

REVIEW ARTICLE

Marine Mammal Zoonoses: A Review of Disease Manifestations

T. B. Waltzek^{1,2,3}, G. Cortés-Hinojosa^{1,2,3}, J. F. X. Wellehan Jr.³ and Gregory C. Gray^{1,2,3}

¹ Department of Environmental and Global Health, College of Public Health and Health Professions, University of Florida, Gainesville, FL, USA

² Emerging Pathogens Institute, University of Florida, Gainesville, FL, USA

³ College of Veterinary Medicine, University of Florida, Gainesville, FL, USA

Impacts

- Contact between marine mammals and humans is increasing as the number of managed animals in oceanaria, rehabilitation facilities and research facilities grows. Furthermore, as coastal communities expand, opportunities for encounters with marine wildlife increase. Encounters with wildlife species, including marine mammals, pose certain risks including traumatic injury and disease transmission. In this review, we provide a synopsis of the known marine mammal zoonotic diseases, their clinical and pathologic manifestation in marine mammals, followed by a review of disease transmission to humans.
- Although marine mammal zoonoses are poorly understood, a growing list of bacterial, viral and fungal agents have been reported. The most common marine mammal zoonotic diseases induce localized self-limiting infections, although life-threatening systemic diseases have been reported. Marine mammal researchers, rehabilitators, trainers, veterinarians, volunteers and subsistence hunters have an increased risk of being injured or acquiring zoonotic diseases through extended occupational exposure.
- Future progress in marine mammal zoonotic disease research will require the coordination of multidisciplinary teams addressing the nexus of human, animal and environment. The information presented here will be useful to public health professionals, physicians, veterinarians and wildlife biologists interested in a better understanding of marine mammal zoonoses.

Keywords:

Marine mammals; zoonosis; one health

Correspondence:

Thomas B. Waltzek. Emerging Pathogens Institute, 2055 Mowry Road, PO Box 100009, Gainesville, FL 32611, USA. Tel.: 530 574 2976; Fax: 352 273 9420; E-mail: tbwaltzek@epi.ufl.edu

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Summary

Marine mammals evoke strong public affection as well as considerable scientific interest. However, the resultant close contact with marine wildlife poses human health risks, including traumatic injury and zoonotic disease transmission. The majority of zoonotic marine mammal diseases result in localized skin infections in man that resolve spontaneously or with appropriate medical therapy. However, other marine mammal zoonoses, if left untreated, induce life-threatening systemic diseases that could pose public health risks. As the number of zoonotic diseases rises, the diagnosis of and treatment for these emerging pathogens pose special challenges requiring the expertise of physicians, veterinarians and wildlife biologists. Here, we provide a comprehensive review of the bacterial, viral and fungal marine mammal zoonotic diseases that we hope will be utilized by public health professionals, physicians, veterinarians and wildlife biologists to better understand, diagnose and prevent marine mammal zoonotic diseases.

Introduction

Recent studies have underscored the importance of domesticated and feral animal populations in both the emergence of novel and re-emergence of existing human pathogens (Woolhouse and Gowtage-Sequeria, 2005). This is illustrated by the fact that 75% of known human pathogens are zoonotic, and the incidences of their associated diseases are increasing (Cunningham, 2005). Most recent emerging diseases have been associated with host switches, including severe acute respiratory syndrome coronavirus, H5N1 avian influenza, Hendra virus, Nipah virus and acquired immunodeficiency syndrome (AIDS) (Woolhouse and Gowtage-Sequeria, 2005). The rise in zoonotic diseases is driven by a complex interplay of environmental (global warming, ocean acidification, pollution), ecological (habitat destruction or fragmentation) and epidemiologic (increasing human densities encroaching on decreasing wildlife populations, global movements of plants and animals) factors (Van Bresse et al., 2009; Bossart, 2011). Humans are having a major impact on marine environments, with negative impacts on marine mammal populations (Bejder et al., 2006). As the closest oceanic relatives of humans, marine mammals are sentinel species for both human and ocean health and they are long-lived, top-tier consumers, inhabiting the same inshore ecosystems utilized by man (Jessup et al., 2004; Bossart, 2011). Our knowledge of the diversity of marine mammal pathogens is now expanding rapidly (Nollens et al., 2010; Palacios et al., 2011; Wellehan et al., 2011). Future progress in zoonotic and emerging disease research will require the coordination of multidisciplinary teams addressing the nexus of human, animal and environment that has been referred to as the 'One Health' paradigm.

Marine mammals are beloved by the general public, and numerous recreational industries permit intimate contact with these charismatic megafauna, including whale-watching tours, 'swim-with-the-dolphin/manatee' programs, and oceanaria. Marine mammal researchers, rehabilitators, trainers, veterinarians and volunteers have an increased risk of being injured or acquiring zoonotic diseases through extended occupational exposure (Hunt et al., 2008). Subsistence hunters (e.g. whalers and sealers) are also at occupational risk of disease acquisition through their direct physical contact with infected marine mammals or through the ingestion of marine mammal food products (Boggild, 1969; Bender et al., 1972; Cawthorn, 1997; Tryland, 2000; McLaughlin et al., 2004). Finally, during marine mammal stranding events, human rescuers have acquired zoonotic infections following contact with infected carcasses (Webster et al., 1981).

The most common marine mammal zoonotic diseases are localized infections, although life-threatening systemic

diseases have been reported. A recent study evaluating the risk of illness associated with occupational contact with marine mammals found that more than 10% of the participants reported having contracted localized infections colloquially referred to as 'seal finger' (Hunt et al., 2008). 'Seal finger' is caused by a variety of bacterial and viral species (Table 1). Here, we provide a comprehensive review of the bacterial, viral and fungal marine mammal zoonotic diseases. The review provides a synopsis of each disease, its clinical and pathologic manifestation in marine mammals, followed by a review of transmission of the disease to humans.

Materials and Methods

Literature search strategy

In July 2011, we searched the PubMed database, without any language restriction, using the search terms 'marine mammals' and 'zoonosis' to find reports describing cases of human infection following contact with marine mammals. Additional articles were identified through the reference sections of the studies retrieved.

Results

Bacteria

Bisgaardia

Pathogen summary

Bisgaardia hudsonensis is a newly described Gram-negative rod-shaped facultative anaerobe within the family Pasteurellaceae in the phylum Proteobacteria (Foster et al., 2011). Investigations into the deaths of ringed seals (*Phoca hispida*) in Eastern Hudson Bay of Northern Quebec, Canada, lead to discovery of the bacteria from normal appearing tissues including: lung, retro-mandibular lymph node and tonsil. This bacterium has only recently been reported as a potential human pathogen following seal bite (Sundeeep and Cleeve, 2011).

Clinical signs in marine mammals

The clinical significance of *B. hudsonensis* in seals is currently unknown, although association with the lung tissues may suggest respiratory disease.

Clinical signs in humans

The sole reported case occurred after a fisherman received a bite on the finger from a seal (Sundeeep and Cleeve, 2011). The localized skin infection had nearly healed following a week of antibiotic therapy. A yellow exudate was

noticed on the lesion at day 10, and by day 13, the lesion showed signs of improvement. *Bisgaardia hudsonensis* is considered one cause of 'seal finger' given the single zoonotic transmission event occurred following a seal bite.

Pathology and histology

The gross and histologic lesions induced by *B. hudsonensis* in seals and man are unknown.

Brucella

Pathogen summary

Brucella species are small (<1.5 µm by 0.7 µm), facultative, intracellular, Gram-negative coccobacilli in the family Brucellaceae in the phylum Proteobacteria (Quinn and Markey, 2003). The first report of *Brucella* infecting marine mammals occurred in 1994 (Ewalt et al., 1994; Ross et al., 1994). At least two species of *Brucella* infect a wide variety of aquatic mammals including pinnipeds, cetaceans and the European otter (Nymo et al., 2011): *Brucella pinnipedialis* is associated with pinnipeds, and *B. ceti* is associated with cetaceans (Foster et al., 2007; Nymo et al., 2011). Although these two species are each others closest relatives, recent molecular data suggest they may require further division into additional species (Maquart et al., 2009; Nymo et al., 2011). Although transmission of *Brucella* in marine mammals is poorly understood, growing evidence suggests that cetaceans and pinnipeds may acquire brucellosis horizontally, vertically and through infection of bacterial laden lungworms (Hernandez-Mora et al., 2008; see (Nymo et al., 2011) and references within).

Clinical signs in marine mammals

Despite repeated isolation and high seroprevalence of *Brucella* within certain marine mammal populations, clinical disease is rarely reported and most commonly consists of neurologic (Hernandez-Mora et al., 2008; Gonzalez-Barrientos et al., 2010) and reproductive (e.g. abortions in *Tursiops truncatus*, Miller et al., 1999) signs.

Clinical signs in humans

Marine mammal workers experience an increased risk of contracting brucellosis when working with infected animals (Brew et al., 1999). Transmission to humans may result in influenza-like illness (e.g. fever, headache, lethargy, myalgia, sinusitis) (Brew et al., 1999) chronic disease signs (e.g. arthritis, fatigue) and in rare cases, neurologic disease. A researcher contracted brucellosis

after a laboratory exposure resulting in fatigue, chronic headaches and a severe sinusitis (Brew et al., 1999). Two cases of neurobrucellosis and a case of osteomyelitis, caused by marine mammal *Brucella* isolates, were reported without direct marine mammal contact following the consumption of raw seafood (Sohn et al., 2003; McDonald et al., 2006).

Pathology and histology

Few consistent gross lesions are observed following necropsy of marine mammals afflicted with brucellosis. Microscopic pathology observed primarily within *Brucella* infected cetaceans includes reproductive (endometritis, placentitis, salpingitis, mastitis, orchitis, epididymitis), neurologic (meningitis, encephalitis, meningoencephalitis) as well other (arthritis, peritonitis, vegetative endocarditis, discospondylitis, lymphadenitis, interstitial pneumonia, hepatic and splenic coagulative necrosis, subcutaneous and hepatic abscesses) lesions (Gonzalez-Barrientos et al., 2010; Goertz et al., 2011; Nymo et al., 2011). Microscopic lesions associated with dolphins that are pregnant or have recently aborted include a necrotizing placentitis with Gram-negative coccobacilli and mixed inflammatory cell infiltrates (mononuclear and polymononuclear cells) within the placental trophoblast (Miller et al., 1999; Gonzalez-Barrientos et al., 2010). Dolphins may develop a non-suppurative meningoencephalitis that is most pronounced in the periventricular regions with an associated perivascular infiltration of mononuclear cells (Hernandez-Mora et al., 2008; Gonzalez-Barrientos et al., 2010). Involvement of respiratory tissues has been reported as non-suppurative interstitial pneumonia in striped dolphin (Gonzalez-Barrientos et al., 2010), and *Brucella* may have contributed to the verminous bronchopneumonia reported among two seal species from the German North Sea (Prenger-Berninghoff et al., 2008).

Erysipelothrix

Pathogen summary

Erysipelothrix rhusiopathiae is a small (<0.4 µm by 2.5 µm), non-motile, Gram-positive, facultative anaerobic, pleomorphic bacillus in the family Erysipelotrichaceae in the phylum Firmicutes. It is catalase-negative, oxidase-negative and resistant to high salt concentrations (Quinn, and Markey 2003). This potential pathogen is ubiquitous and can persist for long periods of time in the environment including marine watersheds (Wang et al., 2010). *Erysipelothrix rhusiopathiae* infects a variety of domesticated and wildlife species including swine, sheep, reptiles, chickens, turkeys, ducks, emus, marine mammals and fish

(Wang et al., 2010). Turkeys and pigs are commonly affected with erysipelas resulting in significant economic losses (Wang et al., 2010). Odontocete cetaceans are highly susceptible to *E. rhusiopathiae*, and infections have been reported since the 1950s (Seibold and Neal, 1956; Simpson et al., 1958; Higgins, 2000). *Erysipelothrix rhusiopathiae* is less frequently reported in pinnipeds (Suer and Vedros, 1988), and its clinical significance has been questioned (Sweeney, 1974). Because they are not kept in captivity, less is known about this organism in mysticetes. Marine mammals are believed to acquire the pathogen from their fish prey that may carry the bacterium in their mucous layer without ill effect (Higgins, 2000). The first definitive zoonotic case was described by Chastel et al., (1975), with more recent reports associated with the isolation of the pathogen from the wounds of marine mammal handlers following traumatic encounters (Suer and Vedros, 1988; Hunt et al., 2008).

Clinical signs in marine mammals

Erysipelothrix rhusiopathiae causes erysipeloid in humans, and the analogous disease in animals is known as erysipelas, or 'diamond skin disease'. Marine mammals present with either a life-threatening acute septicaemic disease (Seibold and Neal, 1956; Kinsel et al., 1997) or a self-limiting, subacute dermatological disease (Simpson et al., 1958; Thurman et al., 1983; Bossart and Eimstad, 1988). The course of disease may be very rapid, progressing from an asymptomatic animal to death in less than a day. Marine mammals afflicted with the dermatologic manifestation may appear normal, whereas septic animals often present with depression and lethargy followed rapidly by death (Kinsel et al., 1997).

Clinical signs in humans

Transmission from marine mammals to humans has been associated with direct contact, necropsy or physical injury (e.g. bite wounds) (Chastel et al., 1975; Suer and Vedros, 1988; Hunt et al., 2008). Zoonotic *E. rhusiopathiae* infections in humans typically presents with localized pain, redness, erythema and swelling of lymph nodes (Chastel et al., 1975; Robson et al., 1998). However, a more serious systemic disease characterized by prolonged malaise and a life-threatening toxæmia was reported in one individual following a minor cutaneous insult and exposure to a harbour porpoise carcass (Hunt et al., 2008).

Pathology and histology

In marine mammals, the subacute form of the disease is characterized by dermal infarcts resulting in sloughing of

the epidermis that occasionally results in rhomboid patterns producing the classic 'diamond skin disease' (Simpson et al., 1958; Higgins, 2000; Wang et al., 2010). Gross pathology in the acute form of the disease includes ascites, thoracic effusions, and enlargement of mesenteric and pleural lymph nodes (Kinsel et al., 1997; Dunn et al., 2001). Histologic examination in the acute form of the disease reveals non-specific multifocal necrosis and inflammation of various organs, intracellular and extracellular Gram-positive bacteria, with a mixed inflammatory infiltrate (macrophages, monocytes, neutrophils) (Kinsel et al., 1997; Dunn et al., 2001).

Leptospira

Pathogen summary

Leptospira spp. are long, helically-coiled, motile Gram-negative bacteria in the family Leptospiraceae in the phylum Spirochaetes. They proliferate in aquatic environments and are organized into 20 species with more than 200 recognized serovars (Bharti et al., 2003). *Leptospira* spp. are globally distributed, infecting humans and a wide variety of domestic and wild mammal species, including several pinniped species (Smith et al., 1977; Gulland et al., 1996; Stamper et al., 1998; Colegrove et al., 2005). Periodic large-scale stranding and mortality events of California sea lions attributed to *Leptospira interrogans* var. *pomona* have been reported along the Pacific coast of North America from southern California to British Columbia since 1970 (Gulland et al., 1996; Cameron et al., 2008; Norman et al., 2008; Zuerner et al., 2009). Although the mode of transmission of *Leptospira* among pinnipeds is poorly understood, it likely involves direct spread among individuals via infected urine at rookeries (Cameron et al., 2008; Norman et al., 2008; Zuerner et al., 2009). *Leptospira* has been detected from faecal and urine-contaminated sand in the vicinity of a stranded California sea lion calling into question whether other species (e.g. humans, domestic and wildlife) might contract disease through environmental exposure (Cameron et al., 2008). California sea lions often strand near densely populated coastal communities as well as stagnant sources of freshwater or river outflow, thereby potentially increasing the zoonotic, anthroponotic and domestic/wildlife species spread of *Leptospira* (Cameron et al., 2008; Norman et al., 2008).

Clinical signs in marine mammals

Leptospirosis in pinnipeds is characterized by depression, dehydration, polydipsia, anorexia, fever, vomiting, icterus, abortion and reluctance to use the rear limbs (Vedros

et al., 1971; Smith et al., 1974; Dierauf et al., 1985; Gulland et al., 1996; Dunn et al., 2001).

Clinical signs in humans

To date, few cases of human leptospirosis have been definitively linked to contact with marine mammals (Smith et al., 1978; Hunt et al., 2008). Transmission to humans has been reported following contact with contaminated fluids from infected sea lions and after contact with contaminated tissues during necropsy of California sea lion that succumbed to *Leptospira* (Smith et al., 1978). The three researchers who became infected developed acute renal failure.

Pathology and histology

On necropsy of infected pinnipeds, the kidneys often appear swollen and the liver may be enlarged and friable. The cortex and medulla often appear pale with loss of renicular and corticomedullary differentiation and occasional infarcts (Gulland et al., 1996; Colegrove et al., 2005; Cameron et al., 2008). Subcapsular haemorrhages and haemorrhage at the corticomedullary junction may also be observed. Aborted fetuses and seal pups may present with subcutaneous haemorrhages and hyphema (Smith et al., 1974). Typical microscopic kidney lesions include a lymphoplasmacytic tubulointerstitial nephritis, intratubular protein casts and abundant associated spirochaetes within the tubular epithelium and lumen (Gulland et al., 1996; Colegrove et al., 2005).

Mycobacterium

Pathogen summary

Mycobacterium spp. are aerobic, non-motile bacilli in the family Mycobacteriaceae in the phylum Actinobacteria. They are acid-fast and often found intracellularly. Zoonotic *Mycobacterium* spp. have been reported from marine mammals, including *M. marinum* (Flowers, 1970) and *M. pinnipedii* (Kiers et al., 2008). *Mycobacterium pinnipedii* is a member of the *M. tuberculosis* complex causing significant disease in pinnipeds and occasionally humans and other animals (Kiers et al., 2008; Moser et al., 2008; Kriz et al., 2011). *Mycobacterium bovis*, another member of the *M. tuberculosis* complex, had been reported from pinnipeds prior to recognition of *M. pinnipedii*, but these older reports may have been *M. pinnipedii* (Thompson et al., 1993). *Mycobacterium marinum* and other environmental species are slow-growing and omnipresent in both freshwater and marine habitats, where they are important pathogens of fish and amphibians and occasional patho-

gens of marine mammals (Lewis, 1987; Bowenkamp et al., 2001; Moeller, 2002; Wuenschmann et al., 2008).

Clinical signs in marine mammals

Pinnipeds infected with *M. pinnipedii* often display non-specific clinical signs including: lethargy, anorexia and weight loss (Forshaw and Phelps, 1991; Kiers et al., 2008). Authors have observed that the classic chronic coughing observed in human tuberculosis cases may not be a prominent sign of active disease in infected marine mammals (Forshaw and Phelps, 1991). Cetaceans infected with environmental *Mycobacteria* spp. typically display disseminated cutaneous lesions (Lewis, 1987; Bowenkamp et al., 2001; Moeller, 2002; Wuenschmann et al., 2008).

Clinical signs in humans

Transmission to humans may occur following direct contact with infected marine mammals that are shedding bacteria in aerosols, mucosal secretions, faeces or urine (Quinn and Markey, 2003). Indirect transmission to humans through prolonged exposure to contaminated environments has also been reported (Kiers et al., 2008). The first zoonotic mycobacteriosis report in the scientific literature occurred after a marine mammal trainer was bitten by a managed dolphin. This trainer noticed a painless swelling at the bite site 2.5 months following the altercation, and *M. marinum* was cultured from the lesion (Flowers, 1970). In another report, a group of managed Southern sea lions (*Otaria flavescens*) were diagnosed with *M. pinnipedii* by tuberculin skin test (TST) and subsequent necropsy. Approximately six of 25 animal keepers that were in close contact with the sea lions were positive by TST, five of 25 keepers were positive by interferon-gamma release assay, but no keepers were symptomatic or had detectable lung lesions by radiography (Kiers et al., 2008). A third report involved an Australian seal trainer who developed pulmonary tuberculosis (*M. tuberculosis* complex), including night sweats, fatigue, weight loss and a chronic productive cough, following close contact with seals that had previously been diagnosed with the same agent (Thompson et al., 1993).

Pathology and histology

On necropsy, pinnipeds infected with *M. pinnipedii* typically display granulomas in some or all of the following organs: lungs, kidneys, spleen, liver and lymph nodes (Forshaw and Phelps, 1991; Kiers et al., 2008; Kriz et al., 2011). Environmental species like *Mycobacterium marinum* may generate chronic cutaneous or subcutaneous

(panniculitis) lesions or poorly defined internal lesions in the lungs or lymph nodes (Lewis, 1987; Bowenkamp et al., 2001; Moeller, 2002; Wuenschmann et al., 2008). Microscopic lesions associated with *M. pinnipedii* involve well-defined granulomas, whereas *M. marinum* is often associated with poorly defined granulomatous lesions. Acid-fast bacteria may be observed in some but not all lesions (Lewis, 1987; Bowenkamp et al., 2001; Kiers et al., 2008; Wuenschmann et al., 2008).

Mycoplasma

Pathogen summary

Mycoplasmas, in the family Mycoplasmataceae, phylum Tenericutes, are the smallest self-replicating prokaryotes and lack a cell wall. They are generally host-specific pathogens found on mucosal surfaces (Quinn and Markey, 2003). *Mycoplasma* spp. have been associated with viral-induced (e.g. influenza viruses or morbilliviruses) marine mammal mass mortality events (Madoff et al., 1982; Giebel et al., 1991; Ruhnke and Madoff, 1992). In pinnipeds, five species are known: *M. phocidae*, *M. phocirhinis*, *M. phocicerebrale*, *M. zalophi* and *M. haemozalophi* (Madoff et al., 1982; Kirchoff et al., 1989; Giebel et al., 1991; Haulena et al., 2006; Volokhov et al., 2011). *Mycoplasma phocidae* was cultured from the respiratory tract and heart of harbour seals during a respiratory epizootic along the New England seaboard from 1979 to 1980 (Madoff et al., 1982). *Mycoplasma phocicerebrale* and *M. phocirhinis* were cultured from seals during a mass mortality event that occurred in the Baltic and North Sea (Kirchoff et al., 1989; Giebel et al., 1991). *Mycoplasma zalophi* was repeatedly isolated from California sea lions (*Zalophus californianus*) undergoing rehabilitation from 1999 to 2001 (Haulena et al., 2006). A recent study isolated *M. phocicerebrale* and at least two novel *Mycoplasma* spp. from cetacean carcasses that washed up off the coast of Scotland over a 12-year period (Foster et al., 2011). *Mycoplasma haemozalophi* was detected by PCR in 12.4% of blood samples from California sea lions (Volokhov et al., 2011).

Clinical signs in marine mammals

In marine mammals, *Mycoplasma* spp. are often associated with respiratory disease signs (Giebel et al., 1991; Ruhnke and Madoff, 1992) and have been associated with significant stranding or mortality events (Giebel et al., 1991; Ruhnke and Madoff, 1992; Foster et al., 2011). *Mycoplasma zalophi* is associated with pneumonia and polyarthritis in California sea lions in rehabilitation (Haulena et al., 2006).

Clinical signs in humans

The disease known as 'seal finger', often associated with *Mycoplasma* spp. in pinniped hosts, is common among individuals with occupational exposure to seals (e.g. sealers and marine mammal trainers) and is usually limited to localized cutaneous infections (see (Hunt et al., 2008) and references within). Transmission occurs principally through physical trauma (e.g. seal bite), or when compromised skin surfaces come in contact with infected marine mammal tissues. Zoonotic *Mycoplasma* spp. infections in humans typically present with localized pain, redness and erythema (Stadtlander and Madoff, 1994; Baker et al., 1998). A typical case was reported by Baker and colleagues (Baker et al., 1998); a trainer at the New England Aquarium received a seal bite that became painful, swollen and erythematous after 6 days. *Mycoplasma phocicerebrale* was cultured from the wound and the mouth of the seal. The trainer fully recovered with tetracycline antibiotic therapy, and the seal never displayed signs throughout the episode.

Pathology and histology

Few gross lesions are associated with *Mycoplasma* infections in marine mammals. Histopathologic findings typically include a pleuritis, interstitial pneumonia or bronchopneumonia, lymphadenitis, subdermal abscessation and septic polyarthritis (Haulena et al., 2006; Foster et al., 2011).

Viruses

Calicivirus

Pathogen summary

San Miguel Sea lion virus (SMSV) is a small positive-sense single-stranded RNA virus in the genus Vesivirus. The virus was first isolated from California Sea Lions (*Z. californianus*) in 1972 (Smith et al., 1973), although it has since been isolated from cetaceans (Smith and Boyt, 1990). This virus is indistinguishable from the vesicular exanthema of swine virus (VESV) (Smith et al., 1973), a reportable foreign animal disease that was declared to be eradicated from the United States in 1956. SMSV displays an extremely wide host range, infecting fish, amphibians, reptiles and mammals (Smith et al., 1980). Of significant concern is the precedent of feline calicivirus, a closely related member of the genus Vesivirus, known to mutate and cause epizootics of a haemorrhagic fever with 33–50% mortality in cats (Ossiboff et al., 2007). This has happened independently in high-density colonies multiple

times; virulent haemorrhagic strains from geographically diverse sites do not form a clade (Ossiboff et al., 2007). SMSV mutates rapidly and acts as a quasispecies (Wellehan et al., 2010).

Clinical signs in marine mammals

In marine mammals, the disease is most often characterized by anorexia followed by the formation of vesicles in the mucocutaneous junctions and on the ventral surface of flippers (Van Bonn et al., 2000). The virus has been associated with clinical diarrhoea. SMSV is easily isolated from vesicles and has also been isolated from females California sea lions that have recently aborted as well as the aborted sea lion fetuses (Smith and Boyt, 1990). In marine mammals, the clinical manifestation lasts between 4 and 20 days (Van Bonn et al., 2000).

Clinical signs in humans

Marine caliciviruses can survive for 15 days in the marine environment (Smith et al., 1981). Caliciviruses can be transmitted by direct contact or indirectly by consumption of contaminated prey (Smith et al., 1998). In one report, a researcher was accidentally exposed to SMSV serotype 5 in the laboratory and developed an influenza-like illness that lasted for 2 days followed by the blistering of both hands and feet. Healing commenced following 1 week and the patient was fully recovered after 2 weeks (Smith et al., 1998). In a study looking at prevalence of antibodies to pooled SMSV types in 765 human blood donors in the northwestern USA, 12% of healthy blood donors were seropositive, whereas 21% of those rejected solely because of an elevation in the hepatocellular marker enzyme alanine transferase were seropositive, a significant difference ($P < 0.001$) (Smith et al., 2006). Further, 29% of patients with hepatitis of unknown cause and 47% of patients with hepatitis associated with blood transfusion or dialysis were seropositive, and 11 of 112 sera tested PCR positive (Smith et al., 2006).

Pathology and histology

Microscopically, vesicular lesions generally consist of spongiosis of the stratum spinosum, which progresses to subcorneal vesicle formation (Moeller, 2002).

Influenza viruses

Pathogen summary

Influenza viruses are negative sense single-stranded RNA viruses that constitute three of the genera (A,B,C) in the

family Orthomyxoviridae. Influenza A viruses are widely distributed among animal populations including humans. Since the late 1970s, influenza A and B viruses have been detected by viral isolation, serologic methods and RT-PCR in wild populations of cetaceans and pinnipeds (Osterhaus et al., 2000; Ohishi et al., 2003; Blanc et al., 2009). Mass strandings attributable to influenza A virus have been reported in both pinnipeds and cetaceans along the New England coast, resulting in population losses up to 20% (Geraci et al., 1982; Hinshaw et al., 1984). Post-mortem examination of infected harbour seal carcasses and contact with symptomatic animals resulted in zoonotic transmission (Webster et al., 1981).

Clinical signs in marine mammals

Influenza A and B virus infections induce upper and lower respiratory disease signs in marine mammals. Disease signs in moribund harbour seals during an influenza A epizootic along the coast of Massachusetts included respiratory distress, lethargy, swelling of the neck and conjunctiva, incoordination and frothy white or bloody nasal discharge (Geraci et al., 1982). Influenza A virus was associated with extreme emaciation and sloughing skin in two 1984 mass strandings of long-finned pilot whales along the coast of Cape Cod, USA (Hinshaw et al., 1986). Influenza B virus was associated with stranded harbour seals in respiratory distress along the Dutch coast in 1999 (Osterhaus et al., 2000).

Clinical signs in humans

Four people developed conjunctivitis after post-mortem examination of H7N7-infected seals from an outbreak in New England (Webster et al., 1981). Experimental transmission studies with the influenza A virus isolate produced a lethal systemic disease in squirrel monkeys (Murphy and Jarrell, 1983). An investigator developed a severe conjunctivitis after an experimentally infected seal subject sneezed directly into his face (Webster et al., 1981). The experimental H7N7 influenza A strain was isolated from the investigator's conjunctiva, and the inflammation subsided by the fourth day.

Pathology and histology

Gross observations of influenza A virus disease in cetaceans are limited but may include enlargement of the hilar lymph node, haemorrhagic lungs and a small friable liver (Hinshaw et al., 1986). Necropsy of the aforementioned New England harbour seals revealed a pneumonia characterized by inflammation and haemorrhage in the upper and lower respiratory tracts (Geraci et al., 1982).

Histopathologic examination of the lungs of seals in that succumbed to influenza A virus revealed necrotizing bronchopneumonia with extensive degeneration, necrosis and desquamation of the bronchial epithelium (Hinshaw et al., 1984).

Poxvirus

Pathogen summary

The family Poxviridae comprises large double-stranded DNA viruses that are grouped into two subfamilies: Chordopoxvirinae and Entomopoxvirinae. The chordopoxviruses, using vertebrate hosts, are currently divided into eight genera (Moss, 2001), although the number of genera is likely to expand. Most poxviruses of pinnipeds have been tentatively classified in the genus Parapoxvirus, although a Steller sea lion pox is clearly distinct and does not cluster in a recognized genus (Bracht et al., 2006; Nollens et al., 2006a). The cetacean poxviruses may also represent a new genus, and one analysis of limited sequence found them to be the sister group to the orthopoxviruses (Bracht et al., 2006). Cetacean and pinniped poxviruses induce cutaneous lesions in their hosts, but only the pinniped parapoxviruses are currently known to be zoonotic (Hicks and Worthy, 1987; Clark et al., 2005).

Clinical signs in marine mammals

Pinniped parapoxviruses typically induce the formation of nodular or villonodular lesions in the skin around the head and neck, mucocutaneous junctions of the conjunctiva and oral mucosal, and the tongue. However, lesions may appear anywhere and in severe cases become quite expansive (Wilson and Poglayen-Neuwall, 1971; Moeller, 2002). Lesions often ulcerate within a couple of weeks and resolve within a month (Hicks and Worthy, 1987). Young or debilitated animals may suffer and/or succumb to the disease (Sweeney and Ridgway, 1975; Geraci et al., 1979; Van Bressemer et al., 1993, 2009; Nollens et al., 2006b). Known cetacean poxviruses cause circular discoloured lesions called 'tattoos' that generally do not have significant health impacts.

Clinical signs in humans

Sealpox has been transmitted to humans after contact (Hicks and Worthy, 1987) or following physical trauma (Clark et al., 2005). The aforementioned zoonotic sealpox cases involved 3 marine mammal technicians with increased exposure to symptomatic grey seals. In each case, a single papule, 'milker's nodule', was noticed on the hand of each individual resembling the lesions

induced by other zoonotic parapoxviruses (e.g. Orf virus, bovine papular stomatitis virus and pseudocowpox virus). The solitary cutaneous lesions were uncomplicated and resolved without treatment over several months (Hicks and Worthy, 1987; Clark et al., 2005; Hunt et al., 2008).

Pathology and histology

Microscopically, skin lesions in seals and sea lions are characterized by a ballooning degeneration of the stratum spinosum with pustule formation. The epidermal hyperplasia is characterized by orthokeratotic and parakeratotic hyperkeratosis and acantholysis (Clark et al., 2005; Nollens et al., 2006b). The greatly enlarged cells usually contain large, eosinophilic intracytoplasmic inclusions (Moeller, 2002; Clark et al., 2005; Nollens et al., 2006b).

Fungi

Ajellomyces

Pathogen summary

Blastomycosis is caused by a saprophytic dimorphic fungi, *Ajellomyces (Blastomyces) dermatitidis*, in the family Ajellomycetaceae in the phylum Ascomycota. It is endemic to the Eastern United States and Canada. Humans and animals are usually infected via inhalation (Migaki and Jones, 1983). Infected animals often develop a primary lesion in the lungs, with subsequent spread to various organs including the skin (Higgins, 2000; Quinn and Markey, 2003). In marine mammals, blastomycosis has been reported in captive bottlenose dolphins (Sweeney et al., 1976; Cates et al., 1986), Steller sea lions and California sea lions (Zwick et al., 2000).

Clinical signs in marine mammals

In marine mammals, the clinical manifestation is variable depending upon the severity of the lesion and affected organs (Migaki and Jones, 1983). Severe systemic blastomycosis results in depression, weakness, anorexia and death.

Clinical signs in humans

In the single human zoonotic transmission report, a veterinarian treating a bottlenose dolphin developed a chronic localized cellulitis and lymphadenitis that resolved without treatment (Cates et al., 1986). However, *A. dermatitidis* is generally only present as a yeast in warm-blooded animal tissues, and yeast forms are considered non-infectious, with conidial forms involved in transmission seen at cooler

temperatures. Because of this, animal to animal transmission is rare, and potential common environmental sources of infection should be investigated when outbreaks are seen (Bradsher et al., 2003).

Pathology and histology

Systemic blastomycosis in marine mammals results in pyogranulomatous inflammation in the lungs, lymph nodes, spleen, liver, thyroid and kidneys (Williamson et al., 1959). Histologically, *A. dermatitidis* is observed either free or phagocytosed in macrophages as a large round yeast cell, with a diameter of 8–25 μm , and a thick ‘doubly contoured’ cell wall (Migaki and Jones, 1983).

Lacazia

Pathogen summary

Lobomycosis is a chronic mycotic disease of the skin caused by *Lacazia (Loboa) loboi*, an obligate pathogen. It is not assigned to a family, but is in the order *Onygenales* in the phylum Ascomycota. The disease affects bottlenose (*Tursiops truncatus*) and Guyana (*Sotalia guianensis*) dolphins as well as humans living in the Americas (Van Bresse et al., 2009). Diagnosis of lobomycosis depends on identification of characteristic yeast-like organisms (5–10 μm) in tissues or exudates (Hay, 2003). The impact of lobomycosis on cetacean populations is unknown but may be responsible for the deterioration in health of chronically infected individuals (Van Bresse et al., 2009).

Clinical signs in marine mammals

In marine mammals, lesions are restricted to the skin and appear whitish to pink with a nodular or cobblestone appearance (Migaki and Jones, 1983; Moeller, 2002). Typically, lobomycosis does not induce significant pathology in dolphins or humans although cutaneous lesions may persist for years.

Clinical signs in humans

Transmission occurs by direct contact with infected animals following abrasion or traumatization of the skin (Migaki and Jones, 1983; Symmers, 1983). A cutaneous granuloma on the hand of an aquarium attendant and an associated supratrochlear lymphadenitis was observed 3 months following an occupational exposure with a bottlenose dolphin infected with *L. loboi*. Biopsies from the infected dolphin and the aquarium attendant’s skin

and lymph node were histologically indistinguishable (Symmers, 1983).

Pathology and histology

Grossly, multiple whitish to pink, nodular or cobblestone, cutaneous lesions are observed in dolphins suffering from lobomycosis (Migaki and Jones, 1983; Moeller, 2002). Histologic lesions have been described as a granulomatous dermatitis involving the papillary dermis. The granulomas are composed of macrophages and multinucleate giant cells that have phagocytosed the fungal agents. The epidermis over affected areas display acanthosis with downward growth of the rete pegs (Migaki and Jones, 1983; Moeller, 2002).

Discussion and Conclusion

The focus of this review was to summarize what is known about marine mammal zoonoses including bacterial, viral and fungal pathogens. Cases of marine mammal zoonoses involve individuals with increased marine mammal contact whether in a research, management or medical setting (Hunt et al., 2008). We found no zoonotic human case reports that involve a member of the general public. This suggests that recreational activities with limited exposure to marine mammals are relatively safe pursuits from an infectious disease standpoint. By excluding anecdotal information or case reports without confirmatory diagnostics, we have likely omitted a subset of lesser known emerging marine mammal zoonoses that future studies may elucidate. However, progress in the diagnosis and characterization of marine mammal zoonotic diseases may be impeded, as a recent survey exploring health risks for marine mammal workers found that infected workers repeatedly reported their physicians were inadequately informed about marine mammal zoonotic diseases (Hunt et al., 2008).

It is probable that the number of known zoonoses from marine mammals will expand. *Streptococcus iniae*, named after a genus of river dolphins from which it was first isolated, can cause disease in humans (Agnew and Barnes, 2007). Methicillin-resistant *Staphylococcus aureus* has recently been identified in marine mammals (O’Mahony et al., 2005; Faires et al., 2009). Recombinants of human and sea lion astroviruses have been identified, implying that marine mammals play a role in human astrovirus ecology (Rivera et al., 2010). Noroviruses, rotaviruses, and sapoviruses have been sequenced from the faeces of sea lions and do not cluster phylogenetically separate from human viruses in these genera (Li et al., 2011).

The risk of acquiring food-borne illnesses following the consumption of uncooked marine mammal meat is

poorly understood but has been reported in native peoples of Arctic and Australasia regions (Hunt et al., 2008). The consumption of raw or undercooked pinniped or cetacean meat has resulted in bacterial (e.g. salmonellosis and botulism) and parasitic (trichinellosis and toxoplasmosis) diseases in man (Bender et al., 1972; Cawthorn, 1997; Tryland, 2000; McLaughlin et al., 2004; Bejder et al., 2006). Southern and Northern sea otters are recognized as sentinels for both ocean health as 'keystone species' in nearshore habitats as well as sentinels of human health, because they accumulate important zoonotic protozoa (e.g. *Toxoplasma gondii* and *Sarcocystis neurona*) from the consumption of infected shellfish (Jessup et al., 2004; Bossart, 2011; Gibson et al., 2011). A recent study found that a variety of Pacific Northwest marine mammal species were coinfecting with *T. gondii* and *S. neurona* indicating pervasive zoonotic parasite flow from terrestrial species (e.g. *T. gondii* oocysts from domestic cats) into

coastal waterways (Gibson et al., 2011). Thus, these parasites contaminate important waterways and bioaccumulate in shellfish that may later infect marine mammals or humans consuming uncooked seafood. The reported high rates of infected marine mammals illustrate a potential public health issue given that coastal watersheds are major sources of food and water for humans (Jessup et al., 2004; Bossart, 2011; Gibson et al., 2011).

Given the popularity of oceanaria and continued marine mammal research and rehabilitation, future zoonotic diseases cases involving bacterial, viral and fungal pathogens are inevitable. Future progress in marine mammal zoonotic disease research will require the coordination of multidisciplinary teams addressing the nexus of human, animal and environment. It is our sincere hope that the information provided within the present review will be utilized by public health professionals, physicians, veterinarians and wildlife biologist to better

Table 1. List of zoonotic marine mammal diseases

Genus species	Disease	Clinical diseases in marine mammals	Clinical diseases in humans ^a	References
Bacteria				
<i>Bisgaardia hudsonensis</i>	Seal finger	Unknown	Dermatitis	Sundeeep and Cleeve (2011)
<i>Brucella pinnipedialis</i> and <i>B. ceti</i>	Brucellosis	Reproductive disorders, neurological disorders, and osteomyelitis	Headache, lethargy, and severe sinusitis	Brew et al. (1999), Kiers et al. (2008)
<i>Erysipelothrix rhusiopathiae</i>	Erysipeloid (humans), erysipelas (marine mammals)	Sepsis (peracute), rhomboid skin lesions (chronic)	Localized dermatitis and sepsis in severe cases	Chastel et al. (1975)
<i>Leptospira interrogans</i> (serovars pomona, gryppotyphosa)	Leptospirosis	Renal failure	Renal failure	Smith et al. (1978)
<i>Mycobacterium marinum</i> and <i>M. pinnipedii</i>	Mycobacteriosis	Failure to thrive (e.g. lethargy, anorexia, and weight loss), granulomatous dermatitis (<i>marinum</i>), granulomatous lesions in lungs and other organs (<i>pinnipedii</i>)	Failure to thrive (e.g. lethargy, anorexia, and weight loss), granulomatous dermatitis (<i>marinum</i>), tuberculosis (<i>pinnipedii</i>)	Flowers (1970), Kiers et al. (2008)
<i>Mycoplasma phocacerebrale</i> , <i>M. phocarhinis</i> , <i>M. phocidae</i>	Mycoplasmosis (seal finger)	Pneumonia and polyarthrits	Localized dermatitis	Baker et al. (1998)
Virus				
Calicivirus (San Miguel sea lion virus)	Seal finger	Vesicular dermatitis	Vesicular dermatitis and influenza-like illness	Smith et al. (1998)
Influenza virus subtypes A	Influenza	Pneumonia	Conjunctivitis	Webster et al. (1981)
Parapoxvirus	Seal finger	Dermatitis	Single papule, Milker's nodule	Clark et al. (2005)
Fungus				
<i>Ajellomyces dermatitidis</i>	Blastomycosis	Granulomatous lesions in lungs and other organs	Lymphadenitis and cellulitis	Cates et al. (1986)
<i>Lacazia loboi</i>	Lobomycosis	Granulomatous dermatitis	Granulomatous dermatitis	Symmers (1983)

^aThe clinical disease signs in humans are those that have appeared in the literature associated with zoonotic disease transmission from marine mammals.

understand, diagnose and prevent marine mammal zoonoses.

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