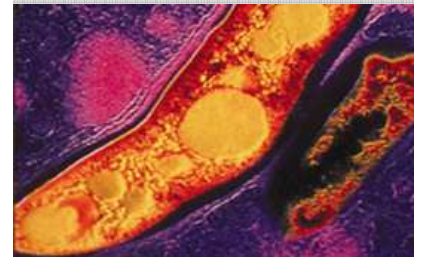
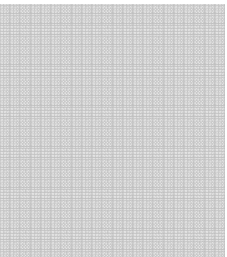


Prevention, Control and Management of Tuberculosis: A National Strategy for Malta



March 2012

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Chapter 1

Introduction

Tuberculosis (TB) is a re-emerging infectious disease of global importance. In 1993, the World Health Organisation (WHO) had declared TB as a 'global emergency'. Worldwide, TB is the second leading cause of death from communicable disease, being responsible for 1.7 million deaths in 2009.¹ Overall, one-third of the world's population is currently infected with the TB bacillus. Sub-Saharan Africa has the highest incidence per capita (over 350 cases per 100,000) but the greatest burden of disease occurs in South-East Asia.¹

1.1 BACKGROUND

1.1.1 Causative organisms

TB is caused by *Mycobacterium tuberculosis* complex, which includes the organisms *M. tuberculosis* and *M. africanum* primarily transmitted from humans, and *M. bovis* primarily transmitted from cattle. *Mycobacterium tuberculosis* is the most frequent cause of TB worldwide.

1.1.2 Transmission of Infection

TB is transmitted by inhalation of infected airborne droplet nuclei produced by people with pulmonary or laryngeal TB during expiratory efforts like coughing and sneezing. Prolonged close contact with an infectious person is usually required for transmission of infection to occur. Uncommonly TB can be contracted through consumption of unpasteurized milk or dairy products contaminated with *M. bovis*. Haematogenous dissemination of mycobacteria in a pregnant mother with extra-pulmonary TB is also possible, and may result in vertical transmission and manifestations of congenital TB in the infant. Laboratory personnel, pathologists and mortuary workers may also be at risk through inoculation of bacilli via cuts and scratches, or by inhalation of droplets when working on tuberculous material or cultures.

1.1.3 Signs and Symptoms

In most cases, primary TB infection is either asymptomatic or presents as a febrile respiratory illness of short duration. In the vast majority (90%) the infection is usually contained by the host's immune system and becomes dormant. This is termed latent tuberculosis infection (LTBI). LTBI can reactivate many years after the initial exposure in settings of advanced age or in cases of immunosuppression such as in patients with HIV infection, prolonged corticosteroid therapy, cancer, genetic factors and diabetes.

LTBI may be detected through a positive Mantoux result and serial Mantoux testing. In recent years, an interferon-gamma release assay (IGRA) test has become available, which excludes false positive Mantoux tests like those secondary to BCG vaccination and many environmental mycobacterial infections.

Primary TB infection most commonly affects the mid-part and lower regions of the lung, with regional spread to the hilar lymph nodes. Reactivation of pulmonary disease often occurs with cavitations in the upper lung zones. Disease may also develop in extra pulmonary sites. The most common sites include the lymph nodes (especially cervical), pleura, larynx, genitourinary system, bones and joints, skin and the central nervous system. Disseminated or miliary TB may also occur.

Patients with pulmonary TB very often have a cough which is usually productive, with occasional breathlessness, chest pain, and haemoptysis. Other non-specific symptoms such as weight loss, malaise and night sweats are important and may also be present. The three most common presenting symptoms are cough of more than 3 weeks duration, unexplained weight loss, and night sweats.

Diagnosis of pulmonary TB may be made by a combination of clinical features, radiological features and sputum smear microscopy and culture, histological examination and molecular studies. Confirmation of the diagnosis is obtained through testing of sputum for acid-fast bacilli and by culture of an organism belonging to the *M. tuberculosis* complex. Those with pulmonary TB are assumed infectious for as long as the mycobacteria are observed in the sputum.

Extrapulmonary TB can be diagnosed clinically, by histology and culture of appropriate specimens. Patients with extrapulmonary TB alone are generally not considered to be infectious except for laryngeal and congenital TB.

1.2 EPIDEMIOLOGY OF TUBERCULOSIS IN MALTA

1.2.1 Tuberculosis by geographic origin

Malta is a low TB incidence country with an average notification rate of 7.1 per 100,000, ranging from 1.8 to 12.9 per 100,000 over the last ten years. Like other Western European countries, the TB notification and incidence rates in Malta have decreased steadily among the indigenous population in recent decades. In fact from 1995 to 2011, the TB rate in the Maltese population has significantly ($p < 0.001$) decreased² (Figure 1). In the local population it occurs mostly in the elderly, mainly due to reactivation of old TB.

However, following the recent wave of immigration from the African subcontinent to Malta since 2002, it was noted that an increasing number and proportion of TB cases were being detected among these immigrants² (Figure 1, 2). In 2011, 73% of total TB cases occurred in migrants (Figure 2). Furthermore during the period 2002 to 2011 the TB rate in the migrant population has significantly ($p < 0.001$) increased.²

The overall TB rate from 1995 to 2011 has also increased significantly ($p < 0.05$ -Figure 1).² This rise seems to reflect the rise in immigrant rate, as the TB rate in the Maltese population has decreased and is likely to be due to the recent large influx of immigrants from a high prevalence country. Similar trends have been observed in many Western European countries which have undergone a

large influx of immigration from countries with a high incidence of TB, like The Netherlands and Switzerland.³

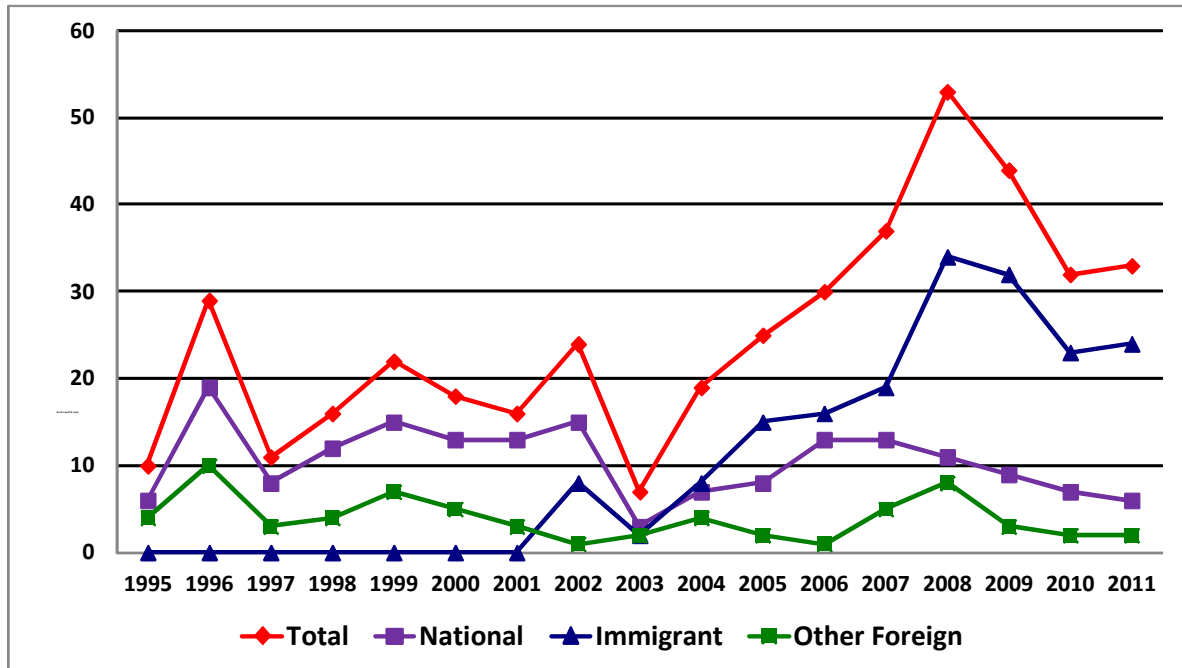


Figure 1: Number of notified* TB cases by geographic origin, Malta, 1995-2011

*Notified TB cases means cases notified to IDCU and ascertained.

Source: IDCU TB Surveillance Database

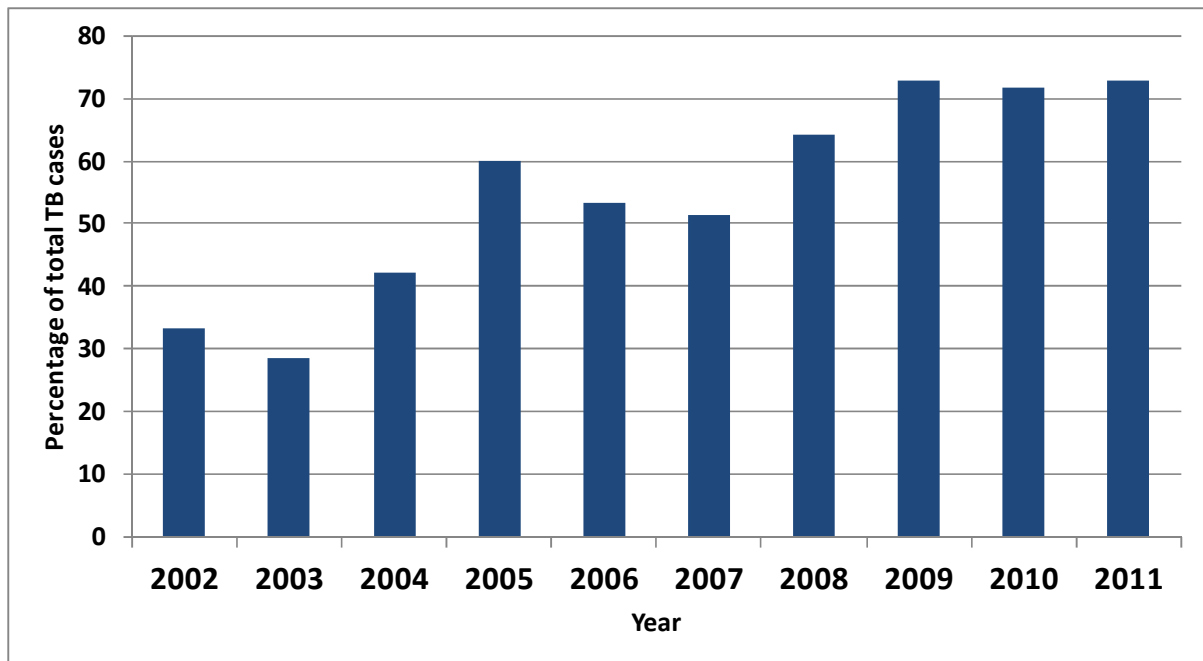


Figure 2: The proportion of total TB cases in migrants, Malta, 2002-2011

Source: IDCU database

TB cases in migrants to Malta occurred most commonly in the younger age groups, with an average age of 26.5 years.² This can denote recent infection most likely imported from their country of origin, where TB is endemic. It may also reflect the age distribution of the migrants coming to Malta, 81% of whom were young adults, with ages ranging from 15 to 34 years.⁴

1.2.2 Site of origin of tuberculosis

Pulmonary TB is much more common than extrapulmonary TB among our TB cases (Figure 3). Among the extrapulmonary TB, the extrathoracic lymph node group is the most predominant site.

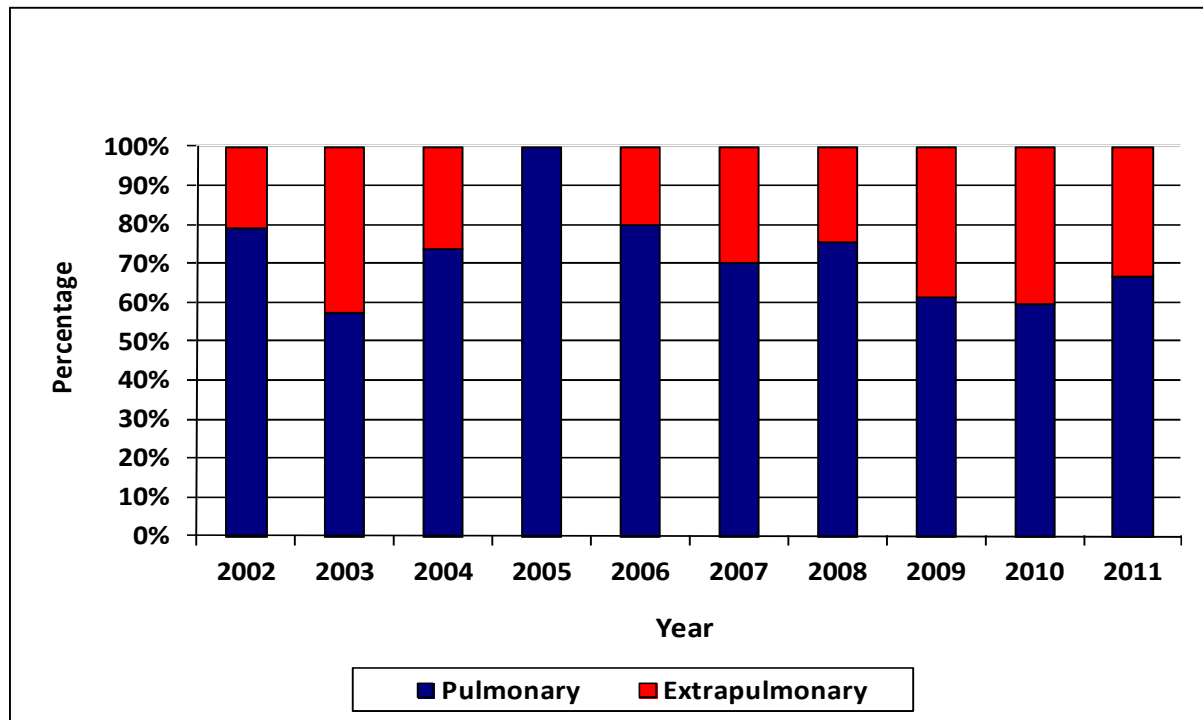


Figure 3: *The proportion of notified* TB cases by site of origin, Malta, 2002-2011*

*Notified TB cases means cases notified to IDCU and ascertained.

Source: IDCU TB Surveillance Database

1.2.3 Tuberculosis age trends

Figure 4 shows the TB age trends in Malta from 2001 to 2011.

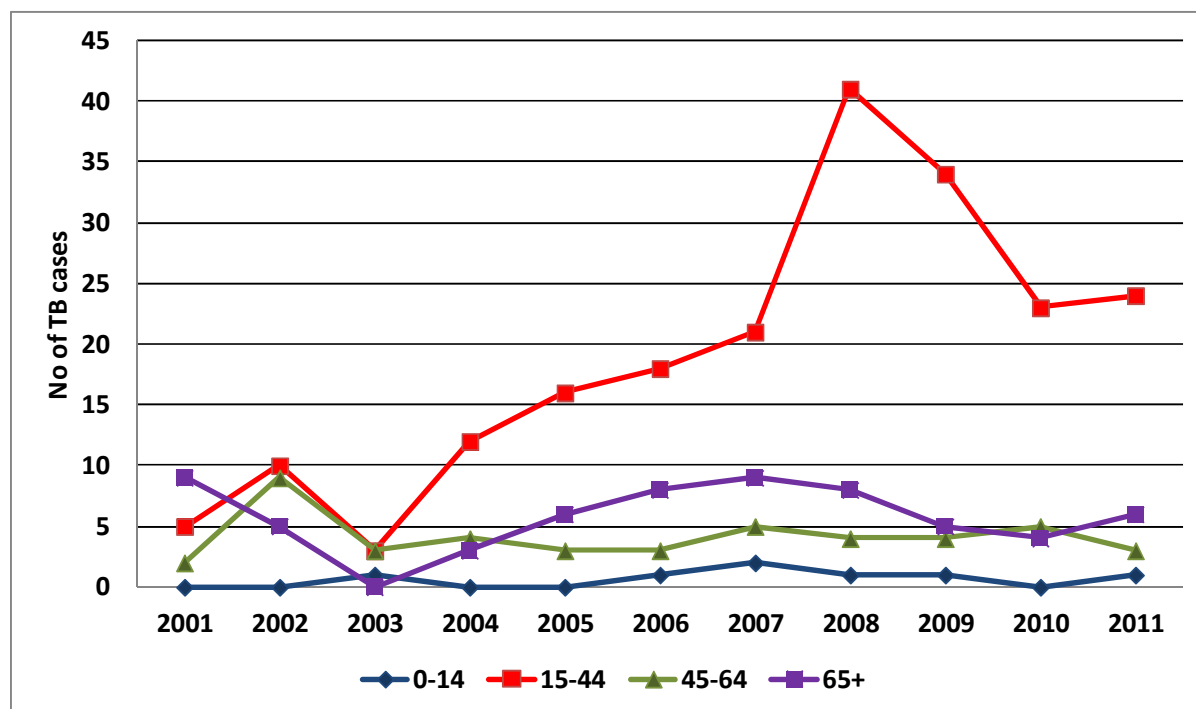


Figure 4: Number of notified TB cases by age group, Malta, 2001-2011

*Notified cases means cases notified to IDCU after ascertainment.

Source: IDCU TB Surveillance Database

Childhood TB seems to be uncommon in Malta. There were only seven notified cases in children in the last decade: three cases were in Maltese children: two pulmonary (one aged 8 years and the other 14 years) and one TB lymph nodes (aged 2 years). The other four notified TB cases were in migrant children. Two were aged 2 years, one aged 8 years and the other aged 10 years. It is important to closely monitor childhood TB using key indicators (Section 3.1.1) as this usually denotes new infection in the population and is a reservoir of infection for future generations. Furthermore although the overall trends in the European Union/ European Economic Area (EU/EEA) show a steady decline in paediatric TB, in certain settings, in some low incidence countries (< 20/100,000) there has been a rise in paediatric TB in all age groups.⁵

The most frequent age group for all TB cases is 15-44 years. This may be due to the fact that a large proportion of the total TB cases in Malta were migrants from high incidence countries (73% in 2011) and these were mostly young adults.²

1.2.4 TB/HIV co-infection

During the period 2007-2011 there were 19 cases of TB/HIV co-infection reported. Of these:

- 74% (14cases) were in migrants from high TB incidence countries
- 11% (2 cases) were in other foreigners
- 16% (3 cases) were in Maltese persons

The number and percentage of total TB cases with positive HIV serostatus during the same time period is shown in Table 1.

	2007	2008	2009	2010	2011
Number of TB/HIV cases	2	5	4	3	5
% of total TB cases that were HIV positive	5.3%	9.4%	9.1%	9.4%	15.2%

Table 1: HIV positive TB cases, Malta, 2007-2011

In 2009 among the countries with complete data, the percentage of TB cases that were HIV positive was highest in Portugal (12.2%), Estonia (9.5%), Latvia (7.5%) and Malta (9.1% representing only 4 cases), compared to 2.3% overall EU/EEA rate.⁶ Furthermore in Malta the proportion of total TB cases that were HIV positive seems to have increased from 5.3% in 2007 to 15.2% in 2011 (Table 1), bearing in mind that this also depends on the number of TB cases that were tested for HIV and the number of TB cases whose HIV result/testing was unknown.

These results warrant our attention and TB/HIV co-infection has been included as one of the strategic areas of action in our National TB strategy.

1.2.5 Multidrug and extensively drug resistant tuberculosis

Like many Western European countries, the prevalence of multidrug resistant (MDR) TB in Malta is very low, all cases of notified MDR-TB were imported. From 2007 to 2011 there were two notified cases of MDR-TB, both being from Eastern European countries. To date no cases of extensively drug resistant (XDR) TB have been reported. To prevent and control drug resistance, Malta has endorsed the consolidated action plan to prevent and combat MDR and XDR TB in the WHO European Region 2011-2015.⁷

1.2.6 Treatment outcome

Figure 5 shows the treatment outcome at 12 months between 2002 and 2009. Success rate is on average 82% over this time period. A case for concern is the number of patients who are transferred out of the country without appropriate medical documentation and those lost to follow up, as interruption of treatment can result in the emergence of drug resistance.

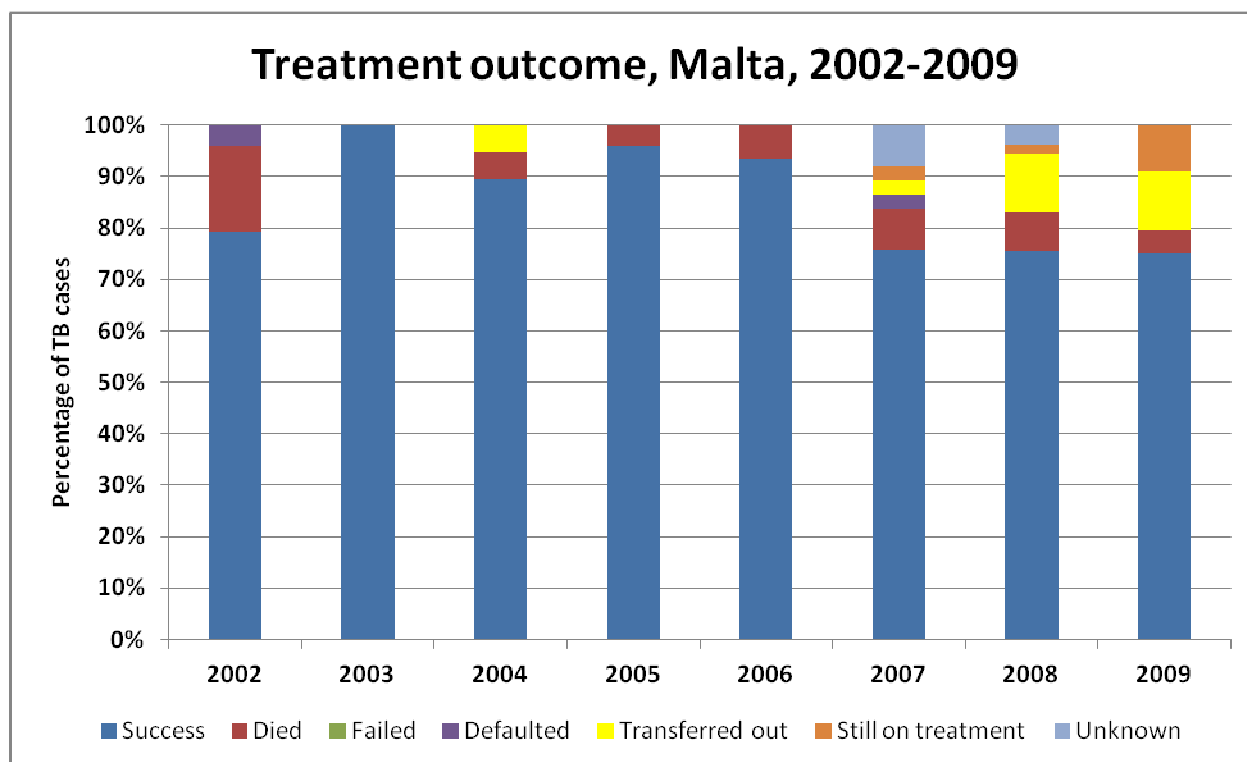


Figure 5: Treatment outcome at 12 months, Malta, 2002-2009

Died= the sum of TB patients who died of TB, those who died of causes other than TB and those whose cause of death is unknown

Source: IDCU TB Surveillance Database

1.3 THE BASIS OF TB CONTROL

The majority of cases of the infectious form of the disease involves the lung or larynx, and is spread from person to person. Left untreated a person with infectious pulmonary TB may infect up to 10-15 people every year, although this figure may be greater if there is very prolonged and intense exposure, or if exposed contacts have a lowered immunity. People with a normal immune system have an approximate 10% lifetime risk of developing TB if they are infected with the organism. Half of those developing TB disease will do so in the first 2 to 3 years from infection, and is higher in the younger and elderly age groups. The presence of HIV infection increases the 10% lifetime risk in uninfected persons to that of 10% per year.

The mainstay of TB control is the early identification, diagnosis and effective treatment of individuals with the infectious form of the disease. In the case of drug sensitive TB about two weeks of appropriate treatment will render most people non-infectious. Completion of a full course of treatment using combination therapy is essential to achieve a cure while reducing the likelihood of emergence of drug resistance.

1.4 THE CASE FOR A NATIONAL TB STRATEGY

A group made of health professionals had performed a communicable disease prioritization exercise and identified TB and blood borne infections as key priority diseases, leading them to formulate a communicable disease strategy. This together with the increasing awareness of TB as a re-emerging disease of global importance in recent decades and a rise of TB in immigrants from high incidence countries to Malta has led the Ministry of Health, the Elderly and Community Care to formulate a strategy which places the patient at the centre of care. This strategy has been developed by a multidisciplinary team of key workers, including public health physicians, clinicians and microbiologists with contribution from a laboratory scientist and pharmacists.

1.5 AIMS, OBJECTIVES AND TARGETS

a) Aims

The aims of the strategy are:

- Early detection and effective treatment of all active TB disease
- Reducing the incidence of TB infection (risk group management and prevention of transmission of infection)
- Reducing the prevalence of TB infection (outbreak management and targeted preventive treatment).⁸

b) Objectives

The objectives of the strategy are:

- Increased and sustained political commitment to TB
- Increased professional and public awareness to TB
- Maintenance of high quality surveillance, targeting vulnerable populations and risk groups, like migrants from high incidence countries, HIV positive persons, the elderly and household contacts of recent TB cases
- Decreasing the burden of TB/HIV co- infection by strengthening the collaboration of TB and HIV programmes and activities.
- Maintenance of high quality clinical services
- Targeted treatment of LTBI
- Strengthening of directly observed treatment (DOTS)
- Maintenance of good quality laboratory services in line with the increasing demands

c) Targets

The programme targets are:

- To achieve a cure rate of 85% among new sputum smear positive TB patients⁹
- To detect 70% of existing cases of sputum smear positive TB⁹
- To prevent the emergence of acquired drug resistant TB
- To halt and begin to reverse the incidence of TB in the Maltese population by 2015
- Reduce the prevalence of and deaths due to TB in the Maltese population by 50% compared with a baseline of 1990 by 2015
- Eliminate TB as a public health problem by 2050¹⁰

Chapter 2

TB prevention and management: the current local set up

Although government commitment is essential for the success of the TB control strategy, the control of TB depends on the many other professionals and key entities:

The Government Health Service

- Public Health
- Infectious Disease Prevention and Control Unit (IDCU)
- Chest Unit
- Advisory Committee on Immunisation Policy (ACIP)
- Community Care
- Primary Health Care
- Community nurses
- Social workers in detention and open centres

Hospital-based service (In/Out patient)

Emergency and Admitting Department

- Medical and surgical firms
- Infectious disease firms
- Paediatric infectious diseases clinic
- Chest Clinic
- Laboratory services
- Pharmaceutical services
- Endoscopy
- Radiology services
- Infection Control Unit
- Surgical Services

Other governmental entities

- Social services
- Detention services
- Agency for the welfare of asylum seekers (AWAS)
- Employment and training corporation (ETC).

Non governmental entities

- Non Government organisations (NGOs)
- International organisation of migration (IOM)
- Patient groups
- General public
- Mass media.

Specific responsibilities of professionals and entities

2.1 PUBLIC HEALTH

2.1.1 Infectious Disease Prevention and Control Unit

- Local surveillance: collection, analysis and interpretation of TB data
- Contact tracing, in collaboration with the Chest Unit / Chest Clinic
- Investigation of clusters
- Screening programmes (Section 3.2, 3.3)
- Continuous liaison with the Chest Clinic, medical consultants and consultants in Infectious Disease in the management of patients
- Organisation and ensuring compliance with treatment through DOTS
- Preparation of national individual datasets for international entities like World Health Organisation (WHO) and European Centre for Disease Prevention and Control (ECDC)
- Dissemination of educational material and provision of education to the general public and to patients
- Point of reference for other health professionals

2.1.2 Chest Unit (branch of IDCU)

- Screening of foreigners requesting work permits, immigrants, detainees and asylum seekers coming from high TB endemic areas.
- Screening of individuals who are potentially at high risk of contracting TB, including those working with immigrants
- Screening of contacts of TB cases
- Vaccination of previously unvaccinated individuals less than 45 years of age
- Liaising with physicians in infectious diseases and Chest Clinic
- Monitoring of DOTS

2.1.3 Advisory Committee on Immunisation Policy

- Advice to Superintendent of Public Health on BCG vaccination policy

2.2 COMMUNITY CARE

2.2.1 Primary Care

- Referral of suspected cases of TB
- Early detection of treatment- induced complications
- Dissemination of educational material and provision of education to patients
- Counselling for patients to improve patient compliance with treatment
- BCG vaccination in schools
- Infection control within primary care setting

2.2.2 Community nurses and care workers

- DOTS services: ensuring compliance with treatment on a daily basis
- Point of reference for patient
- Liaising with other health service providers
- Monitoring patient as regards possible side effects to treatment and other health issues.
- Addressing any issues patient may have regarding their treatment

2.2.3 Social workers

- Assistance with DOTS in detention and open centres
- Assistance with contact tracing

2.3 HOSPITAL-BASED SERVICES

2.3.1 Clinical Service

- Investigation, diagnosis and treatment of suspect cases of latent and active TB
- Treatment and follow-up of patients, both on an in-patient and out-patient basis
- Management of cases suffering from a co- infection of TB and HIV

2.3.2 Laboratory services

- Provision of an efficient service with regard to direct Ziehl-Neelsen (ZN) stained smears
- Provision of cultures for AFB, both in solid and liquid media
- Liaison with reference laboratory in the UK as required

2.3.3 Pharmaceutical services

- Timely procurement and storage of the necessary anti-TB medication by the Government Health Procurement Services
- Provision and dispensation of treatment as prescribed
- Intervention with prescribing physician when difficulties arise
- Provision of TB treatment and TB related treatment free of charge (with TB card)

2.3.4 Endoscopy services

- Bronchoscopy for broncho-alveolar lavage and biopsies

2.3.5 Surgical service

- Timely biopsies of suspicious lesions suggestive of non pulmonary disease

2.3.6 Radiology services

- Timely radiological investigations (chest x-rays) to determine the presence or absence of active TB

2.3.7 Infection Control Unit at MDH and Infection Control Nurses in other hospitals

- Screening of hospital staff
- Contact tracing of exposed patients and staff in wards
- Infection control in hospital/ outpatient clinics
- Education of health care workers

2.4 OTHER GOVERNMENTAL ENTITIES

2.4.1 Social services

- Provision of financial support for patients during the duration of treatment

2.4.2 Detention services

Accommodate migrants while their identities are being verified. Their collaboration with IDCU and clinical services are essential for screening of irregular migrants and the management of cases of TB in detention centres.

2.4.3 Agency for the welfare of asylum seekers

The agency for the welfare of asylum seekers (AWAS):

- oversees the daily management of accommodation facilities
- provide particular services, information and help to asylum seekers

- promote the Government's policy and schemes regarding resettlement and assisted voluntary returns.
- have an essential role in the management of cases of TB in detention centres.

2.4.4 Employment and Training Corporation

The Employment and training corporation (ETC):

- Enhance employability by recommending policies and implementing initiatives aimed at empowering, assisting and training jobseekers to facilitate their entry or re-entry into the active employment market, promoting workforce development through skills and competency development and assist employers in their recruitment and training needs.
- Key player to coordinate screening of persons applying for an employment licence and who are coming from high endemic countries.

2.5 NON GOVERNMENTAL ORGANISATIONS

2.5.1 International organisation of migration

The International organisation of migration (IOM):

- Provides services for persons who require international migration assistance

Chapter 3

Public Health Services

Three public health actions are essential for the prevention and control of tuberculosis (TB):

- Early identification and effective treatment of all active TB cases
- Contact tracing
- Screening populations at a higher risk of TB

3.1 TB SURVEILLANCE

Surveillance is an essential element in the control and elimination of TB, as it provides information on the epidemiology of the disease, identifies risk groups for targeting public health activities and monitors the effectiveness of TB control activities to tailor health care services appropriately. Surveillance can be active or passive. Active surveillance is looking methodically for cases of active TB disease and LTBI in people at a higher risk of TB. Passive surveillance is waiting for people to develop symptoms of TB and go to their doctor.

3.1.1 Surveillance of paediatric TB

High quality surveillance of paediatric TB is essential (Section 1.2.3). The use of key epidemiological indicators, like the time trend of the ratio of notification rates in children versus adults and the time trend in mean age of TB cases, is important to measure the effectiveness of TB control activities. The targets are a decreasing ratio of notification rates in children versus adults and an increasing mean age of TB cases.⁵

3.1.2 Notification

The Public Health Act (2002)¹¹ requires that all forms of TB are notified to the Superintendent of Public Health (SPH). The SPH has delegated the authority of investigation of infectious disease to the Infectious Disease Control Unit (IDCU). Any doctor diagnosing active TB should urgently inform IDCU about the case. If the diagnosis is made after death this should also be reported, stating that the patient is deceased. Sometimes patients may be suspected of having TB yet confirmatory evidence may be lacking. If a decision to start anti-TB treatment is made, a notification should also be done informing that the patient is receiving trial therapy.

All laboratories handling pathological specimens (including private ones) also have the responsibility to inform the SPH when pathological evidence of active disease caused by *M. tuberculosis* complex is present.

3.1.3 TB case definition for surveillance

The definitions and methodology used in TB surveillance are consistent with international recommendations.^{12, 13}

Definite TB case

- In countries where laboratories able to perform culture and identification of *M. tuberculosis* complex are routinely available, a definite case is a patient with culture-confirmed disease due to *M. tuberculosis* complex;
- In countries where routine culturing of specimens is not feasible, patients with sputum smear positive for acid-fast bacilli (AFB) are also considered as definite cases.

Other than definite TB cases meeting the following two conditions are also considered as TB disease:

- A clinician's judgement that the patient's clinical and/or radiological signs and/or symptoms are compatible with TB **and**
- A clinician's decision to treat the patient with a full course of anti-TB treatment.

3.1.4 National TB database

Data on TB cases is collected in the National TB database held by IDCU. The database collects information from 4 main sources: physician and laboratory notifications, TB death certificates from the Health Information and Research Directorate and pharmacy returns of patients receiving anti-TB drugs, from the main government hospital. This is the only pharmacy in the country from where patients can get TB treatment, which is free of charge. HIV data is obtained from the IDCU, Chest Clinic and Infectious Disease Unit, as part of the TB/HIV collaboration activities. There is collaboration of this data with international entities like European Centre for Disease Prevention and Control (ECDC) and World Health Organization (WHO).

3.2 CONTACT TRACING

In low incidence countries, contact tracing of notified TB cases is one of the most important methods for the early identification of persons with active TB, to detect persons with latent tuberculosis infection (LTBI) who are at a higher risk of developing TB and to identify those not infected with TB for whom BCG vaccination may be appropriate. In children contact tracing is done to identify the source of infection.

Once a patient is suspected of or diagnosed with active TB, the diagnosing physician should inform the IDCU immediately so that contact tracing can be initiated. Contact tracing should not be delayed until receipt of notification.

When the IDCU is informed of a case of TB, the extent of contact is determined, after taking into account the infectivity of the index case and the susceptibility of the contacts. Contacts identified should be classified according to the degree of exposure in concentric circles around the index case, as per the stone-in-the-pond principle.¹⁴ Closest contacts (those with the most exposure, usually domestic contacts) are assessed first. When there is evidence of transmission among a ring, one should move on to the next one and so on.

Definition of contacts

The definitions of contacts are based on the National Institute for Clinical Excellence (NICE) TB guidelines¹⁵ and the British Thoracic Society (BTS) guidelines.¹⁶

Close contact: Many studies give no clear definition of close contacts.

Domestic contact: These comprise people from the same household who share a bedroom, kitchen, bathroom or sitting room with the index case and very close associates such as boyfriend/girlfriend or frequent visitors to the home of the index case.

Contacts with a cumulative total exposure to a smear positive case of TB exceeding eight hours within a restricted area equivalent to a domestic room are equivalent to domestic contacts.

Screening tools

Table 2 shows the screening tests of TB contacts. Screening of contacts is done at the Chest Unit. It consists of:

- A standard screening questionnaire looking for signs and symptoms
- A Mantoux test (Mtx) to detect LTBI and identify those not infected with TB (0-5mm)¹⁵ for whom BCG vaccination may be appropriate. This test may be repeated after a window period of 6-8 weeks to check for tuberculin conversion.
- A confirmatory interferon-gamma release assay (IGRA) test if the Mantoux test is positive¹ or 6-8 weeks following high risk exposure: e.g. smear positive pulmonary TB.

If the IGRA test is positive, preventive treatment is offered once active TB has been ruled out (Section 3.3.3).

- A chest x-ray (if no suspicion of pregnancy) in individuals who are symptomatic, in children (0-15 years) with a high Mantoux reaction¹ and in individuals ≥ 16 years of age.
- Infants and children <2years of age have a higher risk of developing TB meningitis or disseminated TB following exposure and should be referred urgently to the Paediatric infectious diseases clinic for immediate initiation of preventive treatment irrespective of the result of their Mantoux test.

Pregnant women are screened by a clinical history and examination and a Mantoux test. Chest x-ray is postponed until after delivery.

¹ in immunocompetent individuals this constitutes an induration of ≥ 6 mm in the absence of a BCG scar or ≥ 15 mm with BCG scar¹⁵

Index patient	Initial screening tests of TB contacts	Screening tests of TB contacts after a window period (6-8wks)
Pulmonary TB sputum smear ZN and/or culture positive	Mtx*/IGRA Chest x-ray	Mtx*/IGRA
Pulmonary TB sputum smear ZN and culture negative	Mtx*/IGRA Chest x-ray	Mtx*/IGRA in children
Extra-pulmonary TB Contact tracing only if the index case is a child, to find the source of infection	Mtx*/IGRA Chest x-ray	

* Mantoux test performed by intradermal injection of 0.1mls of 2TU/1mlsPPD
ZN=Ziehl-Neelsen

Table 2: Screening tests of TB contacts

Depending on the test results, contacts are discharged from Chest Unit or referred to Chest Clinic/ Paediatric Infectious Diseases Clinic. Information and advice should be given to all contacts of a sputum positive TB case.

3.3 TB SCREENING

3.3.1 Screening new entrants from high TB incidence countries

New entrants are people recently arriving or returning to the country (excluding tourists). TB screening for acute illness is mandatory in all new entrants from high TB incidence countries (> 40/100,000 per year, as listed by the WHO Organisation⁸) seeking residency in Malta (Appendix 1) including:

- Migrants
- Those applying for a work permit
- Foreign students

3.3.1.1 Objectives

The objectives of TB screening are:

1. To detect active TB at an early stage and give effective treatment.
2. To detect LTBI and offer preventive treatment.
3. To prevent transmission of disease in the community.
4. To administer the BCG vaccine to those at risk of TB who have been confirmed to be free from TB and who have never been immunised.

3.3.1.2 Screening tools

The screening tests which are recommended for different age groups are shown in Table 3.

Age	Chest x-ray	Mantoux Test*
< 3 months	-	+
3 months – 10 years	±	+
11 – 17 years	+	+
≥ 18 years	+	±

*Mantoux test: performed by intradermal injection of 0.1ml of 2TU/0.1ml PPD

Table 3: Screening tests for new entrants coming from countries with high incidence rates of TB

A chest x-ray is performed to detect active TB at an early stage before the person becomes infectious or shows clinical symptoms of TB.^{17,18,19} To facilitate action and subsequent data analysis chest x-rays are coded into one of the following four categories: 1) an abnormality compatible with TB, 2) an abnormality other than TB, 3) no abnormality or 4) an abnormality of a technical nature.²⁰

Figure 6 shows the algorithm for screening and follow up of adult (≥18 years) new entrants. A chest X-ray is the initial screening test recommended for adults. If the chest x-ray is suspicious of TB disease, the patient is referred to the Chest Clinic/ Infectious Disease Unit for clinical evaluation and further testing (Section 3.3.1.4). A Mantoux test is done in those with radiological evidence of fibrotic changes or who are HIV positive, as these individuals are more likely to progress from LTBI to active disease.²¹ Those with a high Mantoux reading² are referred to Chest Clinic for investigation.

² in immunocompetent individuals this constitutes an induration of ≥6mm in the absence of a BCG scar or ≥15mm with BCG scar¹⁵

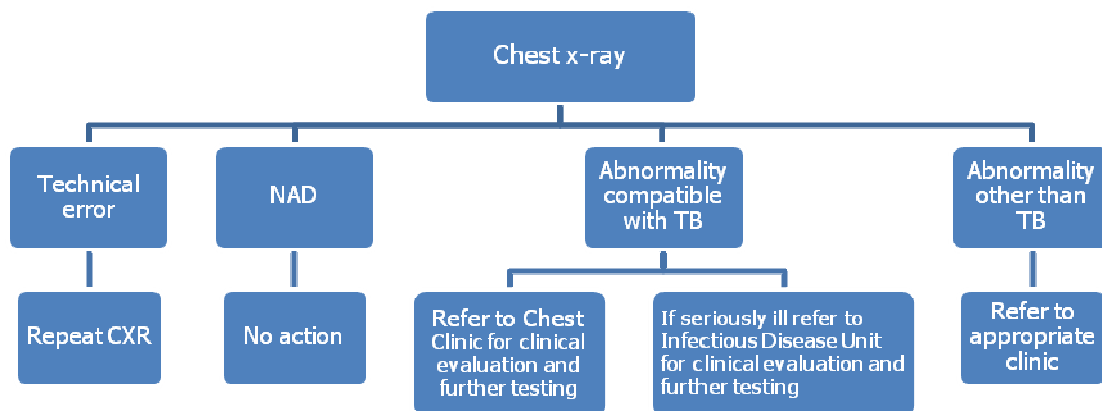


Figure 6: Algorithm for screening and follow up of adult (≥ 18 years) new entrants

All children and adolescents (0-17 years of age) should undergo symptom screening and a Mantoux test. A chest x-ray is performed routinely in those aged 11-17 years, in those who are symptomatic (all ages) and in children <10 years of age with a high Mantoux reaction¹¹ (Figures 7 and 8).

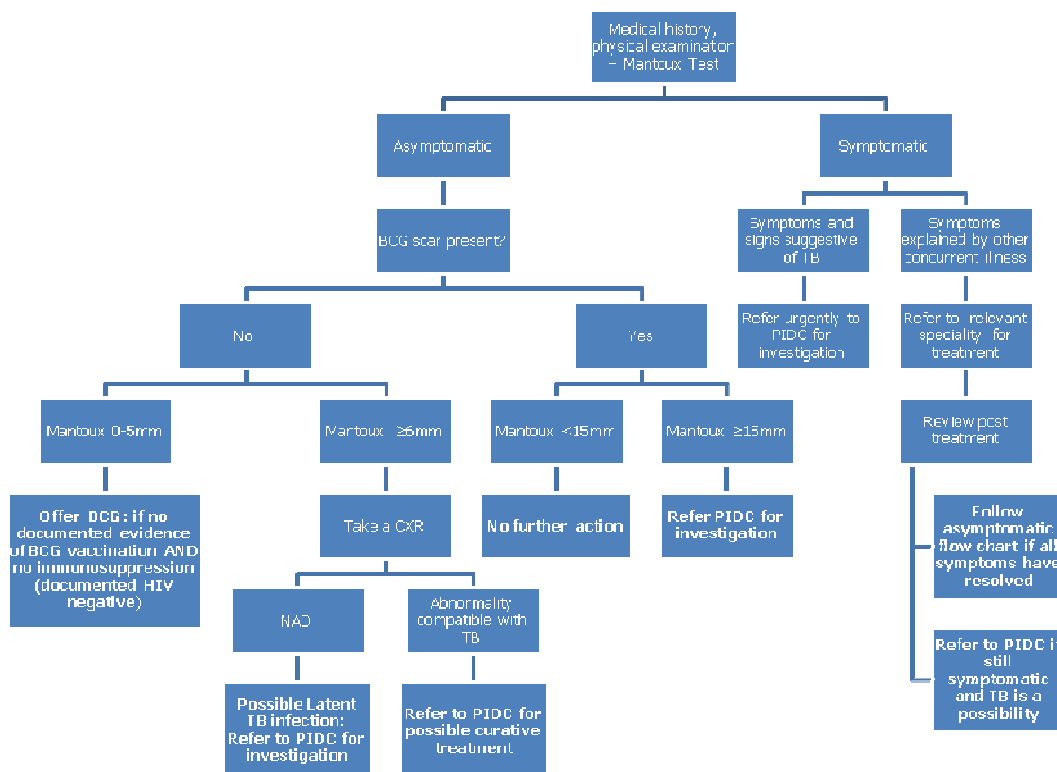


Figure 7: Algorithm of screening and follow up in new entrant children (0-10 years)

PIDC: Paediatric Infectious Diseases Clinic, Children's Outpatients, Mater Dei Hospital: Tel: 2545 4520/1

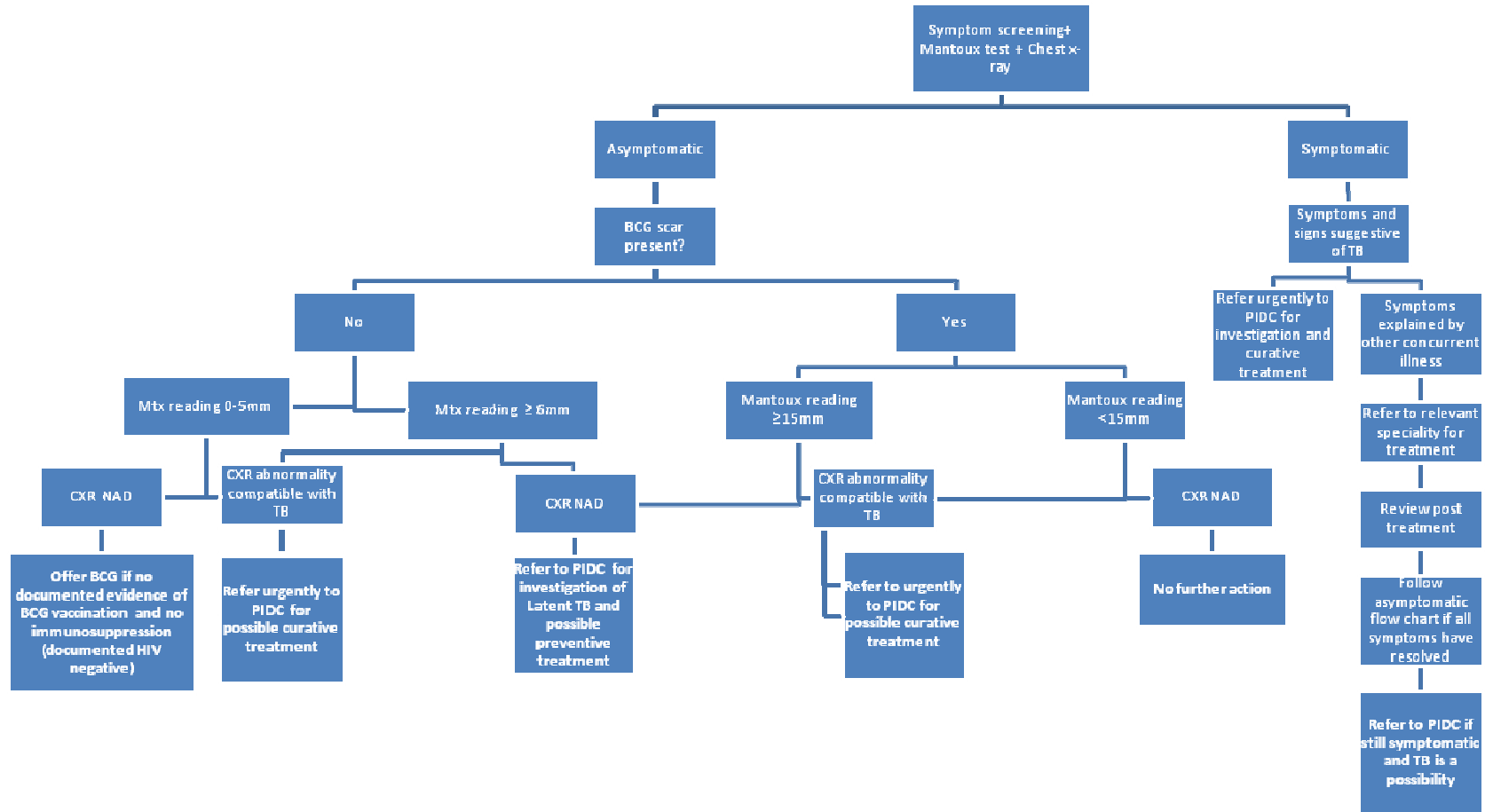


Figure 8: Algorithm of screening and follow up in new entrant children and adolescents (11-17 years)

PIDC: Paediatric Infectious Diseases Clinic, Children’s Outpatients, Mater Dei Hospital: Tel: 2545 4520/1

Those children with a negative Mantoux reaction (0-5mm)¹⁵ who do not have a BCG scar or documented evidence of BCG administration need to be given the BCG vaccine (as long as there is no evidence of immunosuppression: i.e. documented to be HIV negative).

In well looking infants <3 months of age, the Mantoux test is less reliable and should be repeated 3 months later, to check for tuberculin conversion. Pregnant women are screened by a clinical history and examination and a Mantoux test. Chest x-ray is postponed until after delivery (Appendix 2).

3.3.1.3 Screening procedure

In order to prevent transmission of TB, screening will occur shortly (within 2 weeks) after arrival. Irregular migrants are referred by the Immigration Division of the Police Department, whilst regular migrants are referred by the respective occupational health department of the employing company (or prior starting school for children) to the Chest Unit/IDCU where screening is organised. Regular migrants arriving from a country outside the European Union who need a chest x-ray have to do it privately. It is recommended that the police number in irregular migrants/the passport number in regular migrants is used as an individual's identification number. This avoids spelling mistakes resulting in multiple identities and double counting. In terms of need for public health and medical action, evaluation of the chest x-rays should be carried out without delay by a radiologist. Suspected TB cases are to be brought to the attention of the Consultant Physician in charge of the Chest Clinic, who refers such patients for clinical evaluation and necessary management. Suspected or diagnosed TB cases are notified to the Superintendent of Public Health.

New entrants from high TB incidence countries, who were previously residing in Malta and have visited their country of origin, are screened again if they have been away for ≥ 1 year, unless symptomatic at any point in time.

3.3.1.4 Curative interventions

The early identification and effective treatment of patients with active TB is the most important intervention in TB control. In-patient treatment at the Infectious Disease Unit is necessary for patients (≥ 16 years old) with severe illness and for those whose medical circumstances or other reasons make treatment at the immigrant's residence difficult or impossible. Patients with smear positive pulmonary TB should be isolated in a single room with negative pressure ventilation. Directly observed treatment (DOTS) should be instituted as soon as possible after discharge. This is organised by the IDCU through the Chest Unit. Less urgent cases are referred to the Chest Clinic at St. Luke's hospital. Appointments should be as early as possible.

TB in children

Children (<16 years of age) with TB disease who need in-patient treatment are admitted to one of the paediatric wards and isolated according to the guidelines set in section 4.1.1 of the Mater Dei Hospital Infection Control Policy on the prevention of tuberculosis in healthcare settings.²² Less urgent cases are referred to the Paediatric Infectious Diseases Clinic. DOTS or daily therapy is carried out by the community nurses. In the case of daily therapy the community nurses visit the family until they are sure that the parents are able to administer the treatment unsupervised.

3.3.2 Screening people living/working in high risk environments

TB screening is performed in people living/working in high risk environments like:

- Healthcare workers
- Laboratory staff
- People living/working in closed and open migrant centres
- Staff and detainees at correctional facilities
- Veterinary and staff such as abattoir workers who handle animal species known to be susceptible to TB
- Drug /alcohol abusers
- People living/working in care homes for the elderly

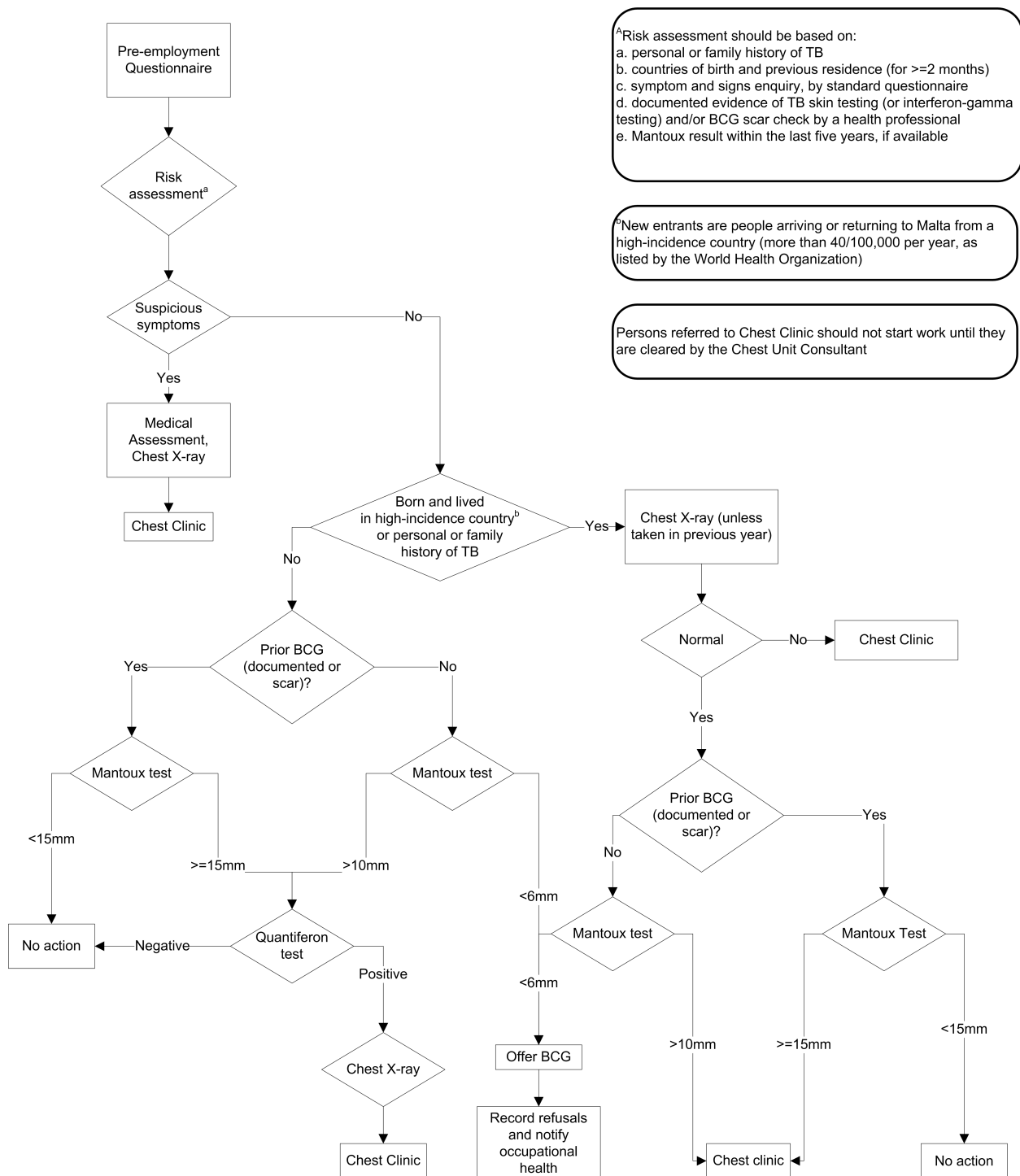
3.3.2.1 Screening of Healthcare workers upon employment

Screening for TB in healthcare workers should be according to the MDH Hospital Infection Control Policy²² as outlined in Figure 9.

1. New employees in the above categories should not start work until they have completed screening for TB
2. Pre-employment screening for TB should include an assessment of the TB risk to and of the employee. This assessment may be based on:
 - a. Personal or family history of TB
 - b. Countries of birth and previous residence
 - c. Symptoms and signs enquiry, by a standard questionnaire
 - d. Documented evidence of TB skin testing (or IGRA) and/or BCG scar check by a health professional
 - e. Mantoux result within the last five years, if available.
3. Any new employee who has suspicious symptoms should undergo a medical examination and chest x-ray. If suspicious of active TB, the employee should be referred to the chest clinic.
4. All employees in the above categories should have a pre-employment / baseline Mantoux test.
5. For an employee who was born and lived in a low-incidence country and with no personal or family history of TB:
 - a. If a new employee has evidence of BCG vaccination, and the TB risk assessment above shows no increased risk, no further tests are necessary if the Mantoux is <15mm.
 - b. If a new employee has no evidence of previous BCG vaccination, and the Mantoux is < 6mm, the employee may receive vaccination.
 - c. If a new employee has a Mantoux test reading of ≥ 10 mm (if no evidence of BCG vaccination) or ≥ 15 mm (if there is evidence of BCG vaccination) they should have an IGRA test performed. If positive, a chest x-ray should be taken and the employee referred to the Chest Clinic for further investigation and possible treatment of latent infection.

6. For an employee who was born or lived for more than one month in a high-incidence country or who has a personal or family history of TB:
 - a. New employees of any age who were born in countries with a high incidence of TB or who have lived in the said countries for more than one month should have a chest x-ray (if not taken in the previous year) apart from their Mantoux test.
 - b. If chest x-ray shows any changes compatible with TB, they should be referred to the Chest Clinic for further investigation.
 - c. If Mantoux is less than 6 mm, and there is no scar/history of vaccination, they are advised to be vaccinated with the BCG vaccine.
 - d. If Mantoux is positive ($\geq 10\text{mm}$ if not BCG vaccinated and $\geq 15\text{mm}$ if vaccinated) they should be referred to the Chest Clinic for diagnosis of active or LTBI and possible treatment. In the meantime, they should not be allowed to work if there are suspicious clinical symptoms. TB should be excluded by the Chest Clinic.

7. Obtaining a baseline of TB status is useful when periodic screening is to be provided.



^aRisk assessment should be based on:
a. personal or family history of TB
b. countries of birth and previous residence (for ≥ 2 months)
c. symptom and signs enquiry, by standard questionnaire
d. documented evidence of TB skin testing (or interferon-gamma testing) and/or BCG scar check by a health professional
e. Mantoux result within the last five years, if available

^bNew entrants are people arriving or returning to Malta from a high-incidence country (more than 40/100,000 per year, as listed by the World Health Organization)

Persons referred to Chest Clinic should not start work until they are cleared by the Chest Unit Consultant

Figure 9: Screening of Healthcare Workers upon employment

Source: Mater Dei Hospital, Hospital Infection Control Policy

3.3.3 SCREENING FOR LATENT TB INFECTION AND TB CHEMOPROPHYLAXIS

3.3.3.1 Objective

The objective is to detect LTBI and offer preventive treatment

3.3.3.2 Screening Tools

Currently, diagnosis of LTBI is based on Mantoux testing, followed by a confirmatory IGRA test if the Mantoux test is positiveⁱⁱⁱ.²³ This is because the IGRA test may be less discriminating in people from high endemic countries.²⁴ One must always rule out active TB disease by physical examination and a chest x-ray prior to initiation of chemoprophylactic treatment.

3.3.3.3 Considerations for preventive treatment

1. Among persons from high endemic areas there is a high proportion with latent infection, often old infection. However the risk of progression from old infection to active disease is low.²⁵ Thus providing them all with preventive treatment would result in over treatment and hence not recommended.
2. Treatment of LTBI requires a large number of resources and a substantial infrastructure. These people are usually asymptomatic and the risk of non-compliance is high. Thus they need regular follow up during the treatment, to ensure compliance and detect any side effects of the treatment.
3. Among asymptomatic persons with LTBI, the most important factors for allowing progression from LTBI to active TB are:
 - Recent infection
 - HIV infection
 - Fibrotic changes on the chest x-ray.²¹
4. Among people detected with LTBI during contact tracing it is assumed that this is recent infection from the index case
5. Children with LTBI may denote new infection.

For these reasons, screening for LTBI in Malta is only done in specific groups like:

- New entrant children and adolescents from high incidence countries
- Contacts of an active TB case
- People working in high risk environments
- HIV positive persons (Section 3.3.3.4)
- People with old TB changes on their chest x-rays

ⁱⁱⁱ in immunocompetent individuals this constitutes an induration of ≥ 6 mm in the absence of a BCG scar or ≥ 15 mm with BCG scar¹⁵

- Patients started on biological agents for various conditions such as rheumatological disease and inflammatory bowel disease.

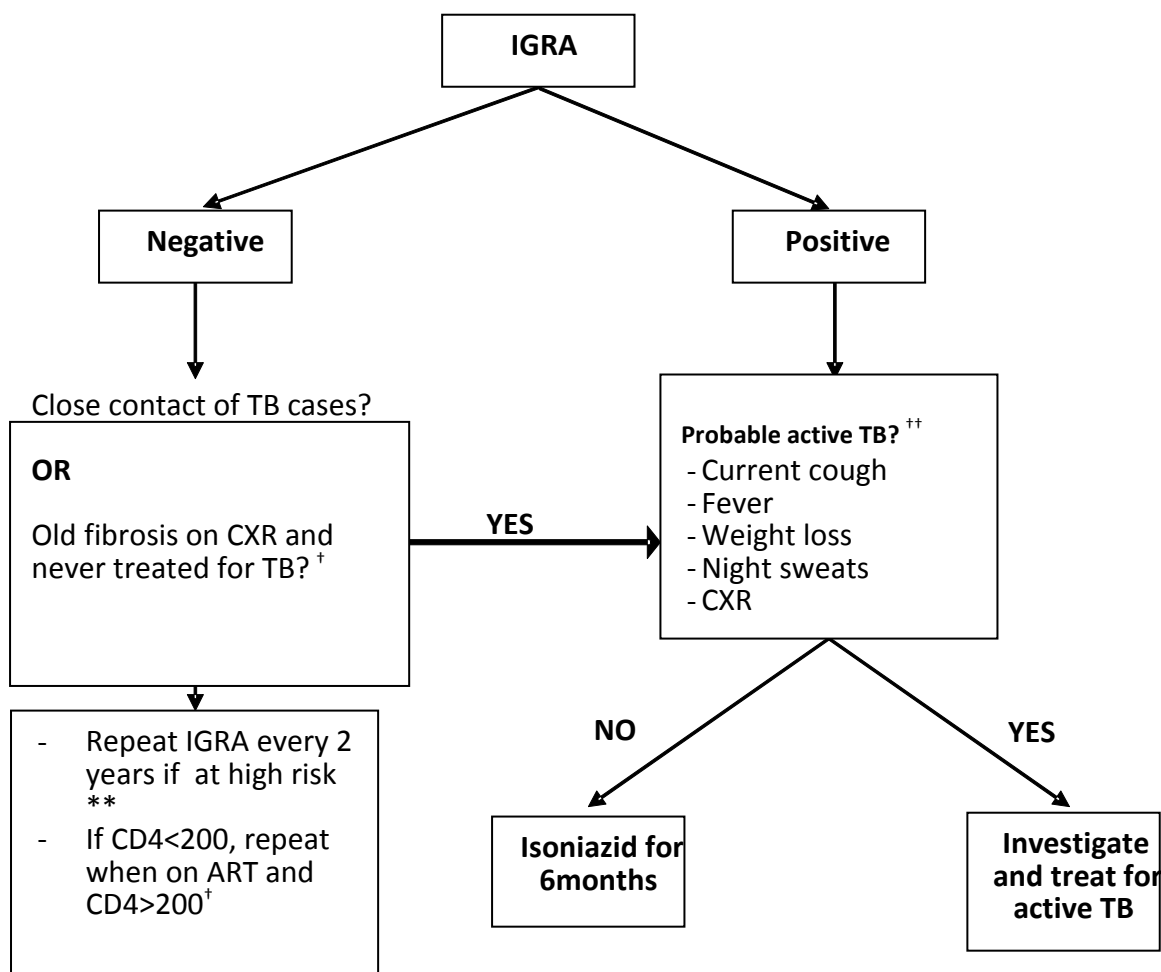
These people are offered TB chemoprophylaxis. Patients who refuse preventive treatment are offered:

- Information and advice and
- A repeat chest x-ray after 2 years time.

3.3.3.4 Screening for Latent TB Infection in HIV Patients

The protocol of screening for LTBI and TB chemoprophylaxis in HIV patients is as per Figure 10. One should consider screening the following groups of HIV-positive patients coming from:²⁶

- Sub-Saharan Africa, if length of current antiretroviral therapy is under 2 years, whatever the current blood CD4 cell count.
- Medium TB incidence* countries, if length of current antiretroviral therapy is under 2 years and current CD4 count is less than 500 cells/ μ L
- Low incidence countries, e.g. Caucasians from the European Union/ European Economic Area (EU/EEA), if not on antiretroviral therapy, or length of current antiretroviral therapy is less than 6 months and current CD4 count is less than 350 cells/ μ L.



* Medium incidence regions include: Eastern Europe, Central Asia, North Africa and the Middle East, South Asia, East Asia and the Caribbean.

** High risk settings include: incarcerated, congregate settings, active drug users and poor socio demographic conditions.

Figure 10: Algorithm of screening for LTBI and TB chemoprophylaxis in HIV patients

CXR= chest x-ray; IGRA=interferon-gamma release assay

† = 27

†† = 28

3.4 MONITORING TB TREATMENT

3.4.1 Improving adherence

To promote compliance, patients should be involved in treatment decisions at the outset of TB treatment. The importance of adherence should be emphasised during discussion with the patient when agreeing to undertake a treatment regimen. A named key worker should be assigned to each patient and be the point of contact with the Health Services. If need be cultural mediators/translators should be present to ensure that communication is effective.

3.4.2 Use of Directly Observed Treatment

Use of DOTS is necessary in cases where patient compliance with treatment might be problematic and particularly when the patient might be a public health risk. A risk assessment for adherence to treatment should be undertaken by clinicians when treatment is started. The risk assessment should consider the following:

- Homelessness
- Family and social circumstances
- Site of infection

Patients at high risk should be referred to IDCU for organisation of DOTS through the Chest Unit. DOTS should be provided by appropriately trained care workers. These employees may be assigned as key workers to the patients on treatment and may serve as a focal point for channelling issues in the care of TB patients. This role would also require liaison with professionals from other governmental and non-governmental agencies. These care workers should provide adequate information, ensure compliance with treatment and report adverse effects.

Patients should be informed to watch for symptoms of relapse and informed how to contact the TB service rapidly, ideally through his/her key worker. Patients who have had drug-resistant TB should be considered for follow-up for a period of 12 months after completing treatment.

3.4.3 Treatment outcome

To evaluate treatment outcome, IDCU must be informed by the clinicians on the date of start of treatment, the date of change of treatment and the envisaged date of termination of treatment.

3.5 BCG Immunisation

BCG vaccine offers protection against the most severe forms of the disease, including meningeal and miliary TB in neonates and children. Mantoux testing is used prior to BCG, in order to determine whether there has been previous infection with any mycobacterial species which would indicate some

protection and thus no need for immunisation. Vaccination requires intra-dermal injection and should be carried out by healthcare workers skilled in this technique.

3.5.1 BCG vaccination in children

Currently voluntary vaccination against TB forms part of the national immunisation programme and is offered once to all children at around 12-14 years of age and to infants in high-risk communities, provided they are free from HIV infection.

3.5.2 Travel vaccination

BCG is recommended for the following two groups of travellers:

- Previously unvaccinated tuberculin-negative travellers under 16 years of age, going to live or work with local populations for three or more months in a country where the annual incidence is > 40/100,000 population
- Individuals at occupational risk (Section 3.3.2) including healthcare workers aged ≤ 35 years of age, irrespective of the duration of stay.²⁹

For travellers for whom BCG vaccination is not an option, pre- and post-travel tuberculin skin testing (6-8 weeks post-travel) may be considered, either as a screening test for latent recent infection or as an aid to the diagnosis of active disease.²⁹

3.5.3 Contraindications for BCG vaccination

- Those who have evidence of previous BCG vaccination
- Those with a past history of TB
- Those with an induration of 6 mm or more following Mantoux testing
- Those with confirmed anaphylaxis to a component of the vaccine
- Pyrexia or generalised infected skin conditions
- HIV positive individuals and infants born to HIV positive mothers (until the infant is proven to be uninfected)
- Immune suppression including systemic corticosteroid therapy, radiotherapy, receiving or planned to receive anti-TNF treatment, malignant conditions, known or suspected HIV infection.

3.5.4 Precautions

- Postpone vaccination in those who are acutely unwell
- Pregnancy

Although no harmful effects on the foetus has been observed from BCG during pregnancy, it is wise to avoid vaccination especially in the first trimester. Whenever possible postpone the vaccination after delivery.

Chapter 4

Clinical Services

Key clinical priorities for implementation are the National Institute for Clinical Excellence (NICE) TB guidelines recommendations¹⁴ which include:

- Treatment of adults and children with active pulmonary disease with a 6 month rifampicin-based, four-drug, initial regimen
- Assignment of a named key worker is to be assigned to each patient with the aim of facilitating education and involving the person with TB in achieving adherence and completion of treatment.
- Use of directly observed treatment (DOTS) and the need to risk-assess all patients for adherence with treatment (See section 3.4.2). DOTS should be considered for patients who have adverse factors in their risk assessment, in particular:
 - Retreatment cases
 - Patients with a history of poor or non-adherence with treatment
 - Migrants who are residing in the community
 - Migrants in closed and open centres
 - The elderly

4.1 INVESTIGATION OF CASES OF ACTIVE PULMONARY TB

It is recommended that for active pulmonary disease:

- Multiple sputum samples (at least two, one being an on 'the spot' test and the second an early morning sample) should be sent for TB microscopy and culture in a case of suspected TB before starting treatment. Broncho-alveolar lavage (BAL) specimens may also be indicated
- In those children who are unable to expectorate sputum, 3 consecutive early morning gastric aspirates or induction of sputum should be considered
- Data including the number of sputum samples taken per patient and the proportion of culture-confirmed cases should be collected
- If there are clinical signs and symptoms consistent with a diagnosis of TB, treatment should be started without waiting for culture results. An observation period may be chosen if no symptoms are present. The standard recommended regimen should be continued in patients whose subsequent culture results are negative
- In case of a fatal suspect TB suitable samples should be sent for TB culture from autopsy material if active pulmonary TB is a possibility, since this would aid in public health action. (Personal protective equipment of mortuary workers as per MDH Hospital Infection Control Policy²²)

4.2 INVESTIGATION OF CASES OF ACTIVE EXTRAPULMONARY TB

If extrapulmonary TB is a possibility, the following specimens may be sent for histology and mycobacterial culture:

- Lymph node biopsy
- Pus aspirated from lymph nodes
- Pleural biopsy
- Any relevant surgical sample
- Histology sample (in an appropriate fixative)
- Any other aspiration sample
- Autopsy sample (consider sending two specimens, one for histology in fixative and the other for TB culture in saline)

Samples should be placed in sterile saline (where appropriate) in sterile, disposable, screw-capped bottles.

- The appropriate treatment regimen should be started without waiting for culture results if the direct Ziehl-Neelsen (ZN) or clinical picture is consistent with a diagnosis of TB.
- All patients with extrapulmonary TB should have a chest x-ray to exclude or confirm co-existing pulmonary TB.
- The appropriate drug regimen should be continued even if subsequent culture results are negative

4.3 TREATMENT REGIMES FOR CASES OF ACTIVE TB

Treatment for active TB is based on a standard regimen as recommended by international guidelines.^{14,30,31} This should be based on a daily 6-9 month rifampicin-based, initial four-drug treatment regimen, depending on the site of infection.

The following regimen is recommended for use locally:

- 6 months of isoniazid and rifampicin supplemented in the first 2 months with pyrazinamide and ethambutol (2RHZE+4RH). Pyridoxine 10mgs daily should be added to prevent isoniazid induced peripheral neuropathy (depending on factors like nutritional status, concurrent co-morbidities)
- Monitoring of clinical response should be aided by sputum smears as necessary.
- Treatment for multidrug resistant (MDR) TB can be prolonged (18-24 months). International guidelines³² on treatment protocols are to be used. Early identification of patients with risk factors for drug resistance is essential. Known risk factors for drug resistance include previous incomplete treatment, treatment failure, contact with a known case of drug-resistant TB and birth in a high MDR-TB incidence country. Countries which have particularly high rates of MDR-TB are available at the WHO website.³² These patients must be referred to an infectious disease consultant who has the required experience and expertise to manage such patients.

4.4 MANAGEMENT OF CASES OF TB IN CHILDREN

Cases of children with TB are uncommon in Malta. Such cases should be managed by a paediatrician specialised in infectious diseases. Emphasis should be made on assessing close contacts of children with TB in an effort to identify the primary source of infection, since children generally contract TB from an adult. Particular efforts should be made to have culture confirmation and drug susceptibility testing (DST) of paediatric TB cases.

4.5 CARE PATHWAY OF A SUSPECT TB CASE REFERRED TO HOSPITAL

A case of suspected active pulmonary TB, either through symptoms and/or a suspicious chest x-ray should be urgently referred to the Chest Clinic or Mater Dei Hospital (emergency and admission) as per care pathway in figure 11. These sections need to be informed of the case, prior to sending a suspected case. The patient is considered for isolation according to the TB diagnostic score in the Hospital Infection Control Policy.²² Two or three sputum samples are taken for smear-microscopy and culture and the patient is treated according to established protocols. IDCU is notified and contact tracing is organised so as to limit spread of infection. The patient is also tested for HIV and if positive, is referred to the Infectious Disease Specialist for appropriate management. Once the initial phase of treatment is over and a patient with pulmonary TB is no longer considered to be infectious, s/he is removed from isolation and referred for DOTS. A patient with extra-pulmonary TB is only referred for DOTS if specific social or medical issues are present. IDCU needs to be informed when treatment is started, changed, stopped, completed and when a patient is not compliant and discontinues treatment.

All patients, except MDR-TB or HIV associated infection should be referred for follow-up to the Chest Clinic. The Chest Clinic should also be informed before discharge and see the patient not more than 2 weeks from date of discharge. The Chest Clinic will follow-up patients on a monthly basis at most, until completion of treatment.

Patients with MDR-TB and HIV associated infection are referred for follow up to outpatient clinics run by Infectious Disease Specialists.

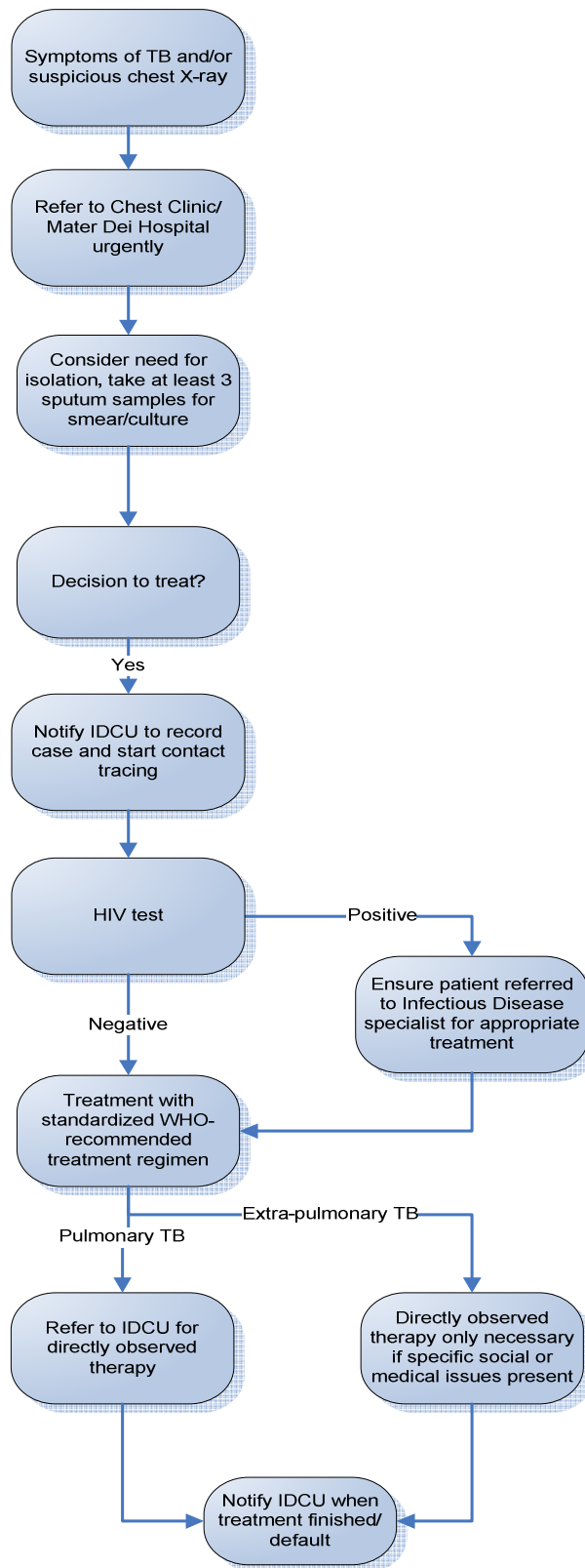


Figure 11: *The care pathway of a suspect active TB case referred to hospital*

4.6 HOSPITAL INFECTION CONTROL POLICY FOR TB PATIENTS

NICE¹⁴ gives the following recommendations with regards to three levels for infection control in hospital settings:

- Negative pressure rooms which have air pressure continuously or automatically measured
- Single rooms that are not negative pressure but are vented to the outside of the building
- Beds on a ward, for which no particular engineering standards are required.

Infection control arrangements in hospital settings are dealt with in detail in the Hospital infection Control Policy²² for prevention of TB in Health Care settings issued by the Hospital Infection Control Team at Mater Dei Hospital. Staff should be aware of appropriate isolation facilities and the infection precautions that need to be taken for cases of TB.

4.7 MANAGEMENT OF LATENT TB

Section 3.3.3. for definition and screening for LTBI. Treatment for LTBI is based on standard regimens as recommended by international guidelines.¹⁴

Chapter 5

Laboratory Services

Bacteriology is one of the fundamental aspects of national tuberculosis (TB) control. In order to enhance case detection, strengthening laboratory services is essential. The World Health Organization (WHO) has recognised the need for supporting laboratory systems as many countries have weak laboratory support. To this effect, the WHO established a subgroup on Laboratory Capacity Strengthening.

It is recommended that the laboratory mycobacteriology service will be led by an identified microbiologist who will be responsible for the implementation and the recommendation of the National TB strategy.

The Stop TB and Global Plan to Stop TB⁸ recommend that the laboratories should have the capacity to perform culture and Ziehl-Neelsen (ZN) stain. Hence the national strategy recommends that our laboratory should have:

- The capacity to provide a ZN stained smear on the same day in urgent cases, while non urgent cases should be processed within 48 hours
- The capacity to provide sputum culture on liquid media
- The capacity to process samples efficiently and expeditiously
- The capacity to perform the necessary amount of Quantiferon tests as required: estimated amount being 500. There is the need to have more than 1 person capable of performing this test.

Another essential element is the standardisation of laboratory documents which include

- A protocol indicating the use of liquid and/or solid media³³
- A standardised method for reporting positive direct ZN stained smears³³
- A laboratory assessment tool which focuses on the following areas
 - Structure and organisation
 - Human resources, training and supervision
 - Diagnostic services
 - External QA
 - Lab equipment, supplies and procurement
 - Biosafety issues

Due to limitations in number of samples available and human resources it is essential to have continued liaison with the reference laboratory for:

- Drug sensitivity testing
- Species identification
- PCR testing
- VNTR DNA fingerprinting

It is recommended that:

- The Laboratory adopts all international standards as recommended and endorsed by European or WHO agencies
- Laboratory staff should receive appropriate training abroad to develop such procedures and to achieve the necessary skills.
- High quality supervision carried out regularly with feedback mechanism
- Laboratory scientists are recruited to match the work load.
- Ensure professional relationship between TB suspects/patients, clinicians and laboratory staff to increase confidence in TB control

Chapter 6

Strategic Areas of action

6.1 ACTION 1: INCREASED PROFESSIONAL AND PUBLIC AWARENESS

Aim: Maintain awareness of TB especially among health care professionals, high risk groups and people working in high risk environments.

Rationale: Since 2002, a large proportion of notified TB cases in Malta were found among migrants coming from high incidence countries: 73% in 2011.² Many of these cases were detected on entry screening⁴ with relatively very few cases being detected later on in the community. Delays in diagnosis may be occurring because people, including health care professionals think that TB has disappeared. Furthermore high risk groups may find it difficult to approach the health care services for various reasons including stigma, lack of education, fears, language or cultural barriers³⁴ resulting in relative inaccessibility. Early detection and effective treatment of TB disease is essential to stop transmission from occurring.

Plan

- Use World TB day (24th March) to launch educative campaigns targeting health care professionals, high risk groups and people working in high risk environments
- Educational campaigns should make a particular effort to ensure that:
 - All foreign patients from high endemic countries with suspicious symptoms of TB approach the health services in the community by:
 - Providing them with culturally appropriate multilingual information about TB and about health centres and how to access them
 - Educating them, addressing their fears of persecution and stigma
 - All foreign patients from high incidence countries with suspected or diagnosed TB are referred to the Infectious Disease/TB specialists at Mater Dei Hospital as soon as possible following the date of first presentation to a health care professional by:
 - Educating health care professionals to “think TB”
 - Making sure that health care professionals are aware of the local arrangements for referring patients with suspected or diagnosed TB to specialists at Mater Dei Hospital.
- Use the media to inform the general public

6.2 ACTION 2: HIGH QUALITY SURVEILLANCE

Aim: Provide information on the epidemiology of the disease to:

- Identify risk groups
- Identify outbreaks/clusters
- Monitor trends
- Monitor the effectiveness of TB control activities
- Inform policy to tailor health care services appropriately
- Collaborate data with international entities

Plan

- Enhanced surveillance of identified high risk groups like new entrants from high TB endemic countries
- Establish a database linking DNA fingerprinting and epidemiological data
- Enhanced surveillance of paediatric TB, given the rise in certain settings, in some low burden countries in the EU⁵
- Use of key indicators (like the ratio of notification rates in children to that of adults) to closely monitor the progress towards elimination⁵
- Update targeted screening protocols among high risk groups including new entrants from high endemic areas seeking residency in Malta and contacts of an active TB case, to standardise procedures
- Update screening protocols of people working in high risk environments
- Update protocols on targeted TB prophylactic treatment
- Review and monitor BCG vaccination policy
- Increase financial resource for continued TB expertise like attendance of international conferences and short courses
- Increase human resource at the Infectious Disease Prevention and Control Unit (IDCU) and Chest Unit to establish this ambitious plan

6.3 ACTION 3: HIGH QUALITY CLINICAL SERVICES

Aims:

- Provide standardised high quality evidence based treatment to all TB patients
- A treatment success rate of at least 85%⁷

Plan:

Ensure that all patients suspected or diagnosed with TB:

1. Are referred to the Infectious disease/TB specialists as soon as possible
2. Are managed according to international guidelines modified according to our requirements
3. Have their diagnosis confirmed by laboratory culture of *M.tuberculosis* complex
4. Have multiple sputum samples sent for TB microscopy and culture for suspected TB before starting treatment

5. Are started on treatment if clinical signs and symptoms are consistent with a diagnosis of TB, even before having culture results
6. Have their treatment outcome recorded. This information should be relayed to the IDCU, who enters the data into the national TB database
7. Are referred to IDCU/Chest Unit who will organise DOTS as soon as feasibly possible.
8. Guidelines for the isolation and discontinuation of isolation period in hospital should be implemented.

Ensure that all patients diagnosed with LTBI are:

1. Referred to the Infectious disease/TB specialists
2. Managed according to the international guidelines modified according to our requirements.

Ensure that all patients diagnosed with LTBI and offered TB chemoprophylaxis are:

1. Followed up regularly throughout the treatment to ensure compliance and check for adverse effects of the treatment.

To facilitate communication between the health care professionals and the patient, the services of cultural mediators is essential when the patient is a foreigner.

6.4 ACTION 4: STRENGTHENING DIRECTLY OBSERVED TREATMENT

Aim: to institute directly observed treatment (DOTS) successfully in cases where patient compliance with treatment might be problematic and particularly when the patient might be a public health risk.

Rationale: DOTS ensures that TB treatment is taken appropriately and consistently making sure that the patient is cured and does not develop drug resistance. Studies show that treatment interruption is more common in immigrants.³⁵ Since a large proportion of notified TB cases in Malta are in migrants from high prevalence countries, strengthening DOTS is essential for treatment success and TB control.

Plan:

TB patients for DOTS should be:

- Referred to IDCU for organisation of DOTS through the Chest Unit
- Provided with an appropriately trained care worker to supervise treatment
- Assigned a key worker who would serve as a focal point for channelling issues in the care of the TB patient and liaise with professionals from governmental and non-governmental agencies. These employees would ensure compliance with treatment and report adverse effects of the treatment
- Informed how to contact the TB service rapidly, ideally through his/her key worker

6.5 ACTION 5: MAINTENANCE OF GOOD QUALITY LABORATORY SERVICES IN LINE WITH INCREASING DEMANDS

Aim: Provide consistent high quality laboratory services in line with increasing clinical and public health needs

Plan:

- The laboratory mycobacteriology service will be led by an identified microbiologist who will be responsible for the development of a local TB strategy
- The laboratory should have:
 - The capacity to provide a ZN stained smear on the same day in urgent cases, while non urgent cases should be processed within 48 hours
 - The capacity to provide sputum culture on liquid media
 - A protocol indicating the use of liquid and/or solid media³³
 - A standardised method for reporting positive direct Ziehl-Neelsen (ZN) stained smears³³
 - Continued liaison with the reference laboratory in the UK for:
 - Drug sensitivity testing
 - Species identification
 - PCR testing
 - VNTR DNA fingerprinting
 - The capacity to process samples efficiently and expeditiously
 - The capacity to perform the necessary amount of Quantiferon tests as required: estimated amount being 500. There is the need to have more than 1 person capable of performing this test.

It is recommended that:

- The Laboratory adopts all international standards as recommended and endorsed by European or WHO agencies
- Laboratory staff should receive appropriate training abroad to develop such procedures and to achieve the necessary skills.
- Laboratory scientists are recruited to match the work load

6.6 ACTION 6: TB/HIV CO-INFECTION

Aim: to decrease the burden of TB/HIV co-infection by strengthening the collaboration of TB and HIV programmes and activities

Rationale: There is an interaction between TB and HIV that tends to worsen both conditions in individuals co-infected with both.³⁶ HIV interacts directly with specific host immunity so as to increase the susceptibility of the host to TB. It increases the risk of progression of LTBI to active TB.²¹ Furthermore both infections have some common risk groups which can lead to an increase in co-infection in these subgroups of the population.³⁷ The spread of HIV in populations has affected the epidemiology of TB in various countries.²² In Malta 15.2 % of notified TB cases in 2011 were co-infected with TB (EU/EEA average of reported TB cases co-infected with HIV in 2009 was 2.3%).

Plan

- TB testing in HIV patients
- Updated screening protocols for LTBI in HIV patients
- HIV testing and counselling in TB patients
- Provide training to healthcare professionals in counselling pre and post HIV testing
- Enhanced TB/HIV surveillance
- Results of HIV testing in TB patients should be relayed to the national TB programme manager at IDCU, who enters the data into the national TB database
- Collaboration of the key stakeholders managing TB and HIV programmes and activities

List of Appendices

Appendix 1: Tuberculosis screening protocol for pregnant irregular immigrants to Malta.

Appendix 2: Residency definitions.

References

- ¹ World Health Organization. Tuberculosis fact sheet. Geneva, Switzerland: WHO, 2007. Available at <http://www.who.int/mediacentre/factsheets/fs104/en/> Accessed March 2012.
- ² IDCU unpublished data.
- ³ Raviglione M C, Sudre P, Rieder H L, Spinaci S, Kochi A. Secular trends of tuberculosis in Western Europe. Bull WHO 1993; 71: 297-306.
- ⁴ Pace-Asciak A, Mamo J. Tuberculosis surveillance and control among new immigrants to Malta, 2002-2005. Unpublished data.
- ⁵ Sandgren A, Hollo V. Childhood Tuberculosis in the European Union/ European Economic Area, 2010. Unpublished data.
- ⁶ European Centre for Disease Prevention and Control/WHO Regional Office for Europe: Tuberculosis surveillance in Europe 2009. Stockholm, European Centre for Disease and Control, 2009.
- ⁷ The consolidated action plan to prevent and combat multidrug- and extensively drug-resistant tuberculosis in the WHO European Region 2011-2015. Available at <http://www.euro.who.int/en/who-we-are/governance/regional-committee-for-europe/sixty-first-session/documentation/working-documents/wd15-consolidated-action-plan-to-prevent-and-combat-multidrug-and-extensively-drug-resistant-tuberculosis-in-the-who-european-region-20112015> Accessed March 2012.
- ⁸ Broekmans J F, Migliori G B, Rieder H L, Lees J, Ruutu P, Loddenkemper R. European framework for tuberculosis control and elimination in countries with a low incidence. Eur Respir J 2002; 19:765- 775.
- ⁹ World Health Organization. 44th World Health Assembly. Resolutions and Decisions. Resolution WHA 44.8. Geneva, Switzerland: WHO, 1991. Available at http://www.who.int/tb/publications/tbresolution_wha44_8_1991.pdf Accessed March 2012.
- ¹⁰ Global tuberculosis control. WHO report 2011. Geneva, World Health Organization.
- ¹¹ Public Health Act (2002), Malta.
- ¹² Rieder H L, Watson J M, Raviglione M C, Fosssbohm M, Migliori G B, Schoobel V. Surveillance of tuberculosis in Europe. Working Group of the World Health Organization (WHO) and the European

Region of the International Union Against Tuberculosis and Lung Disease (IUATLD) for uniform reporting on tuberculosis cases. *Eur Respir J.* 1996; 9 (5): 1097-1104.

¹³ 2008/426/EC: Commission Decision of 28 April 2008 amending Decision 2002/253/EC laying down case definitions for reporting communicable diseases to the Community network under Decision No 2119/98/EC of the European Parliament and of the Council (notified under document number C(2008) 1589). *OJ L* 159, 18.06.2008, p46.

¹⁴ Veen J. Microepidemics of tuberculosis: stone-in-the-pond principle. *Tubercle and lung disease* 1992; 73(2); 73- 76.

¹⁵ National Collaborating Centre for Chronic Conditions. Tuberculosis: clinical diagnosis and management of tuberculosis and measures for its prevention and control. London: Royal College of Physicians, 2006.

¹⁶ Joint Tuberculosis Committee of the British Thoracic Society. Control and prevention of tuberculosis in the United Kingdom: Code of practice 2000. *Thorax* 2000 55: 887-901.

¹⁷ Verver S, Bwire R, Borgdorff M W. Screening for pulmonary tuberculosis among immigrants: estimated effect on severity of disease and duration of infectiousness. *Int J Tuberc Lung Dis* 2001, 5(5): 419 – 425.

¹⁸ Lobue PA, Moser KS. Screening of immigrants and refugees for pulmonary tuberculosis in San Diego County, California. *Chest* 2004, 126(6): 1777-1782.

¹⁹ Monney M, Zellweger J P. Active and passive screening for tuberculosis in Vaud Canton, Switzerland. *Swiss Med Wkly* 2005, 135(31-32): 469-474.

²⁰ Rieder H L, Zellweger J P, Raviglione M C, Keizer S T, Migliori G B. Tuberculosis control in Europe and international migration. *Eur Respir J* 1994; 7: 1545-1553.

²¹ Rieder H L, Cauthen G M, Comstock G W, Snider DE Jr. Epidemiology of tuberculosis in the United States. *Epidemiol Rev* 1989: 11: 79-98.

²² Mater Dei Hospital, Hospital Infection Control Policy. Policy for prevention of tuberculosis in healthcare settings. Policy No: ICU/03Pol/2010v01.0. Available at www.kura.gov.mt Accessed March 2012.

²³ Caevalho A C C, Pezzoli M C, El-Hamad I, Arce P, Bigoni S, Scarcella C. QuantiFERON®- TB Gold Test in the identification of latent tuberculosis infection in immigrants. *Journal of Infection* 2007, 55 (2): 164-168.

²⁴ Kik S, Franken W P, Mensen M, Verver S, Cobelens F G, Arend S M, Borgdorff M W. Predictive value of tuberculin skin test, quantiferon TB gold and T-spot. TB for active tuberculosis. 2007, poster Union Conference Cape Town 2007.

²⁵ Rieder H L. Epidemiologic basis of tuberculosis control, first edn: International Union Against Tuberculosis and Lung Disease; 1999.

²⁶ British HIV Association. Routine investigation and monitoring of adult HIV-1-infected individuals (2011). Available at <http://www.bhiva.org/Monitoring.aspx> Accessed March 2012.

-
- ²⁷ Centres for Disease control and prevention (CDC) MMWR Report. Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents. April 2009. Available at: <http://www.cdc.gov/mmwr/pdf/rr/rr5804.pdf> Accessed March 2012.
- ²⁸ World Health Organization. Guidelines for intensified tuberculosis case-finding and isoniazid preventive therapy for people living with HIV in resource-constrained settings. 2011. Available at: http://whqlibdoc.who.int/publications/2011/9789241500708_eng.pdf Accessed March 2012.
- ²⁹ Health Protection Agency. National Travel Health Network and Centre. Tuberculosis Fact sheet. Health Protection Agency, 2007. Available at <http://www.nathnac.org/pro/factsheets/documents/tb.pdf> Accessed March 2012.
- ³⁰ World Health Organization. Treatment of tuberculosis guidelines. Fourth edition. Geneva: World Health Organization, 2010.
- ³¹ Infectious Diseases Society of America. IDSA practice guidelines. Available at http://www.idsociety.org/IDSA_Practice_Guidelines/ Accessed March 2012.
- ³² World Health Organization. Multidrug and extensively drug-resistant TB (M/XDR-TB): 2010 global report on surveillance and response. Available at <http://www.who.int/tb/publications/2010/978924599191/en/index.html>. Accessed March 2012.
- ³³ Debattista S, Haider J. Investigation of specimens for Mycobacterium species. Malta, 2009.
- ³⁴ Asch S, Leake B, Anderson R, Gelberg L. Why do symptomatic patients delay obtaining care for tuberculosis? *Am J Respir Crit Care Med* 1998; 157: 1244-1248.
- ³⁵ Borgdorff M W, Veen J, Kalisvaart N A, Broekmans J F, Nagelkerke N. Defaulting from tuberculosis treatment in the Netherlands: rates, risk factors and trend in the period 1993-1997. *Eur Respir J*. 2000; 16(2):209-13.
- ³⁶ Interim policy on collaborative TB/HIV activities. Stop TB Department and Department of HIV/AIDS. World Health Organization, Geneva, 2004. Available at http://whqlibdoc.who.int/hq/2004/who_htm_tb_2004.330.pdf Accessed March 2012.
- ³⁷ Corbett E L, Watt C J, Walker N, Maher D, Williams B G, Raviglione M C. The growing burden of tuberculosis. Global trends and interactions with the HIV epidemics. *Arch Intern Med* 2003; 163(9): 1009-21 EuroHIV.