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<th><strong>Title</strong></th>
<th>Tuberculosis in Hong Kong - patient characteristics and treatment outcome; 香港結核病患者的特徵與治療結果</th>
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<td><strong>Author(s)</strong></td>
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Tuberculosis in Hong Kong—patient characteristics and treatment outcome

**Objectives.** To identify the general characteristics of patients with tuberculosis, and to evaluate their treatment outcomes.

**Design.** Retrospective study.

**Setting.** Tuberculosis and Chest Service, Department of Health, Hong Kong.

**Subjects and methods.** All patients with tuberculosis registered for treatment from 1 January 1996 to 31 December 1996 were included in the study. Information was extracted from their medical records at treatment commencement and at 12 and 24 months after treatment was instigated. Data gathered included demographic data, past treatment, site of disease, case category, treatment regimen, bacteriological status, and treatment outcome.

**Results.** There were 5757 patients for analysis. Approximately one third of patients were aged 60 years or older, and 69.1% were male. Pulmonary disease alone occurred in 77.7% of patients, while both pulmonary and extrapulmonary diseases occurred in 8.6%. New patients comprised 84.6% of cases, and 16.3% had concomitant illnesses. There was excess risk of disease among patients who were male, elderly, or who had silicosis. Only 0.1% of patients were co-infected with human immunodeficiency virus infection. Among the 5757 cases evaluated, 1324 (23.0%) were new patients with a positive sputum smear, 299 (5.2%) were patients who were retreated with a positive sputum smear, and 4134 (71.8%) were new or retreatment patients with a negative sputum smear. The overall treatment completion rates at 12 and 24 months were 80.4% and 84.8%, respectively. Males and patients aged 60 years or older had lower treatment completion rates. Non-adherence, transfer to other services, and mortality among the elderly were key factors influencing treatment outcomes. Co-morbidity was associated with better case-holding, and this more than compensated for its effect on prolongation of treatment and mortality.

**Conclusions.** There was an excess risk of tuberculosis among male and elderly patients, who also had a less favourable outcome. Active screening of clearly identified risk groups may be appropriate but requires the completion of more in-depth studies and careful cost-effectiveness analyses. Further efforts with respect to case-holding are indicated to address treatment defaulting and transfer rates.

**Key words:**
- Demography
- Disease management
- Treatment outcome
- Tuberculosis

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Introduction

The notification rate for tuberculosis (TB) in Hong Kong declined significantly between 1950 and 1990. In 1995, the notification rate was at a low of 100.9/100,000. Since 1996, however, there has been an increase in the notification rate—117.3/100,000 in 1998 and 113.7/100,000 in 2000—and the rate has since failed to decline.¹

The exact reasons for the recent stagnant trend in the TB notification rate in Hong Kong are not known. In many countries, poor treatment and acquired HIV infection have been found to be the major reasons for the resurgence of TB.² In view of such observations, the World Health Organization (WHO) has recommended that directly observed treatment (DOT), short course (DOTS) is the treatment of choice for TB.³ Hong Kong, however, was among one of the first places to implement DOT in the 1970s,⁴ and this was the probable reason for the dramatic decline in the rate of TB from 1970 to the 1980s. The local prevalence of HIV infection has always been relatively low.⁵ While there has been an improvement in notification of TB by physicians,⁶ it is likely that other factors are also contributing to the current elevated rates. This study was undertaken to examine the reasons for the failure of the TB rate to decline. The aim was to identify the general characteristics of patients with TB seen by the Hong Kong Government Tuberculosis and Chest Service (TB&CS), and to evaluate their treatment outcome.

Subjects and methods

All patients registered for treatment of TB with the TB&CS (which treats approximately 80% to 90% of all notified TB patients in Hong Kong) from 1 January 1996 to 31 December 1996 were included in the study. The year 1996 was chosen because an increase in the TB notification rate was first noted in that year, and population statistics were also available through a census conducted during that year. In addition, in 1996, a set of programme forms was introduced for systematic data collection of all patients with TB managed by the TB&CS. The programme forms recorded the following information: name, date of treatment commencement, age, sex, previous treatment, site of disease (pulmonary or extrapulmonary), and other medical conditions. The forms also recorded bacteriological status before treatment, at 2 months, 6 months, and at the end of treatment, and treatment outcome at intervals after treatment commencement. Data were obtained for each patient through the completion and submission of programme forms by clinicians at the TB&CS at the start of treatment and at 12 and 24 months after the start of treatment. These data were supplemented by a review of medical records for patients with missing forms, missing information on forms, or inconsistent information between completed forms, and for all patients with extrapulmonary TB. The data were entered into the Epi-Info database (Version 6; Centers for Disease Control and Prevention, Atlanta, US) and checked for accuracy by another person. The data were then exported to the Statistical Package for the Social Sciences (Windows version 6.0; SPSS Inc., Chicago, US) and edited before analysis.

Analysis

Definitions used in the study are outlined in the Box. They were modified slightly from those provided by the International Union Against Tuberculosis and Lung Diseases.⁷

Statistical analyses were carried out using Statistical Package for the Social Sciences (Windows version 6.0). Continuous variables were compared using the Student’s independent samples t test. Proportions were compared using the Chi squared test. Differences were considered significant at P<0.05.

Results

There were 5971 patients registered with the TB&CS for treatment of TB in 1996. Of these, 103 had an incorrect diagnosis, 106 had an atypical mycobacterial infection, and five received chemoprophylaxis only. The number of valid patients for the following analysis was thus 5757.

Patient characteristics

Patient characteristics are summarised in Table 1. This shows that TB affected men more frequently than women (69.1% versus 30.9%; P<0.01) in Hong Kong. Approximately one third of patients were aged 60 years or older. The mean age of male patients was significantly older than that of female patients (50.6 years versus 43.5 years; P<0.01). The male to female ratio was higher among those aged 60 years or older than among those younger than 60 years (3.36:1 versus 1.85:1; P<0.01).

The majority of patients had pulmonary disease. Pulmonary disease alone occurred in 77.7% of patients. Extrapulmonary TB without lung involvement occurred in 13.7%, while both extrapulmonary and pulmonary diseases occurred in 8.6% of patients. Extrapulmonary disease tended to occur more commonly among women.

The majority of patients (84.6%) were new patients. There were more men than women treated for relapsed disease (15.1% versus 8.0%; P<0.01), and also more men with a history of previously defaulting treatment (2.8% versus 0.7%; P<0.01).
Concomitant illnesses occurred in 16.3% of all patients, and was significantly higher among men than women (18.3% versus 11.9%; P<0.01), and also in those aged 60 years or older compared with those younger than 60 years (27.8% versus 10.3%; P<0.01). Diabetes, silicosis, liver disease, and lung cancer were common concomitant medical illnesses associated with TB.

Almost 10% of all patients with TB also had diabetes at the time of diagnosis. Of the 555 patients with diabetes, 75.1% were male, and 57.6% were aged 60 years or older. The mean age (standard deviation) for this group of patients was 60.6 years (12.4 years). Only six (0.1%) patients had documented HIV infection.

### Treatment outcomes

Among the 5757 patients, 1324 (23.0%) were new patients with a positive sputum smear, 299 (5.2%) were retreatment patients with a positive sputum smear, and 4134 (71.8%) were sputum smear-negative patients, including both new and retreatment patients (Table 2).

At 12 months, 80.4% of patients had completed treatment, 8% had defaulted, 3.6% had been transferred, 3.9% had died, and 4.1% were still receiving treatment. However, for retreatment patients with a positive sputum smear at treatment commencement, only 71.6% completed treatment, 10.0% defaulted treatment, 2.3% were transferred, 6.0% had died, and 10.0% were still receiving treatment.
were also significant differences in outcome between men and women, between young and elderly patients, and between those with and without co-morbidity. A total of 82.9% of female patients completed treatment compared with 79.3% of male patients (P<0.05). A greater proportion (82.7%) of patients younger than 60 years completed treatment compared with 76.0% of those aged 60 years or older (P<0.05). Mortality for those younger than 60 years was only 1.0% in sharp contrast to 9.4% for those aged 60 years or older (P<0.01). More patients with concomitant medical conditions (83.3%) completed treatment compared with those without such conditions (83.3% versus 80.0%; P<0.05) [Table 3].

At 24 months, 84.8% of all patients had completed treatment. However, only 81.3% of retreatment cases with an initial positive sputum smear had completed treatment. More female patients than male patients had completed treatment (86.8% versus 83.8%; P<0.05), as had more patients younger than 60 years (86.3% versus 81.9%; P<0.05). The difference in number of patients with concomitant medical conditions who completed treatment compared with those without such conditions was more marked (92.4% versus 83.6%; P<0.001).

Of the 4880 patients who completed treatment, 76 had a relapse of TB, and this was bacteriologically confirmed.
for 50 patients. Only 59 of the 450 patients who defaulted treatment were found and retreated.

**Discussion**

According to the 1996 by-census, only 14.3% of the population were aged 60 years or older while, as shown in Table 1, 34.5% of the patients with TB were in this age-group. There was clearly an excess of elderly patients with TB seen at the TB&CS. The 1996 notification registry figures indicate a generally increasing risk of TB with age (Fig 1). While the overall notification rate was 101.0 patients per 100,000, the notification rate was as high as 361.4 patients for those aged 75 years or older. According to data from the Census and Statistics Department and from the TB notification registry, there have been increasing proportions of elderly citizens within the local population, and an even more marked increase in the proportion of elderly among TB patients during the past few decades (Fig 2). In 1971, only 8.0% of patients with TB were aged 65 years or older, with 1.7% aged 75 years or older. The corresponding percentages had increased to 36.2% and 19.0%, respectively, in 2001. Since the population in Hong Kong is ageing, it is likely that elderly patients will account for an increasing proportion of the total TB caseload. This may be one of the factors accounting for the persistently high rate of TB reported in Hong Kong.

As reported in a previous paper on sex differences in TB, men had a higher rate of TB than women in all age-groups. The male to female ratio was higher among those aged 60 years or older. Male patients aged 60 years or older constituted 26.6% of the total patient pool in this sample, a sizeable risk group.
Although this study covered only 89% (5757/6501) of all TB notifications, excluding patients managed outside the TB&CS, it may serve to highlight other potential risk factors for TB in Hong Kong residents. Silicosis is a well-known risk factor for TB and there were 84 patients with TB and silicosis in this study. If the number of surviving patients with confirmed silicosis in Hong Kong was to be approximately 3000, the annual risk of TB among people with silicosis was approximately 2800/100000. This figure is much higher than the overall annual notification rate of 101/100000 in 1996. However, the absolute number of patients with silico-TB was small, and these patients were unlikely to have affected the overall trend in TB rates in Hong Kong.

In this study, only six patients with TB were known to be infected with HIV. Voluntary HIV testing was offered to all patients with TB attending the TB&CS, and the uptake rate was approximately 90%. The low incidence of HIV infection in this study is supported by the results of unlinked anonymous assays periodically carried out on samples from patients attending the TB&CS. These have given the incidence of HIV infection as approximately 0.13% to 0.70% between 1990 and 2000. Such low incidence reflects the relatively low incidence of HIV infection in the general population. Indeed, the HIV seropositive rate among blood donors is only 5/100000, and the incidence in the general population is likely to be well below 0.1%. These results suggest that while the risk for TB is high among patients with HIV infection, HIV infection is unlikely to have contributed to the stagnation in TB rates seen in Hong Kong during the past decade.

Table 4 shows the estimated rate of TB among patients with diabetes. Using the number of patients with TB identified with diabetes in this study and the population at risk based on local statistics, the rate of TB for each age-group was estimated. In 1996, 10% of all patients with TB treated in the chest clinics had diabetes. The TB rates among individuals with diabetes did not differ greatly from those among the general population, with the exception of men aged between 45 and 54 years. It should be stressed that TB patients with diabetes managed outside the TB&CS have not been included in this study. A higher prevalence of diabetes could well be found among patients managed solely inside hospitals, and thus the rate of TB among patients with diabetes may have been underestimated.

At present, the overwhelming majority of patients with TB in Hong Kong are identified through passive case finding, that is, encouraging patients with symptoms suggestive of TB to come forward for screening. An active screening programme exists mostly for examination of contacts. The finding of high-risk groups raises the question of whether active screening for TB should be extended to these groups. In a series of studies conducted between 1960 and 1973 in different parts of the world, it was shown that, even in places with active case-finding programmes, approximately 60% of sputum smear-positive patients were discovered because of their symptoms. Only 20% of new patients were found through indiscriminate mass radiography alone. This is explained by the relative rapidity with which the infection develops, with symptoms developing more rapidly than repeat screening can be accomplished.

In a survey completed by the TB&CS in 1981, the yield of patients with active TB was 10% to 15% among new clinic attendees, well over the likely yield among any of the risk groups found in this study. Screening directed at latent infection instead of active disease may potentially give a higher yield. However, the existing screening and treatment tools for latent TB infection are far from ideal. The tuberculin test is confounded by previous bacille Calmette-Guérin vaccination and atypical mycobacterial infection, and only about 10% of immunocompetent patients with latent TB infection ever develop the disease. Treatment of latent TB often involves a long duration of treatment with drugs that have potential for adverse events. These factors seriously limit the widespread application of such an approach. Therefore, passive case finding must remain one of the cornerstones of the local TB control programme, as in most other areas of the world.

Among household contacts, a regularly screened high-risk group, the yield of active TB has been in the order of 1% to 2%, doubling to more than 3% at the extremes of

<table>
<thead>
<tr>
<th>Age-groups (years)</th>
<th>No. in Hong Kong population with diabetes in 1996</th>
<th>No. with tuberculosis and diabetes in this study</th>
<th>Estimated No. of patients with tuberculosis among diabetic individuals in Hong Kong* (per 100 000)</th>
<th>No. of patients with tuberculosis in the general population of Hong Kong (per 100 000)</th>
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<tbody>
<tr>
<td>Male</td>
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<tr>
<td>25-34</td>
<td>11 164</td>
<td>8</td>
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<tr>
<td>35-44</td>
<td>34 945</td>
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<td>65-74</td>
<td>61 061</td>
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* Tuberculosis patients with diabetes treated outside the TB&CS have not been included
Drug resistance in Hong Kong during the period from 1986 to 1990 was evaluated by Chaulk and Kazandjian, who reported the findings of the Public Health Tuberculosis Guidelines Panel in 1998 on treatment outcome in the US. The panel chose 27 studies for review of treatment completion for pulmonary TB and, among these, 18 had implemented DOT. They were classified into three categories. In the first category, the 12 studies based on comprehensive, patient-centred DOT strategies, such as fully supervised DOT with multiple incentives and enablers (enhanced DOT), reported the highest treatment completion rates. The completion rates ranged from 86.0% to 96.5% for a variety of patient populations, including alcoholics, patients with substance abuse problems, incarcerated patients, homeless persons, and patients infected with HIV. The rate of TB relapse reported in these studies ranged from 0% to 11.5%. For the four studies of DOT in the second category, without extensive enablers and incentives, treatment completion rates ranged from 85.0% to 87.6%, and reported rates of relapse ranged from 0.8% to 4.9%. For the two studies in the third category with modified DOT, supervision was used for only part of the treatment period (typically during the hospitalisation phase of therapy), and thereafter, patients were self-supervised. This strategy appeared to be less effective, with treatment completion rates ranging from 78.6% to 82.6%. The first two categories included two studies of DOT from Hong Kong, evaluating the treatment programme in the 1970s and 1980s.

In 1996, among patients attending the TB&CS, 80.6% completed treatment at 12 months, but 84.8% completed treatment by 24 months. Thus, the treatment completion rate in Hong Kong at 12 months, although quite reasonable, still fell somewhat short of the goal of the 85% treatment success rate at 12 months for national tuberculosis programmes recommended by the WHO for all active cases. As shown in Table 2, the treatment default rate at 12 months was 8.0%, accounting for 40.7% (460/1129) of all unfavourable outcomes, while the transfer rate was 3.6%, accounting for 18.5% (209/1129) of all unfavourable outcomes. As patients who default treatment may remain a source of infection and also acquire drug resistance, this group may have contributed in part to the persistently high rate of TB in Hong Kong. The current DOT programme employed by the Hong Kong TB&CS uses a combination of incentives and enablers, including education for patients and their families, intermittent client-focused regimens, incentives such as money for extra nutrition, referrals to other social services, as well as the use of outreach teams and tracing of patients who default treatment. Surveillance of Mycobacterium tuberculosis drug resistance in Hong Kong during the period from 1986 to 1999 showed a significant decline in drug resistance. The overall resistance to one or more drugs was reduced from approximately 17% to 12% for new patients and from 36% to 25% for retreatment patients, while the corresponding figures for multidrug resistance were reduced from 2.7% to 1.0% and from 15.9% to 8.3%, respectively. Notwithstanding the data presented, more in-depth studies are required to examine factors that may affect case-holding in Hong Kong among a relatively mobile population with freedom of choice in seeking medical treatment.

In this study, the mortality rate for all patients with TB at 12 months was 3.9%, accounting for approximately 20% (222/1129) of the patients with unfavourable outcome. There was also a sharp contrast in mortality rates between elderly and younger patients. As more than one third of patients were aged 60 years or older, the higher mortality rate may have contributed to the overall low treatment completion rate. The high prevalence of co-morbidity in this study is consistent with the relatively high proportion of elderly patients. As shown in Table 3, 8.8% of patients with co-morbidity were receiving treatment at 12 months compared with 3.4% of those without co-morbidity. This may reflect the more frequent need to modify the treatment regimen, either to decrease the risk of side-effects or as a result of actual side-effects. Although 4.1% of patients were still receiving treatment at 12 months, accounting for another 20% (238/1129) of patients with unfavourable outcomes at 12 months, most of these patients were eventually successfully treated as reflected by the better treatment completion rate at 24 months. It is evident from Table 3 that the lower treatment defaulting and transfer rates associated with co-morbidity more than compensated for the effect of prolonged treatment and higher mortality. Indeed, the treatment completion rates seen for those with concomitant medical conditions were higher than those without co-morbidity at both 12 months and 24 months.

**Conclusion**

This study found an excess of TB disease risk and a less favourable treatment outcome for elderly, male patients in Hong Kong. While consideration should be given to extending active screening programmes to such clearly identified risk groups, further studies and careful cost-effectiveness analyses are called for before implementation of such programmes is indicated on a service-wide scale. The treatment success rate seen at 12 months was reasonably good, although short of the WHO goal of 85%. More in-depth studies and efforts with respect to case-holding should also be considered to address treatment default and transfer rates.

**Acknowledgements**

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