



Antituberculosis drug resistance in New Zealand, 2007

Surveillance of antituberculosis drug resistance is based on the results of susceptibility testing of isolates in the Mycobacteriology Reference Laboratories at Auckland City, Wellington and Waikato Hospitals. The laboratory results are matched with tuberculosis case notifications.

In 2007, 288 cases of tuberculosis were notified, 225 (78.1%) of which were reported by the Mycobacteriology Reference Laboratories as culture positive. Antimicrobial susceptibility testing results were available for all 225 isolates, which comprised 222 *Mycobacterium tuberculosis* and 3 *M. bovis* isolates. The proportion of isolates resistant to isoniazid, rifampicin, ethambutol, pyrazinamide and streptomycin is shown in Table 1.

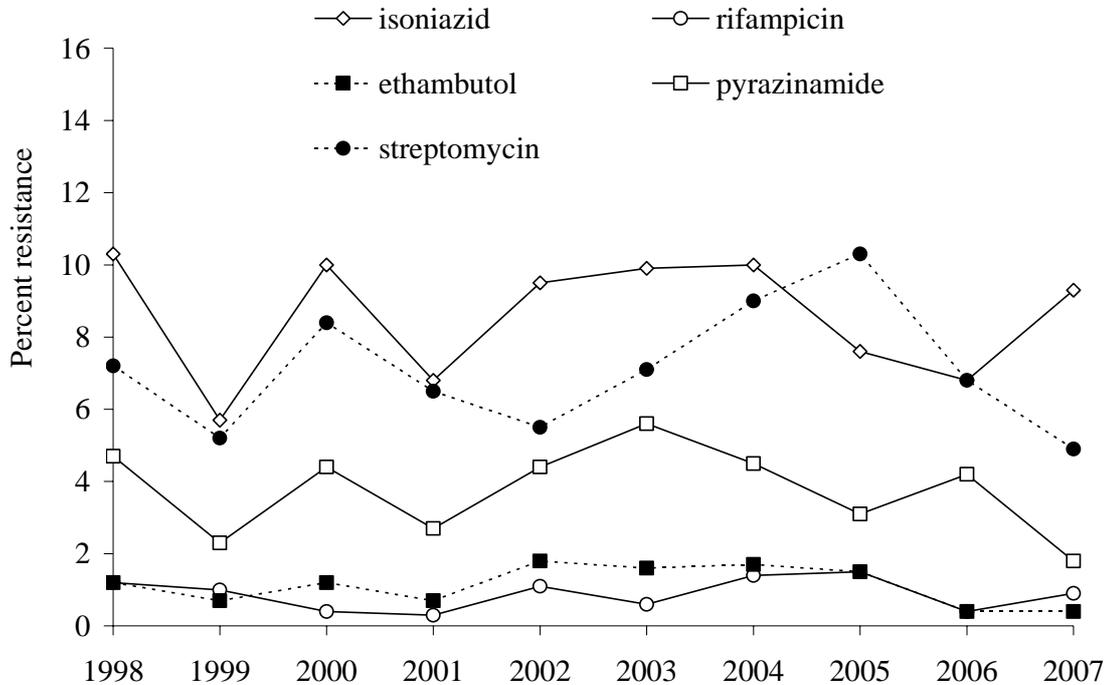
Table 1. Resistance to each antimicrobial, 2007

Antimicrobial	Percent (number) resistant ¹		
	<i>M. tuberculosis</i> n=222	<i>M. bovis</i> n=3	Total n=225
Isoniazid (0.1 mg/L)	9.5 (21)	0	9.3 (21)
Isoniazid (0.4 mg/L) ²	3.2 (7)	0	3.1 (7)
Rifampicin	0.9 (2)	0	0.9 (2)
Ethambutol	0.5 (1)	0	0.4 (1)
Pyrazinamide	0.5 (1)	100 (3)	1.8 (4)
Streptomycin	5.0 (11)	0	4.9 (11)

Notes: 1 includes resistance alone or in combination with other antimicrobials
2 all isolates resistant to isoniazid at the standard breakpoint concentration of 0.1 mg/L were also tested at the higher concentration of 0.4 mg/L

Trends in resistance to the five antimicrobials are shown in Figure 1. Overall, during the last 10 years, 1998-2007, there has been no significant change ($P \leq 0.05$) in resistance to any of the five antimicrobials.

Figure 1. Resistance to each antimicrobial, 1998-2007



In 2007, the majority (88.0%) of the isolates were susceptible to all five antimicrobials tested (Table 2). There were two cases (0.9%) of multidrug-resistant tuberculosis (MDR-TB, resistance to at least isoniazid and rifampicin). Both cases were TB relapses or reactivations. One case was a visitor from Indonesia. The other MDR-TB case appears to have developed resistance during treatment in New Zealand. Treatment of this case was interrupted during the Northland floods in early 2007 during which time the health services were not able to reach the patient.

MDR-TB remains relatively rare in New Zealand, with an average annual incidence of 0.8% and a total of 21 cases recorded during the last 10 years. All but two of these 21 MDR-TB cases were born overseas and assumed to have acquired their MDR-TB overseas.

Any MDR-TB isolates are now tested for susceptibility to an extended range of antibiotics. No cases of extensively drug-resistant TB (XDR-TB) have been identified in New Zealand. XDR-TB is MDR-TB with additional resistance to any fluoroquinolone and at least one of the following second-line drugs: capreomycin, kanamycin or amikacin.

Table 2. Distribution of resistance patterns, 2007

	Percent (number)	Resistance pattern ¹	Percent (number) of isolates with each pattern
Fully susceptible	88.0 (198)		
Resistant to 1 agent	7.6 (17)	H	4.9 (11)
		Z	1.3 (3) ²
		S	1.3 (3)
Resistant to 2 agents	3.6 (8)	HS	3.1 (7)
		HR	0.4 (1) ³
Resistant to 3 agents	0.9 (2)	HRZ	0.4 (1) ³
		HES	0.4 (1)

Notes: 1 H, isoniazid resistance at the standard concentration of 0.1 mg/L; R, rifampicin; E, ethambutol; Z, pyrazinamide; S, streptomycin
2 the three *M. bovis* isolates
3 MDR-TB, multidrug-resistant tuberculosis, that is, resistant to at least isoniazid and rifampicin

A comparison of resistance among isolates from cases born in New Zealand and cases born overseas is presented in Table 3. While, except for pyrazinamide, resistance was higher among isolates from cases born overseas, none of the differences were significant ($P \leq 0.05$). In addition, when the analysis was confined to *M. tuberculosis*, as *M. bovis* are intrinsically resistant to pyrazinamide, pyrazinamide resistance was also higher among isolates from cases born overseas (0.7%) than among isolates from cases born in New Zealand (0%).

Table 3. Resistance by case's place of birth, 2007¹

	Percent		P value ²
	New Zealand-born cases (n=55)	Overseas-born cases (n=156)	
Fully susceptible	92.7	86.5	0.2220
Resistant to:³			
Isoniazid⁴	3.6	10.9	0.1682
Rifampicin	0	0.6	1.0000
Ethambutol	0	0.6	1.0000
Pyrazinamide	3.6	1.3	0.2789
Streptomycin	0	6.4	0.0665
MDR-TB⁵	0	0.6	1.0000

Notes: 1 information on place of birth unknown or not reported for 14 cases, which included one isoniazid- and rifampicin-resistant case (MDR-TB) and one isoniazid- and streptomycin-resistant case
2 rates compared by the Chi-square test or Fishers Exact test, as appropriate
3 includes resistance alone or in combination with other antimicrobials
4 isoniazid resistance at the standard concentration of 0.1 mg/L
5 multidrug-resistant tuberculosis, that is, resistant to at least isoniazid and rifampicin

An analysis of the geographic distribution of resistant isolates among cases born in New Zealand, showed that there were no significant differences in resistance between regions within New Zealand.

Fourteen (6.2%) of the 225 culture-positive cases in 2007 were reported to be tuberculosis disease relapses or reactivations. This category of disease could also include cases of re-infection.

As the number of cases notified as tuberculosis disease relapses/reactivations in any one year is small, the following analysis of relapses/reactivations covers the last 5 years, 2003-2007. During this period, 76 (5.6%) of the 1364 culture-positive tuberculosis cases were reported to be relapses/reactivations. Information on previous treatment was recorded for 62 of the 76 cases, and 55 were recorded as having received previous antituberculosis drug treatment.

Resistance among new cases of tuberculosis, cases reported to be relapses/reactivations, and cases that were reported to have been previously treated, is shown in Table 4. Compared with new cases, previously treated cases were significantly more resistant to isoniazid, rifampicin and ethambutol; more likely to be MDR-TB; and less likely to be fully susceptible to all five antimicrobials.

Table 4. Resistance among new cases, relapses/reactivations and previously treated cases of tuberculosis disease, 2003-2007

	Percent		
	New cases n=1288	Relapse/reactivation cases	
		All n=76 (P value) ²	Previously treated n=55 ¹ (P value) ²
Fully susceptible	84.6	71.1 (0.0019)	65.5 (0.0002)
Resistant to:³			
Isoniazid⁴	7.8	25.0 (<0.0001)	30.9 (<0.0001)
Rifampicin	0.4	10.5 (<0.0001)	12.7 (<0.0001)
Ethambutol	0.6	10.5 (<0.0001)	14.6 (<0.0001)
Pyrazinamide	3.7	7.9 (0.1889)	9.1 (0.1325)
Streptomycin	7.8	6.6 (0.7065)	9.1 (0.6127)
MDR-TB⁵	0.4	10.5 (<0.0001)	12.7 (<0.0001)

Notes: 1 information on previous treatment reported for only 62 of the 76 relapse/reactivation cases

2 rate compared with that among new cases by the Chi-square test or Fishers Exact test, as appropriate

3 includes resistance alone or in combination with other antimicrobials

4 isoniazid resistance at the standard concentration of 0.1 mg/L

5 multidrug-resistant tuberculosis, that is, resistant to at least isoniazid and rifampicin

Compiled by: Helen Heffernan
Senior Scientist
Antibiotic Reference Laboratory
Communicable Disease Group
ESR
P O Box 50 348
PORIRUA 5240
Phone 04 914 0781, Fax 04 914 0770
helen.heffernan@esr.cri.nz

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This report is available at www.surv.esr.cri.nz/antimicrobial/tuberculosis.php