A CONCISE GUIDE TO TUBERCULOSIS CONTROL IN WESTERN AUSTRALIA

By

SC Pang
Perth Chest Clinic
Western Australia
First draft 1999, finalised 2001

TABLE OF CONTENTS

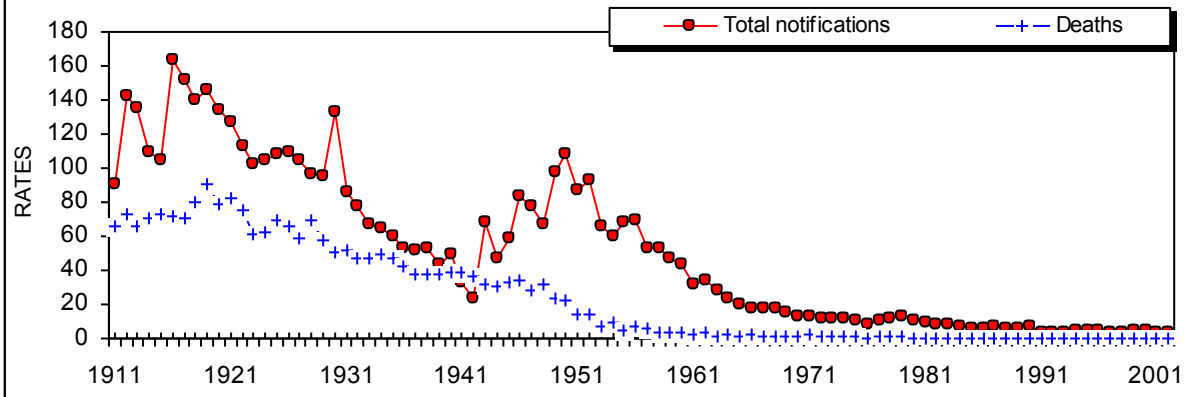
I. INTRODUCTION

The very low rates of annual tuberculosis notification in Australia create a mirage, blurring our vision to the rampant scourge of the disease in many parts of the world and distracting our mission towards a concerted commitment to its elimination.

In 1993 the World Health Organisation (WHO) declared tuberculosis (TB) a global emergency[1] and its latest Report 2002 revealed virtually no change in the global case notification rate since 1980 (60 per 100,000).[2] The decline in the United States and Western Europe following the 1986 resurgence has been offset by the rising trend in Central and Eastern Europe (8% per year) and some Eastern and Southern African countries (10% per year). In a press release at the closure of the fiftieth session of the WHO Regional Committee for the Western Pacific in 1999, the Regional Director, Dr Shigeru Omi, declared a "tuberculosis crisis" in the Region. It was estimated that in 1998 there were 1.96 million new cases and 355,000 people died from TB in the Region.

The situation in Australia, one of the member countries of the Western Pacific Region, however, is quite different. From 1986 to 2000 the national annual notification rate varied between 5 and 6 per 10^5 population and in 2000, 78% of them were from people born overseas.[3] In Western Australia (WA) the corresponding rate has been under 5.0 per 10^5 since 1991 while that of TB-related deaths consistently below 1 per 10^5 person-years (Figures 1) for more than 25 years.

Figure 1: TUBERCULOSIS IN WESTERN AUSTRALIA INCIDENCE RATES PER 100,000 POPULATION 1911-2002



Pulmonary TB only before 1943. Atypical TB excluded after 1954.
Figures to 1990 include, and those after exclude diagnoses outside WA.

The highly successful Australian TB Campaign[4] of 1948-76, which reduced the annual notification rates in this country from 50 to 10 per 10^5 population, led to a premature sense of complacency. Since then the National TB Advisory Council was dissolved and national TB statistics were not maintained for many years. In most States/Territories, the control of the disease has been subsumed within the general medical system and the traditional culture of the TB clinic has largely disappeared. The very low notification rates mean negligible exposure to the disease for most medical practitioners. It is therefore not unexpected that expertise and alertness in TB control have dwindled.

Numerous signs have emerged, indicating that the situation has not continued to improve since the Campaign finished. In the 25-year period of the Campaign the national incidence rates were reduced five-fold but less than halved in the subsequent 25 years. State/Territory TB control bodies are either disorganised or under great resources constraints from what is now well known as governments' "U-shaped curve of concern".[5] "When, with any disease, rates are high, resources are provided to bring

the rates of the disease down. When the disease rates fall, governments eliminate the programs which could potentially eliminate the disease, thus ensuring that the rates go back up." Our obligation and commitment to accept immigrants, including many from high prevalence areas, will suffice to maintain the notification rates. Human immunodeficiency virus (HIV) infection, the greatest ally to TB in inflicting human sufferings, is still lurking around with no sight of a cure or decline. The situation is made worse by the global economic downturn and political turmoils that increase the number and hardship of the socially disadvantaged minority groups. Delay in the detection of TB or initiation of therapy remains common and the annual number of cases undiagnosed until death[6-8] persists with no indication of improvement. Finally we have no idea about the size of the infection source in the community as immigrants continue to reactivate their TB throughout their lifetime after settlement in Australia.

Literature and writings on the subject have grown astronomically since the resurgence of TB in the mid-1980s. They are, however, either too specialised or have little local or practical applications. Due to the vastness of the country and the small number of annual notifications, Australia can no longer sustain the traditional infrastructures of TB clinics. Respiratory, infectious diseases and general physicians have become increasingly involved with the diagnosis and treatment of the disease. Most of them will not be seeing more than a dozen of cases in a year. There is therefore a need for basic information on the control of the disease to this new breed of part-time phthisiologists in Australia.

The monograph is written with this in mind and consists of notes based on available evidence and the author's thirty years of experience with the disease. Since experience, as well as evidence is essential in the management of this condition, the information aims to assist clinicians for whom patients with TB will be in the minority. However, as with any treatment, individuals need to take responsibility for understanding the various scenarios where these general guidelines may not apply.

References

1. Nakajima H. Tuberculosis: a global emergency. *World Health 1993*; 46th Year No 4, July-August. Geneva, Switzerland: World Health Organization, 1993.
2. World Health Organization. Global Tuberculosis Control: Surveillance, Planning, Financing, WHO Report 2002. Geneva, Switzerland, WHO/CDS/TB/2002.295.
3. Lin M, Spencer J, Roche P, McKinnon M and the National TB Advisory Committee for the Communicable Diseases Network Australia. Tuberculosis notifications in Australia, 2000. *Comm Dis Intell* 2002; **26(2)**:214-25.
4. Porter RM, Boag TC. The Australian Tuberculosis Campaign 1948-1976. Melbourne: Robert Menzies Memorial Foundation Ltd 1991.
5. Reichman LB. Tuberculosis elimination-what's to stop us? *Int J Tuberc Lung Dis* 1997; **1**(1):3-11.
6. Rieder HL, Kelly GD, Bloch AB, Cauthen GM, Snider Jr DE. Tuberculosis diagnosed at death in the United States. *Chest* 1991; **100**:678-81.
7. Xie HJ, Enarson DA, Chao CW, Allen EA, Grzybowski S. Deaths in tuberculosis patients in British Columbia, 1980-1984. *Tuberc Lung Dis* 1992; **73**:77-82.
8. DeRiemer K, Rudoy I, Schecter GF, Hopewell PC, Daley CL. The epidemiology of tuberculosis diagnosed after death in San Francisco, 1986-1998. *Int J Tuberc Lung Dis* 1999; **3**(6):488-93.

II. CAUSATION AND TRANSMISSION

In spite of the many horrible names attached to tuberculosis, its causative agent, the M tuberculosis complex, is not an efficient infecting microbe.

The tubercle bacillus

Human TB is the result of infection from the *Mycobacterium tuberculosis complex,* which refers mainly to the following three species:

- *Mycobacterium tuberculosis (hominis),*
- *Mycobacterium (tuberculosis) bovis, and*
- *Mycobacterium africanum*.

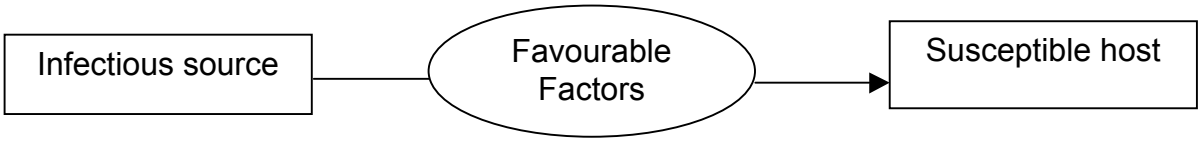
They are collectively called the tubercle bacilli. In Australia *M. tuberculosis* accounts for over 99% of the notifications. Although *M. bovis* is responsible for less than 1% of the cases, it is important to recognise because of its natural resistance to pyrazinamide. Bacille Calmette Guérin (BCG), an attenuated strain of *M. bovis*, is generally non-pathogenic but may cause disseminated disease in the immunocompromised (including the HIV infected) and occasionally in those where BCG is instilled for the treatment of bladder cancer.

Transmission

The disease is most commonly spread by droplet nuclei derived from infectious aerosols generated during expulsive respiratory efforts such as coughing, sneezing, shouting and laughing. Infrequent modes of transmission include ingestion from the digestive system and implantation through body wounds. Spitting alone is an unlikely cause of spread unless it is associated with expectoration or TB in the oral cavity, which is rare.

The transmission of TB requires a combination of three conditions: an infectious source, a susceptible host and favourable environmental factors (Figure 1).

Figure 1: The transmission of tuberculosis



- Sputum smear positive TB
- Lung cavitation
- Respiratory/laryngeal/oral TB
- Cough/forced expiratory manoeuvres
- Not on adequate treatment
- Multidrug resistant TB

- Infectious nuclei
- Sufficient exposure (time/space)
- Overcrowding
- Poor ventilation
- Climatic conditions

- HIV infection
- Immunosuppression
- Other medical conditions
- General resistance complex

THE SOURCE

The infectious source is commonly a patient with pulmonary or upper respiratory TB, whose expectorated sputum samples are positive for acid-fast bacilli (AFB) on microscopy. The degree of infectiousness closely follows the semi-quantitative grading of the smear positivity from a reliable laboratory. In areas like WA where environmental Mycobacteria are prevalent, it is important to ensure that the bacilli are from the *M. tuberculosis complex* (by culture or direct molecular testing).

For public health reasons a patient with positive smears on bronchoscopic aspirates or positive sputum culture only should be considered potentially infectious. The same applies to those with cavitation or extensive infiltrates in their chest x-rays and laryngeal/oral TB before microscopy results are available.

The risk is greatest when cough is present, before the diagnosis is suspected, prior to the start of adequate medical treatment or with multidrug resistant TB before the results of susceptibility tests are known.

That a patient may be considered non-infectious after two weeks of standard therapy is perhaps largely true but should not be taken in isolation. It is acceptable in practice provided that the disease is not extensive, the cough has subsided, the organism is fully sensitive to the drugs used, there is complete treatment compliance and any subsequent contacts are not immunocompromised. For specific purposes such as long distance travel in commercial carriers, a better guide would be the conversion of sputum smears to negative on three consecutive mornings. In other situations such as health workers with TB returning to the direct care of patients, clearance may only be acceptable with negative sputum cultures or on completion of successful antituberculosis treatment.

Extrapulmonary TB alone is not infectious. The inadvertent irrigation of a TB abscess in an enclosed area is a rare exception.

THE HOST

Strictly speaking all human beings, including those with successful BCG vaccinations, are susceptible to infection by the tubercle bacilli. There are, however, groups of conditions that predispose persons to a much higher risk not only of being infected but also of the infection progressing or reactivating to disease. These include:

- HIV infection.
- Other immunodeficiency states and persons on immunosuppressive therapies.
- Certain medical conditions such as diabetes mellitus, chronic renal failure, silicosis, gastro-intestinal bypass surgery, and malignancies.
- Factors that lower the “general resistance complex” such as extreme ages, certain genetic phenotypes, and malnutrition states.

The relative risks[1] of some of the conditions are well publicised and are reproduced in Table 1.

THE ENVIRONMENT

The probability of a susceptible host to be infected relates to the concentration of tubercle bacilli in the environment, which in turn is determined by:

- The number of infectious particles produced by the patient,
- The closeness of the contact,
- The total duration of exposure,
- The ventilation system and any germicidal installations (eg ultraviolet irradiation), and
- Climatic factors (temperature/ humidity).

The tubercle bacilli can survive for long periods of time outside the human body in dark, damp or

cold conditions. On the other hand two minutes under direct sunlight and five minutes in boiling water are sufficient to kill them. Simple common sense such as covering the mouth when the patient coughs or sneezes, expectorating into tissues that can be readily disposed and window extraction fans can go a long way in reducing the spread of the disease. TB is not transmitted by fomites. However the most powerful weapon for its prevention lies in the early detection and proper treatment of patients with active diseases.

Table 1: Risk factors for tuberculosis following infection

Risk factor	Absolute incidence per 1,000 person-years	Relative odds	Relative risk
Infection >7 yrs past	0.7		
Infection <1 yrs past	10.4		
HIV* infection	79		
AIDS†			170.3
Fibrotic lesion	2.0-13.6		
Silicosis		34	30
Carcinoma of head or neck			16
Haemophilia			9.4
Immunosuppressive treatment			11.9
Haemodialysis			10-15
Underweight			2.2-4
Diabetes mellitus			2.0-3.6
HLA‡-A11-B15		3.6	
HLA-DR2		1.6	
Smoking, heavy			2.2
Gastrectomy			5
Jejunoileal bypass			27-63

Adopted from HL Rieder and co-authors (1989)[1].
*Human immunodeficiency virus; †Acquired immunodeficiency syndrome.
‡Human leukocyte antigen.

References

1. Rieder HC, Cauthen GM, Comstock GW, Snider Jr DE. Epidemiology of tuberculosis in the United States. *The John-Hopkins University School of Hygiene and Public Health*, Vol 11, 1989:79-98.

III. THE NATURAL HISTORY OF TUBERCULOSIS

In the caring of an individual with tuberculosis, do not lose sight of the social and community aspects of the disease.

The developments following the introduction of the tubercle bacilli into the human body can be studied pathologically, immunologically, epidemiologically and/or clinically. Although of great fundamental importance, the first two aspects have little direct application in the control of the disease and will be omitted from further discussions.

The natural history of tuberculosis in an individual

The clinical events after the primary infection by the tubercle bacilli in an immunocompetent individual are best described in the timetable of TB first put forward by Wallgren[1] in 1948 (Table 1).

Table 1: The timetable of tuberculosis

Months (from infection)	
	Infection
0	Pre-allergic phase
	Tuberculin sensitivity
1 - 2	Fever
	Erythema nodosum
	Primary complex
	Haematogenous spread
3 – 5	Bacteraemia
	Meningitis
	Miliary/ disseminated tuberculosis
	Pleural effusion
4 – 9	Peritonitis
	Segmental lung lesions
	Regression (majority)
12 - 36	Post-primary tuberculosis
	Skeletal tuberculosis

Modified from A Wallgren (1948)[1]

Usually the affected person is unaware of the infection and has no specific symptoms or signs unless the disease is caused by cutaneous implantation. A latent period called the pre-allergic phase lasts for 4 – 8 weeks during which even the tuberculin test is negative. Then the signs of a primary infection appear, the most consistent of which is the positive tuberculin reaction. A mild or transient febrile episode may be noticed and less commonly erythema nodosum over the shins. A primary complex (consisting of a demonstrable focal lesion and a regional lymphadenitis) if present completes the classical picture.

In the third to fifth months following infection, a brief phase of haematogenous spread or bacteraemia takes place with the lodgement of tubercle bacilli in different parts of the body. This results in the development of the most serious forms of the disease (such as meningeal, miliary and disseminated TB) in a small proportion of people, commonly children under five years of age. At about the same time and up to the ninth month, other forms of primary TB (such as pleural effusion, peritonitis and segmental disease in the lung) may appear.

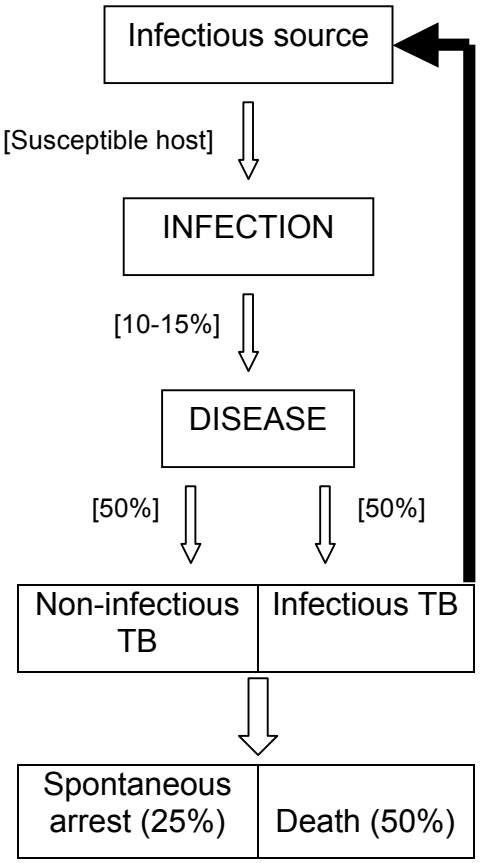
In the great majority of the normal population the disease then regresses into the dormant phase with the gradual building up of one's specific immunity. In a small proportion, however, it progresses directly into the post-primary diseases. It is estimated that the overall life long risk of developing active TB after infection is 10-15%[2] and about half of them will have it within five years. It is important to remember that the disease may reactivate at any time when the body resistance is decreased.

When the disease reactivates or when the person is re-infected the second time, the disease follows the post-primary pattern. It is generally localised and without the haematogenous phase unless the person is immunocompromised.

The natural history of tuberculosis in a community

While we best understand TB in an individual from Wallgren's timetable, to control the disease in a community we need to know its natural behaviour in a population (Figure 1).

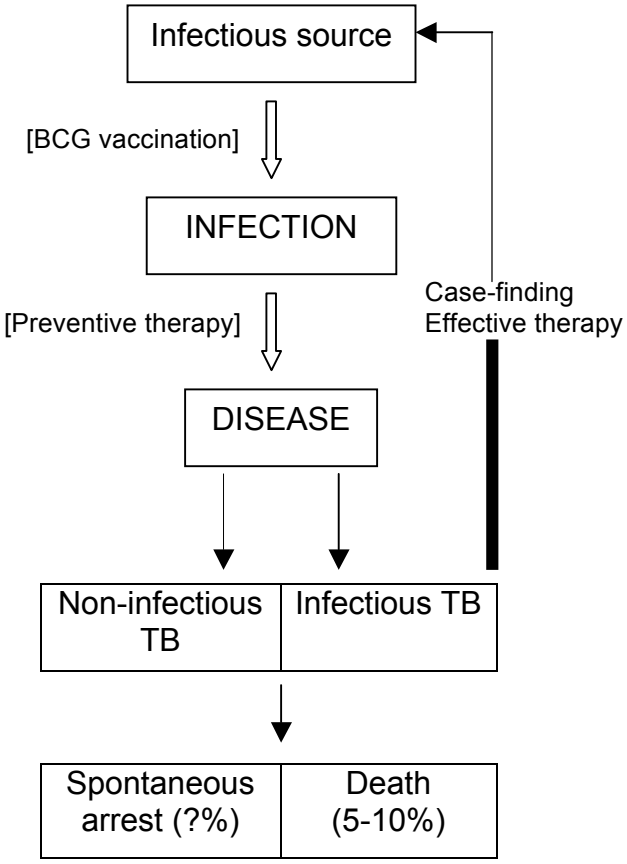
Figure 1: Natural history of tuberculosis



For the disease to persist in a community there must be a pool or pools of infectious source consisting of people with infectious TB. Without treatment they will infect on an average one person a month.[3] Of those thus infected, 10-15% will go on to have active disease in their lifetime. About 50% of them will be sputum smear positive (infectious) and the other half either smear negative or extrapulmonary. Irrespective of their infectious status, about 25% will have their diseases arrested spontaneously and 50% die within five years.[4-6] The survivors will reinforce the infectious pool in the community and the cycle repeats.

It is obvious that to control TB we need to break the vicious cycle (Figure 2).

Figure 2: Tuberculosis control in the community



BCG vaccination that has been widely used to prevent the susceptible from being infected is now considered to be ineffective although, when given at birth in an endemic area, it may protect 60-80% of vaccinated children from the severe forms of primary disease. In other words the vaccine does not prevent infection by the tubercle bacilli but may provide a variable protection by modifying the body response from a primary to a post-primary one. It should be noted that BCG vaccination is directed at people before infection, an event that may not happen. Besides its unsatisfactory efficacy, it also has a low efficiency and negligible impact on the epidemiology of the disease. Its place in TB control is therefore restricted and mainly to provide a simple and inexpensive alternative for individuals in special circumstances.

On the other hand, the use of preventive chemotherapy to stop the progression of infection to active disease has been shown to be highly effective even with isoniazid (INH) monotherapy and in people with HIV infection. It is directed towards those who have already been infected and would otherwise add to the infectious pool in the community. It is an important strategy in low prevalence countries whose aim is the elimination of the disease but as a policy it is difficult to enforce.

However, the most powerful weapons to combat and to eventually eradicate the disease are good chemotherapy and active case finding. Together they effectively remove the infectious cases in the community. In Australia various active case finding programs are in place to screen high-risk groups to detect diseases before they become infectious.

In spite of all the efforts and resources in the economically established countries it is disappointing that there is still an annual TB-related deaths of 5-10% in the notified cases.[7-10] They are mostly elderly people with multiple medical conditions that eventually lead to the reactivation of an old infection.[11]

References

1. Wallgren A. The time table of tuberculosis. *Tubercle* 1948; **29**:245-51.
2. Enarson DA, Rouillon. The epidemiological basis of tuberculosis control. In*:* Davies PDO, ed, *Clinical Tuberculosis.*. London: Chapman and Hall Medical 1994; **2**:19-32.
3. Styblo K. Recent advances in epidemiological research in tuberculosis. *Adv Tuberc Res* 1980; **20**:1-63.
4. National Tuberculosis Institute, Bangalore. Tuberculosis in a rural population of South India: a five-year epidemiological study. *Bull World Health Organ* 1974; **51**:473-88.
5. Rutledge JA, Crouch JB. The ultimate results in 1654 cases of tuberculosis treated at the modern Woodmen of America Sanatorium. *Am Rev Tuberc* 1919; **2**:755-63.
6. Grzybowski S, Enarson DA. The fate of cases of pulmonary tuberculosis under various treatment programmes. *Bull IUAT* 1978; **53(2)**:70-75.
7. Leading Article. Tuberculosis in old age. *Tubercle* 1983; **64**:69-71.
8. Rieder HL, Kelly GD, Bloch AB, Cauthen GM, Snider Jr DE. Tuberculosis diagnosed at death in the United States. *Chest* 1991; **100**:678-81.
9. Xie HJ, Enerson DA, Chao CW, Allen EA, Grzybowski S. Death in tuberculosis patients in British Columbia, 1980-1984. *Tuberc Lung Dis* 1992; **73**:77-82.
10. De Meer G, van Geuns HA. Rising case fatality of bacteriologically proven pulmonary tuberculosis in the Netherlands. *Tuberc Lung Dis* 1992; **73**:83-6.
11. King K, Sheldon C, Cock H, Wilkinson P, Barnes N. Co-existing disease and survival in patients with pulmonary tuberculosis. *Thorax* 1991; **46**:312P.

IV. DIAGNOSIS

In a community tuberculosis control program, if more than 50% of your patients on full treatment have no microbiological and/or histological confirmation, you are probably over-diagnosing active tuberculosis; if the diagnosis in over 80% of your patients is confirmed, ponder whether you have missed chances of early detection.

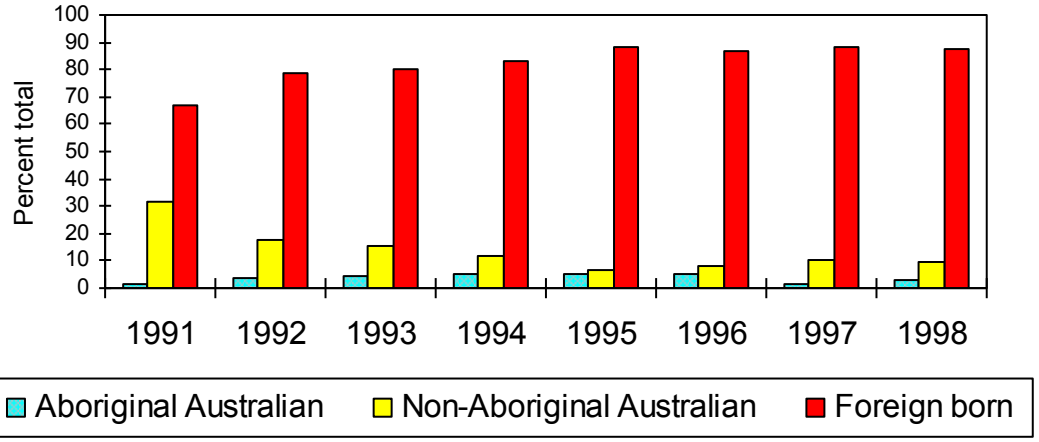
Index of suspicion

The diagnosis of TB does not differ in principle from that for other diseases, but being infectious, it is of public health importance to do so as early as possible. The best way to achieve this is to have a high index of suspicion for which a good working knowledge of the local epidemiology is essential.

COUNTRY OF BIRTH

In Australia the patient's country of birth is the best guide to raise the suspicion for a diagnosis of TB. Nationally 78% of the notifications in 2000 were in people born overseas[1] and in Western Australia the figure reaches almost 90% in the years 1995-98 (Figure 1).

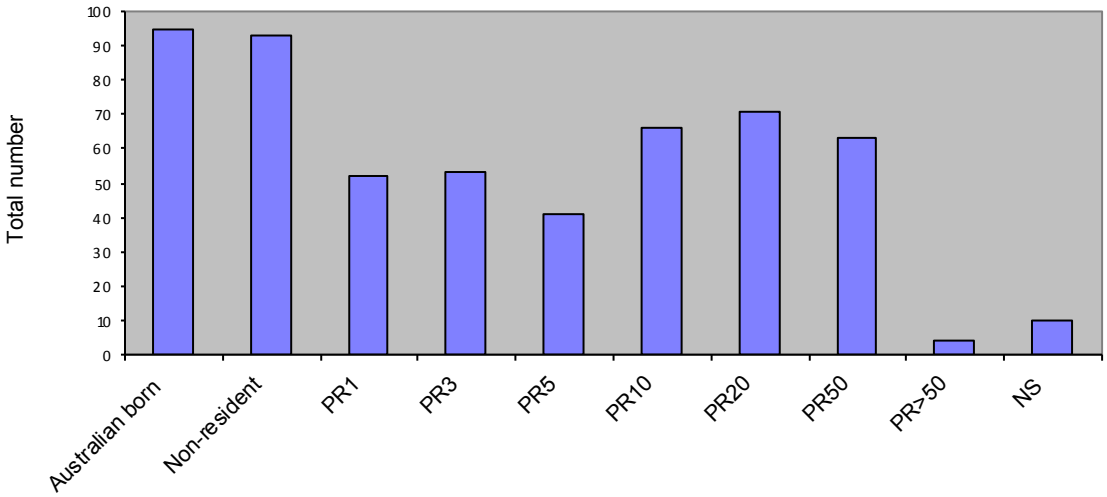
Figure 1: Tuberculosis notifications by origin of birth Western Australia 1991-98



After settlement the disease continues to reactivate throughout the lifetime of these immigrants (Figure 2). It appears that they bring with them the TB incidence rates of their own countries, but because of the strict medical examinations for immigration and the change in the environment, the level is generally lower.

The classification of the Asia Pacific nations by TB notifications (1997) is given in Table 1. Up-to-date information may be obtained electronically from two World Health Organization websites of Global TB Control Report at http://www.who.int/gtb/index.html and of International Travel and Health/Disease Maps at http://www.who.int/ith/disesemaps_index.html.

Figure 2: Tuberculosis notifications by origin of birth and duration of residence in Western Australia 1991-98



Non-resident: person born overseas and having no permanent resident status.
PR: permanent resident; 1 to >50 indicate the number of years since migration to Australia.
NS: resident status non-specified.

Table 1: Tuberculosis incidence in the Asia Pacific region

Annual notifications >100 per 100,000 population	Annual notifications of 25 – 100 per 100,000 population	Annual notifications < 25 Per 100,000 population
SOUTH EAST ASIAN REGION		
India	Banglasdesh	
	Bhutan	
	Indonesia	
	Maldives	
	Myanmar	
	Nepal	
	Sri Lanka	
	Thailand	
WESTERN PACIFIC REGION		
Cambodia	Brunei Darussaiam	American Samoa
Hong Kong	China	Australia
Kirbati	Fiji	Cook Islands
Mariana Islands	French Polynesia	New Zealand
Marshall Islands	Guam	Tonga
Mongolia	Japan	
Niue	Laos	
Palau	Macau	
Papua New Guinea	Malaysia	
Philippines	Micronesia	
Tokelau	Nauru	
Tuvalu	New Caledonia	
	Republic of Korea	
	Samoa	
	Singapore	
	Solomom Islands	
	Vanuatu	
	Vietnam	
	Wallis & Futuna	

Source: World Health Organisation. Global Tuberculosis Control: WHO Report 1997. WHO/TB97.225.

Another important aspect of ethnicity relates to the site of the disease. The Asians and in particular those from the Indian subcontinent have over 80 times the incidence of lymphatic TB than the Caucasians (Table 2).

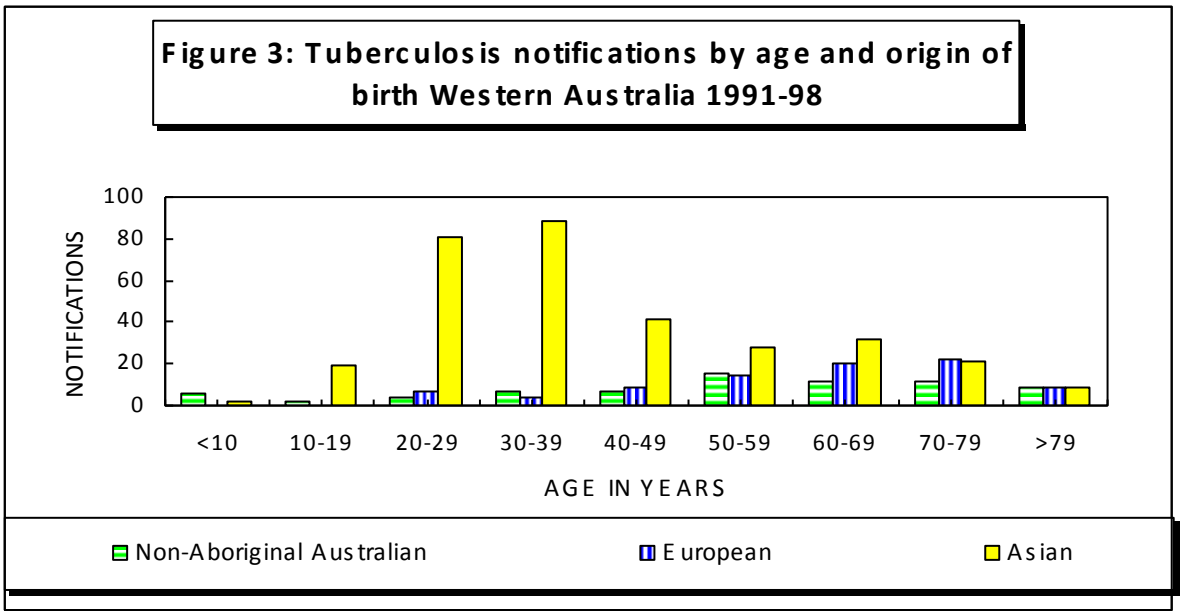
Table 2: Culture-positive non-respiratory tuberculosis* in Western Australia 1980-94.

	Non-Aboriginal Australian and European		Asian excluding those from the Middle East		Others including Aboriginals	All ethnic groups	
	No. (%)	AAIR+	No. (%)	AAIR+	No. (%)	No. (%)	AAIR+
Lymph nodes	14 (20.0)	0.07	48 (69.6)	5.9	2 (12.5)	64 (41.3)	0.29
Genitourinary tract	22 (31.4)	0.11	7 (10.1)	0.9	9 (56.3)	38 (24.5)	0.17
Bones and joints	16 (22.9)	0.08	5 (7.2)	0.6	2 (12.5)	23 (14.9)	0.10
Disseminated and miliary diseases	11 (15.7)	0.05	6 (8.7)	0.7	1 (6.3)	18 (11.6)	0.08
Abdomen	2 (2.9)	0.01	3 (4.4)	0.4	0	5 (3.2)	0.02
Meninges	2 (2.9)	0.01	0		2 (12.5)	4 (2.6)	0.02
Others	3 (4.3)	0.02	0		0	3 (1.9)	0.01
Total	70 (100.1)	0.35	69 (100.0)	8.5	16 (100.1)	155 (100.0)	0.69

*All notifications excluding pulmonary and pleural diseases.
+AAIR (Average annual incidence rates/ 10^5 population) are calculated on the estimated resident population of Western Australia as at June 30, 1987 according to the Australian Bureau of Statistics.

SEX AND AGE

Figure 3 shows the notifications in WA by country of birth and age for the period of 1991-98.



It can be seen that TB in the Australian born and those from European countries peaks at the ages

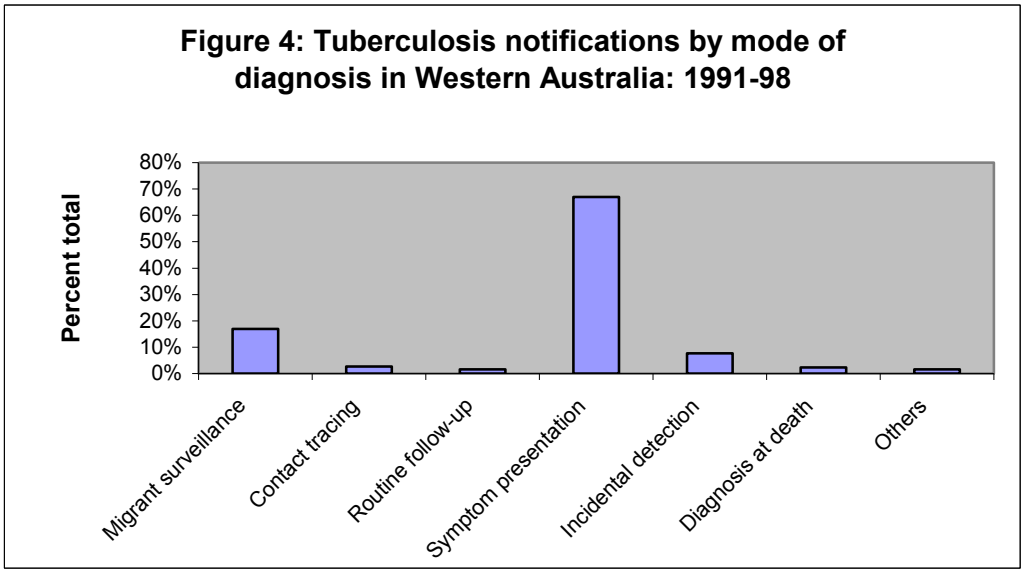
of 50 to 79 years whereas that in the Asians at 20 to 39 years. Furthermore for most age groups, the total number of notifications is highest in those born in Asia. The greater number of Australian born children in the under 10-year age group actually comes from second and later generations of immigrants.

The overall male to female ratio of the disease in WA is 1.2:1; it is roughly even in those below 70 years of age but rises to 2.6:1 in those above. Another distinct difference is the predilection of lymphatic TB in female patients with a M:F ratio of 1:1.7.[2]

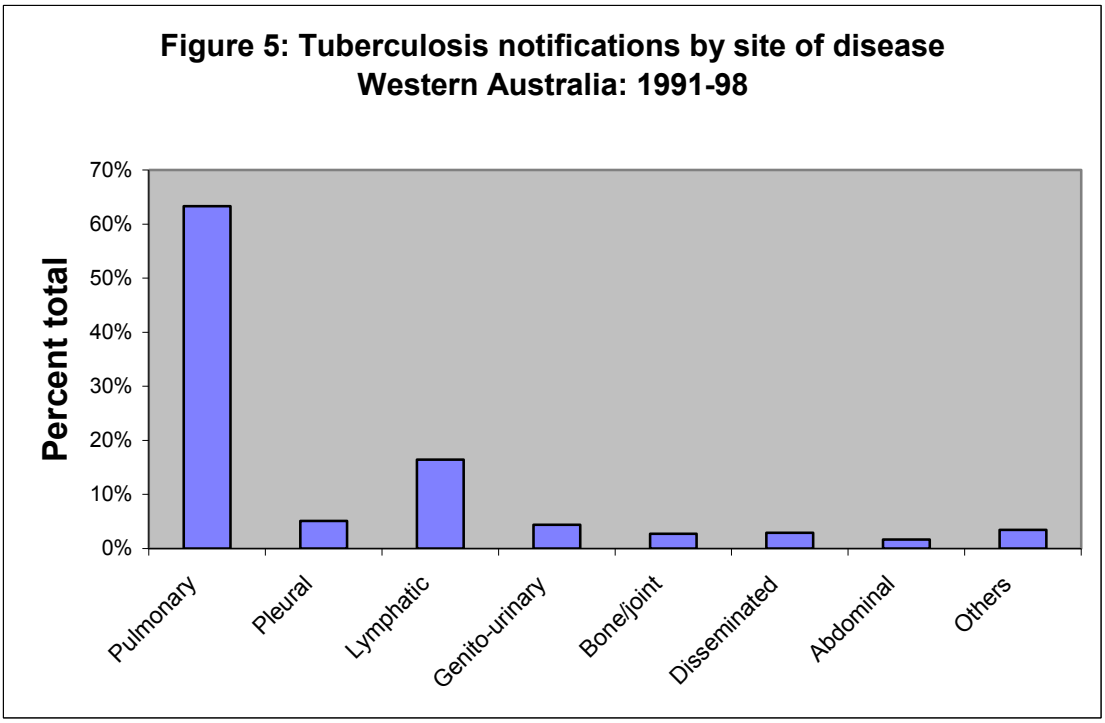
TB-related deaths are dominated by the male sex at a ratio of 4.8:1 (1991-98). They are usually elderly with a mean age at the seventies and have multiple medical conditions.[3] Over a third of them are not diagnosed until death.

CLINICAL PRESENTATION

The clinical features of TB are well known and fully described in standard texts. It is however important to stress that active and even infectious diseases may be asymptomatic. Indeed for public health reasons there is every advantage to detect them before symptoms appear. In WA about two-thirds of the notifications are in persons presenting with symptoms; in another one-fifth the disease is detected by active case finding through migrant screening, contact tracing, routine follow up and tuberculin testing. In up to 8%, the diagnosis is incidental and in about 2% it is not made until death (Figure 4).



The sites of the disease in WA are shown in Figure 5. Although pulmonary TB remains the commonest its proportion has decreased from 79% of the notifications for 1980-89[4] to just over 63% for 1991-98. On the other hand non-respiratory diseases increase from about 17% to almost 32% due largely to the rise of lymphatic TB.



The tuberculin or PPD skin test

When TB is suspected it is always a good practice to request a tuberculin test with PPD-H (purified protein derivative from the human tubercle bacilli) or a double tuberculin test with PPD-H and PPD-A (from M. avium complex) in Australia. The test is the most widely used method for demonstrating infection with the *M. tuberculosis complex* and no better, simpler and cheaper tests are currently available.

The standard method is the Mantoux test that is preferred for all purposes. The reagent used in Australia is Tuberculin PPD from the Commonwealth Serum Laboratories and the recommended dose is 10 TU (tuberculin units) to be given strictly intradermally. If the test is essential in persons known or suspected to have severe reactions, start with 1 TU. The test should only be performed and read by designated and properly trained personnel and in accordance with recommended guidelines.[5]

The use of 10 TU for the test in Australia (as against 5 TU in the United States) dates back to the beginning of the national TB campaign in 1948 when the disease was prevalent and long-term radiological observation was preferred over preventive therapy (PT). The adoption of a higher tuberculin dose to minimise the chance of missing cases in the borderline range was justified. However, with State/Territory bodies more prepared to accept PT since the 1990's there is a strong argument[6,7] in support of reducing the dose to 5 TU in Australia.

A positive Mantoux test is defined according to the purpose of the test and the age of the subject from the size of the induration measured after 48-72 hours. The result should always be reported in measurements to the nearest millimetre of induration, preferably using a vernier calliper and supplemented by stating any associated erythema and/or blisters. The definition of a positive test varies widely, relates to the local epidemiology of the disease and takes into account the consequences to the community of any false classification of the results. A proposal for its interpretation in Australia is given in Table 3.

Table 3: Proposed definition of positive Mantoux reactions in Australia

Risk of infection	Age	Reason for Mantoux test	Positive reaction in mm induration
HIGH	< 5 yrs Any Any	Recent close contact with infectious TB Positive or high risks for HIV infection To exclude person from BCG vaccination	≥ 5 ≥ 5 ≥ 5
MEDIUM	≥ 5 yrs	Recent close contact with infectious TB Abnormal chest x-ray consistent with TB High risk medical conditions High risk immigrants with no BCG scars High risk immigrants with BCG scars	≥ 10 ≥ 10 ≥ 10 ≥ 10 ≥ 15
LOW	Adults	Surveys or routine tuberculin testing (for consideration of preventive therapy)	≥ 15

TB: tuberculosis; HIV: human immunodeficiency virus; BCG: Bacille Calmette Guérin.

There are four practical considerations in applying the test to the control of TB:

1. Diagnosis
    - The test detects a cell-mediated response to a multitude of mycobacterial antigens (tuberculoproteins) that are not exclusive to the *M. tuberculosis complex*.
    - It does not measure immunity and cannot by itself differentiate active TB from old or treated diseases.
    - Generally it has a high sensitivity and low specificity. It is most useful in the detection of recent infection when the test converts from negative to positive and hence fundamental in the decision on preventive therapy.
    - While a positive reaction may not necessarily mean TB, the diagnosis of active disease in the presence of a true negative test (refer false negatives below) should be viewed with suspect and require other strong evidences including an explanation for the anergy.
2. False negatives
    - Faulty techniques: expired tuberculin solution, subcutaneous injection, leakage at site, incorrect reading of results.
    - Pre-allergic phase after TB infection.
    - Within four weeks of an intercurrent viral infection or live viral immunisation.
    - Immunodeficient states: therapeutic (immunosuppressants, radiation), diseases (HIV infection, malignancies, advanced/disseminated TB, any severe illness), malnutrition.
    - Physiological factors: old age, a small proportion of the normal population.
3. False positives
    - Faulty techniques from dilution, injection, reading and interpretation.
    - Prior BCG vaccination that may produce a reaction indistinguishable from those caused by natural infection. If in doubt or in the absence of a good scar, disregard the history of vaccination for clinical decisions.
    - Infection due to environmental mycobacteria (EM), for which a double tuberculin test may prove helpful.
4. A two-step tuberculin test (a second test is carried out within one week of the first that is negative) is indicated:
    - As the true baseline reading to monitor conversion in health care workers with a history of BCG vaccination, and
    - In immigrants from high TB prevalence areas, who are being assessed for PT or ongoing surveillance.

Chest radiography

It is prudent always to include a chest x-ray examination if TB is suspected, even in patients presenting with extra-respiratory symptoms. Disease in multiple sites is not unusual and the presence of consistent radiographic signs may help in the diagnosis.

Chest radiography is a well recognised and effective method of diagnosis for active pulmonary TB in experienced hands.[8,9] It has the distinct advantage over sputum microscopy of detecting within minutes those infectious cases having no or minimal symptoms. On the other hand atypical radiographic findings[10,11] in the HIV infected and culture-positive pulmonary TB with normal chest x-rays[12,13] are well known.

There are no pathognomonic signs for TB in the plain chest x-ray or in the computerised tomographic (CT) scan but with sufficient clinical information any experienced chest physician or radiologist can achieve a reasonable accuracy in being alerted to the disease.

FEATURES SUGGESTIVE OF TB IN THE PLAIN CHEST X-RAY
- Patchy, mottling, miliary, nodular and/or linear shadows;
- Situated mainly in the apical/posterior segments of the upper, or the superior segment of the lower lobes and less commonly in the middle/lingular lobes;
- Bilateral distribution in the upper zones;
- The lesions may be sub-segmental or segmental in the early stages, extending to lobar or multi-lobar involvement as the disease progresses;
- Persistence of the shadows after several weeks with or without antibiotic treatment;
- “Soft” opacities that fluctuate over time suggest activity;
- Cavities are usually thin-walled and if present indicate active and infectious disease;
- Calcifications, dense fibrotic opacities and distortion of intra-thoracic structures indicate chronicity;
- A small tuberculoma may not be differentiated from tumours even in the presence of calcification as a cancer may develop over a TB scar;
- Previous chest films are valuable in assisting the interpretation of the findings.

FEATURES CONSISTENT WITH TB IN THE THORACIC CT SCAN[14,15]
- Multi-segmental involvement;
- Thin-walled cavitation(s);
- Endobronchial disease with centrilobular nodules/branching linear structures, “tree-in-bud” appearance and “acinar” nodules;
- Lobular or greater consolidation;
- Mosaic pattern of reduced lung attentuation from gas trapping, hypoxic vasoconstriction and/or vascular damage;
- Miliary pattern;
- Mediastinal nodes;
- Chronic changes of bronchial wall thickening, bronchiectasis, fibrotic bands, bronchovascular distortion, emphysema and pleural reactions.

Bacteriology

The finding of the *M. tuberculosis complex* in clinical specimens is the only certainty to confirm the diagnosis of TB and it is mandatory making every effort to achieve this before treatment is given. The specimens may be sputa, bronchial/gastric aspirates, morning whole-stream urine collections, discharges and tissues. Multiple samples, if practicable, are preferred.

Common laboratory examinations in increasing time requirements include:
- Direct smear or microscopy (1-2 hours),

- Direct molecular test (2-6 hours),
- Radiometric culture (10-14 days), and
- Conventional culture (4-12 weeks).

The direct smear using the Ziehl-Neelsen or fluorescent stain is quick, simple and inexpensive and should be within the competency of all laboratories. It also identifies the most infectious patients but has the disadvantage of being unable to distinguish *M. tuberculosis complex* from the environmental mycobacteria. The estimate of the number of AFB seen in 1, 10 or 100 oil immersion fields should be reported semi-quantitatively, such as the 1+ (1-9 AFB/100 fields), 2+ (1-9 AFB/10 fields), 3+ (1-9 AFB/field) and 4+ (>9 AFB/field) grading system recommended by the Centers for Disease Control, Atlanta.[16]

The direct molecular test is a rapid but expensive method, using DNA technology to differentiate *M. tuberculosis complex* from other mycobacteria. Depending on the technique and the experience of the laboratory it can have a high sensitivity and specificity for clinical purposes. It cannot, however, differentiate between live and dead bacilli.

The cultures are needed both for the confirmation of active disease and drug susceptibility testing. They are time consuming and not fast enough even with the advancement of the radiometric culture systems.

There is a true entity of active TB with persistent negative microscopy and cultures. For these patients the diagnosis is based purely on clinical grounds. Although full treatment may be warranted, referral to or consultation with a physician experienced in TB is recommended.

Histopathology

Not only is the histopathology of a TB lesion non-specific, it also varies with the stage of the disease. The tubercle is a granulomatous reaction found in a number of conditions besides TB[17], including non-tuberculous mycobacterial infections, sarcoid, tertiary syphilis, brucellosis, primary biliary cirrhosis, hypogammaglobinaemia, fungal infections, chronic berylliosis and foreign body reaction. Most of these can easily be ruled out clinically and if there is associated caseation, TB becomes the most likely cause. It is essential to include culturing part of the tissue specimen if TB is suspected.

Serology

Serological diagnosis of active TB has always been attractive because of its simplicity and rapid results. Most of them are based on the standard enzyme-linked immunosorbent assay. The recent development of a membrane-based antibody assay[18,19] available in a cheap and simple commercial kit (ICT Diagnostics, Australia) can give results in 15 minutes. Its clinical usefulness, however, has not been established.

The well-publicised gamma interferon blood test for TB infection[20] is the equivalent of the Mantoux test. In spite of its rising popularity it has not proved superior to the time-honoured skin test except in the immunocompromised. Apart from a much higher cost, it also has a lower sensitivity for active TB[21] compared to the tuberculin test. This makes it less suitable for screening high-risk immigrants, in whom unexpected active disease is not uncommon. Compared to the tuberculin skin test, proponents of the gamma interferon TB test argue that it only needs a single visit, removes observer errors in reading the results and has less false positives in those with EM infection or previous BCG vaccination. However, a single visit is only advantageous in studies or surveys, whereas for clinical purposes, a second visit is mandatory to have the results explained and acted upon accordingly. In fact if PT is advisable, the willingness or otherwise to attend the second time, may contribute to the initial assessment of the person's treatment compliance. Technical errors with the Mantoux test is well known but can be minimised by proper training and regular quality assurance as with all laboratory tests. On the other hand, any mixing up of blood samples or request forms is non-existent. Cross-reaction from EM infections can be helped by a double tuberculin test and that from

BCG vaccination by adjusting the definition of a positive result. Finally it is important to note that most studies have shown a high degree of concordance between the two tests and cost is the major difference.

The diagnosis

A diagnosis of TB should include one of the following qualifying specifications:

- Disease, active (requiring full antituberculosis treatment) and further classified according to
  Smear, culture and/or histology results (positive, negative or not available), and
  Site(s) of involvement.
- Disease, inactive or treated (requiring preventive therapy, observation or no further action).
- Infection without disease (requiring preventive medication, observation or no further action).

Paucibacillary pulmonary tuberculosis

This is an entity where there are strong clinical and radiographic evidence of active or probably active TB in the lung but multiple (three or more) samples of sputum and/or bronchoscopic aspirates are negative for acid-fast bacilli on microscopy and other causes have been reasonably excluded. The diagnosis of TB remains provisional if subsequent cultures do not isolate the *M. tuberculosis complex*. The significance of its recognition lies in the reported high risks[22-25] of active or reactivated TB of up to 88% over 30 months and the fact that a shorter or less intensive course of medical therapy may be sufficient.[26,27] An inherent disadvantage is that drug susceptibility cannot be ascertained. An alternative to full treatment is close observation. Preventive therapy is inappropriate when active TB is suspected.

Notification

Active or reactivated TB disease is notifiable in Australia. Besides being a statutory requirement the notification which should be done as early as possible, is necessary for the following reasons:

- Contact tracing,
- Information, counselling and supervision of treatment to the patient and family and
- Epidemiological surveillance.

References

1. Lin M, Spencer J, Roche P, McKinnon M and the National TB Advisory Committee for the Communicable Diseases Network Australia. Tuberculosis notifications in Australia, 2000. *Comm Dis Intell* 2002; **26(2)**:214-25.
2. Pang SC. Mycobacterial lymphadenitis in Western Australia. *Tubercle Lung Dis* 1992; **73**:362-7.
3. Pang SC. Epidemiology. In: *Tuberculosis Control in Western Australia*. Perth: Westcare Incorporated 1996; **II**:5-11.
4. Pang SC, Clayton AS, Harrison RH. Culture-positive tuberculosis in Western Australia. *Aust NZ J Med* 1992; **22**:109-13.
5. Rieder HL. Epidemiologic basis of tuberculosis control. *IUATLD* 1999:30-4.
6. Stuart RL, Bennett N, Forbes A, Grayson ML. A paired comparison of tuberculin skin test results in health care workers using 5 TU and 10TU tuberculin. *Thorax* 2000; **55**:693-5.
7. National Tuberculosis Advisory Council. *The Tuberculin Test*. Canberra: Australian Government Publishing Service 1979.
8. Hong Kong Chest Service, Tuberculosis Research Centre Madras and British Medical Research Council. A study of the characteristics and course of sputum smear-negative pulmonary tuberculosis. *Tubercle* 1981; **62**:155-67.
9. Cohen R, Muzaffar S, Capellan J, Azar H, Chinikamwala M. The validity of classic symptoms and chest radiographic configuration in predicting pulmonary tuberculosis. *Chest* 1996; **109**:420-23.
10. Pitchenik AE, Rubinson HA. The radiographic appearance of tuberculosis in patients with acquired immune deficiency syndrome (AIDS) and pre-AIDS. *Am Rev Respir Dis* 1985; **131**:393-6.

11. Long R, Maycher B, Scalcini M et al. The chest roentgenogram in pulmonary tuberculosis patients seropositve for human immunodeficiency virus type 1. *Chest* 1991; **99**:123-7.
12. Schmidek HH, Hardy MA. Pulmonary tuberculosis with normal chest radiographs: report of 8 cases. *Can Med Assoc J* 1967; **97**:178-80.
13. Marciniuk DD, McNab BD, Martin WT, Hoeppner VH. Detection of pulmonary tuberculosis in patients with a normal chest radiograph. *Chest* 1999; **115**:445-52.
14. Im J-G, Itoh H, Shim Y-S, et al. Pulmonary tuberculosis: CT findings – early active disease and sequential change with antituberculous therapy. *Radiology* 1993; **186**:653-60.
15. Long R, Maycher B, Dhar A, Manfreda J, Hershfield E, Anthonisen N. Pulmonary tuberculosis treated with directly observed therapy. Serial changes in lung structure and function. *Chest* 1998; **113**:933-43.
16. Smithwick RW. *Laboratory manual for acid-fast microscopy*. 2nd ed. US Department of Health, Education and Welfare,PHS. Atlanta: Centre for Disease Control 1976.
17. Crofton J, Douglas A. Sarcoidosis. In: *Respiratory Diseases*, 2nd ed. Oxford: Blackwell Scientific Publications Ltd 1975; **25**:404-28.
18. Cole RA, Lu HM, Shi YZ, Wang J, De-Hua T, Zhou AT. Clinical evaluation of a rapid immunochromatographic assay based on the 38 kDa antigen of Mycobacterium tuberculosis on patients with pulmonary tuberculosis in China. *Tubercle Lung Dis* 1996; **77**:363-8.
19. Mathur ML, LoBue PA, Catanzaro A. Evaluation of a serologic test for the diagnosis of tuberculosis. *Int J Tuberc lung Dis* 1999; **3(8)**:732-5.
20. Streeton JA, Desem N, Jones SL. Sensitivity and specificity of a gamma interferon blood test for tuberculosis infection. *Int J Tuberc Lung Dis* 1998; **2(6)**:443-50.
21. Mazurek GH et al. Comparison of a whole-blood interferon [gamma] assay with tuberculin skin testing for detecting latent *Mycobacterium tuberculosis* infection. *JAMA* 2001; **286(14)**:1740-7.
22. Grzybowski S, McKinnon E, Tuters L, Pinkus G, Phillips R. Reactivations in inactive pulmonary tuberculosis. *Am Rev Respir Dis* 1966; **93**:352-61.
23. Hong Kong Chest Service, Tuberculosis Research Centre Madras and British Medical Research Council. A controlled trial of 2-month, 3-month, and 12-month regimens of chemotherapy for sputum-smear-negative pulmonary tuberculosis; results at 60 months. *Am Rev Respir Dis* 1984; **130**:23-8.
24. Cowie RL, Langton ME, Escreet BC. Diagnosis of sputum smear and culture negative pulmonary tuberculosis. *S Afr Med J* 1985; **68**:878.
25. Gordin FM, Slutkin G, Schecter G et al. Presumptive diagnosis and treatment of pulmonary tuberculosis based on radiographic findings. Am Rev Respir Dis 1989; 139:1090-3.
26. Hong Kong Chest Service, Tuberculosis Research Centre Madras and British Medical Research Council. A controlled trial of 3-month, 4-month, and 6-month regimens of chemotherapy for sputum-smear-negative pulmonary tuberculosis; results at 5 years. *Am Rev Respir Dis* 1989; **139**:871-6.
27. Dutt AK, Moers D, Stead WW. Smear- and culture-negative pulmonary tuberculosis: four-month short-course chemotherapy. *Am Rev Respir Dis* 1989; **139**:867-70.

V. MEDICAL TREATMENT OF ACTIVE TUBERCULOSIS

In the treatment of tuberculosis, the physician has two mandatory obligations: to cure the patient of the disease and not to produce iatrogenic drug resistance.

TB is a completely curable disease if the diagnosis is made in time. The success of medical treatment depends not only on the right combination of antituberculosis agents but also their judicious application according to certain simple but strict principles. As drug susceptibility results are invariably unavailable for several weeks, the selection of an initial regimen has to be empirical and standardised according to local surveillance data. The total duration of treatment may vary according to the type and bacteriological status of the disease as well as the immunocompetency of the patient.

Pretreatment considerations

When antituberculosis therapy is indicated, every effort should be made to assess the following:

- Source of infection.
- Co-existing medical conditions and predisposing factors.
- Previous treatment(s).
- Probability of initial drug resistance.
- Possible treatment complications and potential adverse drug reactions and interactions.
- Patient status and compliance.
- Bacteriological confirmation and drug susceptibility testing as far as practicable.

General measures

1. Hospital admission and bed rest are required only for problems of diagnosis, in the very sick, for the socially deprived and under special circumstances such as spinal or multidrug resistant TB. The most infectious period is before TB is even suspected and modern treatment may render a patient non-infectious in as short a time as two weeks.
2. Most patients can carry on with their work although some may need one to two weeks off to get used to the medication or to get over distressing symptoms.
3. Both the patient and the family members need to be counselled about the nature of the disease and the importance of adherence to the prescribed treatment.
4. Regular supervision and reinforcement by the treating physician and visiting nurse are essential. When compliance becomes or is expected to be a problem, fully supervised or directly observed therapy (DOT) should be implemented and combination antituberculosis drugs considered.
5. Alcohol should be discouraged in all patients on TB treatment. The homeless and those in institutions or known to be substance abusers need closer supervision or DOT right from the start.

Drug therapy of active tuberculosis

Of all diseases TB is the most extensively and thoroughly studied in relation to drug treatment.[1] The principles are strict and well known. The results are rewarding and highly cost effective but only if the physician has the right training and experience.

1. At any time in the course of treatment for active TB, the absolute minimum number of chemotherapeutic agents administered is two. There is no general rule on the maximal number permissible as it depends on the possibility of drug resistance, the severity of the disease and the patient's tolerance. In most clinical situations where the organism is likely to be fully sensitive, the optimal number is three or four for the initial two months (intensive phase) and two for another four months (maintenance phase).
2. The dosage of most anti-tuberculosis drugs is standardised and related to the age, body weight, rhythm of administration (daily or intermittent), the presence or absence of impaired body functions in the individual, and/or any concurrent medications.

3. The total duration of therapy depends on the drug regimen used, the severity or site of the disease, the time of sputum conversion and the immune status of the patient. It is important to stress that a six-month course is only applicable to localised diseases caused by susceptible organisms in immunocompetent patients who are treated with rifampicin and isoniazid throughout and supplemented with pyrazinamide in the first two months.
4. The common regimens acceptable in Australia for new patients are given in Table 1 and the drug dosages in Table 2.
5. The standard treatment for new patients in Australia is a combination of daily rifampicin (R), isoniazid (H), pyrazinamide (Z) and ethambutol (E) for 2 months, followed by R and H for another 4 months (2RHZE – 4RH). The choice is dependent on the actions required of the drugs and their potency as indicated in Table 3.
6. Treatment modification may be required if drug resistance is present, when adverse drug reactions occur or when intermittent therapy becomes necessary.
7. Follow up after adequate therapy in patients with fully sensitive organisms is not essential and should not be more than 12 months.

Table 1: Regimens for active tuberculosis in Western Australia

Regimen	Total Duration in Months		
	Pulmonary or extra-pulmonary	Milliary/ meningeal/ disseminated	Patients with immunodeficient states
2RHZE-RH	6	12	≥12
2RHZ-RH	6	12	≥12
2RH(E)-RH	9	18	18-24
RE or EH	12	24	24
2RHZE-R_3H_3	6	12	≥12
2RHZ-R_3H_3	6	12	≥12
$R_3H_3Z_3E_3$	6	12	≥12
$2R_3H_3Z_3E_3$-R_3H_3	6	12	≥12

R=rifampicin; H=isoniazid; E=ethambutol; Z=pyrazinamide.
The front number denotes the duration of the initial phase in months.
Subscripts denote the number of times per week the drug is being administered.

Table 2: Recommended dosages of standard antituberculosis drugs

	BW /Age	Adult Dosage in mg			Children Daily Dose in mg
		Daily	3X/wk	2X/wk	
RIFAMPICIN	<50 Kg >50 Kg	450 600	450 600	450 600	10/Kg
ISONIAZID		300	10/Kg	15/Kg	5-10/Kg
PYRAZINAMIDE	<60 Kg >60 Kg	1,500 2,000	2,000 2,500	3,000 3,500	20-30/Kg
ETHAMBUTOL*		25/Kg 2/12 then 15/Kg	30/Kg	45/Kg	same as in adults
STREPTOMYCIN*	>45 Yr <45 Yr	500 - 750† 750 - 1,000†	500 - 750† 750 - 1,000†		20/Kg

*Avoid in children and those with impaired renal functions.
†Monitor plasma levels to adjust the dosage.

Table 3: Relative activity of the standard antituberculosis drugs

Activity	Bactericidal	Sterilizing	Preventing resistance
High	Isoniazid*	Rifampicin†	Isoniazid
		Pyrazinamide#	Rifampicin
Medium	Ethambutol	Isoniazid	Ethambutol
	Rifampicin		Streptomycin
Low	Streptomycin	Streptomycin	Pyrazinamide
	Pyrazinamide	Thiacetazone	Thiacetazone
	Thiacetazone	Ethambutol	

Adopted from: Mitchison DA, Tubercle 1985; 66:219-25.
*on freely dividing extracellular bacilli in the early phase of disease.
†on intracellular persistent bacilli with occasional bursts of metabolic activity.
#on slowly dividing intra-/extra-cellular bacilli in an acid environment (inflammation).
Note: none of the drugs will have any effect on the dormant bacilli.

DAILY REGIMENS

1. **2RHZE-RH** is recommended in all new patients where there is a ≥5% chance of initial drug resistance to one or two of the standard drugs, eg immigrants from Asia, Africa and Latin America.
2. **2RHZ-RH** may be used in new patients unlikely to have initial drug resistance, i.e. most Australians. When this is not certain start as in 1 and adjust when susceptibility results are available.
3. **2RHE-RH, RH** are used in new patients unlikely to have initial drug resistance and intolerant of pyrazinamide. Ethambutol is added if initial isoniazid resistance cannot be ruled out.
4. **RE** and **EH** are rarely used in patients with multiple drug intolerance (failing the usual measures to overcome them) and fully sensitive organisms. They should be avoided if possible because of the much longer duration required.
5. **Streptomycin** may be used in the initial phase either as a replacement for E or as an adjunct to increase the sterilising potency of the standard regimens in severe diseases like meningitic, peritoneal or disseminated TB. Together with Z, it forms a bactericidal combination. It is less prescribed in Australia than it deserves mainly because of parenteral administration and the necessity to monitor its plasma levels and patients' renal functions.

INTERMITTENT REGIMENS

They are similar in indications to the daily regimens and are alternatives when DOT is necessary or when adverse drug reactions are troublesome.

1. **2RHZE-R_3H_3** and **2RHZ-R_3H_3** are suitable for patients who have extensive disease and/or require initial hospital admission. The subscripts infer the number of times that the drugs are administered per week (usually on Mondays, Wednesdays and Fridays).
2. **$R_3H_3Z_3E_3$** and **$2R_3H_3Z_3E_3$-R_3H_3** are more suited to fully supervised ambulatory therapy in an outpatient clinic. However they are not advisable as initial therapy in those with extensive or severe forms of TB and an initial daily phase of as short as 2-4 weeks could be advantageous to reduce the infectiousness more effectively.
3. Similar regimens administered twice weekly are acceptable but have a higher incidence of rifampicin-related adverse reactions [2] in certain ethnic groups.

PATIENTS WITH PREVIOUS TREATMENTS AND/ OR MULTIDRUG RESISTANT TUBERCULOSIS

1. The majority of previous treatments consisted of combinations of streptomycin, isoniazid, para-aminosalicylate (PAS) and ethambutol. The standard quadruple regimen has taken this into consideration.

2. Where other drugs such as rifampicin and pyrazinamide are suspected to have been used as well, it is recommended that the patient be referred to special centres for management, as are all proven cases of multidrug resistant disease.
3. Multidrug resistant (resistance to both rifampicin and isoniazid plus or minus others) TB is on the rise in certain parts of the world. Treatment is difficult and resources demanding. The drugs required have to be individualised and depend on the detailed knowledge of previous therapy and drug susceptibility results. Reserve or experimental antituberculosis agents will be required. Treatment is prolonged, adverse drug reactions are common and the failure rate is high even in large centres.[3,4] Timely surgery[5] if feasible, may help in a proportion of these patients. Cases should be managed in a specific referral centre at the state or national level.
4. The general principle is to start with at least three antituberculosis drugs that have not been used prior to the retreatment and adjust accordingly when drug susceptibility results (preferably to both standard and reserve drugs) are available. A simplified list of the reserve drugs to consider is given below. No more than one from each group should be included.

    - Prothionamide, ethionamide, and PAS.
    - Kanamycin, capreomycin, amikacin, and viomycin.
    - Ofloxacin, ciprofloxacin, and moxifloxacin.
    - Clarithromycin and azithromycin.
    - Rifabutin and rifapentine.

MONITORING AND FOLLOW-UP OF PEOPLE ON ANTI-TUBERCULOSIS THERAPY

Although there is no fixed rule as to how often a person on antituberculosis medication should be reviewed, a monthly evaluation is usually adequate. This may be extended to two monthly for special circumstances, preferably after the initial two months, with no drug intolerance and in reliable patients. Even so someone in the health-care team should maintain a monthly contact either by telephone or home visits.

The objectives of the follow-up attendance are:

- To reaffirm treatment compliance,
- To assess progress, and
- To monitor adverse drug reactions.

Treatment compliance is reinforced at every patient attendance and double-checked by urine examinations (for isoniazid and rifampicin) or pill counts at surprise home visits.

Progress is assessed mainly through improvements in symptoms and signs, body weight records, and supplemented by sputum (at the second, fourth and sixth months of therapy if available) and chest x-ray (at the second and sixth months) examinations for pulmonary TB.

Adverse drug reactions are monitored both before and during the entire course of medication. The frequency to monitor depends on the age of the patient, any pre-existing medical conditions and the presence or absence of side effects from the treatment. A good knowledge of their manifestations (Table 4) and pharmacokinetic interactions with other drugs (Table 5) as well as alertness to their development are essential. Pre-treatment liver and renal function tests (including uric acid level in appropriate cases) are advisable as three of the four standard initial drugs are potentially hepatotoxic and ethambutol is excreted by the kidneys. Routine referral to the ophthalmologist is not necessary; full explanation on what to watch for and simple testing with the Snellen chart and Ishihara colour plates are adequate if renal functions are normal. If not, assess whether ethambutol can be avoided before adjusting and monitoring the dosage. Ophthalmologic consultation is mandatory when visual symptoms develop during treatment.

Table 4: Adverse reactions to antituberculosis drugs

Occurrence	Common	Uncommon	Rare
Isoniazid		Hepatitis Peripheral neuropathy Cutaneous reactions Hypersensitivity reactions Anorexia/ nausea	Optic neuritis Mental symptoms Difficulty in micturition Giddiness/ drowsiness Tremor Hyper-activity Convulsions Pellagra Lupoid reactions Haemolytic anaemia
Rifampicin (daily) Rifampicin (intermittent)	Reddish discolouration of body secretions and soft contact lenses Anorexia/ nausea Flushing As above	Hepatitis Cutaneous reactions Hypersensitivity reactions "Flu" syndrome Hepatitis	Severe exudative conjunctivitis Vomiting/ diarrhoea Thrombocytopenia Dyspnoea Shock Acute renal failure Haemolytic anaemia Thrombocytopenia
Pyrazinamide	Anorexia/ nausea Flushing Arthralgia	Vomiting Hepatitis Photo-sensitisation	Hyperuricaemia Hypersensitivity reactions Sideroblastic anaemia
Ethambutol		Retrobulbar neuritis Hyperuricaemia	Hepatitis Hypersensitivity reactions Peripheral neuropathy
Streptomycin Kanamycin Capreomycin Viomycin	Hypersensitivity reactions Giddiness Numbness around mouth Minor renal tubular dysfunction	Ototoxicity (vestibular >auditory) Vertigo/ tinnitus Ataxia	Lupoid reaction Aplastic anaemia Agranulocytosis Renal damage Hypokalaemia Hypocalcaemia
Prothionamide Ethionamide	Salivation/ eructation Metallic taste in mouth Anorexia/ nausea/ vomiting Abdominal pain Diarrhoea Giddiness/ headache	Hepatitis Hypersensitivity reactions	Alopecia Gynaecomastia Menstrual irregularity Hypoglycaemia Diplopia Convulsions Impotence Mental disturbance Peripheral neuropathy Hypotension
Ofloxacin Ciprofloxacin	Anorexia/ nausea/ vomiting Dizziness/ headache Insomnia	Hypersensitivity reaction Cutaneous reactions Tremor/ tinnitus Convulsion Acute renal failure Hepatitis Abdominal pain/ diarrhoea	Haemolytic anaemia Agranulocytosis Thrombocytopenia Depression/ confusion Hypoglycaemia
Para-aminosalicylic Acid (PAS)	Anorexia/ nausea/ vomiting Diarrhoea Hypersensitivity reactions	Hepatitis Hypokalaemia	Acute renal failure Hypoprothombinaemia Haemolytic anaemia Thrombocytopenia Hypothyroidism
Cycloserine	Dizziness/ headache Slurred speech Tremor Insomnia Nightmares Depression/ psychosis Suicidal tendency		
Clarithromycin		Diarrhoea/ nausea/ vomiting Abdominal pain Dizziness/ headache Moniliasis Cutaneous reactions	Hepatitis Acute renal failure Haematological Abnormalities

Table 5: Important antituberculosis drug interactions

Drug X	Drug Y			
	Y increases level of X	Y decreases level of X	X increases level of Y	X decreases level of Y
Isoniazid	Prednisolone Ethionamide		Phenytoin Carbamazepine Warfarin Diazepam	Enflurane Ketoconazole Fluconazole
Rifampicin	Protease Inhibitors	PAS Ketoconazole		Warfarin Sulphonylureas Oral contraceptives Glucocorticoids Cyclosporin Phenytoin Diazepam Theophyllines Vitamin D Digoxin Nefidipine Ketoconazole Fluconazole Protease inhibitors *NNRTIs
Ethambutol		Aluminium hydroxide		Methadone
Pyrazinamide			Probenecid	
Ciprofloxacin		Antacids	Theophyllines Warfarin	
Ofloxacin		Antacids	Theophylline	
Clarithromycin	Fluconazole Ritonavir	Rifabutin Rifampicin	Rifabutin Theophylline Terfenadine Astemizole Warfarin Digoxin Disopyramide Triazolam Midazolam Cyclosporin Tacrolimus Carbamazepine Phenytoin	Zidovudine
Ethionamide			Isoniazid	
PAS				Rifampicin

Adopted from: Winstanley PA. The clinical pharmacology of antituberculosis drugs. In: Davies PDO, ed, *Clinical Tuberculosis*. London: Chapman and Hall 1994; **8a**:129-40.
*NNRTIs: nonnucleoside reverse transcriptase inhibitors.

MANAGEMENT OF ADVERSE EFFECTS FROM ANTI-TUBERCULOSIS DRUGS

The adverse side effects from anti-tuberculosis therapy may be divided into four general categories as follows:

1. Minor upsets which are clinically insignificant and should not interrupt medication. Examples are: mild gastric discomfort due to the tablets, reddish discoloration of body secretions (urine, tears and sweat) and facial flushing from rifampicin, photosensitivity with pyrazinamide, light-headedness from streptomycin, etc. Due explanation, preferably prior to the start of treatment, and assurance are sufficient.
2. Specific toxic effects such as peripheral neuropathy (isoniazid), optic neuropathy (ethambutol), thrombocytopenia, febrile and shock syndromes (rifampicin) and renal or eighth cranial nerve impairment (aminoglycosides) usually mean that the offending drug may not be used again.
3. Pharmacokinetic interactions with other concurrent medications are common. A list of them is given in Table 5 but they are growing fast. Management is basically a matter of awareness, priority,

regular monitoring and careful adjustment of the dosage. Particular attention should be paid to introducing and subsequently ceasing one of the interacting drugs.

4. Hypersensitivity drug reactions are not uncommon and their management requires experience. General guidelines are given separately in Section IV.

Corticosteroids in tuberculosis

The increased risk of TB infection and reactivation in immunocompromised persons including those on long-term corticosteroids is well known.[6-8] There is, however, no general consensus on the indications of corticosteroids in the management of active TB. Their use may be divided into three broad categories:

MANDATORY

- Patients critically ill from TB;
- Patients with cerebral or meningeal TB and altered mental states[9];
- Patients with adrenal insufficiency from TB involvement.

BENEFICIAL

- Patients manifesting severe toxic febrile reactions[10];
- Patients with troublesome manifestations of hypersensitivity to tuberculoproteins such as visceral lymphadenopathy and eye complications;
- Patients with severe adverse reactions to antituberculosis agents that need to be continued.

DOUBTFUL

- To prevent or reduce the sequelae from fibrosis in TB serositis, renal and endobronchial diseases.

It is imperative that patients who have active TB and require corticosteroid or immunosuppressive therapy must be covered with adequate antituberculosis drugs to which the organism is fully sensitive.

Therapeutic trial for tuberculosis

When active TB is strongly suspected and no confirmation is obtained after reasonable investigations, a therapeutic trial may be considered both for diagnosis and for management. There are certain prerequisites that must be observed:

- Persistent symptoms or signs for which more common causes have been excluded, such as fever of unknown origin, chronic cough, continuous weight loss, indolent or recurrent skin lesions histologically consistent with TB and chronic uveitis.
- Reasonable probability of TB aetiology such as positive tuberculin reaction or equivalent serological tests, radiological changes consistent with previous infection and history of past TB with or without treatment.
- As the trial may take four to six weeks to complete, the delay must not affect the health of the patient if the diagnosis turns out to be different. In other words every effort should be made to exclude conditions like pyogenic infections and malignancy.
- There must be objective parameters to assess the progress, eg temperature or body weight charts and radiographic changes.
- The physician should have sufficient experience to decide on the outcome of the trial.

The trial should consist of specific antituberculosis combinations such as isoniazid, pyrazinamide and ethambutol. Antibiotics such as rifampicin and streptomycin should be avoided as far as possible because of their action against other microbes.

The paradoxical responses

Even in compliant patients with the correct treatment and no adverse drug reactions, the progression

of the disease is not always smooth. There are a number of well-known phenomena that may lead to unnecessary investigations or change of therapy from those unaware of their occurrence. They are commonly known as paradoxical responses[11] as they complicate an otherwise successful course of treatment. They usually start to appear 3 to 12 weeks after the introduction of antituberculosis therapy. The exact mechanism of their development is unclear but it is generally accepted that these events result from the restoration of a previously depressed immune system and/or a hypersensitivity reaction to the release of tuberculoproteins following effective treatment. Hence they are also known as the immune restoration syndrome.

They include:

1. Enlargement and/or formation of cold abscess from TB lymphadenitis[12];
2. Development of new pulmonary shadows (infiltrative or granulomatous) or pleural effusion (ipsilateral or contralateral) in the presence of pulmonary or extra-pulmonary disease[13-16];
3. Expansion of intracranial tuberculoma[17-19]; and
4. Exacerbation of TB symptoms and/or lesions following the initiation of highly active antiretroviral therapy (HAART) in those co-infected with HIV[20].

The manifestations depend on the site of the paradoxical response. For 1 and 2 above, fever and local signs of nodal enlargement/softening with skin involvement and of pleurisy/radiological changes respectively are the most common. For 3 and 4, the response is usually worsening of the presenting symptoms and signs from the TB disease. One distinct feature of these lesions is that they are either paucibacillary or negative for *M. tuberculosis* on cultures. In their study[20] Narita and co-workers found a 36% (12 of 33) incidence in HIV patients receiving HAART and antituberculosis medication, compared to 7% (2 of 28) in HIV patients on antituberculosis treatment but not HAART and 2% (1 of 55) in non-HIV patients taking antituberculosis drugs alone.

The importance of recognising their occurrence is firstly the TB is actually responding to the treatment and the medications need not be changed or ceased except in those with HIV co-infection where there is interference between the antituberculosis and antiretroviral drugs. Secondly certain timely interventions may be required such as a course of corticosteroids for febrile reactions or pressure effects from expanding lesions and the resection or drainage of cold abscesses. However for the diagnosis it is imperative to be certain of treatment compliance, to confirm full susceptibility of the organism to the treatment regime and to exclude adverse drug reactions or concomitant conditions that may have caused the manifestations.

There has been no study on whether the total treatment duration should be changed when TB is complicated by the development of paradoxical responses but anecdotal reports generally indicated a lengthened course by three to six months. This is most likely the time required to make sure that the new lesions have responded to therapy, which they invariably do.

References

1. Fox W, Ellard GA, Mitchison DA. Studies on the treatment of tuberculosis undertaken by the British Medical Research Council Tuberculosis Units, 1946-1986, with relevant subsequent publications. *Int J Tuberc Lung Dis* 1999; **3(10)**:S231-79.
2. Aquinas M, Allan WGL, Horsfall PAL, et al. Adverse reactions to daily and intermittent rifampicin regimens for pulmonary tuberculosis in Hong Kong. *Br Med J* 1972; **1**:765-71.
3. Mitchison DA, Nunn AJ. Influence of initial drug resistance in the response to short-course chemotherapy of pulmonary tuberculosis. *Am Rev Respir Dis* 1986; **133**:423-30.
4. Goble M, Iseman MD, Madsen LA, Waite D, Ackerson L, Horsburgh Jr CR. Treatment of 171 patients with pulmonary tuberculosis resistant to isoniazid and rifampicin. *N Engl J Med* 1993; **328**:527-32.
5. Iseman MD, Madsen L, Goble M, Pomerantz M. Surgical intervention in the treatment of pulmonary disease caused by drug-resistant Mycobacterium tuberculosis. *Am Rev Respir Dis*

1990; **141**:623-5.
6. Sahn SA Lakshminarayan S. Tuberculosis after corticosteroid therapy. *Br J Dis Chest* 1976; **70**:195-205.
7. Edlin GP. Active tuberculosis unrecognised until necropsy. *Lancet* 1978; **i**:650-2.
8. Millar JW, Horne NW. Tuberculosis in immunosuppressed patients. *Lancet* 1979; **ii**:1176-8.
9. Humphries M. The management of tuberculous meningitis. *Thorax* 1992; **47**:577-81.
10. Bilaçeroglu S, Perim K, Büyüksirin M, Çelikten. Prednisolone: a beneficial and safe adjunct to antituberculosis treatment? A randomised controlled trial. *Int J Tuberc Lung Dis* 1999; **3(1)**:47-54.
11. Smith H. Paradoxical response during the chemotherapy of tuberculosis. *J Inf* 1987; **15**:1-3.
12. Campbell IA, Dyson AJ. Lymph node tuberculosis: a comparison of various methods of treatment. *Tubercle* 1977; **58**:171-9.
13. Bobrowitz ID. Reversible roentgenographic progression in the initial treatment of pulmonary tuberculosis. *Am Rev Respir Dis* 1980; **121**:735-42.
14. Hung SC, Chang SC. New pulmonary lesions during therapy for extrapulmonary tuberculosis. *Chest* 1999; **116**:1794-7.
15. Matthay RA, Neff TA, Iseman MD. Tuberculous pleural effusion developing during chemotherapy for pulmonary tuberculosis. *Am Rev Respir Dis* 1974; **109**:469-72.
16. Vilaseca J, Lopez-Vivancos J, Arnau J, Guardia J. Contralateral pleural effusion during chemotherapy for tuberculous pleurisy. *Tubercle* 1984; **65**:209-10.
17. Chambers ST, Hendrickse WA, Record C, et al. Paradoxical expansion of intracranial tuberculoma during chemotherapy. *Lancet* 1984; 2:181-3.
18. Afghani B, Lierberman JM. Paradoxical enlargement or development of intracranial tuberculosis during therapy: case report and review. *Clin Infect Dis* 1994; **19**:1092-9.
19. Ramdas K, Minamoto GY. Paradoxical presentation of intracranial tuberculomas after chemotherapy in a patient with AIDS. *Clin Infect Dis* 1994; **19**:793-4.
20. Narita M, Ashkin D, Hollender ES, Pitchenik AE. Paradoxical worsening of tuberculosis following antiretroviral therapy in patients with AIDS. *Am Rev Respir Crit Care Med* 1998; **158**:157-61.

VI. HYPERSENSITIVITY DRUG REACTIONS IN ANTI-TUBERCULOSIS THERAPY

Do not ignore minor drug reactions in your patients; attention to these enhances treatment adherence.

Incidence

The exact incidence of hypersensitivity reactions to antituberculosis drugs is unknown and probably population and geographically related. Large chemotherapy studies[1,2] reported its occurrence in 7% to 10% of cases.

Onset

The commonest time of onset is within the first one or two months of treatment.

Manifestations

MILD CUTANEOUS REACTIONS
These consist of pruritus with or without rashes that may be transient. There are no systemic upsets and the person usually can continue with daily activities. No interruption or alteration of medications is necessary. Sometimes a few doses of antihistamines may be needed to relieve the itchiness especially at night.

MODERATE TO SEVERE REACTIONS
These may be localised to one organ system or generalised. Manifestations consist of variable combinations of the following:

- Pruritus, rashes, preiorbital swelling, conjunctivitis, and exfoliative dermatitis;
- Fever, chills, headache, musculoskeletal pains, malaise, nausea and vomiting;
- Lymphadenopathy, jaundice, and hepatosplenomegaly;
- Haemolytic anaemia, granulocytopenia, thrombocytopenia and abnormal liver/renal functions;
- Pulmonary eosinophilia.
- Shock or acute renal failure.

Management of moderate reactions

These are much more common than the severe or life-threatening reactions but the principle of management is similar. Patients with severe reactions may need hospital admission.

1. Stop all drugs and give symptomatic or supportive treatment if necessary until the reactions have subsided.
2. Identify the offending drug or drugs by giving challenge doses, one at a time, beginning with the least likely. The process can be hastened by administering the doses 12-hourly as in the following table (for adults) although the exact order of the drugs may be changed according to the type of adverse reactions.

Drug	Day 1 (12-hourly)		Day 2 (12-hourly)		Day 3
Isoniazid	50 mg;	100mg	200 mg	--	Full dose
Rifampicin	75 mg;	150 mg	300 mg	--	Full dose
Pyrazinamide	250 mg;	500 mg	1000 mg	--	Full dose
Ethambutol	100 mg;	200 mg	400 mg;	800 mg	Full dose
Streptomycin	125 mg	--	250 mg	--	Full dose

3. In most situations it is not necessary to go through all the drugs. As soon as the patient gives no reactions to two drugs in full dosage, resume treatment with them and proceed with desensitisation to the remaining drugs one at a time. The difference between challenge and

desensitisation is the size of the initial dose and the speed of its increase.

4. If the next drug has not been challenged or the drug reaction not severe, start as in the above schedule. If reaction occurs with the initial dose or was severe, restart with approximately one-tenth of that dose and double it every 12-hourly or daily until the full dose is reached. If reaction develops with any subsequent dose, reduce to the previous dosage and increase more gradually. Monitor the progress by clinical or laboratory examinations as appropriate.
5. Desensitise only when necessary. For example, if the organism is fully sensitive, there is no need to desensitise for ethambutol if the patient gives no adverse effects with rifampicin, isoniazid and pyrazinamide. As a general rule do not attempt desensitisation for reactions such as severe exfoliative dermatitis, thrombocytopenia, agranulocytosis, haemolytic anaemia, shock and renal failure.
6. Occasionally corticosteroid cover may be necessary because of:
   - Hypersensitivity to multiple drugs with no good alternatives,
   - Severe reactions requiring corticosteroid therapy, and
   - Critically ill patients requiring continuation or rapid resumption of adequate treatment.

   For severe reactions an accepted procedure is to start the corticosteroid (eg prednisolone at an appropriate dose and preferably four times daily) for 24 to 48 hours before introducing the offending drug(s). Begin the antituberculosis agent with ¼ of the full daily dose in 2 divided administrations and increase by the same amount daily so that on the fourth day it will reach full dosage in 2 divided doses. On the fifth day give the drug in a single dose. After the condition becomes stable, gradually tail off the corticosteroid.

References

1. Hon Kong Chest Service/Tuberculosis Research Centre Madras/British Medical Research Council. A controlled trial of 3-month, 4-month, and 6-month regimens of chemotherapy for sputum smear-negative pulmonary tuberculosis. *Am Rev Respir Dis* 1989; **139**:871-6.
2. Hong Kong Chest Service/British Medical Research Council. Controlled trial of 2, 4, and 6 months of pyrazinamide in 6-month three-times-weekly regimens for smear-positive pulmonary tuberculosis, including an assessment of a combined preparation of isoniazid, rifampicin, and pyrazinamide. *Am Rev Respir Dis* 1991; **143**:700-6.

VII. TREATMENT COMPLIANCE

Check and reinforce treatment adherence in every appointment with your patient; when non-compliance occurs, always reflect first on what you may have overlooked.

Apart from multidrug resistant diseases, TB is totally curable if good chemotherapy is strictly applied. This requires the compliance from both the patient and the health care providers.[1,2]

In spite of the advancements in the last thirty years, active TB still requires a minimum of six-month therapy with multiple drugs to be cured. Because of the effectiveness of modern treatment, most symptoms will disappear after a few weeks of medication. Adherence then becomes an increasing problem in the latter months of the course. If not detected and rectified promptly this will lead to treatment failure, relapse and/or development of secondary drug resistance.

In the past much of the unsatisfactory outcomes of treatment were attributed to patient non-compliance. It has, however, been accepted that the responsibility to ensure completion of therapy rests with the health care providers and/or the local organization for TB control. Since the early chemotherapeutic era of the 1950s various strategies have been developed such as the fully supervised ambulatory therapy, directly observed therapy (DOT), signing of a contract and involuntary detention.

Although admittedly these measures may be needed under certain circumstances, it is important to note that Australia had a highly successful TB campaign for twenty-eight years (1948-76) followed by another twenty-two years (1976-1998) with treatment completion rates consistently over 90%. The Health Act for involuntary confinement was applied sparingly in WA during the campaign and not at all thereafter. For the whole period, universal DOT and the signing of a contract with patients have not been adopted. The routine practice remains individualisation and self-medication under indirect but close supervision. The legal aspects of the issue have been addressed by Annas[3]. In particular, his comments on DOT is pertinent, “Requiring all persons to take therapy under direct observation because it is necessary for some is wasteful, inefficient, and gratuitously annoying, and it undercuts the legitimate desire…. to use the least restrictive and intrusive public health interventions.”

While the arguments from proponents for DOT are valid, other significant aspects of health care need equal considerations in Australia:

- Patience and good communication will make people fully aware of the strict requirements to cure the disease and the importance of their co-operation.
- Good rapport and close supervision throughout the treatment period depends on mutual trust and respect between the patients and the health care providers.
- Authoritarian measures are no substitute for knowledge and experience that will enable the health care team to detect the few who need fully supervised therapy.
- The fact that patients are *voluntarily* attending treatment centres or waiting at home for their dose to be delivered can only mean that they have the motivation to comply with self-medication.
- The occasional miss of a dose in a daily regimen still makes the treatment safe and effective but the same in an intermittent regimen (for DOT to be practical) could be dangerous and inadequate.

A good working system demands the compliance from both the health care providers and the patients.

Compliance from health care providers

The members of the health care team must be adequately trained and have sufficient knowledge and experience for their role in all aspects of TB management.

They must have a clear understanding of the strict principles behind good chemotherapy and the paramount importance of preventing drug resistance. For this they need to be thoroughly familiar with the dosage, the rhythm of administration, the various well-tried effective regimens, the adverse

reactions and their frequency/management as well as willingness to attend to, or discuss, trivial matters relating to medication without a pre-booked appointment.

There must be plenty of pretreatment counselling and information about the disease, emphasising the fact that it is totally curable and that the success of treatment lies in the patients' own hands. The care workers are there just to assist. This should be followed by an adequate explanation about the medication, their possible side effects and how they should be watched or can be managed, the estimated total duration of treatment and the importance of, and reasons for, strict adherence.

There must also be a friendly system of monitoring adherence and progress. Keeping the same team for the entire course of therapy is preferred. Regular and constant contacts in person, by telephone or through home visits are important. Objective but subtle assessment of medication being properly taken such as pill counting and urine/blood testing should be in place. Bacteriological progress in patients with sputum smear positive disease is mandatory while radiography is mostly optional. Monitoring for adverse drug reactions is essential, since the latter have been shown to be significantly related to adherence in preventive therapy[4].

The human side of the disease cannot be ignored. As TB usually affects the socially disadvantaged, every effort should be made to provide needed assistance in living conditions, travel, home help and sickness benefits. TB allowance was one of the major factors in the great success of the Australian campaign. Above all, patients must be treated with dignity and this is why at times DOT can be counter-productive.

Patient compliance

It is generally accepted that patient non-compliance with medication is universal and cannot be accurately predicted[5]. On the other hand certain groups that are more prone need close supervision and assessment for DOT:

- The substance abusers
- The homeless, the vagrants and those institutionalised or living in lodging houses,
- The unemployed or those in social hardships,
- Those having different religious beliefs or cultural backgrounds,
- People with multiple medical conditions or on a multitude of medications, and
- The mentally unstable, the feeble/fragile and those living alone or without a family.

The best way to obtain patient compliance is a combination of respect, understanding, good communication and diligent supervision. There are undoubtedly occasional cases that will challenge the wits and resources of the TB program to the limit but it is fair to say that in the last twenty years the Health Act has not been applied in WA to commit any person for TB treatment.

Take-home information sheets should be available to supplement the pre-medication counselling after the diagnosis. In WA they include "Tuberculosis from A to Z for patients" (Appendix A), "What you should know about the medication for TB treatment" (Appendix B) and/or "About preventive therapy for TB" (Appendix C). They are accessible to all health care providers.

The non-adherent

The experience of the health care team is important not only in the management of the disease, in giving unequivocal and straightforward instructions, but also in detecting early any treatment non-adherence. If the last is suspected, the person should be interviewed sympathetically to ascertain the reason(s). Very often they are simple and easy to rectify. In WA only a few each year require DOT for which experienced community nurses strictly supervise the medication. The person is required either to attend a treatment centre or to wait at home for the administration of medication by the designated nurse. It is also important to arrange convenient times when the person is working and to assist transportation (eg bus/rail passes) whenever necessary. Although parents, partners and family members are always encouraged to provide support, they should not replace the properly

trained health care providers in administrating DOT. Occasionally financial incentives such as food vouchers, assistance in accommodation or a period of hospital admission may be required.

References

1. Fox W. Compliance of patients and physicians: experience and lessons from tuberculosis–I. *Br Med J* 1983; **287**:33-5.
2. Fox W. Compliance of patients and physicians: experience and lessons from tuberculosis–II. *Br Med J* 1983; **287**:101-5.
3. Annas GJ. Control of tuberculosis – the law and the public health. *New Engl J Med* 1993; **328(8)**:585-8.
4. Pang SC, Harrison RH, Brearley J, Jegathesan V, Clayton AS. Preventive therapy for tuberculosis in Western Australia. *Int J Tuberc Lung Dis* 1998; **2(12)**:984-8.
5. Sbarbaro JA. The patient-physician relationship: compliance revisited. *Ann Allergy* 1990; **64**:325-31.

VIII. PREVENTIVE THERAPY

Do not offer preventive therapy if you have no resources or provisions to ensure treatment adherence.

Terminology

Three terms have been used to describe this aspect of TB control, tuberculosis chemoprophylaxis, preventive therapy for tuberculosis and the treatment of latent tuberculosis infection. The first one is a medical jargon and similar in meaning to the second that is much more user friendly. In the third the word "latent" is redundant and inaccurate since the evidence on which we base our recommendation for treatment is simply TB infection as against TB disease. In most cases we are uncertain whether the infection is active, chronic, dormant or arrested. The term is also not applicable when treatment is given to a baby before infection has been confirmed (see below). Preventive therapy for TB is therefore adopted here, implying that the treatment is aimed at preventing the development of active disease.

Definition

For completeness, the broad definition proposed by the Joint Tuberculosis Committee of the British Tuberculosis Association in 1982 is adopted here:

"Preventive therapy for TB is the administration of one or more antituberculosis drugs to persons, whether tuberculin negative or positive, who have no clinical, radiographic or bacteriological evidence of (active) tuberculous disease." The word "active" in parentheses is added here to avoid any ambiguity.

It is conveniently classified into the following:
- Primary: to *prevent infection* in the non-infected person,
- Secondary: to *prevent disease* in an infected individual, and
- Mass: to *prevent both* in an entire community.

Mass preventive therapy is now obsolete but the primary form is still applied when a baby from an infectious mother is given the treatment before there is evidence of infection (see below).

Rationale

The chance of developing active TB after infection varies from a life long risk of 10-15%[1] in persons with normal immune systems and chest x-rays to an annual risk of 8%[2] in those infected with HIV. About half of the former will do so within the first five years after infection and run a small risk of getting the serious forms of the disease. If not detected early, this may lead to further transmission in the community. Preventive therapy has been shown to be effective[3] and is an important strategy in the elimination of TB in the low prevalence countries[4].

Indications

In Australia preventive therapy for TB is *not mandatory*, as the person is healthy at the time and may not even develop the disease. It is, however, of public and individual health reasons to *offer* or *recommend* it to the appropriate persons with full explanation. They in turn should make the ultimate decision from their individual circumstances. Assistance and policy guidelines are available from most State/Territory TB Control Programs. In those where therapy is indicated but declined it would be advisable to follow them up for two years.

Preventive therapy should be offered to the following:

1. HOUSEHOLD/CLOSE CONTACTS OF SPUTUM SMEAR-POSITIVE PATIENTS
   - Tuberculin positives under 35 years of age.
   - All tuberculin converters (see 2 below).
   - For children less than 2 years[5] of age, start preventive therapy as soon as possible irrespective of whether an initial tuberculin test is done. If the initial test is negative, repeat in 3 months; if it remains negative, cease therapy and consider BCG vaccination. If the initial or the second test is positive, complete preventive therapy.

2. RECENT TUBERCULIN CONVERTERS
   Other than TB contacts, they refer mainly to health care workers at risk of TB exposures and are being monitored with regular tuberculin testing. Any tuberculin conversion is likely to be recent and the person at a higher risk of developing active disease.
   For monitoring of TB infection, recent conversion is defined as an increase within two years of the tuberculin reaction of ≥10 mm. In the case of recent close contact with sputum smear-positive TB, it is an increase of ≥ 5 mm within three months for children under 15 years of age, and ≥10 mm for adults.

3. POSITIVE TUBERCULIN REACTORS UNDER 35 YEARS OF AGE AND AT HIGH RISKS
   This indication refers to people with a single positive test carried out for surveillance or diagnostic purposes. It includes both immigrants from high prevalence regions and those with medical conditions that predispose them to increased risk of TB reactivation (refer Section II under the host).

4. HIV INFECTED INDIVIDUALS
   - All tuberculin reactors of ≥ 5 mm with no age limits.
   - Those having had close contact with sputum smear-positive TB irrespective of tuberculin status.

5. PERSONS WITH EVIDENCE OF PAST TUBERCULOSIS AND INADEQUATE TREATMENT
   This indication consists mainly of those having radiographic changes consistent with inactive TB in the chest x-ray. They have been estimated to have a natural incidence to develop active TB of 2.9 per 1,000 person-years[6].
   To justify the recommendation for preventive therapy in the group, the following criteria are essential:
   - TB is a reasonable cause of the abnormality including a positive tuberculin reaction.
   - It shows no sign of activity (asymptomatic, other examinations normal including negative bacteriology, stable lesions over a period).
   - No adequate past treatment.

   Other factors to consider include the type (calcified, 'fibrocaseous', 'infiltrates') and duration of the abnormality, the chance of reactivation in the person's lifetime and any associated medical conditions. In case of doubt about the TB diagnosis or activity it is prudent to proceed with further investigations or to observe for a period.

It should be noted that all indications except 5 assume that the only significant abnormality is a positive tuberculin reaction. In this respect BCG vaccination may produce a reaction that cannot be reliably distinguished from infection by the *M. tuberculosis complex*. For the purpose of preventive therapy as indicated above, disregard any history of BCG vaccination if no convincing scar is present. On the other hand therapy should be withheld if compliance cannot be ensured.

Preventive treatments

In spite of its well-documented effectiveness, preventive therapy is difficult to practise. The persons are invariably healthy, the side effects from the medication real and the chance of their infection progressing to disease may be small. Its main significance lies in reducing the infectious pool in the community and in removing the unpredictability of future TB reactivation in the individual.

REGIMENS

- Isoniazid monotherapy for 6 to 12 months.
- Two-drug combinations such as rifampicin/pyrazinamide for 2 months.
- Standard full treatment as for smear- and culture-negative TB when there are doubts on disease inactivity and therapy is warranted.
- The choice of treatment for contacts with drug resistant TB will depend on the drug susceptibility results from the index case; it may require the use of reserve or experimental drugs and simple observation should be considered as an option.

EFFICACY AND COMPLIANCE

Of the different regimens, only isoniazid monotherapy[6,7] has been adequately assessed. Both the 6- and 12-month regimens are highly effective but the former is more acceptable in terms of compliance. In WA from 1993 to 1996 inclusive, of 369 subjects who had 6 months of isoniazid monotherapy and a median follow up period of 12 months, 333 (90%) completed at least 5 months of medication and only one person subsequently developed active TB in the lymph node[8]. Varying degrees of treatment non-adherence were present in 90 (24%) and this was significantly related to adverse drug reactions. Although the side effects are predominantly minor it is important to attend to them promptly for better compliance.

ADVERSE DRUG EFFECTS

In the same study[8] adverse drug effects were present in 32 (9%) of the 369 subjects. The majority (20) had cutaneous reactions, including four who developed facial acne. Neurological complaints (7) consisted of giddiness, insomnia, drowsiness, headache, lack of concentration and transient paraesthesia. Digestive upsets included nausea, constipation and abdominal pain. Only one had raised liver enzyme levels.

The major concern on isoniazid is its potential hepatotoxicity that is rare in those under 35 years of age and without prior liver damage. A previous study in the United States[9] found the incidences to be 0, 0.3%, 1.2% and 2.3% for the age groups of under 20, 20-34, 35-49 and 50-64 years respectively. Without age restriction to the therapy, the overall mortality rate[6] is 0.14 per 1,000 but this is largely preventable with clinical alertness and proper monitoring.

References

1. Enarson DA, Rouillon. The epidemiological basis of tuberculosis control. In*:* Davies PDO, ed, *Clinical Tuberculosis.*. London: Chapman and Hall Medical 1994; **2**:19-32.
2. Selwyn PA, Hartel D, Lewis IA, et al. A prospective study of the risk of tuberculosis among intravenous drug abusers with human immunodeficiency virus infection. *New Engl J Med* 1989; **320**:545-50.
3. Comstock GW, Baum C, Snider DF. Isoniazid prophylaxis among Alaskan Eskimos: a final report of the Bethel isoniazid studies. *Am Rev Respir Dis* 1979; **119**:827-30.
4. Sbarbaro JA. The plan to eliminate tuberculosis in the United States. In: Reichman LB, Hershfield ES, eds, *Tuberculosis. A comprehensive international approach*. New York: Marcel Dekka Inc 1993; **28**:628-39.
5. Joint Tuberculosis Committee of the British Thoracic Society. Chemotherapy and management of tuberculosis in the United Kingdom: recommendations 1998. *Thorax* 1998; **53**:536-48.
6. International Union Against Tuberculosis Committee on Prophylaxis. Efficacy of various durations of isoniazid preventive therapy for tuberculosis: five years of follow-up in the IUAT trial. *Bull World Health Organ* 1982; **60**:555-64.
7. Ferebee SH. Controlled chemoprophylaxis trials in tuberculosis: a general review. VI. Results. *Adv Tuberc Res* 1970; **17**:41-73.
8. Pang SC, Harrison RH, Brearley J, Jegathesan V, Clayton AS. Preventive therapy for tuberculosis in Western Australia. *Int J Tuberc Lung Dis* 1998; **2(12)**:984-8.
9. Kopanoff DE, Snider DE, Caras GJ. Isoniazid related hepatitis. A US Public Health Service Cooperqtive Surveillance Study. *Am Rev Respir Dis* 1978; **117**:991-1001.

IX. BACILLE CALMETTE GUÉRIN VACCINATION

BCG vaccination has limited applications in Australia but should remain available for small selective groups of individuals.

This is the most controversial aspect in the control of TB. The policies governing its application vary from total rejection to universal vaccination at birth. The problem lies in the absence of convincing evidence of efficacy or otherwise from numerous studies[1-3]. The widely quoted meta-analysis of selected publications in the literature by Colditz and co-authors[4] gives an average of 50% overall protective effect in the vaccinated with 64% and 78% respectively against TB meningitis and disseminated diseases. The individual study results, however, differ from negative to 80% protection. This uncertainty and its negligible impact on TB control make BCG vaccination an unattractive option in the low prevalence countries. On the other hand its long safety record and minimal side effects provide a good alternative in special situations.

Rationale

Compared to preventive therapy, BCG vaccination is not cost efficient, has no impact on the epidemiology of the disease and provides unreliable protection against the development of TB disease.

To decide whether it has any place in the national TB program in Australia, we need to consider:

- The recommendations of the IUATLD[5]in 1994 and the WHO[6] in 1996,
- The wide spectrum of TB prevalence in the different migrant groups in Australia,
- The small direct benefit of the vaccination to the individual, and
- The absence of a preventive therapeutic regimen with proven efficacy and acceptability for multidrug resistant (MDR) TB.

The vaccine

The vaccine presently used in Australia is the *Dried BCG Vaccine* manufactured by the Connaught Laboratories and supplied through the Commonwealth Serum Laboratories. It comes with full explanation and instructions that should be strictly observed.

Method and dosage

The vaccine is given intradermally into the skin of the upper arm above the insertion of the deltoid muscle. Direct BCG vaccination is administered to babies less than two to three months old; otherwise the vaccine will only be given to those whose Mantoux reaction is under 5 mm in induration. Adults with a good BCG scar and a two-step Mantoux reaction (two tests on opposite arms carried out one week apart) of <5 mm should be assessed for anergy if revaccination is considered.

The dose is 0.05 ml for babies under 12 months of age and 0.1 ml for the rest.

Only designated and properly trained personnel should give the vaccination.

Contra-indications

ABSOLUTE:

- HIV seropositives,
- Those at high risk of HIV infection but with unknown serological status,
- Those with impaired immune responses as in leukaemia, lymphoma and generalized malignancy, and
- Those on immunosuppressive therapy including corticosteroids, anticancer/anti-rejection medications and radiation treatment.

NOT ADVISABLE:
- Within 4 weeks of another live vaccine except the oral poliomyelitis vaccine,
- During pregnancy,
- In the convalescent period of acute illnesses,
- In those with skin sepsis or a tendency to form keloid scars, and
- In newborns who are jaundiced, premature or weighing <2.5 Kg.

Complications

The BCG vaccine is one of the safest vaccines in use when given properly. Still it is important to be familiar with the evolution following vaccination and possible side effects.

NORMAL EVOLUTION
The wheal from the intradermal injection of the vaccine disappears within half an hour. A transient small erythema, associated rarely with a few tiny vesicles, may be seen in the first two days. The skin returns to normal to be followed by a small nodule in one to four weeks. It increases in size, becomes red and ulcerates with little serous discharges. The colour deepens to purplish and the ulcer dries up in one to three weeks. The crust that seals the ulcer comes off some weeks later and the lesion continues to heal usually within six months of the vaccination, leaving a small, pale and pitted scar.

LOCAL REACTIONS
- Slow healing or large size (>10 mm) of the local lesion (1%).
- Subcutaneous abscess (1:10,000).
- Secondary infections.
- Keloid formation.
- Lupus vulgaris (<1:100,000).
- Regional lymphadenitis (6-12%).
- Regional suppurative lymphadenitis (1-5%) that may require repeated aspirations or surgical removal.

DISTANT REACTIONS
- Subcutaneous abscesses (rare but no figure available).
- Osteitis (0.1:100,000) that is related to the vaccine type used.
- General BCG disease (0.01:100,000), usually in people with immune deficiency states.

Recommendations

Full informed consent is mandatory for BCG vaccination. All vaccinees should be issued with a record card indicating the date of vaccination, the dose and the batch number of the vaccine.

DIRECT BCG is offered to newborn babies (after obtaining parental informed consent):
- Of Indigenous Australians, or
- From high TB prevalence migrant groups, who are likely to maintain close contact with people in their country of origin.

BCG FOR TUBERCULIN NEGATIVES is available to:
(a) Persons under 6 years of age who are
    - Close contacts of patients with sputum smear-positive MDR-TB, or
    - Working/staying in high TB prevalence areas for over 6 months and preferring vaccination over repeating the Mantoux test for preventive therapy, and
(b) Fully informed health care and related professionals/ trainees in facilities caring for patients with MDR-TB.[7]

In the case of contact with sputum smear-positive and fully drug sensitive TB, the index patient should have been rendered non-infectious and initial contact tracing completed by the time the person shows no Mantoux conversion in three months. The indication for vaccination becomes non-existent unless the treatment fails.

There is no reason why an immunocompetent person of any age cannot receive BCG vaccination. The age limit is set as a guide from available evidences and should not be used to refuse vaccination in persons who are fully informed of the various aspects in relation to the complications and effectiveness or otherwise of the vaccine. For the purpose of vaccinating a person 6 years of age and over, a two-step Mantoux test is recommended to establish true tuberculin negativity.

The Perth Chest Clinic has free information sheets on “What you should know before BCG vaccination” (Appendix D) and “You have been vaccinated with BCG” (Appendix E) to those who intend to have the vaccination.

References

1. British Medical Research Council. BCG and vole bacillus vaccines in the prevention of tuberculosis in adolescence and early adult life. Third report. *Br Med J* 1963; **1**:973-8.
2. Tuberculosis Prevention Trial. Trial of BCG vaccines in South India for tuberculosis prevention: first report. *Bull IUAT* 1980; **55(1)**:14-22.
3. Fine PEM. Variation in protection by BCG: implications of and for heterologous immunity. *Lancet* 1995; **346**:1339-45.
4. Colditz GA, Brewer TF, Berkey CS, Wilson ME, Burdick E, Fineberg HV, Mosteller F. Efficacy of BCG vaccine in the prevention of tuberculosis. Meta-analysis of the published literature. *JAMA* 1994; **271**:698-702.
5. A statement of the International Union Against Tuberculosis and Lung Disease. Criteria for discontinuation of vaccination programmes using Bacille Calmette-Guérin (BCG) in countries with a low prevalence of tuberculosis. *Tubercle Lung Dis* 1994; **75**:179-80.
6. Global programme for vaccines and immunization – Expanded programme on immunization, 1996. Immunization Policy. WHO/Extended Programme on Immunization/Geneva/95.03. Rev 1. World Health Organization, Geneva.
7. Stevens JP, Daniel. Bacille Calmette Guérin immunisation of health care workers exposed to multidrug-resistant tuberculosis: a decision analysis. *Tubercle Lung Dis* 1996; **77**:315-21.

X. TUBERCULOSIS SURVEILLANCE

Good chemotherapy and active case finding are the two most powerful weapons in the fight against tuberculosis.

In the simplest terms TB surveillance refers to on-going programs of active case finding in high-risk groups of individuals. It entails a number of well-known TB control measures:

- Mass (miniature) radiography, either community wide or in selected groups,
- Tuberculin surveys usually in selected or representative groups,
- Contact tracing,
- Migrant surveillance, and
- Screening and protection of health care workers.

Mass miniature radiography[1] that was the main force of disease detection behind the Australian TB Campaign of 1948-76 is not cost-efficient in low prevalence communities. Tuberculin surveys detect infection and will only pick up diseases through chest x-ray/follow-up examinations in the positives. They are useful in estimating the infection risk in a population. Both are labour intensive, have little place in clinical practice and will be omitted from further discussions.

Xa. CONTACT TRACING

Rationale

The rationale of contact tracing in TB control is dependent on two principles:

- The major risk factor for infectiousness from the index case is the presence on microscopy of *M. tuberculosis complex* in the sputum, and
- We need to detect both the person(s) who transmit(s) the disease to, and those who may have been infected by, the index patient.

The study on contact tracing by the British Thoracic Society[2] in 1973-74 showed that the overall yields of new TB cases in England were 3.4% and 3.6% for the Asian and non-Asian communities respectively. They were about three times as high when the index case was positive on sputum smears and about a third when the index case had non-respiratory TB.

For practical purposes the procedure of contact tracing follows the "stone in the pond" principle. That is, we start with the household or close contacts and only extend the examination to work, social and casual contacts if the initial yield is high or when unusual exposure to a highly infectious case has occurred. An information sheet called “About contact examination for tuberculosis” (Appendix F) explaining the process in plain language is available from the Perth Chest Clinic.

Procedure

1. INDEX PATIENT WITH SPUTUM SMEAR-POSITIVE TB
   - 1.1 Household contacts under 2 years[3] of age should be offered preventive therapy irrespective of the result of the initial tuberculin test, which, if negative, will be repeated in 3 months. If the initial reaction is, or if the second test becomes, positive, complete the preventive therapy; if the repeat test remains negative, cease treatment and consider BCG vaccination. Note that the initial tuberculin test is not essential for decision-making.
   - 1.2 Contacts aged 2 years and above will have a tuberculin test:
     - 1.2.1 Positive reactors aged less than 35 years will be offered preventive therapy.
     - 1.2.2 Positive reactors aged 35 years and over will have chest x-ray examinations at 0, 6 and 18 months.
     - 1.2.3 Negative reactors will have a repeat tuberculin test in 2-3 months. All converters irrespective of age will be offered preventive therapy. Persistent negative reactors will be

discharged unless the index case has multidrug resistant TB when BCG vaccination may be considered for those under 15 years of age.

1.2.4 Those not accepting preventive therapy will be x-rayed at 0, 6 and 18 months.

2. INDEX PATIENT WITH SPUTUM SMEAR-NEGATIVE OR EXTRAPULMONARY TB

2.1 All contacts will have a tuberculin test.

2.1.1 Positive reactors under 35 years of age will be assessed for preventive therapy.

2.1.2 Positive reactors aged 35 years and above will be x-rayed at 0, 6, and 18 months if the index patient has pulmonary disease.

2.1.3 Negative reactors having contact with pulmonary TB will have a repeat of the test in 2-3 months. Converters will be offered preventive therapy and persistent negative reactors discharged.

2.1.4 Negative reactors having contact with extrapulmonary TB will be discharged.

3. Contacts who cannot be skin tested should if practicable have chest x-ray examinations as for positive tuberculin reactors.

4. It is understood that all contacts being offered or assessed for preventive therapy should have a chest x-ray.

5. All contacts with symptoms or abnormal chest x-rays not related to other existing medical conditions should be clinically assessed for active disease irrespective of tuberculin or index patient status.

6. BCG vaccination may produce a tuberculin reaction that cannot be reliably distinguished from those caused by infections with the *M. tuberculosis complex*. If no convincing scar is found disregard any vaccination history in the interpretation of the tuberculin test for contact examinations.

7. For definitions of positive reactors refer Table 3 in Chapter IV on Diagnosis.

Xb. MIGRANT SURVEILLANCE

Rationale

The incidence of TB in Australia has remained stable at 5 to 6 per 100,000 population since 1984; in recent years the foreign-born accounts for around 80% of the annual TB notifications.[4] The incidence of the disease in certain migrant groups is 18 to 40 times that of the non-Aboriginal Australians and 4.5 to 8 times that of the Aboriginal Australians (Table 1). The necessity to screen them before and after arrival is therefore obvious.

Table 1: Incidence rates of culture-positive tuberculosis by origin of birth in Western Australia

Origin of birth	Average annual incidence			Total Notifications			
	Rates/100,000		Mean annual	1980-9		1991-3	
	1980-9	1991-3	change	No.	%	No.	%
Australian							
non-Aboriginal	1.7	0.8	-10%	157	32	26	23
Aboriginal	7.0	3.8	- 8%	25	5	5	4
European	5.4	0.9	-21%	134	28	9	8
Asian	31.4	31.8	+0.2%	145	30	64	56
Others	5.7	7.8	+4%	24	5	10	9
Total	3.5	2.3	-5%	485	100	114	100

The primary objective of pre-migration screening is to detect infectious and active TB and any post-migration surveillance should include an assessment for preventive therapy in suitable immigrants or groups. To provide BCG vaccination to their children is not a consideration in Australia although it may be discussed if the parents seek information on the issue.

The Australian tuberculosis screening system

Under the Migration Regulations of the Migration Act 1958, all foreign-born adults applying for long-term stay in Australia require TB clearance. The assessment is being processed through three avenues: (a) offshore visa offices, (b) onshore DIMIA (Department of Immigration and Multicultural and Indigenous Affairs) offices and (c) the International Office for Migration (exclusively for offshore humanitarian immigrants).

The chest x-ray examination is the most important criterion to exclude current infectious TB and Mantoux testing is not required. All persons found to have active disease must be treated or rendered non-infectious before the visa is granted. They, together with those having a past history of TB or chest x-ray changes consistent with the disease are required to sign a health undertaking[5,6] by which they are bound to attend the State/Territory TB Control Body within four weeks of arrival.

The system applies to all applicants for permanent or long-term residence in Australia. Long-term residence includes visa classes for business, work, study, retirement, aged parents and visitors from high-risk countries staying for over three months.

Classification

Three broad categories of immigrants are recognised:

- **Category I** consists of immigrants admitted into Australia subject to health undertakings[5,6] with or without abnormal chest x-rays.
- **Category II** refers to the humanitarian immigrants who come from high TB risk areas and require screening or surveillance although they may not be subject to an undertaking and may have normal chest x-rays. They include those having been assessed by an international migration centre, the illegal entrants, and the asylum seekers.
- **Category III** relates to the remaining majority of immigrants from high-risk regions and with complete medical clearance overseas. They have no regulatory obligation to undergo further TB screening on arrival but are generally advised of such a service in the State or Territory where they come to settle.

Screening

1. CATEGORY I
   - 1.1 Immigrants under this category are required by virtue of their signing the health undertaking, to attend the State/ Territory TB Control Body within four weeks of their first arrival. They are individually assessed, as the reasons behind the undertaking may vary from abnormal chest x-ray findings, present and past TB treatment or recent exposure to poor pre-migration films, hepatitis B infection and pregnancy.
   - 1.2 Those with abnormal chest x-rays would need assessments or follow-up by a chest physician. Further actions and duration of observation are matters of clinical decision. In general they should be evaluated for active TB, preventive therapy or periodic radiographic surveillance.
   - 1.3 Non-TB undertakings may require referral to, or consultation with, other health care services.

2. CATEGORY II
   - 2.1 All migrants under this category will be tuberculin tested:
     - 2.1.1 Positive reactors (>9 mm) under 35 years of age and with no BCG scars are x-rayed and assessed for preventive therapy.

2.1.2 Positive reactors under 35 years of age and with BCG scars are x-rayed at 0, 6, 18 and 30 months if the reaction is <15 mm and offered preventive therapy if >14mm.
2.1.3 Positive reactors aged 35 years and over are x-rayed as under 2.1.2 irrespective of BCG vaccination status.
2.1.4 Persons eligible for but refusing preventive therapy will be followed up as under 2.1.2.
2.1.5 All negative tuberculin reactors should have a two-step Mantoux test. Persistent negative reactors are discharged with those aged 15 years and over subject to a normal chest x-ray.
2.1.6 Immigrants having abnormal chest x-rays at any stage are treated as under Category I.

3. CATEGORY III immigrants who attend voluntarily will be assessed individually by the chest physician as under 1.

Xc. SCREENING AND PROTECTION OF HEALTH CARE WORKERS

Rationale

The increased risk of TB in health care workers (HCWs) and health care facilities (HCFs) has been well recognised and extensively documented[7,8.] Although its prevalence in Australia is unknown, it is expected to be uncommon in view of the very low incidence of the disease and the generally stringent control measures. Comprehensive protocols to deal with the issue have been prepared in the United States[9] but they are resources demanding to implement and applicable only to large referral or tertiary centres in this country.

Recommendations should take into consideration the following:

- HCWs may not only be infected by, but also spread the disease to, those under their care; therefore they need both protection and screening.
- Due to the great variation in the degree of risk in different HCFs in Australia, the infection control bodies of individual institutions and the HCWs should be given the direct responsibility of planning and implementing the control strategies.
- The best intervention is the combination of a high suspicion index coupled with early diagnosis and effective treatment of patients with sputum smear-positive TB according to local epidemiological data and State/Territory guidelines.
- While BCG vaccination is unreliable in preventing TB infection, there is difficulty in compliance with preventive therapy after infection in healthy persons.
- The general standard of infection control, the extent of environmental engineering in the work place and the provision of personal protective gears should best be decided by the risk of infection in individual HCFs rather than a strict blanket national policy.
- The ultimate requirements for the institution should be determined by the infection rate following the implementation of the strategies.

High-risk health care facilities or areas

TB is not a highly infectious condition and most HCFs in Australia do not need a separate control policy for the disease. On the other hand as regular tuberculin testing of HCWs has not been a national policy and the rates of nosocomial TB infection in Australia are not available, the definition of high risks is arbitrary and based mainly on experiences from the United States[10].

- Where nosocomial transmission of TB has occurred,
- Where TB patients are commonly cared for before diagnosis and treatment: the chest or TB clinics, respiratory medical wards, radiology waiting rooms and emergency departments,
- Where procedures such as bronchoscopy, endotracheal intubation, sputum induction, aerosol therapy, open abscess irrigation, processing of secretions/ tissues for TB culture and autopsy are performed, and
- Where patients with multidrug resistant TB and/or immunocompromised conditions are managed.

Pre-employment screening of health care workers

1. All HCWs should have a Mantoux test before employment unless there is adequate documentation of a reliable test result within the last 3 months.
2. Positive reactors without BCG scars should have a chest x-ray and/or be referred to a chest physician with experience in TB for assessment.
3. Positive reactors with or without BCG scars and working in high-risk areas should be offered biennial chest radiography and those working in low risk areas chest x-ray examination whenever exposure occurs.
4. Negative reactors with no BCG scar and working in high-risk facilities should have annual Mantoux testing for conversion while those in low-risk facilities would follow standard contact examination procedures when exposure occurs.
5. Negative reactors with BCG scars should have a two-step Mantoux test to set the baseline reaction size. Persistent negative reactors will follow procedures as in 4 and positive reactors to the second test as in 3.
6. BCG vaccination may be an acceptable alternative to annual Mantoux testing at the request of the negative reacting HCWs who are likely to be exposed to MDR-TB. Full information on the issue should be given and the contra-indications for the vaccination strictly observed.
7. HCWs with immunocompromised conditions or on immunosuppressive therapy should not work in high-risk areas.
8. Staff without direct contact with patients requires neither pre-employment TB screening nor regular monitoring apart form contact examination on exposure.

Post-exposure assessment

1. HCWs monitored by periodic Mantoux testing or chest radiography do not need separate contact examination with each TB exposure at work.
2. HCWs working in low-risk facilities do not need regular monitoring and only require standard contact examination whenever TB exposure occurs.
3. TB exposure is defined here as direct care from an unprotected HCW for four or more total cumulative hours, of a patient who has been or are subsequently diagnosed to have sputum smear-positive pulmonary TB.
4. All HCWs with Mantoux conversion either through periodic monitoring or contact examination should be offered preventive therapy for TB.
5. All HCWs working in high-risk areas and developing symptoms suggestive of TB should be promptly assessed.

The infection control body

The infection control body of the health care facility should be directly responsible for the following:

- The development and implementation of effective policies and protocols to ensure rapid detection, isolation and treatment of patients with infectious TB,
- The engineering controls to prevent the spread and to decrease the concentration of infectious droplets through measures such as local exhaust or dilutional ventilation, unidirectional air flow and air cleaning or filtration,
- The supply of personal respiratory protective equipment in high-risk areas,
- The development, implementation and periodic assessment of the TB infection control plan, including the pre-employment screening procedures,
- The investigation and assessment of any suspected/confirmed nosocomial outbreaks, and
- The education of its staff on TB appropriate to their work category.

Steps to set up a tuberculosis infection control policy in an institution

1. Assign responsibility (TB infection control body).

2. Assess the risk.
    - Identify overall risk and risk areas or groups.
    - Classify the risk:
      Very low – no TB case in the previous year,
      Low - <6 cases in the previous year,
      Moderate - ≥6 in the previous year, and
      High – evidence of nosocomial transmission.
3. Decide on the optimal method of screening HCWs.
    - Regular Mantoux testing for conversion,
    - Entry and exit Mantoux testing,
    - Periodic chest radiography, and/or
    - Contact examination whenever a case arises.
4. Educate and reinforce on work practices:
    - High index of suspicion,
    - Early diagnosis of infectious TB, and
    - Prompt isolation and treatment.
5. Decide on environmental engineering in the work place:
    - Uni-directional ventilation,
    - High efficiency particulate air filtration, and/or
    - Ultra-violet gemicidal radiation.
6. Decide on personal respiratory protection:
    - Disposable particulate masks,
    - Elastometric half-face masks, or
    - Air-purifying respirator hood.
7. Develop, implement and enforce the TB infection control policy.
8. Establish procedures to evaluate and tackle nosocomial transmission of TB.
9. Review regularly the efficacy and efficiency of the policy.

References

1. Pang SC. Chest radiography and tuberculosis case-finding in Western Australia. *Respir Med* 1998; **92**:198-202.
2. British Thoracic and Tuberculosis Association. A study of a standardised contact procedure in tuberculosis. *Tubercle* 1978; **59**:245-59.
3. Joint Tuberculosis Committee of the British Thoracic Society. Chemotherapy and management of tuberculosis in the United Kingdom: recommendations 1998. *Thorax* 1998; **53**:536-48.
4. The Communicable Diseases Network Australia. Tuberculosis notifications in Australia, 2000. *Commun Dis Intell* 2002; **26**:214-25.
5. King K, Dorner RI, Hackett BJ, Berry G. Are health undertakings effective in the follow-up of migrants for tuberculosis? *Med J Aust* 1995; **163**: 407-11.
6. Pang SC, Harrison RH, Brearley J, Jegathesan V, Clayton AS. Tuberculosis surveillance of immigrants through health undertakings in Western Australia. Int J Tuberc Lung Dis
7. Sepkowitz KA. Tuberculosis and the health care worker: a historical perspective. *Ann Intern Med* 1994; **120**:71-9.
8. Menzies D, Fanning A, Yuan L, Fitzgerald M. Tuberculosis among health care workers. *New Engl J Med* 1995; **332(2)**:92-8.
9. ACCP/ATS consensus Conference. Institutional control measures for tuberculosis in the era of multipe drug resistance. *Chest* 1995; **108**:1690-710.
10. Davis YM, McCray E, Simone PM. Hospital infection control practices for tuberculosis. In: Iseman MD, Huitt GA, eds. *Clinics in Chest Medicine*. Philadelphia: WB Saunders 1997; **18(1)**:19-33.

APPENDIX A
TUBERCULOSIS FORM A TO Z FOR PATIENTS

A What is tuberculosis?
Tuberculosis is an infectious disease that untreated may lead to death or years of chronic ill health. It can affect people of all ages but is now most common in older persons.

B Is tuberculosis curable?
Yes. Tuberculosis is almost 100% curable with modern treatment. To be effective, treatment requires the full co-operation of the patient. Early diagnosis, followed by prompt treatment, helps preventing spread to others and in avoiding or diminishing disability after treatment.

C Can a treated patient lead a normal life?
Yes. The outlook has brightened dramatically due to modern drugs. With few exceptions patients return to full work and recreation, even while under treatment.

D What is the cause?
The only cause is a minute germ – the tubercle bacillus – that can grow and multiply in the body.

E How is tuberculosis spread?
It is almost entirely an air-born disease spread to healthy individuals by the germs that come from the lungs of an infected person. Such a person may disseminate the bacilli widely by coughing, sneezing, laughing or shouting. The danger is not in the large visible particles but in the tiny droplets that may be inhaled by those in contact. Tuberculosis is not spread by handling objects that have been used or touched by a patient.

F Is tuberculosis hereditary?
No. This belief arose because naturally those in closest contact with patients are their families who are then most likely to be infected.

G What parts of the body are usually involved?
The blood stream may carry the infection to any part of the body, but by far the commonest part infected is the lungs. This is termed pulmonary tuberculosis.

H What tests are done for tuberculosis?
There are a variety, depending on the part of the body infected, but nearly all cases of tuberculosis have three tests. These are a chest x-ray, a sputum test and a tuberculin test.

I Why is an x-ray necessary and what does it show?
The x-ray is necessary because much of the large volume of the lungs may be involved in disease before major symptoms occur. The x-ray will show the tuberculosis process (lesion) and its extent. Some common terms used are - a cavity, which is a hole in the lung eroded by disease; calcification and fibrosis which are some indications of the body's effort to heal and which may be referred to as "scars'.

J What is a sputum test?
This is a test carried out to ascertain whether tubercle bacilli are present in the sputum (phlegm). Their presence is proof of active pulmonary tuberculosis. In persons with little sputum, small amounts may pass over the top of the windpipe and down to the stomach. Sputum may be coughed up naturally, be induced by a special inhalant or be obtained through a stomach washing or aspirations from the air tubes. The bacilli may be found by a rapid microscopic examination called a 'smear'. A more accurate identification is by growing the actual germs. This may take up to 12 weeks and is called a "culture'.

K What is a tuberculin test?
A tuberculin test is the injection into the skin of a minute dose of some of the proteins (tuberculin)

made by the tuberculosis germ. Persons who have been infected have formed antibodies that react with the tuberculin to give a positive reaction. The test is also called the Mantoux test.

L Does a positive skin test mean that I have tuberculosis?
No. Most people with a positive test do not have active tuberculosis, but have been infected at some time. Usually the body defences have controlled the infection.

M Can animals cause infection to humans?
Very rarely in Australia is tuberculosis caused by milk (bovine disease) and even more rarely is the disease spread between animals and humans by close contact.

N What symptoms does pulmonary tuberculosis cause?
In the early or even moderate case, there may be none. The classical symptoms of fully developed disease are cough, sputum, coughing up blood, weight loss, lethargy and high temperature. Persisting cough or any of the other symptoms indicate the need for a chest x-ray.

O What is the treatment?
Modern treatment is by drugs. It is almost always successful but most patients still need 6 months of medication. Interrupted or too short a period of therapy increases the possibility of treatment failure. The best chance of cure is on the first treatment.

P What drugs are used in treatment?
Many are available, but several that have been proven to be the best are Isoniazid, Rifampicin, Pyrazinamide, Ethambutol and Streptomycin.

Q What can I do to ensure my cure?
Take your drugs absolutely regularly and exactly as prescribed. Never stop taking one of your drugs as treatment problems may result. Consult immediately with your physician about all ill effects that make taking your drugs difficult. In some cases it may be necessary to vary the medication because of reactions.

R What is a reactivation?
A reactivation is a breakdown of previously treated tuberculosis. It is now rare where proper treatment has been completed. However, to guard against breakdown, the patient should consult the doctor if symptoms reappear.

S Are patients with tuberculosis safe to be with or work with?
A patient whose disease is controlled by effective treatment, is no danger to others.

T Are any special hygienic precautions necessary for patients?
Yes. Cough should be guarded at all times and tissues used should be properly disposed of or burnt. Your physician or nurse will advise. Contact with others, particularly with children, should be avoided at certain stages of the illness, but this depends on the individual case and, if necessary, advice should be sought.

U Are there any special precautions necessary with bedding, utensils, etc?
No. Thorough normal cleanliness is all that is necessary. There is no need for such procedures as fumigation, washing walls with Lysol or boiling utensils, etc.

V What is a contact?
A contact is someone who either at home, socially or at work has been in contact with a patient suffering from tuberculosis. As this is an infectious disease, contacts run some risk of catching it and should be checked at a chest clinic.

W What is a BCG?
BCG is a vaccine that gives some protection against tuberculosis. It is offered where appropriate to

certain individuals and groups at high risk in Australia.

X Is treatment free?
All treatment for tuberculosis is free at approved chest clinics, hospitals and institutions in this country.

Y Is there a special tuberculosis allowance?
No. If you are employed and your doctor considers you are not fit to work for a specific period, you may be entitled to a sickness benefit paid through Social Security.

Z Where can I get help or advice?
There are many ready to help in the net work of tuberculosis and chest clinics that cover Australia. The following is a list of them in the capital cities:

Sydney **Phone 02 9828 5980**	TB Services Hugh Jardine Building Locked Mail Bag 7017 Liverpool BD 1871
Melbourne **Phone 03 9637 4115**	TB Program Dept of Human Services 120 Spencer Street Melbourne
Brisbane **Phone 07 3224 5535**	Division of Specialised Health Services 63 George Street Brisbane
Adelaide **Phone 08 8222 5307**	Chest Clinic 275 North Terrace Adelaide
Perth **Phone 08 9325 3922**	Chest Clinic 17 Murray Street Perth
Hobart **Phone 03 6222 7293**	Chest Clinic Royal Hobart Hospital Hobart
Canberra **Phone 02 6244 2066**	Chest Clinic Department of Thoracic Medicine The Canberra Hospital Garran ACT 2606
Darwin **Phone 08 8922 8522**	TB Clinic Royal Darwin Hospital Casuarina

APPENDIX B
WHAT YOU SHOULD KNOW ABOUT THE MEDICATION FOR TB TREATMENT

General

1. Take your medication as single doses every day at about the same time and for the required period. Remember that ***irregular medication will lead to failure of treatment.***
2. Make sure the dose of each kind of medicine is correct and always store them in a cool dry place.
3. Mild stomach upsets may be noted at the beginning but they usually go away with persistence. However if they get worse or affect your daily activities, or if you are in doubt, talk to the doctor who prescribed you the medicine or the visiting nurse.
4. No medication is completely free of side effects but their occurrence varies from person to person. It is important for you to recognise and report them early to this Clinic to prevent any ill effects.
5. Show your doctor the medication card when you need other treatment or going into a hospital.
6. Alcohol should be avoided during the period of treatment.
7. A brief description of the medicine you have been prescribed follows, but it is important to point out that the information is incomplete. Remember: ***when in doubt, talk to your doctor.***

RIFAMPICIN (RIMYCIN/RIFADIN)

The capsules of Rimycin (Rifadin) are in two forms: the maroon and black (red and blue for Rifadin) ones containing 150 mg of Rifampicin, and the all maroon (all red for Rifadin) ones 300 mg. They should be taken about an hour before or two hours after meals. The adult daily dose is 600 mg for those weighing 50 kg and above, and 450 mg for those below 50 kg.
Rifampicin colours your urine, sweat, tears and saliva from orange to reddish, but this is entirely harmless although soft contact lenses may become discoloured. The main side effects are stomach upsets: nausea, loss of appetite and abdominal discomfort, rarely vomiting and diarrhoea. Mild flushing, itchy skin and a faint rash are often transient and treatment can be continued. Occasionally they may get worse or are associated with fever. When that happens you should cease all medication and let this Clinic know as soon as possible. Inflammation of the liver is rare unless your liver has been damaged by other diseases or alcoholism.
Drug interactions occur with the following: the contraceptive pill, warfarin, oral diabetic drugs, digoxin, phenobaritone, methadone, morphine and dapsone. Let the nurse/doctor know if you are taking any of these medications.

ISONIAZID

Each small white tablet contains 100 mg of Isoniazid and the adult dose is 300 mg daily.
Adverse effects of Isoniazid are uncommon, the main ones being inflammation of the liver (especially in those over 35 years of age) and peripheral neuropathy (tingling and numbness of the fingers and toes). The daily tablet of VITAMIN B6 is given to prevent the neuropathy. Itchiness of the skin and rashes are rare.
Drug interactions may occur with the anti-convulsants given for epilepsy. Let the nurse/doctor know if you are on any of them.

PYRAZINAMIDE (ZINAMIDE)

Each large white tablet of Zinamide contains 0.5 gm (500 mg) of Pyrazinamide. The daily adult dose is 1.5 gm, 2.0 gm and 2.5 gm for persons weighing 41-60 kg, 61-80 kg and over 80 kg respectively.
Common side-effects include loss of appetite, nausea and flushing. Pain in the joints is usually mild and can be relieved with simple analgesics. Inflammation of the liver is uncommon, so are skin reactions (itchiness and rashes) and photosensitivity (over-reaction of the skin to sunlight).

ETHAMBUTOL (MYAMBUTOL)

Myambutol has two strengths. The large grey tablet contains 400 mg of Ethambutol and the small yellow tablet 100 mg. The daily adult dose is 25 mg per kg body weight for the first two months and 15 mg per kg thereafter if required. Make sure that this dosage is not exceeded at all times.
The most serious but fortunately uncommon adverse effect of Ethambutol is progressive loss of vision both in sight and in colour (especially red and green). ***Stop the drug at once and report to this Clinic as soon as possible when you notice or even suspect any visual disturbance.*** If you do, there is every chance that your eyesight will fully recover. If you ignore the early symptoms and continue the medication, your eyesight may become permanently damaged.
Other rare side effects include pain in the joints, skin reactions (itchiness and rashes), inflammation of the liver and peripheral neuropathy (tingling and numbness of fingers and toes).

APPENDIX C
ABOUT PREVENTIVE THERAPY FOR TB

Your tuberculin test (skin test for tuberculosis) is found to be positive. This means that at some stage in the past you have had contact with the germ that may cause tuberculosis (TB). We cannot tell from the test when and how this happened.

If you did not have BCG vaccination before, you have about a 10% chance of developing active TB in the future. If you had the BCG vaccine before contact with the TB germ, you could be partially protected. However if contact occurred first, there will not be any protection.

You have two choices to deal with the situation. You can choose to wait and have the full treatment when you develop the active disease later on. Only one in ten persons will need that but the timing cannot be predicted. Alternatively you can take a six-month course of preventive medication now to get rid of the infection. In that case you do not have to worry about it or be checked regularly. You have the options because you are well and not contagious.

If you decide to receive preventive treatment, you will be given ISONIAZID tablets that you should take once every day for a total of six months. You will also be given Vitamin B6 to reduce the side effects from the antibiotic. The most important thing to remember is, **once you decide to have the treatment, you must take the medication continuously for six months without any interruption**. Collect more tablets from the Perth Chest Clinic before the bottle is empty. There is no charge for the treatment.

Adverse effects from Isoniazid are rare, the main ones being inflammation of the liver and tingling in the fingers and toes. Itchiness and/ or rashes in the skin are uncommon. Interference with other drugs may occur. Please let the nurse or doctor know if you are taking any. Avoid alcohol during treatment.

APPENDIX D
WHAT YOU SHOULD KNOW BEFORE BCG VACCINATION

What is BCG?

BCG is a live TB germ found commonly in cattle. It has been modified in the laboratory so that it will not cause disease in a normal person. However it is capable of producing severe or fatal TB in persons with impaired resistance, such as those infected with HIV.

How is the BCG vaccine given?

It is injected into the skin of the upper arm near to the shoulder. Complications are more likely if it is given in any other site.

Is the vaccine safe?

Yes if it is given according to strict guidelines by properly trained personnel. This is the experience from having vaccinated hundreds of millions of people all over the world. Apart from the sore at the injection site (a normal response), occasionally healing may be prolonged or a swelling (enlarged lymph node) with/without pain may develop in the armpit. Both will eventually disappear and very rarely require treatment.

How effective is the vaccine?

Successful vaccination gives a good protection against the severe forms of TB and leprosy **in children** who have not been infected by the TB germ. It is important to realise that protection will only start 6-8 weeks after the vaccination, lasts for about 10 years, and is variable and low in adults.

Who should NOT be vaccinated?

BCG vaccination should not be given to:

1. Those tested HIV positive or having high risk behaviours for HIV infection,
2. Those suffering from certain cancers,
3. Those on treatment with corticosteroids, radiotherapy and anticancer or anti-rejection medication,
4. Those whose Mantoux reaction is $\geq$ 5 mm induration,
5. Those having had a live vaccine within 4 weeks other than the oral poliomyelitis vaccine,
6. Those who are pregnant,
7. Those with inflamed skin conditions or tendency to form keloid scars, and
8. Newborns who are jaundiced, premature or weigh under 2.5 Kg.

Who may be vaccinated in Western Australia?

BCG vaccination to school children in this State ceased in 1985 and is now offered to only a very small and limited group of people who have a high risk of catching TB. However any person referred to this Clinic by a medical practitioner will be considered provided that the implications are well understood and informed consent has been given.

APPENDIX E
YOU HAVE BEEN VACCINATED WITH BCG

Here are some facts that should interest you

What to expect after BCG vaccination

You have been given an injection of BCG vaccine into the skin of the upper arm. A small swelling will appear in one to four weeks time. This is the sign that the vaccine is doing its work. The swelling will enlarge and a small sore may appear. If left alone and not covered, the swelling will go down again and the sore will heal in several weeks.

What to do if a sore appears

Leave the sore uncovered and exposed to the air. This helps it to heal quickly. Do not scratch it or disturb the scab. If it is moist dab it gently with methylated spirit as often as required. This will dry it up. If there is enough discharge to soil the clothing, place a piece of clean dry gauze over the sore and secure it with a narrow strip of adhesive plaster on either side, making sure that air can reach the sore. If at any stage you are worried please contact the Perth Chest Clinic.

What not to do

Do not apply ointment, antiseptics, sticking plaster or any dressing as these may delay healing.

The effect of BCG vaccination

Successful vaccination with BCG gives a good protection against tuberculosis in children and experience shows that protection lasts for years.

KEEP THESE INSTRUCTIONS UNTIL THE VACCINATION HAS COMPLETELY HEALED

APPENDIX F
ABOUT CONTACT EXAMINATION FOR TUBERCULOSIS

What is contact examination?

It is the checking for tuberculosis (TB) in persons who have had recent contact with a patient notified to be suffering from the disease.

Why do we need contact examination?

TB is a contagious disease spread by airborne droplets from persons with the infectious form of the disease. The notified patient must have contracted it from someone and may continue to infect others around him or her. The contact examination will detect both and break the cycle of transmission.

What are the tests carried out in contact examination?

If you are a child or an adult without symptoms we usually do a skin (Mantoux) test followed by a chest x-ray if the test is positive. If you have symptoms or are worried, we may start with the chest x-ray that will give us the results much quicker. You may also request discussing your personal concerns with the Clinic doctor. If your x-ray is abnormal, a full consultation will be arranged.

Do I need follow-up examinations?

The answer is generally yes. To begin with, if you have a skin test you need to come back in three days for the result.

If you had contact with infectious TB, you need to be checked again to allow for the incubation period and the late development of the disease. You may be required to have a repeat of the skin test in 3 months and/or the chest x-ray in 6 and 18 months. Occasionally you may need follow-up appointments with the doctor.

If you had contact with non-contagious TB, your skin test is negative and/or chest x-ray is normal, you will not need further examinations for the contact.

Do I have to book for my follow-up examinations?

No. You will be notified in writing before your next appointment with us for the examinations. Please inform this Clinic if you change your address.