



Herpes B Virus: Implications in Lab Workers, Travelers, and Pet Owners

Presenter:

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Objectives

1. Discuss how Herpes B infection is transmitted
2. List symptoms of Herpes B infection in humans
3. Describe vaccination and treatment options for Herpes B.

The Case of a Lab Worker

- S:
 - 53 y/o clinician/researcher at a local lab went to MGH with **fever, HA, and rigors** 3/27/12.
 - Notes being **scratched by a research monkey (Macaque sp)** 9 days prior on dorsum of L hand.
 - Washed the wound for few minutes but did not report the injury. Negative for neck pain, or difficulty with concentration.
- O:
 - PE: Scar longitudinal between 3rd and 4th MC L hand 3 cm. Negative for vesicular lesions, erythema, signs of infection, or rashes
- Labs:
 - LP's performed weekly with Herpes B negative on PCR
 - Elevated WBC's seen on CBC
- Imaging:
 - 2 MRI's were normal

On week 3 LP again performed with PCR of CSF positive for Herpes B and serology with Ab (+)

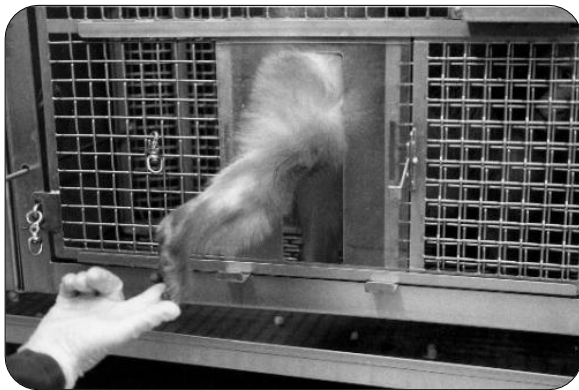
A:

Diagnosed with Meningoencephalitis 2/2 to Herpes B infection



Background (History)

First documented case of B-virus infection in 1932 when a researcher was bitten on the hand by an apparently healthy rhesus macaque and died of progressive encephalomyelitis 15 days later.



Background

- Transmission via contact with oral-secretions
 - Direct (bite, scratch, contact with body fluid or tissue)
 - Indirect (contaminated fomite e.g., needle puncture or cage scratch)
 - Human-to-human transmission has been documented in one case

Pet monkey who wore diapers and dressed as Santa shot dead after 'flipping out' and unleashing attack on his owner

By DAILY MAIL REPORTER

07:42 EST, 24 August 2012 | UPDATED: 16:08 EST, 24 August 2012

How To Fight Monkeys

What should you do if you're surrounded by angry macaques?
By Michelle Tsai | Posted Monday, Oct. 22, 2007, at 6:59 PM



Macaque Attack!!!!

ANIMALS

Macaque Attacks Little Girl in Wal-Mart Parking Lot

Look at Charlie the macaque up there. Doesn't he look terrified? Confused? Distraught? He should be. That sweet-looking little girl, 8-year-old Tayce Nickel, has all but administered the lethal injection that will stop the rapid beating of his tiny, simian heart. In return, he probably

A British woman with fear of monkeys attacked by a pack of macaques while on trip to Thailand
conquer her lifelong fear of primates

by Our Foreign Staff
2:59PM BST 17 Jun 2010

Dee Darwell, 56, from Peterborough lost consciousness as first one monkey then another bit her and then she was surrounded by a whole pack.

She collapsed with blood spurting from her arm and had to be rescued by Thai boatmen.

What About Travelers?

- B virus prevalent in macaques native to SE Asia.
- Frequent contact between humans and macaques sufficient to transmit B virus commonly occur
- At a Bali Hindu temple :
 - **81.6% macaques were B-virus seropositive**
 - No cases consistent with B-virus disease described in humans.
 - **In cases of encephalitis, B virus may not be considered.



Case of a Traveler

- **7 yo** on a Family trip to **Thailand** visited a sanctuary where monkeys can be touched, carried, and fed by tourists.
- She **picked up a banana** on the ground to feed one of the monkeys.
- The monkey jumped on the girl's arm, grabbed her hair, and bit into her forehead.
- No cleaning or rinsing of the wound was performed.
- 10 d later in the ED, no persisting wound
 - Vomited x1 day before ED visit
- Immunoassay was negative.
- Girl remained well with no skin changes at the site of the bite
- Monkey **species identified on photos** provided by the family as pigtail and a rhesus macaques



What About Exotic Pet Owners

- Where macaques have been domesticated as pets, opportunities for exposure to B virus are possible.
- One report showed many instances of potential exposures
 - Bites
 - Scratches
 - Food sharing
 - Close physical contact
 - Shared chewing gum
 - Report also found that children were three times more likely than adults to be bitten by pet macaques.



Exotic Pet Owner Case

- **2 y.o.** boy presented to the ED 30 min after being **attacked by a neighbor's pet Bonnet Macaque** monkey while playing in his grandmother's backyard
- PE- multiple minor abrasions, scratches and puncture wounds on the face, and scalp
- Admitted and was stable throughout his hospital course. D/c after 3 days.
 - B-virus serologies (acute and 21 days) for both the monkey and the boy neg



- What could have/should have been done in these cases?
- What is Herpes B?
- What is the treatment?
- How to prevent

Thomas Winters, MD, FACOEM

- Chief Medical Officer and Principal Partner OEHN
 - Board Certified in Occupational Medicine
 - Board Eligible in Infectious Diseases
 - Board Certified in Internal Medicine
 - Certified Medical Review Officer
 - Certified Independent Medical Examiner
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- over 25 years experience in occupational and environmental medicine.
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- Previous positions have included:
 - Medical Director of a national occupational medicine provider
 - Medical Director for several manufacturing companies
 - State Police Surgeon - Massachusetts State Police
 - Owner/Medical Director of Medsite - an occupational and primary care medicine center.



What is Herpes B and Why Macaques in Research?

- Belongs to genus: Simplexvirus
 - Other members include: HSV 1 and 2
 - Symptoms in monkeys are similar i.e vesicular lesions
 - High rate of seropositivity in Macaques
- Discovery of simian immunodeficiency virus (SIV) and its identification as a model for HIV infection



Virus breakthrough
**Hope for
new HIV
vaccine**

ASCCJUG

Herpes B in Monkeys

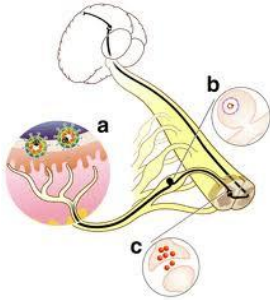
- **Asymptomatic** Infxn in rhesus and cynomolgus
 - Also stumptail, pig-tailed, Japanese, bonnet, and Taiwan sp.
 - Used in biomedical research.
 - ****Monkeys become aggressive as they age past 2 years and have higher rates of seropositivity.**
- B virus from rhesus may be more pathogenic for humans
- Herpes B is **transmissible to other monkey sp**, but is usually deadly

Herpes B in Humans (Sxs)

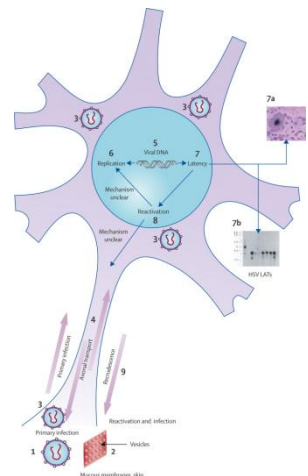
- Onset usually within 1 mo of exposure
 - Incubation period of a few days to a week.
- Progression dependent on site and size of exposure
- Sxs:
 - **Influenza-like** (fever, muscle aches, fatigue, and headache)
 - **Skin- vesicles** may be seen at site of exposure
 - Occasionally: lymphadenitis, lymphangitis, N/V, abd pain, and hiccups
 - **Neuro (variable and ominous):** Hyperesthesias, ataxia, diplopia, agitation, ascending flaccid paralysis



MOA/Virulence



- **Infects mucosal epithelia** and can spread to and from nerve ganglia by **axonal transport**,
 - Latency in the nerve ganglia.
- Virus spreads along peripheral nervous system to the spinal cord then to brain
- Can lead to fatal encephalomyelitis in humans
 - **80% mortality if untreated**
 - **20% mortality with treatment**
 - Neurologic sequelae common in survivors



Transmissibility:

- Small percentage of macaques actively shedding
 - 2-3% in a group with 100% seroprevalance
 - Shedding more likely if under stress, or ill
- Estimated risk of exposure is **32% for non-SPF** (specific pathogen free) colony, and **0.5% with SPF**
 - 50 reported cases since 1932, 26 well documented
 - No known cases of B-virus infection at USMRAID during 66 incidents since 1972.
 - At least one case in a Boston area lab
 - Over 26 exposures in 2012

Diagnosis

- Patient:
 - Culture of wound site sent for PCR (controversial)
 - **Serology** recommended initially and at 3 wks
- Source:
 - **Exam** of monkey looking for lesions
 - **Culture** of buccal mucosa, conjunctiva, and urogenital area of source also controversial since viral shedding can be intermittent
 - **Serology** is recommended (still **not perfect**)



Exposure Treatment

- Clean the wound or exposure site**
 - **Non-mucosal surfaces**- cleanse with soap or detergent for at least 15 min
 - **Mucosal surfaces**- rinse with sterile saline or running water for 15 min.
- Antiviral Prophylaxis?? (Controversial)
 - H/o proper cleansing initiated immediately determines need for prophylaxis
 - **Unnecessary in most cases** –can confound diagnostic testing
 - Use if herpetic lesions in source animal, injuries of the head or neck, and mucosal exposures



Tourist and Exotic Pet Owner Considerations

- Tetanus vaccine if >5 yrs or less than 3 lifetime doses
- For bites consider:
 - Rabies immunoglobulin
 - And rabies vaccination



Treatment (for Symptomatic pt):

- Lab worker:
 - Initially started on IV Acyclovir, but changed to **IV Gancyclovir** a few days later when dx confirmed
 - Completed 2 weeks of high dose gancyclovir
 - Discharged on Valgancyclovir (a pre-drug of gancyclovir).
 - Switched to **life long Valacyclovir****.

Prevention

- According to USMRAID:
 - wear protective long-sleeved garment (Tyvek suit or long-sleeved scrubs),
 - protective gloves,
 - protective eyewear,
 - face mask,
 - booties,
 - hair bonnet.



Prevention

- Pathogen-Free Colony Development (**SPF**)
 - Serologic methods are used to screen and monitor animals for consideration as pathogen free
 - Demand exceeds supply
 - A safer option, but **still must use proper PPE**
- **Vaccination** of macaques
 - Promising results in rabbits and macaques,
 - No development plans



Recommendations

- **Tourists-** stay away from monkey infested areas
- **Exotic pet owners-** Monkeys belong in the wild and zoos. Choose New world vs. Old world.
- **Lab workers-** proper PPE, training, SPF have lower risk, and establishment of SOP in case of exposure (next slide)

****Keep in mind B virus is classified as a Biosafety Level-4 biologic agent (belonging to the same group as Ebola virus and Marburg virus)**



SOP - Post Exposure Procedures Following NHP Macaques Injuries

I. Purpose:

To describe procedures for providing immediate care to personnel exposed to B-virus or Cercopithecine herpes virus 1 (formerly known as Herpes virus simiae or Herpes B.)

II. Introduction/Background:

- A. Cercopithecine herpes virus 1 (CHV1), also known as B-virus, occurs naturally in Macaque monkeys. The virus is enzootic among Old World macaques and usually causes minimal or undetectable morbidity in its natural host. Employees who have contact with these animals' tissues or secretions, may be exposed to B-virus through bites, scratches, cuts, contaminated needle-sticks and other contact of mucous membranes or broken skin with infected body fluids from macaques or with wet, unfixed tissues or primary cell culture material. In addition contaminated husbandry and research equipment can potentially spread B-virus.
- B. Persons exposed to contact with blood, tissue or secretions of nonhuman primates are at risk for B-virus infection through:
1. Bites
 2. Eye splash
 3. Mucous membrane exposure
 4. Contaminated needle-sticks
 5. Exposure of cuts or broken skin to contaminated material.
 6. Scratch from an animal or cage/equipment
 7. Exposure at necropsy (i.e., cut from a scalpel blade)
 8. Saliva contamination of an existing wound
 9. Exposure to infections tissue or fluids of NHP (i.e., , ocular, oral, genital secretions CNS tissue and CSF), that are potentially infectious.
 10. Exposure of broken skin to primary cell cultures de-rived from macaque kidneys are a

Questions?



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