DETECTION *and* TREATMENT OF LATENT

tuberculosis infection

in MASSACHUSETTS
COLLEGE *and* UNIVERSITY STUDENTS

Recommendations of the *Medical Advisory Committee for the Elimination of Tuberculosis (MACET)*

RECOMMENDATIONS OF THE MEDICAL ADVISORY COMMITTEE FOR THE ELIMINATION OF TUBERCULOSIS (MACET)

DETECTION AND TREATMENT OF LATENT TUBERCULOSIS INFECTION IN MASSACHUSETTS COLLEGE AND UNIVERSITY STUDENTS

MACET College Health Subcommittee

Janice Allen, NP
John Bernardo, MD
Michelle Bowdler, MSPH
Jennifer S. Daly, MD
Sue Etkind, RN, MS
Martha Favre, FNP
Pamela Harris, RN
Margaret Higham, MD
Robert N. Husson, MD
Karen Kalamkis, NP
A. J. Lardner, RN
Stephen J. Lerman, MD, MPH (Principal Author)
Art Nahill, MD
Thomas I. Nary, MD
Kay Petersen , MD
Mitchell H. Pysznik, RN, MPH
Linda Singleton, RN, MPH
Janice Sundnas
Ian Wong, MSPH
Carole Worsh, NP

MACET Members

Carlos Alvarez, MA
Timothy F. Brewer, MD, MPH (Vice-Chair)
Robert T. Cooper, RS
Jennifer S. Daly, MD
C. Robert Horsburgh, MD
Robert N. Husson, MD
Bonnie Johnston, RN
Stephen J. Lerman, MD, MPH (Chair)
Edward Nardell, MD
Joel Piton, MD, MEd

Ex-Officio Members, Massachusetts Department of Public Health

John Bernardo, MD
Jennifer Cochran, MPH
Sue Etkind, RN, MS
Alfred DeMaria, MD
Kathleen Hursen, RN
Jill Northrup, MPH
Sharon Sharnprapai, MS
Linda Singleton, RN, MPH

Staff Facilitator

Tony Palomba, The Medical Foundation

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Please Note

This guide and updates of it will be posted on the website of the Massachusetts Department of Public Health – Division of Tuberculosis Prevention and Control (www.state.ma.us/dph/cdc/tb/index.htm).

INTRODUCTION

With 85 colleges and universities, Massachusetts has a large (387,508, according to the 2000 census) and richly diverse population of students seeking a higher education. During the five-year period 1996-2000, 60 (4%) of 1,365 reported active tuberculosis cases in Massachusetts occurred in college students.

Although risk-based, targeted testing to detect latent tuberculosis infection is recommended by the American Thoracic Society and the Centers for Disease Control and Prevention[1] and the American College Health Association,[2] the recommendations of these national organizations differ in some respects and, importantly, Massachusetts college health services vary widely in their implementation approaches. Some test all incoming students, some test none, and some test only students who are at high risk of exposure to tuberculosis. In addition, programs aimed at treating students who have latent tuberculosis infection generally have had low success rates.

Responding to numerous requests from college health services for clarification and guidance, the Massachusetts Department of Public Health asked its expert tuberculosis advisory group, the Medical Advisory Committee for the Elimination of Tuberculosis (MACET), to address the issue. MACET, in turn, formed a College Health Subcommittee composed of several members of MACET, representatives of the Division of Tuberculosis Prevention and Control of the Massachusetts Department of Public Health, the college health specialist of the Massachusetts Department of Public Health, and college health service physicians, nurses, and administrators. The latter were selected to represent the wide variety of types of schools in Massachusetts, ranging from public two-year community colleges to large private research universities. The Subcommittee produced this practical, step-by-step operational guide intended for use by college health services. This guide was endorsed by MACET and will be submitted to the Massachusetts Department of Public Health for adoption as an official policy recommendation.

Format of the Guide

The goal of this guide is to help Massachusetts college health services improve their ability to detect and treat latent tuberculosis infection. The aim is to benefit both the individual student and the college community by reducing the risk of active tuberculosis in a way that makes the best use of limited financial resources and personnel time.

There are four components of the MACET recommendations and a chapter in the guide is devoted to each. Those components are:

1. Administer a tuberculosis risk assessment questionnaire to all incoming students to identify those who have been at increased risk of exposure to tuberculosis.

[1] Centers for Disease Control and Prevention. Targeted tuberculin testing and treatment of latent tuberculosis infection. MMWR 2000; 49 (No. RR-6):1-51.
[2] American College Health Association. ACHA Guidelines. Tuberculosis screening of college and university students. November 2000; 1-3.

2. Administer a tuberculin skin test to all students identified as having been at increased risk of exposure to tuberculosis, but do not test students identified as having been at low risk of exposure.

3. Perform a clinical evaluation and chest x-ray for students found to have a positive tuberculin skin test.

4. Offer students with latent tuberculosis infection treatment with nine months of isoniazid or an alternative recommended drug regimen.

In each chapter there are four sections: (a) scientific rationale, (b) operational guidance, (c) sample forms, and (d) program evaluation.

Educational materials that are appropriate for college students, particularly foreign-born students, will be essential for the success of this program, but their availability is limited. MACET decided that development of needed educational materials was beyond its scope and that it would rely on the Massachusetts Department of Public Health to develop them.

Health Science Students

Hospitals, nursing homes, and other health-related work sites frequently ask college health services to perform tuberculin skin tests for health science students who are applying for clerkships or employment. Because these practices are controlled by the rules and regulations of the Occupational Safety and Health Administration and the various health institutions involved, MACET decided to make no recommendations in regard to screening of health science students for these purposes.

Special Health Conditions

The type of screening described here is designed for a healthy population. The relative risk of developing active tuberculosis is higher and the course of disease is worse in patients with a number of underlying conditions, such as HIV/AIDS, silicosis, diabetes mellitus, chronic renal failure, and neoplasms, and in those receiving prolonged treatment with corticosteroids and other immunosuppressive agents. **This guide will not address tuberculosis screening for students with these special health conditions.** The recommended frequency and interpretation of tuberculin skin testing in each of these clinical situations varies and is best handled by the individual student's health care provider, who should consult for guidance the Centers for Disease Control and Prevention publication *Targeted tuberculin testing and treatment of latent tuberculosis infection* (MMWR 2000; 49 [No. RR-6]:23-5) or the "Tuberculosis" section in the American Academy of Pediatrics *Red Book*: *Report of the Committee on Infectious Diseases.* (Pickering LK, ed., 25th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2000:593-9).

College Health Service Tuberculosis Programs

College health services should review how they market and implement tuberculosis control; tuberculosis control programs should be unintimidating, accessible, and convenient for the students. To counter erroneous information and overcome resistance to testing and treatment of tuberculosis, we encourage colleges to develop innovative, culturally sensitive educational programs. One noteworthy example: The college health service at Virginia Commonwealth University trained students who had completed treatment as peer educators (see **APPENDIX 1** for their website). Finally, students must be completely confident that their privacy in this highly sensitive area will be respected.

New Definitions

Latent tuberculosis infection is the currently accepted term for the stage of *Mycobacterium tuberculosis* infection that is asymptomatic, dormant, and non-contagious; the patient is not sick due to *M. tuberculosis* infection and has a normal chest x-ray. A positive tuberculin skin test is the only evidence of latent tuberculosis infection. This stage may continue for the patient's entire lifetime or, in a matter of weeks to years from the time of infection, may progress to the stage of active disease called **tuberculosis** that can affect the lung or other parts of the body (lymph nodes, meninges, bones, joints, liver and spleen) and may then be contagious to others. **Treatment of latent tuberculosis infection**, previously termed preventive treatment or prophylaxis, aims to prevent the future development of active disease.

EXECUTIVE SUMMARY

Tuberculosis continues to be a significant public health threat in the United States, and it affects college students. During the five-year period 1996-2000, 60 of the 1,365 reported cases of active tuberculosis in Massachusetts occurred in college students. The appearance of even a single case of contagious tuberculosis on a college campus causes great anxiety and disruption for students, parents, and staff. If these cases could be prevented, both the individual student and the college community would benefit.

Current approaches to screening Massachusetts college students for tuberculosis show little consistency. Some colleges test every incoming student and some test none. Moreover, treatment programs for latent tuberculosis infection in college students generally report low success rates. Responding to numerous requests from college health services for clarification and guidance, the Massachusetts Department of Public Health asked its expert tuberculosis advisory group, the Medical Advisory Committee for the Elimination of Tuberculosis (MACET), to address the issue. MACET, in turn, sought the help of a group of college health physicians, nurses, and administrators selected to represent the wide range of types of colleges and universities in Massachusetts. Working together, they prepared this step-by-step operational guide for college health services on the detection and treatment of latent tuberculosis infection. It aims to combine practicality, consistency of practice, and sound judgment based on available scientific data.

To prevent development of tuberculosis in college students, MACET recommends risk-based, targeted tuberculin skin testing--the same approach advocated by the American Thoracic Society, the Centers for Disease Control and Prevention, and the American College Health Association. All incoming students should complete a simple questionnaire about the three major risk factors for exposure to tuberculosis that have been identified in epidemiological studies. These are (1) close contact with a case of active tuberculosis, (2) birth in a country that has a high rate of tuberculosis (defined as 50 or more cases/100,000 people), and (3) travel or residence for more than one month in a country that has a high rate of tuberculosis. Students who have one or more risk factor for exposure to tuberculosis should have a tuberculin skin test. Those with a positive tuberculin skin test should have a chest x-ray and clinical evaluation to determine whether they have latent tuberculosis infection or active disease. Students with latent tuberculosis infection have a lifetime chance of up to 10% of developing active, contagious tuberculosis. They should be offered nine months of treatment with isoniazid, an antibiotic that kills the tuberculosis organisms and reduces by more than 90% the danger of becoming ill and spreading infection to others.

Students from countries where bacillus Calmette-Guerin (BCG) vaccine is widely used should be managed in the same manner as those from countries that do not use BCG vaccine. Prior BCG vaccination, administered according to World Health Organization guidelines, neither prevents latent tuberculosis infection nor interferes with correct interpretation of tuberculin skin tests.

Most college students in Massachusetts will be identified by the questionnaire as being at low risk of exposure to tuberculosis. They should not have a tuberculin skin test because the majority of positive tests in a low-risk population are false positive results. This testing subjects students to unnecessary anxiety and to the side effects and expense of medication for an infection that they may not have.

Each college health service is encouraged to quantitatively evaluate the success of each step of its program for detecting and treating latent tuberculosis infection. This can serve as a basis for continual improvement.

Using the targeted approach recommended in this guide, college health services can make the best use of limited financial resources and personnel time to prevent tuberculosis.

CHAPTER 1. TUBERCULOSIS RISK ASSESSMENT

The first step in the process of diagnosing latent tuberculosis infection is to assess the risk of previous exposure to tuberculosis. This assessment can be accomplished using a simple questionnaire. Individuals who report increased risk of exposure to tuberculosis should be tuberculin skin tested, while those reporting low risk should not.

A. SCIENTIFIC RATIONALE

In Massachusetts in 2002, there were 271 reported cases of tuberculosis (case rate 4.27 per 100,000 population).[3] Persons born outside the United States were the largest risk group; 76% of the tuberculosis cases fell into this category. As stated in the Introduction, during the five-year period 1996-2000, 60 of 1,365 reported cases of tuberculosis cases in Massachusetts occurred in college students (annual case rate 3.10 per 100,000 students). Although the case rate was low and similar to that of the general population, it is striking that 54 (90%) of the 60 students with tuberculosis were born outside the United States.

Risk Factors

A number of studies in children and adolescents living in the United States have examined the rates of latent tuberculosis infection in potential risk groups.[4] [5] [6] [7] [8] Foreign birth was by far the strongest predictor of latent tuberculosis infection. Visiting or traveling in a country with a high rate of tuberculosis, having contact with an adult with active tuberculosis, or having a relative with a positive tuberculin skin test were also validated as risk factors. On the other hand, poverty, exposure to individuals with HIV/AIDS, homelessness, illicit drug use and recent incarceration were not independent predictors of latent tuberculosis infection.

University Study

There is only one recent study of risk factors for latent tuberculosis infection among university students.[9] Performed among incoming students at Virginia Commonwealth University, this large-scale evaluation of a risk assessment questionnaire found a strong association (unadjusted odds ratio 44.9) between birth in a high-prevalence country and

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[3] Massachusetts Department of Public Health. Division of Tuberculosis Prevention & Control. Summary of statistics for the year 2002. Boston, MA; 2003.

[4] Froehlich H, Ackerson LM, Morozumi PA. Targeted testing of children for tuberculosis: Validation of a risk assessment questionnaire. Pediatrics 2001; 107:e54.

[5] Saiman L, San Gabriel P, Schulte J, et al. Risk factors for latent tuberculosis infection among children in New York City. Pediatrics 2001; 107:999-1003.

[6] Besser RB, Pakiz B, Schulte JM, et al. Risk factors for positive Mantoux tuberculin skin tests in children in San Diego, California: Evidence for boosting and possible food-borne transmission. Pediatrics 2001; 108:305-10.

[7] Lobato MN, Hopewell PC. *Mycobacterium tuberculosis* infection after travel to or contact with visitors from countries with a high prevalence of tuberculosis. Am J Respir Crit Care Med 1998; 158:1871-5.

[8] Sewint JR, Hall BS, Baldwin RM, Virden JM. Outcomes of annual tuberculosis screening by Mantoux test in children considered to be at high risk: Results from one urban clinic. Pediatrics 1997; 99:529-33.

[9] Koppaka VR, Harvey E, Mertz B, Johnson BA. Risk factors associated with tuberculin skin test positivity among university students and the use of such factors in the development of a targeted screening program. Clin Infect Dis 2003; 36:599-603 and personal communication, 2002.

a positive tuberculin skin test. The risk was lower for the subgroup of foreign-born students called "international students" (unadjusted odds ratio 25.9). ["International students" are foreign-born students who are not residents of the United States. The Immigration and Naturalization Service issues them temporary student visas that have no requirement for tuberculin skin tests or chest films]. Close contact with a tuberculosis patient was also a risk factor (unadjusted odds ratio 3.5). This study found that there was no association between a number of other potential risk factors and a positive tuberculin skin test. These included symptoms of tuberculosis such as cough or fever, injection drug use, homelessness, incarceration, prior experience in health care, travel in a country with a high rate of tuberculosis, and diseases and treatment known to affect the progression of latent tuberculosis infection to tuberculosis. In this university population, use of a questionnaire that simply identified as candidates for skin testing the 10% of students who were born in high-prevalence countries had a high level of sensitivity and specificity. Adding a question about close contact with a tuberculosis patient improved the sensitivity of the questionnaire and only slightly expanded the number of students to be tested.

Travel

Although visiting or traveling in a country with a high rate of tuberculosis had no detectable effect on the risk of latent tuberculosis infection in the university study, it did in the pediatric studies cited above. The minimum time required for significant exposure, however, was not determined in the pediatric studies.

A study of adult Dutch travelers who were skin tested for tuberculosis before and after long-term (3-12 months) travel to highly endemic countries provided insight into the dynamics of acquiring tuberculosis abroad.[10] With a minimum three-month stay, the risk was elevated to a level similar to that of the local population and that risk level did not increase with longer stays of up to 12 months. Health care work involving direct patient contact was a significant and independent risk factor for acquiring latent tuberculosis infection.

Countries with High Tuberculosis Rates

The World Health Organization provides figures for every country of the annual number of tuberculosis case notifications and the estimated number of cases, an adjusted figure that takes into account incomplete coverage by health services, inaccurate diagnosis, or deficient recording and reporting.[11] The Virginia Commonwealth University study of risk factors[12] and the American College Health Association recommendations[13] used tuberculosis case notification figures and a rate of 15 or more cases per 100,000

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[10] Cobelens FGJ, van Duetekom H, Draayer-Jansen IWE, et al. Risk of infection with *Mycobacterium tuberculosis* in travelers to areas of high tuberculosis endemicity. Lancet 2000; 356:461-5.

[11] World Health Organization. Global tuberculosis control. WHO report 2002. http://www.who.int/gtb/publications/globrep02.

[12] Koppaka VR, Harvey E, Mertz B, Johnson BA. Risk factors associated with tuberculin skin test positivity among university students and the use of such factors in the development of a targeted screening program. Clin Infect Dis 2003; 36:599-603 and personal communication, 2002.

[13] American College Health Association. ACHA Guidelines. Tuberculosis screening of college and university students. November 2000; 1-3.

population to define a high prevalence country. MACET, in contrast, used estimated case figures and a higher rate, **50 or more estimated cases per 100,000 population**, to define a country with a high rate of tuberculosis. Among foreign-born college students with tuberculosis in Massachusetts during the period 1996-2000, 50 of 54 cases (93%) were from countries that met this definition (see **APPENDIX 2**). In addition, a tuberculosis case rate of 50 or more cases per 100,000 population was consistently associated with an elevated rate of latent tuberculosis infection in that country; between 16 and 64% of the people in the countries identified as having a high tuberculosis case rates had latent tuberculosis infection.[14]

The American Thoracic Society and the Centers for Disease Control and Prevention[15] and the American College Health Association[16] recommend testing for and treating latent tuberculosis infection only in foreign-born persons who have arrived in the United States within the past five years, on the grounds that the greatest risk of developing active tuberculosis occurs within a short time after arrival. Indeed, half of the active tuberculosis cases overall were diagnosed within five years of arrival. This means, however, that half of the active tuberculosis cases occurred later; the proportion of disease after five years ranged from 37% to 59% depending on the person's country of origin.[17] Moreover, the incidence of active tuberculosis diagnosed after arrival in the United States declined at different rates, depending not only on the country of origin, but also on age at time of arrival. The incidence remained elevated in some subgroups for more than 20 years.

Why Test Only High-Risk Students?

The tuberculin skin test is currently the best way to tell if someone has tuberculosis infection. However, like all tests used in medicine, the tuberculin skin test is not perfect. It can be negative in people who actually have latent tuberculosis infection (a result called a false negative) and it can be positive in people who are not infected (a result called a false positive). When a test is less than perfect, it performs better in a group of people more likely to have the condition for which they are being tested than in those less likely to have the condition. This means that people at increased risk of having been exposed to tuberculosis are the best candidates for the tuberculin skin test. Many more of them will have a positive test result and, importantly, very few of the positive test results will be false positives. In contrast, people who are unlikely to have been exposed to tuberculosis, such as most people born in the United States and attending college today, are poor candidates for the tuberculin skin test. Not only will smaller numbers of them have a positive test result, but also the majority of the positive test results that do occur will be false positives.

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[14] Dye C et al. Global burden of tuberculosis. Estimated incidence, prevalence, and mortality by country. JAMA 1999: 282:677-86.

[15] Centers for Disease Control and Prevention. Targeted tuberculin testing and treatment of latent tuberculosis infection. MMWR 2000; 49 (No. RR-6):1-51.

[16] American College Health Association. ACHA Guidelines. Tuberculosis screening of college and university students. November 2000; 1-3.

[17] Talbot EA, Moore M, McCray, Binkin NJ. Tuberculosis among foreign-born persons in the United States, 1993-1998. JAMA 2000; 284:2894-900.

It is recommended that **students who report a low risk of previous exposure to tuberculosis should not be skin tested, because of the high likelihood of false positive test results in this population.** A false positive test result means that the student will be burdened with unwarranted anxiety, will be exposed unnecessarily to the side effects and expense of medication, and will gain no benefit.

B. OPERATIONAL GUIDANCE

In Massachusetts, the law requires certain immunizations for entering college and university students.[18] The law is directed at full-time undergraduate and graduate students, part-time undergraduate and graduate students in a health science program, and full- or part-time students attending institutions of higher education while on student or other visas. The latter category corresponds roughly to the "international student" as previously defined.

The law does not address tuberculosis risk assessment or tuberculin skin tests for college students, and MACET does not feel that it is advisable to make tuberculosis screening a legal requirement. However, **MACET strongly recommends tuberculosis risk assessment for all incoming full-time undergraduate and graduate students and for all other groups covered by the immunization law.** Coupling tuberculosis risk assessment with immunizations would be an efficient way to gather, process, and monitor information about both because college health services are diligent about the immunization requirements and have established mechanisms for ensuring compliance.

C. SAMPLE FORM

The **TUBERCULOSIS RISK QUESTIONNAIRE FOR COLLEGE AND UNIVERSITY STUDENTS** (**APPENDIX 3**) should be incorporated into the form used to gather immunization data that is sent out prior to matriculation. The incoming student should fill it out.

It asks three questions: about exposure to tuberculosis, birth in a country with a high rate of tuberculosis, and travel or residence for more than a month in a country with a high rate of tuberculosis. The questionnaire also lists the countries that have high rates of tuberculosis (50 or more cases/100,000 population). A positive response to any of these questions indicates that the student has had an increased risk of exposure to tuberculosis and should have a tuberculin skin test. A negative response to all three questions indicates that the student has had a low risk of exposure to tuberculosis and should not have a tuberculin skin test.

Three points about the questionnaire should be noted. First, the minimal duration of travel or residence in a country with a high rate of tuberculosis that constitutes a risk for acquiring infection is unknown, and one month has been arbitrarily selected; living with a local family or participating in health care work may be more important determinants than duration. Second, as the global epidemiology of tuberculosis changes, the list of countries with high rates of tuberculosis will have to be updated. Third, MACET has deviated from the approach taken by the the American Thoracic Society, the Centers for Disease Control and Prevention, and the American College Health Association by

[18] 105 CMR 220.600: Immunization Requirements for Postsecondary Students.

including **all** students born in countries with high tuberculosis rates, not just those who have arrived in the United States within the past five years. Not only does the proportion of active tuberculosis cases that occur more than five years after arrival show variation from country to country, but also consideration of this time factor complicates the evaluation of risk because of return trips to the country of birth and interim stays in other countries with high rates of tuberculosis.

D. PROGRAM EVALUATION

MACET encourages college health services to keep their own step-by-step statistics to evaluate the success of the program, to understand barriers, and to serve as a basis for continually improving the process.

The initial steps of the process, discussed in this chapter, can be evaluated by comparing the number of incoming students to the number who completed the risk questionnaire and the number who were found to be at high risk for tuberculosis exposure.

Step 1

$$\% \text{ Risk Assessment} = \frac{\text{Number Who Completed Risk Questionnaire}}{\text{Number of Incoming Students}} \times 100$$

Step 2

$$\% \text{ High Risk} = \frac{\text{Number of High Risk Students}}{\text{Number Who Completed Risk Questionnaire}} \times 100$$

In a successful program, a high proportion of incoming students completes the tuberculosis risk assessment form. The proportion of students at a particular college who are identified as having an increased risk of exposure to tuberculosis will depend largely on the number of students at that college born in countries with high rates of tuberculosis.

CHAPTER 2. TUBERCULIN SKIN TEST

A student who has been at increased risk of exposure to tuberculosis should have a tuberculin skin test. The intradermal Mantoux test containing 5 tuberculin units (TU) of purified protein derivative (PPD), referred to as **intermediate PPD**, is the only recommended tuberculin skin test. Other strengths of Mantoux skin tests (1 and 250 TU) should not be used. Multiple puncture tests, such as Tine and Mono-vacc, are not recommended, because they lack adequate sensitivity and specificity.

Since the tuberculin skin test is positive with both latent tuberculosis infection and active tuberculosis, a negative chest x-ray and clinical evaluation are required to establish whether a student with a positive test has latent infection or active disease, as will be discussed in Chapter 3.

QuantiFERON®-TB Test

Although the tuberculin skin test remains the standard, QuantiFERON®-TB, a new test for detecting latent tuberculosis infection, has recently been approved by the Food and Drug Administration and guidelines for its use have been formulated by the Centers for Disease Control and Prevention.[19] The test uses a whole blood sample and measures the release of interferon-gamma from the patient's lymphocytes when incubated with PPD from *M. tuberculosis* and control antigens. QuantiFERON®-TB showed moderate concordance with the tuberculin skin test in one study,[20] but poor concordance in another.[21]

The new test requires only one patient visit and the reading is less subject to reader error and bias than the tuberculin skin test, but it requires a laboratory that is capable of performing the assay and is more expensive. As with the tuberculin skin test, risk assessment is required, because QuantiFERON®-TB test interpretation is stratified according to risk factors. The Centers for Disease Control and Prevention recommends that QuantiFERON®-TB should not be used for people who have been in close contact with a case of tuberculosis (one of the three risk factors used in this guide), in persons suspected of having active tuberculosis, in children less than 17 years of age, in pregnant women, or for confirmation of tuberculin skin test results. With further experience and technologic improvements, this type of test may eventually replace the tuberculin skin test for detection of latent tuberculosis infection.

[19] Centers for Disease Control and Prevention. Guidelines for using the QuantiFERON-TB test for diagnosing latent *Mycobacterium tuberculosis* infection. MMWR 2003; 52 (RR-2):15-8.

[20] Mazurek GH, LoBue PA, Daley CL, et al. Comparison of a whole-blood interferon γ assay with tuberculin skin testing for detecting latent *Mycobacterium tuberculosis* infection. JAMA 2001; 286:1740-7.

[21] Bellete B, Coberly J, Barnes GL, et al. Evaluation of a whole-blood interferon-γ release assay for the detection of *Mycobacterium tuberculosis* infection in 2 study populations. Clin Infect Dis 2000; 34:1449-56 and Nadal D. Is the in vitro interferon-γ release assay an adequate replacement for the tuberculin skin test? (Editorial). Clin Infect Dis 2000; 34:1457-9.

A. SCIENTIFIC RATIONALE

BCG Vaccine

Many students from countries with high rates of tuberculosis have been previously vaccinated with bacillus Calmette-Guerin (BCG). Misconceptions about BCG vaccine held by many foreign-born students and their physicians have created resistance to the use of the tuberculin skin test to detect latent tuberculosis infection and reluctance to treat those identified as having latent tuberculosis infection.

Effectiveness of BCG Vaccine

BCG vaccine is a live, attenuated bacterial vaccine. Widely used since 1921, it has been given to more people than any other vaccine. The Expanded Programme for Immunization of the World Health Organization recommends its use at birth or shortly thereafter for infants in countries with high rates of tuberculosis, because it is highly effective in preventing two life-threatening forms of tuberculosis in infants and young children, tuberculous meningitis and disseminated (miliary) tuberculosis.[22] For preventing tuberculosis of the lung in children and adults, the most common form of tuberculosis, BCG vaccine may be effective only about half of the time, with some field trials showing little or no protection.[23] [24] Because of the modest and variable protective effect of BCG vaccine for tuberculosis of the lung, public health authorities in the United States have not endorsed its general use here.[25]

On the basis of experimental studies, experts agree that when a person inhales the tuberculosis bacteria, *M. tuberculosis*, prior BCG vaccine does not prevent the initial infection, and it may then persist in a person's body for his or her lifetime.[26] In other words, **BCG vaccine does not prevent latent tuberculosis infection**. Given exposure to tuberculosis, latent tuberculosis infection may result and, if it does, the tuberculin skin test is as likely to be positive in someone who has had BCG in the past as in someone who has not had the vaccine.

BCG Vaccine and the Tuberculin Skin Test

Misunderstanding may arise, however, because BCG vaccine itself may cause some reaction to the tuberculin skin test. The key questions are: how much reaction does BCG vaccine cause and for how long does it last?

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[22] Colditz GA, Berkey CS, Mosteller F, et al. The efficacy of bacillus Calmette-Guerin vaccination of newborns and infants in the prevention of tuberculosis: Meta-analyses of the published literature. Pediatrics 1995; 96:29-35.
[23] Colditz GA, Brewer TF, Berkey CS, et al. Efficacy of BCG vaccine in the prevention of tuberculosis: Metaanalysis of the published literature. JAMA 1994; 271:698-702
[24] Fine PEM. Bacille Calmette-Guerin vaccines: A rough guide. Clin Infect Dis 1995; 20:11-4.
[25] Centers for Disease Control and Prevention. The role of BCG vaccine in the prevention and control of tuberculosis in the United States. MMWR 1996; 45 (No. RR-4):1-18.
[26] Brewer TF, Wilson ME, Nardell EA. BCG immunization: Review of past experience, current use, and future prospects. In: Remington JS, Swartz MN, eds. Current Clinical Topics in Infectious Diseases. Boston: Blackwell Scientific Publications, 1995:255.

When BCG vaccine is given to young infants using the dose and method recommended by the World Health Organization, most have small (1-9 mm) tuberculin skin test reactions at 3-11 months of age, but only 7-11% develop a reaction sufficiently large (10 mm or more) to be called "positive". The skin test reaction size attributable to BCG vaccine becomes progressively smaller over the next year or two. Eventually, in the absence of intervening infection, the test shows little or no reaction. At the same time, infants in countries with high rates of tuberculosis are exposed to contagious tuberculosis at a young age. In many countries, the prevalence of infection starts to go up among children as young as six months of age. By 2-3 years of age the likelihood is very strong that a "positive" tuberculin skin test is due to latent tuberculosis infection, not to BCG vaccine.[27] [28] [29]

Further support for the view that the tuberculin skin test can be used to accurately identify latent tuberculosis infection in BCG vaccine recipients comes from studies in a variety of settings. Native Americans living in remote communities in Northern Canada where tuberculosis is endemic, received BCG at birth and only 0-2% in early childhood had positive skin tests, but the rate rose to 25% by mid-adolescence.[30] In Botswana, the country with the world's highest rate of tuberculosis and one with universal BCG coverage, 7% of children 3-60 months of age who had no contact with a case of active tuberculosis had a positive tuberculin skin test, but twice as many (13%) tested positive among those who had known contact with tuberculosis. If the child had contact with a mother or an aunt with active tuberculosis, the rates were significantly higher, 33% and 36%, respectively.[31] In Brazil, 61% of children less than 15 years of age, most of whom had received BCG vaccine, and all of whom had close household exposure to an adult with active tuberculosis, had a positive skin test. Only 4% of unexposed neighborhood controls with similar BCG coverage had a positive test.[32] Among immigrants to Montreal, Canada from countries with high tuberculosis incidence rates, the prevalence of positive tuberculin skin tests was similar among those who did and did not report prior BCG vaccination and was directly related to age at the time of immigration.[33]

Thus, there is a high degree of probability that a positive tuberculin skin test indicates infection with *M. tuberculosis* in a college student who received BCG vaccine in infancy and who had close contact with a person with active tuberculosis or came from a country with a high rate of tuberculosis.

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[27] Karalliedde S, Katugaha LP, Uragoda CG. Tuberculin response of Sri Lankan children after BCG vaccination at birth. Tubercle 1987; 68:33-8.

[28] Lockman S, Tappero JW, Kenyon TA, et al. Tuberculin reactivity in a pediatric population with high BCG coverage. Int J Tuberc Lung Dis 1999; 3:23-30.

[29] Floyd S, Ponninghaus JM, Bliss L, et al. Kinetics of delayed-type hypersensitivity to tuberculin induced by bacilli Calmette-Guerin vaccination in northern Malawi. J Infect Dis 2002; 186:807-14.

[30] Young TK, Mirdad S. Determinants of tuberculin sensitivity in a child population covered by mass BCG vaccination. Tubercle and Lung Dis 1992; 73:94-100.

[31] Lockman S, Tappero JW, Kenyon TA, et al. Tuberculin reactivity in a pediatric population with high BCG coverage. Int J Tuberc Lung Dis 1999; 3:23-30.

[32] Almeida LMD, Barbieri MA, Carvalho A, et al. Use of purified protein derivative to assess the risk of infection in children in close contact with adults with tuberculosis in a population with high Calmette-Guerin bacillus coverage. Pediatr Infect Dis J 2001; 20:1061-5.

[33] Menzies R, Vissandjee B, Amyot D. Factors associated with tuberculin reactivity among the foreign-born in Montreal. Am Rev Respir Dis 1992; 146:752-6.

Several factors may influence the tuberculin skin test result in a student with prior BCG vaccination: vaccination after infancy, recent vaccination, multiple doses of vaccine, and prior administration of multiple tuberculin skin tests. However, since most persons who have received BCG vaccine also have a high risk of exposure to tuberculosis, risk-based interpretation of the tuberculin skin test, discussed below, should be followed.

B. OPERATIONAL GUIDANCE

The tuberculin skin test is recommended for students whom the **TUBERCULOSIS RISK QUESTIONNAIRE FOR COLLEGE AND UNIVERSITY STUDENTS** has shown to be at high risk for exposure to tuberculosis. It is not recommended for those at low risk of exposure to tuberculosis. It is also not recommended for students who have had a positive tuberculin skin test in the past.

Many colleges will accept the results of skin tests performed by outside health care providers, while some may prefer to perform all tuberculin skin tests themselves.

MACET encourages each college health service to institute a simple and reliable system for listing all incoming students and for recording the results of the tuberculosis risk assessment questionnaire (high or low risk). For those at high risk, the dates and results of the tuberculin skin test, performed either by the student's health care provider or the college health service, should be noted.

Vaccines and the Tuberculin Skin Test

Prior receipt of BCG vaccine is not a contraindication to administration of a tuberculin skin test.

It is not necessary to delay immunization with MMR vaccine until after the student has been tested for tuberculosis. Unlike measles (the disease), measles vaccine does not activate latent tuberculosis infection. The tuberculin skin test can be administered at the same time MMR vaccine and other live virus vaccines are given, but it should not be administered later in the 4-6 week period after a live virus vaccine has been administered, because transient anergy may cause a false negative skin test result.

Technique

The 5 TU intradermal Mantoux test (intermediate PPD) is administered with a 1 ml tuberculin syringe with a 27 g ½″ needle. Draw up 0.1 ml of intermediate PPD solution. Use the flat volar surface of the forearm, not the side. Insert the needle with the bevel up and inject the dose intradermally. If a bleb is not raised, it means that the test material was delivered subcutaneously. If this happens, try again at a different site.

Reading the Tuberculin Skin Test

Ideally, the tuberculin skin test should be read 48-72 hours after application. If the student fails to have the test read within three days, however, a test reading within four or five days (96-120 hours) is probably still valid, although this point has not been

rigorously studied. Test readings more than four or five days after application may not be accurate and should not be accepted.[34] [35] If there was vesiculation, however, the test should be regarded as positive and should not be repeated.

All test results – whether positive or negative – must be read by qualified health care personnel. Reports of readings by students, their friends, or their parents are unreliable. Students or students' parents who themselves are medical personnel should be gently discouraged from reading the test, because denial may erode their objectivity.

Induration, not redness, is the basis of the reading. Induration can be determined by palpation or by the technique of running a ballpoint pen along the skin until resistance is met. Fewer positive reactions are missed with the ballpoint pen technique.[36] Since the area of induration is seldom a perfect circle, the result will be different depending on which dimension is selected for measurement. In the past, some have recommended measuring the largest diameter. Now, all authorities recommend measuring the diameter of induration on the transverse axis (i.e., at a right angle to the long axis) of the arm. This technique was the standard in the studies used to establish cut-off points for Mantoux test results.

The test result should be expressed in millimeters (mm). When using a ruler, the reader must guard against being influenced by seeing the cut-off points (e.g., 10 mm). An inexpensive sewing gauge or a special tuberculin skin test caliper supplied by the Massachusetts Department of Public Health helps to avoid this source of bias. The reader can measure the induration with the blank side of the sewing gauge or caliper up and then turn it over to see the number that was measured.

Interpreting the Tuberculin Skin Test Result

Cut-off points are used to stratify the test result as **positive** or **negative** depending on the risk factor(s) reported by the individual. This risk-based interpretation serves to minimize false positive and false negative results. Three factors were considered in the assessment of tuberculosis exposure risk, and their cut-off points are shown in the table below:

[34] Slutkin G, EJ Perez-Stable, PC Hopewell. Time course and boosting of tuberculin reactions in nursing home residents. Am Rev Respir Dis 1986; 134:1048-5l.
[35] Cauthen GM, SE Valway. Tuberculin reactions read at 2 days and 7 days. Am J Respir and Crit Care Med 1994; 149 (Pt 2):A101.
[36] Carter ER, Lee CM. Interpretation of the tuberculin skin test reaction by pediatric providers. Pediatr Infect Dis J 2002; 21:200-3.

INTERPRETATION OF TUBERCULIN SKIN TEST	
RISK FACTOR	**POSITIVE RESULT**
Close contact with a case of tuberculosis	5 mm or more
Born in a country that has a high rate of tuberculosis	10 mm or more
Traveled or lived for a month or more in a country that has a high rate of tuberculosis	10 mm or more
None [test not recommended]	15 mm or more

Consider the individual's risk factors for tuberculosis exposure when interpreting the tuberculin skin test. For example, a test result of 8 mm would be positive in a student with household exposure to tuberculosis, but would be negative in a student who was born in a country that has a high rate of tuberculosis and who had no direct contact with a case of tuberculosis. A test result of 13 mm in a student with no known risk factors who was inadvertently given a skin test should be interpreted as negative.

The same criteria for a positive tuberculin skin test should be used whether a student has or has not received BCG vaccine in the past.

When to Repeat the Tuberculin Skin Test

If a student has had a negative tuberculin skin test three or more months after a risk factor has ended (e.g., the end of contact with a tuberculosis case or arrival in the United States from a country with a high rate of tuberculosis), the test does not have to be repeated. If a student has had a documented and reliable positive tuberculin skin test at any time in the past, the test should not be repeated.

C. SAMPLE FORM

The form for **MEDICAL EVALUATION OF COLLEGE AND UNIVERSITY STUDENTS FOR LATENT TUBERCULOSIS INFECTION** (**APPENDIX 4**) will be used to collect information about tuberculin skin test and chest x-ray results. Although presented separately for the sake of clarity, it should be combined with the **TUBERCULOSIS RISK QUESTIONNAIRE FOR COLLEGE AND UNIVERSITY STUDENTS** (**APPENDIX 3**) and incorporated into the form the college uses to gather immunization data prior to matriculation. The student's health care provider should fill it out. The college health service can use the same form if it performs tuberculin skin testing of students found to be at increased risk of previous exposure to tuberculosis.

D. PROGRAM EVALUATION

To evaluate the operational success of this stage of the program, the number of high-risk students should be compared with the number who had tuberculin skin tests, whether they were administered by outside health care providers or by the college health service. Completion of the tuberculin skin test requires two steps: administration of the test and reading of the test.

Step 3

$$\% \text{ Test Administered} = \frac{\text{Number Who Had Tuberculin Skin Test Administered}}{\text{Number Of High-Risk Students}} \times 100$$

Step 4

$$\% \text{ Test Read} = \frac{\text{Number Who Had Tuberculin Skin Test Read}}{\text{Number Who Had Tuberculin Skin Test Administered}} \times 100$$

Step 5

$$\% \text{ Positive} = \frac{\text{Number with Positive Tuberculin Skin Test}}{\text{Number Who Had Tuberculin Skin Test Read}} \times 100$$

In a successful program a high proportion of students who are at high risk of previous exposure to tuberculosis have a tuberculin skin test administered and read. The proportion of students with positive test results will vary from one college to another, largely depending on the rates of tuberculosis in the countries of origin of the foreign-born students attending the particular college.

CHAPTER 3. CHEST X-RAY AND CLINICAL EVALUATION

The tuberculin skin test is positive with both latent tuberculosis infection and active tuberculosis. A chest x-ray and clinical evaluation are required to distinguish between the two. A positive tuberculin skin test, a negative chest x-ray, and a normal clinical evaluation establish the diagnosis of latent tuberculosis infection. No additional laboratory studies are needed to rule out active tuberculosis.

A. SCIENTIFIC RATIONALE

Rarely, a seemingly healthy student with a positive tuberculin skin test has been found to have active disease. For this reason, prior to treatment, all students with a positive tuberculin skin test should have a chest x-ray and clinical evaluation.

B. OPERATIONAL GUIDANCE

Chest X-ray

A single posterior-anterior chest x-ray is recommended. If the college health service does not have radiologic capability, it should arrange for a chest x-ray at a local hospital, radiology center, or Massachusetts Department of Public Health Tuberculosis Clinic (listed in **APPENDIX 5**). Most student health insurance covers this diagnostic test. The Massachusetts Tuberculosis Clinics do not require payment for services, including for the chest x-ray, although they may bill the student's health insurance plan.

Clinical Evaluation

The clinical evaluation should focus on symptoms suggestive of tuberculosis (cough, fever, weight loss, and night sweats) and the relevant physical findings pertaining to those symptoms.

When to Repeat the Chest X-ray

A student who has been diagnosed with latent tuberculosis infection in the past and who has received appropriate treatment does not need to have another chest x-ray. Also, a student who has had a positive tuberculin skin test in the past but did not receive treatment and does not plan to embark on treatment now, does not need a chest x-ray. On the other hand, a student should have a chest x-ray if he or she has had a positive tuberculin skin test in the past, received no treatment, and now plans to start treatment. In a student with no symptoms suggestive of tuberculosis, a chest x-ray obtained within the past 3-6 months is considered timely and does not need to be repeated.

In all cases, a student with a prior diagnosis of latent tuberculosis infection, whether treated or not, who develops symptoms suggestive of tuberculosis should have a chest x-ray and clinical evaluation to rule out active disease.

C. SAMPLE FORM

MEDICAL EVALUATION OF COLLEGE AND UNIVERSITY STUDENTS FOR LATENT TUBERCULOSIS INFECTION (**APPENDIX 4**) requests information about the chest x-ray, clinical evaluation, and treatment of a student with a positive tuberculin skin test. As noted in Chapter 2, the student's health care provider or the college health service may complete this form.

D. PROGRAM EVALUATION

The number of students with a positive tuberculin skin test either before or at the time of enrollment and the number who have a chest x-ray and clinical evaluation form the basis for evaluating this stage of the process.

Step 6

$$\% \text{ Chest X-ray} = \frac{\text{Number Who had Chest X-ray}}{\text{Number with Positive Tuberculin Skin Test}} \times 100$$

In a successful program, a high proportion of students who have had a positive tuberculin skin test result will have had a chest x-ray and clinical evaluation to define their tuberculosis status.

CHAPTER 4. TREATMENT OF LATENT TUBERCULOSIS INFECTION

The identification of a college student with latent tuberculosis infection is beneficial only if the student receives appropriate treatment. Consequently, a college health service should not embark on a program to identify students with latent tuberculosis infection unless it also has a clear plan in place for their treatment.

A. SCIENTIFIC RATIONALE

Risk of Tuberculosis

After individuals become infected, they have a lifetime risk of up to 10% of developing tuberculosis. Half to three-quarters of the cases of active disease occur in the first 1-2 years after infection and the remainder occur at a later time in life.[37] [38] [39] [40] College students who have latent tuberculosis infection are at special risk for developing active tuberculosis by virtue of their age. Following infection in childhood, tuberculosis case rates are elevated after 12 years of age, peak at 19 years of age, and fall to a lower, stable rate at 24 years of age.[41]

A number of factors can interfere with the ability of the immune system to control latent infection and thereby precipitate active tuberculosis. These include taking corticosteroid and other immuno-suppressive agents (e.g., infliximab, a monoclonal antibody to tumor necrosis factor, used in the treatment of Crohn's disease and rheumatoid arthritis[42]); having measles, leukemia, Hodgkin's disease, cancer, silicosis, diabetes mellitus, HIV infection, malnutrition, or chronic renal failure; injection drug use; and old age.

Isoniazid Recommended

MACET recommends that latent tuberculosis infection in college students be treated with isoniazid[43] for nine months. However, if adherence to the preferred nine months of treatment is not feasible, use of isoniazid for six months is an acceptable alternative. Although nine months of isoniazid is significantly more effective than six months, as discussed below, completion rates may be lower with a nine-month course

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[37] Comstock GW, VT Livesay, SF Woolpert. The prognosis of a positive tuberculin reaction in childhood and adolescence. Am J Epidemiol 1974; 99:131-8.

[38] Ferebee SH. Controlled chemoprophylaxis trials in tuberculosis: A general review. Adv Tuberc Res 1970; 17:28-106.

[39] Sutherland I. The ten-year incidence of clinical tuberculosis following "conversion" in 2550 individuals aged 14 to 19 years. TSRU Progress Report 1968 (KNCV, The Hague, Netherlands), cited in: Centers for Disease Control and Prevention. Targeted tuberculin testing and treatment of latent tuberculosis infection. MMWR 2000; 49 (No. RR-6):7.

[40] Lincoln EM, EM Sewell. Tuberculosis in children. New York: McGraw-Hill Book Company, 1963: 24.

[41] Comstock GW, VT Livesay, SF Woolpert. The prognosis of a positive tuberculin reaction in childhood and adolescence. Am J Epidemiol 1974; 99:131-8.

[42] Keane J, Gershon S, Wise RP, et al. Tuberculosis associated with infliximab, a tumor necrosis factor α-neutralizing agent. N Engl J Med 2001; 345:1098-104.

[43] Isoniazid is isonicotinic acid hydrazide; hence, the commonly used acronym INH.

of treatment than with six months because of the limited motivation of some students and practical considerations such as summer vacation.

Three situations that might call for use of drugs other than isoniazid are described in the **Alternatives to Isoniazid** box at the end of this section.

Efficacy of Isoniazid

Effective treatment of latent tuberculosis infection kills *M. tuberculosis* and prevents the development of active disease. The high efficacy of isoniazid in preventing tuberculosis has been solidly established through many controlled clinical trials, most of which compared 12 months of isoniazid with placebo.[44] When analysis was restricted to people who were compliant with the medication, protective efficacy was 90% or more. Protection lasted at least 20 years, the longest period of follow-up,[45] [46] and probably lasts a lifetime, according to expert opinion.

Only one trial was specifically designed to compare 12 months with shorter durations of isoniazid.[47] For the participants who took 80% or more of their medication, the efficacy of a 12-month regimen was 93%, compared with 69% for a 6-month regimen and 31% for a 3-month regimen. The trial did not include a 9-month regimen. A recent analysis of a community-based study in Alaska, although not designed to compare durations of isoniazid administration, concluded that the protection conferred by taking nine months of treatment was significantly greater than that conferred by taking six months; it appeared that no further protection was conferred by extending the duration of treatment from nine to 12 months.[48] Thus, according to this analysis, the optimal duration of isoniazid administration is nine months, not six or 12 months.

Side Effects of Isoniazid

Isoniazid has two noteworthy side effects: hepatitis and peripheral neuropathy.

The frequency of clinically overt isoniazid-induced hepatitis was studied in almost 14,000 patients given isoniazid as treatment for latent tuberculosis infection in 1971-72.[49] [50] The rate of hepatitis increased with advancing age:

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[44] Centers for Disease Control and Prevention. Targeted tuberculin testing and treatment of latent tuberculosis infection. MMWR 2000; 49 (No. RR-6):1-51.

[45] Hsu KHK. Isoniazid in the prevention and treatment of tuberculosis. A 20-year study of the effectiveness in children. JAMA 1974; 229: 528-33.

[46] Comstock GW, Baum C, Snider DE. Isoniazid prophylaxis among Alaskan Eskimos: A final report of the Bethel isoniazid studies. Am Rev Respir Dis 1979; 119:827-30.

[47] International Union Against Tuberculosis Committee on Prophylaxis. Efficacy of various durations of isoniazid therapy for tuberculosis: Five years of follow-up in the IUAT trial. Bull WHO 1982; 60:555-64.

[48] Comstock GW. How much isoniazid is needed for prevention of tuberculosis among immunocompetent adults? Int J Tuberc Lung Dis 1999; 3:847-50.

[49] Mitchell JR, Zimmerman HJ, Ishak KG, et al. Isoniazid liver injury: Clinical spectrum, pathology and probable pathogenesis. Ann Intern Med 1976; 84:181-92.

[50] Kopanoff DE, Snider DE, Caras GJ. Isoniazid-related hepatitis. A U.S. Public Health Service cooperative surveillance study. Am Rev Respir Dis 1978; 117:991-1001.

AGE (YEARS)	HEPATITIS RATE (%)
Under 20	0
20-34	0.3
35-49	1.2
50-64	2.3

An association of hepatitis with alcohol consumption was also found. Compared with nondrinkers, rates were 4.1 times higher among persons who drank daily and 1.7 times higher among persons who drank occasionally.

Nearly half of the patients who developed evidence of hepatitis did so within two months of starting treatment. It characteristically had a prolonged prodromal period. Severe, potentially fatal disease usually occurred in patients who continued to take isoniazid long after the onset of symptoms. If isoniazid was discontinued shortly after symptoms appeared, the clinical course was usually self-limited. Symptoms of isoniazid hepatitis included loss of appetite, fatigue, nausea, vomiting, right upper quadrant abdominal discomfort, fever, dark urine, and jaundice. The results of liver function tests in isoniazid hepatitis were indistinguishable from those in viral hepatitis. Among those who developed hepatitis due to isoniazid, the fatality rate was 8%.

Asymptomatic, usually mild serum transaminase elevations attributable to isoniazid occurred in nearly one-quarter of people; elevated levels returned to normal while treatment continued.[51] Because of the high frequency of transient and harmless increases in the serum transaminase levels, clinical, rather than biochemical, monitoring has become standard practice. Clinical monitoring involves educating patients about symptoms of hepatitis and advising them to stop treatment immediately if such symptoms occur and to report to the clinician for evaluation. Using careful clinical monitoring exclusively, one tuberculosis clinic recently reported a rate of hepatitis of less than 0.1% and no deaths among more than 11,000 persons with latent tuberculosis infection during isoniazid treatment over a seven-year period.[52]

Although isoniazid can lower the serum level of pyridoxine (vitamin B_6), paresthesias and other symptoms of peripheral neuropathy are uncommon. Supplemental pyridoxine (see **OPERATIONAL GUIDANCE** below) will prevent peripheral neuropathy in individuals whose diets are deficient in pyridoxine.

Rare side effects of isoniazid include nausea and vomiting not related to hepatitis, diarrhea, fever, rash, and allergic reactions. There have been a few reports in patients taking isoniazid of flushing following ingestion of certain cheeses and wine, presumably due to inhibition by isoniazid of the liver enzymes that metabolize tyramine.

[51] Mitchell JR, Zimmerman HJ, Ishak KG, et al. Isoniazid liver injury: Clinical spectrum, pathology, and probable pathogenesis. Ann Intern Med 1976; 84:181-92.
[52] Nolan CM, Goldberg SV, Buskin SE. Hepatotoxicity associated with isoniazid preventive therapy: A 7-year survey from a public health tuberculosis clinic. JAMA 1999; 281:1014-8.

Hematological disorders and a variety of neuropsychiatric symptoms have also been reported.

Pregnancy and Lactation

Pregnant women may be more vulnerable to isoniazid hepatitis. However, isoniazid is not teratogenic for the human fetus. If a pregnant woman with latent tuberculosis infection is HIV positive, has had recent contact with an infectious tuberculosis case, or is otherwise at high risk for disease, treatment should not be delayed, even during the first trimester. In pregnant women with a lesser risk of progression to active disease, it may be prudent to delay treatment until after delivery. Isoniazid can be given to lactating mothers. Although isoniazid is excreted in breast milk, no adverse effect on nursing infants has been demonstrated.

Drug Interactions

Isoniazid may inhibit phenytoin (Dilantin®) and carbamazapine (Tegretol®) metabolism in the liver, thereby increasing their serum concentrations. The serum level of phenytoin or carbamazapine should be monitored and the anticonvulsant dose decreased if necessary.

Acetaminophen (Tylenol® and others) taken in doses that exceed those recommended in the package insert (4000 mg per day), either inadvertently or in a suicide attempt, can cause hepatic necrosis. Case reports suggest that excessive doses of acetaminophen cause greater liver damage in individuals who are taking isoniazid.[53] [54] [55] Although there is little evidence that recommended doses of acetaminophen in conjunction with isoniazid enhance the risk of liver damage, experts believe that concurrent use of isoniazid and acetaminophen should be avoided.[56]

Women taking combination oral contraceptive pills, including those with low dose estrogen, can be reassured that isoniazid has not been associated with breakthrough bleeding or contraceptive failure.

Alternatives to Isoniazid

Although isoniazid is the preferred treatment for most college students with latent tuberculosis infection, there are three situations in which to consider an alternative regimen. (1) Latent tuberculosis infection resulting from contact with a case of tuberculosis resistant to isoniazid and sensitive to rifampin should be treated with

- continued -

[53] Murphy R, Swartz R, Watkins PB. Severe acetaminophen toxicity in a patient receiving isoniazid. Ann Intern Med 1990; 113:799-800.
[54] Moulding TS, Redeker AG, Kanel GC. Acetaminophen, isoniazid, and hepatic toxicity (Letter). Ann Intern Med 1991; 114:431.
[55] Crippin JS. Acetaminophen hepatotoxicity: Potentiation by isoniazid. Am J Gastroenterol 1993; 88:590-2.
[56] Kim RB and the Editors of the Medical Letter. The Medical Letter handbook of adverse drug interactions. The Medical Letter, Inc, New Rochelle, NY. 2003:9.

rifampin. (2) If an individual cannot tolerate isoniazid, rifampin should be used. (3) A recent study suggested that treatment with a rifampin-containing regimen might be more cost-effective than isoniazid for latent tuberculosis infection in immigrants from Vietnam, Haiti, and the Philippines where isoniazid resistance rates are high.[57] However, this approach has not been tested and is not yet widely endorsed.

Recommendations published in 2000 on the treatment of latent tuberculosis infection in adults added two new, shorter treatment regimens--rifampin plus pyrazinamide for two months and rifampin for four months--as alternatives to the long-established use of isoniazid for 6-9 months.[58] [59]

Since publication of the latent tuberculosis treatment recommendations, experience with rifampin plus pyrazinamide has shown a much higher rate of severe and fatal hepatitis than was initially anticipated, even with intensive clinical and biochemical monitoring.[60] [61] [62] As a result, use of this regimen is no longer recommended.[63] **Rifampin plus pyrazinamide should NOT be prescribed for college students.**

The other alternative, rifampin for four months, is considered by experts to be effective, but has never been subjected to a controlled clinical trial in healthy individuals with latent tuberculosis infection. Although rifampin alone can cause hepatitis, the rate seems to be much lower than when rifampin and pyrazinamide are given together. It should be noted that rifampin causes important drug interactions by inducing liver enzymes that increase the metabolism of many drugs and markedly reduce their serum levels. One noteworthy example: Women using birth control pills or hormonal implants should be advised to use an alternative form of contraception, because rifampin may reduce contraceptive effectiveness by increasing hormone metabolism.[64] Also, rifampin can permanently discolor soft contact lenses. If treatment with rifampin is selected, review the latest recommendations on the website of the Centers for Disease Control and Prevention (www.cdc.gov/nchstp/tb) and consider consultation with an expert, using the resources described in the ***Consultation*** section below.

[57] Khan K, Muennig P, Behta M, Zivin JG. Global drug-resistance patterns and the management of latent tuberculosis infections in immigrants to the United States. N Engl J Med 2002; 347:1850-9.
[58] Centers for Disease Control and Prevention. Targeted tuberculin testing and treatment of latent tuberculosis infection. MMWR 2000; 49 (No. RR-6):26-39.
[59] Medical Advisory Committee for the Elimination of Tuberculosis. Latent tuberculosis infection: A guide for Massachusetts providers. Boston, MA; November, 2000.
[60] Centers for Disease Control and Prevention. Update: Fatal and severe liver injuries associated with rifampin and pyrazinamide for latent tuberculosis infection, and revisions in American Thoracic Society/CDC recommendations – United States, 2001. MMWR 2001; 50:733-5.
[61] Centers for Disease Control and Prevention. Update: Fatal and severe liver injuries associated with rifampin and pyrazinamide treatment for latent tuberculosis infection. MMWR 2002; 51:998-9.
[62] Jasmer RM, Saukkonen JJ, Blumberg HM, et al. Short-course rifampin and pyrazinamide compared with isoniazid for latent tuberculosis infection: A multicenter clinical trial. Ann Intern Med 2002; 137:640-7.
[63] Centers for Disease Control and Prevention. Update: Adverse event data and revised American Thoracic Society/CDC recommendations against the use of rifampin and pyrazinamide for treatment of latent tuberculosis infection–-United States, 2003. MMWR 2003; 52:735-9.
[64] Kim RB and the Editors of the Medical Letter. The Medical Letter handbook of adverse drug interactions. The Medical Letter, Inc, New Rochelle, NY. 2003:243.

B. OPERATIONAL GUIDANCE

MACET supports the concept that treatment of latent tuberculosis infection is part of primary health care, an activity that a college health service can manage with skill and confidence, with physician supervision or in consultation with a Massachusetts Department of Public Health Tuberculosis Clinic (**APPENDIX 5**). Alternatively, a college health service may prefer to refer students to a Tuberculosis Clinic for treatment.

Isoniazid

Isoniazid is an inexpensive drug that is supplied as 100 mg and 300 mg tablets and as a 50 mg/tsp syrup. The adult dose is 5 mg/kg to a maximum of 300 mg given as a single daily dose. Administered twice weekly, the isoniazid dose is 15 mg/kg to a maximum of 900 mg. Twice weekly administration should be used **only** in conjunction with directly observed therapy (see below), because the impact of a missed dose is greater than with daily administration. The recommended duration of treatment is nine months, with six months as an alternative. Most student health insurance covers this treatment. Medication is free at the Massachusetts Department of Public Health Tuberculosis Clinics.

Pyridoxine 25 mg once daily is recommended for students on meat- and milk-deficient diets, for those who are malnourished, and for women who are pregnant.

Counseling

Prior to starting treatment, students should be counseled about the importance of taking their medication regularly and for the full course of treatment, strategies for improving adherence, and the symptoms of hepatitis (loss of appetite, fatigue, nausea, vomiting, right upper quadrant abdominal discomfort, fever, dark urine, and jaundice). Although the rate of hepatitis associated with isoniazid is low in the college age group, it does occur and fatal cases have been reported. **Students should be instructed to stop isoniazid IMMEDIATELY and to call the college health service if they develop any symptoms suggestive of hepatitis, even if they think the symptoms are unrelated to treatment.** The college health service should obtain liver function tests and seek consultation if results are abnormal.

Students should be advised that abstaining from or minimizing alcohol intake during the treatment period would lessen their risk of hepatitis.

It seems prudent to advise students taking isoniazid to avoid use of acetaminophen and to substitute aspirin or a non-steroidal anti-inflammatory agent, such as ibuprofen (Advil®, Motrin®) or naproxen (Aleve®, Naprosyn®) for it, if needed. Students should note that acetaminophen is used in more combination products than any other drug and for a number of different indications.[65] Taking more than one of these products, or taking plain acetaminophen in addition, can lead to inadvertent overdosage and the potential for enhanced liver damage with isoniazid.

[65] Anon. Acetaminophen safety. The Medical Letter on Drugs and Therapeutics 2002; 44:91-3.

Liver Function Tests

Routine monitoring of liver function tests before and during treatment is not recommended. For selected college students whose behavior puts them at risk for viral hepatitis (intravenous drug use and males who have sex with other males) or alcoholic hepatitis (heavy alcohol consumption), as well as for those taking potentially hepatotoxic drugs, pregnant women, and those who are known hepatitis B surface antigen carriers, a baseline SGPT (ALT) before starting isoniazid is indicated. If baseline liver function tests are normal, they do not need to be repeated during treatment unless students develop symptoms of hepatitis. For those with abnormal baseline liver function tests, serial testing during treatment may be warranted; expert consultation should be obtained.

Clinical Monitoring

During the period when students are taking isoniazid, a health care worker should see them at monthly intervals to question them about symptoms of hepatitis, to review with them the procedure to follow if they develop any adverse effects, and to assess their compliance with treatment. To facilitate clinical monitoring, isoniazid should be dispensed one month at a time.

Adherence to Treatment

A number of techniques may improve adherence to self-supervised treatment. Students should take medication at the same time each day to help make pill-taking a habit. They should have a calendar in which they check off each day when they take their pill. This serves as a reminder and also as a deterrent to taking more than one dose per day. The same ends are met by supplying a month of isoniazid in a tablet-dispensing package that is arranged by days of the week and weeks of the month, similar to the packaging of oral contraceptive tablets. Students should keep medication in a place that they visit consistently, such as on the dining table, next to their toothbrush, or beside their alarm clock. They can put a reminder sign in a prominent location, such as on their computer, refrigerator, or bathroom mirror. With proper sensitivity to privacy issues, voice mail or email reminders may prove helpful in selected instances.

The health care worker can determine adherence to the treatment regimen in several ways. If there is good rapport with students, asking about pill taking or reviewing their calendar with them will usually give an accurate picture of adherence. In some instances, checking on prescription refills from the pharmacy is helpful. If adherence to treatment is uncertain, urine samples can be checked with test strips that detect isoniazid metabolites (Bacto INH Test Strips, Mycodyn Uritec test strips).

To improve adherence, MACET suggests that treatment of latent tuberculosis infection with twice a week directly observed therapy should be considered. Directly observed therapy is defined as treatment provided directly to the patient by a health care worker or trained third party (not a relative or friend) to document that the patient takes each dose of medication. This approach has greatly enhanced adherence to treatment for active tuberculosis and shows similar promise with latent tuberculosis infection. College health services will need to consider issues of resource allocation and logistics when

implementing this suggestion. On some campuses directly observed therapy might be a practical approach for all students requiring treatment and on others it might be employed for selected students with adherence problems.

Interrupted Treatment

Completion of treatment is based on total number of doses administered, not on duration of treatment alone. The 9-month regimen of daily isoniazid should consist of 270 doses completed within a 12-month time period and the 6-month regimen should consist of 180 doses completed within a 9-month time period.[66] If isoniazid was stopped for less than three months (either cumulative interruptions or a single interruption), simply resume the treatment course and add the missed days. For example, if isoniazid was not taken during a 2-week vacation, resume treatment and extend the course by two weeks. If isoniazid was stopped for more than three months, start the treatment course over.

Repeat Chest X-rays and Tuberculin Skin Tests

During or after treatment with isoniazid, students with latent tuberculosis infection should not have additional chest x-rays unless they have symptoms suggestive of active tuberculosis. Likewise, tuberculin skin tests should not be rechecked during or after treatment. They will remain positive for many years, often for a lifetime. Moreover, once a positive tuberculin skin test is documented, additional tests have no utility as aids in the diagnosis of active tuberculosis.

Consultation

For help and advice, consult an infectious disease or pulmonary disease expert, the Massachusetts Tuberculosis Clinic in your area (listed in Appendix 5), or Dr. John Bernardo, Tuberculosis Control Officer, Massachusetts Department of Public Health (617-983-6970 or john.bernardo@state.ma.us).

C. SAMPLE FORM

WORKSHEET: TREATMENT OF LATENT TUBERCULOSIS INFECTION (**APPENDIX 6**) is provided for use by clinicians who administer treatment to students with latent tuberculosis infection.

D. PROGRAM EVALUATION

Evaluation of the final, crucial steps in the proper management of latent tuberculosis infection compares the number of students who have latent tuberculosis infection with the number who start treatment and the number who complete treatment. For statistical purposes, use one year as the time period within which treatment should be completed.

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[66] Centers for Disease Control and Prevention. Targeted tuberculin testing and treatment of latent tuberculosis infection. MMWR 2000; 49 (No. RR-6):32-3.

Step 7

$$\% \text{ Start Treatment} = \frac{\text{Number Who Start Treatment}}{\text{Number with Latent Tuberculosis Infection}} \times 100$$

Step 8

$$\% \text{ Complete Treatment} = \frac{\text{Number Who Complete Treatment}}{\text{Number Who Start Treatment}} \times 100$$

In a successful program a high proportion of students with latent tuberculosis infection start treatment and a high proportion of those who start treatment complete it.

In summary, by examining a series of eight steps from risk assessment of incoming students to completion of treatment of students who have latent tuberculosis infection, a college health service can measure the success of its tuberculosis control program and identify specific areas that need improvement.

APPENDIX 1. USEFUL WEBSITES

NAME AND WEBSITE ADDRESS	RESOURCES AVAILABLE
American College Health Association www.acha.org/info_resources	2000 guidelines on screening college students for tuberculosis.
Centers for Disease Control – Division of Tuberculosis Elimination www.cdc.gov/nchstp/tb	Easy access to CDC guidelines, MMWR articles, and training materials.
Francis J. Curry National Tuberculosis Center www.nationaltbcenter.edu	Training materials on the tuberculin skin test and treatment of latent tuberculosis infection.
Charles P. Felton National Tuberculosis Center at Harlem Hospital www.harlemtbcenter.org	Useful pocket guides on treatment of latent tuberculosis infection.
Massachusetts Department of Public Health – Division of Tuberculosis Prevention and Control www.state.ma.us/dph/cdc/tb/index.htm	This guide and updates of it will be posted on the Massachusetts Department of Public Health website. It also contains fact sheets, policy statements, laws, and educational resources.
Virginia Commonwealth University – Student Health Services http://ush1.ush.vcu.edu/tb	An excellent website that shares their tuberculosis case tracking system, peer educator program, and list of tuberculosis resources in foreign languages.
World Health Organization www.who.int/gtb/publications/globrep	The annual WHO report on Global Tuberculosis Control contains figures to update the list of countries with high rates of tuberculosis.

APPENDIX 2. TUBERCULOSIS IN MASSACHUSETTS COLLEGE STUDENTS BY COUNTRY OF BIRTH (1996-2000)

TUBERCULOSIS CASE RATE IN COUNTRY OF BIRTH*		NUMBER OF STUDENTS (%)
50 Or More Cases/100,000		**50 (83%)**
Botswana	757	1
Kenya	484	4
Ethiopia	397	7
Somalia	360	1
Haiti	350	4
Cameroon	341	1
Indonesia	280	1
Nepal	208	2
Vietnam	189	10
India	184	10
Dominican Republic	147	2
China	107	4
Korea	62	2
Portugal	52	1
10 - 49 Cases/100,000		**4 (7%)**
Japan	36	1
Turkey	36	1
Spain	34	2
Less Than 10 Cases/100,000		**6 (10%)**
USA	5	6
Total		**60**

* World Health Organization. Global tuberculosis control. WHO report 2002.

APPENDIX 3. TUBERCULOSIS RISK QUESTIONNAIRE FOR COLLEGE AND UNIVERSITY STUDENTS

The questionnaire is on the following page and can be printed on the letterhead of either the Massachusetts Department of Public Health or the college, at the college's discretion.

TUBERCULOSIS RISK QUESTIONNAIRE FOR COLLEGE AND UNIVERSITY STUDENTS

	YES	NO
1. To the best of your knowledge have you ever had close contact with anyone who was sick with tuberculosis (TB)?	☐	☐
2. Were you born in one of the countries listed below?	☐	☐
3. Have you traveled or lived for more than one month in one or more of the countries listed below?	☐	☐

COUNTRIES WITH HIGH RATES OF TUBERCULOSIS (TB)*

Afghanistan	Colombia	India	Moldova, Rep.	Senegal
Angola	Comoros	Indonesia	Mongolia	Sierra Leone
Armenia	Congo	Iran	Morocco	Solomon Islands
Azerbaijan	Congo, DR	Iraq	Mozambique	Somalia
Bahamas	Cote d'Ivoire	Kazakhstan	Myanmar	South Africa
Bahrain	Croatia	Kenya	Namibia	Sri Lanka
Bangladesh	Djibouti	Kiribati	Nepal	Sudan
Belarus	Dominican Rep.	Korea, DPR	New Caledonia	Suriname
Benin	Ecuador	Korea, Rep.	Nicaragua	Swaziland
Bhutan	El Salvador	Kyrgyzstan	Niger	Syrian Arab Rep.
Bolivia	Equatorial Guinea	Lao PDR	Nigeria	Tajikistan
Bosnia & Herzegovina	Eritrea	Latvia	Niue	Tanzania, UR
Botswana	Estonia	Lesotho	Northern Mariana Islands	Thailand
Brazil	Ethiopia	Liberia	Pakistan	Togo
Brunei Darussalam	Gabon	Lithuania	Palau	Tokelau
Burkina Faso	Gambia	Macedonia, TFYR	Panama	Turkmenistan
Burundi	Georgia	Madagascar	Papua New Guinea	Uganda
Cambodia	Ghana	Malawi	Paraguay	Ukraine
Cameroon	Guam	Malaysia	Peru	Uzbekistan
Cape Verde	Guatemala	Maldives	Philippines	Vanuatu
Central African Rep.	Guinea	Mali	Portugal	Vietnam
Chad	Guinea-Bissau	Marshall Islands	Romania	Yemen
China	Guyana	Mauritania	Russian Federation	Zambia
China, Hong Kong SAR	Haiti	Mauritius	Rwanda	Zimbabwe
China, Macao SAR	Honduras	Micronesia	Sao Tome & Principe	

* World Health Organization. Global tuberculosis control. WHO report 2002.

If the answer to **any** of the above questions is **YES**, the Massachusetts Department of Public Health **strongly recommends** that you have a tuberculin skin test to check for latent tuberculosis infection. If the answer to **all** of the above questions is **NO**, a tuberculin skin test should not be done. Please note: If you have had a positive tuberculin skin test in the past, you do not need another test.

APPENDIX 4. MEDICAL EVALUATION OF COLLEGE AND UNIVERSITY STUDENTS FOR LATENT TUBERCULOSIS INFECTION

The evaluation form is on the following page.

MEDICAL EVALUATION OF COLLEGE AND UNIVERSITY STUDENTS FOR LATENT TUBERCULOSIS INFECTION

Tuberculin Skin Test Date _____/_____/_____

Result (48 – 72 hours) _____ mm of induration
(If no induration, mark "0")

Note: Use 5 TU Mantoux test (Intermediate PPD) only; result of multiple puncture tests, such as Tine or Mono-vacc, not accepted.

Risk-based Interpretation

- ☐ Negative
- ☐ Positive

INTERPRETATION OF TUBERCULIN SKIN TEST	
RISK FACTOR	**POSITIVE RESULT**
Close contact with a case of tuberculosis	5 mm or more
Born in a country that has a high rate of tuberculosis	10 mm or more
Traveled or lived for a month or more in a country that has a high rate of tuberculosis	10 mm or more
None [test not recommended]	15 mm or more

If the tuberculin skin test is positive:

Chest X-ray Date _____/_____/_____

- ☐ Normal
- ☐ Abnormal _____
(Describe)

Clinical Evaluation Date _____/_____/_____

- ☐ Normal
- ☐ Abnormal _____
(Describe)

Treatment

- ☐ Yes _____
- ☐ No (Drug, dose, frequency, and dates)

APPPENDIX 5. MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH TUBERCULOSIS CLINICS

The current list of clinics is on the following page. To obtain an updated list, call the Massachusetts Department of Public Health, Division of Tuberculosis Prevention and Control at 617-983-6970.

Massachusetts Department of Public Health
Division of TB Prevention & Control
State Laboratory Institute, 305 South St., Jamaica Plain, MA 02130
Phone: (617) 983-6970 Fax: (617) 983-6990 24hr Reporting Line: 1-888-627-7682

April 2003 – Free TB Clinics

Listed By Tuberculosis Surveillance Areas (TSA)

TB Clinics provide diagnostic and treatment services for Massachusetts residents who are:
*Diagnosed/suspected of having TB disease
*Diagnosed/suspected of having latent TB infection
*Contacts to persons with active TB disease
*In need of treatment for old TB disease
Services do not include routine or initial TB skin testing.
Local medical providers/health departments are sources for these services.

TSA 1 — **CLINIC APPOINTMENTS MADE BY:**

Baystate Medical Center
Attn: TB Clinic
Neighborhood Health Center
11 Wilbraham Road
Springfield, MA 01199

Clinic Coordinator (413)794-5435
FAX (413)794-8861

Clinic hours Tuesday, 8:00-11:00 AM

Berkshire Medical Center
Attn: TB Clinic
510 North Street
Suite 18
Pittsfield, MA 01201

Berkshire Medical Center (413)447-2654
FAX (413)447-2355
Attn: Jackie Roy Elliot, RN

Clinic hours 1st & 3rd Thursday, 9:30 AM-Finish

Health Alliance or Health Alliance
Burbank Campus P. Workum, MD
Attn: TB Clinic 50 Memorial Drive
275 Nichols Road Suite 111
Fitchburg, MA 01420 Leominster, MA 01453

Lynn Sarro (978)466-4252
FAX (978)466-4250

Clinic hours Tuesday every other week,
8:30-11:30 AM

Franklin Medical Center
Attn: TB Clinic
164 High Street
Greenfield, MA 01301

Cardio/Pulmonary (413)773-2289
FAX (413)773-2080

Clinic hours last Tuesday of month,
1:00-4:30 PM

Harrington Memorial Hospital
Attn: TB Clinic
100 South Street
Southbridge, MA 01550

Harrington Home Health Care (508)765-1515
FAX (508)765-1517

Clinic hours Wednesday, 1:00-4:00 PM

Family Health & Social Services
Attn: Medical Specialty Clinic
Worcester City Hospital
26 Queen Street
Worcester, MA 01610
(Formerly called Getchell Ward Clinic)

Clinic (508)860-7700
FAX (508)860-7775

Clinic hours Tuesday, Wednesday, Thursday,
7:00 AM-3:30 PM

TSA 2

CLINIC APPOINTMENTS MADE BY:

Cambridge Hospital
Attn: TB Clinic
1493 Cambridge Street
Cambridge, MA 02139

Cambridge Clinic (617)665-1291
FAX (617)665-1925
BOH Telephone (617)665-3803
BOH FAX (617)665-3888

Clinic hours Monday, 2:00-4:00 PM
Tuesday, 3:00-6:00 PM
Thursday, 9:00-11:00 AM

Lahey Clinic
Attn: TB Clinic
41 Mall Road
Burlington, MA 01805

Clinic (781)744-8480
FAX (781)744-3171

Clinic hours Wednesday, 1:00-5:00 PM

TSA 3

CLINIC APPOINTMENTS MADE BY:

Hallmark Health (Malden Hospital)
Attn: TB Clinic
100 Hospital Road
Malden, MA 02148

Malden Health Dept. (781)397-7052
FAX (781)397-7356
Everett Health Dept. (617)394-2314
FAX (617)394-2339
Medford Health Dept. (781)393-2449
FAX (781)393-2562
Melrose Health Dept. (781)979-4130
FAX (781)979-7696

Clinic hours 10:00 AM-1:00 PM
Two Tuesdays a month, varying Tuesdays

Lawrence General Hospital
Attn: TB Clinic
One General Street
Lawrence, MA 01812

Lawrence Health Dept. (978)794-5690
FAX (978)794-5759

Clinic hours two Wednesdays a month, Noon

North Shore Pulmonary PHC
Salem Hospital
Attn: TB Clinic
81 Highland Avenue
Salem, MA 01970

TB Clinic (978)354-4455
FAX (978)740-4776

Clinic hours Monday and Wednesday
MD Clinic starts at 1:45 PM
RN Clinic 9:00 AM-4:00 PM

Saints Memorial Hospital
Attn: West, Chest Clinic
220 Pawtucket Street
Lowell, MA 01854

SMMC Clinic (978)446-1626
FAX (978)446-1901

Clinic hours
MD visits Wednesday, 1:30-3:30 PM
RN visits Fridays
1st & 5th (if one) 9:00-11:00 AM
2nd, 3rd, 4th 1:30-3:30 PM

TSA 4

CLINIC APPOINTMENTS MADE BY:

Boston Medical Center
Attn: TB Clinic
850 Harrison Avenue
ACC Bldg., 3rd Floor
Boston, MA 02118

Clerk/BMC (617)534-4976
FAX (617)534-4976

Clinic hours
MD-Mon, Tues, Thurs, Fri 8:30-11:30 AM
Wed 12:30-3:30 PM

RN-Mon, Tues 9:00 AM-4:00 PM
Wed 12:00-6:00 PM
Thurs, Fri 9:00 AM-Noon

Children's Hospital*
Attn: TB Clinic
300 Longwood Avenue
Mailstop: HU-208
Boston, MA 02115

Pulmonary Services (617)355-7881
FAX (617)566-7810

Clinic hours Monday 1:00-4:00 PM
Friday 9:00 AM-1:00 PM

Lemuel Shattuck Hospital
Attn: TB Clinic
170 Morton Street
Jamaica Plain, MA 02130

Lemuel Shattuck (OPD) (617)971-3443
FAX (617)971-3850

Clinic hours Friday 1:00-4:00 PM (not last Fri of month)

*For Children's Hospital, Boston can only be up to age 18 years old.

TSA 5	CLINIC APPOINTMENTS MADE BY:
Brockton Hospital Attn: TB Clinic 680 Centre Street Brockton, MA 02302-3395	Brockton TB Clinic (508)584-1200 FAX (508)941-6310 William Stenson, MD Devi Vedula, MD Stephanie Morin, RN Clinic hours Tuesday 10:00 AM-Noon
Cape Cod Hospital Attn: TB Clinic (Held at Dr. Mohr's office) 91 Camp Street Hyannis, MA 02601	Chester Mohr, MD (508)790-5955 FAX (508)755-8654 Timothy Herrick, MD Deborah Fisher, NP Clinic hours by appointment
Morton Hospital Attn: TB Clinic (Held at Dr. McCrone's office) 72 Washington Street Taunton, MA 02780	Dr. McCrone's office (508)828-6733 FAX (508)828-6736 Clinic hours 3rd Wed 1:00-4:00 PM
St. Anne's Hospital Attn: TB Clinic 795 Middle Street Fall River, MA 02721-1798	Fall River Health Dept. (508)324-2445 FAX (508)324-2544 Linda Sarvao, RN William Sheehan, MD Clinic hours one Wednesday a month 8:00 AM until finished
Sturdy Memorial Hospital Attn: TB Clinic 211 Park Street Attleboro, MA 02703	Attleboro Health Dept. (508)223-2222 X 3244 FAX (508)222-3046 Beth Collins, RN Hesameddin Karimeddiny, MD Clinic hours 1st Tues. of month 5:30-7:30 PM
VNS Martha's Vineyard Community Services	Refer to Dr. Mohr's office (508)790-5955 Clinic hours by appointment only

Revised March, 2003

APPENDIX 6. WORKSHEET: TREATMENT OF LATENT TUBERCULOSIS INFECTION

The worksheet is on the following page.

WORKSHEET: TREATMENT OF LATENT TUBERCULOSIS INFECTION

Clinician _____

Positive Tuberculin Skin Test _____ (Date)

Negative Chest X-ray _____ (Date)

Drug(s) _____

Dose(s) _____

Other Treatment _____

Planned Duration _____

Name of Student _____

Unit Number _____

Date of Birth _____

Address _____

_____

Phone _____

E-mail _____

	Initial Appointment	Follow-up Appointments											
		1M	2M	3M	4M	5M	6M	7M	8M	9M	10M	11M	12M
Date													
Compliance													
Symptoms And Signs													
Laboratory Studies													
Patient Education													
Next Appointment													
Other													