CHAPTER 3.10.5.

# ZOONOSES TRANSMISSIBLE FROM NON-HUMAN PRIMATES


## SUMMARY

*The* Terrestrial Animal Health Code (*chapter 6.12*) *requires tests for certain diseases in non-human primates imported for research, educational or breeding purposes. This chapter indicates where to find further information on such tests. It is important to recognise that primate species represent a significant risk of pathogen transmission to humans in contact, including the collection of samples for laboratory testing, and the handling of those samples in the laboratory. Veterinary laboratories should seek advice from medical authorities on the appropriate health protocols that should be followed by staff handling such materials. All laboratory manipulations with live cultures or potentially infected or contaminated material must be performed at an appropriate biosafety and containment level determined by biorisk analysis* (*Chapter 1.1.4* Biosafety and biosecurity: Standard for managing biological risk in the veterinary laboratory and animal facilities)*.*

*In addition to the specific tests required by the WOAH* Terrestrial Code *as detailed below, additional information on the health monitoring of non-human primate colonies, including a list of potential zoonotic diseases and the types of tests used for diagnosis, is provided by the Federation of European Laboratory Animal Science Associations* (*FELASA*) (*Balansard* et al., *2019*) *and also by the Committee on Occupational Health and Safety in the Care and Use of Nonhuman Primates* (*2003*)[1].


## 1. Tuberculosis

The test procedures and preparation of reagents are described in Chapter 3.1.13 *Mammalian tuberculosis* (*infection with* Mycobacterium tuberculosis *complex*)*.* The delayed hypersensitivity skin test in non-human primates is usually carried out by the intradermal injection of at least 1500 units (0.1 ml) of undiluted "mammalian old tuberculin"[2] into the edge of the upper eyelid using a sterile 25–27 gauge needle. Tuberculins prepared for use in humans are not of sufficient potency to elicit a response in non-human primates. Purified protein derivatives (PPD) as described in chapter 3.1.13 may also be used, but are generally considered less sensitive for non-human primates. The animal must be suitably restrained or drug-immobilised. For smaller species such as marmosets, tamarins or small prosimians the test can be carried out in the abdominal skin, but this approach requires handling of animals multiple times. A repeat test by the abdominal route may be used in cases where the palpebral reaction is difficult to interpret. False positive and false negative reactions can occur with the tuberculin skin test (Miller, 2008), but nonspecific responses to tuberculin are more common than either a false positive or a false negative response. Nonspecific responses are usually caused by immunological sensitisation to non-pathogenic *Mycobacteria*, often environmental saprophytes, that result in cross reaction to antigens common to both pathogenic and non-pathogenic *Mycobacteria*. Clarification of false positive, false negative, and nonspecific responses can sometimes be done by a battery of testing including *Mycobacterial* culture of faeces, tracheal, bronchial or gastric lavage fluids; radiography to detect tuberculous lesions; haematology and biochemical screens and culture or polymerase chain reaction (PCR) assay of tissue biopsies. Immunological tests can also be used, amongst which the interferon gamma release assay is most widely accepted for verification of the tuberculin test. The combination of a tuberculin test with confirmation by interferon gamma production would be reasonable first steps for screening. However, in species for which little is known about the immunological responses to *Mycobacterial* infection and for which these

1 http://www.nap.edu/catalog/10713.html

2 Mammalian old tuberculin is available from the Colorado Serum Company, 4950 York St, P.O. Box 16428, Denver, Colorado 80216-0428, United States of America.

tests have not been validated, it can be difficult despite battery testing to determine with confidence the tuberculosis status of a non-human primate.

## 2. Enteric bacteria (*Salmonella, Shigella* and *Yersinia*)

These organisms can be detected by standard bacteriological culture methods on samples of fresh faeces or rectal swabs. Culture techniques for *Salmonella* are described in Chapter 3.10.3 *Salmonellosis.* Methods for the collection, transport and processing of faecal samples are described by WHO (2003). Methods for culture of *Shigella* are described in Appendix 9. Commercial panels of PCR reagents covering the main pathogens are also available for screening faecal samples.

Enteric species of *Yersinia* include *Y. enterocolitica* and *Y. pseudotuberculosis.* Culture and enrichment are more effective if carried out at lower temperatures (4°C rather than 25°C). Details of culture methods including suitable enrichment media are described by Laukanen *et al.* (2010) and Arrausi-Subiza *et al.* (2014). The latter also describe real-time PCR methods for the identification of culture isolates. A general overview of *Y. enterocolitica* and *Y. pseudotuberculosis* is given by Fredriksson-Ahomaa *et al.* (2007), including biochemical methods for the identification of culture isolates.

## 3. Hepatitis B

Hepatitis B virus (HBV) is classified in the family *Hepadnaviridae*, and is associated with severe disease in humans, where infection is widespread. Although other hepadnaviruses have been identified, and chimpanzees, gorillas, orang-utans, gibbons and woolly monkeys carry similar viruses to those from humans, transmission to humans has not been reported.

## 4. Macacine herpesvirus 1 (Simian herpes B virus, Cercopithecine herpesvirus 1)

Macacine herpesvirus affects macaques (*Macaca* spp.) and is associated with fatal laboratory infection of humans. It is lethal to some other Old World species, such as colobus, patas and De Brazza's monkeys (Elmore & Eberle, 2008). The situation in New World monkeys is unclear, since human herpesvirus can be lethal for marmosets, but capuchins may be infected with macacine herpesvirus by contact with macaques without developing lethal infection (Coulibaly *et al.,* 2004; Huemer *et al.,* 2002). Non-human primates that have been in contact with macaques may therefore pose a risk of human infection from macacine herpesvirus. Diagnosis is best done by serology with recombinant macacine herpesvirus antigens (Elmore & Eberle, 2008). PCR has not found widespread use for identification of Macacine herpesvirus 1 infected macaques as only those monkeys actually shedding virus at the time of sampling would test positive; latently infected animals not actively shedding virus would not test positive (Eberle & Jones-Engel, 2017). Specified pathogen free colonies of macaques without macacine herpesvirus are being developed.

## 5. Simian retroviruses

These include simian immunodeficiency virus (SIV), simian type D retrovirus (SRV), simian T-lymphotropic virus, simian foamy virus and gibbon ape leukaemia virus. They pose a potential risk to humans. Diagnostic procedures for infections in non-human primates rely on serology, virus isolation and PCR. See Murphy & Switzer (2008).

## 6. Endo- and ectoparasites

Non-human primates should be screened during quarantine for the presence of parasites by standard parasitological techniques, according to the parasite under investigation. Methods for these tests may be found in standard parasitological textbooks (Cogswell, 2007; Smith *et al.,* 2007).

## 7. Other zoonotic pathogens

As well as those infections and infestations referred to above, there is a long list of zoonotic agents that may be carried by various species of non-human primate. Given the close phylogenetic relationship between humans and other primates it must be assumed that most pathogens can transmit zoonotically. Further details including the likely host species, and a suitable regimen for health monitoring in primate colonies, are given in Balansard *et al.,* 2019). The following table is derived from that publication, but is not exhaustive.

Table 1 should be interpreted in context, taking into account the species of primate, its origin (captive bred or wild caught) and its housing. Animals held in cages where they can come into contact with other species or their excreta can acquire infections from one group to the next, which may be subclinical but would cause an infection risk if they were transferred to another room or centre. Wild-caught animals may harbour additional conditions e.g. yaws (*Treponema pallidum*), depending on their origin. Not all pathogens are relevant: wild caught macaques (and most captive bred ones) are a risk for macacine herpesvirus, but this is NOT a risk for other species that have not been in direct contact with macaques so testing would be pointless and unnecessary. Similarly, based on current research, Marburg virus is a risk in wild-caught African non-human primates, and is unlikely to present a risk to New World primates (but it can infect humans). Yellow fever is unlikely to be a risk in primates of Asian origin, but it can infect humans. An individual risk assessment should be made for each case, and screening applied accordingly. Similarly, when screening animals for infection prior to transferring them to another room, centre or back to the wild, a risk assessment should be made on relevant pathogens for the species and any additional risks from the environment in which they were held. Animals exposed to antibiotics repeatedly, or multi-resistant pathogens during their captivity, may also pose a risk for infecting other colonies and human contacts. In addition, the anthropozoonotic potential for humans to transmit pathogens to non-human primates should be considered.

***Table 1. Microorganisms and parasites of current concern in non-human primates***

| **(1) Viruses** |
|---|
| Adenoviruses |
| Ebola virus |
| Foamy virus |
| Hepatitis A virus |
| Hepatitis B virus |
| *Herpes T, Herpesvirus platyrrhinae, Saimiriine herpesvirus 1* |
| *Herpesvirus cercopithecus*, (SA 8), *Cercopithecine herpesvirus 2* |
| *Herpesvirus saimiri, Saimiriine herpèsvirus 2* |
| Lyssa virus (rabies) |
| Macacine herpesvirus (formerly B virus, *Herpesvirus simiae*, Cercopithecine herpesvirus 1) |
| Marburg virus |
| Monkeypox virus |
| Papiine herpesvirus 2 (formerly *Cercopithecine herpesvirus 16*) |
| Simian haemorrhagic fever virus |
| Simian immunodeficiency virus (SIV) |
| Simian retroviruses or<br>Simian betaretroviruses (formerly Simian retrovirus, type D (SRV) |
| Simian T-cell lymphotropic virus-1 (STLV-1) |
| SV 40 |
| West Nile virus |
| Yellow fever virus |
| Zika virus |

*Table 1.* (*cont.*) *Microorganisms and parasites of current concern in non-human primates*

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|---|
| **(2) Bacteria** |
| *Burkholderia pseudomallei* |
| *Campylobacter fetus* |
| *Campylobacter jejuni* |
| *Leptospira interrogans* (various serovars) |
| *Mycobacterium africanum* |
| *Mycobacterium bovis* |
| *Mycobacterium tuberculosis* |
| *Salmonella enteritidis* |
| *Salmonella typhimurium* |
| *Shigella flexneri* |
| *Yersinia pseudotuberculosis* |
| **(3) Parasites** |
| Ectoparasites:<br>• Mites<br>• Lice<br>• Ticks |
| *Entamoeba histolytica* |
| *Giardia* spp. |
| *Plasmodia malariae, vivax* |
| *Plasmodium brasilianum* |
| *Plasmodium cynomolgi* |
| *Plasmodium* species |
| *Pneumonyssus simicola* |
| *Prosthenorchis elegans* |
| *Strongyloides stercoralis* |
| *Toxoplasma gondii* |
| *Trichuris* |
| **(4) Dermatomycosis** |
| *Trichophyton* |

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**NB**: FIRST ADOPTED IN 2008. MOST RECENT UPDATES ADOPTED IN 2021