



Date: July 24, 2023

To: National Association of State Public Health Veterinarians

**From: Division of Global Migration and Quarantine
Centers for Disease Control and Prevention**

Subject: Tuberculosis in Imported Nonhuman Primates

Dear Colleague:

Due to recent cases of [tuberculosis](#) (TB) in imported nonhuman primates (NHP), the Centers for Disease Control and Prevention's Division of Global Migration and Quarantine (CDC DGMQ) is providing information, including the attached fact sheet, to stakeholders who may have occupational exposure to imported NHP.

CDC requires all imported NHP to be quarantined for a minimum of 31 days upon entry to the United States, during which time they are monitored for signs of illness and tested for TB infection. Imported NHP must undergo at least three tuberculin skin tests (TST) at minimum two-week intervals, all of which must be negative before the NHP can be released from quarantine. During CDC-mandated quarantine, controls are in place to protect workers from exposure to TB. NHP must be housed in negative pressure rooms. Personnel must wear, at minimum, NIOSH-approved N95 respirators while working in animal rooms, as part of an Occupational Safety and Health Administration (OSHA)-compliant Respiratory Protection Program ([29 CFR 1910.134](#)) that includes medical evaluation, training, and fit testing. CDC also requires personnel working in NHP quarantine facilities to be evaluated for TB on a regular basis.

Since 2021, CDC has noted an increase in the rate of positive TST reactions and culture-confirmed *Mycobacterium tuberculosis* complex (MTBC) disease in imported NHP during CDC-mandated quarantine. From 2013 to 2020, there were no reported cases of MTBC in imported NHP during the CDC-mandated quarantine period. In 2021 and 2022, 0.02% and 0.03%, respectively, of total imported NHP were identified as MTBC culture positive during quarantine. From January 1, 2023 to June 30, 2023, 0.2% of NHP imported had culture-confirmed TB during quarantine*. All MTBC-positive NHP identified during CDC-mandated quarantine were captive-bred cynomolgus macaques (*Macaca fascicularis*) from Southeast Asia. None demonstrated obvious clinical signs of disease. In most cases, MTBC was isolated from lung lesions and tracheobronchial lymph nodes; less common sites of infection included liver, spleen, and peripancreatic lymph nodes.

While the majority of imported NHP with TB infection were identified and euthanized during CDC-mandated quarantine, some were detected after NHP had been released from quarantine. Infected NHP identified post-quarantine included cynomolgus macaques (*Macaca fascicularis*) imported from Mauritius and Southeast Asia between 2020 and 2022. These cases were identified 5 months to 2 years

* From January 1, 2013 to December 31, 2020, the number of NHP imported to the United States was 215,228. In 2021, the number imported was 32,276. In 2022, the number imported was 29,667. From January 1, 2023 to June 30, 2023, the number of NHP imported to the United States was 8,025.

after NHP were released from quarantine and had epidemiologic links to other TB cases in imported NHP.

MTBC species isolated from imported NHP during and after CDC-mandated quarantine included *M. bovis*, *M. caprae*, *M. orygis*, and *M. tuberculosis*.

Institutions receiving imported NHP after quarantine may not implement the same level of controls to reduce the risk of TB transmission as do quarantine facilities. Employers should inform employees who have occupational exposure to NHP of the increased TB prevalence and limitations of available tests for detecting TB infection in imported NHP; employers should ensure appropriate exposure controls are in place. Procedures to decrease the risk of introduction and spread of TB in NHP colonies and workers in NHP facilities are listed below.

- *CDC-Registered NHP Importers*
 - Ensure all personnel or contractors having occupational exposure to imported NHP, including those involved in transport (air and ground transport) or offloading of NHP crates from aircraft at ports of entry:
 - Are informed about associated zoonotic disease hazards, including TB
 - Strictly adhere to your CDC-approved standard operating procedures (SOPs) for worker protection during quarantine
 - Participate in an Occupational Safety and Health Administration (OSHA)-compliant Respiratory Protection Program (29 CFR 1910.134) that includes medical evaluation, training, and fit testing
 - Ensure that quarantine facility personnel have a baseline evaluation for TB prior to working with NHP and an evaluation at least annually thereafter. CDC also recommends that contracted personnel involved in the transport of imported NHP undergo regular TB testing in consultation with an occupational healthcare provider.
 - If an NHP is found to have culture-confirmed TB, ensure that workers who had previously entered the room where the NHP was housed promptly undergo post-exposure TB evaluation, and report results to CDC in accordance with 42 CFR 71.53(i)(7)(iii).
 - Use enhanced biosafety measures (e.g., powered air purifying respirator, biosafety cabinet, downdraft table) during necropsy of NHP when TB is suspected.
 - For TST reactors that die or are euthanized in quarantine, submit fresh tissue specimens, including lung, tracheobronchial lymph node, spleen, liver, and granulomas found at necropsy, to the US Department of Agriculture (USDA) [National Veterinary Services Laboratory](#) for MTBC PCR, mycobacterial culture, and whole genome sequencing.
 - For non-TST reactors, or animals that have not yet been tested, that die or are euthanized in quarantine, submit granulomas found at necropsy to the [USDA National Veterinary Services Laboratory](#) for MTBC PCR, mycobacterial culture, and whole genome sequencing.
 - Within 24 hours, report any positive or suspicious TST¹, necropsy findings, or laboratory results to CDC Division of Global Migration and Quarantine (DGMQ) by emailing nhpimporters@cdc.gov. Report TB-culture positive NHP to state and local [animal](#) and [public health](#) officials.
 - Inform recipients of NHP that were imported and quarantined with TB-culture positive NHP of the risk of exposure, the potential for prolonged TB incubation period, and that

negative TB infection test results do not completely rule out the possibility of animals developing TB after quarantine.

- *Recipients of imported NHP that have cleared the CDC-mandated quarantine period (e.g., researchers, zoos)*
 - Follow established guidelines and state and local regulations for quarantine of newly acquired NHP and regular TB testing in maintenance colonies^{2,3}.
 - Develop occupational health and safety protocols that address:
 - Wearing a NIOSH-approved N95 respirator or higher-level respirator while working in rooms housing NHP, as part of an OSHA-compliant Respiratory Protection Program ([29 CFR 1910.134](#)) that includes medical evaluation, training, and fit testing
 - Baseline evaluations for TB prior to working with NHP and subsequent evaluations, preferably at least annually, for personnel with occupational exposure to NHP
 - Submit NHP diagnostic specimens to the [USDA National Veterinary Services Laboratory](#) for MTBC PCR, mycobacterial culture, and whole genome sequencing.
 - Report TB-culture-positive NHP to state and local [animal](#) and [public health](#) officials.
 - Refer personnel who were exposed to infected NHP, test positive for TB infection, or develop symptoms of TB disease, to a healthcare provider for medical evaluation. The local public health department should be notified immediately if TB disease is diagnosed.

Additional Information:

TB is caused by infection with bacteria in the MTBC, which includes *M. tuberculosis*, *M. bovis*, *M. caprae*, *M. orygis*, *M. africanum*, *M. pinnipedii*, *M. canettii*, *M. microti*, and *M. mungi*. While each species within the MTBC is adapted to a particular host or group of hosts, any species can infect any susceptible host. People and all species of NHP are susceptible to TB infection, which is spread primarily through respiratory droplets in the air. Although less common, TB transmission through ingestion, direct contact, and contact with fomites (e.g., thermometers and tattoo needles) has been documented in NHP⁴.

Because TB is more common in captive NHP than in wild NHP, it is thought that TB is likely introduced to captive NHP from people. Once TB is introduced to an NHP colony, it can spread between NHP and back to people. In 2020, around the start of the COVID-19 pandemic, the primary supply of NHP imported to the United States shifted from China to countries in Southeast Asia where the World Health Organization estimates the TB incidence in people to be higher than in China⁵.

In both humans and NHP, TB infection can remain latent or progress to TB disease. In humans, progression to disease is often associated with an immune compromising condition. In NHP, the triggers that result in progression from latent TB infection (LTBI) to TB disease are not well understood⁶.

People with TB disease typically experience symptoms including cough, weight loss, loss of appetite, and fever. Those with pulmonary or laryngeal disease are infectious to others. However, NHP with TB disease may not demonstrate obvious signs of illness for weeks to months, during which time they can shed infectious organisms, posing a risk to other NHP and human caregivers⁷.

Both LTBI and TB disease can be treated with antimicrobial medications. Without proper treatment, TB disease can be fatal. In people, treatment typically involves the administration of multiple drugs for

several months⁸. In NHP, multiple drug regimens administered for up to a year have been recommended, but ideally the NHP should be isolated during this time⁴. Isolating and treating NHP with multiple drugs for an extended period of time can be logistically challenging. Additionally, confirming that TB has completely resolved in NHP following treatment may be difficult. For these reasons, as well as associated public health risks, treatment is rarely considered except for endangered or threatened species in zoo collections. Alternatively, euthanasia of infected NHP may be considered.

Detecting TB infection in NHP can be challenging. The mainstay of detection of TB infection in live NHP is the tuberculin skin test (TST) using mammalian old tuberculin (MOT). The TST can give false positive and false negative results. There are numerous reasons that an NHP with TB infection could have a false negative TST, including recent infection, advanced infection, latent infection, concomitant viral infection, recent vaccination with a modified-live vaccine, and recent administration of medications that affect the immune system. Other diagnostic tests include interferon-gamma release and serological assays; however, the TST is currently the only validated, USDA-approved test for TB detection in live NHP in the United States⁶. The gold standard for TB diagnosis in NHP is isolation of MTBC from clinical specimens. Collection of specimens for culture from live NHP requires relatively invasive procedures such as bronchoalveolar and gastric lavage, but unless the infected NHP is actively shedding the agent at the time of sampling, culture will be negative. During CDC-mandated quarantine, culture is generally performed using tissue samples that are collected during necropsy of animals that died during quarantine or were euthanized due to a TST reaction. *Mycobacterium* organisms grow slowly, so it may take 8 weeks or more before a diagnosis of TB can be confirmed by culture. A direct PCR test for MTBC is a faster diagnostic test that is available through the USDA National Veterinary Services Laboratory; however, this test has not been validated for NHP, and sensitivity and specificity are unknown.

Resources:

- [Tuberculosis \(TB\) | CDC](#)
- [Questions and Answers | Pamphlets, Brochures, Booklets | Publications & Products | TB | CDC](#)
- [Monkeys | Bringing an Animal into U.S. | Importation | CDC](#)

References:

1. Bennett, B., Abee, C. & Henrickson, R. *Nonhuman Primates in Biomedical Research*. (1998).
2. Institute of Laboratory Animal Resources (ILAR). Laboratory Animal Management: Nonhuman Primates. Available as a publication from ILAR, NRC. ILAR News. Institute of Laboratory Animal Resources (ILAR). Laboratory Animal Management: Nonhuman Primates.
3. *Guide for the Care and Use of Laboratory Animals. Guide for the Care and Use of Laboratory Animals* (National Academies Press, 2011). doi:10.17226/12910.
4. Simmons, J. & Gibson, S. Bacterial and Mycotic Diseases of Nonhuman Primates. in *Nonhuman Primates in Biomedical Research* (eds. Christian, R., Abee, K., Tardif, M. & Morris, T.) 105–172 (Academic Press).
5. World Health Organization. Global tuberculosis report 2022. <https://www.who.int/publications/i/item/9789240061729>.
6. Yee, J. L. *et al.* Tuberculosis detection in nonhuman primates is enhanced by use of testing algorithms that include an interferon- γ release assay. *Am. J. Vet. Res.* **83**, 15–22 (2022).
7. Lerche, N. W., Yee, J. A. L., Capuano, S. V. & Flynn, J. L. New approaches to tuberculosis surveillance in nonhuman primates. *ILAR Journal* vol. 49 170–178 (2008).
8. CDC. Treatment for Latent TB Infection and TB Disease. available at <https://www.cdc.gov/tb/topic/treatment/default.htm>.