Antituberculosis drug resistance in New Zealand, 2006

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 2006, 357 cases of tuberculosis were notified, 266 (74.5%) of which were reported by the Mycobacteriology Reference Laboratories as culture positive. Antimicrobial susceptibility testing results were available for all 266 isolates, which comprised 258 *Mycobacterium tuberculosis* and eight *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, 2006

	Percent (number) resistant[1]		
Antimicrobial	***M. tuberculosis*** **n=258**	***M. bovis*** **n=8**	**Total n=266**
Isoniazid (0.1 mg/L)	6.6 (17)	12.5 (1)	6.8 (18)
Isoniazid (0.4 mg/L)[2]	4.7 (12)	12.5 (1)	4.9 (13)
Rifampicin	0.4 (1)	0	0.4 (1)
Ethambutol	0.4 (1)	0	0.4 (1)
Pyrazinamide	1.2 (3)	100 (8)	4.1 (11)
Streptomycin	7.0 (18)	0	6.8 (18)

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

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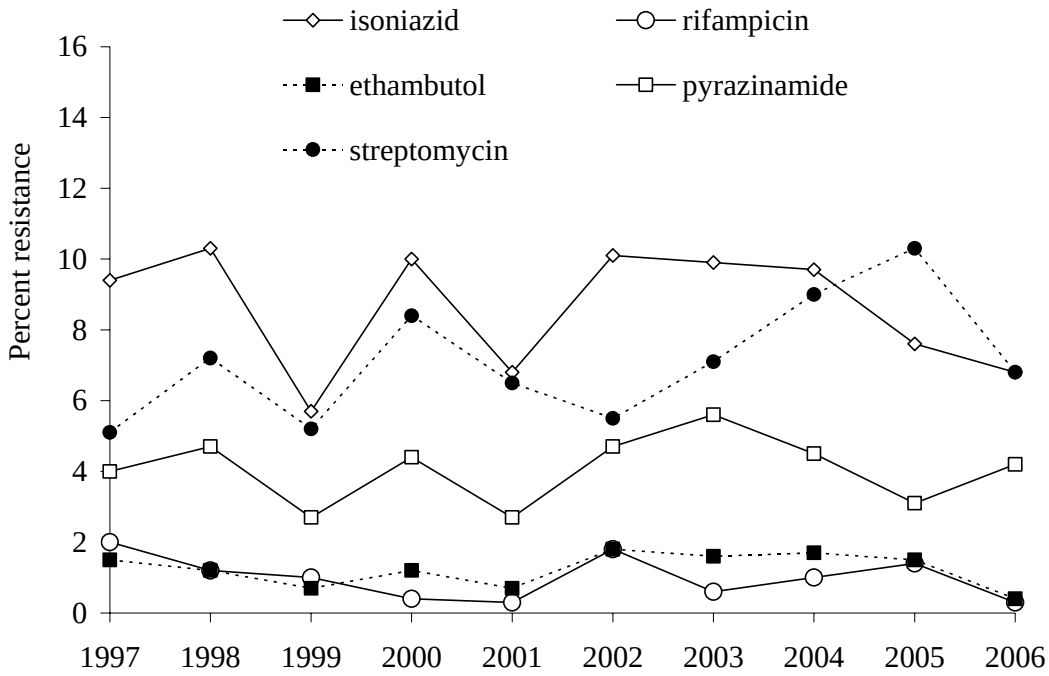
Trends in resistance to the five antimicrobials are shown in Figure 1. Overall, during the last 10 years, 1997-2006, there has been no significant change ($p \leq 0.05$) in resistance to any of the five antimicrobials.

Figure 1. Resistance to each antimicrobial, 1997-2006



In 2006, the majority (86.5%) of the isolates were susceptible to all five antimicrobials tested (Table 2). There was one case (0.4%) of multidrug-resistant tuberculosis (MDR-TB, resistance to at least isoniazid and rifampicin). This MDR-TB case was from China and had arrived in New Zealand in late 2002. MDR-TB is rare in New Zealand, with an average annual incidence of 0.8% and a total of 24 cases recorded in the 12 years since national surveillance of antituberculosis drug resistance began in 1995. All but one of the 24 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, 2006

	Percent (number)	Resistance pattern[1]	Percent (number) of isolates with each pattern
Fully susceptible	86.5 (230)		
Resistant to 1 agent	9.8 (26)	H	3.0 (8)
		Z	3.4 (9)[2]
		S	3.4 (9)
Resistant to 2 agents	3.0 (8)	HS	2.6 (7)
		HZ	0.4 (1)[3]
Resistant to 3 agents	0.4 (1)	HZS	0.4 (1)
Resistant to 4 agents	0.4 (1)	HRES[4]	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 includes seven of the eight *M. bovis* isolates
3 the eighth *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. Pyrazinamide resistance was the only resistance that differed significantly depending on the case's place of birth, with cases born in New Zealand more likely to be resistant. However, when the *M. bovis* isolates were excluded from this analysis, there was no significant difference (p = 0.5787) in pyrazinamide resistance among *M. tuberculosis* isolated from cases born overseas (1.6%) and cases born in New Zealand (0%).

Table 3. Resistance by case's place of birth, 2006[1]

	Percent		P value[2]
	New Zealand-born cases (n=56)	Overseas-born cases (n=188)	
Fully susceptible	85.7	85.6	0.9886
Resistant to:[3]			
Isoniazid[4]	1.8	8.5	0.1309
Rifampicin	0	0.5	1.0000
Ethambutol	0	0.5	1.0000
Pyrazinamide	10.7	2.7	0.0340
Streptomycin	3.6	8.5	0.3801
MDR-TB[5]	0	0.5	1.0000

Notes: 1 information on place of birth unknown or not reported for 22 cases, which included one isoniazid-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 only pyrazinamide resistance varied significantly between regions within New Zealand. Pyrazinamide resistance was highest (50.0%) in the Southern region (Canterbury, South Canterbury, West Coast, Otago, and Southland Health Districts). However, when the *M. bovis* isolates were excluded from this analysis, there were no significant regional differences (p = 0.7940) in pyrazinamide resistance among *M. tuberculosis*.

Sixteen (6.0%) of the 266 culture-positive cases in 2006 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, 2002-2006. During this period, 69 (4.9%) of the 1415 culture-positive tuberculosis cases were reported to be relapses/reactivations. Information on previous treatment was recorded for 56 of the 69 cases, and 51 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, 2002-2006

	Percent		
	New disease n=1346	**Disease relapses/reactivations n=69 (P value)[1]**	**Previously treated cases n=51 (P value)[1]**
Fully susceptible	83.4	73.9 (0.0402)	70.6 (0.0166)
Resistant to:[2]			
Isoniazid[3]	8.3	20.3 (0.0007)	25.5 (<0.0001)
Rifampicin	0.7	8.7 (<0.0001)	11.8 (<0.0001)
Ethambutol	0.9	11.6 (<0.0001)	15.7 (<0.0001)
Pyrazinamide	4.2	8.7 (0.2104)	7.8 (0.4567)
Streptomycin	7.9	4.4 (0.2838)	5.9 (0.6025)
MDR-TB[4]	0.6	8.7 (<0.0001)	11.8 (<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 isoniazid resistance at the standard concentration of 0.1 mg/L
4 multidrug-resistant tuberculosis, that is, resistant to at least isoniazid and rifampicin

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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.