SECTION I - INFECTIOUS AGENT

NAME: Mycobacterium tuberculosis and Mycobacterium tuberculosis complex (including M. bovis, M. africanum, M. pinnipedii, M. microti, M. caprae and M. canettii)

SYNONYM OR CROSS REFERENCE: TB, Tuberculosis, Mycobacterium tuberculosis complex (MTBC)

CHARACTERISTICS: These bacteria are acid-fast, aerobic, non-spore forming, non-motile bacteria (1). They form slightly curved or straight rods which may branch (0.2 to 0.6 μm by 1.0 to 10 μm). They are slow growers, i.e. they require more than 7 days to form colonies when sub cultured on Lowenstein-Jensen medium (1). M. tuberculosis forms off-white, rough colonies on Lowenstein-Jensen solid media (1). Colonies formed by M. bovis are small and rounded with irregular edges on egg based media (1).

SECTION II - HAZARD IDENTIFICATION

PATHOGENICITY/TOXICITY: Tuberculosis infection can be of many different types. Primary tuberculosis may be asymptomatic and may only be recognized by a positive skin test. Following the inhalation of the bacteria, primary complex develops in the lungs, which usually heals and forms calcifications (2). In 90-95% of the cases, the host immune response generated against the bacteria is capable of limiting its growth and multiplication, leading to a latent infection with no clinical symptoms (3). It may become progressive in 5-10% of the cases (3). If the disease becomes progressive, patients present with cough, weight loss, night sweats, low-grade fever, dyspnea, lymphadenopathy, chest pain, and even pneumonia or phthisis (1, 2). Along with the formation of the cavernous lesions, primary tuberculosis may also have an exudative course (2). Exudative course involves pleural effusion along with high fever and chest pain (2). The latent infection may develop into active TB in 5-10% of the individuals (4). Extrapulmonary tuberculosis may affect any organ system and may cause cervical lymphadenitis, pleuritis, pericarditis, synovitis, meningitis, and infections of the skin, joint or bones (1, 2). Milliary tuberculosis (disseminated tuberculosis) is characterized by high and sustained fever, night sweats, dry cough, malaise, splenomegaly, and skin lesions. Meningitis (high fever, cranial nerve deficits, and psychic changes) develops in 50% of the cases with a high mortality rate, if left untreated (2). Furthermore, these patients may also develop tuberculous peritonitis with fever, ascites, and increase in abdominal girth (2). Although M. bovis infection in humans causes a disease very similar to M. tuberculosis, non-pulmonary lesions are more frequent than pulmonary lesions, since M. bovis infection is mainly acquired by consuming contaminated milk or meat (4). Farm workers, however, are prone to pulmonary lesions since they are exposed to droplets from the infected cattle (5).

EPIDEMIOLOGY: Tuberculosis is a major health problem worldwide (1). The greatest risk factor for tuberculosis progression from a latent infection to an active one is HIV infection (1). World Health Organization (WHO) reported that in 2008, there were an estimated 8.9–9.9 million incident cases and 9.6–13.3 million prevalent cases of tuberculosis, worldwide (5). They also reported that...
tuberculosis infection resulted in 1.1–1.7 million deaths among HIV-negative people and an additional 0.45–0.62 million deaths among HIV-positive people (6). The highest number of estimate cases of tuberculosis occurred in Asia (55% of the total TB cases) and Africa (30% of the total TB cases) (6). The number of reported cases appears to be decreasing in the western hemisphere (3% of the total cases in North America: prevalence of 24 cases/100,000) owing to effective strategies to prevent, detect, and treat the infection, implemented by these countries (1, 5). An estimated 0.5 million cases of MDR-TB (Multiple drug resistant TB) occurred worldwide in 2007, with most cases being reported from India and China (6). WHO also reported an increase in the number of Extensively Drug Resistant TB strains (XDR-TB) cases in the year 2009 (6). In Canada, 1,600 new active and re-treatment tuberculosis (TB) cases (a rate of 4.8/100,000) were reported to the Canadian Tuberculosis Reporting System (CTBRS) in 2008 (2). Furthermore, out of the 1359 isolates tested for resistance to anti-tuberculosis drugs, 1.1% were MDR and 0.07% were XDR-TB strains (8). Incidence of tuberculosis is more concentrated in foreign-born people in Canada (7). Human tuberculosis due to M. bovis was found among 1.4% of all the tuberculosis cases reported during the period 1995-2005 in the United States (9). Patients not born in the United States, Hispanic patients, patients <15 years of age, HIV infected patients, and patients with extrapulmonary disease were reported to have a higher risk for having infection with M. bovis versus M. tuberculosis (9).

HOST RANGE: Monkeys, humans, parrots, cattle, sheep, goats, dogs, cats (1, 2).

INFECTIOUS DOSE: M. tuberculosis has a very low infectious dose (1, 4). The ID$_{50}$ is estimated to be <10 bacilli in humans (1).

MODE OF TRANSMISSION: Transmission can be nosocomial or airborne (inhalation of droplet nuclei carrying M. tuberculosis, which are generated when patients with tuberculosis cough) (1). Other modes of transmission include exposure to autopsy material, venereal transmission, and even percutaneous transmission (direct injury to the skin and mucous membranes through breaks in skin (10, 11). Infected animals can spread the infection to laboratory workers through aerosols, fomites, bites (10). Bovine tuberculosis can occur from exposure to infected cattle (airborne, ingestion of raw milk or dairy products) (5).

INCUBATION PERIOD: 4-6 weeks (2). For latent TB infections, 5% of patients develop an active infection within 2 years and 5% develop an infection within their lifetime (12).

COMMUNICABILITY: Highly communicable. For bovine tuberculosis, infected humans can transmit the disease to cattle and vise versa (2).

SECTION III - DISSEMINATION

RESERVOIR: Humans, and diseased animals (2).

ZOOONOSIS: Yes, through monkeys, parrots, cattle, sheep, goat, dogs, cats (2).

VECTOR: None.

SECTION IV - STABILITY AND VIABILITY

DRUG SUSCEPTIBILITY: Pan susceptible tuberculosis is defined as tuberculosis susceptible to all 4 first-line drugs used to treat the disease: isoniazid, ethambutol, rifampin, and pyrazinamide (13, 14). M. bovis strains are resistant to pyrazinamide, but susceptible to streptomycin (2, 9).

DRUG RESISTANCE: Multiple drug resistant TB (MDR-TB) strains of mycobacterium are resistant to at least isoniazid and rifampin (13, 14). Extremely drug resistant TB (XDR-TB) is the most severe form of the disease, caused by strains of mycobacteria which are not only resistant to isoniazid and rifampin, but also show resistance to fluoroquinolones and at least one of three injectable second line anti-tubercular drugs (amikacin, kanamycin, and/or capreomycin) (13, 14).

SUSCEPTIBILITY TO DISINFECTANTS: Mycobacterium species show greater resistance to disinfectants than vegetative bacteria (11). M. tuberculosis is more resistant than M. bovis (15). Amphy1 and other phenol soap mixtures and 0.05 % to 0.5% sodium hypochlorite can be used for
Mycobacterium Tuberculosis Complex - Pathogen Safety Data Sheets

3/6


6/9/2014

1. Mycobacterium tuberculosis is susceptible to N-dodecyl-1,3-propanediamine supplemented with sodium hydroxide, ethylene oxide, a mixture 7.5% hydrogen peroxide and 0.85% phosphoric acid, phenolics, 0.35% peracetic acid, orthophthaldehyde and superoxidized water. Higher concentrations of chlorine are required for efficacy against M. tuberculosis. A 2% solution of aqueous glutaraldehyde is required to kill M. tuberculosis within 10-20 minutes at room temperature. A 2% solution of alkaline glutaraldehyde has slower action against M. tuberculosis. Some disinfectants such as quaternary ammonium compounds, chlorhexidine gluconate, and iodophore have been reported to be ineffective against M. tuberculosis.

PHYSICAL INACTIVATION: UV light can be used for surface disinfection. Most bacteria are sensitive to moist heat (121°C for at least 15 min). Mycobacteria are easily killed by heat (> 65°C for at least 30 min).

SURVIVAL OUTSIDE HOST: M. tuberculosis can survive for months on dry inanimate surfaces. M. bovis can survive on dry surfaces at 4°C. M. tuberculosis can survive in cockroach feces for 8 weeks, sputum on carpet (19 days) and wood (over 88 days), moist and dry soil (4 weeks), and in the environment for more than 74 days if protected from light (possibly longer if in feces).

SECTION V- FIRST AID / MEDICAL

SURVEILLANCE: Monitor for symptoms. Diagnosis can be done by chest X-ray, direct smear microscopy for detecting acid-fast bacilli, culture of the bacillus from clinical specimens, or by nucleic acid amplification techniques such as PCR, followed by southern blotting. Diagnosis of TB infection in asymptomatic individuals can be done using tuberculin skin tests, such as the Mantoux test, or gamma interferon releasing assays.

Note: All diagnostic methods are not necessarily available in all countries.

FIRST AID/TREATMENT: New smear or culture positive cases of TB are treated with 4 first-line anti-tuberculosis drugs: oral isoniazid, oral rifampicin, oral pyrazinamide, and oral ethambutol. If the tuberculosis strain is fully susceptible, then treatment is continued with isoniazid and rifampin for an additional 4 months. If the M. tuberculosis strain is resistant to the first line drugs, group 2-5 drugs are given according to the drug susceptibility testing of the isolated strains. M. bovis is resistant to pyrazinamide, and is thus treated with isoniazid and rifampin for 9 months.

IMMUNIZATION: Bacille Calmette and Guerin (BCG), is the vaccine currently being used to prevent tuberculosis. It is derived from an attenuated, avirulent strain of M. bovis, and is also known as M. bovis BCG. It has been shown to be effective in preventing the most severe disseminated forms of disease in children and newborns, but its efficacy against active TB in adults has been challenged. BCG vaccine is successful mainly due to its efficacy in preventing tuberculosis meningitis in children and its safety for use in humans. New live and attenuated strains of M. tuberculosis, recombinant BCG strains and subunit vaccines are currently being tested for their efficacy and safety.

PROPHYLAXIS: Isoniazid may be used for prophylaxis in tuberculin-negative individuals who have come into contact with tuberculous individuals. Isoniazid in combination with rifampin should be used for prophylaxis on tuberculin positive, asymptomatic individuals.

SECTION VI-LABORATORY HAZARD

LABORATORY-ACQUIRED INFECTIONS: Incidence of tuberculosis in laboratory workers working with M. tuberculosis is three times higher than those not working with the agent. More than 200 cases of laboratory acquired infections with M. tuberculosis and M. bovis have been reported up to 1999. Up to 1976, 176 cases were reported with 4 deaths.

SOURCE/SPECIMENS: Sputum, gastric lavage fluids, cerebrospinal fluids, urine or lesions from a variety of infected tissues.

PRIMARY HAZARDS: Nosocomial transmission of the bacteria while working with patients or during handling of clinical specimens, litter from the naturally or experimentally infected animals such as...
Guinea pigs or mice, and exposure to infectious aerosols generated during manipulation of cultures or during handling infected animals, accidental parenteral inoculation (1, 25, 26).

SPECIAL HAZARDS: Bacilli can survive in heat-fixed smears and may be aerosolized during the preparation of frozen stocks or during manipulation of cultures (25). The annual tuberculin conversion rate is higher among personnel working with infected non human primates than in the general population (25).

SECTION VII-EXPOSURE CONTROLS / PERSONAL PROTECTION

RISK GROUP CLASSIFICATION: Risk group 3 (28).

CONTAINMENT REQUIREMENTS: Containment Level 3 facilities, equipment, and operational practices for work involving infectious or potentially infectious materials, animals, or cultures. Work involving clinical specimens may be done at a lower containment level based on a local risk assessment, and in consultation with the Pathogen Regulation Directorate, Public Health Agency of Canada.

PROTECTIVE CLOTHING: Personnel entering the Containment Level 3 laboratory should remove street clothing and jewellery, and change into dedicated laboratory clothing and shoes, or don full coverage protective clothing (i.e., completely covering all street clothing). Additional protection may be worn over laboratory clothing when infectious materials are directly handled, such as solid-front gowns with tight fitting wrists, gloves, and respiratory protection. Eye protection must be used where there is a known or potential risk of exposure to splashes (29).

OTHER PRECAUTIONS: All activities with infectious material should be conducted in a biological safety cabinet (BSC) or other appropriate primary containment device in combination with personal protective equipment. Centrifugation of infected materials must be carried out in closed containers placed in sealed safety cups, or in rotors that are loaded or unloaded in a biological safety cabinet. The use of needles, syringes, and other sharp objects should be strictly limited. Open wounds, cuts, scratches, and grazes should be covered with waterproof dressings. Additional precautions should be considered with work involving animals or large scale activities (29).

SECTION VIII-HANDLING AND STORAGE

SPILLS: Allow aerosols to settle and, wearing protective clothing, gently cover spill with paper towels and apply an appropriate disinfectant, starting at the perimeter and working towards the centre. Allow sufficient contact time before clean up.

DISPOSAL: All wastes should be decontaminated before disposal either by steam sterilization, incineration or chemical disinfection.

STORAGE: The infectious agent should be stored in a sealed and identified container.

SECTION IX-REGULATORY AND OTHER INFORMATION

REGULATORY INFORMATION: The import, transport, and use of pathogens in Canada is regulated under many regulatory bodies, including the Public Health Agency of Canada, Health Canada, Canadian Food Inspection Agency, Environment Canada, and Transport Canada. Users are responsible for ensuring they are compliant with all relevant acts, regulations, guidelines, and standards.

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PREPARED BY: Pathogen Regulation Directorate, Public Health Agency of Canada

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REFERENCES:


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