg/L)				Sources of Antibiotics
	S	I	R	RS	
Penicillin	≤ 0.06	0.12- 1.0	≥ 2.0		Sigma #P 7794
Tetracycline	≤ 0.25	0.5 - 1.0	≥ 2.0		Sigma #T 3383
Erythromycin	≤ 1.0		≥ 2.0		Sigma #E 5389
Spectinomycin	≤ 32.0	64.0	≥ 128.0		Sigma #S 9007
Ceftriaxone	≤ 0.25			> 0.25	Sigma #C 5793
Ciprofloxacin	≤ 0.06	0.12 - 0.5	≥ 1.0		Bayer Health Care
Cefixime	≤ 0.25			> 0.25	Wyeth - Ayerst
Azithromycin	≤ 1.0		≥ 2.0		Pfizer

S= Susceptible, I=Intermediate, R= Resistant, RS= Reduced susceptibility

**Table 3. *Neisseria gonorrhoeae* Antimicrobial Resistance Characterization Definitions**

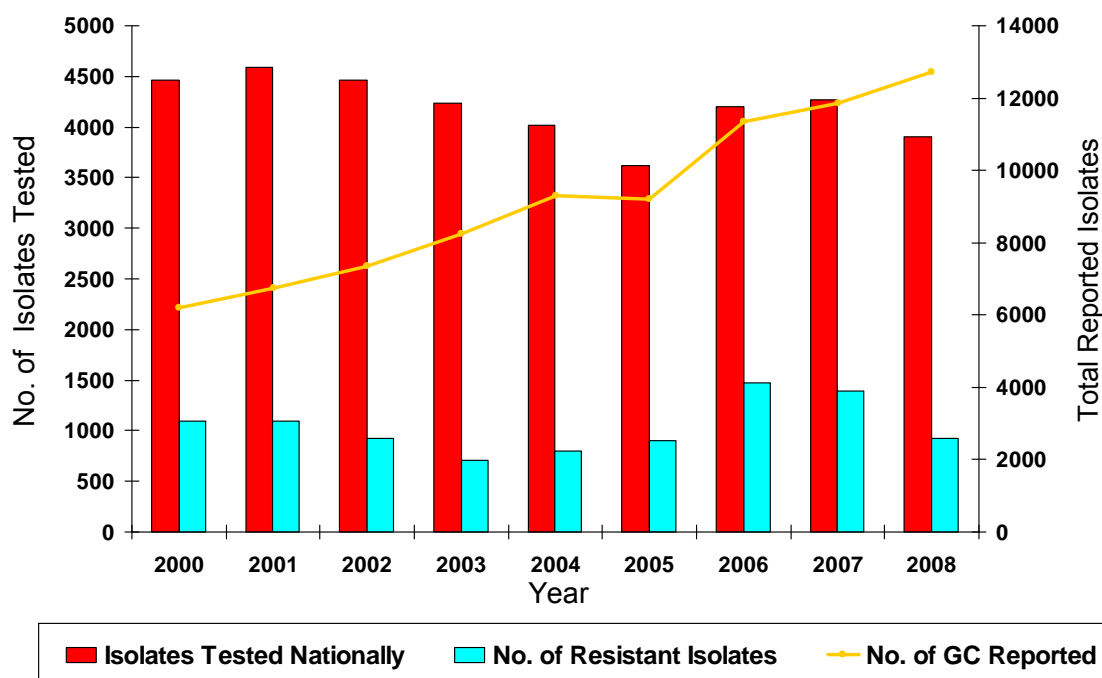
<b>Characterization</b>		<b>Definition</b>
PPNG	Penicillinase Producing <i>Neisseria gonorrhoeae</i>	Pen MIC $\geq$ 2.0 mg/L, $\beta$ -lactamase positive, $\beta$ -lactamase plasmid (3.05, 3.2 or 4.5 Mdal plasmid)
TRNG	Tetracycline Resistant <i>Neisseria gonorrhoeae</i>	Tet MIC $\geq$ 16.0 mg/L, 25.2 Mdal plasmid, TetM PCR positive
CMRNG	Chromosomal Mediated Resistant <i>Neisseria gonorrhoeae</i>	Pen MIC $\geq$ 2.0 mg/L, Tet MIC $\geq$ 2.0 mg/L but $\leq$ 8.0 mg/L, and Ery MIC $\geq$ 2.0 mg/L
Probable CMRNG	Probable Chromosomal Mediated Resistant <i>Neisseria gonorrhoeae</i>	One of the MIC values of Pen, Tet, Ery = 1 mg/L, the other two $\geq$ 2.0 mg/L
PenR	Penicillin Resistant <i>Neisseria gonorrhoeae</i>	Pen MIC $\geq$ 2.0 mg/L, $\beta$ -lactamase negative
TetR	Tetracycline Resistant <i>Neisseria gonorrhoeae</i>	Tet MIC $\geq$ 2.0 mg/L but $\leq$ 8.0 mg/L
EryR	Erythromycin Resistant <i>Neisseria gonorrhoeae</i>	Ery MIC $\geq$ 2.0 mg/L
CipR	Ciprofloxacin Resistant <i>Neisseria gonorrhoeae</i>	Cip MIC $\geq$ 1.0 mg/L
AzR	Azithromycin Resistant <i>Neisseria gonorrhoeae</i>	Azi MIC $\geq$ 2.0 mg/L
SpecR	Spectinomycin Resistant <i>Neisseria gonorrhoeae</i>	Spec R $\geq$ 128 mg/L
CxRS	Ceftriaxone Reduced Susceptibility <i>Neisseria gonorrhoeae</i>	Cx MIC $\geq$ 0.5 mg/L
CeRS	Cefixime Reduced Susceptibility <i>Neisseria gonorrhoeae</i>	Ce MIC $\geq$ 0.5 mg/L



## Results and Discussion

Of the 10,080 isolates tested at the NML between 2000 and 2008, 9,269 isolates (91.9%) were found to be resistant to at least one of the following antibiotics: penicillin, tetracycline, ciprofloxacin, azithromycin, and erythromycin. A total of 723 (7.1%) isolates were found to be susceptible to all of these antibiotics. In 2008, 23.8% (929 of 3907) of all *N. gonorrhoeae* isolates tested were found to be resistant to at least one antibiotic (Figure 1). The characterization of each resistant *N. gonorrhoeae* isolate is provided in Table 4.

**Figure 1. *Neisseria gonorrhoeae* Isolates in Canada, 2000 to 2008**

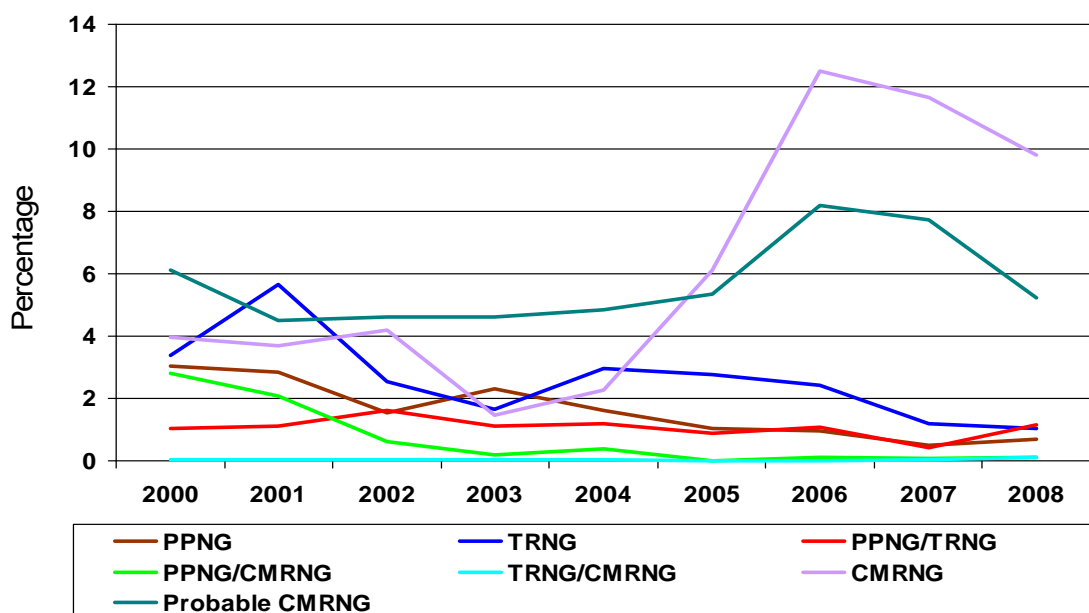


**Table 4. Characterization of all *Neisseria gonorrhoeae* isolates submitted to National Microbiology Laboratory, 2000-2008**

Characterization		2000	2001	2002	2002	2004	2005	2006	2007	2008	Totals
Plasmid Mediated Resistances	PPNG	21	43	44	73	41	17	26	12	10	287
	PPNG/CipR	2	11	6	5	3	10	3	3	13	56
	PPNG/CipR/EryR	1	1	2	0	0	1	0	0	0	5
	PPNG/CipR/TetR	3	3	3	3	7	3	2	0	0	24
	PPNG/TetR	108	66	14	16	12	6	10	6	1	239
	PPNG/EryR	0	6	0	1	2	0	0	1	3	13
	PPNG/CMRNG	125	96	27	8	15	0	5	3	0	279
	PPNG/CMRNG/CipR	0	0	0	0	0	0	0	0	5	5
	PPNG/TRNG	33	37	48	26	24	8	10	4	10	200
	PPNG/TRNG/CipR	7	7	20	17	22	23	31	9	31	167
	PPNG/TRNG/CipR/EryR	1	7	4	4	2	1	4	4	4	31
	PPNG/TRNG/EryR	6	1	1	0	0	0	0	0	0	8
	PPNG/TRNG/AziR/CipR/EryR	0	0	0	0	0	0	0	1	0	1
	TRNG	102	236	106	57	112	82	84	37	29	845
	TRNG/CipR	1	10	6	8	4	14	12	11	8	74
	TRNG/CipR/EryR	2	6	1	3	1	2	1	3	3	22
	TRNG/EryR	8	4	1	3	1	1	5	0	0	23
	TRNG/PenR	38	3	0	0	1	1	0	0	0	43
	TRNG/CipR/PenR	0	0	0	0	0	0	0	1	1	2
	TRNG/CMRNG	1	0	0	0	0	0	0	0	0	1
	TRNG/CMRNG/CipR	1	1	1	1	1	0	0	2	5	12
Chromosomal Mediated Resistances	AziR/EryR	0	0	0	0	3	3	3	0	0	9
	AziR/EryR/TetR	0	0	0	0	1	1	0	2	0	4
	AziR/CipR	0	0	0	0	0	1	0	0	0	1
	AziR/CipR/EryR/TetR	0	0	0	0	0	1	0	0	0	1
	AziR/CipR/EryR	0	0	0	0	0	0	0	1	0	1
	CeRS/CipR	0	0	0	0	0	0	0	1	0	1
	CeRS/CipR/EryR	0	0	0	0	0	0	0	0	1	1
	CipR	5	13	3	11	27	44	163	161	87	514
	CipR/EryR	2	4	0	1	7	8	54	214	62	352
	CipR/EryR/TetR	1	0	8	9	39	39	22	28	8	154
	CipR/TetR	4	5	16	12	30	71	100	34	48	320
	CipR/PenR	0	0	0	0	0	1	6	0	2	9
	EryR	16	4	4	4	4	8	7	2	0	49
	EryR/TetR	49	8	21	29	32	23	16	0	0	178
	PenR	0	2	2	0	0	0	2	0	1	7
	PenR/TetR/CipR/CeRS	0	0	0	0	1	0	0	0	0	1
	PenR/TetR	0	0	0	0	0	0	0	3	2	5
	TetR	105	148	194	154	125	67	37	23	9	862
	CMRNG	167	139	162	49	43	10	6	3	3	582
	CMRNG/AziR	5	3	10	1	1	0	3	0	0	23
	CMRNG/CipR	5	30	16	12	47	209	514	494	375	1,702
	CMRNG/AziR/CipR	0	0	0	0	0	2	2	2	4	10
	Probable CMRNG	257	185	195	182	145	55	24	11	5	1,059
	Probable CMRNG/CipR	16	21	11	14	49	137	320	318	198	1,084
	Probable CMRNG/AziR/CipR	0	0	0	0	0	1	0	1	1	3
	Susceptible Strain	104	114	222	76	48	48	56	37	18	723
Contaminated or No Growth	Insufficient/No Growth/Contaminated	10	20	15	21	5	7	4	6	0	88
Totals		1,206	1,234	1,163	800	855	905	1,532	1,438	947	10,080

Between 2000 and 2008, there was an increasing prevalence of *N. gonorrhoeae* isolates that were classified as CMRNG, while the plasmid-mediated resistance strains (PPNG, TRNG, and PPNG/TRNG) all had a declining trend, shown in Figure 2. The rate of CMRNG increased from 3.9% in 2000 (177 of 4458 cultures) to 9.8% by 2008 (382 of 3907 cultures) and 5.2 % of isolates were characterized as Probable CMRNG. During the same time period, the PPNG isolates decreased from 3.0% (135 of 4458 cultures) to 0.7% (27 of 3907 cultures). The TRNG isolates decreased from 3.4% (151 of 4458 cultures) in 2000 to 1.05% (41 of 3907 cultures) in 2008 (Figure 2).

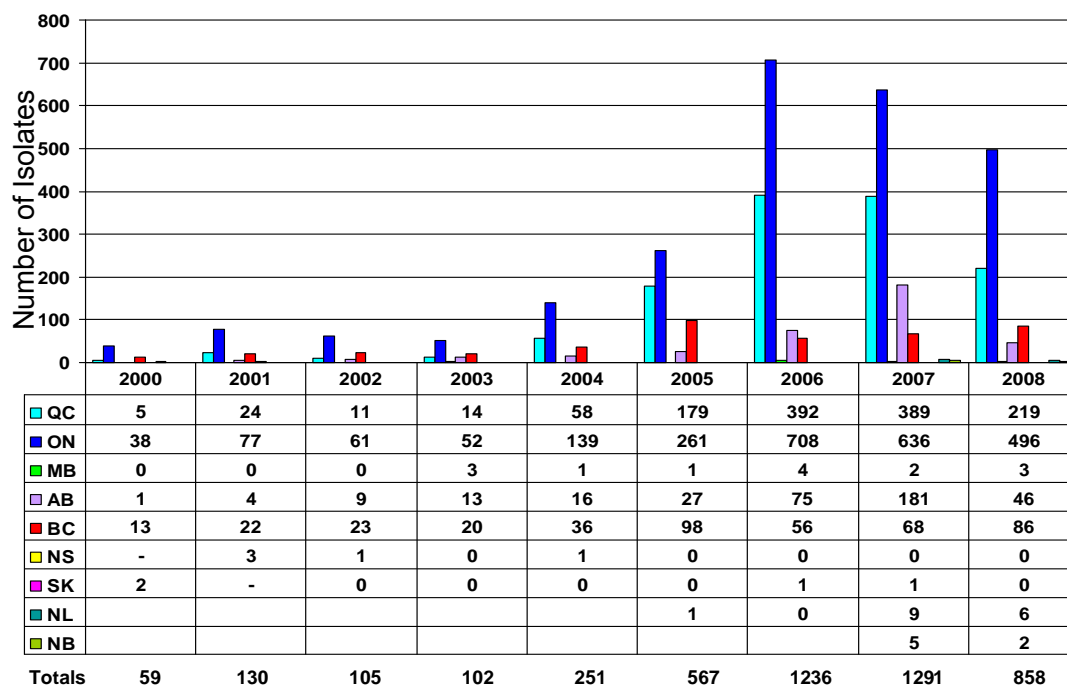
**Figure 2. Trends of PPNG, TRNG, CMRNG, Probable CMRNG *Neisseria gonorrhoeae* in Canada from 2000 to 2008**



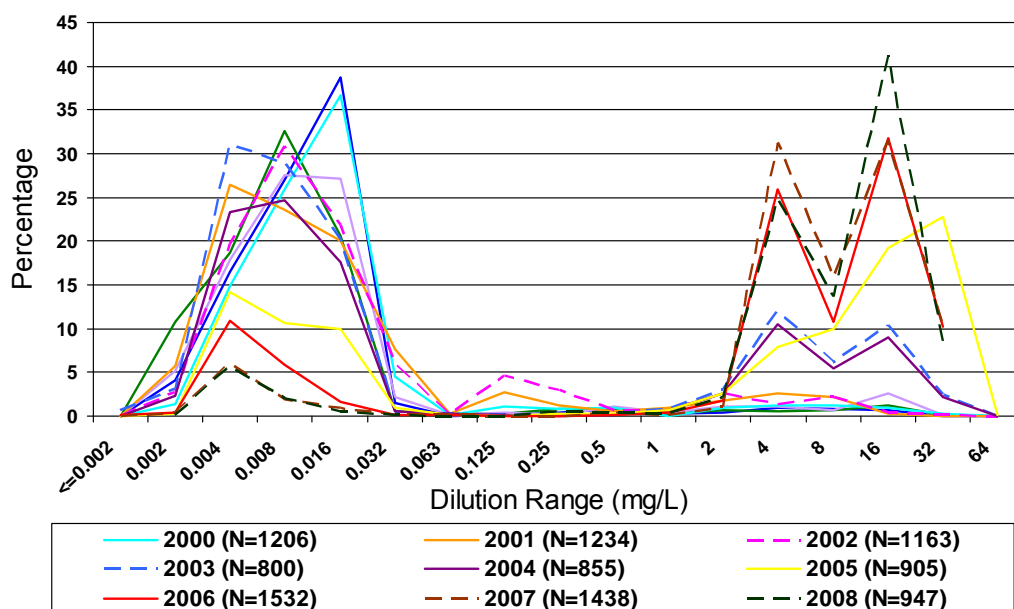
Percentage based on total number of isolates tested nationally: 2000=4458; 2001=4591; 2002=4465; 2003=4235; 2004=4018; 2005=3619; 2006=4201; 2007=4275; 2008=3907

Ciprofloxacin resistant *N. gonorrhoeae* accounted for 11.0% (4601 of 37,769) of all strains isolated between 2000 and 2008 (Figure 3). The number of isolates increased from 59 in 2000 (1.3%) to 858 in 2008 (22.0%). The mode of MICs of ciprofloxacin has shifted from 0.016 µg/ml in 2000 to 16.0 µg/ml in 2008 (Figure 4). Of the 858 ciprofloxacin resistant isolates identified in 2008, 89.8% (n=771) were also resistant to at least one other antibiotic; 379 (44.2%) were characterized as CMRNG. Ciprofloxacin resistant isolates predominate in the central and western provinces. Of all the isolates identified between 2000 and 2008 in the central provinces, 9.9% were ciprofloxacin resistant (n=3759). During the same period, 2.1% of all the *N. gonorrhoeae* cultures isolated in the western region were ciprofloxacin resistant (n=794). Rates of ciprofloxacin resistance in the prairie and eastern provinces were considerably lower at 0.05% and 0.08%, respectively (Figure 3).

**Figure 3. Geographical Distribution of Ciprofloxacin Resistant *Neisseria gonorrhoeae* Isolates, 2000 to 2008**



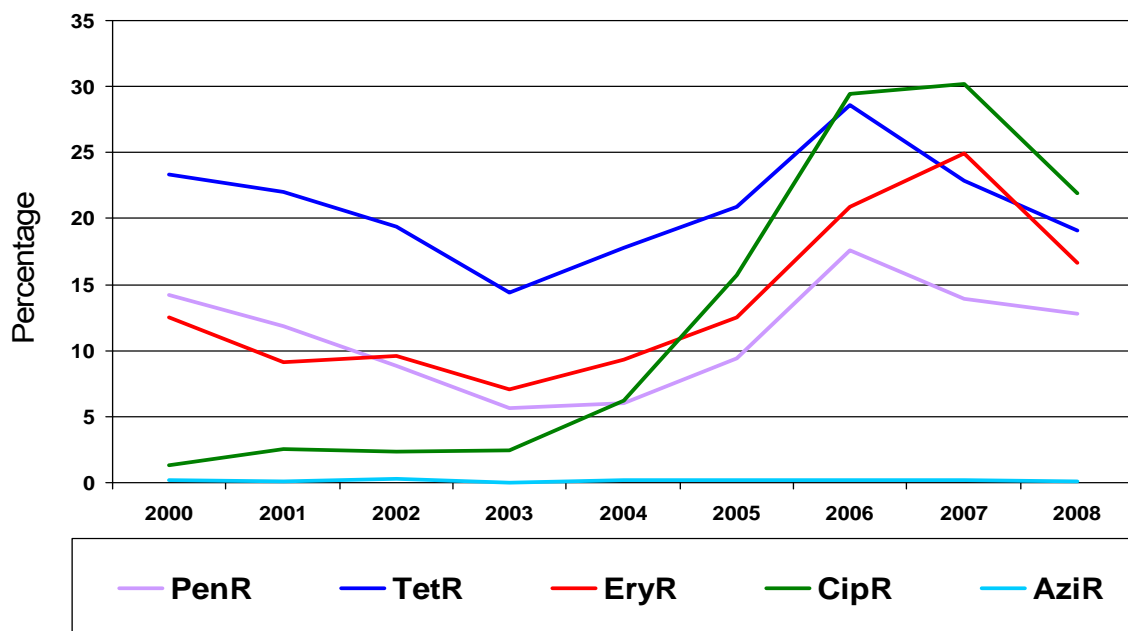
**Figure 4. Trends of Ciprofloxacin Susceptibilities of *Neisseria gonorrhoeae* Resistant Isolates Received by NML from 2000 to 2008**



Percentages were calculated using the total number of viable strains (both resistant and susceptible isolates) tested by NML as the denominator (N).

Erythromycin resistance in *N. gonorrhoeae* continues to rise and accounted for 13.6% (5127 of 37,769) of all strains isolated between 2000 and 2008. In 2000, only 12.5% (559 of 4458 isolates) were found to be erythromycin resistant (Figure 5). By 2007, the rate increased to 24.9% (1064 of 4,278 isolates) and then decreased again to 16.7% (653 of 3907 isolates) by 2008. Of the 653 erythromycin resistant isolates identified during in 2008, all were also resistant to at least one other antibiotic. A total of 382 (58.5%) of these were characterized as CMRNG. Strains with higher MICs to erythromycin also have higher MICs to azithromycin. Penicillin resistance experienced a decrease in levels between 2000 and 2003 from 14.2% (633 of 4,458 isolates) to 5.6% (240 of 4235 isolates) and then increased again to 12.8% by 2008 (500 of 3,907). Tetracycline followed this same pattern with a decrease in levels between 2000 and 2003 from 23.3% (1040 of 4,458 isolates) to 14.3% (608 of 4235 isolates) and then increased again to 19.1% by 2008 (746 of 3,907) (Figure 5).

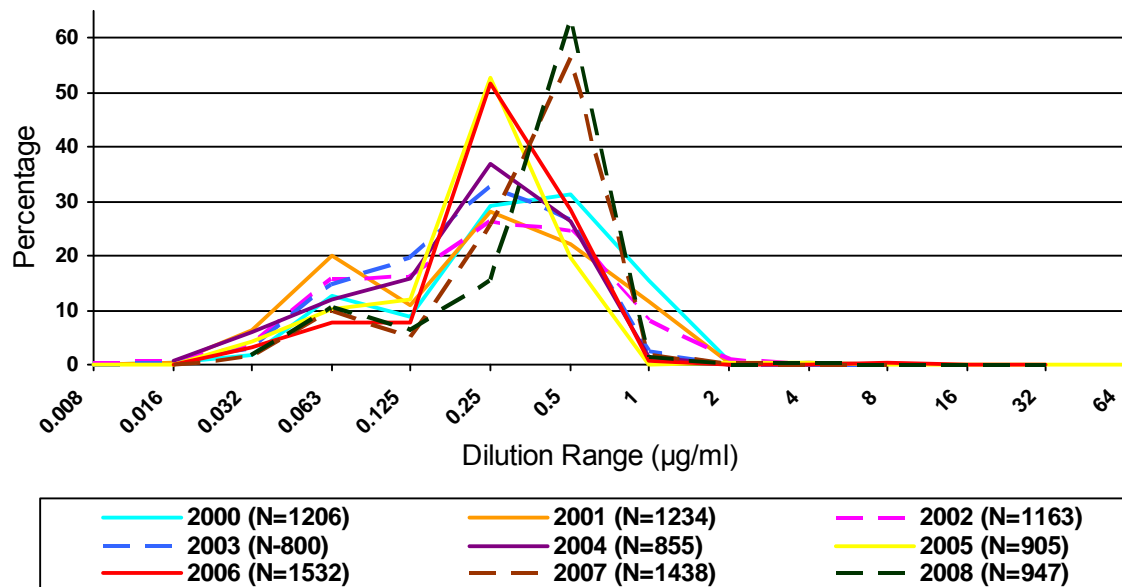
**Figure 5. Antimicrobial Susceptibility of *Neisseria gonorrhoeae* Isolates Tested in Canada Between 2000-2008**



Percentage based on total number of isolates tested nationally: 2000=4458; 2001=4591; 2002=4465; 2003=4235; 2004=4018; 2005=3619; 2006=4201; 2007=4275; 2008=3907.

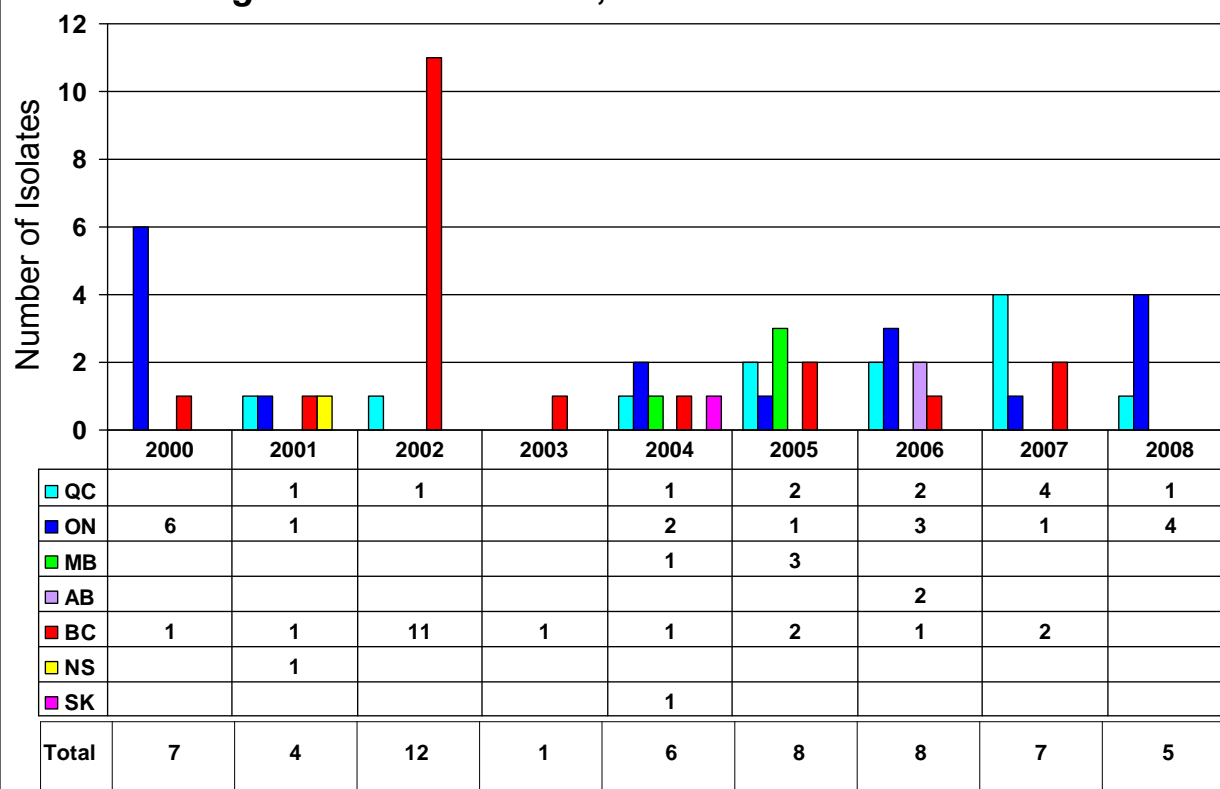
Azithromycin resistant *N. gonorrhoeae* accounted for 0.15% (58 of 37,769) of all strains isolated between 2000 and 2008. The mode of MICs of azithromycin has shifted from 0.25 µg/ml in 2001 to 0.5 µg/ml in 2007 (Figure 6). Each of the 58 azithromycin resistant isolates is associated with resistance to at least one other antibiotic (Figure 7).

**Figure 6. Trends of Azithromycin Susceptibilities of *Neisseria gonorrhoeae* Isolates in Canada from 2000 to 2008**

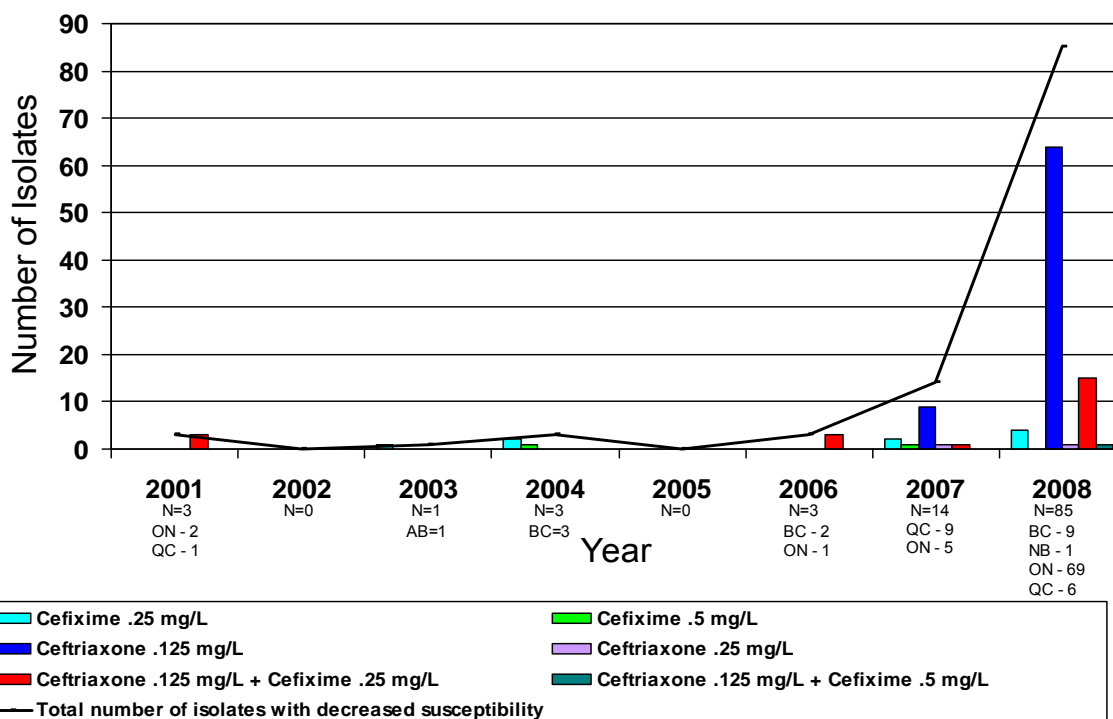


Percentages were calculated using the total number of viable strains (both resistant and susceptible isolates) tested by NML as the denominator (N).

**Figure 7. Geographical Distribution of Azithromycin Resistant *Neisseria gonorrhoeae* Isolates, 2000 to 2008**



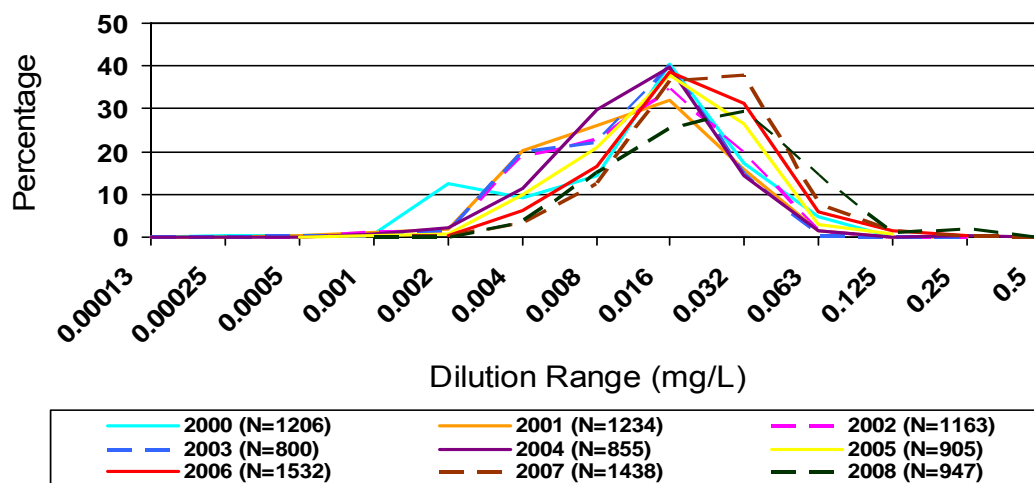
**Figure 8. 109 *Neisseria gonorrhoeae* Isolates with Decreased Susceptibility to Cefixime (0.25 mg/L and 0.5 mg/L) and Ceftriaxone (0.125 mg/L and 0.25 mg/L) MICs Isolated between 2001-2008**



Of the 10,080 isolates tested at NML between 2000 and 2008, none were identified with resistance to spectinomycin, cefixime or ceftriaxone. A total of 109 *N. gonorrhoeae* isolates with decreased susceptibility MICs to ceftriaxone and cefixime were identified between 2001 and 2008 (Figure 8). Three isolates (one each in 2004, 2007 and 2008) were identified with a cefixime MIC of 0.5 mg/L, classified as reduced-susceptibility by CLSI guidelines. These isolates with decreased susceptibility MICs to 3rd generation cephalosporins have been identified from several provinces around the country. In 2001, isolates were identified from Ontario (n=2) and Québec (n=1). Between 2003 and 2006, isolates were identified from Alberta (n=1), British Columbia (n=5) and Ontario (n=1). In 2007, an increase in incidence of these isolates was seen in only two provinces, Québec (n=9) and Ontario (n=5). By 2008, 85 isolates were identified in Canada (Ontario, n=69; British Columbia, n=9; Québec n=6 and New Brunswick, n=1). However, based on testing conducted at the NML, there has been a shift in the mode of the MICs of both cefixime and ceftriaxone from 0.016 mg/L in 2000 to 0.032 mg/L in 2008 (Figures 9 and 10). Preliminary data suggest the trend towards a “right” shift in MICs continued during 2009 (data not shown). These results indicate that the MICs of these 3rd generation cephalosporins are likely increasing over time.

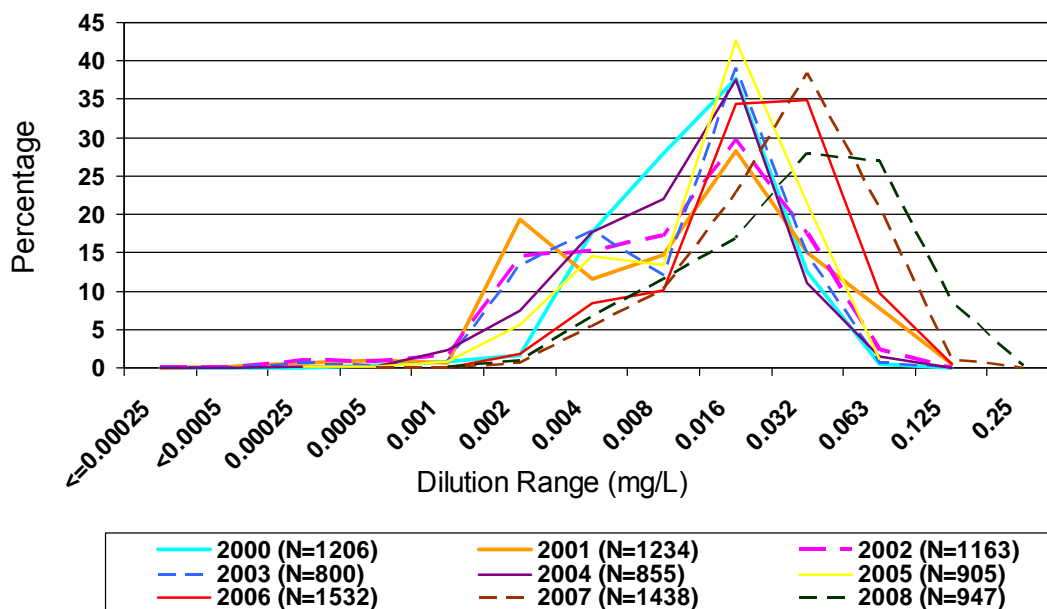


**Figure 9. Trends of Cefixime Susceptibilities of *Neisseria gonorrhoeae* Isolates Received by NML from 2000 to 2008**



Percentages were calculated using the total number of viable isolates (resistant and susceptible isolates) tested by NML as the denominator.

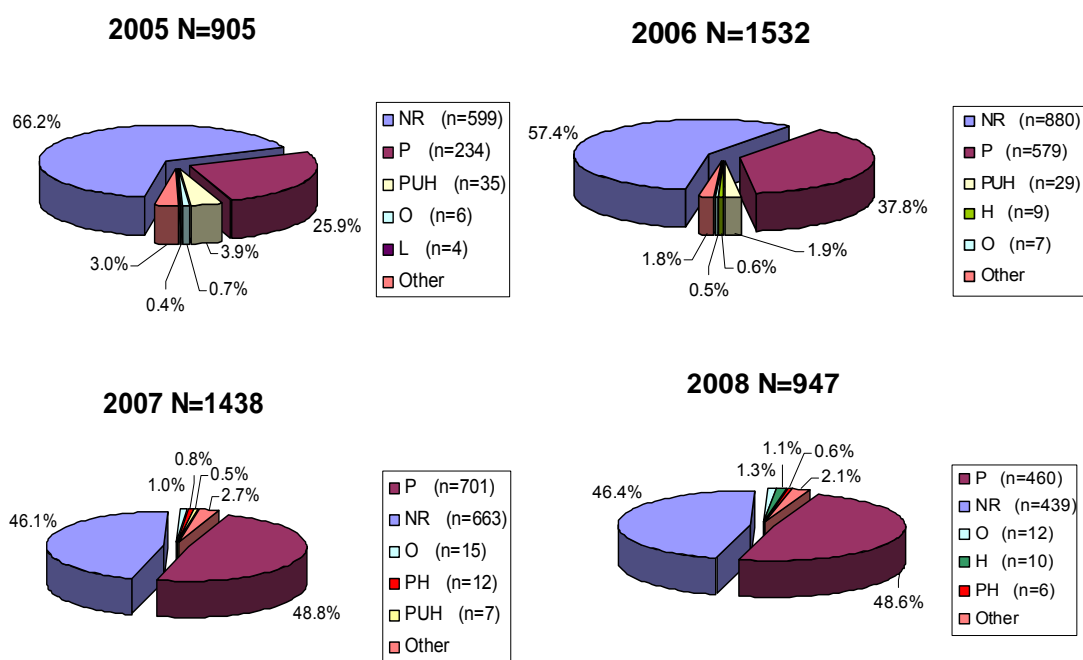
**Figure 10. Trends of Ceftriaxone Susceptibilities of *Neisseria gonorrhoeae* Isolates Received by NML from 2000 to 2008**



Percentages were calculated using the total number of viable isolates (both resistant and susceptible isolates) tested by NML as the denominator.

Auxotypes for all isolates were also determined. The majority of isolates in 2005 and 2006 were non-requiring (NR) at 66.2% and 57.4%, respectively. The next most common auxotype in 2005 and 2006 was proline-requiring (P) at 25.9% and 37.8%, respectively. In 2007 and 2008 P-requiring isolates became the most common auxotype at 48.8% and 48.6%, respectively followed by NR at 46.1% in 2007 and 46.4% in 2008. A variety of other auxotypes were also identified at a low frequency including proline, uracil and hypoxanthine-requiring (PUH) at 6.3%, ornithine-requiring (O) at 3.5%, H-requiring at 1.7% and PH-requiring at 1.4% of all the isolates examined between 2005 and 2008 (Figure 11).

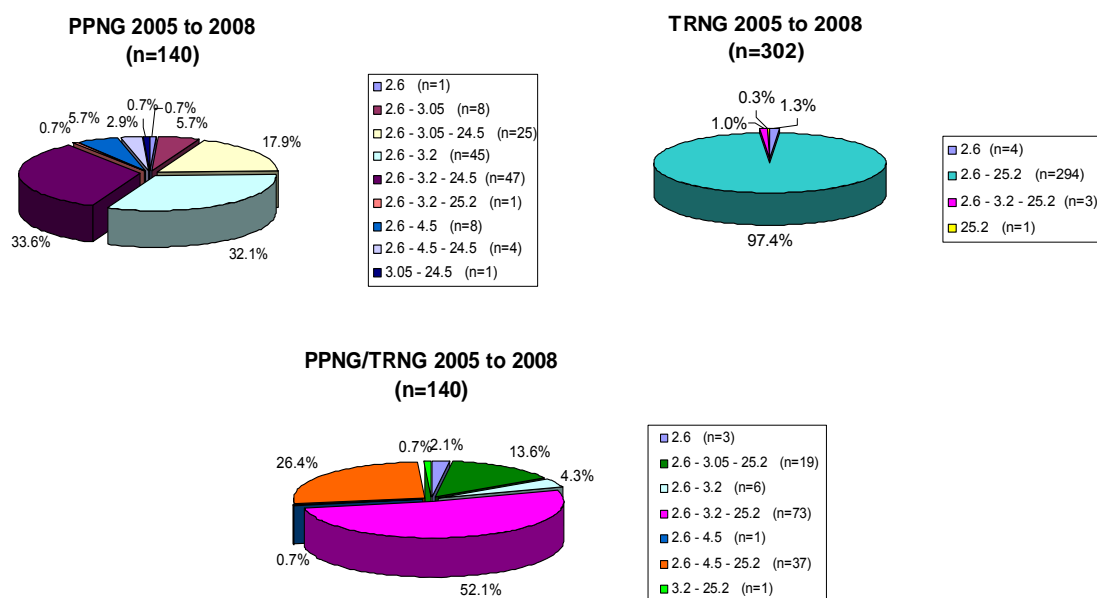
**Figure 11. Auxotype Distribution of *Neisseria gonorrhoeae* Isolates in Canada, 2005 - 2008**



Auxotype Definitions: Non-requiring (NR), leucine (L) - requiring, ornithine (O) - requiring, citrulline (C) - requiring, proline (P) - requiring, arginine (A) - requiring, hypoxanthine (H) - requiring, uracil (U) - requiring and methionine (M) - requiring

Plasmid profiles for PPNG, TRNG and PPNG/TRNG isolates are shown in Figure 12. The  $\beta$ -lactamase gene was encoded in three different types of plasmids of sizes 3.05 Mda, 3.2 Mda and 4.5 Mda. The 3.2 Mda plasmid was the most common type amongst the 140 PPNG strains isolated between 2005 and 2008 at 66.4%, followed by the 3.05 Mda plasmid at 24.3% and then the 4.5 Mda plasmid at 8.6%. These plasmids co-existed with the 2.6 Mda cryptic plasmid and sometimes with the 24.5 Mda conjugal plasmid. The 3.2 Mda plasmid is also the most common  $\beta$ -lactamase encoding plasmid in PPNG/TRNG strains at 56.4%. The 25.2 Mda plasmid that encodes tetracycline resistance (Tet M) co-existed with the cryptic plasmids in most TRNG and PPNG/TRNG strains. Among the TRNG isolates tested between 2005 and 2008, 98.3% had the 2.6 and 25.2 Mda plasmids. TRNG isolates accounted for 75.9% of all the plasmid mediated resistance in *N. gonorrhoeae* between 2005 and 2008 (442 of 582 PPNG, PPNG/TRNG and TRNG strains).

**Figure 12. Plasmid Distribution within Antimicrobial Classifications of *Neisseria gonorrhoeae* Isolates in Canada, 2005 - 2008**



Plasmid sizes displayed in megadaltons (Mda)

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## Conclusion

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The current Canadian treatment guidelines recommend a single dose treatment of 125 mg of intramuscular ceftriaxone or a single dose of 400 mg of oral cefixime (8) for the treatment of gonorrhea. Although penicillin and tetracycline have not been used in gonorrhea treatment for many years, the identification of the penicillin and tetracycline resistance phenotypes assist in monitoring the susceptibilities to the 3rd generation cephalosporins since these isolates also exhibit higher MICs of ceftriaxone and cefixime. Continued surveillance of the antimicrobial susceptibilities of *N. gonorrhoea* is important to monitor changes in the prevalence of the resistant isolate populations and their spread across the country. These surveillance data can be used to anticipate the need to revise treatment guidelines before resistance becomes prevalent in a region and weakens gonorrhea control measures.

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