Johns Hopkins University
Animal Care and Use Committee

Preventing and Responding to B-Virus Exposures in Animal Care and Research Personnel Handling Macaques

PURPOSE: This standard operating procedure (SOP) establishes macaque handling requirements that are designed to (1) assist members of the JHU community understand the health risks posed by macaque monkeys, (2) outline practices that will protect an individual from contact with macaque fluids that contain the potentially deadly B virus, and (3) provide specific information on steps to take if fluid contact occurs or is suspected.[1]

BACKGROUND: Nonhuman primates of all types can harbor diseases that are infectious for personnel handling these animals, but the risk of human infection with B virus from macaque monkeys (e.g., *Macaca mulatta*, *M. nemestrina* or *M. fascicularis*) is particularly threatening due to the high morbidity and mortality it can produce in exposed untreated humans. Thus it is important that all who work with or around macaques are familiar with information about the transmission of this infection and the methods for protection against it.

B-virus is enzootic in the rhesus, pig-tail, cynomolgus and other Asiatic monkeys of the genus *Macaca*. This means that the risk is present even in animals that have completed a quarantine period following arrival at the institution. The clinical detection of B-virus infection in these animals is difficult because, as with human oral herpes infection, infected animals are frequently asymptomatic and occasional false negative results do occur in the serological monitoring of B-virus-infected macaques. Even when a negative test has previously been obtained, no macaque should be regarded as non-infectious. Re-activation of infection under spontaneous or stress-induced conditions with viral shedding in the saliva, tears, and genital fluids has been documented. Thus when a person is exposed to fluids from a macaque, it is essential to test the animal to determine its status at that time.

Personnel are at risk of contracting infection both through direct contact with infected macaques as well as by indirect contact with environmental sources contaminated by virus. Of the approximately 50 cases of B virus infection in humans, 26 have been well documented. As

[1] The information in this document is consistent with and/or derived from (1) Jeffrey I. Cohen, David S. Davenport, John A. Stewart, Scott Deitchman, Julia K. Hilliard, Louisa E. Chapman, and the B Virus Working Group, "Recommendations for the Prevention of and Therapy for Exposure to B-Virus (*Cercopithecine herpesvirus* 1), *Clinical Infectious Diseases* 35: 1191-203, 2002. and (2) National Research Council, *Occupational Health and Safety in the Care and Use of Nonhuman Primates*, The National Academies Press, Washington, D.C., 2003.

described in Cohen et al. (footnote 1), most cases resulted from direct inoculation by macaque bites (10 cases), and 2 cases each resulted from monkey scratches, possible aerosol, or scratch from a cage in which a macaque had been housed. Any exposure of broken skin or mucous membrane to potentially contaminated secretions or material places the individual at risk of infection. Although frequency of infection may be relatively low compared to frequency of contact with macaques, the mortality rate has been about 80%, which is why protection and appropriate treatment if exposed is so critical.

All macaques used for research at Johns Hopkins are serologically tested for a number of viral agents including B-virus. Rhesus and pigtailed macaques from the Johns Hopkins University Research Farm colonies are serologically negative for B-virus. Whenever possible, Research Animal Resources (RAR) will supply B-virus serologically negative macaques from its own colony or from outside sources. Animals serologically positive for B-virus will be used only when similar negative animals are not available.

None of the negative B-virus macaques from the colony at the Farm have seroconverted (i.e., from negative to positive). Due, however, to the possibility of false negative B virus status of laboratory macaques and the severe consequences of B virus infection, all macaque monkeys must be regarded as potentially infected with B virus and are considered capable of transmitting the infection regardless of their colony of origin or prior testing results for this agent.

The following policies and practices apply to the handling and housing of macaques at JHU:

1. Areas where macaques are maintained or used must have limited access to ensure that only workers who are properly trained in the procedures to avoid risk of infection or those who are accompanied by such workers may enter.
2. Personnel must be cognizant of the importance of adhering to established traffic patterns (i.e., working with negative first, positive last) when macaques are segregated into B-virus infection positive and negative housing areas. Signage will be used to identify monkey's that have tested serologically positive for B-virus. Once a positive test is obtained, the sign will not be changed even the monkey tests negative at a later date.
3. Cages and other equipment used for macaque housing or procedures should be considered contaminated with infectious B-virus. This equipment should be designed and maintained to prevent personnel injury from sharp edges or corners and be arranged in the animal housing area to minimize the risk of workers being accidentally grabbed or scratched by the animals.
4. The publication "Occupational Health and Safety in the Care and Use of Nonhuman Primates" (see footnote 1) provides a checklist (p. 113) for choice and use of personal protective equipment (PPE) in working with nonhuman primates. The selection of appropriate PPE is to be based on "hazard identification, assessment of risks associated with specific tasks, and the level of training of individual workers." Given the various types of activity in which faculty, staff, and trainees may be in the proximity of macaques, Table 1 provides the minimum level of PPE for a range of activities (table adapted from NIH Policy Manual 3044-2).

Requirements for handling potential exposures to macaque secretions:

1. Bites and scratches incurred from macaques or injuries from equipment contaminated with macaque secretions that result in bleeding must be handled urgently according to the instructions given in the **Monkey Splash/Injury Kit Instructions**. These incidents must be immediately referred to **5-STIX (410-955-7849).**
2. Any skin lesions or neurological symptoms (such as itching, pain or numbness) that occur near the site of the wound and any illness following the original assessment of the injury must be reported immediately to the supervisor and the Occupational Injury Clinic (locations provided below).
3. Because B virus infections have occurred in animal caretakers who had no recall of an obvious exposure, workers must be made aware that any prolonged fever (>48 hours), flu-like symptoms or symptoms compatible with B virus infection should be reported to their supervisor and to the Occupational Injury Clinic.
4. Personnel in the Occupational Injury Clinic will be responsible for monitoring the clinical status of the individual at appropriate intervals as per the most current clinical guidance for macaque secretion exposures.
5. JHU Policy is that prophylactic treatment with an antiviral agent be administered until a second serum sample comes back negative. Otherwise, handling of the clinical monitoring and post-exposure prophylaxis for persons potentially exposed to B virus will be according to currently recommended best practices (e.g., per B Virus Research and Resource Laboratory, Georgia State University; cf., Cohen et al., footnote 1).

Table 1

Protective Clothing Requirements for a Range of Activities with or near Macaques

ACTIVITY	REQUIREMENTS
View animals in the primate room. No contact with the animals or the cages	Mucous membrane protection as appropriate* and street clothes covering.
Contact with a restraint device (e.g., chair or transfer cage) holding an awake animal.	Mucous membrane protection as appropriate,* street clothes covering and light gloves.**
Transfer of an alert monkey using a stand-off method, such as pole/collar technique or transfer cage	Mucous membrane protection as appropriate*, street clothes covering and light gloves.**
Handling (e.g., hand catching or restraining) of an alert monkey.	Mucous membrane protection as appropriate for this high risk situation,* street clothes covering, and arm-length bite-protection gloves.

Physical contact with an anesthetized monkey.	Mucous membrane protection as appropriate,* street clothes covering and light gloves.**
Physical contact with restrained alert monkey.	Mucous membrane protection as appropriate,* street clothes covering and light gloves.**
Physical contact with infant monkeys.	Mucous membrane protection as appropriate,* street clothes covering and light gloves.** As infants mature, heavier gloves may be required.
Handling/moving and/or cleaning cages or pans.	Mucous membrane protection appropriate for high risk situations,* dedicated clothing, dedicated shoes, and appropriate gloves as determined by Research Animal Resources.
Perform portions of experiments that involve only handling tissues or biological materials in a laboratory.	Lab coat and light gloves.** Wear eye/face protection for any manipulation that could involve a splash or spray.

Note: This table has been adapted from NIH Policy Manual Section 3044-2.

* Mucous membrane protection should be appropriate to the potential for splash hazard in the course of the course of the listed activity.

**Light gloves means gloves that are vinyl, latex, nitrile, or similar material.

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