



Antituberculosis drug resistance in New Zealand, 2005

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 2005, 344 cases of tuberculosis were notified, 262 (76.2%) of which were reported by the Mycobacteriology Reference Laboratories as culture positive. Antimicrobial susceptibility testing results were available for all 262 isolates, which comprised 257 *Mycobacterium tuberculosis* and five *M. bovis* isolates. The proportion of isolates resistant to isoniazid, rifampicin, ethambutol, pyrazinamide and streptomycin is shown in Table 1.

In this report we are introducing some additional isoniazid resistance data in Table 1 by reporting on resistance at two concentrations: the standard breakpoint concentration of 0.1 mg/L and also 0.4 mg/L. All isolates resistant to 0.1 mg/L isoniazid are also tested at the higher concentration of 0.4 mg/L. Most (17/20) of the isolates resistant to the lower isoniazid concentration were also resistant to the higher concentration. The results at the higher concentration may correlate better with the clinical efficacy of isoniazid than the results at the lower concentration.¹ For the other analyses presented in this report, where the concentration of isoniazid is not specified, the data are for resistance at the standard concentration of 0.1 mg/L.

Table 1. Resistance to each antimicrobial, 2005

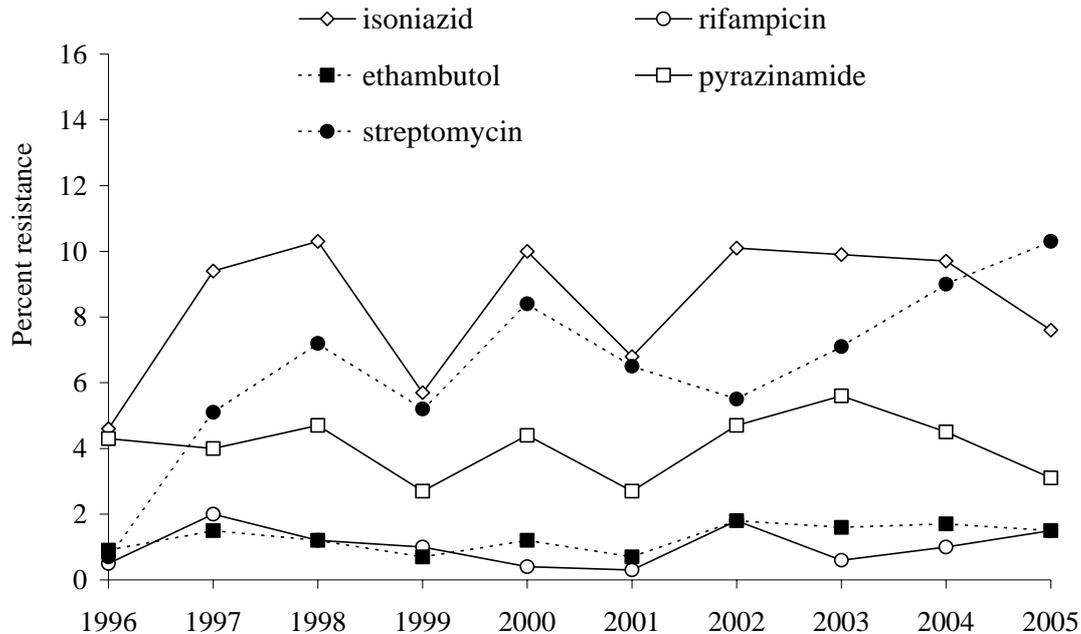
Antimicrobial	Number resistant ¹	Percent resistance ¹
Isoniazid (0.1 mg/L)	20	7.6
Isoniazid (0.4 mg/L) ²	17	6.5
Rifampicin	4	1.5
Ethambutol	4	1.5
Pyrazinamide	8 ³	3.1
Streptomycin	27	10.3

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

¹ National Committee for Clinical Laboratory Standards. Susceptibility testing of mycobacteria, nocardiae, and other aerobic actinomycetes; approved standard M24-A. Wayne, PA; 2003.

Trends in resistance to the five antimicrobials are shown in Figure 1. Over the whole 10-year period, 1996-2005, only streptomycin resistance changed significantly ($p \leq 0.05$). Streptomycin resistance increased between 1996 and 1998, but the increase was only significant among cases reported to have been born overseas. In contrast, the further increase in streptomycin resistance evident since 2002 occurred in both NZ- and overseas-born cases.

Figure 1. Resistance to each antimicrobial, 1996-2005



In 2005, the majority (84.0%) of the isolates were susceptible to all five antimicrobials tested (Table 2). There were four cases (1.5%) of multidrug-resistant tuberculosis (MDR-TB, resistance to at least isoniazid and rifampicin). Two of the MDR-TB cases were from China and the other two from Korea. They had arrived in New Zealand within five years of their TB being diagnosed. MDR-TB is rare in New Zealand, with an average annual incidence of 0.8% and a total of 23 cases recorded in the 11 years since national surveillance of antituberculosis drug resistance began in 1995. All but one of the 23 MDR-TB cases were born overseas and assumed to have acquired their MDR-TB overseas. The remaining case, while born overseas, appears to have developed MDR-TB during treatment in New Zealand, which was complicated due to the patient being immune compromised, having disseminated extra-pulmonary TB, and adverse reactions to rifampicin, ethambutol and pyrazinamide.

Table 2. Distribution of resistance patterns, 2005

	Number (%)	Resistance pattern ¹	Number (%) of isolates with each pattern
Fully susceptible	220 (84.0)		
Resistant to 1 agent	30 (11.5)	S	18 (6.9)
		H	8 (3.1)
		Z	4 (1.5) ²
Resistant to 2 agents	7 (2.7)	HS	6 (2.3)
		HZ	1 (0.4) ³
Resistant to 3 agents	2 (0.8)	HRE ⁴	1 (0.4)
		HZS	1 (0.4)
Resistant to 4 agents	2 (0.8)	HREZ ⁴	1 (0.4)
		HRES ⁴	1 (0.4)
Resistant to 5 agents	1 (0.4)	HREZS ⁴	1 (0.4)

Notes: 1 H, isoniazid; R, rifampicin; E, ethambutol; Z, pyrazinamide; S, streptomycin
2 four of the five *M. bovis* isolates
3 the fifth *M. bovis* isolate
4 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. There were no significant differences in resistance by place of birth.

Table 3. Resistance by case's place of birth, 2005¹

	Percent		P value ²
	New Zealand-born cases (n=42)	Overseas-born cases (n=198)	
Fully susceptible	83.3	83.3	1.0000
Resistant to:³			
Isoniazid	4.8	8.6	0.5407
Rifampicin	0	2.0	1.0000
Ethambutol	0	2.0	1.0000
Pyrazinamide	7.1	2.0	0.1048
Streptomycin	9.5	11.6	1.0000
MDR-TB⁴	0	2.0	1.0000

Notes: 1 information on place of birth unknown or not reported for 22 cases, which included one isoniazid-resistant and one pyrazinamide-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 multidrug-resistant tuberculosis, that is, resistant to at least isoniazid and rifampicin

There were no significant differences in resistance between regions within New Zealand when either all cases or just those cases born in New Zealand were considered.

Fourteen (5.3%) of the 262 culture-positive cases in 2005 were reported to be tuberculosis disease relapses or reactivations. This category of disease would also include cases of re-infection. Three of the four MDR-TB cases were reported to be previously treated disease relapses/reactivations.

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 five years, 2001-2005. During this period, 76 (5.3%) of the 1442 culture-positive TB cases were reported to be relapses/reactivations. Information on previous treatment was recorded for 57 of the 76 cases, and 50 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 5. 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 5. Resistance among new cases, relapses/reactivations and previously treated cases of tuberculosis disease, 2001-05

	Percent		
	New disease n=1366	Disease relapses/reactivations =76 (P value) ¹	Previously treated cases n=50 (P value) ¹
Fully susceptible	83.4	73.7 (0.0290)	66.0 (0.0014)
Resistant to:²			
Isoniazid	8.4	18.4 (0.0026)	28.0 (<0.0001)
Rifampicin	0.7	6.6 (<0.0001)	10.0 (<0.0001)
Ethambutol	1.0	9.2 (<0.0001)	14.0 (<0.0001)
Pyrazinamide	3.9	9.2 (0.0346)	8.0 (0.1380)
Streptomycin	7.7	6.6 (0.7233)	10.0 (0.5855)
MDR-TB³	0.6	6.6 (<0.0001)	10.0 (<0.0001)

Notes: 1 rate compared with that among new cases by the Chi-square test or Fishers Exact test, as appropriate

2 includes resistance alone or in combination with other antimicrobials

3 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
helen.heffernan@esr.cri.nz

Acknowledgements: Ross Vaughan, Mycobacteriology Reference Laboratory, Auckland City Hospital; Leo McKnight, Mycobacteriology Reference Laboratory, Wellington Hospital; and Kathryn Coley, Mycobacteriology Reference Laboratory, Waikato Hospital, for supplying their susceptibility test results. Dr Tim Blackmore, ESR and Capital and Coast Health, for clinical peer review.

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