ORGANISM OR AGENT: Macaque herpesvirus 1
EXPOSURE RISK: Herpes B virus
UCSF OCCUPATIONAL HEALTH SERVICES: 415/885-7580 (Available during work hours)
UCSF NEEDLESTICK EXPOSURE HOTLINE: 415/353-7842 (Available 24 hours)
OFFICE OF ENVIRONMENTAL HEALTH & SAFETY: 415/476-1300 (Main number; available during work hours) or 9-911 (Available 24 hours)
EH&S PUBLIC HEALTH OFFICER: 415/514-3531
BIOSAFETY OFFICER: 415/514-2824
ON-CALL LARC VETERINARIAN: 415/502-8687

PROTOCOL SUMMARY

In the event of an accidental exposure or injury, the protocol is as follows:

1. MODES OF EXPOSURE:
   a. Bite from an infected animal.
   b. Scratch from an infected animal or contaminated equipment.
   c. Contact with mucous membranes (eyes, nose, or mouth) with monkey contaminated material.
   d. Contact with non-intact skin with monkey contaminated material.
   e. Needlestick puncture.

2. FIRST AID
   a. Bites, Scratches or Lacerations: Scrub or irrigate wound immediately with a chlorhexidine impregnated sponge from the first aid kit for at least 15 minutes. You must do this within 2-3 minutes of exposure. Wash all the chlorhexidine solution out of the wound after you are done scrubbing so that the wound can be cultured. Cover wound with a Band-Aid dressing from first aid kit.
   b. Splash to Eye(s), Nose or Mouth: irrigate with sterile eye solution in first aid kit immediately and then find an eye wash station to continue rinsing your eyes for 15 to 20 minutes. NEVER use a bleach solution in your eyes.
   c. Splash Affecting Garments – remove garments that may have become soiled or contaminated and place them in a double red plastic bag.

3. TREATMENT
   a. In the event of an exposure, with or without an injury, call the Needlestick Exposure Hotline in order to get access to medical care for the exposure. If possible, have another person call the Needlestick Hotline while the exposed individual is following first-aid procedures. The Needlestick Exposure hotline responder will provide guidance to the injured individual on necessary medical treatment and post exposure follow-up.
   b. In the event of a severe injury, the injured individual should report to the Emergency Department for acute medical treatment. The injured individual must inform their supervisor, and take a copy of this entire protocol document to the Emergency Department.

4. FOLLOW-UP IS NEEDED IN THE EVENT OF ANY LABORATORY EXPOSURE
   a. In the event of a large spill in a secure area, leave the area and secure the lab to prevent entry of other personnel and possible secondary exposures. In the event of a spill in a non-secure area, contact the emergency response team (9-911) for clean-up.
   c. Contact the on-call LARC veterinarian to identify the monkey and to have the veterinarian collect monkey specimens for Herpes B testing. (415) 502 – 8687.
   d. Contact the Public Health Office to report the injury or exposure.
ROLES & RESPONSIBILITIES AFTER ACCIDENTIAL EXPOSURE TO HERPES B VIRUS

1. WORER’S RESPONSIBILITIES (Employee/Student Initial Self-Care)
   a. First Aid: Perform the recommended first aid and decontamination according to the posted instructions.
   b. Treatment:  
      i) In the event of an exposure, with or without an injury, call the Needlestick Exposure Hotline in order to get access to medical care for the exposure. The Needlestick Exposure Hotline responder will provide guidance to the injured individual on necessary medical treatment and post exposure follow-up. 
      ii) In the event of a severe injury, the injured individual should report to the Emergency Department for acute medical treatment. The employee should bring a copy of this protocol.
   c. Access to Needlestick Hotline: Call the Needlestick Exposure Hotline in order to get access to medical care for the exposure. Dial 415/353-7842. If there is no call back in 15 minutes, call again. If there is no call back the second time, proceed to the nearest Emergency Department with a copy of this protocol.
   d. Reporting: Inform your laboratory supervisor / principal investigator of the exposure.
   e. Secure the laboratory: Identify the non-human primate or equipment involved in the exposure and the mechanism of exposure. Make sure that the laboratory area has been secured and that notification of contamination has been posted to prevent other individuals from entering the area. Remove any garment that may have become soiled/contaminated and place them in a double red biohazardous bag.
   f. Follow up: Contact Occupational Health Services (OHS) at (415) 885-7580 for any needed follow up care.

2. SUPERVISOR’S RESPONSIBILITIES
   a. First Aid and Decontamination: Verify that the worker has washed and decontaminated himself/herself. Ensure that appropriate first aid has been received.
   b. Verify that the contact animal is a macaque or trace the source if possible.
   c. Secure the laboratory: Confirm that the laboratory area has been secured and that notification of contamination has been posted to prevent other individuals from entering the area.
   d. Laboratory clean-up (as needed): Contact the Office of Environmental Health & Safety (OEH&S) through the UC Police Department Emergency Dispatch (From a campus telephone 9-911, from a non-campus phone (415) 476 – 1414.
   e. Report the exposure: Call the Public Health Officer at (415) 514 - 3531 during regular business hours to discuss the exposure. A report summarizing any suspected Herpes B exposures will be submitted to the Biosafety Committee.
   The report must include the following:
   - A brief description of the exposure event, a description of the area involved, and the extent of the employee’s exposure.
   - Corrective action taken to prevent the re-occurrence of the incident.
   - Decontamination procedures.
   - Follow-up and treatment procedures.
   f. Follow-up: Confirm that the worker has called for an appointment at the UCSF Occupational Health Clinic. Confirm that the on-call LARC veterinarian has been contacted about the potential exposure.
g. **Report the Injury:** Within 24 hours, report the injury to the UCSF Human Resources Disability Management Services (HR DMS) Office on the Supervisor’s Report of Injury (SRI) form, available here:

   [http://ucsfhr.ucsf.edu/files/SIR.pdf](http://ucsfhr.ucsf.edu/files/SIR.pdf)

3. **PRINCIPAL INVESTIGATOR RESPONSIBILITIES**

   a. The PI will ensure that all lab personnel are trained in the use of safe laboratory procedures to prevent accidental exposure before assignment to any laboratory where non-human primate or non-human primate tissues are used.

   b. The PI may request assistance from UCSF OEH&S in providing information about safe laboratory procedures. For assistance, the PI should call the Public Health Officer or Biosafety Officer.

   c. The PI must ensure that all researchers who will be working with non-human primates or non-human primate tissues have read the entire protocol. The PI will also ensure that the protocol will be reviewed on a yearly basis by all laboratory workers.

   d. The PI shall ensure that any known Herpes B exposure is reported to the Public Health Officer and Biosafety Officer.

   e. The PI will provide consultation on an as needed basis to the Needlestick Exposure and/or Emergency Department regarding information.

4. **VETERINARY RESPONSIBILITIES**

   a. Verify the macaque species and ID of the animal involved. Note any previous B virus results.

   b. Immediately anesthetize the macaques and check for oral ulcerations or conjunctivitis (may be indicative of active infection and shedding). If any suspicious lesions are seen, contact the Needlestick Hotline at (415) 353 – 7842. Draw 5 ml of blood from the monkey, separate serum. Place 1 ml in an unbreakable plastic vial (minimum 0.5 ml). Label with monkey identification and collection date.

   c. Collect five primate virology samples: 1 buccal, 2 conjunctival (each eye) and 1 genital. Use sterile swabs provided with the viral transport medium. Aseptically break off each swab in the screw top vials containing transport medium.

   d. Label all vials with the monkey identification number, collection date and site of virology sample. Fill out NIH B Virus Request Form available at [www.gsu.edu/bvirus](http://www.gsu.edu/bvirus).

   e. LARC will supply transport medium to the Needlestick Hotline Clinician.
SECTION I – Infectious Agent

Organism or Agent: Macacine herpes virus 1 (MHV-1).

Synonym or cross reference: Herpes simiae virus, herpesvirus simiae, B virus, herpes B virus, herpes B, monkey B virus, monkey herpes infection, simian herpesvirus B infection, and B virus infection.

Characteristics: MHV-1 belongs to the subfamily Alphaherpesvirinae, genus Simplexvirus, and is closely related to herpes simplex virus-1 and -2. MHV-1 is the only non-human primate herpesvirus that has been shown to infect humans. MHV-1 is an enveloped icosapentahedral virion, measuring approximately 160 to 180 nm in diameter, and has a double-stranded DNA genome.

Reservoir: The rhesus macaque (M. mulatta) and the long-tailed macaque (M. fascicularis) are the main natural reservoirs.

Zoonosis: Yes, through direct or indirect contact with the bodily fluids of MHV-1 infected monkeys.

Vectors: None.

SECTION II – Recommended Precautions

Risk Groups Classification: Risk Group 2.

Containment Requirements: Containment Level 2 facilities, equipment, and operational practices for work involving infectious or potentially infectious materials, animals, and cultures. Animal Biosafety Level 2 for non-human primates in laboratory setting.

Protective Clothing: Personnel are required to follow University of California, San Francisco Institutional Biosafety Committee’s Personal Protective Equipment guidelines when working with old world non-human primates or their tissues. Please contact the Biosafety Officer for more information (415) 514 – 2824.

Other Precautions: All activities with infectious material should be conducted in a biological safety cabinet (BSC). Centrifugation of infected materials must be carried out in closed containers placed in sealed safety cups, or in rotors that are unloaded in a biological safety cabinet. The use of needles, syringes, and other sharp objects should be strictly limited. Open wounds, cuts, scratches, and grazes should be covered with waterproof dressings. Additional precautions should be considered with work involving animal activities.

SECTION III - Handling Information

Spills: Allow aerosols to settle and, wearing protective clothing, gently cover spill with paper towels and apply 0.5% sodium hypochlorite, starting at the perimeter and working towards the center. Allow sufficient contact time before clean-up.
Disposal: Decontaminate all materials for disposal from the containment laboratory by steam sterilization, chemical disinfection, incineration or by gaseous methods. Contaminated materials include both liquid and solid wastes. Dispose all waste as biohazardous waste.

SECTION IV – Health Hazards

Pathogenicity: After a brief incubation period, a localized vesicular eruption near the site of inoculation is accompanied by fever, myalgia, headache, and/or nausea. The vesicular eruption is clinically and pathologically similar to that caused by herpes simplex virus. Neurological symptoms follow 3 to 7 days later, including meningismus, nausea, vomiting, persistent headache, confusion, diplopia, dysphagia, dizziness, dysarthria, cranial nerve palsies, and ataxia.

Virus spread to the central nervous system is an ominous sign, since, even with antiviral therapy and supportive care, most patients die. Deaths are often attributed to respiratory failure associated with ascending paralysis. The mortality rate is over 70% in untreated individuals, and neurological sequelae are common in those who survive.

Epidemiology: Human infection with MHV-1 is rare, and around 40 to 50 cases have been described worldwide. The first human case of MHV-1 was reported in a laboratory researcher in 1932, who was bitten on the finger by an apparently healthy rhesus macaque and died of progressive encephalomyelitis 15 days later.

Host Range: Humans, monkeys of the genus Macaca, including the stump-tailed macaque (M. arctoides), pig-tailed macaque (M. nemestrina), Japanese macaque (M. fuscata), bonnet macaque (M. radiate), and Taiwan macaque (M. cyclopis).

Experimental hosts include rabbits, dogs, mice and guinea pigs.

Infectious Dose: Unknown.

Modes of Transmission: Humans are infected in most cases by monkey bites, but transmission has also occurred following direct inoculation of the eye or respiratory tract with the bodily fluids of MHV-1 infected monkeys. Direct contamination of a pre-existing wound with MHV-1 infected monkey saliva is a less common mode of transmission. Indirect contact, such as injury from a contaminated fomite (e.g. needlestick injury, cuts from broken tissue culture bottles containing infected monkey cells, or cage scratch), has also resulted in human infection.

Incubation Period: Reported range is 2 days to 5 weeks, although most cases fall into a range of 5 to 21 days.

Communicability: Person-to-person transmission from intimate contact with vesicular lesions has been documented in a single case.

FOR USE BY THE NEEDLESTICK EXPOSURE HOTLINE RESPONDER

SECTION V – Stability and Viability

Drug Susceptibility: MHV-1 is susceptible to the antiviral drugs acyclovir, valacyclovir, and famciclovir.

Susceptibility to Disinfectants: MHV-1 is susceptible to fresh 0.5% sodium hypochlorite solution, povidone-iodine, and chlorhexidine.

Physical Inactivation: Like all other enveloped viruses, it is likely that exposure to ultraviolet light and heat (56°C for at least 30 minutes) will inactivate MHV-1.
Survival Outside Host: Storage of MHV-1 in tissue culture medium (pH 7.2, 4°C) was shown to result in a slight loss in viability after 8 weeks. A single episode of freezing at either -20°C or -72°C resulted in an initial loss of 2 logs of infectivity of tissue culture medium stored specimens. All infectivity of MHV-1 is lost after storage in tissue culture media at 40°C for 2 weeks.

SECTION VI – First Aid/ Medical

Surveillance: Methods of detection of MHV-1 in suspected cases include viral culture of the agent from swab specimens, cerebrospinal fluid, and punch-biopsied material from possible sites of infection (bites and scratch wounds), PCR, ELISA, Western blot and PCR-microplate hybridisation assay. Due to significant cross-reactivity with herpes simplex virus -1 and -2, serological testing is of human sera is of limited diagnostic merit. MRI, CT and EEG of the brain can also be used to detect the neurological signs of MHV-1 infection.

First Aid/Treatment: All bite and scratch wounds should be immediately scrubbed with a chlorhexidine impregnated sponge for 15 to 20 minutes. Wash all the chlorhexidine solution out of the wound after you are done scrubbing so that the wound can be cultured. Cover wound with a Band-Aid dressing from first aid kit. For exposures to the eyes and mucous membranes, irrigate with the sterile eye solution in the monkey bite scratch first aid kit immediately and then find an eye wash station to continue rinsing for 15 to 20 minutes. Never use a bleach solution in your eyes. Antiviral therapy is administered if the individual is thought to be at risk.

Immunization: None.

Prophylaxis: Yes, individuals thought to be at high risk for infection following a bite, laceration, or puncture wound when working with infected neural tissue are administered antivirals. Prophylaxis is started as soon as possible after exposure (within hours), but only after wound cleaning has been completed. Three orally administered agents are currently available for post-exposure prophylaxis of MHV-1 infection: acyclovir, valacyclovir, and famciclovir. The drug of choice is valacyclovir.

SECTION VII – Laboratory Hazards

Laboratory-Acquired Infections: Virtually all known MHV-1 infections were laboratory acquired and of approximately 40 to 50 cases reported worldwide only 26 have been well documented. Of those 26, the majority were contracted from the bite of a MHV-1 infected monkey.

Sources/Specimens: Blood, saliva, conjunctival fluid, or urogenital secretions of infected macaques. Central nervous system tissues and cerebrospinal fluid of monkeys are also potentially infectious.

Primary Hazards: Bite or scratches from MHV-1 infected monkeys, exposure of broken skin or mucous membranes to infected secretions of monkeys, contact with mucous membranes (eyes, nose, mouth) or broken skin with monkey contaminated material, needlestick or sharps injuries when handling infected samples, and scratch from a contaminated equipment.

Special Hazards: Cell culture and autopsy materials derived from infected monkeys can present a potential hazard. Exposure to virus from the natural aerosols that surround monkeys is a possibility but is considered to be of unknown or low risk.

Source:  

FOR THE USE OF THE EMERGENCY DEPARTMENT:
UCSF Occupational Health Services
Monkey Bite/Exposure
Instructions for Emergency Department Personnel

This employee has had an occupational exposure to Herpes B, a disease with an 80% fatality rate in humans. Transmission has been linked to even trivial exposures to monkey body fluids and cage materials. Timely provision of first aid to the exposure site and post-exposure prophylactic medication by emergency services is essential and time sensitive even if the employee appears to have an insignificant presentation.

TRIAGE NURSE:

Confirm proper exposure site cleansing and repeat if inadequate:

- Mucous membranes/eyes -15 minute rinse with water or sterile saline.
- Skin -15 minute wash with a solution containing detergent soap i.e. chlorhexidine or povidone iodine

TREATING PROVIDER

- Call needlestick/exposure hotline at (415) 353-STIC (7842) for advice.
- Wear gloves, eye protection and use universal precautions.
- Evaluate general health (including medications) and determine when the last tetanus booster was received.
- Perform a careful baseline neurological examination.
- Collect culture of wound or exposure site only after thoroughly scrubbing wound area using viral transport medium and swabs located in the ED laboratory. If vesicular lesion is present, unroof and swab across the base of the lesion. Send to the lab with instructions to refrigerate and hold for Occupational Health Services.
- Draw 10 ml of blood in red top or serum separator tubes. Send to the lab with instructions to refrigerate and hold for Occupational Health Services.
- Strongly consider prophylaxis
  - Valcyclovir 1 g TID x 14 days or Acyclovir 800 5mg 5xday for 14 days.
  - For deep bites, Augmentin 875/125 mg PO BID plus Flagyl 500 mg PO 4x/day.
- Counsel the patient:
  - Return for skin lesions, flu-like symptoms or neurological symptoms.
  - Contact Occupational Health Services at 353-4341 on the next business day.
  - Begin medication immediately and take all doses.

RESOURCES

- UCSF 24 hour needlestick and exposure hotline 415-353-STIC (7842).
- National B Virus Resource Center [http://www2.gsu.edu/~wwwvir/index.html](http://www2.gsu.edu/~wwwvir/index.html)
- Dr. Julia Hilliard, National B Virus Resource Center
  - Lab Phone: (404) 651-0808
  - Emergency contact: (404) 358-8168

For acute injuries that require immediate medical attention, please take a copy of these instructions with you to the Emergency Department.
Appendix A

Center for Disease Control and Prevention – Herpes B Virus, 2010

Risks for Infection

Persons at greatest risk for B virus infection are veterinarians, laboratory workers, and others who have close contact with Old World macaques or monkey cell cultures. Infection is typically caused by animal bites or scratches, by exposure to the tissues or secretions of macaques, or by mucosal contact with body fluid or tissue. Human infection can also result from indirect contact via, for example, a needlestick injury from a contaminated needle.

Macaques housed in primate facilities usually become B virus positive by the time they reach adulthood. B virus establishes latent infection in macaques and can only be transmitted during active viral shedding into mucosal surfaces. This happens only on reactivation from the latent state, which occurs rarely—most commonly in animals that have been stressed or immunosuppressed.

In late 1997, a worker at a primate center died from B virus infection that developed after biologic material from a monkey was splashed into the worker's eye. In response to this case, CDC formed a working group to reassess the existing recommendations for the prevention, evaluation, and treatment of B virus infection in humans. The group's report, Recommendations for Prevention of and Therapy for Exposure to B virus (Cercopithecine Herpesvirus 1), was published in Clinical Infectious Diseases in 2002. The 2002 report updates previous recommendations and describes the use of newer antiviral agents in post-exposure prophylaxis. (Also see the Prevention section.)

Prevention

There are no vaccines available for B virus. Experimental vaccines have been evaluated in animal models, but none are being considered for human trial.

With the substantial increase in the use of macaque models for research (e.g., HIV), the number of potential human exposures to B virus has increased concomitantly. This has led to the publication of guidelines, which have been updated several times, by expert panels of virologists, veterinarians, and physicians—the Recommendations for Prevention of and Therapy for Exposure to B virus (Cercopithecine Herpesvirus 1) in Clinical Infectious Diseases, 2002.

Principal Recommendations for Prevention

While exposures that involve unpredictable, potentially aggressive animals are not completely preventable, adherence to appropriate laboratory and animal facility protocols will greatly reduce the risk of B virus transmission.

- Work with B virus–susceptible monkeys should be done using humane restraint methods that reduce the potential for bites and scratches.
- Proper personal protective equipment, including a lab coat, gloves, and a face shield, must be used when working with macaque monkeys.
- Any bites, scratches, or exposure to the tissues or secretions of macaques must be cleansed immediately, as detailed in the Recommendations mentioned above.
Following B virus exposure, samples from both the exposed human and the implicated macaque should be sent for B virus diagnostic testing (see Specimen Collection section).

Transmission

B virus infection in humans usually occurs as a result of bites or scratches from macaques—a genus of Old World monkeys that serve as the natural host—or from direct or indirect contact of broken skin or mucous membranes with infected monkey tissues or fluids. The virus can be present in the saliva, feces, urine, or nervous tissue of infected monkeys and may be harbored in cell cultures derived from infected monkeys.

Possible routes of transmission to humans include

- Bite or scratch from an infected animal
- Needlestick from contaminated syringe
- Scratch or cut from contaminated cage or other sharp-edged surface
- Exposure to nervous tissue or skull of infected animal (especially brain)

B virus may survive for hours on the surface of objects, particularly on surfaces that are moist. The injury need not be severe for infection to occur, although non-penetrating wounds are thought to carry a lower risk of transmission.

Transmission risks of B virus to humans should be considered in the context of the rarity of observed transmission, even among broadly infected populations of animals. Hundreds of macaque bites and scratches occur annually in primate facilities in the United States, but B virus infection in humans occurs only rarely. In a study of more than 300 animal care workers, among whom, 166 reported possible transmission risk exposures to macaques, none of the workers was considered to be B virus positive.

Only one case of human-to-human transmission has been documented; the case, which was reported in a study of a B virus outbreak involving 4 persons in Florida, resulted from direct physical contact with lesions (see Epidemiologic Notes and Reports B-virus Infection in Humans -- Pensacola, Florida. Morbidity and Mortality Weekly Report 1987). Among the 4 case patients, 3 were animal handlers (2 suffered bite wounds and 1 had close contact with the sick macaque but was not injured or exposed to other bodily fluids and did not develop symptoms). The fourth patient was the wife of 1 of the animal handlers. She used an ointment to treat her husband's lesions and subsequently used it on herself to treat contact dermatitis. She seroconverted to B virus but never developed symptoms. The study found no evidence of B virus infection among 130 close contacts of the 4 patients, healthcare workers, or primate workers. Moreover, even though B virus seroprevalence among adult macaques is >70%, only a few people in the study developed laboratory evidence of B virus exposure. Thus, transmission of this virus, both human-to-human and primate-to-human, is quite rare.

REFERENCES

Biosafety in Microbiological and Biomedical Laboratories, CDC/NIH 4th edition

Center for Disease Control and Prevention – Herpes B virus
http://www.cdc.gov/herpesbvirus/index.html

National B Virus Resource Center
http://www2.gsu.edu/~wwwvir/

Recommendations for Prevention of and Therapy for Exposure to B Virus – Clinical Infectious Disease 2002
http://cid.oxfordjournals.org/content/35/10/1191.full