

III-17. NONHUMAN PRIMATE BODY FLUID EXPOSURE

- I. Purpose
 - A. To reduce the risk of infection following exposure to nonhuman primate (NHP) body fluids.
 - B. To utilize information from these injuries to enhance worker safety.
- II. Relevant Occupational Medical Service (OMS) Procedure Manual Sections
 - A. Occupational Injury and Illness. Chapter III Section 18
 - B. Wound Care Guidelines. Chapter III Section 32
 - C. Animal Exposure Program. Chapter IV Section 1
 - D. Retrovirus Exposure. Chapter III Section 24
- III. Attachments
 - A. Information and Specimens Requested Following an Exposure to a NHP Body Fluid. [Attachment I](#)
 - B. B Virus Backgrounder. [Attachment II](#)
 - C. B Virus Wallet Card. [Attachment III](#)
- IV. Background
 - A. The significance of an injury involving NHP body fluid depends, among other things, upon the type of NHP, the body fluid, and the route of exposure. The following is a brief description of some viruses found in NHP body fluids, how they are transmitted to humans and the significance of the resulting infection.
 - B. Rhesus, cynomolgus, pig-tail and stump-tail NHPs and other macaques may be infected with B virus (*Macacine herpesvirus 1*, formerly *Cercopithecine herpesvirus 1* [CHV-1]), or simian type D retrovirus serotypes (SRVs). In addition, these NHPs can be experimentally infected with simian/human immunodeficiency virus (SHIV).
 1. B virus
 - a. Like herpes simplex virus (HSV) infections in humans, B virus may persist in the NHP's sensory ganglia and be shed periodically in oral, ocular, or genital secretions. Usually viral shedding occurs without any clinical findings. Two percent of NHPs infected with B virus are likely to shed on any given day. This percentage will rise, if the infected NHP's immune system is compromised or if the animal is stressed.
 - b. Transmission to humans has resulted from bites, scratches, and other incidents that expose the worker to NHP's mucous membrane fluids, cerebral spinal fluid, or neurologic tissue. B virus is not transmitted by exposure to blood from an infected animal.
 - c. HSV may enter sensory nerve endings within five minutes. B virus is thought to infect the same sensory nerve cells just as rapidly.

III-17. Non-Human Primate Body Fluid Exposure

- d. The incubation period for human infection ranges from two days to five weeks. Most cases present within three weeks of the exposure. Initial complaints frequently include flu-like symptoms (i.e., fever, myalgias, fatigue and headache) with or without localized findings at the injury site such as herpetic vesicles, pain or tingling. Peripheral or central nervous system manifestations of infection may vary.
 - e. Although human infection with B virus is a very infrequent occurrence, approximately 70% of workers infected with B virus have died from complications of their infections. As a result, appropriate first aid should be administered immediately and consideration should be given to the prompt administration of post exposure prophylaxis.
2. SRV
- a. SRVs, a group of closely related retroviruses, naturally infect rhesus macaques. SRV has been identified as the etiologic agent of an infectious immunodeficiency disease in macaques that resembles infection with human immunodeficiency virus type 1 (HIV-1) in humans. Vaccines are under development to prevent this infection with devastating consequences in captive populations of macaque species.
 - b. SRV is present in blood, saliva, urine and other body fluids.
 - c. The CDC has reported that two of 398 individuals (0.5%) with occupational contact with nonhuman primates had seroreactivity to SRV antigens. The investigators were unable to detect SRV-infected cells by polymerase chain reaction (PCR) testing or to culture the virus. Although SRV replicates in human cells, neither worker has developed symptoms suggestive of an infection with a retrovirus.
3. SHIV
- a. SHIV strains are chimeric viruses that combine genetic sequences from HIV-1 with genes of the simian immunodeficiency virus (SIV). They are designed to study how HIV-1 behaves in animal research models by making the new viral constructs mimic HIV-1 infection more closely than SIV does.
 - b. SHIV can be recovered from the same body fluids and tissues as HIV-1.
 - c. Occupational transmission of SHIV has not yet been reported. As a result, the consequences of infection with SHIV are not yet defined.
- C. African green monkeys, baboons, sooty mangabeys and chimpanzees may be naturally infected with SIV or Simian Foamy Virus (SFV).
1. SIV
- a. SIV is genetically and antigenically related to HIV-2. Animals naturally infected with SIV typically do not develop immunodeficiency disease. However, when SIV crosses over to infect other NHP species, either experimentally or by accidental exposure of a colony, it may be lethal to susceptible NHPs.
 - b. The virus has been isolated from blood, plasma, cerebrospinal fluid,

III-17. Non-Human Primate Body Fluid Exposure

and parenchymal tissues. Transmission to man may occur following percutaneous and mucous membrane exposures to body fluids containing white blood cells.

- c. Testing at the CDC has shown that three of 472 individuals (0.6%) with nonhuman primate contact have developed laboratory evidence of infection with SIV. However, the virus could not be cultured in any of these cases. So far, none of these individuals has developed clinical evidence of disease or of immune suppression.

2. SFV

- a. There is no recognized human analogue retrovirus for SFV and there is no recognized disease state associated with SFV infection in its natural host or in man.
- b. SFV can be experimentally transmitted by blood transfusions. It is suspected that transmission to workers may be associated with percutaneous wounds such as bites, scratches, and sharps injuries.
- c. The CDC has reported that 13 of 398 individuals (3.3%) who worked with nonhuman primates have serologic evidence of exposure to SFV. PCR testing was positive from several of these workers and the virus was cultured from two individuals.

- V. Nonhuman primate testing following a reported injury is based upon the type of NHP and body fluid involved in the incident (the rationale for this is outlined in Section IV above and in [Attachment I](#)). In addition, the OMS healthcare provider routinely asks whether the NHP has any known natural or experimental infections. If the NHP was used in an experiment with a human pathogen OMS staff may request additional testing.

- A. Macaque blood. If the incident involves blood from a macaque (e.g., rhesus, cynomolgus, pig-tail, stump-tail monkeys) and there is a possibility that the area could be contaminated with the NHP oral, ocular, or genital fluids the following information and biologic specimens are requested:
 1. A report of physical exam findings including whether or not the NHP has oral or genital vesicles, ulcerations, or crusts, or conjunctivitis.
 2. One virus culture that contains swabs from the macaque's mouth, conjunctival sacs, and genitalia. Special care should be taken to swab all vesicles, ulcerations, or crusts. More than one cotton swab may be placed in the transport media. Cultures should be obtained as soon as feasible.
 3. Serum only from animals that have never tested positive for antibodies to B virus.
- B. Macaque saliva. If the incident involves saliva from a macaque, the following information and biologic specimens are requested:
 1. A report of physical exam findings including whether or not the NHP has oral or genital vesicles, ulcerations, or crusts, or conjunctivitis.
 2. Two virus cultures:
 - a. One from the macaque's mouth, using care to swab any ulcers that might be present.
 - b. The second from the macaque's conjunctival sacs and genitalia. Any

III-17. Non-Human Primate Body Fluid Exposure

vesicles, ulcerations, or crusts should be swabbed. More than one cotton swab may be placed in the transport media. Cultures should be obtained as soon as feasible.

3. Serum only from animals that have never tested positive for antibodies to B virus.
- C. Macaque unidentified body fluid. If the accident involves a potential exposure to an unidentified macaque body fluid by way of a scratch, mucous membrane splash, or injury involving a soiled cage, OMS requests:
1. A report of physical exam findings including whether or not the NHP has oral or genital vesicles, ulcerations, or crusts, or conjunctivitis.
 2. One virus culture that contains swabs from the macaque's mouth, conjunctival sacs, and genitalia. Special care should be taken to swab all vesicles, ulcerations, or crusts. More than one cotton swab may be placed in the transport media. Cultures should be obtained as soon as feasible.
 3. Serum only from animals that have never tested positive for antibodies to B virus.
- D. African green monkey, baboon, sooty mangabey, or chimpanzee blood. If the incident involves exposure to blood from one of these NHPs by way of a percutaneous injury or a splash to non-intact skin or mucous membranes, OMS requests serum for SIV testing only from animals that have not previously tested positive for antibodies to SIV.
- E. African green monkey, baboon, sooty mangabey, or chimpanzee saliva or other, unidentified body fluid. If the injury involves potential exposure to a body fluid other than blood, biologic testing is not routinely required.
- F. Marmoset, squirrel, or owl monkey body fluids. Pathogens found in marmosets, squirrel and owl monkeys generally do not constitute a health risk for humans. Routine laboratory testing is not necessary following an exposure to body fluids from these NHPs. The OMS healthcare provider will ask if the animal involved may have been exposed to NHPs of different species to determine any indirect risk to the worker of human pathogen exposure from those NHPs.

VI. Specimen Identification and Handling

- A. Virus cultures use the same transport media as listed in V.D.3.b and specimens are labeled with the following information:
1. The animal's identifying information,
 2. The date the specimen was obtained,
 3. The sites swabbed (e.g., mouth, eyes, genitalia), and
 4. The date that the injury occurred.
- B. Blood must be obtained using a red top plastic tube. The blood should be permitted to sit and clot for 30 minutes before centrifuging. Alternately, for work groups off campus, blood can be obtained in a serum separator tube (SST), to avoid delaying the medical evaluation. Regardless, the label on the tube should include the following information:
1. The animal's identifying information
 2. The date the specimen was obtained.

III-17. Non-Human Primate Body Fluid Exposure

- C. Virus cultures and blood specimens should be placed on ice and delivered to OMS or refrigerated (4°C) until delivery the next business day. It is important that the swabs remain submerged in the viral medium during storage and/or transport. Specimens should be accompanied with the name, phone number, building and room number of the IC and Facility Veterinarian.

VII. Employee Medical Assessment and Treatment

- A. Reporting. Anyone (e.g., NIH employees, contractors, others) exposed to NHP body fluids in an NIH facility is expected to notify OMS immediately with a telephone call. During non-clinic hours, workers contact the on-call OMS healthcare provider by calling the NIH page operator on 301-496-1211.
- B. First aid. First aid procedures are outlined in the OMS Wound Care Guidelines.
 - 1. First aid should be performed at the worksite, unless the worker can get to OMS in less than five minutes. Employees working in animal care facilities off campus, frequently call OMS to discuss the medical significance of the injury.
 - 2. If the employee reports to OMS within eight hours of the incident, first aid is repeated, regardless of whether or not it was performed at the worksite.
- C. Medical assessment. As first aid is being administered, a standardized, targeted medical history is obtained using the Accident Reporting System in the OMS electronic medical record system. The OMS healthcare provider completes the CAM (Clinical Access Manager) injury report as well as the NHP expanded fields. The following information is obtained:
 - 1. When the injury occurred.
 - 2. Safety measures employed at the time of the injury.
 - 3. Type of injury (e.g., skin or a mucous membrane exposure, percutaneous injury).
 - 4. Type and amount of fluid contacted.
 - 5. Circumstances of the accident.
 - 6. The identity of the nonhuman primate involved in the injury.
 - 7. Details regarding first aid provided at the work site.
- D. Laboratory Testing
 - 1. B virus. If the injury involved a potential percutaneous or mucous membrane exposure to B virus, a virus culture is obtained from the wound following the administration of first aid at OMS. Decisions regarding bacterial cultures are made on a case-by-case basis.
 - 2. Retroviruses. If the injury involved skin or mucous membrane contact or a percutaneous exposure to blood or another blood contaminated body fluid from a nonhuman primate suspected to be infected with SIV or SHIV, the worker is offered serologic monitoring for infection. The utility of monitoring for conversion after potential exposure to other retroviruses will be determined with each case individually. If post exposure prophylaxis with an antiretroviral is started, baseline testing will include a complete blood count, a chemistry panel, amylase, lipase, and urinalysis.
 - 3. Laboratory specimens.

III-17. Non-Human Primate Body Fluid Exposure

- a. A blood sample is obtained following every suspected injury involving an exposure to NHP body fluids, unless a sample was obtained in the preceding six months. The serum is stored at -20°C for possible future reference.
- b. The virus culture is obtained using Hank's Buffered Salts Solution (Bartel's Viral Transport Media) and labeled with the employee's name, date the specimen was obtained and that it was from the wound post scrub. Virus cultures obtained after 2 pm on Thursday are stored at -70°C and shipped Monday morning.

E. Treatment

1. B virus. Because B virus may infect sensory nerves quickly, when treatment is indicated every effort is made to initiate it as soon after the injury as possible. A worker who sustains a possible percutaneous or mucous membrane exposure to B virus is:
 - a. Counseled regarding the significance of the incident while still at the worksite;
 - b. Directed to initiate treatment with the valacyclovir stored in the bite-scratch kit in their work area (two 500 mg tablets) noting the time treatment was started;
 - c. Instructed to proceed to OMS;
 - d. Issued a B Virus Handout ([Attachment II](#)) and a related wallet-sized card ([Attachment III](#));
 - e. Provided additional 500 mg tablets (so that the worker has a total of 42 tablets) and instructed to take two tablets every eight hours; and
 - f. Given an appointment to return to clinic in one week.
2. Retroviruses. A worker who sustains a suspected percutaneous or mucous membrane exposure to SIV or SHIV is counseled, treated and followed as outlined in the OMS Retrovirus Exposure procedure. If the accident is reported during clinic hours, appropriate treatment is initiated in OMS. If the accident is reported after OMS clinic hours, and:
 - a. The worker is within driving range of the Clinical Center (CC), the OMS medical provider:
 - i. Instructs the worker to go to the CC Pharmacy to obtain the prescribed medications;
 - ii. Calls the CC Pharmacy (301-496-2867) to order the medications; and
 - iii. Asks the pharmacist to identify the patient only with the worker's initials and the last four digits of the worker's social security number.
 - b. The worker is not within driving range of the CC, the OMS medical provider:
 - i. Obtains contact information for the closest pharmacy and directs the worker to proceed there directly, and
 - ii. Calls the pharmacy and orders sufficient medications to supply the worker until additional medications can be acquired from the OMS clinic.

III-17. Non-Human Primate Body Fluid Exposure

3. Nurse coordinator. The OMS medical provider alerts the nurse coordinator for injuries potentially involving NHP body fluids of the injury. The coordinator tracks all related laboratory test results and employee compliance with follow-up appointments.
- F. Follow-up
1. Possible B virus exposure – receiving treatment.
 - a. One-week follow-up visit. The worker is interviewed for symptoms suggestive of an infection with B virus, compliance with treatment, and possible side effects to the medication. In addition, the wound is checked, an additional 42 tablets of valacyclovir is provided and the worker is given an appointment to return in a week.
 - b. Two-week follow-up visit. The worker again is interviewed for symptoms suggestive of an infection with B virus, compliance with treatment, and possible side effects to the medication. The worker is given an appointment to return in another four weeks.
 - c. Six-week follow-up visit. The worker is interviewed for symptoms suggestive of an infection.
 - d. The employee's serum may be tested for antibodies to B virus, if there are symptoms suggestive of an infection with B virus.
 2. Possible B virus exposure – treatment recommended but declined.
 - a. One-week follow-up visit. The worker is interviewed for symptoms suggestive of an infection with B virus and the wound is checked.
 - b. Two- and four-week follow-up visit. The worker is again questioned for symptoms suggestive of infection with B virus and blood is obtained for serum storage.
 3. Possible retrovirus exposure.
 - a. The OMS guidelines for follow-up evaluations are outlined in the OMS Retrovirus Exposure procedure.

VIII. Record Keeping and Reporting

- A. The injury is recorded in the OMS Accident Reporting System and, if indicated, a CA-1 form is issued. Details are provided in the OMS guidelines for Reporting Occupational Injuries and Illnesses.
- B. All injuries potentially involving NHP body fluids are reported to a safety specialist by the OMS healthcare provider at the time the injury is reported. The safety specialist interviews the employee, performs a work site assessment and offers appropriate safety advice to the employee and supervisor.
- C. The OMS lab coordinator maintains a log of B virus related laboratory test results. The following information is recorded in the log:
 1. The date the injury occurred and the date the sample was shipped for testing,
 2. Name of the worker,
 3. The employee/worker's employer (e.g., IC, contractor),
 4. Location (e.g., building, room) at the time of the injury,
 5. Identification of the nonhuman primate,
 6. Name address and telephone number of the IC and facility veterinarian,

III-17. Non-Human Primate Body Fluid Exposure

7. The type of injury (e.g., bite, scratch), and
 8. Tests requested and results received for the nonhuman primate.
- D. All laboratory test results for the nonhuman primate are shared with the animal's IC veterinarian.

IX. Bibliography

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Information and Specimens Requested following an Exposure to a NHP Body Fluid

Injury involving a rhesus, cynomolgus, pig tail, stump tail or other macaque body fluid:							
NHP Body Fluid	NHP Medical History		NHP Physical Exam Findings			NHP Laboratory Testing	
	Known Infections	Last Test for B virus Result & Date	Oral	Genital	Ocular Conjunctivitis	B Virus Culture	Blood Testing for B Virus
			Vesicles, Ulcerations, Crusts				
Blood	Provide	Provide	Provide*	Provide*	Provide*	Combine oral, ocular, genital	If not previously positive for B virus*
Saliva	Provide	Provide	Provide	Provide	Provide	One oral, combine ocular and genital	If not previously positive for B virus
Unknown	Provide	Provide	Provide*	Provide*	Provide*	Combine oral, ocular, genital	If not tested or previous test negative for B virus*

* Only if the injury may have involved exposure to saliva or other mucous membrane fluid.

Possible exposure to a body fluid from an African green monkey, baboon, sooty mangabey, or chimpanzee:							
NHP Body Fluid	NHP Medical History		NHP Physical Exam Findings			NHP Laboratory Testing	
	Known Infections	Last SIV Test Result Date	Oral	Genital	Ocular Conjunctivitis	SIV Culture	Blood Testing for SIV
			Vesicles, Ulcerations, Crusts				
Blood	Provide	Provide	NA	NA	NA	NA	If not previously positive for SIV
Saliva	Provide	NA	NA	NA	NA	NA	NA
Unknown	Provide	NA	NA	NA	NA	NA	NA

Possible exposure to a body fluid from a **marmoset, squirrel or owl monkey:**

Body Fluid:	NHP Medical History, Known Infections, Contact with NHPs of Other Species	NHP Physical Exam Findings	NHP Laboratory Testing
Blood	Provide	NA	NA
Saliva	Provide	NA	NA
Unknown	Provide	NA	NA

B Virus Backgrounder

Q: What is B virus?

A: B virus is a herpes virus. Old World nonhuman primates (NHPs) such as rhesus, cynomolgus, pig-tail and stump-tail NHPs are frequently infected with B virus. Infection with B virus produces a very mild disease in NHPs. Most infected NHPs have no obvious evidence that they are infected. Some NHPs may develop tiny blisters which quickly develop into small, shallow ulcers. The blisters and ulcers may occur in the mouth, face, lips, eyes, or genitals. Although the rash heals quickly, the virus remains in the NHP's involved nerves permanently. Later, the NHP may shed the virus in the same areas when it is "stressed". There usually is no obvious evidence that shedding is occurring.

Q: How is B virus passed from an infected monkey to a human?

A: For transmission to occur several things must happen. First, the NHP must have been infected with B virus. Second, if the injury involves a NHP fluid, the NHP must be currently shedding the virus. Third, the virus must be found in the NHP fluid or tissue involved in the injury. Finally, the NHP fluid or tissue must get through the worker's skin (for example by a puncture or laceration) or onto the worker's mucous membrane or non-intact skin. Each of these requirements must be met in order to transfer B virus to the worker.

Q: Who is at risk for infection with B-virus?

A: Those at risk include animal caretakers, laboratory staff, or anyone who has possible contact with Old World NHPs or their unfixed tissues. Persons whose immunity is weakened due to a medical condition or medical treatment may be at higher risk for infection. That said, the risk of being infected with B virus is probably very low. Thousands of persons have handled macaques since human infection with B virus infection was first reported in 1932. Yet, less than 30 cases of human infection have been documented.

Q: How can I protect myself from infection?

A: Proper work practices markedly reduce the chances of infection. When working with NHPs:

1. Exercise caution at all times. Remember NHPs are wild animals.
2. Wear appropriate personal protective equipment, as instructed.
3. Minimize direct handling of NHPs. Work with at least one other person when handling awake NHPs, if necessary.
4. Report all NHP blisters and ulcerations to a staff veterinarian.
5. If possibly exposed to oral, genital or ocular secretions or neural tissues from an Old World NHP, immediately initiate first aid. Contaminated skin and wounds should be washed thoroughly with soap and water for 15 minutes. Contaminated eyes and mucous membranes should be irrigated with saline or water for 15 minutes. As soon

as you have completed the first aid, notify your supervisor and report to the Occupational Medical Service (OMS) for further care. If OMS is closed, call the NIH operator (301-496-1211) and ask the operator to page the OMS physician immediately.

Q: What are the signs and symptoms of B virus infection in humans?

A: B-virus is characterized by a variety of signs and symptoms, which generally occur within one month of exposure. The early signs and symptoms can occur within hours to days of being infected with the virus. The following list describes early B virus infection symptoms. Note that there is no orderly sequence of events.

1. Fever and chills.
2. Flu-like symptoms including headache, fatigue, and muscle aches.
3. Itching, pain, numbness or loss of feeling at the injury site that increases toward the body.
4. Twenty to thirty percent of workers develop blisters or shallow open ulcers at or near the injury site.

If any of the above symptoms occur following an injury involving an Old World NHP, or equipment contaminated with their secretions or tissues, immediately call OMS.

OMS Contact Information:

During business hours from 7:30 am to 5 pm, Monday to Friday, except federal holidays call the nearest OMS clinic:

OMS Bethesda, MD 301-496-4411,
OMS Frederick, MD 301-631-7233,
Baltimore, MD 443-740-2309, or
Hamilton, MT 406-375-9755.

When OMS is closed (weekdays from 5:00 pm to 7:30 am, weekends and federal holidays), call the NIH operator (301-496-1211) and ask to speak with the OMS on-call physician. Please allow for the two-hour time difference between the Eastern and Mountain time zones.

(B Virus Wallet Card)

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Symptoms of B virus (*Macacine herpesvirus-1*) Infection

Very few people have been infected with B virus. However, if an infection does occur, it can be life-threatening. Prompt medical evaluation and treatment are important. Please read the following list of symptoms which may be related to a B virus infection.

1. Flu-like symptoms:
 - a. Fever and chills,
 - b. Muscle aches, or
 - c. Headache and fatigue.

2. At the injury site:
 - a. Itching or pain,
 - b. Tiny blisters or shallow ulcers, or
 - c. Numbness or loss of feeling.

-reverse-

Contact the Occupational Medical Service (OMS) if you have any questions about these symptoms.

If any of these symptoms occur within a month from the date of your injury, you should immediately contact OMS for an emergency evaluation. When OMS is closed (5:00 pm to 7:30 am, weekends and federal holidays), call the NIH operator (301-496-1211) and ask to speak with the OMS on-call physician. Give the operator your name and a phone number where you can be reached. An OMS physician will contact you within 15 minutes.

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