MANAGING THE RISK OF B-VIRUS INFECTION FROM MACAQUE-DERIVED MATERIALS: THE CONTROL BANDING APPROACH

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Content

1. Background
2. What are the Occupational Safety & Health (OSH) concerns when working with Macaque-derived materials?
3. Risk management approach - Control banding
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1. Background

1. In institutes of higher learning in Singapore, Principal Investigator (PIs) and their researchers work with Non Human Primates (NHPs) including Macaques and their samples.

2. In NUS, the samples are obtained from sources from within Singapore and other parts of the world.

Types of work include:

a) Anatomical and histochemical studies
b) Electrophysiological studies
c) Molecular biology studies including tissue culture
d) Material compatibility studies
Dr Willam Barnet Brebner

1. Dedicated researcher
2. Asst. Professor
3. Macaque bite
4. Fatal Neuroencephalomyelitis
5. Invaluable postmortem sample

1. B-Virus discovered !!
2. Safety awareness triggered

(Pimentel, 2008)
Dr Elizabeth R Griffin

i. Dedicated researcher
ii. Macaque body fluid splash into eyes
iii. Fatal Neuroencephalomyelitis

i. Lab-acquired infection from Macaque-material
ii. The Elizabeth R Griffin Research Foundation
iii. B-Virus working group

(http://www.ergriffinresearch.org/)
B-virus ulcers in rhesus macaque

Electron microscopy of the liver sample showing intranuclear viral capsids with circular profile (Carlson et al., 1997)
2. What are the OSH concerns when working with Macaque-derived materials?

1. Zoonotic pathogens from NHPs
2. B-virus from Macaque (endemic)
3. Fatal (80%), if untreated
4. It can survive for hours on an exposed dry surface
5. Transmission: splashes, needlestick or aerosols, contaminated equipment etc.
6. There are no vaccines available for prevention of B virus infection
OSH concerns

1. In March 1989, Southwest Foundation Laboratory identified B-virus contamination in a batch of primary monkey (Rhesus) kidney cells (pMK) from a commercial supplier (Wells et al 1989).

2. “The virus can be present in the *saliva, feces, urine, or nervous tissue* of infected monkeys and may be found in *cell cultures* derived from infected monkeys. (CDC)”

3. Macaque samples used in NUS- e.g., blood, brain tissue, whole carcass & cell lines
In vivo and in vitro work

Hazard

http://carnivoraforum.com/topic/9328619/1/
B-virus pathology

Incubation period is 2 days - 5 weeks

- Vesicles at inoculation site
- Pruritic rash
- Tingling, pain & numbness
- Fever
- Myalgias
- Weakness
- Abdominal pain
- Sinusitis
- Conjunctivitis
- Paresthesias
- Lymphadenopathy
- Persistent Headache
- Diplopia
- Confusion
- Dizziness
- Ataxia

Exposure

Brain stem
Encephalomyelitis

Respiratory Failure

Ascending Paralysis

Coma

Brain
Spinal cord
B-virus pathology

- Vesicles at inoculation site
- Pruritic rash
- Tingling, pain & numbness
- Lymphadenopathy
- Paresthesias
- Fever
- Myalgias
- Weakness
- Abdominal pain
- Sinusitis
- Conjunctivitis
- Persistent Headache
- Diplopia
- Confusion
- Dizziness
- Ataxia
- Brain stem Encephalomyelitis

Exposure to head and neck leads to CNS symptoms

Exposure to periphery allows Non-CNS symptoms

Ascending Paralysis

Respiratory Failure

Coma
Rationale for developing this programme and working team

1. Risk of B-virus infection from Macaque-derived materials
2. AAALAC requirement
3. World class safety standards
4. Safety awareness in staff

OSHE - Office of Safety, Health & Environment
IBC - Institutional Biosafety Committee
OH - Occupational Health Clinic
CM - Comparative Medicine (NUS animal facility)
3. Risk management approach - Control banding

Technique to guide the assessment and management of workplace risks (NIOSH)

1. A system that makes use of previous knowledge
2. Task-based advice
3. Prioritized hazards based on levels of risks & exposure
4. Focused on controls
Principles of control banding

1. Effective occupational hygiene practices, supplemented by using appropriate personal protective equipment (PPE)
2. Engineering controls, including local exhaust ventilation & containment
3. Seeking specialist advice
The difference…

Traditional approach

Hazard → Exposure → Control

Control banding approach

Hazard → Control → Exposure

Keith Tait, Corporate Health & Safety, Pfizer
National Control Banding Workshop, Washington, DC March, 2005
Control banding - key components

Categorise the hazards by linking

1. Hazard category (Eg. Biological)
2. Hazard classification (Eg. Infectious)
3. Associated containment levels (Eg BSL-1)
4. Recommendations for each hazard category (Eg. administrative and engineering controls)
Control Banding when handling NHP (Macaque)- derived materials

NHP derived materials

- Non-Macaque
  - Chemically fixed
  - Untreated material
  - BSL-1
  - BSL-2

- Macaque
  - Chemically fixed
  - Untreated material
  - BSL-1
  - BSL-2 (Enhanced)

Hazard

Engineering control

- Authorization from IBC/OSHE prior to work/possession (iORC)
- Restricted access and signage
- OH programme
- Class room training
- B-virus exposure kit and post exposure response procedure

Seeking expert advice

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Process flow

Circular to Deans, HODs and Directors

Identify researchers handling Macaque-derived materials through a survey

Database

Researchers attending the class room training on safe handling of NHP (Macaque)-derived materials

BSL-2 (enhanced) practices

Monitoring

New researchers declaring the use of NHP (Macaque) derived materials in the iORC*

* iORC - Integrated Online Research Compliance System
Survey results: NHP-derived materials use in NUS

- 60% PIs using Non-Macaque derived materials or Inactivated samples
- 30% PIs using Macaque-derived materials (fresh)

Roles:
- Students
- Research Assistants
- Research Fellows
- Lab Technologists
- Safety & Health Coordinators
Title : SAFE HANDLING OF NON-HUMAN PRIMATE (MACAQUE) DERIVED MATERIALS

Trainees : All staff and students handling Macaque-derived materials

Content : 1. Introduction – Biological Hazards of working with NHP derived materials
          2. NUS requirements for handling Macaque-derived materials
          3. Dealing with exposure to Macaque-derived materials
          4. Summary and references
4. Monitoring

1. Regular Safety & Health Management System (SHMS) audits for PIs
2. Project risk assessment (on iORC) review and database update
3. Inspections (regular and adhoc)
4. Overall effectiveness of the training - increase in mean Likert score from 3.46 to 6.23 on a scale of 1-7
Learning gained in the class room training on safe handling of NHP (macaque)-derived materials

Columns represent mean of scores from . Error bars represent SEM. (N=35). **P≤0.001. Paired t test.
Compliance by researchers - current status

1. 100% of the researchers attended training since the programme launched in October 2016

2. B-virus exposure kit procured by PIs prior to the commencement of work
5. Summary

1. B-virus is a potential zoonotic pathogen present in Macaque-derived materials which can cause serious disease in humans.

2. An integrated programme on safe use of Macaque-derived materials was launched in NUS.

3. Excellent response from the research community
   a. 100% of researchers handling Macaque-derived materials attended the training
   b. PIs procured B-virus exposure kits prior to the commencement of work
   c. Increased awareness as observed from training scores.

4. Principles of control banding were useful and this tool could be extended to other similar programmes.
6. References


11. http://www.egriffinresearch.org/


15. https://www.cdc.gov/niosh/topics/ctrlbanding/

Thank you