Mycobacterium tuberculosis (MTB)
or Mycobacterium tuberculosis complex

Tuberculosis

- Skin puncture or injection
- Ingestion
- Contact with mucous membranes (eyes, nose, mouth)
- Exposure to aerosols containing TB; Airborne exposure to droplet nuclei

First Aid:
- Skin Exposure, immediately go to the sink and thoroughly wash the skin with soap and water. Decontaminate any exposed skin surfaces with an antiseptic scrub solution.
- Skin Wound, immediately go to the sink and thoroughly wash the wound with soap and water and pat dry.
- Splash to Eye(s), Nose or Mouth, immediately flush the area with running water for at least 5-10 minutes.
- Splash Affecting Garments, remove garments that may have become soiled or contaminated and place them in a double red plastic bag.

Emergency Treatment:
- In the event of an acute injury resulting from a laboratory incident which requires immediate medical care, the injured employee/student should report to the emergency department for acute medical treatment. The injured individual must take a copy of this entire protocol document to the Emergency Department.

Follow up is needed in the event of any Laboratory Exposure:
- After first aid has been administered, immediately inform your supervisor of the exposure.
- In the event of a large spill, contact the emergency response team (9-911) for clean-up.
- In the event of a percutaneous exposure, call the Exposure Hotline at 415/353-7842. The responder will provide guidance to the injured individual on necessary medical treatment and post exposure follow-up.
- Contact Occupational Health Services, after first aid is complete, for a follow-up care.
UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
ROLES & RESPONSIBILITIES
AFTER ACCIDENTAL EXPOSURE TO MYCOBACTERIUM TUBERCULOSIS (MTB)

1. WORKER’S RESPONSIBILITIES (Employee/Patient Initial Self-Care)
   a. First Aid: Perform the recommended first aid and decontamination according to the posted instructions.
   b. Treatment: i) In the event of an acute injury resulting from a laboratory incident which requires immediate medical care, the injured individual should report to the Emergency Department for acute medical treatment. ii) In the event of an exposure, with or without an injury, call the Exposure Hotline for access to medical care.
   c. Provide any treating physicians with information regarding the strain of MTB, and whether it has any known drug resistance.
   d. Reporting: Inform your laboratory supervisor / principal investigator of the exposure.
   e. Secure the laboratory: Identify the equipment involved in the exposure and the mechanism of exposure. Make sure that the laboratory area has been secured and that notification of contamination has been posted to prevent other individuals from entering the area.

2. SUPERVISOR’S/PI’S RESPONSIBILITIES
   a. First Aid and Decontamination: Verify that the worker has washed and decontaminated himself/herself. Ensure that appropriate medical treatment has been received.
   b. Secure the laboratory: Confirm that the laboratory area has been secured and that notification of contamination has been posted to prevent other individuals from entering the area.
   c. Laboratory Clean-up (as needed): Contact the Office of Environment Health & Safety (EH&S) through the UC Police Department Emergency Dispatch (from a campus telephone 9-911, from a non-campus phone 415/476-1414).
   d. Report the exposure: Ensure that the Biosafety Officer, the Public Health Officer and other appropriate departments have been notified, as outlined in this protocol. Provide an incident report summarizing any suspected MTB exposure. The report must include the following:
      - A brief description of the exposure event, a description of the area involved, and the extent of employee exposure
      - If applicable, specification of the amount of infectious material released, time involved, and explanation of procedures used to determine the amount involved
      - Report that medical treatment has been provided
      - Corrective action taken to prevent the re-occurrence of the incident
   e. Follow Up: Confirm that the patient has called for an appointment with UCSF-OHS for evaluation
on the next weekday the clinic is open. Confirm that the patient has been evaluated.

f. **Report of Injury:** Within 24 hours, report the injury to the UCSF Human Resources Disability Management Services (HR DMS) Office on the Supervisor’s Report of Injury (SRI) form. Here is a link to the form: [http://ucsfhr.ucsf.edu/files/SIR.pdf](http://ucsfhr.ucsf.edu/files/SIR.pdf)

5. **EH&S/BIOSAFETY/PUBLIC HEALTH OFFICER RESPONSIBILITIES**

a. The UCSF-PHO and Biosafety Officer will review the incident report, provide an analysis of the incident, and produce a report containing the date(s), location(s) and list of potentially exposed personnel.

b. For all research related exposures, the incident report and analysis will be prepared for the UCSF Institutional Biosafety committee.

c. The UCSF-PHO will ask the exposed individuals to report to UCSF-OHS for baseline TB assessment, and will be reassessed 12 weeks following exposure.
SECTION I – Infectious Agent
Organism or Agent: Mycobacterium tuberculosis (MTB)
Synonym or Cross Reference: T.B. or Mycobacterium tuberculosis complex
Characteristics: A bacterial disease caused by Gram positive rods, non-spore forming, non-motile, slightly curved, forming strands and cords, acid-fast staining, aerobic, slow growing mycobacterium.
Infectious Dose: As low as 10 organisms
Pathogenicity: Initial infection usually unnoticed, tuberculin sensitivity appears in a few weeks and lesions commonly heal; may progress to pulmonary tuberculosis (fatigue, fever, cough, chest pain, hemoptysis fibrosis, cavitation) or extrapulmonary involvement (miliary, meningeal) by lymphohematogenous dissemination; serious outcome of initial infection more frequent in infants and children; infection with bovine bacillus rare; drug resistant strains can cause irreversible damage in the lungs.
Special issues: The organism has a thick, lipid-rich cell wall that renders bacilli resistant to harsh treatments including alkali and detergents. Any laboratory working with high titer MTB should have semi-annual surveillance using the tuberculin skin test or QFT.

SECTION II – Recommended Precautions
Containment Requirements: Biosafety level 3 practices, safety equipment, and facilities for activities involving the manipulation of MTB that could generate aerosols. BSL-2 precautions for non-aerosol-producing manipulations of clinical specimens.
UCSF Required Personal Protective Equipment: gloves, safety goggles, lab coat, N95 respiratory protection or higher.

SECTION III – Handling Information
Spills: Allow aerosols to settle; wearing protective clothing, gently cover spill with paper towel and apply 10% sodium hypochlorite, starting at perimeter and working towards the centre; allow sufficient contact time before clean up (30 min)
Biohazardous Waste: Collect solid waste in double red bags and transport in a rigid container. Decontaminate liquid waste with a 1:10 dilution of 5% bleach for a minimum of 15 minutes before disposing down the drain.
Disposal: Decontaminate before disposal; steam sterilization, chemical disinfection, incineration
Storage: Store in sealed containers that are appropriately labeled.

SECTION IV – Health Hazards
Pathogenicity: Initially causes a sub-clinical infection which can be detected 8-10 weeks after exposure. Pulmonary TB may arise from exogenous reinfecion or endogenous reactivation of a latent focus originating from the initial sub-clinical infection, persons with immunodeficiencies, such as HIV infection, have a higher risk of extrapulmonary TB. If untreated, about 65% of patients with sputum smear-positive pulmonary tuberculosis die within 5 years, most of these within 2 years. Extrapulmonary TB occurs less commonly (30%) than pulmonary TB (70%). Sensitive to moist heat (121° C for at least 15 min) and light.
**Modes of Transmission:** Inhalation of aerosolized bacteria as well as mucosal and percutaneous routes of infection. Portal entry is the lung; pathogen is carried as airborne particles (droplet nuclei); exposure to airborne bacilli from sputum of infected persons; direct invasion of mucous membranes or breaks in skin; bovine tuberculosis from exposure to infected cattle (via airborne exposure, or ingestion of raw milk or dairy products); medical personnel at risk while performing autopsies, intubation, bronchoscopies or by dermal inoculation.\(^4\)  
**Incubation Period:** 2-10 weeks  
**Communicability:** Any laboratory procedure that aerosolizes bacteria, or person to person spread.

**FOR THE USE OF THE EXPOSURE HOTLINE**

**SECTION V – Viability**  
**Drug Susceptibility:** Many drug resistant strains.  
**Susceptibility to Disinfectants:** Intermediate-level disinfection—Chemical germicides used in this category correspond to Environmental Protection Agency (EPA)-approved “hospital disinfectants” that are also “tuberculocidal”.\(^3\) Greater resistant to disinfectants and require longer contact times for most disinfectants to be effective; 5% phenol, 1% sodium hypochlorite (only if low organic matter and longer contact times), iodine solutions (high concentration of available iodine required), glutaraldehyde and formaldehyde (longer contact time) are effective.\(^3\)

**Physical Inactivation:** Sensitive to UV inactivation. Less sensitive to heat inactivation; tubercule bacilli may survive in heat-fixed smears and may be aerosolized from frozen sections.\(^3\)

**Survival Outside Host:** Survives for extended period of time in the environment. Guinea pig carcasses - 49 days; carpet - up to 70 days; dust - 90 to 120 days; cockroaches - 40 days; manure 45 days; paper book - 105 days; sputum (cool, dark location) - 6 to 8 months; clothing - 45 days.\(^4\)

**SECTION VI – Medical**  
**Surveillance:** Any exposed worker should contact UCSF-OHS on the work next day to set up a baseline evaluation followed by reevaluation in 12 weeks. Wound sites should be monitored for the development of any non-healing lesions.  
**First Aid/Treatment:** Decontamination  
**Immunization:** BCG not recommended  
**Conversion:** Any reevaluation with a positive skin test or QFT test will be considered a conversion and a case of latent TB.

**SECTION VII – Laboratory Hazards**  
**Laboratory-Acquired Infections:** Well documented hazard.  
**Sources/Specimen:** Any tissue from infected animals may pose a risk of infection. The greatest hazard is from concentrated cultured materials.  
**Primary Hazards:** Inhalation, followed by percutaneous or mucosal exposures. Laboratory acquired infections have occurred from exposed skin and attempts to incinerate organisms from a bacteriological needle or loop.\(^2\)

**Special Hazards:** Environmentally persistent.
FOR THE USE OF THE EMERGENCY DEPARTMENT

SECTION VIII – Emergency Medical Treatment

Treatment Indications: Emergency department treatment is only indicated for wounds that occur ancillary to exposure.

Decontamination: Ensure that any wounds have been adequately decontaminated.

(Format/Content adapted directly from Canadian MSDS and the 5th Edition of Biosafety in Microbiological and Biomedical Laboratories (BMBL) with additional information from subsequent portions of the protocol)

SECTION IX – References

A. DEFINITION OF TUBERCULOSIS EXPOSURE AND RISK OF TRANSMISSION:

1. Through manipulation of infective materials containing *Mycobacterium tuberculosis*, an exposure can occur in the following ways:
   - Contact with mucous membranes (e.g., eyes, nose, mouth)
   - Contact with skin (through possible microfissures)
   - Percutaneous exposure/Contact with non-intact skin (e.g. abrasions, rash, cuts)
   - Inhalation

2. Face-to-face or same room contact without personal respiratory protection to either a patient or employees with AFB smear positive TB

B. DESCRIPTION AND IMPLICATIONS OF RISK:

*M. tuberculosis* is carried in airborne particles called droplet nuclei that can be generated when persons who have pulmonary or laryngeal TB disease cough, sneeze, shout, or sing. Airborne particles can also be generated in research labs where MTB is manipulated. Airborne particles of greatest concern are approximately 1–5 μm; normal air currents can keep them airborne for prolonged periods and spread them throughout a room or building. *M. tuberculosis* is usually only transmitted through air, not by surface contact. After the droplet nuclei are in the alveoli, local infection might be established, followed by dissemination to draining lymphatics and hematogenous spread throughout the body. Infection occurs when a susceptible person inhales droplet nuclei containing *M. tuberculosis*, and the droplet nuclei traverse the mouth or nasal passages, upper respiratory tract, and bronchi to reach the alveoli. Persons with TB pleural effusions might also have concurrent unsuspected pulmonary or laryngeal TB disease. Usually within 2–12 weeks after initial infection with *M. tuberculosis*, the immune response limits additional multiplication of the tubercle bacilli, and immunologic test results for *M. tuberculosis* infection become positive. However, certain bacilli remain in the body and are viable for multiple years. This condition is referred to as latent tuberculosis infection (LTBI). Persons with LTBI are asymptomatic (they have no symptoms of TB disease) and are not infectious.

In the United States, LTBI has been diagnosed traditionally based on a purified protein derivative (PPD)-based tuberculosis skin test (TST) result after TB disease has been excluded. In vitro cytokine-based immunoassays for the detection of *M. tuberculosis* infection have been the focus of intense research and development. One such blood assay for *M. tuberculosis* (or BAMT) is an interferon gamma release assay (IGRA), the QuantiFERON®-TB test (QFT), and the subsequently developed version, QFT-G. The QFT-G measures cell-mediated immune responses to peptides from two *M. tuberculosis* proteins that are not present in any Bacille Calmette-Guérin (BCG) vaccine strain and that are absent from the majority of nontuberculous mycobacteria (NTM), also known as mycobacteria other than TB (MOTT). QFT-G was approved by FDA in 2005 and is an available option for detecting *M. tuberculosis* infection. CDC recommendations for the United States regarding QFT and QFT-G have been published, and are available at http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5202a2.htm
Because this field is rapidly evolving, in this report, BAMT will be used generically to refer to the test currently available in the United States. Additional cytokine-based immunoassays are under development and might be useful in the diagnosis of *M. tuberculosis* infection. Future FDA-licensed products in combination with CDC-issued recommendations might provide additional diagnostic alternatives. The latest CDC recommendations for guidance on diagnostic use of these and related technologies are available at [http://www.cdc.gov/nchstp/tb/pubs/mmwr html/Maj_guide/Diagnosis.htm](http://www.cdc.gov/nchstp/tb/pubs/mmwr html/Maj_guide/Diagnosis.htm). Typically, approximately 5%–10% of persons who become infected with *M. tuberculosis* and who are not treated for LTBI will develop TB disease during their lifetimes. The risk for progression of LTBI to TB disease is highest during the first several years after infection.

**Persons at Highest Risk for Exposure to and Infection with *M. tuberculosis***

Characteristics of persons exposed to *M. tuberculosis* that might affect the risk for infection are not as well defined. The probability that a person who is exposed to *M. tuberculosis* will become infected depends primarily on the concentration of infectious droplet nuclei in the air, and the duration of exposure. The closer the proximity, and the longer the duration of exposure, the higher the risk of being infected.

**Persons at High Risk for Progression from LTBI to TB Disease**

The following persons are at high risk for progressing from LTBI to TB disease:

- persons infected with HIV;
- persons infected with *M. tuberculosis* within the previous 2 years;
- infants and children aged <4 years;
- persons with any of the following clinical conditions or other immunocompromising conditions
  - silicosis,
  - diabetes mellitus,
  - chronic renal failure,
  - certain hematologic disorders (leukemias and lymphomas),
  - other specific malignancies (e.g., carcinoma of the head, neck, or lung),
  - body weight >10% below ideal body weight,
  - prolonged corticosteroid use,
  - other immunosuppressive treatments (including tumor necrosis factor-alpha [TNF-α] antagonists),
  - organ transplant,
  - end-stage renal disease (ESRD), and
  - intestinal bypass or gastrectomy

HIV infection is the greatest risk factor for progression from LTBI to TB disease. Therefore, voluntary HIV counseling, testing, and referral should be routinely offered to all persons at risk for LTBI. All workers should be informed regarding the risk for developing TB disease after being infected with *M. tuberculosis*. However, the rate of TB disease among persons who are HIV-infected and untreated for LTBI in the United States is substantial, ranging from 1.7–7.9 TB cases per 100 person-years. Persons infected with HIV who are already severely immunocompromised and who become newly infected with *M. tuberculosis* have a greater risk for developing TB disease, compared with newly infected persons without HIV infection. Because the risk for disease is particularly high among HIV-infected persons with *M. tuberculosis* infection, HIV-infected contacts of persons with infectious pulmonary or laryngeal TB disease must be evaluated for *M. tuberculosis* infection, including the exclusion of TB disease, as soon as possible after learning of exposure. Vaccination with BCG probably does not affect the risk for infection after exposure, but it might decrease the risk for progression from infection with *M. tuberculosis* to TB disease, preventing the development of miliary and meningeal disease in infants and young children. Although HIV infection increases the likelihood of progression from LTBI to TB
disease, whether HIV infection increases the risk for becoming infected if exposed to \textit{M. tuberculosis} is not known.

Adapted directly from \textit{Guidelines for Preventing the Transmission of Mycobacterium tuberculosis I Health-Care Settings}, 2005, with minor edits: http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5417a1.htm

Although typically considered a chronic disease, tuberculosis (TB) has protean acute manifestations. The pathogenesis of acute TB, although still incompletely understood, may be related to both epidemiologic and genetic host factors. Miliary TB manifests as a nonspecific clinical syndrome with a high mortality rate. The most well-known form of acute TB is meningitis, characterized by fever, nuchal rigidity, and a lymphocytic pleocytosis of the cerebrospinal fluid. Acute abdominal TB may present with obstruction or, less commonly, as perforated viscera or peritonitis. Critically ill patients may have acute respiratory distress syndrome, shock, or disseminated intravascular coagulopathy. The spectrum of disease makes diagnosis of acute TB difficult unless clinical suspicion of disease is high, but the high mortality mandates its consideration. Early initiation of therapy is crucial to optimize clinical outcome.

- Acute tuberculosis can manifest in nearly any organ system
- Diagnosis requires a high index of suspicion; clinical, radiographic, pathologic and laboratory findings are often nonspecific, but helpful when considered together.
- The diagnosis of acute TB is frequently made postmortem.


\textbf{All UCSF employees who work with MTB should be aware of the OEH&S policy on workers with immune compromise. Please refer to Campus Research Exposure Protocols, Immune Compromised Worker: http://www.occupationalhealthprogram.ucsf.edu/ohpEE.asp#EP}