## TABLE OF CONTENTS

## 1.0 INTRODUCTION

Simian B virus (Herpes simiae, *Cercopithicine herpesvirus* -1) is a naturally occurring infectious agent that is endemic among macaque monkeys (including rhesus macaques, pig-tailed macaques, cynomolgus monkeys, and other macaques). Infected monkeys often have no or very mild symptoms, although oral and genital lesions may develop. Infections due to Simian B virus in humans are rare and occur as a result of exposure to either macaques or their secretions. Only ~50 cases of Simian B virus infection in humans have been identified worldwide to date. All reported cases have been in researchers and laboratory workers handling captive macaques or infected tissue/body fluid from captive macaques. **So far there have been no confirmed cases of Simian B virus infection in travelers or in countries where there is frequent human-monkey contact despite the fact that monkey bites in travellers are common.**

## 2.0 CLINICAL DESCRIPTION

**Mode of transmission:** Infection occurs by a percutaneous or permucosal exposure to the infectious tissues or fluids of macaque monkeys. The ocular, oral and genital secretions are potentially infectious. Monkey bites and scratches are well documented routes of Simian B virus infection.

In infected humans, Simian B virus replicates at the site of exposure which may manifest as a vesicular rash. The virus spreads along the peripheral nervous system to the spinal cord and then to the brain.

**Incubation period**: This is reported to range from as little as 2 days to 5 weeks with most well-documented cases presenting **5 – 21 days** after exposure.

**Clinical description:** A vesicular rash may develop at the site of exposure. Additional symptoms can include tingling, itching, pain, or numbness at the site although many patients report no symptoms at the site of infection beyond the discomfort of the wound. Some patients develop lymphadenopathy proximal to the site of inoculation. Within the first 3 weeks after exposure, paresthesias may develop and proceed proximally along the affected extremity. Associated symptoms can include fever, myalgias, weakness of the affected extremity, abdominal pain, sinusitis and conjunctivitis. The virus spreads along the nerves of the peripheral nervous system to the spinal cord and then to the brain. Once at

this stage symptoms include headache, meningismus, nausea, vomiting, confusion, cranial nerve palsies, ataxia etc. Asymptomatic infection of humans has not been documented.

**Among untreated humans, the mortality rate associated with B virus infection is estimated to be 80%. With effective antiviral treatment this is expected to be lower, however, there are too few cases reported to determine this rate.**

## 3.0 DEFINITIONS

**Confirmed case of B virus infection:** B virus seropositive, as defined by both ELISA and Western Blot analysis.

**Exposure:** Skin exposure (macaque bites; macaque scratches; or contact with ocular, oral, or genital secretions, nervous tissue, or material contaminated by macaques) with loss of skin integrity **OR** mucosal exposure with or without injury.

For each primate exposure, 3 major variables need to be assessed:

1) **Source of exposure:** Macaques are the **only** primates known to transmit Simian B virus. Other primates pose no known risk unless they have had the opportunity to acquire infection directly from a macaque; this has not been documented but is theoretical. Macaques with oral lesions are more likely to be shedding virus. Primates that are ill, stressed or gravid are all more likely to shed Simian B virus. Captive macaques are much more likely to be seropositive for Simian B virus and in one study 100% of captive macaques over 2.5 years of age were seropositive.

2) **Adequacy of wound first aid:** Adequate wound care includes: cleansing within 5 minutes of exposure for a full 15 minutes.

3) **Type of wound:** The type of wound or exposure, the depth of the wound, and the location of the wound should all be considered in the management. Infections from exposure of the head, torso or neck may present with no signs or symptoms before the CNS is involved and should be classified as high risk. Superficial wounds and scratches are easily cleaned and, therefore, usually are considered of lower risk. Deep punctures – in particular, those caused by bites – are likely to result in inadequately cleansed wounds and pose a higher risk.

**Note: Prophylaxis is strongly recommended for cases with:** skin puncture exposure that could not be adequately cleaned or mucosal exposure to a high-risk source (macaque monkey in captivity) particularly if there was a deep puncture bite or laceration of the head, neck or torso.

**Prophylaxis is not recommended for:** skin exposure in which the skin remains intact; exposure associated with non-macaque species of nonhuman primates.

## 4.0 GUIDELINES FOR POST-EXPOSURE PROPHYLAXIS

Post-exposure prophylaxis is defined as administration of an antiviral medication to a person potentially exposed to simian B virus but not documented to be infected. There have been no noted cases in which humans who received post exposure prophylaxis within 72 hours of exposure developed disease.

### 4.1 Was the person exposed to a macaque primate?

Simian B virus disease in humans usually results from macaque bites or scratches. Following is a web site to assist with identification of the type of monkey involved: http://www2.gsu.edu/~wwwvir/VirusInfo/macaque.html

### 4.2 First Aid

The most critical period for the prevention of B virus infection and other infections is during the first few minutes after an exposure occurs. Both the adequacy and the timeliness of wound or mucosa cleansing are the important factors for reducing the risk of infection. Washing of the involved site should last for at least 15 minutes with a solution containing detergent soap (e.g. chlorhexidine). In addition to being washed, wounds may be gently massaged to increase their contact with the cleansing solutions. Incision of wound sites is not recommended.

### 4.3 Detailed History

A detailed history should be obtained and the time, source, type of exposure, and the time and adequacy of cleansing after the exposure should be documented.

### 4.4 Diagnostic Testing

**Consultation with the BCCDC virologist-on-call is required before the collection of specimens for Simian B virus testing.**

Simian B virus is classified as a Biosafety Level-4 biologic agent and testing of material known or suspected to contain this virus should be done at a facility designated as having a Biosafety Level of 4. In North America, there are three laboratories that perform diagnostic testing for the agent. All specimens are to be sent to BCCDC Laboratory Services and will then be forwarded to an appropriate laboratory.

PCR testing to identify Simian B virus is feasible but only if clinically appropriate; consultation with the BCCDC virologist on-call is required before PCR testing is considered. The US CDC advises against PCR testing of lesions from concern the test may force virus into the wound.

The need for serologic testing of people potentially exposed to simian B virus is controversial and is unlikely to be helpful. Serology is not effective for clinical diagnosis of Simian B exposure in humans because it takes approximately 3-6 weeks before a serological response can be diagnosed. By this time it is too late to consider antiviral prophylaxis. Serology may be appropriate for laboratory workers handling Macaques or to manage high risk exposures in individuals who have received post-exposure prophylaxis.

## 5.0 EPIDEMIOLOGY/HISTORICAL INFORMATION

There have been no documented cases of Simian B virus infections in British Columbia to date. Only ~ 50 cases of B virus infection in humans have been reported worldwide, with only 26 of these being well documented cases:

| Exposure | No. of cases |
|---|---|
| Monkey bite | 10 |
| Monkey scratch | 2 |
| Wound contamination with monkey saliva | 2 |
| Tissue culture-bottle cuts | 1 |
| Needlestick injury | 2 |
| Possible aerosol | 2 |
| Cleaning monkey skull | 1 |
| Needle scratch and monkey bite | 1 |

| | |
|---|---|
| Cage scratch | 2 |
| Possible reactivation of simian B virus | 1 |
| Human to human contact | 1 |
| Mucosal splash | 1 |
| Unknown | 1 |

All reported cases have been in researchers and laboratory workers handling captive macaques or infected tissue/body fluid from captive macaques. So far there have been no confirmed cases of Simian B virus infection in travelers or in countries where there is frequent human-monkey contact despite the fact that monkey bites in travellers are common. This may be due to a number of factors including: wild macaques may be less likely to shed virus; wild animals may have less virulent strain of the virus; the viral load transmitted by bites in travellers may be insufficient for infection; disease may be undiagnosed in non-laboratory associated settings; testing for Simian B virus is not widely available and infection may not be diagnosed particularly in resource-poor countries. Studies in macaques and local human populations with contact with macaques in SE Asia have shown high rates of carriage of Simian B antibodies in the monkey population but no evidence of illness in locals who had contact with the macaques including those who had received frequent bites or scratches.

The US CDC and others have developed comprehensive occupational health guidelines for workers who have exposures to captive macaques including use of gloves and mucosal protection, protocols for immediate first aid and reporting of possible exposures and education of workers on the risks of Simian B virus infection. Travelers should be warned of the risks of contact with macaques while traveling and to avoid high risk activities such as feeding of the primates. Children are more likely to be bitten than adults and should be prevented from contact with primates. Given the small but real risk for simian B virus shedding, macaques are not suitable as pets.

## 6.0 POST-EXPOSURE PROPHYLAXIS

Prophylaxis is recommended when: there has been skin exposure or mucosal exposure to a high-risk source (a captive macaque monkey), **and** there was

inadequate cleansing of the exposed area **or** the exposure was a deep puncture bite.

To be effective prophylaxis should be started within hours after the exposure but given the extended incubation period for illness may be effective even after several days. Effectiveness in humans has not been proven, however, PEP recommendations are based on studies showing increased survival in rabbits treated with acyclovir. In these studies there was no effectiveness demonstrated if PEP was given after 5 days, however Herpes B virus infection in rabbits results in more rapid progression of disease than in humans suggesting PEP after 5 days may still be of benefit in humans.

**For occupational exposures (i.e. laboratory workers or others working with captive macaques) PEP should be considered up to 5 weeks (the longest known incubation period) from the time from exposure, as this is the highest risk group for development of illness.**

**While some organizations (including infectious disease and pediatric associations) have recommended assessing and providing PEP to travelers who received bites by wild macaques this is currently not recommended by public health as there is evidence that risk in these situations is exceedingly small. In BC, infectious disease experts may recommend PEP in individual cases based on risk assessment.**

Three orally administered agents – acyclovir, valacyclovir, and famciclovir – are currently available for post-exposure prophylaxis of simian B virus infection. These drugs have not been approved by the US Food and Drug Administration for the treatment of simian B virus infection.

The recommended anti-viral agent of choice is **valacyclovir, 1 g, given 3 times daily for 14 days.**

The first alternate choice is Acyclovir, 800 mg 5 times daily for 14 days. Acyclovir is the preferred agent if post-exposure prophylaxis is to be initiated in pregnancy.

Famciclovir 500mg po 5 times daily may be an effective alternative, however, lack of animal studies of effectiveness for PEP limit its use.

If the patient remains asymptomatic after 14 days, discontinuation of the PEP is recommended with a careful follow up at 3-6 weeks after exposure.

**Consultation with an Infectious Disease specialist is strongly recommended before or immediately after initiation of prophylaxis**.

## 7.0 AUTHORITY

Public Health Act (2009) and Communicable Disease Regulation

## 8.0 REFERENCES

Cohen, J.I., Davenport, D.S., Stewart, J.A., Deitchman, S., Hilliard, J.K., Chapman, L.E., and the B Virus Working Group. (2002). Recommendations for Prevention of and Therapy for Exposure to B Virus (Cercopithecine Herpesvirus - 1) Clinical Infectious Diseases, 2002; 35:1191-203

Johnson, G., Dick, D., Ayers, M., Petric, M., Tellier, R. Detection and species-level identification of primate herpesviruses with a comprehensive PCR test for human herpesviruses. J. Clin. Microbiol. 2003;41:1256 – 1258.

U.S. Department of Health and Human Services. (1987). Guidelines for Prevention of Herpesvirus Simiae (B Virus) Infection in Monkey Handlers. Morbidity and Mortality Weekly Report, 36 (41).

Ritz, Nicole MD; Curtis, Nigel FRCPCH, PhD; Buttery, Jim MD ; Babl, Franz E. MD, MPH. Monkey Bites in Travelers: Should We Think of Herpes B Virus? Pediatric Emergency Care. 25(8):529-531, August 2009

Harold T. Zwartouw, Christopher R. Humphreys and Peter Collins. Oral chemotherapy of fatal B virus (herpesvirus simiae) infection Antiviral Research Volume 11, Issues 5-6, June-July 1989, Pages 275-283

Perlino, C, Hilliard, J, Koehler, J. Fatal Cercopithecine herpesvirus 1 (B virus) infection following a mucocutaneous exposure and interim recommendations for worker protection. MMWR: Morbidity & Mortality Weekly Report, 01492195, 12/18/98, Vol. 47, Issue 49

Engel G, Jones-Engel L, Schillaci M, Suaryana M, Putra A, Fuentes A, and Henkel R. Human Exposure to Herpesvirus B–Seropositive Macaques, Bali, Indonesia Emerging Infectious Diseases • Vol. 8, No. 8, August 2002