

## Risks and Management of SIV in Mandrills (*Mandrillus sphinx*) and Drills (*Mandrillus leucophaeus*)

### A. Background

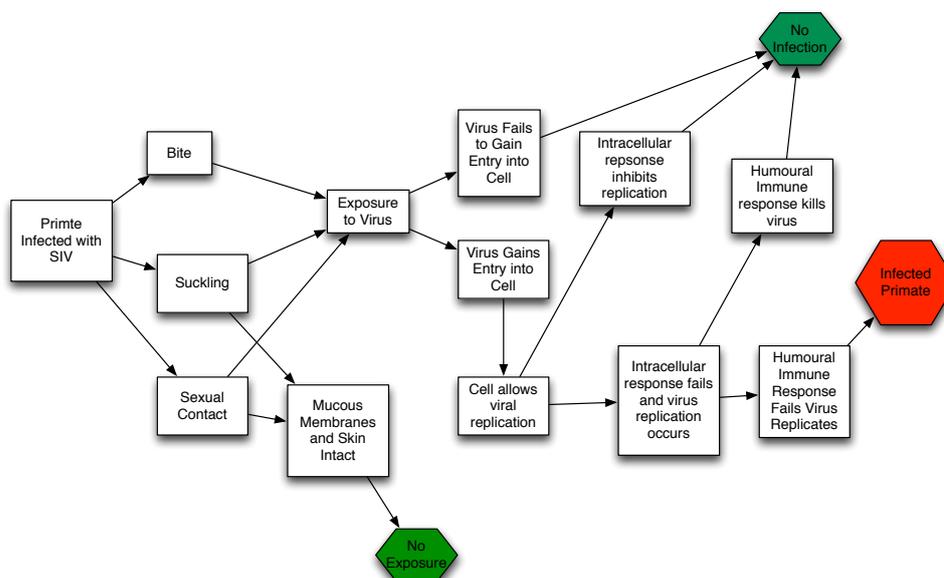
Simian Immunodeficiency Viruses (SIV) are primate lentiviruses, which infect a wide variety of non-human primates species in sub-Saharan Africa. The evolution of the lentiviruses is very complex but there is evidence to suggest that the viruses are ancient and co-evolved with specific species. The virus that naturally infects the specific species does not cause clinical disease but causes lifelong but unapparent infection. However there is significant evidence of multiple cross species infections. In African primates these rarely cause clinical disease but in Asian primates can cause clinical disease characterized by immunosuppression, meningoencephalitis and lymphoproliferative disease.

### B. Managing SIV in Mandrills and Drills

The Mandrill and Drill are naturally infected with their own SIV viruses. The mandrill is the natural host for at least three different strains of SIV and the drill has its own single SIV virus. There is however evidence that the two species can cross infect each other, but with no clinical signs developing (van der Kuyl et al, 2004). The SIV viruses identified are non-pathogenic to their host species. Wild mandrills and drills are infected with SIV, research suggests that up to 30% of wild animals are infected. (Clewley et al, 1998; Peeters et al, 2002). It is therefore quite possible that a similar number are infected in captive populations.

The virus is primarily transmitted horizontally through bite wounds and less commonly through sexual contact and breast milk. Indeed the virus can rarely be isolated from semen, cervical secretions and breast milk (CDC,1988). This does vary between species with research suggesting that SIV in sooty mangabeys is definitely spread sexually and that SIV in Mandrills is transmitted in breast milk more commonly than in other species.

Figure 1 - The risk scenario tree – the pathway of transmission between an infected Mandrill or Drill and an uninfected animal.



This raises a number of issues for captive management.

Recommendations for the EEP;

1. There is NO justification for euthanasia of Mandrill or Drill testing positive for SIV – this should be a direct instruction for all participants.
2. When ever possible zoos should routinely screen for SIV so a known status for each animal is obtained.
3. It should not be assumed that offspring of positive parents will be positive, – they should be tested for confirmation.
4. There is no need to manage to separate populations (one SIV positive and one SIV negative) of Drill or Mandrill

Recommendations for managing an SIV positive Mandrill or Drill Group are:

1. Little research has been undertaken to investigate cross-infection of other primates except it is known that SIV Mandrill and SIV Drill can cross infect each other. Therefore Mandrill and Drill should never be mixed. SIV positive Drill or Mandrill should not be housed in a mixed exhibits with other primates. The primary route of transmission would be from bite wounds. African old world monkey species should never be mixed with Asian old world monkey species.
2. The greatest risk of SIV transmission is through biting – stable family groups are at a lower risk. The group should be managed to encourage this.
3. It must not be presumed that all animals in a group are SIV positive – each animal should be tested individually. It is possible that offspring are negative.
4. If one animal tests positive for SIV the whole group should be tested.

### **Laboratory Testing and Interpreting Results.**

Due to the species specific SIV viruses, laboratory testing for SIV can be difficult as often tests for HIV are used and not SIV specific tests. In addition to this different tests have different sensitivity (ability to detect a positive result).

There are several different test types undertaken.

1. Viral Culture produces the most reliable test results however this requires the laboratory to have primate cell lines to culture the virus in. As the most commonly used cell lines come from Rhesus macaque it is often difficult to get the virus to grow at all.
2. A nested PCR with degenerated primers (e.g. PolOR and Polis4 and then Unipol and polis2) and subsequent sequencing is more broader applicable and bring final evidence of infection. However, it is once more mostly down to the operator's experience, the equipment and connected to substantial costs if this technique is not carried out routinely. This can be arranged through the Old World Monkey TAG.

3. Immunostrip ELISA ,which has a very broad cross-reactivity. However, this serological test normally gives a good idea on which animals are negative if the result is negative, yet intermediate and positive animal require additional work, which can sometimes be very difficult. Due to the low numbers of drills, species-specific ELISA techniques do not exist yet. This test can be arranged through the TAG as well.

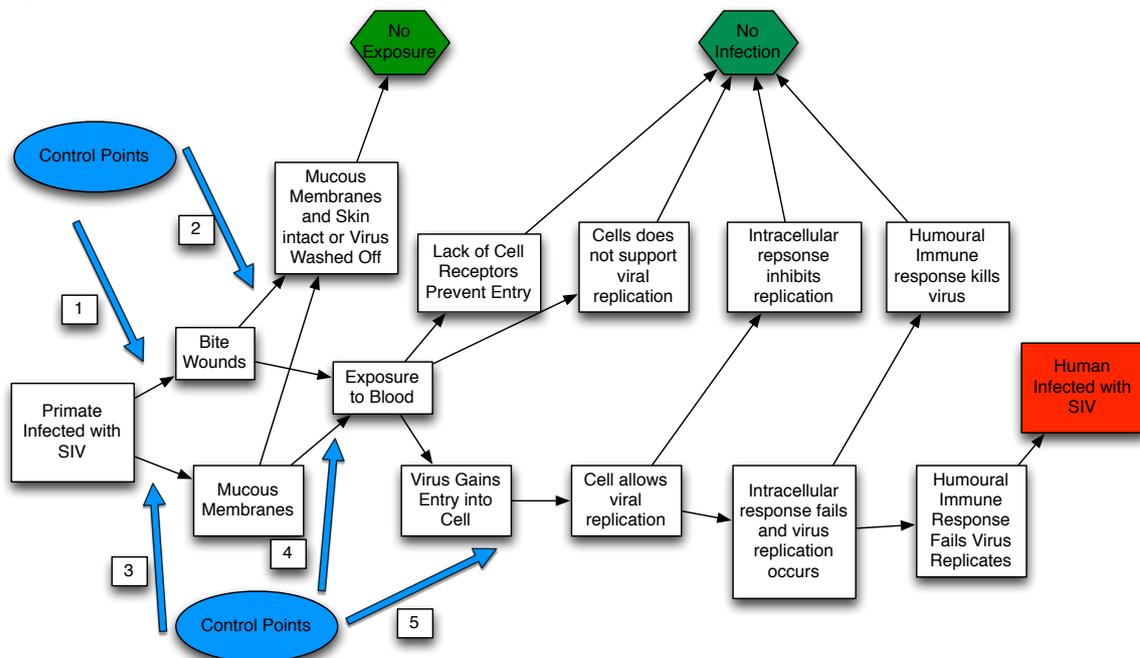
4. Western Blot – This is the least reliable of the tests due to the cross reactivity of the SIV strains used. Increasingly the human HIV-2 western blot test is being used but interpretation of this test requires great expertise. We would recommend that this test is not used.

### General Principles of Laboratory Testing

- If an animal tests negative it could have been recently infected and the virus has not yet replicated to detectable levels. As the amount of virus in the animal is so low it will not yet be able to transmit disease. This animal can be considered negative but at some undeterminable point will test positive when virus reaches detectable levels. This is rare as all the tests can detect virus at very low levels.
- If an animal tests negative and then at a later date tests positive it has been infected by the virus in the intervening period and the animals which it has been in contact with should be tested for SIV.

### C. Human Risks Associated with SIV in Mandrills and Drills

Figure 2- Transmission Pathway from SIV Infected Mandrill and Drill to a Human



### **Can SIV Infect Humans ?**

Cross species infection from the natural host to other species can occur and can result in pathological disease. Cross species transmission of the specific Chimpanzee and Sooty Mangabeys to humans has been linked to the origin of the HIV-1 and HIV-2 virus respectively. It is thought that the SIVs entered human cells, underwent genetic changes, which then allowed human-to-human transmission. This is supported by the fact that humans in Africa have been exposed for centuries to SIVs and yet the HIV epidemic has only apparently emerged in the second half of the last century, which suggests that some other factor influenced the virus. This suggests that viral cross –species transmission is in itself not the only factor required for development of pathological disease.

Despite the large exposure of humans to SIV-infected primates in central and west Africa, through consumption of bushmeat, extensive molecular epidemiological studies have shown only 10 cross-species transmission events during the last century only four of these resulted in epidemic transmission.

Experimental cross species infection of SIVs in different species of primates has shown that in many cases the virus is harmless or cleared by the new hosts immune system

### **Can SIV<sub>deb</sub> Infect Humans ?**

There are over 40 SIV species specific virus and only those from chimpanzees SIV<sub>cpz</sub> and sooty managabeys SIV<sub>sm</sub> have been shown to be associated with HIV.

The general experimental approach to determine this is to try and grow virus in human cells (human peripheral blood mononuclear cells, PBMCs) *in vitro*. A major difference between the guenon SIV viruses and those of the Mandrill and Drill is that all three SIV<sub>mnd</sub> strains and SIV<sub>drl</sub> **do** grow in human cells, which, in theory, could allow the virus to establish persistent infections in humans.

### **What route would SIV be transmitted to humans by ?**

A study of people with occupational exposure to primates was conducted by the USA CDC. 3,000 samples from people potentially exposed to SIV were tested only two demonstrated antibodies cross reactive to SIV, a prevalence of less than 1%. One of these people handled known (experimentally) SIV infected material without gloves whilst having an severe dermatitis of the hands and forearms. The second person had suffered from a needle stick injury whilst handling known experimentally infected blood.

Both of these people had virtually undetectable levels of virus and this explains the lack of AIDS like symptoms as a high circulating viral load is required for disease and transmission in HIV infected humans.

Evidence of SIV infection in zoo keepers has not been reported (Switzer et al, 2004).

Epidemiologic surveys of 1800 persons from nine villages in Cameroon suggested very high (>60%) exposure to primate blood and body fluids and

demonstrated that 1% of exposed individuals were seropositive for SIV of three different nonhuman primate origins (Wolfe et al., 2004). One epidemiological study in Cameroon did reveal a single case of a human infected by the SIVmnd virus (Hu et al, 2003).

Despite the fact that these events clearly demonstrate that human-primate contact occurs commonly, and can result in primate to human retroviral transmissions, human exposure to SIVs resulting in patent infections has been extremely rare. Therefore, exposure of humans to SIVs does not result in successful cross-species infection. Seropositivity merely demonstrates exposure to SIV and a subsequent immune reaction. It does not demonstrate infection.

### **Managing Risk of Infection to Humans:**

The above evidence suggests that routine precautionary measures should be implemented for working with Mandrill and Drills.

- The risk of transmission from urine and faeces is negligible.
- SIV virus is susceptible to household bleach and disinfectants, which should be used routinely for general cleansing.
- As with all primates – latex gloves should be used when handling Mandrill and Drills

There are a number of 'Control Points' identified in Diagram

1. Blood is the main risk to humans. Unknown status or SIV positive Mandrills or Drills should not be handled when conscious to avoid biting injuries and should not be netted but should be darted or a put in a crush cage and then anaesthetic should be used.
2. Should biting injuries occur they should be immediately thoroughly washed and lavaged with Chlorhexidine.
3. During blood collection or other invasive procedures; on unknown status or SIV positive animals, goggles, gloves and face-masks should be worn to prevent mucous membrane contamination.
4. If mucous membranes (eyes, mouth, nose, ears) be contaminated by SIV infected primate bodily fluids the area should be immediately washed with Chlorhexidine.
5. Post Exposure Prophylaxis with anti-retroviral drugs may be indicated following potential exposure. Medical intervention should be sought. (Weston Murphy et al, 2006).

**Risk Assessment:**

|                              |  |   |   |  |
|------------------------------|--|---|---|--|
| <b>Stage in Risk Pathway</b> | Bite Wound or MM Exposure                                  | Virus Infects Cell  | Virus replicates in Cell  | Virus causes active disease in human   |
| <b>Mitigating Action</b>     | Handling Precautions, Gloves, Goggles, Face Mask, Washing, | Post Exposure Prophylaxis   | Human Immune Response<br><br>Anti-retroviral drugs.             | Anti-retroviral drugs.   |
| <b>Further Evidence</b>      |  | In both occupational at risk workers and bush meat hunters seroprevalence was less than 1%. Infection in Zoo keepers has not been reported. | SIVmnd and SIVdrl do replicate in human peripheral blood cells. | Despite regular and widespread exposure cross for centuries only 10 incidences of cross-species infection have been identified and only 4 of these have resulted in human disease. |
| <b>Risk</b>                  | Low  | Negligible  | Low   | Very Low   |
| <b>Uncertainty</b>           | Low  | Medium  | Low   | Medium   |

**Overall Risk Assessment = Low  
Uncertainty = Medium to Low.**

**D. References and Further Reading:**

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