Antituberculosis drug resistance, 2002

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

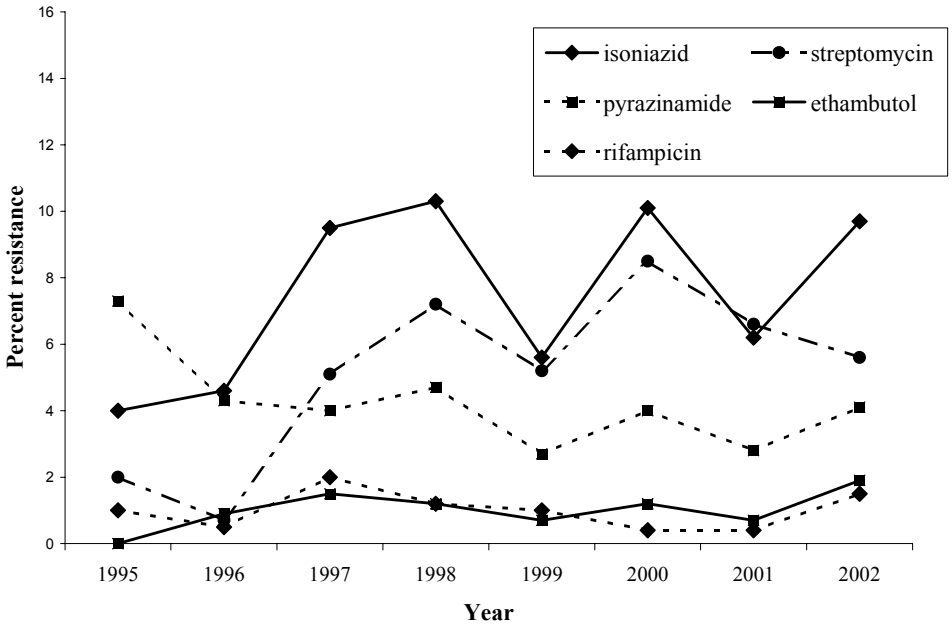
In 2002, 385 cases of tuberculosis were notified, 268 (69.6%) of which were reported by the Mycobacteriology Reference Laboratories as culture positive. Antimicrobial susceptibility testing results were available for all 268 isolates, which comprised 264 *Mycobacterium tuberculosis* and four *M. bovis* isolates. The proportion of isolates resistant to isoniazid, rifampicin, ethambutol, pyrazinamide and streptomycin is shown in Table 1, and trends in resistance to these five antimicrobials are shown in Figure 1. Over the last eight years, there has been a trend of increasing streptomycin resistance (p=0.0078). Isoniazid and pyrazinamide resistance has fluctuated, while rifampicin and ethambutol resistance has been relatively stable and remained ≤2%.

Table 1. Resistance to each antimicrobial, 2002

Antimicrobial	Number tested	Number resistant[1]	Percent resistance[1]
Isoniazid	268	26	9.7
Rifampicin	268	4	1.5
Ethambutol	268	5	1.9
Pyrazinamide	268	11[2]	4.1
Streptomycin	268	15	5.6

Notes: 1 includes resistance alone or in combination with other antimicrobials
2 includes the four *M. bovis* isolates

Figure 1. Resistance to each antimicrobial, 1995-2002



Multidrug-resistant TB (MDR-TB, resistance to at least isoniazid and rifampicin) is rare in New Zealand, with an average annual incidence of 0.7% (14 cases) recorded in the eight years since national surveillance of antituberculosis-drug resistance began in 1995. In 2002, the majority (83.2%) of the isolates were susceptible to all five antimicrobials tested (Table 2). Three isolates (1.2%) were MDR-TB. Two of these isolates were from cases who had arrived in New Zealand ≤2 years prior to their TB being diagnosed. The third MDR isolate was also from an immigrant, but multidrug resistance appears to have developed during treatment in New Zealand. The isolate, which was resistant to isoniazid, rifampicin, pyrazinamide and ethionamide, was a repeat isolation from the patient who was immune compromised due to SLE and steroid treatment. The patient originally presented with disseminated extra-pulmonary TB involving the CNS. Two earlier isolates were resistant to isoniazid alone. The MDR isolate was cultured from a CSF specimen taken after 12 months of treatment, which had been complicated by adverse reactions to rifampicin, ethambutol and pyrazinamide. Molecular typing confirmed the original isoniazid-resistant isolates and the MDR isolate to be the same type and a type not previously identified among TB isolates in New Zealand. This appears to be the first case of MDR-TB developing during treatment in New Zealand. The other 13 MDR-TB cases recorded since 1995 have all been in people born overseas and assumed to have acquired their MDR-TB overseas.

Table 2. Distribution of resistance patterns, 2002

	Number (%)	Resistance pattern[1]	Number (%) of isolates with each pattern
Fully susceptible	223 (83.2)		
Resistant to 1 agent	32 (11.9)	H	13 (4.9)
		R	1 (0.4)
		Z	9 (3.4)[2]
		S	5 (1.9)
		E	4 (1.5)
Resistant to 2 agents	11 (4.1)	HR[3]	1 (0.4)
		HZ	1 (0.4)
		HS	9 (3.4)
Resistant to 3 agents	1 (0.4)	HRZ[3]	1 (0.4)
Resistant to 4 agents	1 (0.4)	HRSE[3]	1 (0.4)

Notes: 1 H, isoniazid; R, rifampicin; Z, pyrazinamide; S, streptomycin; E, ethambutol
2 includes the four *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. Cases born overseas were significantly more likely to be resistant to isoniazid (p=0.0053). Cases born in New Zealand were more likely to be pyrazinamide resistant (p=0.0153). This effect is due to all four *M. bovis* infections being in New Zealand-born cases and this species' intrinsic pyrazinamide resistance.

Table 3. Resistance by case's place of birth, 2002[1]

	Percent		P value[3]
	New Zealand-born cases (n=52)	Overseas-born cases (n=187)	
Fully susceptible	88.5	80.2	0.1708
Resistant to:[2]			
Isoniazid	0	13.4	0.0053
Rifampicin	0	2.1	0.5793
Ethambutol	0	2.7	0.5883
Pyrazinamide	11.5	2.7	0.0153
Streptomycin	0	7.0	0.0769
MDR-TB[4]	0	1.6	1.0000

Notes: 1 information on place of birth unknown or not reported for 29 cases; these 29 cases included one isoniazid-resistant case and two streptomycin-resistant cases.
2 includes resistance alone or in combination with other antimicrobials
3 rates compared by the Chi-square test or Fishers Exact test, as appropriate
4 multidrug-resistant tuberculosis, that is, resistant to at least isoniazid and rifampicin

The geographic distribution of resistant isolates, based on aggregated health districts, is shown in Table 4. There were no statistically significant differences ($p \leq 0.05$) in resistance rates between the areas.

Table 4. Geographic distribution of resistance, 2002

Antimicrobial	Percent resistance (number resistant/number tested)[1]			
	Northern[2]	Midland[2]	Central[2]	Southern[2]
Isoniazid	11.9 (19/160)	3.9 (1/26)	7.1 (4/56)	7.7 (2/26)
Rifampicin	1.9 (3/160)	0 (0/26)	1.8 (1/56)	0 (0/26)
Ethambutol	3.1 (5/160)	0 (0/26)	0 (0/56)	0 (0/26)
Pyrazinamide	4.8 (7/160)	0 (0/26)	5.4 (3/56)	3.9 (1/26)
Streptomycin	8.1 (13/160)	3.9 (1/26)	0 (0/56)	3.9 (1/26)

Notes: 1 includes resistance alone or in combination with other antimicrobials
2 the Northern area includes the Northland, North West Auckland, Central Auckland, and South Auckland Health Districts; the Midland area includes the Waikato, Tauranga, Eastern Bay of Plenty, Gisborne, Rotorua, Taupo, Taranaki, and Ruapehu Health Districts; the Central area includes the Hawkes Bay, Wanganui, Manawatu, Wairarapa, Hutt, Wellington, and Nelson-Marlborough Health Districts; and the Southern area includes the Canterbury, South Canterbury, West Coast, Otago, and Southland Health Districts

Nine (3.4%) of the total 268 isolates were from cases categorised as tuberculosis reactivations. There were no significant differences in resistance among reactivations compared with new cases of tuberculosis.

Acknowledgements: Ross Vaughan, Mycobacteriology Reference Laboratory, Auckland Hospital; Leo McKnight, Mycobacteriology Reference Laboratory, Wellington Hospital; and Vivienne Talbot, Mycobacteriology Reference Laboratory, Waikato Hospital, for supplying their susceptibility test results.

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