Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

84

Marine Mammal Viruses

JIM WELLEHAN AND GALAXIA CORTES-HINOJOSA

Viral abundance in the ocean has been estimated at 10^{30} virions, one or two orders of magnitude greater than the estimated number of bacterial and eukaryotic cells, so viruses are the most abundant life in the oceans.[1,2] Marine mammals live in intimate contact with the ocean, and therefore a vast diversity of viruses. Advances in molecular techniques have allowed a rapid expansion of knowledge on viral diversity, enabling greater understanding of evolution, causes of mortalities, and pathogen interactions.

Clinical Implications of Viral Biology

Viruses are classified on the basis of their genomic material and key elements of structure and replication. A basic knowledge of these elements is also clinically useful for predicting disease risk and epidemiologic characteristics, and for establishing appropriate management protocols (Table 84.1). DNA viruses often replicate in the nucleus of the host cell, and tend to be more species specific. RNA viruses tend to replicate in the cytoplasm and are more prone to jumping between species. There are exceptions, such as poxviruses, asfarviruses, and iridoviruses, which are DNA viruses that replicate in the cytoplasm and have significantly lower host fidelity, and bornaviruses, which are RNA viruses with intranuclear replication.

Viral genome size is also important. Large viruses with many genes are better at evolving complex host interactions for things like latency. Smaller viruses are capable of more rapid evolution and therefore more capable of adapting to different hosts and tissues, resulting in host jumping and differing clinical presentations.

Genome organization is also clinically relevant; nonsegmented viruses that are not very capable of recombination, such as paramyxoviruses, largely change through mutation. Mutations are much more likely to be deleterious rather than beneficial, limiting rates of change. Segmented viruses, such as orthomyxoviruses or reoviruses, may swap segments, much like sexual reproduction in a eukaryote. This enables an organism to use homologous genes that have been functional in another conspecific, which is much more likely to be beneficial than random mutations. As a result, they may change much more rapidly, and this is why a segmented influenza virus changes to the extent where novel vaccines are needed every year or two, whereas vaccines for an otherwise biologically similar nonsegmented morbillivirus result in lifelong immunity, because the virus cannot change as rapidly.

Presence of an envelope is also clinically relevant. Viruses with envelopes tend to need them to infect target cells. This lipid layer is more susceptible to environmental conditions and disinfectants, consequently making cleaning easier and decreasing environmental persistence.

RNA Viruses

Astroviridae

Astroviruses are small (28–30 nm), spherical, nonenveloped, positive-sense, single-stranded viruses with intracytoplasmic replication. Astroviruses often cause diarrhea and have a high prevalence in children; most children over 5 years of age have antibodies to human astroviruses. There are also several astroviruses documented in association with encephalitis in nonmarine mammals. In the order *Carnivora*, astroviruses have been associated with diarrhea in mink *(Neovison vison)*, domestic dogs, cheetahs *(Acinonyx jubatus)*, and domestic cats.[3] In marine mammals, astroviruses have been reported in bottlenose dolphins *(Tursiops truncatus)*,[4] Steller sea lions *(Eumetopias jubatus)*,[4] minke whales *(Balaenoptera acutorostrata)*, and California sea lions *(Zalophus californianus)*.[4,5] Five different astroviruses have been found: one in bottlenose dolphins, one in Steller sea lions, and three in California sea lions.[4] Next-generation sequencing (NGS) has identified a total of eight additional astroviruses in California sea lions.[5] This study was done using fecal swabs of animals in rehabilitation facilities and found an astrovirus prevalence of 51%.[5] Bottlenose Dolphin Astrovirus 1 (BDAstV1) was found in 86% of stranded bottlenose dolphins and in 50% of healthy bottlenose dolphins from a managed collection. A subset of dolphins who were persistent shedders were identified. The clinical significance of astroviruses in marine mammals is likely to be greatest in young animals as a cause of diarrhea, as is seen in other species.

TABLE 84.1 Virus Taxa Associated With Clinical Presentations in Marine Mammals

Clinical Signs	Differentials
Mucocutaneous lesions	Poxvirus, herpesvirus, calicivirus, papillomavirus, picornavirus
Skin	Poxvirus, herpesvirus, calicivirus, papillomavirus
Respiratory	Influenza, morbillivirus, calicivirus, coronavirus, adenovirus
Enteritis	Adenovirus, astrovirus, coronavirus
Neurologic	Morbillivirus, herpesvirus
Neoplasia	Herpesvirus, retrovirus, polyomavirus, papillomavirus
Hepatitis	Adenovirus, coronavirus, herpesvirus
Ocular	Adenovirus, herpesvirus, calicivirus

Caliciviridae

San Miguel sea lion virus (SMSV) is a small (30–38 nm) icosahedral, nonenveloped, positive-sense, single-stranded virus with intracytoplasmic replication that belongs to the genus *Vesivirus* in the family *Caliciviridae*. This virus is genetically indistinguishable from vesicular exanthema of swine virus (VESV), which is a reportable foreign animal disease that has officially been considered eradicated in the United States since 1956. Perhaps most concerning, related vesiviruses have been found to rapidly evolve greater virulence where there are high host population densities.[6] Serologic studies suggest exposure to vesiviruses in cetaceans and pinnipeds.[7] In pinnipeds, SMSV clinical manifestations include vesicular lesions on the flippers and the mouth, as well as gastroenteritis in California sea lions.[8] Clinical presentations in premature pups include respiratory distress and locomotor impairment, with possible fatal consequences. Cutaneous lesions typically resolve without supportive care. SMSV has zoonotic potential, causing an influenza-like syndrome followed by blisters on the hands and feet.[9] SMSV has also been associated with hepatitis in humans.[10,11]

Coronaviridae

Coronaviruses are large (120–160 nm), round, toroidal or bacilliform, enveloped, positive-sense, single-stranded viruses with intracytoplasmic replication. In marine mammals, viruses in the genus *Gammacoronavirus* have been characterized in a captive beluga whale *(Delphinapterus leucas)*[12] and bottlenose dolphins,[13] and an *Alphacoronavirus* has been found in both captive and wild harbor seals *(Phoca vitulina)*.[14,15] Clinical signs in the beluga whale included generalized pulmonary disease and acute liver failure. For the captive harbor seals, the clinical signs included anorexia with abnormal behavior after the sudden death of two other harbor seals in the same pool. At clinical examination, the mucosa was purple and injected, and abnormal pulmonary sounds were auscultated; blood work abnormalities included leukocytosis, hypernatremia, and hyperchloremia. Postmortem findings included acute necrotizing enteritis and pulmonary edema. Confirmation of coronavirus was attempted on cell culture but was not possible at the time. In the epizootic event in wild harbor seals, the five carcasses in suitable condition had lymphocytic/histocytic necrotizing pneumonia diagnosed histologically. An *Alphacoronavirus* was diagnosed in lung tissue using consensus polymerase chain reaction (PCR) with product sequence identification.

Orthomyxoviridae (Influenza Virus)

Orthomyxoviruses are medium sized (80–120 nm), segmented, pleomorphic, enveloped, negative-sense, single-stranded RNA viruses with intranuclear and intracytoplasmic replication. Influenza viruses are further divided into the genera *Influenzavirus A*, *Influenzavirus B*, and *Influenzavirus C*. Influenza A viruses tend to be the most pathogenic and have been well known to cause pandemic outbreaks in humans since 1918/1919. In marine mammals, both Influenza A and Influenza B have been diagnosed in wild populations of cetaceans and pinnipeds since the late 1970s. Mass mortalities in association with several different strains of Influenza A have been reported in harbor seals since 1979. Influenza B has been reported in stranded harbor seals since 1999, but not in association with epidemics. In cetaceans, Influenza A has been detected in stranded long-finned pilot whales. Additionally, South American fur seals *(Arctocephalus australis)*,[16] Caspian seals *(Pusa caspica)*,[17] Baikal seals *(Phoca sibirica)* and ringed seals *(Phoca hispida)*,[18] Dall's porpoises *(Phocoenoides dalli)*,[19] beluga whales, and other species have been reported to be seropositive for influenza.[20] Clinical signs include epistaxis, conjunctivitis, subcutaneous emphysema, and general weakness. Diagnosis of influenza can be based on a combination of clinical signs, qPCR, serology, and postmortem findings (gross pathology, histopathology, and immunohistochemistry). Seal-to-human influenza transmission has been described. Direct contact on massive mortalities and one case of direct contact with respiratory secretion are associated with conjunctivitis in humans.[21] A comprehensive review of influenza in marine mammals is available.[20]

Paramyxoviridae

Morbillivirus

Paramyxoviruses are pleomorphic, enveloped, negative-sense, single-stranded viruses with intracytoplasmic replication. This family causes respiratory, neurologic, and multisystemic diseases in mammals.[22] In marine mammals, three viruses in the genus *Morbillivirus* have been described: canine distemper virus (CDV), phocine distemper virus (PDV), and cetacean morbillivirus (CeMV). CeMV has

significant diversity and may eventually be split into more than one species; morbilliviruses from the Northern Hemisphere [porpoise morbillivirus (PMV), dolphin morbillivirus (DMV), pilot whale morbillivirus (PWMV), and Longman's beaked whale morbillivirus (BWMV)] show significant divergence from CeMV from the Southern Hemisphere (from Swan River, Australia and from Brazil). Morbilliviruses have been recognized as causes of mass mortalities in pinnipeds and cetaceans since the early 1980s. Diagnosis in cetaceans is usually postmortem, but clinical signs include cachexia, abnormal mentation, and respiratory distress. In pinnipeds, clinical signs include respiratory distress, ocular and nasal discharge, pyrexia, and erratic swimming. Morbilliviruses infect via the signaling lymphocytic activation molecule (SLAM [CD150]) receptor, taking out memory T cells and leaving the host significantly immunosuppressed. Coinfection with other pathogens such as *Aspergillus fumigatus* or *Brucella* become more clinically significant.[23,24] Comprehensive reviews are available for both pinnipeds[22] and cetaceans.[23]

Respirovirus

The genus *Respirovirus* contains parainfluenza viruses infecting several mammal hosts. Parainfluenza virus was first identified in marine mammals in a bottlenose dolphin kept in an open water enclosure in 2008. Clinical signs included respiratory stridor, halitosis, and exudate from the blowhole.[25] Serologic data suggested that exposure may be common in wild and captive bottlenose dolphins.[26] This virus is closely related to *Bovine respirovirus virus 3* and *Human respirovirus virus 3*, and potential risks for host jumping of these viruses should be considered.

DNA Viruses

Adenoviridae

Adenoviruses are medium-sized (70–90 nm) icosahedral, nonenveloped, double-stranded DNA viruses with intranuclear replication. In marine mammals, adenoviruses have been reported in pinnipeds, mustelids, and cetaceans. Adenoviruses have been associated with death in yearling California sea lions in rehabilitation; clinical signs included photophobia, emaciation, blood-tinged diarrhea, leukopenia, and monocytosis.[27] In 2011 California sea lion adenovirus 1 (CSLAdV-1) was characterized as a cause of viral hepatitis in wild animals and has since been detected in several pinniped species in captivity, especially in elder animals.[28–30] California sea lion adenovirus 2 and phocid adenoviruses 1 and 2 have been identified in ocular lesions and in unaffected eyes of pinnipeds.[31] In cetaceans, adenoviruses have been associated with gastrointestinal (GI) symptoms in bottlenose dolphins and harbor porpoises from Europe[32,33] and the United States.[34] Recently, a novel adenovirus with unknown clinical significance was found in Southern sea otters.[35] Diagnosis of adenoviral disease may be made with a combination of clinical signs and use of PCR diagnostics and/or negative staining electron microscopy of feces from clinical cases, with intranuclear inclusions present on histologic examination in postmortem cases.

Herpesviridae

Herpesviruses are large (100–150 nm), icosahedral, enveloped, double-stranded viruses with intranuclear replication. Herpesviruses can be latent in different sites, with certain subfamily tendencies; alphaherpesviruses often establish latency in neurons, whereas betaherpesviruses and gammaherpesviruses establish latency in leukocytes. Herpesviruses infect a wide range of vertebrates. *Trichechid herpesvirus* 1 (TrHV-1) is a gammaherpesvirus reported in West Indian manatees *(Trichechus manatus)* and may be a biomarker for stress.[36]

Polar bears *(Ursus maritimus)* are susceptible to encephalitis caused by the alphaherpesvirus equine herpes virus 9 (EHV-9), which may be fatal (see Chapter 33).[37] This virus appears to be endemic in Grevy's zebras *(Equus grevyi)* and is associated with fatalities in diverse laurasiatherian mammals. Although it is unlikely to be significant in wild populations due to low contact rates with the endemic host, it is a more significant concern in zoological collections.

In pinnipeds, 11 herpesviruses have been reported to date.[38,39] Otarine herpesvirus 1 (OtHV-1) is a gammaherpesvirus associated with urogenital carcinoma in California sea lions. OtHV-1 was also detected in a captive South American fur seal *(Arctocephalus australis)* with urogenital carcinoma.[40] This virus has a high prevalence in wild adult California sea lions (46% in males and 22% in females). Rates of metastasis are high, with sublumbar lymph nodes and liver as common sites.[41,42] Otarine herpesvirus 4, found in clinically unaffected northern fur seals *(Callorhinus ursinus)*, is a very close relative of OtHV-1; investigation of this virus as a potential vaccine against OtHV-1 is merited.

Phocid herpesvirus 1 (PHV-1) is an alphaherpesvirus seen in fatal outbreaks in harbor seals and gray seals *(Halichoerus grypus)* in rehabilitation facilities, affecting mainly young and immunosuppressed individuals. This virus may target the respiratory system as well as the GI tract, adrenal glands, and liver. Clinical signs may include nasal and ocular discharge, coughing, inflammation of the oral mucosa, vomiting, diarrhea, lethargy, anorexia, and fever.[43–45]

In cetaceans, diverse alpha- and gammaherpesviruses have been reported. Delphinid herpesviruses 1 and 2, both alphaherpesviruses, have been associated with fatal necrosis of the spleen, thymus, and lymph nodes in bottlenose dolphins, with intranuclear inclusions present in affected tissues.[46] A harbor porpoise herpesviral encephalitis case was also likely to have been caused by an alphaherpesvirus. Delphinid herpesvirus 4, a gammaherpesvirus highly prevalent in bottlenose dolphins, is associated with plaque-like genital lesions, and gammaherpesviruses have been associated with similar lesions in other cetacean species.[38,47,48]

Papillomaviridae

Papillomaviruses are small (55 nm) icosahedral, nonenveloped, double-stranded viruses with intranuclear replication. In marine mammals, papillomaviruses have been found in manatees,[49] cetaceans,[50] and pinnipeds.[51] Clinical signs include warty lesions in lingual and genital mucosa, as well as cutaneous lesions. The possibility of progression to neoplasia should be considered. Treatments against papillomaviruses in marine mammals have not been studied, but imiquimod and cidofovir have shown efficacy in other mammal models. Diagnosis may be accomplished with a combination of histopathology and molecular diagnostics such as PCR or NGS.

Poxviridae

Poxviruses are large, brick- or ovoid-shaped, enveloped double-stranded viruses with intracytoplasmic replication. Viruses in the subfamily *Chordopoxvirinae* can be transmitted directly, indirectly, and by vectors. In general, viruses in this subfamily cause proliferative skin disease in vertebrates. Poxviruses in the genera *Orthopoxvirus* and *Parapoxvirus* have known zoonotic potential. In marine mammals, chordopoxviruses have been found in cetaceans,[52] pinnipeds,[52,53] and sea otters.[54] Clinical signs on cetaceans are typically called "tattoo skin lesions" and present as irregular gray, yellow, or black cutaneous lesions. These lesions usually do not present a risk for the animals and resolve in a few weeks. In pinnipeds, lesions include skin nodules and ulceration. Diagnosis can be accomplished with a combination of histopathology and molecular diagnostics such as PCR or NGS.

Overview of Viral Diagnostics

Virus diagnoses can be accomplished using different approaches, and it is important to be aware of the applications and limitations of each approach. Histopathology and electron microscopy are essential for diagnosis of viral disease, and provide clues to narrow down candidate viruses on the basis of affected tissues, replication site within the cell, structure, shape, and size. Although other techniques are useful for identifying virus presence or exposure, histopathology is usually critical for identification of viral disease.

Immune assays are used to determine whether the patient has been exposed to a particular agent, but it is important to be aware of limitations. The two branches of acquired immunity are humoral immunity and cellular immunity. Recognition of pathogens is done by antibodies in humoral immunity and by T-cell receptors in cellular immunity. Most commonly used assays look for antibodies and not for cellular immunity. The type of acquired immune response is dependent on how a pathogen is presented; humoral immunity is generally more effective for extracellular pathogens, and cellular immunity is more effective for intracellular pathogens such as viruses. Although both branches of acquired immunity may be stimulated, this is not always the case, and it is certainly possible to have a negative antibody titer in an exposed animal with an acquired cellular immune response; for some agents this is common. Antibodies may also cross react to related viruses that have significantly different clinical implications. This is especially important in host taxa whose viral diversity is not yet well known, such as marine mammals. Development of an acquired immune response also requires time; it is often a week or more after infection before a response is seen. Finally, there are limitations on available reagents; many techniques require host-specific reagents to detect antibody responses. Although there may be cross reaction when using reagents from closely related hosts, this needs to be validated for each host species.[55]

Methods for detection of virus rather than immune response include virus isolation, immunohistochemistry, and nucleic acid-based diagnostics. Virus isolation on cell cultures enables many other possible studies including experimental infections and construction of genetically modified viruses for vaccines or understanding of biology. However, culture conditions have not been determined for most marine mammal viruses. There are few available marine mammal cell lines, and when possible, culture is often comparatively very slow. Immunohistochemistry may detect viral proteins in tissue sections, but the availability of validated antibodies for specific detection of marine mammal viruses is very limited, and cross-reactivity concerns exist. In situ hybridization (ISH) is similar to immunohistochemistry but detects viral nucleic acids rather than viral proteins. The cost barriers to ISH assay development are significantly lower, and use of ISH is expanding. However, nucleic acids are much more badly damaged by formalin than proteins, and it is critical that tissues be processed into paraffin blocks rapidly and not remain in formalin for excessive periods of time.

Nucleic acid-based techniques are currently most broadly used for virus detection. PCR-based protocols are used for a wide range of viruses. PCR primers may be designed to amplify only specific viruses or clades of related taxa. It is critical that a PCR product is identified properly; the most rigorous methods are product sequencing and probe hybridization. Sequencing will provide absolute identification of the product amplified; any assay using broad-range primers to identify clades of viruses needs to have a product sequence ID. Probe hybridization uses a labeled complementary nucleic acid strand that will bind very specifically to the expected product under correct salt and temperature conditions. This is currently most commonly done in probe hybridization quantitative PCR (qPCR, a.k.a. real-time PCR) assays, such as TaqMan assays. These assays require less time, are less expensive, and provide quantitative information about the amount of virus present. However, a properly designed and validated probe hybridization qPCR will identify only known target viruses and is not useful for identification of novel agents. Note that methods other than probe hybridization are also

commonly called qPCR or real-time PCR, such as SYBR Green, which involves dye incorporation of dye into any amplified DNA and is less rigorous.

PCR-based methods are limited because they require a known conserved area of sequence for primer design. The detection of novel phylogenetically distant viruses may be challenging or even impossible. In the last few years, NGS technologies have developed. Rather than targeted sequencing of a single DNA template, NGS methods may sequence literally millions of different nucleic acid templates in a sample. Although NGS can obtain sequences from previously unknown and divergent pathogens, it must also recognize and sift through literally millions of nontarget sequences. This is a major bioinformatics challenge but has already resulted in significant advances in infectious disease. Costs for NGS and the time required for data analysis are still high but have dramatically decreased, and NGS technologies are already in use for marine mammal virus discovery.

References

1. Suttle CA: Marine viruses—major players in the global ecosystem, *Nature Rev Microbio* 5:801–812, 2007.
2. Suttle CA: Viruses in the sea, *Nature* 437:356–361, 2005.
3. Atkins A, Wellehan J, Childress A, et al: Characterization of an outbreak of astroviral diarrhea in a group of cheetahs *(Acinonyx jubatus)*, *Vet Microbiol* 136:160–165, 2009.
4. Rivera R, Nollens H, Venn-Watson S, et al: Characterization of phylogenetically diverse astroviruses of marine mammals, *J Gen Virol* 91:166–173, 2010.
5. Li L, Shan T, Wang C, et al: The fecal viral flora of California sea lions, *J Virol* 85:9909–9917, 2011.
6. Schorr-Evans E, Poland A, Johnson W, et al: An epizootic of highly virulent feline calicivirus disease in a hospital setting in New England, *J Feline Med Surg* 5:217–226, 2003.
7. Akers T, Smith A, Latham A, et al: Calicivirus antibodies in California gray whales *(Eschrichtius robustus)* and Steller sea lions *(Eumetopias jupatus)*, *Arch Virol* 46:175–177, 1974.
8. Schmitt TL, Reidarson TH, St. Leger J, et al Novel presentation of San Miguel sea lion virus *(Calicivirus)* epizootic in adult captive sea lions, *Zalophus californianus*. In Proceedings of the 40th International Association for Aquatic Animal Medicine, 2009.
9. Smith AW, Skilling DE, Cherry N, et al: Calicivirus emergence from ocean reservoirs: zoonotic and interspecies movements, *Emerg Infect Dis* 4:13–20, 1998.
10. Smith AW, Iversen PL, Skilling DE, et al: Vesivirus viremia and seroprevalence in humans, *J Med Virol* 78:693–701, 2006.
11. Lee H, Cho YH, Park JS, et al: Elevated post-transfusion serum transaminase values associated with a highly significant trend for increasing prevalence of anti-Vesivirus antibody in Korean patients, *J Med Virol* 84:1943–1952, 2012.
12. Mihindukulasuriya KA, Wu G, St Leger J, et al: Identification of a novel coronavirus from a beluga whale by using a panviral microarray, *J Virol* 82:5084–5088, 2008.
13. Woo PC, Lau SK, Lam CS, et al: Discovery of a novel bottlenose dolphin coronavirus reveals a distinct species of marine mammal coronavirus in Gammacoronavirus, *J Virol* 88:1318–1331, 2014.
14. Nollens HH, Wellehan JF, Archer L, et al: Detection of a respiratory coronavirus from tissues archived during a pneumonia epizootic in free-ranging Pacific harbor seals Phoca vitulina richardsii, *Dis Aquat Organ* 90:113–120, 2010.
15. Bossart G, Schwartz J: Acute necrotizing enteritis associated with suspected coronavirus infection in 3 harbor seals *(Phoca vitulina)*, *J Zoo Wildl Med* 21:84–87, 1990.
16. Blanc A, Ruchansky D, Clara M, et al: Serologic evidence of influenza A and B viruses in South American fur seals *(Arctocephalus australis)*, *J Wildl Dis* 45:519–521, 2009.
17. Ohishi K, Ninomiya A, Kida H, et al: Serological evidence of transmission of human influenza A and B viruses to Caspian seals *(Phoca caspica)*, *Microbiol Immunol* 46:639–644, 2002.
18. Ohishi K, Kishida N, Ninomiya A, et al: Antibodies to human-related H3 influenza A virus in Baikal seals *(Phoca sibirica)* and ringed seals *(Phoca hispida)* in Russia, *Microbiol Immunol* 48:905–909, 2004.
19. Ohishi K, Maruyama T, Ninomiya A, et al: Serologic investigation of influenza A virus infection in cetaceans from the western North Pacific and the Southern oceans, *Mar Mam Sci* 22:214–221, 2006.
20. Fereidouni S, Munoz O, Von Dobschuetz S, et al: Influenza virus infection of marine mammals, *Ecohealth* 13:161–170, 2016.
21. Webster RG, Geraci J, Petursson G, et al: Conjunctivitis in human beings caused by influenza A virus of seals, *N Engl J Med* 304:911, 1981.
22. Wang L, Collins P, Fouchier R, et al: Family paramyxoviridae. Virus taxonomy: Ninth Report of the International Committee on Taxonomy of Viruses 2012:672–685.
23. Cassle SE, Landrau-Giovannetti N, Farina LL, et al: Coinfection by Cetacean morbillivirus and Aspergillus fumigatus in a juvenile bottlenose dolphin *(Tursiops truncatus)* in the Gulf of Mexico, *J Vet Diagn Invest* 28:729–734, 2016.
24. West KL, Levine G, Jacob J, et al: Coinfection and vertical transmission of *Brucella* and Morbillivirus in a neonatal sperm whale *(Physeter macrocephalus)* in Hawaii, USA, *J Wildl Dis* 51:227–232, 2015.
25. Nollens HH, Wellehan JFX, Saliki JT, et al: Characterization of a parainfluenza virus isolated from a bottlenose dolphin *(Tursiops truncatus)*, *Vet Microbiol* 128:231–242, 2008.
26. Venn-Watson S, Rivera R, Smith CR, et al: Exposure to novel parainfluenza virus and clinical relevance in 2 bottlenose dolphin *(Tursiops truncatus)* populations, *Emerg Infect Dis* 14:397–405, 2008.
27. Dierauf L, Lowenstine L, Jerome C: Viral hepatitis (adenovirus) in a California sea lion, *J Am Vet Med Assoc* 179:1194–1197, 1981.
28. Inoshima Y, Murakami T, Ishiguro N, et al: An outbreak of lethal adenovirus infection among different otariid species, *Vet Microbiol* 165:455–459, 2013.
29. Goldstein T, Colegrove K, Hanson M, et al: Isolation of a novel adenovirus from California sea lions *(Zalophus californianus)*, *Dis Aquat Organ* 94:243–248, 2011.
30. Cortés-Hinojosa G, Doescher B, Kinsel M, et al: Coinfection of California sea lion adenovirus 1 and a novel polyomavirus in Hawaiian monk seal *(Neomonachus schauinslandi)*, *J Zoo Wildl Med* 47:427–437, 2016.
31. Wright EP, Waugh LF, Goldstein T, et al: Evaluation of viruses and their association with ocular lesions in pinnipeds in rehabilitation, *Vet Ophthalmol* 18(Suppl 1):148–159, 2015.
32. Rubio-Guerri C, García-Párraga D, Nieto-Pelegrín E, et al: Novel adenovirus detected in captive bottlenose dolphins *(Tursiops*

truncatus) suffering from self-limiting gastroenteritis, *BMC Vet Res* 11:53, 2015.
33. van Beurden SJ, IJsseldijk LL, van de Bildt MW, et al: A novel cetacean adenovirus in stranded harbour porpoises from the North Sea: detection and molecular characterization, *Arch Virol* 162:2035–2040, 2017.
34. Standorf K, Cortés-Hinojosa G, Venn-Watson S, et al: Phylogenetic analysis of the genome of an enteritis-associated bottlenose dolphin mastadenovirus supports a clade infecting the *Cetartiodactyla*, *J Wildl Dis* 54:112–121, 2018.
35. Siqueira JD, Ng T, Miller M, et al: Endemic infection of stranded Southern Sea Otters *(Enhydra lutris nereis)* with novel parvovirus, polyomavirus, and adenovirus, *J Wildl Dis* 2017.
36. Ferrante JA, Cortés-Hinojosa G, Archer LL, et al: Development of a quantitative PCR assay for measurement of Trichechid herpesvirus 1 (TrHV1) load in the Florida manatee *(Trichechus manatus latirostris)*, *J Vet Diagn Invest* 29:476–482, 2017.
37. Donovan T, Schrenzel M, Tucker T, et al: Meningoencephalitis in a polar bear caused by equine herpesvirus 9 (EHV-9), *Vet Pathol* 46:1138–1143, 2009.
38. Maness H, Nollens H, Jensen E, et al: Phylogenetic analysis of marine mammal herpesviruses, *Vet Microbiol* 149:23–29, 2011.
39. Cortés-Hinojosa G, Gulland FM, DeLong R, et al: A novel gammaherpesvirus in Northern fur seals *(Callorhinus ursinus)* is closely related to the California sea lion *(Zalophus californianus)* carcinoma-associated otarine herpesvirus-1, *J Wildl Dis* 52:88–95, 2016.
40. Dagleish M, Barrows M, Maley M, et al: The first report of otarine herpesvirus-1-associated urogenital carcinoma in a South American fur seal *(Arctocephalus australis)*, *J Comp Pathol* 149:119–125, 2013.
41. Buckles E, Lowenstine L, DeLong R, et al: Age-prevalence of otarine herpesvirus-1, a tumor-associated virus, and possibility of its sexual transmission in California sea lions, *Vet Microbiol* 120:1–8, 2007.
42. Lipscomb T, Scott D, Garber R, et al: Common metastatic carcinoma of California sea lions *(Zalophus californianus)*: Evidence of genital origin and association with novel gammaherpesvirus, *Vet Pathology* 37:609–617, 2000.
43. Gulland FM: Stranded seals: important sentinels, *J Am Vet Med Assoc* 214:1191–1192, 1999.
44. Gulland F, Lowenstine L, Lapointe J, et al: Herpesvirus infection in stranded Pacific harbor seals of coastal California, *J Wildl Dis* 33:450–458, 1997.
45. Harder T, Vos H, deSwart R, et al: Age-related disease in recurrent outbreaks of phocid herpesvirus type-1 infections in a seal rehabilitation centre: Evaluation of diagnostic methods, *Vet Rec* 140:500–503, 1997.
46. Blanchard T, Santiago N, Lipscomb T, et al: Two novel alphaherpesviruses associated with fatal disseminated infections in Atlantic bottlenose dolphins, *J Wildl Dis* 37:297–305, 2001.
47. van Beurden SJ, IJsseldijk LL, Ordonez SR, et al: Identification of a novel gammaherpesvirus associated with (muco)cutaneous lesions in harbour porpoises *(Phocoena phocoena)*, *Arch Virol* 160:3115–3120, 2015.
48. van Elk C, van de Bildt M, de Jong A, et al: Genital herpesvirus in bottlenose dolphins *(Tursiops truncatus)*: cultivation, epidemiology, and associated pathology, *J Wildl Dis* 45:895–906, 2009.
49. Ghim S-J, Joh J, Mignucci-Giannoni AA, et al: Genital papillomatosis associated with two novel mucosotropic papillomaviruses from a Florida manatee *(Trichechus manatus latirostris)*, *Aquatic Mammals* 40:195–200, 2014.
50. Robles-Sikisaka R, Rivera R, Nollens H, et al: Evidence of recombination and positive selection in cetacean papillomaviruses, *Virology* 427:189–197, 2012.
51. Rivera R, Robles-Sikisaka R, Hoffman E, et al: Characterization of a novel papillomavirus species (ZcPV1) from two California sea lions *(Zalophus californianus)*, *Vet Microbiol* 155:257–266, 2012.
52. Bracht A, Brudek R, Ewing R, et al: Genetic identification of novel poxviruses of cetaceans and pinnipeds, *Arch Virol* 151:423–438, 2006.
53. Burek K, Beckmen K, Gelatt T, et al: Poxvirus infection of Steller sea lions *(Eumetopias jubatus)* in Alaska, *J Wildl Dis* 41:745–752, 2005.
54. Tuomi PA, Murray MJ, Garner MM, et al: Novel poxvirus infection in northern and southern sea otters *(Enhydra lutris kenyoni)* and *Enhydra lutris neiris)*, Alaska and California, USA, *J Wildl Dis* 50:607–615, 2014.
55. Nollens H, Ruiz C, Walsh M, et al: Cross-reactivity between immunoglobulin G antibodies of whales and dolphins correlates with evolutionary distance, *Clin Vaccine Immunol* 15:1547–1554, 2008.