Clinical aspects of tuberculosis in nonhuman primates

H. W. Steinmetz1 and C. Wenker2

[1] {Knies Kinderzoo, Rapperswil, Switzerland}
[2] {Zoo Basel, Basel, Switzerland}
Correspondence to: H. W. Steinmetz (hp.steinmetz@knieskinderzoo.ch)

1. Extended abstract

Tuberculosis induced by *Mycobacterium (M.) tuberculosis and M. bovis* is an important zoonotic disease in humans and animals worldwide. In 2010, the tuberculi bacilli caused an estimated 8.5 - 9.2 million cases and 1.2 - 1.5 million deaths in humans (*Global tuberculosis* 13 *control: WHO report 2011*, 2011). Pathology and clinical symptoms can vary between species, and diagnosis is complicated by a wide variety of potential hosts with unspecific clinical signs. Nevertheless, similarities between the pathology of *M. tuberculosis* infection observed in some species, e. g. nonhuman primates and guinea pigs (*Cavia porcellus)*, and the disease process in humans have been detected (Flynn et al., 2003; Kraft et al., 2004; Thoen et al., 2009). For treatment and prevention early diagnosis of infected animals and humans is necessary, but despite enormous efforts to increase sensitivity and specificity of diagnostic methods *ante mortem* recognition and diagnosis of tuberculosis is still challenging.

Humans are the only reservoir hosts of *M. tuberculosis* (Une and Mori, 2007). It is estimated that about one-third of the world's population is infected with tuberculosis (*Global tuberculosis control: WHO report 2011*, 2011). Due to the high infection rate the human to human infection cycle rotates continuously; however, *M. tuberculosis* has a wide host range and has been detected in fish, reptiles, birds, and other mammals. Naturally, humans cause the first contamination of these animals with *M. tuberculosis*, and then infection occurs among animals, which become the source of infection in humans (Une and Mori, 2007). Similarly, in nonhuman primates, transmission occurs primarily from man to monkey followed by monkey to monkey and monkey to man transmission (Michel and Huchzermeyer, 1998). Therefore *M.*

tuberculosis is mainly a disease of captive primates or in situations (e. g. ecotourism for primate watching), where close human-monkey contact is present. Although little evidence exists of *M. tuberculosis* infections in wild populations, it is suspected that with the growing human population and the disappearance of undeveloped wildlife areas, in addition to rescue and rehabilitation projects with potentially infected animals, tuberculosis will pose an increasing risk to native primate populations. Infected primates develop a broad spectrum of disease, and clinical differentiation between *M. tuberculosis* and *M. bovis* is impossible, because both tuberculi bacteria primarily affect the respiratory and digestive tract with almost the same pathology (Isaza, 2003). Infection of nonhuman primates occurs by inhalation of infectious aerosols or ingestion of contaminated food items (Sapolsky and Else, 1987). In addition, it is important to emphasize that early clinical signs are only rarely apparent in wild animals. Therefore it is not surprising that textbook literature on tuberculosis in nonhuman primates lists various different unspecific clinical signs such as behavioral changes, anorexia, lethargy, sudden death in good condition, respiratory disease, diarrhea, enlarged lymph nodes, ulceration of the skin, paralysis of hind limbs, palpable splenomegaly, and hepatomegaly. Approximately 90 % of human *M. tuberculosis* infections are clinically latent (Ulrichs et al., 2005). A short review of the literature over the last 20 years revealed similar results for nonhuman primates in that 80 % of confirmed *M. tuberculosis* infections were clinically inapparent. Infections were mostly detected during routine screening with additional diagnostics, e. g. radiology, intracutaneous TB tests, or during pathology. Nevertheless, detection of both active and latent infections is essential for prevention.

Any primate is susceptible, although Asian Old World monkeys seem to be most susceptible; especially rhesus macaques are affected by a short, severe illness with survival times of less than 1 year (Isaza, 2003). Apes and African monkeys are intermediately susceptible, while New World monkeys and prosimians have shown to be relatively resistant (Isaza, 2003). An exception is the African green monkey (*Chlorocebus aethiops*), which seems to be very sensitive to *M. tuberculosis* developing a rapidly progressive disease (Lyashchenko et al., 2007).

2. Conclusion

Despite recent progress in the accuracy of diagnostic imaging and laboratory methods to prove tuberculosis infection, *ante mortem* detection of tuberculosis is still

challenging. Latent infections and very vague clinical signs that are present only in the late disease process make additional disease investigations necessary. Tuberculosis prevention and surveillance of a captive primate population should include a thorough population health management plan with routine and regular screening for tuberculosis (Bushmitz et al., 2009; Lerche et al., 2008). The health program should be based on a variety of tests and should never rely on a single test result only. Regular clinical examinations with pulmonary diagnostic imaging (e. g. radiology, computer tomography, magnetic resonance imaging), bacterial culture (e. g. tracheal wash, gastric lavage), cell mediated (e. g. intradermal skin test, γ-interferon) and immunologic tests (e.g. ELISA, MAPIA) besides biologic sample storage and *post mortem* examinations are recommended.

3. References

Bushmitz, M., Lécu, A., Verreck, F., Preussing, E., Rensing, S., and Mätz-Rensing, K.: Guidelines for the prevention and control of tuberculosis in non-human primates: recommendations of the European Primate Veterinary Association Working Group on Tuberculosis. J. Med. Primatol., 38(1), 59-69, 2009.

Flynn, J. L., Capuano, S. V., Croix, D., Pawar, S., Myers, A., Zinovik, A., et al: Non-human primates: a model for tuberculosis research. Tuberculosis (Edinb), 83(1-3), 116-118, 2003.

Global tuberculosis control: WHO report 2011, Geneva: World Health Organisation, 2011.

Isaza, R.: Tuberculosis in all taxa. In M. E. Fowler, and R. E. Miller (Eds.), Zoo and wild animal medicine (5th ed., pp. 689-696). Pennsylvania: W. B. Saunders, 2003.

Kraft, S. L., Dailey, D., Kovach, M., Stasiak, K. L., Bennett, J., McFarland, C. T., et al.: Magnetic resonance imaging of pulmonary lesions in guinea pigs infected with Mycobacterium tuberculosis. Infect. Immun, 72(10), 5963-5971, 2004.

Lerche, N. W., Yee, J. L., Capuano, S. V., and Flynn, J. L.: New approaches to tuberculosis surveillance in nonhuman primates. ILAR J, 49(2), 170-178, 2008.

Lyashchenko, K. P., Greenwald, R., Esfandiari, J., Greenwald, D., Nacy, C. A., Gibson, S., et al: PrimaTB STAT-PAK assay, a novel, rapid lateral-flow test for tuberculosis in nonhuman primates. Clin. Vaccine Immunol., 14(9), 1158-1164, 2007.

Michel, A. L., and Huchzermeyer, H. F.: The zoonotic importance of Mycobacterium tuberculosis: transmission from human to monkey. J. S. Afr. Vet. Assoc., 69(2), 64-65, 1998.
Sapolsky, R. M., and Else, J. G.: Bovine tuberculosis in a wild baboon population: epidemiological aspects. J. Med. Primatol., 16(4), 229-235, 1987.
Thoen, C. O., Lobue, P. A., Enarson, D. A., Kaneene, J. B., and de Kantor, I. N.: Tuberculosis: a re-emerging disease in animals and humans. Vet. Ital., 45(1), 135-181, 2009.
Ulrichs, T., Kosmiadi, G. A., Jorg, S., Pradl, L., Titukhina, M., Mishenko, V., et al.: Differential organization of the local immune response in patients with active cavitary tuberculosis or with nonprogressive tuberculoma. J. Infect. Dis., 192(1), 89-97, 2005.
Une, Y. and Mori, T.: Tuberculosis as a zoonosis from a veterinary perspective. Comp. Immunol. Microbiol. Infect. Dis., 30(5-6), 415-425, 2007.