

# MMWR: Weekly

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## Fatal Cercopithecine herpesvirus 1 (B Virus) Infection Following a Mucocutaneous Exposure and Interim Recommendations for Worker Protection

On December 10, 1997, a 22-year-old female worker at a primate center died from Cercopithecine herpesvirus 1 (B virus) infection 42 days after biologic material (possibly fecal) from a rhesus macaque (*Macaca mulatta*) splashed into her right eye. This report summarizes the clinical features of her illness and the subsequent investigation by CDC in response to a technical assistance request from the Occupational Safety and Health Administration (OSHA) and presents interim recommendations to prevent ocular splash exposures. This investigation documented the hazard of ocular splashes and indicated that dendritic corneal lesions, such as herpetic skin vesicles, are not always present in B virus infection (1).

The exposure occurred on October 29, 1997, while the worker moved the animal within cages during a routine capture of free-ranging monkeys. She was not wearing protective eyewear because the activities in which she was engaged involved caged macaques, and the activities were judged by the primate center to carry a low risk for exposure to B virus. Following the exposure, the worker wiped her eye with a paper towel and, approximately 45 minutes later, irrigated the eye for 2-3 minutes with tap water but did not file an incident report. The monkey involved was not identified.

On November 8, the worker's eye was red and swollen. At the emergency department (ED) of a medical center affiliated with the same university as the primate center, she informed the physician that she worked with nonhuman primates and may have been exposed to B virus. Dendritic corneal lesions typical of ocular herpes infections were not observed by Wood's lamp examination. The ED physician consulted the B virus protocol in place in the ED and then consulted an infectious diseases specialist by telephone. On the basis of the reported circumstances of the contact and the absence of previous recognized transmission of B virus following mucocutaneous exposure, the infectious diseases specialist concluded that B virus infection was unlikely but recommended follow-up with the infectious diseases clinic within the next few days. The ED physician prescribed sulfonamide eye drops.

An appointment at the infectious diseases clinic was not available immediately. On November 11, the worker called her primary-care physician for a referral because her eye symptoms were worsening. The physician referred her to an ophthalmologist, who elicited history of a recent cat scratch and prescribed doxycycline for suspected Parinaud's oculoglandular syndrome secondary

to cat-scratch fever. Routine eye cultures were obtained. Confirmatory serologic testing for *Bartonella* species, also ordered during the visit, subsequently was negative.

On November 13, the worker sought care from another ophthalmologist because of increased right retro-orbital pain and onset of photophobia, anorexia, nausea, and abdominal pain. After reconsultation with the infectious diseases specialist, the worker was immediately hospitalized for suspected B virus infection. The worker's temperature, normal on admission, reached 101.4 F (38.6 C) during the first day of hospitalization. Physical examination identified a swollen right orbit with conjunctivitis and one small tender right preauricular lymph node. Laboratory examination of urine found trace proteinuria. Cerebrospinal fluid (CSF) analysis identified 8 white blood cells per milliliter (83% lymphocytes {normal: 0-10 cells, 100% mononuclear}). Serum for Western blot testing and CSF specimens and eye swabs for B virus culture were sent to the B Virus Research and Resource Laboratory. All previously collected eye cultures were retrieved from commercial laboratories to minimize biosafety hazards to laboratory workers.

Acyclovir therapy (15 mg/kg intravenously every 8 hours) was started within 2 hours of hospital admission. On November 14, therapy was changed to ganciclovir (5 mg/kg every 12 hours) when a vesicular eruption was noted in the distribution of the first and second branches of the right trigeminal nerve. Magnetic resonance imaging (MRI) of the head was normal. The vesicles resolved over the following week. A sharp mid-cervical/high thoracic back discomfort occurred on November 19 but subsided over an 8-hour period. All symptoms resolved, and on November 24 the worker was discharged on outpatient intravenous (IV) ganciclovir therapy.

Despite uninterrupted ganciclovir therapy, on November 25 the worker woke with right foot weakness, inability to urinate, and lower abdominal pain, followed by a rapidly progressive ascending myelitis. The hospital readmission examination found profound right leg weakness, moderate left leg weakness, decreased hand grip strength bilaterally, and urinary retention. MRI revealed abnormalities extending from the cervical spinal cord to the upper thoracic cord. The worker was intubated electively within 13 hours and developed flaccid paralysis from C2 caudad.

The diagnosis of postviral acute demyelinating encephalomyelitis was considered by neurology consultants, and a short course of plasmapheresis and steroids was administered. On November 30 seizure activity (involuntary facial and eye movements) developed, and foscarnet, usually not recommended for B virus infection because of its toxicity, was added to ongoing ganciclovir therapy. During December 1-9, the worker developed nosocomial pneumonia with bacteremia, followed by adult respiratory distress syndrome. Repeat MRI revealed abnormalities extending from midbrain through the thoracic spinal cord. On December 10, the worker died from refractory respiratory failure.

Eye and CSF cultures obtained in the hospital on November 13 and November 14 were negative for B virus when tested at the B Virus Research and Resource Laboratory. Serum collected November 13 and November 21 and tested for reactivity to B virus by Western blot showed indeterminate and positive reactivity, respectively, confirming B virus infection.

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## **Editorial Note**

Editorial Note: C. herpesvirus 1 (B virus) causes persistent latent infections in greater than or equal to 70% of captive adult macaques (2) but not other primates. During intermittent reactivations, the macaque may shed B virus from the buccal mucosa, urogenital tract, and in conjunctival fluid (2). Reactivations may be asymptomatic or accompanied by clustered vesicles on an erythematous base.

This is the first report of a worker developing a recognized B virus infection following mucocutaneous exposure without injury. Previously reported human infections usually have been attributed to macaque bites or scratches, injuries from needles used near a macaque's mucous membranes or central nervous system, or contact with infective biologic materials from macaques (3-5). One human-to-human transmission has been identified (6). The incubation period in humans has been as short as 2 days but more frequently is 2-5 weeks. Previously reported patients infected with B virus who were treated aggressively with either IV acyclovir or ganciclovir after onset of symptoms but before respiratory arrest or coma have survived (3). The death of this patient despite aggressive antiviral therapy may have resulted from factors related to the route of virus inoculation, the virulence of the virus infecting the patient, the patient's immune response, or timing of initiation of treatment following the exposure.

## **Interim Recommendations to Prevent Ocular Splash Exposures**

Preventing worker exposure to biohazardous material is the best protection against infection. Reviews of injuries and biohazard exposures among workers exposed to nonhuman primates suggest that mucocutaneous contact with nonhuman primate body fluids is common; 16 (94%) of 17 contacts with primate body fluids in one survey involved ocular exposure (6,7). Each institution working with macaques should develop a written comprehensive personal protective equipment (PPE) program based on thorough hazard assessments of all work procedures, potential routes of exposure (e.g., bites, scratches, or mucosal exposures) and potential adverse health outcomes. This plan should clearly identify the PPE required for each task or working area and address training, inspection, maintenance, and periodic assessment of program effectiveness.

Previous recommendations for preventing B virus infections in humans advise presuming that all macaques are infected with B virus and protecting workers with a faceshield (or surgical mask and goggles or glasses) when handling uncaged active macaques (3,8). The incident described in this report indicates that proper eye protection also should be mandatory during activities such as entering areas containing macaques, conducting captures, and transporting caged macaques. Other activities where eye protection is necessary should be determined by the hazard assessment. All personnel who work in situations determined to be hazardous should wear eyewear conforming to established standards for eye and splash protection (9). Personal eyeglasses are not PPE.

Protective goggles designed for splash protection (available with antifog lenses for humid environments and in models that preserve peripheral vision) should be worn to protect the eyes against splash hazards in combination with a mask designed to protect other mucous membranes. Faceshields are commonly considered secondary eye protectors that are worn in combination with protective goggles (9,10). Although previous guidelines indicate a faceshield may be sufficient, ocular exposures have occurred to workers wearing faceshields, including to a worker who was wearing a combination surgical mask/faceshield while moving a macaque within cages. To minimize the potential for mucous membrane exposure, faceshields must prevent droplet splashes to the head from running down into the eyes and prevent mucous membrane exposure around the edges (sides, top, and bottom to below the chin) (10). Decisions to use faceshields as the sole means for preventing ocular exposure should only be made after full consideration of both the limitations of faceshields and regulatory (OSHA) considerations.

### Exposure Management

If exposure prevention fails, the adequacy and timeliness of wound or exposure decontamination procedures are critical factors determining the risk for infection. Institutions that house or conduct procedures involving nonhuman primates or potentially contaminated tissues should develop institution-specific postexposure procedures (3,8). Such procedures would eliminate institutional barriers to patient access and ensure appropriate diagnostic testing and infection control. First, animal handlers should be instructed to cleanse immediately and thoroughly all bites, scratches, and/or mucosal surfaces or abraded skin exposed to macaque biologic materials and to report these exposures immediately (3). Following an exposure to the eye, existing guidelines recommend immediately flushing the eye with water for at least 15 minutes (3). Second, postexposure procedures also should provide potentially exposed workers with direct and rapid access to a local medical consultant knowledgeable about B virus and other biohazards associated with nonhuman primates. The employer should ensure that direct access to the knowledgeable consultant is available immediately following exposures and at any time the worker is concerned that potential occupational exposure to B virus may be relevant to worker symptoms. Finally, postexposure procedures also should include routing diagnostic specimens to the B Virus Research and Resource Laboratory, now at Georgia State University in Atlanta. These interim recommendations will be reviewed and may be revised or augmented following additional consideration by a working group convened by Office of Health and Safety, CDC.

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