



CITY OF PHILADELPHIA

DEPARTMENT OF PUBLIC HEALTH
500 S. Broad Street
Philadelphia, PA 19146

Joseph Cronauer
Assistant Health Commissioner

Caroline Johnson, MD
Director, Division of Disease Control

David Schlossberg, MD, FACP
TB Control Program Medical Director

Barry Dickman
TB Control Program Director

PEDIATRIC TUBERCULOSIS PROTOCOL

Pediatric tuberculosis (TB) is the disease state caused by *Mycobacterium tuberculosis*, an acid-fast bacillus (AFB). Pediatric TB should be regarded as a spectrum of exposure, from infection to disease, because progression from an infected individual (exposure) to infection and subsequently disease can occur much faster in children under 2 years of age (occurring within the incubation of the disease stated below). Progression through this spectrum is age-dependent, being 40% to 50% for 0- up to 2-year-old, approximately 20% for 2- to 4-year-olds, and 10% to 15% for those 5 years old and over, the 5- to 10-year-olds being the most protected age group. Adolescence is another vulnerable age group.

Incidence of Tuberculosis in Philadelphia

In calendar year (CY) 2004, the Philadelphia TB Control Program reported 129 confirmed cases of TB. This represents a 7.5% increase from the prior year when 120 new cases of tuberculosis were reported. Despite this increase, there has been a 68% decrease in the number of tuberculosis cases reported in Philadelphia in the past decade, from 309 cases in 1995 to 129 last year. In Philadelphia, the TB case rate for CY2004 was approximately 8.7 per 100,000 population; this is above the Healthy People 2010 Objective of no more than 3.5 per 100,000 population. The number of cases and case rates for the period 1995-2004 are presented in below:

Table 1. Philadelphia TB Cases (all ages) and Case Rates per 100,000 population, 1995-2004

Year	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004
Cases	309	251	236	179	184	169	144	147	120	129
Rate	20.3	16.7	16	12.3	12.8	11.2	9.6	9.9	8	8.7

Foreign-born cases now account for nearly half of all reported cases in Philadelphia, and they originate from 26 different countries. Asians account for 65 percent of the foreign-born cases, with Vietnam (17.7%), China (11.3%), Cambodia and India (6.5% each) indicated as country of origin for nearly 42 percent of the foreign-born cases.

Tuberculosis in children, less than 15 years of age, increased from 4 cases in 2003 to 7 cases in 2004 (Graph 1). Since tuberculosis disease in children indicates recently acquired infection and

transmission, these data are of sentinel importance. Source contact investigations are initiated for all cases in children less than 15 years of age. Also, a case of latent TB in a child may lead to an unreported adult case of TB.

The incidence of Latent TB Infection in the Philadelphia Ambulatory Clinics was 447 per 100,000 per year for the years 1994-2004. Although these data represent only ~5% of the pediatric (0–18 years) population of Philadelphia, this 5% represents the pediatric patients at highest risk.

Whom to Screen

Children with any of the following risk factors are considered high-risk and should be tested annually:

- *Exposure to a family member (highest risk), OR anyone known to have TB: The national TB control goal is to ensure that at least 85 percent of infected contacts who are started on treatment for latent TB infection will complete therapy*
- Contact with adults from regions of the world with high prevalence
- Those spending time in homeless shelters
- Those with HIV and immunosuppressed states
- Those with Hodgkin disease, lymphoma, diabetes, chronic renal failure, and malnutrition
- Incarcerated adolescents
- Exposure to high-risk adults, such as incarcerated and homeless persons
- Exposure to milk from untested herds

TUBERCULIN MANTOUX TEST (PPD)

A. GENERAL INFORMATION

1. In order to prevent or control the spread of tuberculosis, it is necessary to evaluate those persons at greatest risk for contracting tuberculosis. Philadelphia residents should be tested according to the above risk assessment.
2. Through skin testing, infected individuals are identified. The tuberculin skin test is indispensable in the control of tuberculosis, for the identification of tuberculosis infection, recent or remote, with or without disease. The test is based on the fact that infection with *Mycobacterium tuberculosis* produces sensitivity to certain products of this organism. These products are contained in tuberculin extracts used in the skin test. A sensitized individual is one who has been infected with *Mycobacterium tuberculosis* and, when injected intradermally with tuberculin, will form an indurated area with or without erythema at the site of injection. The size and intensity of the reaction vary according to the dose of tuberculin and sensitivity of the person. **Induration is what is measured.**
3. The tuberculin preparation used for the skin test is called purified protein derivative or PPD. It is obtained from heat-killed cultures of tubercle bacilli grown on synthetic medium. A person who is sensitive to PPD is called a reactor.

4. Sensitivity to tuberculin develops 2 to 12 weeks after initial infection with *M. tuberculosis*. Once acquired, sensitivity tends to persist although several circumstances may influence the reaction. Sensitivity may: 1) wane with increasing age; 2) decrease or disappear if treatment of the infection is given in the earliest stage (usually in children); 3) decrease or disappear temporarily during any severe or febrile illness such as measles, overwhelming infection with *M. tuberculosis*, sarcoidosis, or cancer; or 4) decrease or disappear temporarily after receiving steroids, immunosuppressive drugs, or live virus vaccines, particularly measles, mumps and rubella virus vaccines, and HIV infection.
5. Skin tests become positive 2 to 12 weeks after exposure, but may not turn positive for 3 months. Hence, this is the rationale for treating an exposed child with INH and re-testing with a PPD in 3 months.
6. Repeat testing of infected persons does not sensitize them to tuberculin. However, since delayed hypersensitivity measured during skin testing may wane over the years, a subsequent test given in a person with an initially negative or doubtful reaction, as early as one week after the initial PPD, may be reactive. This is referred to as the booster effect or the 2-step PPD screening. If both tests are negative, the patient is considered non-reactive; if the first test is negative and the second test is positive, the patient is considered reactive (the positive second test is not simply a result of stimulation by the first test). CDC recommends the 2-step PPD in any individual who is likely to have repeated PPDs such as health care workers, or individuals at high risk for TB whose immunity may have waned- such as individuals who have been in refugee camps.
7. Cross-reaction to infection with mycobacteria other than *M. tuberculosis* may occur. The larger the reaction to the tuberculin skin test, generally, the greater probability that the reaction is specific for *M. tuberculosis*.
8. Once infected individuals have been identified, a chest x-ray and a sputum examination for children who can produce sputum from a cough i.e. any child over 8 years of age, should be obtained. Having the results of skin testing and chest x-rays, a physician can decide on a course of therapy after performing a history and physical examination.

DEFINITION OF LATENT TUBERCULOSIS INFECTION AND TREATMENT

Latent Tuberculosis Infection (LTBI) is defined as an infected child who is free of active disease. Treatment requires only isoniazid (INH) at 10 mg/kg/day or up to a maximum of 300 mg daily for 9 months for chemoprophylaxis (2003 Red Book committee of the AAP), if the source case is known to have an organism that is sensitive to first line anti-tuberculosis drugs. Management does not require consultation with Tuberculosis Control, but we ask you to report ALL children receiving INH prophylaxis, as this will help epidemiologic control of LTBI.

CASE MANAGEMENT OF LTBI

Report families where you suspect problems of compliance, side effects of INH, or the source case is Multi-Drug Resistant (MDR) tuberculosis; AND complete the INH PROPHYLAXIS FORM, which should be faxed to TB Control at each encounter. Reporting infected children is anticipated to improve TB control. Directly Observed Preventative Therapy (DOPT) has been

shown to improve TB control and reduce the number of persons with and the emergence of drug resistance. Therefore, in any case where non-compliance with well child care has been demonstrated, DOPT should be considered using INH 30 mg/kg (up to 900 mg) twice weekly and also considered through the school DOPT for children less than 12 years of age. Such children may receive DOPT at The American Lung Association DOT Center, situated at 309 South 13th Street, or DOPT may be given at the District Health Center, at school, child care, or at home. DOPT at the DOT Center requires registration with TB Control (register packages have been supplied to all Health Center Clinical Directors). Home DOPT requires arranging with TB Control (tel. 215-685-6873).

TREATMENT OF TB DISEASE

- 4 drugs for the first two months (i.e., INH 10 mg/kg/day, Rifampin 10 mg/kg/day, Pyrazinamide 30 mg/kg/day, and Ethambutol 25 mg/kg/day if > 2 years of age. If the child is younger than 2 years of age, use INH 10 mg/kg/day, Rifampin 10 mg/kg/day, PZA 30 mg/kg/day AND Streptomycin 20-40 mg/kg intramuscular (IM) instead of Ethambutol unless source case is resistant).
- **TB CONTROL PROGRAM WILL ASSUME CASE MANAGEMENT**

B. SCREENING

1. Close and household contacts of active pulmonary tuberculosis cases.
2. Contacts or associates of PPD reactors referred in by the Tuberculosis Program Staff.
3. Prior to PPD testing, a risk assessment should be performed for all patients attending Philadelphia District Health Centers without known prior positive tests or diagnosis of TB, including those who have received BCG vaccine.
4. Walk-in PPD testing may be performed under the same standards that apply to walk-in immunization. Persons seeking a test only as part of pre-employment physical are eligible for walk-in PPDs.
5. Since no other screening test used in pediatrics is interpreted by a non-professional, the child tested needs to return to have the PPD reaction documented or be followed up by an outreach worker.

C. CONSENT REQUIRED

The patient, parent, or guardian should have completed and signed the Philadelphia Department of Public Health Consent Form and have had the opportunity to have his or her questions answered satisfactorily before the Mantoux test is given.

D. RESTRICTIONS AND/OR CONTRAINDICATIONS

1. Do not give tuberculin to documented tuberculin-positive reactors because they will remain positive. If unable to elicit a satisfactory history, repeat PPD for the record.
2. Defer test in an individual recently immunized with a live virus vaccine (measles, mumps, rubella, polio) or who has had natural disease of measles, mumps, rubella, or polio for 6 weeks. However, PPD can be given the same day as live virus vaccines.
3. Pregnancy is not a contraindication for the Mantoux test. A positive PPD should be followed by a chest x-ray (lead-shielded abdomen) and a sputum specimen for AFB smear and culture. If active TB is diagnosed (by clinical, radiographic or bacteriologic means), the mother must receive INH and Rifampin for 9 months, with Ethambutol added for the first two months. Consultation with the Tuberculosis Control Consultant is recommended. Women with a positive PPD and no active disease, who are HIV positive or have been recently infected, should start INH preventive therapy. There is no evidence of harmful effects of INH to the fetus. Pyridoxine should be administered to pregnant women taking INH and to breast-feeding infants whose mothers are taking INH.
4. Children with cancer or on immunosuppressive drugs or with HIV infection should be skin tested and concurrently tested for anergy to mumps or tetanus (only 50% of normal healthy children less than ONE year old will be anergic- ANY acute viral illness suppresses this further). Any concerns the Family Medical Care Physician has in regard to TB should be discussed with the TB consultant.

E. CONCURRENT IMMUNIZATIONS AND TESTS

The Mantoux test may be given simultaneously with DTaP, Td, Tdap, Haemophilus Influenza type B vaccine (HIB), MMR, Varicella, IPV, pneumococcal, influenza, yellow fever, or Hepatitis B, Hepatitis A, Twinrix (HAV and HB) or Menactra at another site.

F. ADMINISTRATION

1. Preparation

The site of the test is usually the flexor, volar or dorsal surface of the forearm, approximately 4 inches below the elbow. However, testing may be done on any part of the body. The skin at the injection site is cleansed with 70% alcohol and allowed to dry. The syringe and needle used for the test should be a sterile, disposable, single dose type. The diaphragm of the vial stopper should be wiped with 70% alcohol. The needle is pushed through the stopper diaphragm of the inverted vial. When drawing back on the solution, be sure to exclude all air bubbles.

2. Dosage

The Mantoux test is performed by injection of 0.1 ml of intermediate strength tuberculin PPDs containing 5 tuberculin units.

3. **Route**

The test material is injected intradermally with a 0.5 ml or 1.0 ml syringe fitted with a short (1 1/4 or 1/2 inch) 26 or 27 gauge needle. The point of the needle is inserted into the most superficial layers of the skin with the needle bevel pointing upward. As the tuberculin solution is injected, a pale bleb of 6 to 10 mm in diameter will rise over the point of the needle. No dressing is needed.

4. **Special Comments**

If the injection is delivered subcutaneously (no bleb will form) or if a significant portion of the dose leaks from the injection site, the test should be repeated immediately at another site at least 5 mm away.

G. MANAGEMENT OF REACTIONS

1. All results should be read routinely by qualified medical personnel.
2. In highly sensitive individuals, strongly positive reactions may very rarely lead to vesiculation, ulceration, or necrosis at the injection site. If this were to happen, instruct the individual to see a physician (either their private physician or health center physician at the discretion of the patient). Hydrocortisone cream 1% can be applied topically every 6 hours for 2 to 3 days.

H. STORAGE

Tuberculin PPD should be stored in a refrigerator at 36 to 46°F (2 to 8°C) and protected from light. Do not draw up the solution until ready to perform the skin test.

I. INTERPRETATION

Results should always be recorded in “mm,” not “positive.” A “negative” test means 0 mm induration. Induration represents the swelling (not the redness) caused by the immune response.

1. Forty-eight hours to 72 hours after administration of PPD, the skin test should be interpreted as follows:
 - a. Fifteen mm or more of induration equals TB infection in children *more* than 4 years old without any risk factor. This requires a chest x-ray and referral to a physician for workup for active TB and/or evaluation for preventive therapy (see Section J. Case Management below).
 - b. Ten mm of induration equals TB infection in a child <4 years old, or any child with increased environmental exposure to TB such as those exposed to active cases of TB, born to parents from regions of the world with a high prevalence or children exposed to HIV-infected adults, to homeless, to poor and to medically indigent city dwellers, to institutionalized individuals or to migrant farm workers. This requires a chest x-ray and referral to a physician for workup for active TB and/or evaluation for preventive therapy (see Section J. Case Management below).

- c. Five mm through 9 mm of induration equals a questionable reaction. However, a close contact of a person with sputum positive for *M. tuberculosis* or if the child is suspected to have tuberculosis or is immunosuppressed in any way would make this reading positive and the child should have a chest x-ray and be referred to a physician for further evaluation. Others should have their PPD repeated in 3 months.
 - d. Zero mm through 4 mm of induration equals a negative reaction. However, if the person is a close contact of a person with tuberculosis, refer the patient to a physician for further management and recommend INH prophylaxis. A skin test should be repeated in three months. Infants and children less than 2 years of age should still get a CXR, since TB may progress in the face of a negative PPD, and should be referred to TB Control Pediatric Consult.
2. Record the date and result of the skin test in the patient's medical record and on the Philadelphia Department of Public Health Report of Patient Services Form. In the case of pediatric patients, record results in the yellow Child Health Record also. NOTE: All individuals from foreign countries should receive a PPD and chest x-ray before seeing the physician.

J. TUBERCULOSIS CONTACT: CASE MANAGEMENT

Introduction

All contacts of a case of tuberculosis who have not reached their 18th birthday will remain under the care of the Family Medical Care pediatrician whether or not a diagnosis of tuberculosis is made or drug treatment is initiated.

Health Supervision

All tuberculosis contacts who have not reached their 18th birthday should be enrolled in the Family Medical Care Services Program for routine health supervision. All routine Family Medical Care forms shall be used. The patient's chart should be identified as a TB contact and the status and whereabouts of the source case should be noted. The frequency of visits (physician and nurse visits) shall be determined primarily by Family Medical Care routines, which may be modified as needed for contact follow-up purposes and treatment. Contacts will receive therapy, where necessary, as indicated below. Patients who are on anti-tuberculosis therapy will be given a physician and/or a nurse appointment every month during the time they are receiving anti-tuberculosis therapy.

Tuberculin Testing

All contacts will be evaluated for tuberculin skin testing as already detailed. However, because the consequences of newly acquired tuberculosis in children can be life threatening, it is recommended that all close contacts to pulmonary tuberculosis who initially have an insignificant reaction (negative or 0-4 mm reading) receive three months of isoniazid (INH) prophylaxis (primary prophylaxis) and be retested at the end of that period. If the test is 0 mm (negative), INH can be discontinued.

All tuberculin tests are to be done with intermediate strength PPD by techniques specified at the time of the tuberculin skin test.

1. If the tuberculin skin test is read as significant (5 mm or more for close contacts), the nurse reading the test shall order a chest x-ray as a routine procedure.
2. The Family Medical Care Program pediatricians will route the record and chest x-ray to the Tuberculosis Control Program Consultant for review.
3. If the report of the first chest x-ray is normal, the result of the significant PPD will be discussed with the parents by the Family Medical Care pediatrician within three weeks of the time the tuberculin test was read and the child started on INH 10 mg/kg/day for preventive therapy for 9 months.
4. If the report of the first chest x-ray is ABNORMAL, the result of the significant PPD will be discussed with the parents by the Family Medical Care pediatrician PROMPTLY AND REPORTED to TB CONTROL and the child will be started on anti-tuberculous treatment (INH, rifampin, pyrazinamide, and ethambutol or streptomycin according to the child's age); or admitted to the hospital for collection of specimens for bacteriology and initiation of therapy.
5. If a child is determined to have a significant tuberculin response without disease, further screening of family members should be undertaken to try to determine the source of the tuberculous infection.

Disposition of Family Medical Care Contacts Following Tuberculin Skin Testing and Chest X-Ray

1. The Tuberculin Test is Positive and the Chest X-Ray is Normal: Tuberculosis Infection

If the tuberculin skin test reaction is positive and the chest X-Ray is negative, and the patient shall be classified as a Latent Tuberculosis Infection, with the exception that individuals with AIDS may be symptomatic –ie fever, cough with sputum, weight loss and have a negative chest x-ray –hence the importance of also obtaining an a history of symptoms when performing any TB screening, the following procedure is to be followed: The pediatrician will order INH 10 mg/kg/day, (maximum of 300 mg) for a period of 9 months, for children over 12 years of age and report to TB control. All children younger than 12 years of age with a diagnosis of LTBI should be reported to TB Control, and according to the pediatrician and the TB consultant treatment to be decided as above. To assure compliance, renewals of drugs should be filled monthly, the INH Prophylaxis Form should be sent to TB Control, and the child seen by the Family Medical Care Provider monthly. The parent will be informed of side effects of the drug and to return to clinic sooner than the month if there are problems of administration or drug toxicity. Following completion of isoniazid prophylaxis, the patient will be returned to routine Family Medical Care Supervision.

2. The Tuberculin Skin Test is Positive and The Chest X-Ray Shows Evidence of Lung Involvement, Adenopathy, Infiltrate or Pleural Disease: TB Disease

The child is started on 4-drug therapy, and the record is reviewed by both the Tuberculosis Control Program Consultant and the physician taking care of the child.

3. The Tuberculin Skin Test Is Negative after a Repeat PPD in The Case of a Child who is a Contact.

The Family Medical Care pediatrician will consult with the Pediatric Medical Specialist and/or the Tuberculosis Control Program Consultant, and they will evaluate the total situation and elect one of the following regimens:

If the contact has been permanently broken (i.e., the index case has left the household) for more than eight weeks but less than three months, and/or the source case now has sputum that is smear and culture negative, then INH prophylaxis should be continued for three months and the patient should have a repeat PPD test done at the end of the 3-month period.

- a. If the repeat PPD remains negative, the INH is discontinued and the patient remains under regular Family Medical Care supervision.
- b. If the repeat PPD is positive and the chest X-Ray is normal, the diagnosis becomes Latent Tuberculosis Infection (LTBI), and the patient is treated with INH prophylaxis for a 9-month period.
- c. If the contact has not been permanently broken, and the source case remains smear and culture positive, the Family Medical Care pediatrician and the Pediatric Medical Specialist shall evaluate the total family situation with the Tuberculosis Control Consultant and decide on a course of action.

4. TB Contacts Who Have Had BCG before Registering in the Family Medical Care Program

Tuberculosis contacts who have had BCG shall have a tuberculin skin test. If the test is negative, the patient receives a second PPD after one week, and if the repeat is negative, the patient will be returned to routine Family Medical Care health supervision. If the test is positive (10 mm or more), the patient shall have a chest x-ray. If the chest x-ray shows pulmonary involvement, the patient will be treated as a case of TB with 4 drugs pending culture results. If the chest x-ray is normal, the patient should be considered a latent tuberculosis infection and treated with INH for 9 months.

Tuberculin Reactors Who Are Not Contacts

- a. A chest X-Ray will be done
- b. If the chest x-ray is normal, the patient will be put on the same regimen as contacts who have significant tuberculin skin test, i.e. 9 months INH.
- c. If the chest x-ray shows pulmonary involvement, the patient should be treated as having active TB pending culture results, and the TB Control Program should be notified and the total family situation evaluated with the Tuberculosis Control Program.

Associates of Tuberculin Reactors

Associates of tuberculin reactors are defined as members of the household of patients who are found to have significant tuberculin skin test reaction on routine tuberculin testing. They need careful evaluation, as they might be the source of infection. Associates of tuberculin reactors will receive a tuberculin skin test. If the tuberculin skin test is positive, a chest x-ray is done. Follow policy previously outlined. If the tuberculin skin test is negative, the patient will be returned to routine Family Medical Care supervision.

K. BCG VACCINATION IN FAMILY MEDICAL CARE PROGRAM

Eligibility: The ACIP recommends consideration of BCG Vaccine for PPD negative children at high-risk of exposure to Tuberculosis or MDRTB WHEN NO OTHER more effective measure that can be maintained exists. Since TB control measures have been shown to terminate outbreaks, authorities are not routinely recommending BCG.

BCG vaccine will not be used in Philadelphia. Any proposed use of this vaccine or queries about individual patients should be directed to the Tuberculosis Control Program.

L. RECORDS AND RECORDING

The following records will be used for all Family Medical Care patients who are close contacts of a case of tuberculosis.

1. Family Medical Care Record forms
2. Yellow Child Health Record booklets (if preschool age)
3. Report suspects and cases who receive any treatment on the New form
4. Report patients placed on **INH** prophylaxis on INH preventive Rx form.