Herpesviruses and 
macropods

Fact sheet

Introductory statement

Despite the widespread distribution of herpesviruses across a large range of macropod species there is a lack of detailed knowledge about these viruses and the effects they have on their hosts. While they have been associated with significant mortality events infections are usually benign, producing no or minimal clinical effects in their adapted hosts. With increasing emphasis being placed on captive breeding, reintroduction and translocation programs there is a greater likelihood that these viruses will be introduced into naïve macropod populations. The effects and implications of this type of viral movement are unclear.

Aetiology

Herpesviruses are enveloped DNA viruses that range in size from 120 to 250nm. The family Herpesviridae is divided into three subfamilies. Alphaherpesviruses have a moderately wide host range, rapid growth, lyse infected cells and have the capacity to establish latent infections primarily, but not exclusively, in nerve ganglia. Betaherpesviruses have a more restricted host range, a long replicative cycle, the capacity to cause infected cells to enlarge and the ability to form latent infections in secretory glands, lymphoreticular tissue, kidneys and other tissues. Gammaherpesviruses have a narrow host range, replicate in lymphoid cells, may induce neoplasia in infected cells and form latent infections in lymphoid tissue (Lachlan and Dubovi 2011, Roizman and Pellet 2001). There have been five herpesvirus species isolated from macropods, three alphaherpesviruses termed Macropodid Herpesvirus 1 (MaHV1), Macropodid Herpesvirus 2 (MaHV2), and Macropodid Herpesvirus 4 (MaHV4) and two gammaherpesviruses including Macropodid Herpesvirus 3 (MaHV3), and a currently unclassified novel gammaherpesvirus detected in swamp wallabies (Wallabia bicolor) (Callinan and Kefford 1981, Finnie et al. 1976, Johnson et al. 1985, Smith et al. 2008, Stalder unpublished, Vaz, et al. 2013, Wilcox et al. 2011).

Natural hosts

MaHV1 has caused mortalities in parma wallabies (Macropus parma), while MaHV2 has caused mortalities in dorcopsis wallabies (Dorcopsis muelleri luctuosa) and quokkas (Setonix brachyurus). MaHV3 has been associated with cloacal ulceration, respiratory disease and possibly with mammary neoplasia in eastern grey kangaroos (Macropus giganteus). MaHV4 infection was associated with rhinitis and conjunctivitis in an

**World distribution**

MaHV3 has been found in a group of captive eastern grey kangaroos with cloacal ulcers in the United States (Smith et al. 2008). An unidentified herpesvirus was detected in a red kangaroo with hepatitis, also in the United States (Britt et al. 1994). Herpesvirus antibodies have been found in macropods in New Zealand (Webber and Whalley 1978). Given the high prevalence of macropod herpesviruses in captive Australian macropods it seems likely that prevalence is similarly high in animals outside Australia.

**Occurrences in Australia**

Macropod herpesviruses occur Australia-wide with all macropod species assumed to be susceptible to infection (Vogelnest and Portas 2008).

**Epidemiology**

Herpesviruses tend to form latent infections that are periodically reactivated during times of stress or immune-compromise. This capacity has been demonstrated in macropods through a study of MaHV1 seropositive eastern grey kangaroos that began excreting an alphaherpesvirus similar to MaHV1/2 during treatment with corticosteroids. Virus was found in nasal swabs indicating a probable respiratory route of transmission. Herpesvirus DNA was also detected in the trigeminal nerve ganglia of two kangaroos with either reactivated or latent infection. No herpesvirus DNA was detected in cloacal swabs or blood from these animals (Guliani et al. 1999). Herpesviruses have been identified in cloacal swabs of tammar wallabies suffering ulcerative cloacitis, indicating that virus transmission may also occur via the venereal route (Holz, unpublished.).

Herpesviruses are fragile and do not survive well outside the body. They are killed by all common disinfectants including bleach and F10 (benzalkonium chloride/polyhexamethylene biguanide hydrochloride).

Transmission of other herpesviruses generally requires close contact such as mating, licking, nuzzling or sneezing resulting in aerosol spread over short distances.

**Clinical signs**

Clinical disease has predominantly been described in captive animals. Signs include sudden death, depression, fever, incoordination, conjunctivitis, increased respiratory sounds, and vesicles and ulcers on the oral mucosa, cloaca and penis (Ladds 2009). Tammar wallabies have developed cloacal ulcers which heal but then recur
An association between MaHV3 infection and mammary neoplasia has also been postulated (Smith et al. 2008). In a mob of free ranging eastern grey kangaroos, MaHV3 was implicated in an outbreak of respiratory disease, lethargy, inappetence and ataxia, leading to mortality in some cases (Wilcox et al. 2011). MaHV4 was isolated from a free ranging eastern grey kangaroo showing signs of rhinitis and conjunctivitis (Vaz et al. 2013).

**Diagnosis**

Diagnosis in the live animal is largely dependent on demonstrating a rising serum antibody titre via the serum neutralisation test. The collection of swabs from conjunctivae, nostrils, oropharynx or cloaca may also demonstrate the presence of herpesvirus DNA in actively shedding infections (Stalder unpublished). This test may be more sensitive in the presence of cloacal lesions or mucocutaneous ulceration. At necropsy multifocal hepatic necrosis together with intranuclear inclusion bodies is suggestive of herpesvirus infection. This can be confirmed through electron microscopy, viral culture or PCR (Ladds 2009, Vogelnest and Portas 2008).

**Pathology**

Detailed information on the pathology of macropod herpesviruses is available at the Australian Registry of Wildlife Health (ARWH: [http://www.arwh.org/](http://www.arwh.org/)). Post mortem lesions can include a mucoid tracheitis, pulmonary congestion and pneumonia and pale foci in the liver corresponding to multifocal areas of necrosis. Affected liver cells may contain intranuclear inclusion bodies. Diphtheritic plaques can be found on the oesophageal and gastric mucosa and focal ulceration and necrosis of the genitalia may also occur. Inclusion bodies are also found on occasion in affected areas of skin and mucosa (Vogelnest and Portas 2008).

**Differential diagnoses**

Differential diagnoses include macropod diseases associated with sudden death, such as toxoplasmosis and encephalomyocarditis virus infection, diseases causing hepatic necrosis, such as yersiniosis and salmonellosis and diseases causing mucosal ulceration, such as *Treponema spp.* infection (Vaughan-Higgins et al. 2011).

**Laboratory diagnostic specimens**

Detailed information on laboratory diagnostic specimens required for diagnosis of macropod herpesvirus infections is available at the ARWH ([http://www.arwh.org/](http://www.arwh.org/)). For live animals, submit serum and plain swabs from oculonasal, oropharyngeal and cloacal mucosae. For dead animals a complete necropsy should be performed. Collect a range of tissues, including liver and any obvious lesions, and submit them in formalin for histopathology. Fresh tissues should also be submitted for viral culture and PCR (Vogelnest and Portas 2008).

**Laboratory procedures**

Detailed information on laboratory procedures required for diagnosis of macropod herpesvirus infections is available at the ARWH ([http://www.arwh.org/](http://www.arwh.org/)). Serum from live animals can be tested for antibodies using the serum neutralisation test. As many macropods have antibodies to herpesviruses paired samples and a rising titre are required to demonstrate active infection. Both viral culture and PCR can be performed on tissues to demonstrate the presence of herpesvirus spp. PCR performed on oculonasal, oropharyngeal or cloacal swabs can confirm infection in the live animal.
Treatment

Currently there is no treatment. An in vitro study evaluated the ability of the anti-herpetic compounds (E)-5-(2′-bromovinyl)-2′-deoxyuridine (BVDU), acyloguanosine (ACV), 5-iodo-2′-deoxyuridine (IdU), 5-iodo-2′-deoxycytidine (IdC), triflurothymine deoxyribose (TFR), adenine 9-D-arabino-furanoside (Ara-A), cytosine β-D-arabino-furanoside (Ara-C), and thymine 1-D-arabino-furanoside (Ara-T) to inhibit the ability of MaHV2 to form plaques in potoroo kidney cells. Ara-A was the best performing compound, followed by BVDU, but there are no reports of in vivo use in macropods (Smith 1996).

Prevention and control

Given the high prevalence of antibodies in captive macropods it is difficult to maintain a herpesvirus free population. As clinical disease appears to occur infrequently the difficulty and expense associated with maintaining negative populations will likely outweigh the benefits. If a negative population is required newly arrived animals should be quarantined and serviced separately from collection macropods until their herpesvirus status can be ascertained. Macropods with cloacal ulcers should not be used in breeding programs as joeys are presumably susceptible to infection during the birth process. Significant clinical disease and mortality outbreaks have generally been associated with periods of stress, primary exposure of immunologically naïve individuals or in novel host species, which should be considered in the management of captive or free-living macropods.

Surveillance and management

Wildlife disease surveillance in Australia is coordinated by the Wildlife Health Australia. The National Wildlife Health Information System (eWHIS) captures information from a variety of sources including Australian government agencies, zoo and wildlife parks, wildlife carers, universities and members of the public. Coordinators in each of Australia’s States and Territories report monthly on significant wildlife cases identified in their jurisdictions. NOTE: access to information contained within the National Wildlife Health Information System dataset is by application. Please contact admin@wildlifehealthaustralia.com.au.

There is no targeted surveillance program or AUSVETPLAN for macropod herpesviruses in Australia. Cases identified as part of Australia’s general wildlife surveillance system are recorded in the national wildlife health information system.

Statistics

Neutralising antibodies are widespread in both captive and wild populations. Results from one survey are presented in Tables 1 and 2 (Webber and Whalley 1978). A second survey found 98 out of 129 eastern grey kangaroos and 52 out of 89 western grey kangaroos with antibodies (Kerr et al. 1981). Unpublished surveys in 2007 identified seven out of 11 seropositive tammar wallabies and six out of 14 brush-tailed rock wallabies housed in captive institutions in South Australia, and two out of two seropositive yellow-footed rock wallabies (Petrogale xanthopus), four out of four brush-tailed rock wallabies, and two out of eight tammar wallabies housed in Victoria. An unpublished survey conducted in 2011 at a fauna park in the ACT found no actively shedding herpesvirus infections on the basis of PCR performed on swabs from eight brush-tailed rock wallabies, three yellow-footed rock wallabies, four eastern bettongs (Bettongia gaimardi), nine long-nosed potoroos, and eight tammar wallabies despite two of the tammar wallabies having cloacal ulcers at the time of sampling. The serological status of these animals is yet to be determined.
Unfortunately, these serological reports do not differentiate between viruses. As cross-neutralisation is common between herpesviruses, and virus isolation was not performed, it is not possible to determine which viruses these animals were exposed to. A recent study found that antibodies against MaHV4 cross-neutralised MaHV2 (Vaz et al. 2013).

Table 1. Serum neutralising antibodies to macropod herpesvirus in wild macropods (Webber and Whalley 1978).

<table>
<thead>
<tr>
<th>Species (Latin)</th>
<th>No. tested</th>
<th>No. positive</th>
<th>% positive</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Petrogale</em> (rock-wallaby) species</td>
<td>102</td>
<td>20</td>
<td>19.6</td>
</tr>
<tr>
<td><em>Thylagale thetis and stigmata</em> (red-necked and red-legged pademelon)</td>
<td>7</td>
<td>2</td>
<td>28.6</td>
</tr>
<tr>
<td><em>Lagorchestes conspicillatus</em> (spectacled hare-wallaby)</td>
<td>2</td>
<td>2</td>
<td>100</td>
</tr>
<tr>
<td><em>Macropus parma</em> (parma wallaby) (Aus)</td>
<td>13</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><em>Macropus parma</em> (parma wallaby) (NZ)</td>
<td>23</td>
<td>12</td>
<td>52.2</td>
</tr>
<tr>
<td><em>M. robustus robustus</em> (eastern wallaroo)</td>
<td>5</td>
<td>2</td>
<td>40</td>
</tr>
<tr>
<td><em>M. robustus erubescens</em> (euro)</td>
<td>12</td>
<td>1</td>
<td>8.3</td>
</tr>
<tr>
<td><em>M. giganteus</em> (eastern grey kangaroo)</td>
<td>7</td>
<td>5</td>
<td>71.4</td>
</tr>
<tr>
<td><em>M. rufogriseus</em> (red-necked wallaby)</td>
<td>6</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><em>M. rufus</em> (red kangaroo)</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><em>Potorous tridactylus</em> (long-nosed potoroo)</td>
<td>13</td>
<td>3</td>
<td>23.1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>192</strong></td>
<td><strong>47</strong></td>
<td><strong>24.5</strong></td>
</tr>
</tbody>
</table>

Table 2. Serum neutralising antibodies to macropod herpesvirus in captive macropods (Webber and Whalley 1978).

<table>
<thead>
<tr>
<th>Species (Latin)</th>
<th>No. tested</th>
<th>No. positive</th>
<th>% positive</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Macropus eugenii</em> (tammar wallaby) (healthy)</td>
<td>17</td>
<td>5</td>
<td>29.4</td>
</tr>
<tr>
<td><em>M. eugenii</em> (sick)</td>
<td>10</td>
<td>10</td>
<td>100</td>
</tr>
<tr>
<td><em>M. eugenii</em> (Garden Island)</td>
<td>16</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><em>Setonix brachyurus</em> (quokka) (Garden Island)</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><em>M. parma</em> (parma wallaby)</td>
<td>13</td>
<td>4</td>
<td>30.8</td>
</tr>
<tr>
<td><em>M. parma x M. eugenii</em></td>
<td>2</td>
<td>1</td>
<td>50</td>
</tr>
<tr>
<td><em>M. robustus erubescens</em> (euro)</td>
<td>4</td>
<td>3</td>
<td>75</td>
</tr>
<tr>
<td><em>M. robustus robustus</em> (eastern wallaroo)</td>
<td>9</td>
<td>9</td>
<td>100</td>
</tr>
<tr>
<td><em>M. giganteus</em> (eastern grey kangaroo)</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><em>M. rufus</em> (red kangaroo)</td>
<td>6</td>
<td>5</td>
<td>83.3</td>
</tr>
</tbody>
</table>
### Research

As most of the available prevalence data is based on information that was acquired over 30 years ago prior to the molecular identification and classification of macropod herpesvirus species that is currently accepted, further surveys are required, and are currently in progress, to determine the present prevalence of macropod herpesviruses in wild macropod populations. Research is also necessary to determine how infection is acquired, the relationship between infection and clinical disease and the impact of infection at a population level. Thought needs to be given to the implications and management of herpesviruses in re-introduction programs. Possible treatment options for captive macropods could also be explored. As cloacal ulcers can occur in the absence of herpesvirus infections further research is required to determine the aetiology of non-herpesvirus-associated ulcers.

### Human health implications

None.

### Conclusions

Herpesvirus infections appear to be extremely common in both captive and wild macropods. However, clinical disease is rare indicating that the virus is likely well adapted to its host. As with other herpesvirus infections disease generally occurs if the virus finds its way into a naïve, novel or immunocompromised host. With ongoing research, it seems likely that further macropod herpesvirus species will be discovered.

### References and other information


**Acknowledgements**

We are extremely grateful to Peter Holz and Kathryn Stalder who provided the initial draft of this fact sheet and to those individuals, agencies and organisations that provided comment and external review.

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**To provide feedback on this fact sheet**

We are interested in hearing from anyone with information on this condition in Australia, including laboratory reports, historical datasets or survey results that could be added to the National Wildlife Health Information System. If you can help, please contact us at admin@wildlifehealthaustralia.com.au.

Wildlife Health Australia would be very grateful for any feedback on this fact sheet. Please provide detailed comments or suggestions to admin@wildlifehealthaustralia.com.au. We would also like to hear from you if you have a particular area of expertise and would like to produce a fact sheet (or sheets) for the network (or update current sheets). A small amount of funding is available to facilitate this.

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