

# B Virus (Herpes Simiae Virus) Infection: Global and Local Epidemiology

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30 May 2024



### **Causative agent**

 B virus 猴疱疹病毒 (also known as herpes simiae virus, cercopithecine herpesvirus 1, or macacine alphaherpesvirus 1) is an α-herpesvirus, belonging to the family of Herpesviridae under the genus of Simplexvirus.



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### NEW TAXONOMIC ORDER







- B virus is an enveloped double-stranded DNA virus with numerous open reading frames, some of which share approximately 79% amino acid sequence identity with HSV-1 and HSV-2.
- Glycoproteins B and D have 80% and 56% identity with the respective HSV-1 glycoproteins, whereas glycoproteins G and C exhibit significant sequence variation.



Picture from: J Lu, et al. Front. Immunol., 16 November 2023



# **Discovery of B virus**

- The first case of human B virus infection was documented in 1932.
- On Oct 22, 1932, A researcher (patient Dr. W.B.) was bitten on the dorsum of the left ring and little fingers at the terminal phalangeal joints, by an apparently normal Macacus rhesus monkey, while engaging in experimental work on poliomyelitis.
- He died of progressive encephalomyelitis on Nov 9, 1932 (15 days after the injury) in Bellevue Hospital, New York.





# **B** virus infection in monkeys

- Macaques are the natural host of herpes B virus, a type of wild monkeys commonly found in Hong Kong.
- B-virus infection has been reported most commonly in the rhesus and cynomolgus macaque (M. facicularis).
- B virus has also been isolated from the following macaque:
  - stumptail (M. artoides)
  - pig-tailed (M. nemestrina)
  - Japanese (M. fuscata)
  - bonnet (M. radiata)
  - Taiwan(M. cyclopis)
- Strain differences between B virus isolates from different macaque species.
- Herpes B virus from rhesus macaques seems more pathogenic for humans than those of other macaque species.





Macaque 獼猴



# **B** virus infection in monkeys

- B virus infection in macaques are usually latent and asymptomatic or cause only mild disease.
- Oral herpetic lesions such as gingivostomatitis, oral and lingual ulcers, and conjunctivitis have been described,

usually associated with immunosuppression or stress (attributable to breeding season, recent importation or crowded housing conditions).

- The virus can be latent in the trigeminal ganglia and lumbosacral nerve for a long time, and be reactivated and shed from the oral, nasal, or genital mucosa without signs of clinical illness.
- The shedding probability of monkeys infected with the B virus is 1-2%.





# **B** virus infection in monkeys

- Infection is usually acquired at sexual maturity (2–4 years of age for rhesus macaques).
- The incidence rises with age.

生防護中心

- Seropositivity 80% to 100% in some adult macaque groups.
- It is mainly transmitted through mating, scratching or biting among macaques.



Cynomolgus macaque 食蟹獼猴



# **B** virus infection in humans

- B virus infections in humans are rare.
- Around 50 people (21 of them died) have been documented to have B virus infections worldwide.
- Human infection has been reported in United States, Canada, Mainland China and Japan.
- Most cases of human B-virus infection have involved direct contact with macaques, such as a bite, scratch, or mucosal contact with body fluid or tissue.
- Untreated human B virus infections have a fatality rate of 70-80%.





> J Med Primatol. 1987;16(2):99-130.

### B virus, Herpesvirus simiae: historical perspective

A E Palmer

PMID: 3035187

### Abstract

Between 1932 and 1972, 24 known infections of man by B virus caused 23 cases of encephalitis and 18 fatalities. The virus has been isolated from dermal lesions and neural ganglia from macaque monkeys. Serological evidence of infection is complicated by close antigenic relationships between B virus, Herpesvirus simplex, and SA8. Hyperimmune globulin produced from monkey, horse, and rabbit sera has not proved highly effective. Formalin-inactivated vaccine appears safe and antigenic in man but has not been licensed. Half of all human subjects have neutralizing B virus antibody related to their H. simplex titer. More stable animal populations and the improved use of protective apparel have reduced, but not eliminated, the risk of B virus to man.







### **Guidelines for Prevention of Herpesvirus Simiae (B Virus) Infection in Monkey** Handlers

The report of a case of encephalitis caused by B virus in a monkey handler in 1932 indicated that B virus can be highly pathogenic for humans (1). Seventeen additional cases of B virus infection in humans were described through 1973 (2)\* and four cases, including the first known case of person-to-person transmission of the virus, occurred in Pensacola, Florida, in 1987 (5). Twenty of the 22 cases resulted in encephalitis; 15 of these patients died. This extreme degree of morbidity and mortality has given the impression that B virus infection in humans nearly always results in severe or fatal disease. The frequency of mild or asymptomatic B virus infection, however, has never been adequately assessed.

The occurrence of the four 1987 cases of B virus infection prompted CDC to convene a working group to discuss guidelines for preventing B virus infection in monkey handlers. In

- B virus infections in humans—Michigan. MMWR Morb Mortal Wkly Rep. 1989 Jul 7;38(26):453-4.
- Fatal Cercopithecine herpesvirus 1 (B virus) infection following a mucocutaneous exposure and interim recommendations for worker protection. MMWR Morb Mortal Wkly Rep. 1998 Dec 18;47(49):1073-6, 1083.







### **EMERGING INFECTIOUS DISEASES**<sup>®</sup>

EID Journal > Volume 30 > Number 1—January 2024 > Main Article

Volume 30, Number 1—January 2024

Dispatch

### Macacine alphaherpesvirus 1 (B Virus) Infection in Humans, Japan, 2019

Souichi Yamada, Harutaka Katano, Yuko Sato, Tadaki Suzuki, Akihiko Uda, Keita Ishijima, Motoi Suzuki, Daigo Yamada, Shizuko Harada, Hitomi Kinoshita, Phu Hoang Anh Nguyen, Hideki Ebihara, Ken Maeda, Masayuki Saijo, and Shuetsu Fukushi

### Abstract

Two human patients with *Macacine alphaherpesvirus* 1 infection were identified in Japan in 2019. Both patients had worked at the same company, which had a macaque facility. The rhesus-genotype B virus genome was detected in cerebrospinal fluid samples from both patients.





China CDC Weekly

### First Human Infection Case of Monkey B Virus Identified in China, 2021

Wenling Wang<sup>1,&</sup>; Wenjie Qi<sup>2,&</sup>; Jingyuan Liu<sup>3,&</sup>; Haijun Du<sup>4,&</sup>; Li Zhao<sup>1</sup>; Yang Zheng<sup>5</sup>; Guoxing Wang<sup>2</sup>; Yang Pan<sup>5</sup>; Baoying Huang<sup>1</sup>; Zhaomin Feng<sup>5</sup>; Daitao Zhang<sup>5</sup>; Peng Yang<sup>5</sup>; Jun Han<sup>4,#</sup>; Quanyi Wang<sup>5,#</sup>; Wenjie Tan<sup>1,#</sup>

- The patient was a 53-year-old male veterinary surgeon who worked in an institute specialized in nonhuman primate breeding and experimental research in Beijing.
- He dissected two dead monkeys on March 4 and 6, 2021.
- After one month, he had nausea and vomiting followed by fever with neurological symptoms.
- B virus genome was detected as PCR positive in the CSF specimen.
- He eventually passed away on May 27, 2021.





### Transmission

- B virus is commonly found among macaques, which can be found in their saliva, urine, feces, brain or spinal cord tissue.
- **Direct contact**: bite, scratch, mucosal contact with body fluid or tissue of macaques .
- Indirect contact: injury from contaminated tools

FIGURE. Macaque monkey biting an Oregon resident in a public park in Thailand and the resultant wound — 2018







### Transmission

- Laboratory workers, veterinarians, and others who may be exposed to monkeys or their specimens have a higher risk of getting infection.
  - The cynomolgus (Macaca fascicularis) and the rhesus macaque (Macaca mulatta) are the most widely used nonhuman primate models in various biomedical research fields, including genomic analysis and neurodegenerative disease, as well as reproductive biomedical research.
- Human-to-human transmission is very rare only one case has been documented through direct physical contact with the infected person's wounds.





# **Clinical features**

- Incubation period: typically occur within 1 month after exposure, commonly 3 to 7 days.
- Initially present with flu-like symptoms such as fever and chills, muscle ache, fatigue and headache.
- Vesicular skin lesions may then occur at the exposure site (bite or scratch, or where contacted with macaque).
- Patient may develop nausea and vomiting, abdominal pain, shortness of breath and hiccups.





# **Clinical features**

- As disease progresses, the virus can spread to the central nervous system and develop hyperesthesia, ataxia, diplopia, agitation and ascending flaccid paralysis.
- Most patients with CNS complications may die even with treatments. Those who survive usually suffer serious long-term neurologic problems.

The risk of B-virus infection is low, but the risk for death is high.





# Diagnosis

- Isolated culture of B virus is the standard for diagnosis, but it requires a biosafety level 4 containment facility.
- B virus has extensive antigen crossover with HSV, SA8, and HVP-2, causing falsepositive results frequently.
- Although the gB, gC, and gD antigens used for B virus serological detection have a high sensitivity of 88-100%, the development of serologic assays that can reliably differentiate herpes B virus from HSV infections is also problematic.
- The detection of antiviral antibodies are unable to detect infections until an antiviral immune response has developed (at least 7 to 10 days after infection).





# Diagnosis

- Real-time fluorescence quantitative PCR is one of the most effective laboratory diagnostic methods.
- PCR assays have the advantage that they can rapidly and specifically detect minute quantities of virus.
- PCR can be used to test swabs from the site of a bite or scratch for the presence of virus.





## Prevention

- No vaccine available to protect people against B virus infection. Experimental vaccines have been evaluated in animal models.
- Stay away from macaque monkeys and avoid touching or feeding them.
- All personnel who work with macaques should wear personal protection equipment, particularly eyewear conforming to established standards for eye and splash protection.
- If exposure prevention fails, the adequacy and timeliness of wound or exposure decontamination procedures are critical factors in determining the risk for infection.
  - Wash and gently scrub the exposure site in contact with infected monkey immediately with soap, detergent, or iodine for 15 minutes.
  - > Then run water over the exposure site for another 15-20 minutes.





### Hong Kong's first human case of B virus fighting for his life after monkey attack

简生防護中心 Centre for Health Protection **scmpnews ♀**・追蹤 Hong Kong

scmpnews Hong Kong's first recorded human case of the deadly B virus is fighting for his life in hospital after he was attacked by a wild monkey, health authorities have said.

The man, 37, was admitted to Tsuen Wan's Yan Chai Hospital with a fever and decreased conscious level on March 21.

It added that a test of his cerebrospinal fluid came back positive for the B virus, also known as the human simiae virus.

The man was currently in a critical condition and receiving treatment in the hospital's intensive care unit.

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### First B virus human infection in Hong Kong

- A 37-year-old male with good past health
- Patient initially presented with fever, coryzal symptoms and right upper eyelid swelling.
- Patient was found drowsy and was admitted to Yan Chai Hospital through accident and emergency department on March 21 due to fever and decreased conscious level.
- He received treatments at the Intensive Care Unit of the hospital and his condition was critical on April 3.
- Cerebrospinal fluid specimen of the patient tested positive for B virus by the Public Health Laboratory Services Branch.





### **Exposure** history

- The patient's relative met the patient in Feb for meal and noticed that he had rather fresh bite wound on hand and some scratch wounds on legs.
- Upon questioning, the patient volunteered that he transferred fruits to feed the monkeys at Kam Shan Country Park.
- He was wounded when trying to drive away elder monkeys and save the food for the smaller ones.





### First B virus human infection in Hong Kong

The Government of the Hong Kong Special Administrative Region Press Releases

繁體版 简体版

CHP investigates case of B virus human infection

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CHP investigates case of B virus human infection

GovHK 香港政府一站通

The Centre for Health Protection (CHP) of the Department of Health (DH) is today (April 3) investigating a case of human infection of B virus (also known as herpes simiae virus), and urged the public to refrain from touching or feeding wild monkeys to minimise the risk of contracting the virus.

The case involves a 37-year-old male with good past health, who was admitted to Yan Chai Hospital through accident and emergency department on March 21 due to fever and decreased conscious level. He is now receiving treatment at the Intensive Care Unit of the hospital and his condition is critical. Cerebrospinal fluid specimen of the patient tested positive for B virus by the Public Health Laboratory Services Branch of the CHP today.

According to the information provided by his family members and preliminary investigations, the patient had contacts with wild monkeys and was wounded by them during his visit to Kam Shan Country Park in late February. Epidemiological investigations are ongoing.

A spokesman for the CHP said that this is the first B virus human infection case recorded by the CHP, but these cases had been reported in other places such as the United States, Canada, the Mainland and Japan, and were mainly caused by bites or scratches by monkeys while human-to-human transmissions are very rare. Members of the public are strongly urged to refrain from touching or feeding wild monkeys.

The spokesman supplemented that B virus is naturally carried in the saliva, urine and stool of macaques, which is a type of wild monkeys commonly found in Hong Kong. Infected persons may initially present with flu-like symptoms that may progress to infection of the central nervous system.

) 衞 生 防 護 中 心 Centre for Health Protection • CHP press release was issued on April 3, 2024.



### **Risk Communication**

Fact sheet @ chp.gov.hk





♣ Home > Health Topics > Communicable Diseases > B virus infection

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CHP Facebook

CHP Channel

< Back

Communicable Diseases	B virus infection						
Non-Communicable Diseases and Healthy Living	5 April 2024 Causative agent						
Healthy Life Course	hy Life Course       B virus (also known as herpes simiae virus) is a type of herpes virus that is usually found among macaques, a type of wild monkeys commonly found in Hong Kong. B virus is naturally carried in the saliva, urine and stool of macaques. Most infected macaques are usually asymptomatic or having mild disease.         I Health       Human infection of B virus is rare, with about 50 people documented to have been infected globally since 1932. Human infection has been reported in United States, Canada, Mainland China and Japan, and were mainly caused by bites or soratches by monkeys.         Clinical features       Clinical features						
Organ Donation							
Travel Health							
Health and Hygiene							
Antimicrobial Resistance	Infected persons may initially present with flu-like symptoms, such as fever and chills, muscle ache, fatique and bea	dache Vesicular					
Poisoning	skin lesions may then occur at the bite or scratch site. As disease progresses, the virus can spread to the central nervous syst resulting in pain/numbness/itchiness near the wound, problems with muscle coordination, damage to the nervous system and						
	death.						
General Public	Mode of transmission						
+ Health Professionals	Human infections are mainly caused by bites or scratches by infected monkeys, while human-to-human transmissions are very						
Institutions & Schools	Incubation period Symptoms usually occur within 1 month of the patient being exposed.						
Business & Workplace	Management						
	Human infection requires professional medical management.						
	Prevention						
Ť	To minimise risk of acquiring B virus, members of the public are advised to note the following:						
Λ	1. Stay away from wild monkeys and avoid touching or feeding them;						
Department of Health	<ol><li>In case there are wounds caused by monkeys, wash the wound with a plenty of running water and seek med immediately.</li></ol>	lical attention					
The Centre for Health Protection	Members of the public may also visit website of the Agriculture, Fisheries and Conservation Department for more in	formation on do's					
is a professional arm of the	and don'ts when encountering monkeys:						
Department of Health for disease prevention and control	www.atcd.gov.hk/english/conservation/con_fau/con_fau_nui/con_fau_nui_str/con_fau_nui_str.html						

衞生署 Department of Health

### **Risk Communication**

### Facebook post on April 5

【慎防B病毒 不要觸摸或餵飼野生猴子 1.】

衛生署衞生防護中心正調查一宗人類感染B病毒(又稱猴疱疹病毒)個案, 並提醒市民應避免觸摸或誤詞野生猴子,以減低感染病毒的風險。

B病毒可自然存在於獼猴的唾液、尿液及糞便等,而獼猴是香港常見的 一種野生猴子。為人類感染B病毒主要由猴子咬傷或抓傷而引起。受感 染的人最初會出現流感樣病徵,受傷部位可能會出現水泡性的皮膚損 傷。病情可能惡化演變為中樞神經系統感染。▲… See more







### **Risk Communication**

Media interview on April 5



使 衛生防護中心 Centre for Health Protection

### **Enhanced Surveillance**

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本署檔號 來函檔號	Our Ref. : (36) Your Ref :	) in DH SEB CD/1 - 115/3			2.	Clostridium botulinum (肉毒桿菌)
電話傳真	Tel. : Fax No. :				3.	Crimean-Congo haemorrhagic fever virus (克里米亞 —— 剛果 出血熱病毒)
			11 July 2008		4.	Dengue virus (登革病毒)
Dear Doctor,						Ebola virus (埃博拉病毒)
<u>Prevention and Control of Disease Ordinance (Cap. 599)</u> <u>effective since 14 July 2008</u>					6. 7.	Francisella tularensis (土拉桿菌) Guanarito virus (瓜納瑞托病毒)
					8.	Hantavirus (漢坦病毒)
Please be informed that the Secretary for Food and Health has appointed 14 July 2008 as the day on which the Prevention and Control of					9.	Hendra virus (亨德拉病毒)
Disease Ordinance (PCDO, Cap. 599) and its subsidiary legislation, the Prevention and Control of Disease Regulation (PCDR, Cap. 599A) shall						Herpes simiae virus (B virus) (猴疱疹病毒(B病毒))
	Gazette today. Prevention of Dise	The PCDO will replace the existi ease Ordinance, Cap 141.	ng Quarantine and			

衞生署 Department of Health

### **Enhanced Surveillance**

 Addition of B virus infection to the list of "Other communicable diseases of topical public health concern".

#### OTHER COMMUNICABLE DISEASES OF TOPICAL PUBLIC HEALTH CONCERN

Though not specified in the First Schedule to the Prevention and Control of Disease Ordinance, medical practitioners are urged to report suspected or confirmed cases of the following diseases to CENO for arrangement of investigation and control as appropriate:

- Acute flaccid paralysis
- B virus infection
- Brucellosis

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- Cryptosporidiosis
- Myiasis (flesh fly)
- · Severe paediatric enterovirus infection (other than EV71 and poliovirus)
- · Severe paediatric influenza-associated complication/death
- · Vibrio vulnificus infection (with necrotising fasciitis)
- · Other communicable diseases of topical public health concern

### @CENO On-line

![](_page_27_Picture_14.jpeg)

### **Enhanced Surveillance**

#### **B** virus infection

(Last updated on 5 April 2024)

#### Description

 Surveillance case definition and reporting criteria of B virus infection were uploaded to CENO On-line on April 5, 2024.

![](_page_28_Picture_5.jpeg)

B virus (also known as herpes simiae virus) is a type of herpes virus that is usually found among macaques. B virus can be found in the saliva, urine and stool of infected macaques. Human infections are mainly caused by bites or scratches by infected macaques.

Symptoms usually occur within 1 month of the patient being exposed. Infected persons may initially present with flu-like symptoms, such as fever and chills, muscle ache, fatigue and headache. Vesicular skin lesions may then occur at the bite or scratch site. As disease progresses, the virus can spread to the central nervous system (CNS) resulting in pain/numbness/itchiness near the wound, problems with muscle coordination, damage to the nervous system and even death. Other symptoms suggestive of CNS involvement include hyperesthesia, ataxia, diplopia, agitation and ascending flaccid paralysis.

#### **Reporting criteria**

An individual with history of monkey scratch/bite with wound within 1 month of illness onset <u>AND</u> features suggestive of CNS infection

OR

An individual with detection of nucleic acid of B virus in a clinical specimen.

**Confirmed** case

A clinically compatible illness that is laboratory confirmed.

![](_page_28_Picture_14.jpeg)

![](_page_29_Picture_0.jpeg)

![](_page_29_Picture_1.jpeg)

Communicable Disease Branch

Protecting Hong Kong's health

本署	腎檔 號	Our Ref.	:	(1) in DH CDB/8/104/1
來會	函檔 號	Your Ref	:	
電	話	Tel.	:	
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5 April 2024

Dear Doctor.

病

### Vigilance against B virus infection and addition of the infection to the list of "Other communicable diseases of topical public health concern"

I would like to draw your attention to the recently confirmed case of human infection of B virus (also known as herpes simiae virus), and new arrangement on reporting of this disease by adding it to the list of "Other communicable diseases of topical public health concern" with immediate effect.

The case involves a 37-year-old male with good past health, who was admitted to Yan Chai Hospital through accident and emergency department on March 21 due to fever and decreased conscious level. He is now receiving treatment at the Intensive Care Unit of the hospital and his condition is critical. Cerebrospinal fluid specimen of the patient tested positive with detection of nucleic acid for B virus by PCR by the Public Health Laboratory Services Branch of the Centre for Health Protection (CHP). According to the information provided by his family members, the patient had contacts with wild monkeys and was wounded by them during his visit to Kam Shan Country Park in late February. Epidemiological investigations are ongoing.

 Letter to doctors and private hospitals on April 5.

![](_page_29_Picture_12.jpeg)

# **Prevention** – People at high risk of infection

- Adherence to appropriate laboratory and animal facility protocols.
- Work with B virus–susceptible monkeys using human restraint methods that reduce the risk of bites and scratches.
- Use proper PPE- including a lab coat, gloves, and a face shield when working with macaque monkeys.
- Cleanse any bites, scratches, or exposure to the tissues or secretions of macaques immediately.
  - First, thoroughly wash and gently scrub the wound with soap, detergent, or iodine for 15 minutes.
  - After, run water over the wound or area for 15 to 20 minutes more.
- If exposed, seek medical help promptly.

![](_page_30_Picture_8.jpeg)

![](_page_30_Picture_9.jpeg)

![](_page_30_Picture_10.jpeg)

### **Prevention** – General population

- Stay away from wild monkeys and avoid touching or feeding them;
- In case there are wounds caused by monkeys, wash the wound with a plenty of running water and seek medical attention immediately.

![](_page_31_Picture_3.jpeg)

![](_page_31_Picture_4.jpeg)

![](_page_31_Picture_5.jpeg)