**TUBERCULOSIS IN NON-HUMAN PRIMATES**

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<th>Animal Group(s) Affected</th>
<th>Transmission</th>
<th>Clinical Signs</th>
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<td>Non-human primates</td>
<td>Inhalation and ingestion predominates; fomite potential documented</td>
<td>Varies: rough hair coat, weight loss, cough, lymphadenopathy</td>
<td>Highly variable: asymptomatic to severely debilitating disease.</td>
<td>Limited efficacy even with multi-modal treatment; but may be considered for extremely valuable animals. However, culling of positive animals highly recommended</td>
<td>Skin test is routine and gold standard; but nonspecific responses occur.</td>
<td>Yes – and anthroponotic</td>
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**Fact Sheet compiled by:** Charles O. Thoen  
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**Fact Sheet Reviewed by:** Patrice Frost; Heather Cole; Paul P. Calle; Hilton Klein; Ana Cristina Leandro  
**Susceptible animal groups:** All primates, including humans.  
**Causative organisms:** *Mycobacterium tuberculosis*; *M. bovis*, *M. avium ss avium*.  
**Zoonotic potential:** Yes  
**Distribution:** Old World non-human primates and great apes – usually with typical mycobacterial infection; New World non-human primates – usually with other mycobacterial infection(s).  
**Incubation period:** Variable from weeks to months; animals can develop latent infections with reactivation in weeks, months or even years later. Development of disease is dependent on organism, route of infection, dose and immunologic status of animal. Susceptibility, morbidity and mortality are variable for different species.  
**Clinical signs:** The clinical signs are often nondescript and ill-defined. Tuberculosis can imitate a multitude of diseases such as pneumonia, neoplasia or fungal infections. The clinical spectrum of signs range from asymptomatic to multi-symptomatic; the profile is highly dependent on the route of exposure, the system involved and the infecting agent. General signs can include a roughened hair coat, anorexia, depression, lethargy, fever (low grade; intermittent or persistent), weight loss, hepatomegaly, splenomegaly, and local or general lymphadenopathy which may or may not have draining tracts. A chronic or paroxysmal cough and dyspnea indicate pulmonary involvement, which mirrors acute bronchitis, or pneumonia. Neurological presentation with signs including anisocoria or ataxia may implicate meningitis or central nervous system involvement, and paresis to paralysis can indicate a peripheral neurological component that may be a result of spondylitis.  
**Post mortem, gross, or histologic findings:** At necropsy, tuberculosis indications vary with the duration and degree of disease. Organs of predilection are the lung and adjacent hilar lymph nodes. Dissemination occurs to the spleen kidney, liver and associated lymph nodes. Additional sites less frequently seen include omentum, ovary, cerebrum, spinal column, peripheral lymph nodes skin and mammary gland. The extent of the lesions can range from no detectable lesions to wide dissemination of caseous granulomas varying in size from pinpoint to large coalescing lesions. Appearance of lesions within the lung can be focal, coalescing or cavitary.
Lesions in parietal pleural with adjacent adhesion maybe caused by collapse of large granulomas expelling contents into the adjacent airway in this process referred to as cavitation.

**Diagnosis:**

**Intradermal tuberculin skin test (TST):** Using Mammalian Old Tuberculin (mOT) produced by Symbiotics, Inc. is currently the only USDA approved tuberculin for non-human primates. Intradermal injection of 0.1 ml of MOT using a 26 gauge needle in the palpebrae. In small primates, reduced dose (0.05ml) can be used. Injection sites are observed at 24, 48 and 72 hours post injection for hyperemia, edema, and induration. (Grading systems can be found in the Guidelines for the Prevention and Control of Tuberculosis in Nonhuman Primates). The test is interpreted as positive when palpebral swelling is present in conjunction with droop. A minimum of two weeks should occur between skin tests.

Detection of positive animals is difficult in early infections and in advanced stages of disease animals may be nonresponsive. An immunologically competent animal is required for the test to be effective. False positives may occur due to trauma during administration of antigen or nonspecific response caused by cross reactivity with nonpathogenic *Mycobacteria* or previous exposure to Freund’s Complete adjuvant. A comparative TST - using biologically balanced purified protein derivatives (PPD) of *M. bovis* and of *M. avium* – placed into separate palpebrae or at separate sites on the abdomen is useful in differentiating nonspecific sensitization.

Limitations to testing can be challenged by the quality and purity of the tuberculin injected, skill in administration, thorough recording of bruise or palpebral trauma, visual access in group settings, accurate interpretation at all time periods, inadequate interval between tests or lack of documentation. All of these can jeopardize a surveillance program. Thoracic radiographs facilitate diagnosis in conjunction with additional diagnostics.

**Laboratory testing:** This methodology can augment TST.

**PRIMAGAM** (Prionics USA, Inc.) Cell mediated Immunity IFN-γ assay–fully licensed by USDA in 2007 for *in vitro* testing of cynomologus and Rhesus macaques and tests for *M. tuberculosis*, *M. bovis* and *M. avium*. No antigen is administered to the animals so re-testing can be conducted immediately. Questionable ability to detect latent.


**PrimaTB STAT-PAK Assay** (Chembio Diagnostic Systems, Inc., Medford, NY) which detects IgM and IgG antibodies, rapid (20 minute) lateral flow immunoassay. Licensed by USDA in 2007 for use in nonhuman primates. Advantage test uses serum, plasma or whole blood and requires small quantity (30µl) although interpretation is difficult due color of blood. Test is used to detect *M. tuberculosis* and *M. bovis*. A combination of diagnostic techniques may provide for an improved diagnosis.

**Material required for laboratory analysis:**

**Antemortem:** Polymerase chain reaction (PCR) may be conducted on lesion or granuloma, feces, bronchoalveolar and gastric lavage. Culture and speciation: To optimize isolation of organisms from specimens it is recommended that the samples be centrifuged at 3,500 rpm for 30 minutes in sterile polypropylene conical tubes. Success of isolation is dependent on quality of specimen, appropriate processing and culture techniques in the laboratory. The process requires 4-8 weeks for isolation and longer to speciate. Microbiological staining: Specimens include lesions or granulomas in lymph nodes (i.e., broncho-alveolar) and gastric lavage. Fine needle aspirates, impression smears or tissue suspensions that are air dried in a thin layer on slides that is heat fixed and stained for the appearance of acid fast bacilli.

**Post-mortem:** All primates euthanized or found dead should receive complete necropsies to include gross examination and histological examination of lesions including acid fast stains. PCR, culture and staining for organism: blood, lesion or granuloma, feces, lymph nodes and bronchial or
gastric lavage.

**Products Available:**
- AFB Kinyoun Kit (Polysciences, Inc.): stain of slides for acid-fast bacilli.
- PRIMAGAM (Prionics USA, Inc.): heparinized whole blood
- T-SPOT.TB (Oxford Immunotec, Oxford, UK): heparin PBMCs

**Relevant diagnostic laboratories:**
- National Veterinary Services Laboratories (NVSL)
  1920 Dayton Ave.
  Ames, Iowa 50010
  Provides IFN-γ, Histopathology, Isolation and PCR. NVSL is the reference center for U.S. animal health and contribute to public health by ensuring that timely and accurate laboratory support is provided by their nationwide animal-health diagnostic system.

- PCR-Zoologix Primate Diagnostics
  Zoologix Inc.
  9811 Owensmouth Ave., Suite 4
  Chatsworth CA 91311-3800
  info@zoologix.com

**Treatment:** Isoniazid, ethambutol and rifampin is usual starting point. However, even this combination has limited efficacy and is not recommended for tuberculous animals.

**Prevention and control:** Non-human primate colonies should be maintained closed and have minimal direct contact with public. Establish a routine surveillance program using the skin testing to identify infected animals; additional diagnostics may augment TST. Segregate or cull positive animals during confirmation. Identify designated quarantine area for all new nonhuman primates; hold animals for a minimum of 30 days and retest using TST. Animals of unknown source or high risk animals should be quarantined for longer duration for retest.

**Suggested disinfectant for housing facilities:** All primate primary housing, clinics and caging should incorporate tuberculocidal products. The Environment Protection Agency Antimicrobials Division Test oversees the testing of these products for efficacy. Consideration for product selection will depend on surfaces, caging and equipment needing tuberculocidal products.

**Notification:** USDA

**Measures required under the Animal Disease Surveillance Plan:** None

**Measures required for introducing animals to infected animal:** It is not recommended to introduce new animals to collections holding tuberculous animals.

**Conditions for restoring disease-free status after an outbreak:** Cull all positive animals or treat all extremely valuable animals in isolation. Continue to conduct routine surveillance testing to include TST and other diagnostic testing. Maintain proper PPE and Occupational Health Program for all people in contact with nonhuman primates.

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References: