PHR 420
Zoonoses of Non Human Primates

Tuberculosis
and other mycobacterial zoonoses

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Tuberculosis: Importance

• Tuberculosis is one of the most serious and economically devastating diseases of non-human primates.

• Most cases of tuberculosis in non-human primates are caused by *Mycobacterium tuberculosis* (75%) and *M. bovis* (24%). Infection by *M. africanum* has also been reported from chimpanzees and african green monkeys.

• In the recent years, many reports have been published on *M. avium, M. kansasii, M. scrofulaceum, M. intracellulare* and even *M. paratuberculosis* in monkeys.

• Old World monkeys are usually more susceptible than New World monkeys to tuberculosis. They are also more susceptible to *M. tuberculosis* than *M. bovis*. 
Leprosis and NHP

• 1978, first naturally acquired case of leprosy reported in non-human primates reported in a chimpanzee.

• 1981, case reported in sooty mangabey (Cercocebus atys).

• 1986, second case in a sooty mangabey indicated a monkey-to-monkey transmission of leprosy.

• 1989, leprosy was diagnosed in two male chimpanzees after been held in research facilities in the US for over 25 years.

• 1998 first case of naturally acquired leprosy in a wild-caught cynomolgus macaque from the Philippines.

Leprosis and NHP

• Experimental inoculation of *M. leprae* in mangabeys: resulted in 80% of the monkeys developing leprosy. Rhesus monkeys (*Macaca mulatta*) and African green monkeys (*Cercopithecus aethiops*) also susceptible experimentally.

• Out of 46 Rhesus monkeys inoculated with *M. leprae*, 21 (45.7%) developed leprosy.

• Diagnosis confirmation was based on PCR specific for *M. leprae*.

• No human-to-monkey or monkey-to-human cases have been reported, but the natural susceptibility of non-human primates makes leprosy a potential zoonosis.
The earliest reported observation of tuberculosis in a zoo dates from 1836 in a chimpanzee in the London Zoo. In zoos, the highest incidences of tuberculosis (caused by $M. tuberculosis$ and $M. bovis$) were in zoo primates with losses up to 40% in some collections.

In recently imported monkeys, incidence varied from < 1% to 1.4-6.6% in newly received rhesus monkeys (study done in the early 1970s). Tribe reported an incidence of tuberculosis in newly imported rhesus and baboons of 1/1,000; in Patas 1/2,000. The expected incidence is thus not high.

Nevertheless, even in recent times a number of instances have occurred in which tuberculosis has been introduced to primate colonies, resulting in the destruction of a large number of valuable animals.

### Tuberculosis: Background, Prevalence

<table>
<thead>
<tr>
<th>Mycobacterium species</th>
<th>Primate Species</th>
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<tbody>
<tr>
<td>$M. africanum$</td>
<td>Chimpanzee, African Green Monkey</td>
</tr>
<tr>
<td>$M. tuberculosis$</td>
<td>Spider monkey, Babbon, Orangutan</td>
</tr>
<tr>
<td>$M. bovis$</td>
<td>Rhesus monkey, Dusky langur</td>
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<tr>
<td>$M. gordonae$</td>
<td>Squirrel monkey</td>
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• of 249 shipments of 23,913 NHP imported into the USA from 1990 through 1993 (health records from 18 quarantine facilities), most monkeys were cynomolgus ($M. fascicularis$) monkeys with natural TB infection rate of 0.4% (81/20,580), mainly from Mauritius.
• 9 (0.5%) of 1621 Rhesus monkey ($M. mulatta$) were infected, but none of the 712 imported African green monkeys ($C. aethiops$).
Tuberculosis: Epidemiology

- Primates usually become infected from human contact, often at time of capture.
- In laboratory colonies, the disease usually spreads to monkeys throughout the entire room, if left unchecked.
- Experimentally, the rhesus monkey is very susceptible to infection induced by aerosols. Infected monkeys will transmit the disease to cage mates or monkeys in nearby cages. Aerosolized droplets from a coughing monkey probably are the most common mechanism.
- Fomites, such as cages, thermometers, hypodermic needles and tattoo needles are sources of contamination. Similarly contaminated food represents a source of infection (especially atypical mycobacteria and bovine type), as do bites of cage-mates infected with tuberculosis.

Tuberculosis: Zoonotic aspect

The hazard to people in contact with tuberculous animals is appreciable.
In 1970-1971, CDC estimated the annual rate of tuberculosis infection in individuals having direct contact with non-human primates to be 60 to 100 times that of the population at large.
Tuberculin skin test conversion rates in persons working with tuberculous non-human primates are on the order of 70/10,000 compared to 3/10,000 in the general population (Richardson, 1987).

Pets: case of tuberculosis caused by *M. tuberculosis* in a 3-year-old pet marmoset (*Callithrix jacchus*). Owner had had tuberculosis diagnosed in 1988 in his left lung. At the time of the pet monkey case, he was diagnosed with pulmonary tuberculosis of the right lung. PCR/RFLP revealed a similar pattern for the human and monkey isolates.
• All primates are considered susceptible, but it varies according to the species.

• Clinical signs are very often very discrete.

• Disease, particularly in Old World monkeys, can evolve quickly to death.

• Diagnostic and prevention are not easy and still quite controversial.

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Macaques, especially Rhesus monkeys (*Macaca mulatta*) are very susceptible to tuberculosis. Baboons and apes usually have a slower form of disease, similar to that seen in older rhesus monkeys and people. In rhesus monkeys, clinical signs are minimal or absent until the disease is far advanced.
In Old World monkeys, such as rhesus monkey,
•Clinical signs are minimal or absent until the disease is far advanced.
•usually leads to death in macaques in 4-6 months.
•The most striking signs are often behavioral (psychological changes): weakness, lassitude and reluctance to move. hair rough and dishevelled.
•As the disease progresses, the monkey sits in a crouched position, exhibits little interest in food, tires easily after exercise and has dyspnea. of
•Coughing not an adequate sign, since monkeys frequently cough, especially if infected with lung mites. The infected monkey may lose weight and cutaneous abscesses or enlarged lymph nodes may develop. Diarrhea can occur.

One of the suspicions one can have is the persistence of symptoms despite antimicrobial treatment.

*M. tuberculosis* causes more fulminant disease than *M. bovis* in most non-human primates. However, *M. tuberculosis* is less virulent in baboons and great apes.

In general tuberculosis is less frequent in species originating in Africa and uncommon in species from South America.
Cynomolgus macaques (*M. fascicularis*) infected with low doses of virulent *M. tuberculosis* via bronchoscopic instillation into the lung (Capuano et al., 2003). All monkeys successfully infected. Progression of infection in the 17 monkeys studied was variable. Active-chronic infection, observed in 50 to 60% of monkeys, was characterized by clear signs of infection or disease on serial thoracic radiographs and in other tests and was typified by eventual progression to advanced disease. Approximately 40% of monkeys did not progress to disease in the 15 to 20 months of study, although they were clearly infected initially. These monkeys had clinical characteristics of latent tuberculosis in humans.

Among Old World primates suffering from human-type disease, primary lesions in the lungs occurred in 60% of the cases, in the intestines in 30% and in the throat in 5% of the cases. Four routes of spread were reported: 1) the vascular system and the blood; 2) the lymphatic system; 3) the bronchial tree; 4) contiguity of organs. The most common sequence of generalization was lungs, spleen, liver, kidneys and serous membranes.
Tuberculosis: Lesions

1. Pulmonary origin without alimentary infection:
   a. Early lesions
   b. Advanced lesions
   c. Advanced pulmonary lesions with beginning dissemination by blood stream
   d. Generalized infection spread by the blood-vascular route.
2. Pulmonary origin with secondary alimentary infection from swallowing sputum:
   a. Infection of lungs & intestines without generalization.
   b. Infection of lungs & intestines with generalization (blood stream).
3. Alimentary origin:
   a. Early or primary intestinal lesions.
   b. Later stages of such lesions.
4. Alimentary origin with secondary pulmonary infection.
5. Anomalous cases.

Tuberculosis: Lesions

The lesions are caseous, sometimes with liquefaction, calcification is extremely rare, and giant cells are rather uncommon.
In the lungs, are found large coalescing, caseous tubercles, which lead to consolidation of a great part of the pulmonary tissue, with extensive necrosis and cavitation.

The spleen is invariably affected, being enlarged and containing large tubercles in the pulp.
Infection of the liver is often of miliary type with very small pinhead tubercles, peppered throughout the substance.

Tubercles or tuberculous ulcers may occasionally, but rarely, be found in the bowel wall, perhaps more commonly in New World primates than Old.