### HERPESVIRUS B

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<th>Animal Group(s) Affected</th>
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<td>Macaques; other non-human primates; humans</td>
<td>Bites, scratches, fomites, saliva or bodily fluids, mucosal absorption possible, laboratory transmission (i.e., needle puncture)</td>
<td>Macaques: generally intermittent mucosal pustules. Non macaque species: Sometimes are herpes-like mucosal lesions are associated with the point of infection. Most cases present with fever, and encephalitis manifesting neurologic signs, including: dysphagia, ataxia, confusion, paresthesia and paralysis</td>
<td>Non macaque species: Without treatment, it is very fatal (70 - 80%). Some patients continue to have neurologic sequelae after recovery</td>
<td>Anti-virals, such as: ganciclovir, valacyclovir, and famciclovir. Many patients opt to remain on drugs for years after initial infection</td>
<td>Personal protective equipment, including gowns or coveralls, gloves, goggles and a mask or respirator.</td>
<td>Yes</td>
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**Fact Sheet compiled by:** Melinda Rostal  
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**Fact Sheet Reviewed by:** Richard Eberle; Jan Ramer  

**Susceptible animal groups:** The disease occurs naturally in all macaques. Humans and other nonhuman primates are susceptible.  
**Causative organism:** Macacine herpesvirus 1, also called herpes B virus or B virus  
**Zoonotic potential:** Yes  

**Distribution:** All reported cases in humans have been people that work with captive macaques or have been exposed in the field. Macaques are usually asymptomatic and may have been seronegative at the last screening or even at the time of the exposure prior to seroconversion. One report of human infection from Vietnam has been documented otherwise no cases from individuals has been reported in Asia in areas that macaques inhabit.  
**Incubation period:** < 2 days to 2-3 weeks, usually 5-8 days. Two cases were reported where the patient had no previous exposure to macaques or exposure had occurred over 10 years previously.  
**Clinical signs:**  
**Macaques:** 80-100% of sexually mature macaques, especially if they have contact with other macaques, are seropositive for B virus. They rarely have clinical signs indicating infection or recrudescence; however, they will occasionally have herpes-like skin mucosal pustules. Research on shedding frequency is inconclusive, although it increases during periods of stress, including the breeding season.  
**Humans:** Sometimes there are herpes-like skin/mucosal lesions associated with the point of infection accompanied by pain and itching and erythema. Most cases present with fever, and encephalitis manifesting in neurologic signs including: dysphagia, ataxia, confusion, paresthesia and paralysis. Latency is established.
and reactivation can occur.

**Post mortem, gross, or histologic findings:**
Macaques: Most often, histological evidence of acute infection is present without gross pathology. The virus often remains latent in the trigeminal or sacral nerve ganglia, from which culture or PCR may be used to detect the virus. If oral or genital lesions are present there may be vesicle formation with leukocytic invasion of the area; when keratinized cells overlying the vesicle slough, a plaque of necrotic fibrinous material remains overlaying the base of the ulcer. Intranuclear inclusions can be seen in tissues showing recent signs of degeneration.

Humans: Few reports of histological findings have been documented. Inclusion bodies are not typically found. Reported findings include severe inflammatory and degenerative changes in the spinal cord, particularly in the cervical cord and brainstem; the thalamus and hypothalamus may also be infected.

**Diagnosis:** B virus antibody ELISA or B virus recombinant ELISA assays are used. A negative antibody titer does not indicate the animal is not infected, only that it is not currently producing antibodies. Rising titers may be associated with viral shedding period. Diagnosis is often based on Western blot or virus neutralizing antibodies as well as virus isolation. PCR has been developed as well.

**Material required for laboratory analysis:**
For serology: 0.5-2.0 ml serum in plastic tube. Store and ship at -20ºC or with dry ice.
For virology: Swabs of vesicle or other lesions. Place swab in 1-2 ml viral transport media, store at -80ºC. CSF, autopsy samples of brainstem, biopsies from the site of inoculation: place in plastic storage/shipment tubes. Ship samples on dry ice according to US Department of Transportation regulations.

**Relevant diagnostic laboratories:** B-virus is a BSL 4 agent.
B Virus Research and Resource Laboratory
Dr. Julia Hilliard
Georgia State University, Viral Immunology Center
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Atlanta, GA 30302-4118
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Dr. David Brown
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Virus Reference Laboratory (non-human primates only)
VRL – San Antonio
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San Antonio, Texas 78229
(210) 614-7350
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**Treatment:** Non macaques: Anti–virals are used to attempt to control or prevent encephalitis. Recommended medications include: ganciclovir, valacyclovir, and famciclovir. Many patients must remain on anti–virals for years after exposure. FEAU (2’-fluoro-5-ethyl-Ara-U) is a new anti-viral that appears effective in cell culture, but has not been used in a human case.

**Prevention and control:** All macaques need to be treated as B virus-infected. Due to the severity of
infection with B virus in humans the US Centers for Disease Control and Prevention (CDC) developed guidelines to prevent B virus in workers handling macaques (http://www.cdc.gov/mmwr/preview/mmwrhtml/00015936.htm.) The most recently updated version of these recommendations was given in 2002 by the B Virus Working Group. The recommendations are briefly outlined below.

- Personnel must wear appropriate personal protective equipment including glasses and face shields, masks, long sleeve protecting clothing, and nitrile or latex gloves. If the animal is not sedated, leather gloves extending to the shoulder should be used.
- Personnel must be trained in the associated risks of infection and appropriate response protocols.
- Upon possible exposure, the person should immediately wash the wound or lavage the mucous membrane exposed for 15 minutes.
- Collect baseline serum and culture samples from the person and the macaque.
- Starting prophylaxis with an anti-viral within 24 hours is recommended if the case meets one of the following criteria:
  - Exposure of mucosa or injured skin to an ill or immunocompromised or shedding macaque.
  - Exposure of mucosa or injured skin that is not adequately cleaned.
  - Laceration is of the head, neck or torso.
  - Deep puncture bite or a needle puncture associated with macaque CSF fluid, herpes-like lesions, eyelids or mucosa.
  - A post-cleaning culture of wound is positive for B virus.
  - A laceration is caused by an object contaminated by macaque mucosal, genital or saliva secretions.
- Prophylaxis with an anti-viral should be considered if the case meets one of the following criteria:
  - Exposure of mucosa or injured skin that has been adequately cleaned.
  - A needles puncture was associated with blood from an ill or immunocompromised macaque.
  - Skin that was recently exposed to contaminated macaque body fluid or cell culture has been lacerated.

**Suggested disinfectant for housing facilities:** Macaque housing should be cleaned with hot water and detergent by staff utilizing appropriate PPE such as masks and face protection while cleaning. Currently efforts are underway to create specific pathogen free (SPF) colonies of macaques and some groups has successfully maintained populations of macaques that are 99.3% free of B virus for longer than 7 years. This process involves initially keeping the macaques isolated and culling seropositive animals. No current recommendations for disinfecting housing facilities are available since in seropositive populations the virus tends to be ubiquitous and in SPF populations positive animals should be culled. All macaques should be treated as if positive for B virus. Research is also underway to create a B virus vaccine for macaques.

**Notification:** B virus has been a CDC Select Agent; however, as of 4 December 2012, it is no longer a select agent. B virus infections are not reportable on a national level, although states may vary in their reporting requirements.

**Measures required under the Animal Disease Surveillance Plan:** This virus is not listed under Annex A or B.

**Measures required for introducing animals to an infected animal(s):** If a seronegative animal is introduced to a seropositive animal it should be expected that the animal will seroconvert eventually, especially after the onset of sexual maturity. SPF colonies must cull seropositive animals and closely monitor cagemates to prevent the virus from becoming established in the colony.

**Conditions for restoring disease-free status after an outbreak:** No specific standards exist at this time; however, it is recommended to test the animals for antibodies one month apart and again following a time
period of greater than 6 months, but less than 12 months.

**Experts who may be consulted:**
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**References:**