GLOBAL PERSPECTIVES

Drug-resistant tuberculosis in Taipei, 1996-1999

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Objectives: To determine the trends, patterns, and risk factors associated with drug-resistant tuberculosis, we conducted a hospital-based retrospective study in Taipei.
Methods: Clinical and bacteriologic data were routinely collected from 453 patients with a diagnosis of tuberculosis who were treated at Taipei Municipal Chronic Disease Hospital from January 1996 through December 1999 for whom drug-susceptibility testing was done.
Results: Resistance to at least one drug was identified in 154 (34%) out of the 453 patients, and 34 (7.5%) patients were resistant to at least isoniazid and rifampin. Among the 199 patients with recurrent tuberculosis, 98 (49.2%) had isolates that showed resistance to at least one drug. Among the 254 new patients, 56 (22.0%) had isolates that were drug resistant. For all 453 patients, resistance to rifampin was most common (17.4%), followed by resistance to isoniazid (13.9%), streptomycin (13.7%), ethambutol (8.2%), and kanamycin (3.5%). A history of previous tuberculosis therapy (odds ratio = 9.4; 95% CI, 2.9-28) and being born outside of Taiwan (odds ratio 3.3; 95% CI, 1.1-34) were significant risk factors for multidrug resistance.
Conclusions: Our data suggest that the Taipei tuberculosis control program should be rapidly strengthened by expanded use of directly observed therapy and more careful bacteriologic and clinical follow-up, particularly in cases of recurrence and in persons born outside of Taiwan in tuberculosis endemic areas. Our results also indicate that the regular measuring of rates of drug resistance and the monitoring and guiding of tuberculosis treatment programs could increase the therapeutic response rate and prevent the appearance of newly acquired resistance in patients with tuberculosis. In addition, with high rifampin resistance (17.4%), the regulated market for rifampin is essential in Taiwan. (AJIC Am J Infect Control 2001;29:41-7)

Tuberculosis (TB) rates remain as high as 67 per 100,000 persons in 1999 in Taipei despite the existence of a national tuberculosis control program. All persons with TB can be rendered noninfectious and cured if they receive adequate therapy.[1] Adequate therapy requires the use of two or more drugs to which the microorganism is susceptible.[2] Spontaneous mutations resulting in drug resistance occur rarely in *Mycobacterium tuberculosis,* and multidrug regimens can prevent the emergence of drug resistance.[3] The problem of resistance often results from the nonadherence to drug regimens on the part of Taiwanese patients.[4] Resistance to anti-TB drugs after lack of compliance is a serious challenge to effective control of TB in Taipei.[4]

Tubercle bacilli are resistant to anti-TB drugs in two ways: primary resistance and acquired resistance. Primary resistance is defined as the presence of drug resistance to at least one anti-TB drug in a patient with TB who has never received prior treatment. Primary resistance is caused by infection with organisms already resistant to antimicrobial agents. Thus primary resistance is an indicator of the efficacy of TB control efforts in the past.[5] Acquired resistance is defined as resistance to at least one anti-TB drug during treatment by a strain that was originally drug sensitive. The latter process is believed to be a result of the selection of drug-resistant mutants of the original strain as a consequence of inadequate treatment.[6] A high level of this type of resistance is a mark of weakness in the current TB control program.[7]

The prevalence of resistance to anti-TB drugs shows marked geographic difference and has important implications for selecting an appropriate initial treatment regimen for the patient. Reported rates are low from England and Wales (4.6%)[8] and Finland (2%),[9] intermittent from Japan (10.6%)[10] and the United States

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(14.2%),[11] and high from Thailand (52%),[9] Egypt (34%),[9] India (26%),[12] Haiti (22%),[13] and Saudi Arabia (21.3%).[14] These differences reflect the effectiveness of national tuberculosis control programs, particularly in high-rate countries that have failed to achieve high cure rates. A recent study[15] drew attention to the importance of measuring rates of drug resistance as an element of surveillance in national tuberculosis programs; however, to be effective, such measurement requires rigorous methodology both in collecting bacteriologic and clinical data and in defining representative groups of patients so that results can be both useful and comparable.

Multiple drug–resistant (MDR) TB is extremely expensive and difficult to treat and cure.[16] Even in very sophisticated care settings that specialize in the care of TB, the cure rates are less than 50%.[17] In many developing countries, MDR TB is virtually incurable. Furthermore, case-fatality rates from MDR TB are as high as 70% to 90% among persons with HIV infection[18] and 22% among persons without HIV infection.[16] Thus from the perspective of controlling MDR TB, the first priority is to prevent its occurrence. Determination of the risk factors for drug resistance and implementation of the appropriate intervention strategies is urgently needed. The purpose of this study was to determine the prevalence, trends, and patterns of drug-resistant TB and identify populations at high risk for drug-resistant tuberculosis at a hospital in Taipei during the period from 1996 through 1999.

PATIENTS AND METHODS

Selection of study subjects

Taipei Municipal Chronic Disease Hospital (TMCDH), a 60-bed, government-run hospital, provides preventive, diagnostic, and therapeutic services to patients with TB in Taipei. It is also the referral center for patients with pulmonary TB in Taipei. This prevalence study collected data retrospectively from all 522 patients with a diagnosis of tuberculosis who were treated at the TMCDH from January 1996 through December 1999 for whom drug-susceptibility testing was done. The study did not include multiple isolates from a single patient.

Information on demographic characteristic including age, sex, residence, occupation, country of origin, history of TB, and previous therapy was recorded after careful review of the available medical records for each patient.

Bacteriologic examinations and drug susceptibility testing

Patients with any abnormal radiologic findings or with clinical suspicion of TB received bacteriologic evaluation. Three expectorated specimens of sputum were collected in sterile tubes and immediately taken to the TMCDH mycobacterial laboratory for decontamination with 1% Cetylphidium chloride. The sediment obtained after centrifugation was stained using Ziehl Neelsen's method and implanted on fresh Löwenstein-Jensen culture media. Isolates were tested for susceptibility to 5 first-line anti-TB drugs by using the proportions method. The concentration of drugs in the medium was isoniazid (INH) (0.2μg/mL concentrations), ethambutol (EMB) (5.0 μg/mL), rifampin (RIF) (1.0 μg/mL), streptomycin (SM) (2.0 μg/mL), and kanamycin (KM) (0.2 μg/mL).

In this study, the strain was considered resistant if colonies grew on 1% or more of the surface area of the drug-containing medium at 4 weeks of incubation and good growth occurred on the drug-free medium for any of the drug concentrations specified previously. "Drug-resistant TB" was defined as a TB isolate that was resistant to one or more anti-TB drugs. "MDR TB" refers to organisms that are resistant to two or more anti-TB drugs, including RIF and INH.

Statistical analysis

The prevalence of drug-resistant TB from 1996 through 1999 was calculated only for TB isolates tested for drug susceptibility and for those with previous TB therapy separate from those without previous TB therapy. The drug resistance trends over time were evaluated by the Mantel-Haenszel trend test.[19] Both univariate and multivariate logistic regressions were performed to calculate odds ratio (OR) and 95% confidence intervals (CI) for INH- or RIF-resistant TB and MDR TB. The SAS statistical package was used for the analysis.[20]

RESULTS

Of 522 patients who had isolates that were subjected to susceptibility testing during the study period, 69 patients were excluded from the analysis as a result of growth of mycobacteria other than TB (40 cultures) or nonviability (29 cultures). The remaining 453 patients in our study did not differ significantly ($P > .05$) in age, sex, origin of country, history of TB, previous treatment, or proportion with HIV seropositivity from the 6800 cases of TB reported in Taipei from 1996 through 1999 that were not included in our study.[3]

The trend of resistance rates to the 5 first-line drugs against TB is shown in Table 1. The resistance rate to INH was 22.1% in 1996, and it steadily decreased to 10.8% in 1998, rising to 13.1% in 1999. A similar decrease was seen in the resistance rate to EMB, KM, and MDR TB. In contrast, the prevalence of TB isolates resistant to RIF increased from 17.6% to 19.9% from 1996 through 1998, then decreased to 13.1% in 1999. For SM, an increase from 10.3% to 18.2% was observed in the same period.

Table 1. Trend in resistance to the five first-line drugs against tuberculosis in 453 patients at TMCDH, Taipei, 1996-1999

Drug	Resistant/tested (%) 1996	1997	1998	1999	*P* value for trend
INH	15/68 (22.1)	12/82 (14.6)	18/166 (10.8)	18/137 (13.1)	.004
EMB	21/68 (30.9)	9/82 (11.0)	3/166 (1.8)	4/137 (2.9)	.001
RIF	12/68 (17.6)	16/82 (19.5)	33/166 (19.9)	18/137 (13.1)	.216
SM	7/68 (10.3)	11/82 (13.4)	19/166 (11.4)	25/137 (18.2)	.571
KM	7/68 (10.3)	1/82 (1.2)	5/166 (3.0)	4/137 (2.9)	.154
Any drug	34/68 (50.0)	31/82 (37.8)	46/166 (27.7)	43/137 (31.4)	.240
MDR TB	8/68 (11.8)	7/82 (8.5)	10/166 (6.0)	9/137 (6.6)	.562

Table 2. Resistance to 5 anti-TB drugs in culture-positive TB cases; Taipei, 1996-1999

Drug	New cases (n = 254) resistant (%)	Recurrent cases (n = 199) resistant (%)	All cases (n = 453) resistant (%)
INH	12(4.7)	51 (25.6)	63 (13.9)
EMB	15 (5.9)	22 (11.1)	37 (8.2)
RIF	15 (5.9)	64 (32.2)	79 (17.4)
SM	28 (11.0)	34 (17.1)	62 (13.7)
KM	8 (3.1)	8 (4.0)	16 (3.5)
Any drug	56 (22.0)	98 (49.2)	154 (34.0)

Resistance to one or more of the 5 drugs tested was encountered in 154 (34.0%) of the 453 isolates. Of the 199 patients who received previous TB therapy, 98 (49.2%) had drug resistance (secondary resistance) compared with 56 (22.0%) of the 254 patients without evidence of previous therapy. Resistance to RIF was most common (17.4%), followed by INH (13.9%) and SM (13.7%). EMB and KM had resistance rates of less than 10%. Drug resistance rates for all drugs tested were higher in recurrent cases than they were in new cases (Table 2).

Multiple drug resistance was present in 7.5% of all isolates, with a greater proportion of patients (15.1%) with evidence of previous tuberculosis therapy than without evidence of previous tuberculosis therapy (1.6%) having resistance to more than one drug (Table 3).

A total of 89 (57.8%) of the 154 drug-resistant isolates were resistant to 1 drug, 34 (22.1%) to 2 drugs, 24 (15.6%) to 3 drugs, 6 (3.9%) to 4 drugs, and 1 to 5 drugs. Of the 89 cases with isolates resistant to a single drug, 20 (22.5%) were resistant to INH, 11 (12.4%) to EMB, 31 (34.8%) to RIF, 24 (27.0%) to SM, and 3 (3.4%) to KM. Of 56 drug-resistant isolates from new cases, 42 (75.0%) were resistant to 1 drug. In contrast, the resistance rate to 2 or more drugs was higher in recurrent cases (52.0%) than it was in new cases (25.0%) (Table 3).

As expected, patients with recurrent TB were significantly associated with increased risk of both INH-resistant TB (OR = 5.4; 95% CI, 2.2-12) and RIF-resistant TB (OR = 5.5; 95% CI, 2.2-13). Resistance to INH for new cases and recurrent cases was different in different age groups. New cases were more likely to be associated with the younger age group (<25 years old). Recurrent cases were most likely to be associated with persons aged 25 to 44 years. In contrast, resistance to RIF was rare among patients older than 65 years for either new cases or recurrent cases. Sex, education, nationality, homelessness, HIV infection, excess alcohol use, diabetes mellitus, occupation as a miner, and smoking were not significantly associated with resistance to either of these 2 drugs (data not showing in table form).

The prevalence and ORs for MDR TB associated with potential risk factors are shown in Table 4. Like INH- or RIF-resistant TB, MDR TB was also significantly associated with recurrent TB (OR = 9.4; 95% CI, 2.9-24).

Women were more likely to have MDR TB than were men (OR = 2.2; 95% CI, 1.0-33). The risk of MDR TB was significantly increased among persons who had a college or greater level of education (OR = 2.4; 95% CI, 1.0-3.6). Persons born outside of Taiwan in TB endemic areas were more likely to have MDR TB than were persons born in Taiwan (OR = 3.3; 95% CI, 1.1-34). No significant differences in the overall rates of MDR TB were found for the different age groups.

Table 3. Resistance to one or more drugs in culture-positive TB cases, by combination of drugs in Taipei, 1996-1999

Resistance	Drug combination	New cases (n = 254) resistant (%)	Recurrent cases (n = 199) resistant (%)	All cases (n = 453) resistant (%)
1 Drug	INH	6 (2.4)	14 (7.0)	20 (4.4)
	EMB	7 (2.8)	4 (2.0)	11 (2.4)
	RIF	8 (3.1)	23 (11.6)	31 (6.8)
	SM	18 (7.1)	6 (3.0)	24 (5.3)
	KM	3 (1.2)	0 (0.0)	3 (0.7)
	Total	42 (16.5)	47 (23.6)	89 (19.6)
2 Drugs	INH + RIF	0 (0.0)	10 (5.0)	10 (2.2)
	INH + SM	1 (0.4)	6 (3.0)	7 (1.5)
	EMB + RIF	0 (0.0)	5 (2.5)	5 (1.1)
	EMB + SM	1 (0.4)	0 (0.0)	1 (0.2)
	EMB + KM	3 (1.2)	1 (0.5)	4 (0.9)
	RIF + SM	2 (0.8)	1 (0.5)	3 (0.7)
	RIF + KM	0 (0.0)	1 (0.5)	1 (0.2)
	SM + KM	1 (0.4)	2 (1.0)	3 (0.7)
	Total	8 (3.1)	26 (13.1)	34 (7.5)
3 Drugs	INH + EMB + RIF	1 (0.4)	3 (1.5)	4 (0.9)
	INH + EMB + SM	1 (0.4)	1 (0.5)	2 (0.4)
	INH + RIF + SM	1 (0.4)	12 (6.0)	13 (0.7)
	EMB + RIF + SM	1 (0.4)	1 (0.5)	2 (0.4)
	EMB + RIF + KM	0 (0.0)	3 (1.5)	3 (0.7)
	Total	4 (1.6)	20 (10.1)	24 (5.3)
4 Drugs	INH + EMB + RIF +SM	1 (0.4)	3 (1.5)	4 (0.9)
	INH + RIF + +SM +KM	1 (0.4)	1 (0.5)	2 (0.4)
	Total	2 (0.8)	4 (2.0)	6 (1.3)
5 Drugs	INH + EMB + RIF + SM + KM	0 (0.4)	1 (0.5)	1 (0.2)
Total INH + RIF		4 (1.6)	30 (15.1)	34 (7.5)

However, recurrent cases were more likely to be associated with younger age groups (<25 and 25-44 years). There was no significant association between MDR TB and homelessness, HIV infection, excess alcohol use, diabetes mellitus, occupation as a miner, and smoking.

All of the 154 resistant cases reported were residents of Taipei City (12 districts) and Taipei County. Significantly more patients who lived in Taipei County than those who lived in Taipei City had drug-resistant tuberculosis for all of the drugs examined in this study. Most of resistant to INH, RIF, and multiple drugs was found in Nankang CH'U, Taan CH'U, and Chungchen CH'U, respectively (Table 5).

DISCUSSION

In this study, we estimated the prevalence of drug resistance in culture-positive pulmonary TB cases in Taipei to be very high—34.0%. This prevalence rate is higher than those reported by recent surveys in other countries such as 4.8% in 1995-1996 in New Zealand,[21] 8.2% in 1995 in England and Wales,[21] and 12.9% in 1995 in the United States.[21] Drug resistance among patients without a history of previous therapy had a higher prevalence (22.0%) than was estimated in Japan[9] (5.6%) and Puerto Rico[22] (15.9%). This could be an indication of transmission from inadequately treated persons and a measure of the lack of effectiveness of the treatment programs for patients in the past.

As expected, the prevalence of drug-resistant TB was higher in patients who had previously received therapy. This finding is similar to findings in other studies.[1,13,14,23] Patient noncompliance has been well documented as the most important reason for the relapse of TB disease and the development of drug resistance.[4,16,24,25] It is generally believed that a high level of this type of resistance

Table 4. Risk factors for patients with TB isolated resistant to INH and RIF in Taipei, 1996-1999

	New cases (n = 254)		Recurrent cases (n = 199)		All cases (n = 453)	
Risk factor	**Resistant (%)**	**OR (95% CI)**	**Resistant (%)**	**OR (5% CI)**	**Resistant (%)**	**OR (95% CI)**
Sex						
Men	2/180 (1.1)	1.0	17/152 (11.2)	1.0	19/332 (5.7)	1.0
Women	2/74 (2.7)	2.5 (1.0-3.8)	13/47 (27.7)	2.5 (1.0-4.8)	15/121 (12.4)	2.2 (1.0-3.3)
Age, y						
<25	1/47 (2.1)	1.0	2/9 (22.2)	1.0	3/56 (5.4)	1.0
25-44	0/78 (0.0)	–	10/40 (25.0)	1.1 (0.5-2.2)	10/118 (8.5)	1.6 (0.7-3.0)
45-64	1/72 (1.4)	0.7 (0.2-2.4)	8/55 (14.5)	0.7 (0.2-1.9)	9/127 (7.1)	1.3 (0.4-3.2)
≥65	2/57 (3.5)	1.7 (0.6-4.2)	10/95 (10.5)	0.5 (0.1-2.0)	12/152 (7.9)	1.5 (0.5-2.9)
Education						
Illiterate	0/5 (0.0)	–	1/8 (12.5)	1.0	1/13 (5.6)	1.0
Primary	1/25 (4.0)	1.0	4/35 (11.4)	0.9 (0.2-2.6)	5/60 (8.3)	1.5 (0.5-4.2)
Junior	0/17 (0.0)	–	2/13 (15.4)	1.2 (0.3-4.7)	2/30 (6.7)	1.2 (0.4-3.0)
Senior	0/42 (0.0)	–	3/34 (8.9)	0.7 (0.1-3.2)	3/76 (4.0)	0.7 (0.2-1.9)
College and higher	0/33 (0.0)	–	7/20 (35.0)	2.8 (1.0-5.2)	7/53 (13.2)	2.4 (1.0-3.6)
Nationality						
Taiwanese	3/245 (1.2)	1.0	28/194 (14.4)	1.0	31/439 (7.1)	1.0
Born outside of Taiwan	1/9 (11.1)	9.3 (0.8-40)	2/4 (50.0)	3.5 (0.9-40)	3/13 (23.1)	3.3 (1.1-34)
Previous TB						
No	–	–	–	–	4/254 (1.6)	1.0
Yes					30/199 (15.1)	9.4 (2.9-24)
Homeless						
No	4/252 (1.6)	1.0	30/196 (15.3)	1.0	34/448 (7.6)	1.0
Yes	0/1 (0.0)	–	0/1 (0.0)	–	0/2 (0.0)	–
HIV infection						
No	4/253 (1.6)	1.0	30/197 (15.2)	1.0	34/450 (7.6)	1.0
Yes	0/0 (0.0)	–	0/1 (0.0)	–	0/1 (0)	–
Excess alcohol use						
No	4/229 (1.7)	1.0	27/175 (15.4)	1.0	31/404 (7.7)	1.0
Yes	0/24 (0.0)	–	3/23 (13.0)	0.8 (0.2-4.2)	3/47 (6.4)	0.8 (0.2-2.4)
Diabetes mellitus						
No	2/203 (1.0)	1.0	27/173 (15.6)	1.0	29/376 (7.7)	1.0
Yes	2/50 (4.0)	4.0 (0.9-36)	3/25 (12.0)	0.8 (0.2-4.2)	5/75 (6.7)	0.9 (0.3-2.0)
Occupation as a miner						
No	4/245 (1.6)	1.0	28/187 (15.0)	1.0	32/432 (7.4)	1.0
Yes	0/5 (0.0)	–	1/3 (33.3)	2.2 (0.3-16.1)	1/8 (12.5)	1.7 (0.6-4.6)
Smoking						
No	1/49 (2.0)	1.0	12/56 (21.4)	1.0	13/105 (12.4)	1.0
Yes	1/21 (4.8)	2.4 (0.8-48)	4/17 (23.5)	1.1 (0.5-2.6)	5/38 (13.2)	1.1 (0.5-2.0)

is an indicator of a poorly functioning TB control program at the current time. In this study, resistance to RIF (32.2%) was most common, followed by resistance to INH (25.6%). This finding is consistent with results of studies from Saudi Arabia[14] and India.[12] It is surprising that RIF resistance and not INH resistance was the most frequent resistance found. This may have been due to the relatively early introduction of RIF in 1978 in Taiwan, its more extensive use outside the national TB program for more than 20 years until now, and the unregulated market for antibiotics (ie, RIF is available on the open market) in Taiwan.

Multiple drug resistance was frequent (7.5%), particularly among patients who had been previously treated for TB (15.1%). This prevalence rate is higher than the rates of recent surveys in other countries including France,[21] where MDR isolates were cultured from 15 (0.9%) of 1686 cases of TB reported in 1995, and in England,[21] where 1.9% of 2890 *M tuberculosis* isolates from 1995 were resistant to INH and RIF. The goal of TB therapy is to provide the most effective treatment in the shortest period. In Taiwan, the protocol for the treatment of new cases of TB is a 6-month regimen of medication, such as 2 months of INH, EMB, RIF, and

Table 5. Resistance to INH or RIF in culture-positive TB cases, according to district in Taipei, 1996-1999

District	Resistance		
	INH (%)	RIF (%)	INH and RIF (%)
Taipei County	20/118 (16.9)	23/118 (19.5)	14/118 (11.9)
Taipei city	42/331 (12.7)	55/331 (16.6)	19/331 (5.7)
Sungshan CH'U	3/26 (11.5)	6/26 (231)	2/26 (7.7)
Hsinyi CH'U	3/27 (11.1)	3/27 (11.1)	0/27 (0.0)
Taan CH'U	5/37 (13.5)	11/37 (29.7)	3/37 (8.1)
Chungshan CH'U	4/41 (9.8)	4/41 (9.8)	1/41 (2.4)
Chungchen CH'U	6/24 (25.0)	6/24 (25.0)	4/24 (16.7)
Tatung CH'U	1/15 (6.7)	2/15 (13.3)	1/15 (6.7)
Wanhwa CH'U	4/44 (9.1)	3/44 (6.8)	1/44 (2.3)
Wenshan CH'U	2/29 (6.9)	6/29 (20.7)	1/29 (3.5)
Nankang CH'U	3/8 (37.5)	2/8 (25.0)	1/8 (12.5)
Shihlin CH'U	4/36 (11.1)	6/36 (16.7)	3/36 (8.3)
Neihu CH'U	5/15 (33.3)	3/15 (20.0)	2/15 (13.3)
Peiton CH'U	2/29 (6.9)	3/29 (10.3)	0/29 (0.0)
Total	62/449 (13.8)	78/449 (17.4)	33/449 (7.3)

pyrazinamide, followed by 4 months of INH, EMB, and RIF with a standard dose administered daily. Although this regimen is regarded as highly effective, supplies of effective anti-TB drugs must be accompanied by full supervision of their use. Unfortunately, only a small number of patients with TB are treated with directly observed therapy in Taipei, which has led to noncompliance with prescribed treatment. The results of our preliminary TB epidemiology and its control study[3] revealed that only 47.2% of patients completed a recommended course of therapy within 1 year. Available evidence[4] also indicates that patients with TB in Taipei have great difficulty adhering to therapy; 14.7% of patients undergoing treatment for TB in our study were lost to follow-up and could not be documented as completing therapy. Treatment of patients with pulmonary TB due to *M tuberculosis* resistant to INH and RIF is extremely complicated. Physicians and society must recognize that MDR TB is an ominous, deadly disease. Patients who are treated unsuccessfully but remain alive pose a major public health problem. They must be isolated because of the risk of transmitting virtually untreatable drug-resistant disease. The problem of drug resistance is manmade and thus can be prevented. Intervention strategies should focus on the prevention of patient noncompliance.

Another important reason for the high prevalence of MDR TB (7.5%) in Taipei is the increasing number of TB cases among persons born outside Taiwan. The effect of foreign persons on MDR TB is predominantly an urban phenomenon (OR = 3.3; 95% CI, 1.1-34) in Taipei, where the number of foreign persons in Taipei comprised nearly 80% of total national foreign persons. Foreign persons mostly come from Southeast Asian countries, particularly Thailand and the Philippines, where TB is most prevalent. It is speculated that persons born outside Taiwan who have TB may have a higher prevalence of drug resistance than do persons born in Taiwan because TB control programs in these countries have failed to achieve high cure rates, even after the introduction of short-course chemotherapy.[26] Import of either primary or secondary drug-resistant TB is thus possible and cannot be prevented in Taipei because persons born outside of Taiwan and in the country illegally can escape screening, and legal immigrants, like Taiwanese persons, may have drug-resistant TB years after the screening process.

The American Thoracic Society and the Centers for Disease Control and Prevention[27] suggested that standard initial regimens contain INH, EMB, RIF, and pyrazinamide until drug susceptibility results are available. EMB should be included in the initial regimen unless community rates of INH resistance are less than 4%.[28,29] In view of the high prevalence of INH resistance (13.9%) and low EMB resistance (8.2%) in Taipei, we recommend that all persons in Taipei in whom TB is diagnosed should initially receive 4-drug therapy (INH, EMB, RIF, and pyrazinamide) to prevent the emergence of drug-resistant TB.

In conclusion, despite the decline in MDR TB over the 1996 through 1998 period, the prevalence of INH resistance remains as high as 13.1% in 1999. An initial 4-drug regimen should be encouraged for the treatment of patients with TB to prevent treatment failure. We also recommend that all initial cultures of *M tuberculosis* in Taipei be tested for drug susceptibility because of the

impact of drug resistance on the response to therapy. Patients who have previously received therapy and who were born outside Taiwan in TB endemic areas should receive directly observed therapy with careful clinical and bacteriologic follow-up. All their contacts should have priority for evaluation to identify secondary cases. The TB control program surveillance system should collect data on drug resistance so that the incidence and prevalence can be tracked and analyzed. Implementation of these recommendations should increase the therapeutic response rate of patients with TB, diminish the transmission of drug-resistant disease, and prevent the appearance of newly acquired resistance. In addition, with high rifampin resistance (17.4%), the regulated market for RIF is essential in Taiwan.

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