Veterinary Pathology Online
http://vet.sagepub.com/

Marine Mammals as Sentinel Species for Oceans and Human Health

Vet Pathol 2011 48: 676 originally published online 15 December 2010
DOI: 10.1177/0300985810388525

The online version of this article can be found at:
http://vet.sagepub.com/content/48/3/676

Published by:
SAGE
http://www.sagepublications.com

On behalf of:
American College of Veterinary Pathologists, European College of Veterinary Pathologists, & the Japanese College of Veterinary Pathologists.

Additional services and information for *Veterinary Pathology Online* can be found at:

Email Alerts: http://vet.sagepub.com/cgi/alerts

Subscriptions: http://vet.sagepub.com/subscriptions

Reprints: http://www.sagepub.com/journalsReprints.nav

Permissions: http://www.sagepub.com/journalsPermissions.nav

Downloaded from vet.sagepub.com at FLORIDA ATLANTIC UNIV on May 17, 2011

Veterinary Pathology
48(3) 676-690
© The American College of
Veterinary Pathologists 2011
Reprints and permission:
sagepub.com/journalsPermissions.nav
DOI: 10.1177/0300985810388525
http://vet.sagepub.com

Marine Mammals as Sentinel Species for Oceans and Human Health

G. D. Bossart[1]

Abstract

The long-term consequences of climate change and potential environmental degradation are likely to include aspects of disease emergence in marine plants and animals. In turn, these emerging diseases may have epizootic potential, zoonotic implications, and a complex pathogenesis involving other cofactors such as anthropogenic contaminant burden, genetics, and immunologic dysfunction. The concept of marine sentinel organisms provides one approach to evaluating aquatic ecosystem health. Such sentinels are barometers for current or potential negative impacts on individual- and population-level animal health. In turn, using marine sentinels permits better characterization and management of impacts that ultimately affect animal and human health associated with the oceans. Marine mammals are prime sentinel species because many species have long life spans, are long-term coastal residents, feed at a high trophic level, and have unique fat stores that can serve as depots for anthropogenic toxins. Marine mammals may be exposed to environmental stressors such as chemical pollutants, harmful algal biotoxins, and emerging or resurging pathogens. Since many marine mammal species share the coastal environment with humans and consume the same food, they also may serve as effective sentinels for public health problems. Finally, marine mammals are charismatic megafauna that typically stimulate an exaggerated human behavioral response and are thus more likely to be observed.

Keywords

marine mammals, sentinel species, ecosystem health, human health

As the effects of climate change and potential environmental degradation are debated and better characterized, worldwide concern is being raised about the health of the earth's aquatic ecosystems.[40,148,206,212] The long-term consequences of environmental change on aquatic ecosystems are not well characterized but are likely to include aspects of disease emergence in aquatic plants and animals.[206] In turn, these emerging diseases may have epizootic potential, zoonotic implications, and a complex pathogenesis involving other cofactors such as anthropogenic contaminant burden, genetics, and immunologic dysfunction.[30,181] Emerging diseases have themselves become new drivers of environmental change since they can cause extinction of endangered species; alter the ratios of predators, prey, competitors, and recyclers necessary for healthy, well-functioning ecosystems; and alter habitat already threatened by the emergence of discontinuities (ie, habitat fragmentation) and climate change.[62]

Ocean health is inextricably linked to human health on a global scale as well. Connections between the health of humans, animals, and the environments in which they live are well recognized and recently have been referred to as "one health, one medicine." The "one health, one medicine" worldwide strategy for expanding interdisciplinary collaborations and communications in all aspects of health begins to address these critical relationships.

The concept of marine sentinel organisms provides one approach to evaluating aquatic ecosystem health. Such sentinels are used to gain early warnings about current or potential negative impacts on individual- and population-level animal health.[29] In turn, such warnings permit better characterization and management of these impacts that ultimately affect human and animal health associated with the oceans. Marine mammals are described as prime sentinels because many species have long life spans, are long-term coastal residents, feed at a high trophic level, and have large blubber stores that can serve as depots for anthropogenic chemicals and toxins.[7,15,29,30,110,111,154,155,184,234] Finally, marine mammals are charismatic megafauna that typically stimulate an exaggerated human behavioral response and are thus more likely to be observed.[21] Therefore, health concerns that affect these species

[1] Georgia Aquarium, Atlanta, Georgia, and Division of Comparative Pathology, Department of Pathology, School of Medicine, University of Miami, Miami, Florida

Corresponding Author:
Gregory D. Bossart, VMD, PhD, Georgia Aquarium, 225 Baker St. N.W., Atlanta, GA 30313
Email: gbossart@georgiaaquarium.org

Downloaded from vet.sagepub.com at FLORIDA ATLANTIC UNIV on May 17, 2011

may make humans more likely to pay attention to ocean health issues.

Emerging Infectious and Neoplastic Disease in Marine Mammals

Emerging and reemerging viral, bacterial, protozoal, and fungal diseases have been described in marine mammals. Additionally, complex diseases involving emerging infectious and neoplastic components have been reported, and these diseases may provide important information on aquatic ecosystem and public health.

Morbillivirus Infection

Morbillivirus infections are responsible for recent widespread epizootics and mortality in cetaceans.[129,130,131,177,225,226] A cetacean morbillivirus caused a massive epizootic that resulted in the death of an estimated 2,500 dolphins or approximately 50% of the inshore population of Atlantic bottlenose dolphins (*Tursiops truncatus*) in 1987–1988.[129] This large-scale epizootic was followed by further die-offs of bottlenose dolphins in the Gulf of Mexico in 1993 and 1994. Morbillivirus antigen and characteristic lesions were detected in tissues from both epizootics, and morbillivirus RNA was demonstrated by reverse transcription polymerase chain reaction (PCR) testing.[129,130,120,204]

A second major morbillivirus epizootic killed several thousand striped dolphins (*Stenella coeruleoalba*) along the Spanish Mediterranean coast from 1990 to 1992, and more recently an epizootic occurred in 2007.[57-59,177] Historically, 2 strains of cetacean morbillivirus have been reported to infect odontocete cetacean populations worldwide: dolphin morbillivirus (DMV) and porpoise morbillivirus (PMV).[57,58,223] DMV and PMV appear to be closely related strains of a cetacean morbillivirus and are distinct from phocine distemper virus and canine distemper virus and more closely related to the ruminant morbilliviruses and measles virus.[14,10,232] Additionally, a novel morbillivirus was identified in a long-finned pilot whale (*Globicephala melas*) that died off the coast of New Jersey and may represent a third member of the cetacean morbillivirus group.[217] A central role for infection in pilot whales (*Globicephala* sp.) has been suggested on the basis of high seroprevalence in samples obtained during multiple stranding events for both *G. melas* and *G. macrorhynchus* dating back to 1982.[61] The high rates of seroprevalence and gregarious nature of the species led to the hypothesis that pilot whales may serve as reservoirs for cetacean morbilliviruses and transmit the agent to other cetaceans; however, the nature of enzootic infection in *Globicephala*, if it occurs, remains unresolved.[61]

In general, DMV infection is not considered an endemic infection, and it is speculated that a decline in herd immunity and an increase in population density will render dolphin populations susceptible to new epizootics.[33] However, evidence for chronic infection consisting of nonsuppurative encephalitis characterized by DMV antigen in the brain in the absence of other systemic involvement has been reported in striped dolphins.[59] Similarly, DMV titers and antigen persistence in the brain, in the absence of typical morbillivirus lesions or systemic involvement, have both been observed in Indo-Pacific bottlenose dolphins (*Tursiops aduncus*), further illustrating the complexity of this infection (G. D. Bossart, unpublished data). Furthermore, in an ongoing comprehensive Atlantic bottlenose dolphin health assessment program in the Indian River Lagoon (IRL), Florida, positive fluctuating morbillivirus titers and seroconversion were recently reported in this dolphin population that has strong site fidelity.[33] Seropositivity was detected in IRL dolphins less than 6 years of age as well as in dolphins that were alive during the 1987–1988 epizootic. During the study period, pathologic and immunohistochemical findings from stranded IRL dolphins did not demonstrate typical morbillivirus-associated lesions or the presence of morbillivirus antigen. The findings suggest that recurring endemic morbillivirus transmission and subclinical infections are occurring in the absence of widespread mortality in IRL dolphins. In cases of widespread cetacean morbilliviral disease, disease surveillance becomes an important component of population health and epidemiology and may provide information on population susceptibility to epizootics that can significantly impact ecosystem health and stability.

Brucellosis

Brucellosis is a zoonotic disease of terrestrial and marine mammals. *Brucella* spp. were first isolated in 1994 from tissues collected at necropsy from stranded harbor seals (*Phoca vitulina*), harbor porpoise (*Phocoena phocoena*), and common dolphins (*Delphinus delphis*) from Scotland and from an aborted fetus of a bottlenose dolphin in the United States.[63,194,195] The isolation of *Brucella* has since been described from a wide variety of marine mammals including Atlantic white-sided dolphin (*Lagenorhynchus acutus*), striped dolphin, hooded seal (*Cystophora cristata*), gray seal (*Halichoerus grypus*), Pacific harbor seal (*Phoca vitulina richardsi*), minke whale, and white beaked dolphin (*Lagenorhynchus albirostris*).[42,75,76,78,105,176] Furthermore, strong serological evidence exists to suggest that marine mammal *Brucella* infections are globally widespread among marine mammal species and have a high prevalence.[46,107,161-163,169,191,195,214,221,224] Marine mammal *Brucella* strains are distinct from the terrestrial *Brucella* species, and recently 2 new species, *B. pinnipedialis* and *B. ceti*, were described.[77] New molecular data confirm that there are significant subtypes within the newly described marine mammal *Brucella* species, which add to a body of evidence that could lead to the recognition of additional species or subspecies within this group.[47,136]

Compared with the reported high global seroprevalence of marine mammal *Brucella* spp. infection, clinical disease does not appear to be common. In one study, minke whales (*Balaenoptera acutorostrata*) and Bryde's whales (*Balaenoptera edeni*) in the western North Pacific were reported to have chronic purulent or granulomatous orchitis associated with positive *Brucella* antibody titers.[169] Two cases of *Brucella* placentitis and abortion

Downloaded from vet.sagepub.com at FLORIDA ATLANTIC UNIV on May 17, 2011

have been reported in captive Atlantic bottlenose dolphins.[149] Neurobrucellosis recently was reported in striped dolphins and was characterized by lymphoplasmacytic and histiocytic nonsuppurative meningoencephalitis.[84,95] Dolphins with neurobrucellosis typically are PCR, serologically, and immunohistochemically positive to *Brucella* spp and *Brucella ceti* and may be isolated from cerebrospinal fluid. In dolphins, *B. ceti* has tropism for placental and fetal tissues. Vertical transmission and the possibility of horizontal transmission to newborns have been postulated.[95] Thus, bacteria may be shed as in *Brucella*-infected domestic livestock. Moreover, the localization of the bacteria in particular organs suggests the possibility of transmission through sexual intercourse and may ensure the prevalence of both clinical and latent infections.[95] It appears that striped dolphins constitute a highly susceptible host and a potential reservoir for *B. ceti* transmission.[84,95,158] Marine mammal *Brucella* strains are capable of infecting humans and livestock and thus represent an important zoonotic consideration despite the observation that human clinical disease does not appear to be common.[174,207,235] Notably, in one review, none of the 3 human patients infected with marine mammal brucellosis had direct contact with marine mammals, although all had consumed raw seafood.[235] These findings suggest that more extensive studies of the presence and distribution of marine mammal *Brucella* genotypes are needed before the zoonotic significance can be evaluated. Additionally, global surveillance is required to fully understand the distribution, ecology, and genetic relatedness of *Brucella* isolates from marine mammals that become valuable sentinels for evaluating the aquatic health impacts of this infectious agent.

Leptospirosis

Leptospirosis is a zoonotic disease infecting a broad range of mammalian hosts and is reemerging globally.[12] California sea lions (*Zalophus californianus*) have experienced recurrent outbreaks of leptospirosis since 1970, and the infection is thought to be enzootic.[1,142,228] Leptospirosis, primarily caused by *L. interrogans* serovar Pomona, is known to cause abortions and renal disease in California sea lions with clinicopathologic features similar to domestic animals.[56,87] Histologically, a lymphoplasmacytic interstitial nephritis with tubular necrosis is present with the spirochete identified in the renal tubular epithelium and free in the lumina. In newborns and aborted fetuses, the disease is characterized by subcutaneous hemorrhage and hyphema.[142,228]

Recent research to elucidate the epidemiology of leptospirosis in California sea lions demonstrated that the disease is enzootic but also occurs in outbreaks of acute disease every 4–5 years.[133] The latter findings call into question the apparent contradiction between maintenance hosts of leptospirosis, which experience chronic but largely asymptomatic infections, and accidental hosts, which suffer acute illness or death as a result of disease spillover from reservoir species. Furthermore, environmental risk factors for sea lion leptospirosis may include exposure to dogs and dog parks or factors associated with them.[167] The sea lion/leptospirosis system raises questions regarding the accepted view of the epidemiology of this important zoonosis, especially since leptospirosis has resurged in humans and domestic dogs in California.[4,144]

Protozoal Infection

Protozoal infection is a major cause of mortality among southern sea otters (*Enhydra lutris nereis*). Infections with protozoal pathogens *Toxoplasma gondii* and *Sarcocystis neurona* were the cause of death in approximately 25% of the freshly dead sea otters examined from 1998 to 2001.[121,122] Introduced and invasive terrestrial mammals including domestic cats and opossums are the respective definitive hosts for these protozoa. Oocysts from cat feces wash into seawater, where they can survive for at least 24 months and serve as a source of infection via transport hosts.[128] A seroprevalence analysis showed *T. gondii* infection in 52% of beached sea otters and 38% in live sea otters sampled along the California coast, with a clear association between proximity of freshwater inputs into the ocean and infection.[147] Southern sea otters consume a wide variety of benthic marine invertebrates; their daily food consumption is equivalent to 25–35% of their body weight.[111] In the laboratory, filter feeding sea otter prey species such as blue mussels (*Mytilis* spp.) accumulate *T. gondii* oocysts that remain infective for weeks.[8] As nearshore predators, otters serve as sentinels of protozoal pathogen flow into the marine environment since they share the same environment and consume some of the same foods as humans such as mussels, clams, and crabs.[111,146] Eating improperly prepared seafood containing oocysts may result in human toxoplasmosis, which is a potentially fatal infection in immunocompromised patients and a well-documented cause of serious fetal malformations.[37,60] Investigation into the processes promoting protozoal infections in sea otters provides a better understanding of terrestrial parasite flow and the emergence of disease at the interface between wildlife, domestic animals, and humans.[44,68,146]

Mycotic Disease

The emergence of lobomycosis was recently reported in dolphins along Florida's Atlantic coast and in North Carolina.[26,29,189,198] Lobomycosis is a rare chronic mycotic disease of the skin and subcutaneous tissues caused by a yeast-like organism known as *Lacazia loboi*.[17] Dolphins and humans are the only species known to be naturally susceptible to infection with *Lacazia loboi*. The clinicopathologic manifestations of lobomycosis in humans and dolphins are similar and consist of focal to locally extensive verrucoid to nodular lesions that typically progress slowly over the course of years without involvement of internal organs. The tissue response consists of multifocal dermal granulomas. Within granulomas, *Lacazia* can be demonstrated as yeast-like organisms, 6–12 μm in diameter with thick, refractile walls, arranged singly or in chains connected by tube-like bridges.[17,189] The organism has not been cultured to date in vitro; therefore, diagnosis depends on identification of the characteristic yeast-like cells in tissue or exudates.

Downloaded from vet.sagepub.com at FLORIDA ATLANTIC UNIV on May 17, 2011

The IRL is an endemic area for the lobomycosis in dolphins with a prevalence of 10–12%.[189] Recent research indicates that the disease is associated with humoral and cell-mediated immunosuppression.[17,188] The spatial distribution of lobomycosis within the IRL suggests that environmental factors contribute to the expression of the disease.[159] Mercury levels in dolphin tissues in the IRL are high and may play a role in the disruption of immune function, increasing susceptibility to opportunistic infections.[188,208,209] Limited evidence exists to suggest that lobomycosis may be transferred from infected animals to people.[189] However, the high prevalence of lobomycosis in the dolphin population of a Florida coastal region, which is used extensively for recreational purposes, raises concerns for zoonotic or common source transmission. Thus, from several perspectives, lobomycosis in bottlenose dolphins represents an animal sentinel of environmental and ecosystem change, with particular implications for human health in populations inhabiting coastal environments.

Viral Disease

Diseases with complex multifactorial etiologies associated with novel viral infections are being characterized in marine mammals. For example, approximately 20% of sexually mature stranded California sea lions have urogenital cancer, which often metastasizes and is associated with a novel gammaherpesvirus, designated otarine herpesvirus-1 (OtHV-1).[38,39,118,132] Other cofactors potentially involved in the pathogenesis of urogenital carcinoma in sea lions include exposure to anthropogenic contaminants that persist in the sea lions' feeding grounds and genetic factors, specifically inbred sea lions and those with a specific MHC genotype.[2,35,238]

Recently, sexually transmitted orogenital papillomatosis that occasionally undergoes transformation to metastatic squamous cell carcinoma was found to be frequently associated with a novel herpesvirus and newly sequenced papillomaviruses (TtPV-1, TtPV-2) in Atlantic bottlenose dolphins.[28,32,183,185-187] The dolphin disease is associated with immunologic perturbations and, in some instances, with high levels of anthropogenic contaminants, including mercury and infection with immunosuppressive cetacean morbilliviruses.[32,33,208,209] Cutaneous papillomatosis associated with another novel papillomavirus (TmPV-1) was documented in Florida manatees (*Trichechus manatus latirostris*) with virally productive papillomas associated with immunosuppression.[23,182] In manatees, it is thought that cutaneous papillomas are caused by activation of latent infection and reinoculation from active infection with concurrent immunologic suppression as a cofactor in disease pathogenesis.[23] Because related papillomaviruses are associated with human disease, including cervical cancer, dolphins and manatees may be good models for understanding oncogenesis mechanisms in humans. These combined data suggest that interactions occur among genes, anthropogenic toxins, immunologic factors, and/or oncogenic viruses in these common marine mammals that share a coastal environment with humans.[2,29,188,238]

Antibiotic Resistant Bacteria

Other confirmed or suspected infectious disease agents have been reported in marine mammals that may have ecosystem or human health implications.[19,94,135,165,166,230,226] One significant concern to public health authorities is the emergence of antibiotic-resistant species of bacteria among animals and humans. Widespread evidence of antibiotic-resistant bacteria was recently described in northern elephant seals (*Mirounga angustirostris*) and bottlenose dolphins, the latter as part of health assessment studies from the coastal waters of Charleston (CHS), South Carolina, and the IRL.[85,201,202,211] Direct release of resistant bacterial species and/or unused antimicrobial agents into the aquatic environment appears to affect these dolphin populations. Twenty-five percent of *Escherichia coli* fecal isolates from IRL and CHS dolphins demonstrated resistance to 1 or more antibiotics. Disturbingly, a small number of methicillin-resistant also were reported from dolphins. The results suggest that the transfer of resistance from humans or domestic animals may occur or that antibiotics are reaching the marine environment, creating selective genetic adaptation.[85,201,202] Thus, from an aquatic perspective, dolphins appear to be prime sentinels for this important public health problem.

Anthropogenic Chemicals

Marine mammals are exposed to a variety of persistent organohalogen compounds (POCs) and inorganic pollutants that bioaccumulate in marine ecosystems, resulting in high tissue contaminant concentrations. In particular, marine mammals from coastal regions associated with dense human populations and greater industrial and agricultural activities have high tissue concentrations of POCs.[6,64,101,171-173] In addition to being apex predators, small cetaceans have several anatomic and life-history features that contribute to the accumulation of lipophilic pollutants, which may increase susceptibility to other anthropogenic stressors.[64] Cetacean species have extensive fat stores that accumulate high levels of POCs. During periods of fasting, starvation, lactation, or other physiological demands, these contaminants may be mobilized, which may redistribute traditional contaminants as well as emerging chemicals of concern. The redistribution of these contaminants may affect adult and perinatal health. Furthermore, the lower capacity for degradation of these chemicals in these species exacerbates toxic effects.[16,215]

High levels of contaminants documented in marine mammals include legacy chemicals such as the organochlorine pesticides including dichlorodiphenylethanes (ie, DDTs), dieldrin, chlordanes, hexachlorocyclohexanes (HCHs), polychlorinated dioxins, dibenzofurans, and polychlorinated biphenyls (PCBs)[64,86,93,115,116,151,153,164] and emerging compounds such as polybrominated diphenyl ethers (PBDEs),[64,65,103,112,116,143,222] perfluorinated chemicals (PFCs),[34,64,117] hexabromocyclododecanes, and polybrominated dimethoxybiphenyls.[113,231,240] Hydroxylated PCBs and PBDEs were reported in various tissues

Downloaded from vet.sagepub.com at FLORIDA ATLANTIC UNIV on May 17, 2011

of beluga whales, bottlenose dolphins, and killer whales (*Orcinus orca*).[11,102,143]

In particular, the widespread coastal distribution of bottlenose dolphins and their role as apex predators support their relevance as important sentinel species for biomonitoring spatial and temporal trends in contaminants.[29,64,66,67,184,210,234] Interestingly, in a novel POC risk assessment model, marine mammals also have been used as sentinel species for Arctic ecosystem and public health.[97-100,123,134,236] The accumulation of POCs in Native populations from Arctic subsistence communities has raised questions concerning the suitability of terrestrial and marine wildlife from this region for human consumption.[100,168,199,200] For Arctic residents dependent upon marine resources, a clear human connection exists with marine mammal health since Arctic marine mammal species consume similar prey and many marine mammal species are themselves consumed by indigenous peoples.

Persistent organohalogen compounds are resistant to environmental degradation and persist for long periods, becoming widely distributed geographically and accumulating in the fatty tissue of humans and wildlife. The associations of adverse health effects with POCs in marine mammals have been arguably linked to increased infectious disease susceptibility,[5,91,108,109,196,197] immunosuppression,[43,51,54,55,156,157,196] reproductive impairment,[3,43,190,109] endocrine disruption,[73,74,106,175,213,216] and neoplasia.[43,138,140,160,238] In toxicology testing in laboratory species, convincing evidence exists for the toxicopathologic effects of many of these contaminants on endocrine, neurologic, reproductive, developmental, immunologic, and cellular systems.[13,41,45,53,67,79,104,125,126,170,193,229]

Beluga whales (*Delphinapterus leucas*) from the St. Lawrence estuary are one of the most extensively and consistently studied groups of free-ranging marine mammals in relation to POCs and other contaminants and the development of neoplasia.[50,92,137,140,141,160] Beluga whales from the St. Lawrence region develop a wide variety of neoplasms, many of which are of similar types to those seen in domestic species and in humans.[48,49,139,140,160] Exposure to carcinogenic contaminants such as POCs in the food chain is a speculated cause of the high prevalence of neoplasia in this population of whales.[50,92,137,140]

Heavy metal levels have often been measured from the blood of marine mammals, but the significance of the levels found is not fully understood. High levels of mercury have been reported in dolphins from the Gulf and Atlantic coasts of Florida and Australia.[127,208,209,237] For example, the IRL dolphin population has the highest mean concentrations of mercury in blood and skin from the limited set of studies of free-ranging bottlenose dolphins reported to date. The concentrations of mercury found in IRL dolphins exceeded the EPA benchmark of mercury in cord blood for humans.[208,209] Correlations between mercury and selenium have been reported in many marine mammal species, and the ability of marine mammals to withstand large concentrations of mercury is believed to be partly due to this protective pairing with selenium.[127,237] Further studies are required to explore the effects of mercury on these marine mammal populations as well as the potential implications for humans that inhabit the same coastal ecosystems.

The interactions of mercury and selenium may play a role in the cardiomyopathy (CMP) reported in pygmy sperm whales (*Kogia breviceps*) and dwarf sperm whales (*Kogia sima*). The disease in *Kogia* spp. has been described primarily in stranded adult male whales from the southeastern Atlantic Ocean, but it also occurs in Pacific Ocean whales.[18,31] More than half of documented adult *Kogia* spp. strandings exhibit signs of chronic progressive idiopathic CMP or some state of myocardial degeneration. The cause of this complex disorder remains unknown. However, factors speculated to contribute to the development of CMP in these species include genetics, infectious agents, contaminants, biotoxins, and dietary intake (vitamins, selenium, mercury, and prooxidants).[31] In a recent age-controlled study of *K. breviceps*, both mercury and selenium concentrations increased with animal age and progression of CMP (C. E. Bryan, personal communication). Whales with CMP had greater overall protein oxidation, and selenium protein patterns were different between animals with no myocardial lesions and those with CMP, suggesting that selenium protein expression is altered with the disease state in pygmy sperm whales. The latter studies increased knowledge of CMP in pygmy and dwarf sperm whales and may also provide complementary information benefiting other affected species.

Using marine mammals as sentinels may provide important clues about the cumulative and synergistic effects of the mixture of the aforementioned contaminants, which is an emerging issue that requires attention.[150,153,172] Marine mammals are exposed to a wide admixture of legacy POCs and PCBs, emerging contaminants such as PBDEs and PFCs, their metabolites and/or degradation products, heavy metals, and natural marine biotoxins associated with harmful algal blooms (see below). The significance of these multiple co-exposures is still unclear, but the potential exists for additive and/or synergistic effects on the immunologic, neurologic, endocrine, and reproductive systems of not only marine mammals but also humans who inhabit the same coastal ecosystems.

Harmful Algal Blooms

Harmful algal blooms (HABs), and the potent neurotoxins they produce, have been associated with mass mortalities of dolphins, sea lions, southern sea otters, Florida manatees, Mediterranean monk seals (*Monachus monachus*), gray whales (*Eschrichtius robustus*), and humpback whales (*Megaptera novaeangliae*).[22,24,71,72,80,88,111,220] The range of biotoxins produced by HABs is extensive, and these toxins directly or indirectly affect human health. Biotoxins associated with HABs include brevetoxins, the cause of neurotoxic shellfish poisoning; saxitoxins, the cause of paralytic shellfish poisoning; okadaic acid, the cause of diarrheic shellfish poisoning; domoic acid, the cause of amnesic shellfish poisoning; and others.[124,227] The HAB problem is significant, is growing worldwide, and poses a major threat to human and ecosystem health.[81,119] The global pandemic of HABs has been

Downloaded from vet.sagepub.com at FLORIDA ATLANTIC UNIV on May 17, 2011

interpreted as a reflection of ecosystem instability and a threat to public health.[62] Thus, marine mammals appear to be good sentinels for the ecosystem and public health effects of HABs.[20,29]

Domoic Acid

Domoic acid (DA) is a neurotoxin produced by diatoms of the genus *Pseudo-nitzschia*, which targets the limbic system. This toxin causes excitotoxicity and damage to neuronal pathways responsible for the learning and recall of sequences underlying spatial memory as well as restraining seizure-prone circuitry associated with temporal lobe epilepsy.[89,179] A unique hallmark of DA intoxication in humans is loss of short-term memory, thus the term amnesic shellfish poisoning. Recurrent outbreaks of DA poisoning along the California coast have caused stranding of several thousand sea lions, and DA is now viewed as a major cause of reproductive failure.[36,52,83,89,203] The primary peracute microscopic lesions of DA toxicity in adult sea lions are microvesicular hydropic degeneration within the neuropil of the hippocampus, amygdala, pyriform lobe, and other limbic structures. Acutely, ischemic neuronal necrosis develops and is particularly apparent in the granular cells of the dentate gyrus and the pyramidal cells within the hippocampus cornu ammonis (CA) sectors CA4, CA3, and CA1. Chronically, gliosis, mild nonsuppurative inflammation, and loss of laminar organization in affected areas are found.[205] Myocardial necrosis and edema have also been reported.[88] Histopathologic findings associated with abortion and premature birth include systemic and localized inflammation and bacterial infections of amniotic origin, placental abruption, and brain edema.[83] A degenerative cardiomyopathy associated with exposure to DA, which is beyond central neurologic disease, represents another recently reported syndrome in California sea lions and may contribute to morbidity and mortality.[239] Furthermore, it has been suggested that DA intoxication may be potentiated by organochlorine burden.[219]

Recent observations have defined a chronic disease in juvenile California sea lions characterized by epilepsy and unusual behaviors.[82] This emerging chronic juvenile sea lion disease has been proposed to result from in utero toxicity to DA.[180] Research suggests that sublethal DA doses may progress to chronic epileptic disease similar to temporal lobe epilepsy in humans[178] and that magnetic imaging the hippocampus of sea lions exposed to DA may be a useful antemortem diagnostic technique.[152] Acute high-dose DA intoxication may lead to sudden death but those animals that survive the initial bout of seizures may develop neurological disease with behavioral changes and increased severity of spontaneous seizures in the absence of the DA diatom blooms. Thus, sea lions may provide important information on how marine mammals and other species, including humans, respond to DA intoxication including the possible association with epilepsy. Additionally, since sea lion strandings in California appear to be a very sensitive indicator of DA in the marine environment, it has recently been suggested that their monitoring be included in public health surveillance plans.[52]

Domoic acid also may affect southern sea otters, gray whales (*Eschrichtius robustus*), and pygmy and dwarf sperm whales. In 2003, an unusual mortality event was declared in southern sea otters by the US Fish and Wildlife Service and NOAA/National Marine Fisheries Service. Blooms of *Pseudo-nitzschia australis* were associated with this event.[111] In 2000, an abnormally high number of gray whales were stranded in California, and these strandings were associated with *Pseudo-nitzchia australis* blooms and high tissue levels as of DA.[227] Finally, DA was recently detected in urine and fecal samples recovered from pygmy sperm whales and dwarf sperm whales stranding along the US Atlantic coast from 1997 to 2008.[69] Although blooms of *Pseudo-nitzschia* are associated with repeated large-scale marine mammal mortalities on the west coast of the United States, there is no documented history of similar blooms on the southeast US coast, and there were no observed *Pseudo-nitzschia* blooms in the region associated with any of the *Kogia* spp. strandings. Since myocardial damage is a feature of DA toxicity in sea lions and DA intoxication has been identified as a risk factor for myocarditis and dilated CMP in southern sea otters, an association may exist between this toxin and the *Kogia* cardiomyopathy described above.[89,122,239] Toxin accumulation in these pelagic whale species may be an indication of harmful algal bloom activity in offshore areas not currently being monitored and thus reflect shifts in ecosystem health that deserve further investigation.

Brevetoxins

Recent, and often unprecedented, endangered Florida manatee and Atlantic bottlenose dolphin epizootics have been associated with potent marine neurotoxins known as brevetoxins, which are produced by the "red tide" dinoflagellate *Karenia brevis.*[20,24,70] Brevetoxins are known to kill large numbers of fish and cause illness in humans who ingest toxic filter-feeding shellfish (neurotoxic shellfish poisoning) or inhale toxic aerosols. The pathogenesis of brevetoxicosis is suspected to involve direct inhalation of toxins (in manatees) or ingestion of toxins in food sources (in manatees and dolphins).[20,25,27] At least 149 manatees died in an unprecedented epizootic along the southwest coast of Florida, and a detailed pathologic investigation was conducted.[20] At about the same time, a bloom of *K. brevis* was present in the same area. Brevetoxins were isolated in quantities from 2- to 15- fold above control levels in stomach contents, liver, kidney, and lung from dead manatees using a synaptosomal binding assay. Grossly, severe nasopharyngeal, pulmonary, hepatic, renal, and cerebral congestion was present in all cases. Nasopharyngeal and pulmonary edema and hemorrhage were also seen. Consistent microscopic lesions consisted of severe catarrhal rhinitis, pulmonary hemorrhage and edema, multiorgan hemosiderosis, and nonsuppurative leptomeningitis. Immunohistochemical staining using a polyclonal primary antibody to brevetoxin (GAB) showed intense positive staining of lymphocytes and macrophages in the lung, liver, and secondary lymphoid tissues. Lymphocytes and macrophages associated with the inflammatory lesions of the

Downloaded from vet.sagepub.com at FLORIDA ATLANTIC UNIV on May 17, 2011

nasal mucosa and meninges were also positive for brevetoxin. These findings implicated brevetoxicosis as a component of and the likely primary cause of the epizootic.[20] It was postulated that the route of brevetoxin exposure was inhalation of aerosolized toxins causing the upper respiratory inflammation and dissemination of toxin via macrophages and lymphocytes, ultimately resulting in acute agonal cardiovascular collapse. A chronic hemolytic process was also postulated resulting in the widespread hemosiderosis since similar changes have been reported in birds and fish exposed to brevetoxins. Additionally, retrospective histopathologic and immunohistochemical studies demonstrated that other manatee epizootics were likely due to the incidental ingestion of filter-feeding ascidians that contained brevetoxins.

Manatees from Florida's coastlines have frequent potential brevetoxin exposure because red tide blooms are common in these areas. Important new data indicate that brevetoxin vectors such as seagrasses can result in delayed or remote manatee exposure, causing intoxication in the absence of toxin-producing dinoflagelates.[71] Thus, unexpected toxin vectors may account for manatee deaths long after or remote from a dinoflagellate bloom. Therefore, manatee mortality resulting from brevetoxicosis may not necessarily be acute but may occur after chronic inhalation and/or ingestion.[20,24] Immunohistochemical studies of manatee tissues with interleukin-1β–converting enzyme showed positive staining with a cellular tropism similar to GAB.[20,24] The data suggested that brevetoxicosis might initiate the release of inflammatory mediators that culminate in fatal toxic shock. Additionally, prolonged nonlethal toxin exposure may compromise normal immunologic responses, predisposing manatees exposed to brevetoxins to opportunistic disease.[233] Interestingly, the inhalational route of brevetoxin exposure in manatees is shared with humans, making manatees an important sentinel species for this emerging health problem. Increases in human pulmonary emergency room visits are temporally related to red tide and can have significant human health and economic impact.[9,96,119]

Over the past 20 years, investigations into marine mammal mortality events have provided insight into the ecosystem events, vectors, clinical signs, and pathologic effects of HAB biotoxin exposure. Compelling evidence supports the involvement of saxitoxins, DA, and brevetoxins in marine mammal morbidity and mortality.[20,72,80,89] However, confirmation that these toxins are sole etiologic agents for disease remains problematic because the peracute, acute, and chronic biotoxin effects in marine mammals are unknown. Additionally, it is likely these toxins are involved in multifactorial disease involving infectious agents, immunologic perturbations, and other pathologic processes that makes interpretation challenging.

Conclusion

In the past 20 years, dedicated marine mammal research has resulted in an increase in reporting of marine mammal disease.[90] At the same time, the appearance of true emerging and reemerging diseases in marine mammals is also suggested historically and by the scientific literature. This phenomenon may be related to complex factors such as climate change, toxins, and immunosuppression, with coastal marine mammals particularly at risk since many inhabit an environment more affected by human activity.[29,226] Potential increased environmental pressure on marine mammals may provoke more frequent epizootics, help disseminate possible zoonotic pathogens, and increase the prevalence and severity of infectious illnesses worldwide. Marine mammals are useful sentinels for emerging and reemerging infectious and neoplastic disease, the effects of anthropogenic toxins, and the impacts of the global pandemic of harmful algal blooms. Many of these diseases have direct public health implications, whereas others may be indicative of an environmental distress syndrome. To this end, marine mammals are proving to be good sentinels for ocean and human health given their many unique natural attributes. Marine mammal research will undoubtedly expand as new species are evaluated and better tools to assess health are developed. This approach provides a new avenue for better understanding the interface between evolving ecosystem and public health issues.[29] Ultimately, it is in our own best interest to investigate all wildlife health patterns that could potentially affect our own well-being since three-fourths of all emerging infectious diseases of humans are zoonotic, most originate in wildlife, and their incidence is increasing.[114,145,192,218]

Acknowledgements

Tissues from free-ranging dolphins were collected under National Marine Fisheries Service Scientific Research Permit No. 998-1678 issued to Dr. Bossart as part of the Health and Risk Assessment of Bottlenose Dolphin Project (HERA) conducted in the Indian River Lagoon, Florida, and the coastal waters of Charleston, South Carolina. The author thanks the entire dedicated dolphin HERA project staff, with special thanks extended to Dr. Pat Fair, Dr. Juli Goldstein, Dr. John Reif, Dr. Forrest Townsend, Larry Hansen, and the members of the NMFS Marine Mammal Stranding program. Special thanks to Bruce Gordon, Dr. Pat Fair, and Dr. R. H. DeFran for editorial assistance and Dr. Mike Hyatt for data collection assistance. Finally, the author gratefully acknowledges Stephen D. McCulloch for his tireless energy and contributions to marine mammal research.

Declaration of Conflicting Interests

The authors declared that they had no conflicts of interest with respect to their authorship or the publication of this article.

Financial Disclosure/Funding

Harbor Branch Oceanographic Institute at Florida Atlantic University "Protect Florida Dolphin" program and NOAA Fisheries Marine Mammal Health and Stranding Response Program partially supported this work.

References

1. Acevedo-Whitehouse K, de la Cueva H, Gulland FMD, et al: Evidence of Leptospira interrogans infection in California sea lion pups from the Gulf of California. J Wildl Dis **39:**145–151, 2003.
2. Acevedo-Whitehouse K, Gulland FMD, Greig D, et al: Disease susceptibility in California sea lions. Nature **422:**35, 2003.

Downloaded from vet.sagepub.com at FLORIDA ATLANTIC UNIV on May 17, 2011

3. Addison RF: Organochlorines and marine mammal reproduction. Can J Fish Aquat Sci **46:**360–368, 1989.
4. Adin CA, Cowgill LD: Treatment and outcome of dogs with leptospirosis: 36 cases (1990–1998). J Am Vet Med Assoc **216:**371–375, 2000.
5. Aguilar A, Borrell A: Abnormally high polychlorinated biphenyl levels in striped dolphins (Stenella coeruleoalba) affected by the 1990–1992 Mediterranean epizootic. Sci Total Environ **154:**237–347, 1994.
6. Aguilar A, Borrell A, Reijnders PJH: Geographical and temporal variation in levels of organochlorine contaminants in marine mammals. Mar Environ Res **53:**425–452, 2002.
7. Aguirre AA, Tabor AA: Introduction: marine mammals as sentinels of marine ecosystem health. EcoHealth **1:**236–238, 2004.
8. Arkush KD, Miller MA, Leutenegger CM, et al: Molecular and bioassay-based detection of Toxoplasma gondii oocyst uptake by mussels (Mytilius galloprovincialis). Int J Parasitol **33:**1087–1097, 2003.
9. Backer LC, Fleming LE, Rowan A, et al: Recreational exposure to aerosolized brevetoxins during Florida red tide events. Harmful Algae **2:**19–28, 2003.
10. Barrett T, Visser IKG, Mamaev LV, et al: Dolphin and porpoise morbilliviruses are genetically distinct from phocine distemper virus. Virology **193:**1010–1012, 1993.
11. Bennett ER, Ross PS, Alaee M, et al: Chlorinated and brominated organic contaminants and metabolites in the plasma and diet of a captive killer whale (Orcinus orca). Mar Pollut Bull **58**(7):1078–1083, 2009.
12. Bharti AR, Nally JE, Ricaldi JN, et al: Leptospirosis: a zoonotic disease of global importance. Lancet Infect Dis **3:**757–771, 2003.
13. Birnbaum LS, Staskal DF: Brominated flame retardants: cause for concern? Environ Health Perspect **112:**9–117, 2004.
14. Blixenkrone-Moller M, Bolt G, Gottschalck E, et al: Comparative analysis of the gene encoding the nucleocapsid protein of dolphin morbillivirus reveals its distant evolutionary relationship to measles virus and ruminant morbilliviruses. J Gen Virol **75:**2829–2834, 1994.
15. Bonde R, Aguirre AA, Powell J: Manatees as sentinels of marine ecosystem health: are they the 2000 pound canaries? Ecohealth **1:**255–262, 2004.
16. Boon JP, Oostingh I, Van der Meeer J, et al: A model for the bioaccumulation of chlorobiphenyl congeners in marine mammals. Environ Toxicol Pharmacol **270:**237–251, 1994.
17. Bossart GD: A suspected acquired immunodeficiency in an Atlantic bottlenosed dolphin with lobomycosis and chronic-active hepatitis. J Am Vet Med Assoc **185:**1413–1414, 1984.
18. Bossart GD, Odell DK, Altman NH: Cardiomyopathy in stranded pygmy and dwarf sperm whales. J Am Vet Med Assoc **187:**1137–1140, 1985.
19. Bossart GD, Ewing R, Herron AJ, et al: Immunoblastic malignant lymphoma in dolphins: ultrastructural and immunohistochemical features. J Vet Diagn Invest **9:**454–458, 1997.
20. Bossart GD, Baden DG, Ewing R, et al: Brevetoxicosis in manatees (Trichechus manatus latirostris) from the 1996 epizootic: gross, histologic and immunohistochemical features. Toxicol Pathol **26:**276–282, 1998.
21. Bossart GD: The Florida manatee: on the verge of extinction? J Am Vet Med Assoc **214:**10–15, 1999.
22. Bossart GD. Manatees. *In:* Marine Mammal Medicine, ed. Dierauf L and Gulland F, pp. 939–960. CRC Press, Boca Raton, FL, 2001.
23. Bossart GD, Ewing R, Lowe M, et al: Viral papillomatosis in Florida manatees (Trichechus manatus latirostris). Exp Mol Pathol **72:**37–48, 2002.
24. Bossart GD, Baden DG, Ewing RY, et al: Manatees and brevetoxicosis. *In:* Molecular and Cell Biology of Marine Mammals, ed. Pfeiffer C, pp. 205–212. Krieger, Melbourne, FL, 2002.
25. Bossart GD, Meisner R, Rommel SA, et al: Pathological features of the Florida manatee cold stress syndrome. Aquatic Mammals **29**(1):9–17, 2003.
26. Bossart GD, Meisner R, Varela R, et al: Pathologic findings in stranded Atlantic bottlenose dolphins (Tursiops truncatus) from the Indian River Lagoon, Florida. Florida Scientist **66**(3):226–238, 2003.
27. Bossart GD, Meisner R, Rommel SA, et al: Pathologic findings in Florida manatees (Trichechus manatus latirostris). Aquatic Mammals **30**(3):434–440, 2004.
28. Bossart GD, Ghim S, Rehtanz M, et al: Orogenital neoplasia in Atlantic bottlenose dolphins (Tursiops truncatus). Aquatic Mammals **31**(4):473–480, 2005.
29. Bossart GD: Marine mammals as sentinel species for oceans and human health. Oceanography **19**(2):44–47, 2006.
30. Bossart GD: Emerging diseases in marine mammals: from dolphins to manatees. Microbe **11**(2):544–549, 2007.
31. Bossart GD, Hensley G, Goldstein J, et al: Cardiomyopathy and myocardial degeneration in stranded pygmy (Kogia breviceps) and dwarf sperm (Kogia sima) whales. Aquatic Mammals **33**(2):214–222, 2007.
32. Bossart GD, Romano TA, Peden-Adams, et al: Hematological, biochemical and immunological findings in Atlantic bottlenose dolphins (Tursiops truncatus) with orogenital papillomas. Aquatic Mammals **34**(2):166–177, 2008.
33. Bossart GD, Reif JS, Schaefer AM, et al: Morbillivirus infection in free-ranging Atlantic bottlenose dolphins (Tursiops truncatus) from the southeastern United States: seroepidemiologic and pathologic evidence of subclinical infection. Vet Microbiol **143:**160–166, 2010.
34. Bossi R, Riget FF, Dietz R, et al: Preliminary screening of perfluorooctane sulfonate (PFOS) and other fluorochemicals in fish, birds and marine mammals from Greenland and the Faroe Islands. Environ Pollut **136**(2):323–329, 2005.
35. Bowen L, Aldridge BM, Delong R, et al: An immunogenetic basis for the high prevalence of urogenital cancer in a free-ranging population of California sea lions (Zalophus californianus). Immunogenetics **56**(11):846–848, 2005.
36. Brodie EC, Gulland FMD, Greig DJ, et al: Domoic acid causes reproductive failure in California sea lions (Zalophus californianus). Mar Mammal Sci **22**(3):700–707, 2006.
37. Brown AS, Schaefer CA, Quesenberry CP Jr, et al: Maternal exposure to toxoplasmosis and risk of schizophrenia in adult offspring. Am J Psychiatry **162:**767–773, 2005.

Downloaded from vet.sagepub.com at FLORIDA ATLANTIC UNIV on May 17, 2011

38. Buckles EL, Lowenstine LJ, DeLong RL, 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**(1–2):1–8, 2007.
39. Buckles EL, Lowenstine LJ, Funke C, et al: Otarine herpesvirus-1, not papillomavirus, is associated with endemic tumours in California sea lions (Zalophus californianus). J Comp Pathol **135**(4):183–189, 2006.
40. Cao L, Caldeira K: Atmospheric CO2 stabilization and ocean acidification. Geophys Res Lett **35:**L19609, 2008.
41. Capdevielle M, Van Egmond R, Whelan, M, et al: Consideration of exposure and species sensitivity of triclosan in the freshwater environment. Integr Environ Assess Manag **4:**15–23, 2008.
42. Clavareau C, Wellemans V, Walravens K, et al: Phenotypic and molecular characterization of a Brucella strain isolated from a minke whale (Balaenoptera acutorostrata). Microbiology **144:**3267–3273, 1998.
43. Colborn T, Smolen MJ: Cetaceans and contaminants. *In:* Toxicology of Marine Mammals, ed. Vos JG, Bossart GD, Fournier M, and O'Shea T, pp. 291–232. Taylor & Francis, London, 2003.
44. Conrad P, Kreuder C, Mazet J, et al: Linkages between cats, run-off and brain disease in sea otters. Paper presented at the Symposium, Marine Mammals on the Frontline: Indicators for Ocean and Human Health. American Association for the Advancement of Science, Annual Meeting, St. Louis, MO, February 18, 2006.
45. Crofton KM, Paul KB, DeVito MJ, et al: Short-term in vivo exposure to the water contaminant triclosan: evidence for disruption of thyroxine. Environ Toxicol Pharmacol **24:**194–197, 2007.
46. Dawson CE: Anti-Brucella antibodies in pinnipeds of Australia. Microbiology Aust **26:**87–89, 2005.
47. Dawson CE, Stubberfield EJ, Perrett LL, et al: Phenotypic and molecular characterization of Brucella isolates from marine mammals. BMC Microbiol **8:**224, 2008.
48. De Guise S, Lagace A, Beland P: Gastric papillomas in eight St. Lawrence beluga whales (Delphinapterus leucas). J Vet Diagn Invest **6:**385–388, 1994.
49. De Guise S, Lagace A, Beland P: Tumors in St. Lawrence beluga whales (Delphinapterus leucas). Vet Pathol **31:**444–449, 1994.
50. De Guise S: Possible mechanisms of action of environmental contaminants on St. Lawrence beluga whales. Envir Health Perspect **103:**73–77, 1995.
51. De Guise S, Martineau D, Beland P, et al: Effects of in vitro exposure of beluga whale leukocytes to selected organochlorines. J Toxicol Environ Health A **55:**479–493, 1998.
52. de la Riva GT, Johnson CK, Gulland FM, et al: Association of an unusual marine mammal mortality event with Pseudo-nitzschia spp. blooms along the southern California coastline. J Wildl Dis **45**(1):109–121, 2009.
53. DeLorenzo ME, Keller JM, Arthur CD, et al: Toxicity of the antimicrobial compound triclosan and formation of the metabolite methyl-triclosan in estuarine systems. Environ Toxicol **23:**224–232, 2008.
54. de Swart RL, Ross PS, Vedder EJ, et al: Impairment of immunological function in harbour seals (Phoca vitulina) feeding on fish from polluted coastal waters. Ambio **23:**155–159, 1994.
55. de Swart RL, Ross PS, Vos JG, et al: Impaired immunity in harbour seals (Phoca vitulina) exposed to bioaccumulation environmental contaminants: review of a long term feeding study. Environ Health Perspect **104:**823–828, 1996.
56. Dierauf LA, Vandenbroek DJ, Roletto J, et al: An epizootic of leptospirosis in California sea lions. J Am Vet Med Assoc **187:**1145–1148, 1985.
57. Domingo ML, Ferrer L, Pumarola M, et al: Morbillivirus in dolphins. Nature **348:**21, 1990.
58. Domingo M, Visa J, Pumarola M, et al: Pathologic and immunocytochemical studies of morbillivirus infection in striped dolphins (Stenella coeruleoalba). Vet Pathol **29:**1–10, 1992.
59. Domingo M, Vilafranca M, Visa J, et al: Evidence for chronic morbillivirus infection in the Mediterranean striped dolphin (Stenella coeruleoalba). Vet Microbiol **44:**229–239, 1995.
60. Dubey JP, Beattie CP: Toxoplasmosis of Animals and Man. CRC Press, Boca Raton, FL, 1998.
61. Duignan PJ, House C, Geraci JR, et al: Morbillivirus infection in two species of pilot whales (Globicephala sp.) from the western Atlantic. Mar Mammal Sci **11:**150–162, 1995.
62. Epstein PR, Chivian E, Frith K: Emerging diseases threaten conservation. Environmental Health Perspectives **111:**A506–A507, 2003.
63. Ewalt DR, Payeur JB, Martin BM, et al: Characteristics of a Brucella species from a bottlenose dolphin (Tursiops truncatus). J Vet Diagn Invest **6:**448–452, 1994.
64. Fair P, Adams J, Mitchum G, et al: Contaminant blubber burdens in Atlantic bottlenose dolphins (Tursiops truncatus) from two southeastern US estuarine areas: concentrations and patterns of PCBs, pesticides, PBDEs, PFCs, and PAHs. Sci Total Environ **408:**1577–1597, 2010.
65. Fair PA, Mitchum G, Hulsey TC, et al: Polybrominated diphenyl ethers (PBDEs) in blubber of free-ranging bottlenose dolphins (Tursiops truncatus) from two southeast Atlantic estuarine areas. Arch Environ Contam Toxicol **53:**483–494, 2007.
66. Fair PA, Becker PR: Review of stress in marine mammals. J Aquat Ecosyst Stress Recovery **7:**335–354, 2000.
67. Fair PA, Lee H-B, Adams J, et al: Occurrence of triclosan in plasma of wild Atlantic bottlenose dolphins (Tursiops truncatus) and in their environment. Environ Pollut **157:**2248–54, 2009.
68. Fayer R, Dubey J, Lindsay DS. Zoonotic protozoa: from land to sea. Trends Parasitol **20**(11):531–536, 2004.
69. Fire SE, Wang Z, Leighfield TA, et al: Domoic acid exposure in pygmy and dwarf sperm whales (Kogia spp.) from southeastern and mid-Atlantic U.S. waters. Harmful Algae **8:**658–664, 2009.
70. Fire SE, Fauquier D, Flewelling LJ, et al: Brevetoxin exposure in bottlenose dolphins (Tursiops truncatus) associated with Karenia brevis blooms in Sarasota Bay, Florida. Mar Biol **152:**827–834, 2007.
71. Flewelling LJ, Naar JP, Abbott JP, et al: Red tides and marine mammal mortalities. Nature **435:**755–756, 2005.
72. Forcada J, Hammond PS, Aquilar A: Status of the Mediterranean monk seal Monachus monachus in the western Sahara and implications of a mass mortality event. Mar Ecol Prog Sev **188:** 249–261, 1999.

Downloaded from vet.sagepub.com at FLORIDA ATLANTIC UNIV on May 17, 2011

73. Fossi MC, Marsili L, Casini S, et al: Development of new-tools to investigate toxicological hazard due to endocrine disruptor organochlorines and emerging contaminants in Mediterranean cetaceans. Mar Environ Res **62**(Suppl):S2000–S2004, 2006.
74. Fossi MC, Casini S, Marsili L: Potential toxicological hazard due to endocrine-disrupting chemicals on Mediterranean top predators: state of art, gender differences and methodological tools. Environ Res **104:**174–182, 2007.
75. Foster G, Jahans KL, Reid RJ, Ross HM: Isolation of Brucella species from cetaceans, seals and an otter. Vet Rec **138:**583–586, 1996.
76. Foster G, MacMillan AP, Godfroid J, et al: A review of Brucella sp. infection of sea mammals with particular emphasis on isolates from Scotland. Vet Microbiol **90:**563–580, 2002.
77. Foster G, Osterman BS, Godfroid J, et al: Brucella ceti sp. nov. and Brucella pinnipedialis sp. nov. for Brucella strains with cetaceans and seals as their preferred hosts. Int J Syst Evol Microbiol **57:**2688–2693, 2007.
78. Garner MM, Lambourn DM, Jeffries SJ, et al: Evidence of Brucella infection in Parafilaroides lungworms in a Pacific harbor seal (Phoca vitulina richardsii). J Vet Diagn Invest **9:**298–303, 1997.
79. Gee RH, Charles A, Taylor N, et al: Oestrogenic and androgenic activity of triclosan in breast cancer cells. J Applied Toxicol **28:**78–91, 2008.
80. Geraci JR, Anderson DM, Timperi RJ, et al: Humpback whales (Megaptera novaeangliae) fatally poisoned by dinoflagellate toxin. Can J Fish Aquat Sci **46:**1895–1898, 1989.
81. Glibert PM, Anderson D, Gentien PE, et al: The global, complex phenomena of harmful algal blooms. Oceanography **18:**137–147, 2005.
82. Goldstein T, Mazet JAK, Zabka TS, et al: Novel symptomatology and changing epidemiology of domoic acid toxicosis in California sea lions (Zalophus californianus): an increasing risk to marine mammal health. Proc R Soc Ser B Biol **275**(1632):267–276, 2008.
83. Goldstein T, Zabka TS, Delong RL, et al: The role of domoic acid in abortion and premature parturition of California sea lions (Zalophus californianus) on San Miguel Island, California. J Wildl Dis **45**(1):91–108, 2009.
84. González L, Patterson IA, Reid RJ, et al: Chronic meningoencephalitis associated with Brucella sp.infection in live-stranded striped dolphins (Stenella coeruleoalba). J Comp Pathol **126:**147–152, 2002.
85. Greig TW, Bemiss JA, Lyon BA, et al: Prevalence and diversity of antibiotic resistant Escherichia coli in bottlenose dolphins (Tursiops truncatus) from the Indian River Lagoon, Florida, and Charleston Harbor area, South Carolina. Aquatic Mammals **33**(2):185–194, 2007.
86. Greig DJ, Ylitalo GM, Hall AJ, et al: Transplacental transfer of organochlorines in California sea lions (Zalophus californianus). Environ Toxicol Chem **26**(1):37–44, 2007.
87. Gulland FMD, Koski M, Lowenstine LJ, et al: Leptospirosis in California sea lions (Zalophus californianus) stranded along the central California coast, 1981–1994. J Wildl Dis **32:**572–580, 1996.
88. Gulland F: Domoic acid toxicity in California sea lions (Zalophus californianus) stranded along the central California coast, May-October 1998. Report to the National Marine Fisheries Service Working Group on Unusual Marine Mammal Mortality Events. US Dept Commerce, NOAA Tech. Memo. 2000. NMFS-OPR-17, 45 p.
89. Gulland FM, Haulena M, Fauquier D, et al: Domoic acid toxicity in California sea lions (Zalophus californianus): clinical signs, treatment and survival. Vet Rec **150**(15):475–480, 2002.
90. Gulland FM, Hall AJ: Is marine mammal health deteriorating? Trends in the global reporting of marine mammal disease. EcoHealth **4:**135–150, 2007.
91. Hall AJ, Hugunin K, Deaville R, et al: The risk of infection from polychlorinated biphenyl exposure in the harbor porpoise (Phocoena phocoena): a case–control approach. Environ Health Perspect **114:**704–711, 2006.
92. Hammill MO, Lesage V, Kingsley MC: Cancer in beluga from the St. Lawrence estuary. Environ Health Perspect **111:**A77–A78, 2003.
93. Hansen L, Schwacke LH, Mitchum GB, et al: Geographic variation in polychlorinated biphenyl and organochlorine pesticide concentrations in the blubber of bottlenose dolphins from the US Atlantic coast. Sci Total Environ **319:**147–172, 2004.
94. Harms CA, Maggi RG, Breitschwerdt EB, et al: Bartonella species detection in captive, stranded and free-ranging cetaceans. Vet Res **39**(6):59, 2008.
95. Hernández-Mora G, González-Barrientos R, Morales JA, et al: Neurobrucellosis in stranded dolphins, Costa Rica. Emerg Infect Dis **14**(9):1430–1433, 2008.
96. Hoagland P, Jin D, Polansky LY, et al: The costs of respiratory illnesses arising from Florida Gulf coast Karenia brevis blooms. Environ Health Perspect **117:**1239–1243, 2009.
97. Hoekstra PF, O'Hara TM, Fisk AT, et al: Trophic transfer of persistent organochlorine contaminants (OCs) within an Arctic marine food web from the southern Beaufort-Chukchi Seas. Environ Pollut **124:**509–522, 2003.
98. Hoekstra PF, O'Hara TM, Karlsson H, et al: Enantiomer-specific biomagnification of α-hexachlorocyclohexane and selected chiral chlordane-related compounds within an Arctic marine food web. Environ Toxicol Chem **22:**2482–2491, 2003.
99. Hoekstra PF, Letcher RJ, O'Hara TM, et al: Hydroxylated and methylsulfone-containing metabolites of polychlorinated biphenyls in the plasma and blubber of bowhead whales (Balaena mysticetus). Environ Toxicol Chem **22:**2650–2658, 2003.
100. Hoekstra PF, O'Hara TM, Backus SM, et al: Concentrations of persistent organochlorine contaminants in bowhead whale tissues and other biota from northern Alaska: implications for human exposure from a subsistence diet. Environ Res **98:**329–340, 2005.
101. Houde M, Wells R, Fair P, et al: Polyfluoroalkyl compounds in free-ranging bottlenose dolphins (Tursiops truncatus) from the Gulf of Mexico and Atlantic Ocean. Environ Sci Technol **39:**6591–6598, 2005.
102. Houde M, Pacepavicus G, Wells R, et al: Polychlorinated biphenyls and hydroxylated polychlorinated biphenyls in plasma of bottlenose dolphins (Tursiops truncatus) from the Western

Downloaded from vet.sagepub.com at FLORIDA ATLANTIC UNIV on May 17, 2011

Atlantic and the Gulf of Mexico. Environ Sci Technol **40**(19):5860–5866, 2006.
103. Houde M, Pacepavicius G, Darling C, et al: Polybrominated diphenyl ethers and their hydroxylated analogs in plasma of bottlenose dolphins (Tursiops truncatus) from the United States east coast. Environ Toxicol Chem **28:**2061–2068, 2009.
104. Ishibashi H, Matsumura N, Hirano, M, et al: Effects of triclosan on the early life stages and reproduction of medaka Oryzias latipes and induction of hepatic vitellogenin. Aquatic Toxicol **67:**167–179, 2004.
105. Jahans KL, Foster G, Broughton ES: The characterization of Brucella strains isolated from marine mammals. Vet Microbiol **57:**373–382, 1997.
106. Jenssen BM. Endocrine-disrupting chemicals and climate change: a worst-case combination for arctic marine mammals and seabirds? Environ Health Perspect **114:**76–80, 2006.
107. Jepson PD, Brew S, MacMillan AP, et al: Antibodies to Brucella VR in marine mammals around the coast of England and Wales. Vet Rec **141:**513–515, 1997.
108. Jepson PD, Bennett PM, Allchin CR, et al: Investigating potential associations between chronic exposure to polychlorinated biphenyls and infectious disease mortality in harbour porpoises from England and Wales. Sci Total Environ **243/244:**339–348, 1999.
109. Jepson PD, Bennett PM, Deaville R, et al: Relationships between PCBs and health status in UK-stranded harbour porpoises (Phocoena phocoena). Environ Toxicol Chem **24:**238–248, 2005.
110. Jessup DA, Miller M, Ames J, et al: Southern sea otter as a sentinel of marine ecosystem health. Ecoheath **1:**239–245, 2004.
111. Jessup DA, Miller M, Kreuder-Johnson C, et al: Sea otters in a dirty ocean. Jour Am Vet Med Assoc **231**(11):1648–1652, 2007.
112. Johnson-Restrepo B, Kannan K, Addink R, et al: Polybrominated diphenyl ethers and polychlorinated biphenyls in a marine foodweb of coastal Florida. Environmental Science and Technology **39:**8243–8250, 2005.
113. Johnson-Restrepo B, Adams DH, Kannan K: Tetrabromobisphenol (TBBPA) and hexabromocyclododecanes (HBCDs) in tissues of humans, dolphins, and sharks from the United States. Chemosphere **70:**1935–1944, 2008.
114. Jones KE, Patel NG, Levy MA, et al: Global trends in emerging infectious disease. Nature **451:**990–993, 2008.
115. Kajiwara N, Matsuoka S, Iwata H, et al: Contamination by persistent organochlorines in cetaceans incidentally caught along Brazilian coastal waters. Arch Environ Contam Toxicol **46**(1):124–134, 2004.
116. Kannan K, Perrotta E, Thomas NJ, et al: A comparative analysis of polybrominated diphenyl ethers and polychlorinated biphenyls in Southern sea otters that died of infectious diseases and noninfectious causes. Arch Environ Contam Toxicol **53**(2):293–302, 2007.
117. Kannan K, Perrotta E, Thomas NJ: Association between perfluorinated compounds and pathological conditions in southern sea otters. Environ Sci Technol **40**(16):4943–4948, 2006.
118. King DP, Hure MC, Goldstein T, et al: Otarine herpesvirus-1: a novel gammaherpesvirus associated with urogenital carcinoma in California sea lions (Zalophus californianus). Vet Microbiol **2277:**1–7, 2002.
119. Kirkpatrick B, Fleming LE, Squicciarini D, et al: Literature review of Florida red tide: implications for human health effects. Harmful Algae **2:**99–115, 2004.
120. Krafft A, Lichy JK, Lipscomb TP, et al: Postmortem diagnosis of morbillivirus infection in bottlenose dolphins (Tursiops truncatus) in the Atlantic and Gulf of Mexico epizootics by polymerase chain reaction-based assay. J Wildl Dis **31:**410–415, 1995.
121. Kreuder C, Miller M, Jessup DA et al: Patterns of mortality in the southern sea otter (Enhydra lutris nereis) from 1998–2001. J Wildl Dis **39:**495–509, 2003.
122. Kreuder C, Miller M, Lowenstine LJ, et al: Evaluation of cardiac lesions and risk factors associated with myocarditis and dilated cardiomyopathy in southern sea otters (Enhydra lutris nereis). Am J Vet Res **66:**289–299, 2005.
123. Kucklick JR, Struntz WDJ, Becker PR, et al: Persistent organochlorine pollutants in ringed seals and polar bears collected from northern Alaska. Sci Total Environ **287:**45–59, 2002.
124. Landsberg JH: The effects of harmful algal blooms on aquatic organisms. Reviews in Fisheries Science **10:**113–390, 2002.
125. Lau C, Butenhoff J, Rogers J: The developmental toxicity of perfluoroalkyl acids and their derivatives. Toxicol Appl Pharmacol **198:**231–2341, 2004.
126. Lau C, Anitole C, Hodes D, et al: Perfluoroalkyl acids: a review of monitoring and toxicological findings. Toxicol Sci **99:**366–394, 2007.
127. Lavery TJ, Butterfield N, Kemper CM, et al: Metals and selenium in the liver and bone of three dolphin species from South Australia, 1988–2004. Sci Total Environ **390:**77–85, 2008.
128. Lindsay DS, Dubey JP: Long-term survival of Toxoplasma gondii sporulated oocysts in seawater. J Parasitol **95**(4):1019–1020, 2009.
129. Lipscomb TP, Schulman FY, Moffett D, et al: Morbilliviral disease in Atlantic bottlenose dolphins (Tursiops truncatus) from the 1987–1988 epizootic. J Wildl Dis **30:**567–571, 1994.
130. Lipscomb TP, Kennedy S, Moffett D, et al: Morbilliviral disease in an Atlantic bottlenose dolphin (Tursiops truncatus) from the Gulf of Mexico. J Wildl Dis **30:**572–576, 1994.
131. Lipscomb TP, Kennedy S, Moffett D, et al: Morbilliviral epizootic in bottlenose dolphins of the Gulf of Mexico. J Vet Diagn Invest **8:**283–290, 1996.
132. Lipscomb TP, Scott DP, Garber RL, et al: Common metastatic carcinoma of California sea lions (Zalophus californianus): evidence of genital origin and association with novel gammaherpesvirus. Vet Pathol **37**(6):609–617, 2000.
133. Lloyd-Smith JO, Greig DJ, Hietala S, et al: Cyclical changes in seroprevalence of leptospirosis in California sea lions: endemic and epidemic disease in one host species? BMC Infect Dis **7:**125, 2007.
134. Macdonald RW, Barrie LA, Bidleman TF, et al: Contaminants in the Canadian Arctic: 5 years of progress in understanding sources, occurrence and pathways. Sci Total Environ **254:** 93–234, 2000.
135. Maggi RG, Raverty SA, Lester SJ, et al: Bartonella henselae in captive and hunter-harvested beluga (Delphinapterus leucas). J Wildl Dis **44**(4):871–877, 2008.
136. Maquart M, Le Flèche P, Foster G, et al: MLVA-16 typing of 295 marine mammal Brucella isolates from different animal and

Downloaded from vet.sagepub.com at FLORIDA ATLANTIC UNIV on May 17, 2011

geographic origins identifies 7 major groups within Brucella ceti and Brucella pinnipedialis. BMC Microbiol **9:**145, 2009.
137. Martineau D, Lagace A, Beland P, et al: Pathology of stranded beluga whales (Delphinapterus leucas) from the St. Lawrence estuary, Quebec, Canada. J Comp Pathol **98:**287–310, 1988.
138. Martineau D, De Guise S, Fournier M, et al: Pathology and toxicology of beluga whales from the St. Lawrence estuary, Quebec Canada. Past, present and future. Sci Total Environ **154:**201–215, 1994.
139. Martineau D, Lair S, De Guise S, Beland P: Intestinal adenocarcinomas in two beluga whales (Delphinapterus leucas) from the estuary of the St. Lawrence river. Can Vet J **36:**563–565, 1995.
140. Martineau DK, Lemberger A, Dallaire P, et al: Cancer in wildlife, a case study: beluga from the St. Lawrence Estuary, Quebec, Canada. Environ Health Perspect **110:**285–292, 2002.
141. Martineau DK: Potential synergism between stress and contaminants in free-ranging cetaceans. International Journal of Comparative Psychology **20:**194–216, 2007.
142. McIlhattan TJ, Martin JW, Wagner RJ, et al: Isolation of Leptospira pomona from a naturally infected California sea lion, Sonoma County, California. J Wildl Dis **7:**195–197, 1971.
143. McKinney MA, De Guise S, Martineau D, et al: Organohalogen contaminants and metabolites in beluga whale (Delphinapterus leucas) liver from two Canadian populations. Environ Toxicol Chem **25:**30–41, 2006.
144. Meites E, Jay MT, Deresinski S, et al: Reemerging leptospirosis, California. Emerg Infect Dis **10:**406–412, 2004.
145. Miller D, Ewing RY, Bossart GD: Emerging and resurging diseases. *In:* Marine Mammal Medicine, ed. Dierauf L and Gulland F, pp. 15–25. CRC Press, Boca Raton, FL, 2001.
146. Miller MA, Miller WA, Conrad PA, et al: Type X Toxoplasma gondii in a wild mussel and terrestrial carnivores from coastal California: new linkages between terrestrial mammals, runoff and toxoplasmosis of sea otters. Int J Parasitol **38**(11):1319–1328, 2008.
147. Miller, MA, Gardner IA, Kreuder C, et al: Coastal freshwater runoff is a risk factor for Toxoplasma gondii infection of southern sea otters (Enhydra lutris nereis). Int J Parasitol **32:**997–1006, 2002.
148. Miller AW, Reynolds AC, Sobrino C, et al: Shellfish face uncertain future in high CO2 world: influence of acidification on oyster larvae calcification and growth in estuaries. PLoS One **4:**e5661, 2009.
149. Miller WG, Adams LG, Ficht TA, et al: Brucella–induced abortions and infections in bottlenose dolphins **(**Tursiops truncatus**).** J Zoo Wildlife Med **30:**100–110, 1999.
150. Mollenhauer MA, Carter BJ, Peden-Adams MM, et al: Gene expression changes in bottlenose dolphin, Tursiops truncatus, skin cells following exposure to methylmercury (MeHg) or perfluorooctane sulfonate (PFOS). Aquat Toxicol **91**(1):10–18, 2009.
151. Montie EW, Fair PA, Bossart GD, et al: Cytochrome P4501A1 expression, polychlorinated biphenyls and hydroxylated metabolites, and adipocyte size of bottlenose dolphins from the Southeast United States. Aquat Toxicol **86**(3):397–412, 2008.
152. Montie EW. Pussini N, Schneider GE, et al: Neuroanatomy and volumes of brain structures of a live california sea lion (Zalophus californianus) from magnetic resonance images. Anat Rec **292:**1523–1547, 2009.
153. Montie EW, Reddy CM, Gebbink WA, et al: Organohalogen contaminants and metabolites in cerebrospinal fluid and cerebellum gray matter in short-beaked common dolphins and Atlantic white-sided dolphins from the western North Atlantic. Environ Pollut **157:**2345–2358, 2009.
154. Moore SE: Marine mammals as ecosystem sentinels. J Mammal **89:**534–540, 2008.
155. Moore SE: Long-term environmental change and marine mammals. *In:* Marine Mammal Research: Conservation Beyond Crisis, ed. JE Reynolds III, WF Perrin, RR Reeves, S Montgomery and TJ Ragen, pp. 137–147. Johns Hopkins University Press, Baltimore, MD, 2005.
156. Mori C, Morsey B, Levin M, et al: Effects of organochlorines, individually and in mixtures, on B-cell proliferation in marine mammals and mice. J Toxicol Environ Health A **71**(4):266–275, 2008.
157. Mos L, Morsey B, Jeffries SJ, et al: Chemical and biological pollution contribute to the immunological profiles of free-ranging harbour seals. Environm Toxicol Chem **25:**3110–3117, 2006.
158. Muñoz PM, García-Castrillo G, López-García P, et al: Isolation of Brucella species from a live-stranded striped dolphin (Stenella coeruleoalba) in Spain. Vet Rec **158:**450–451, 2006.
159. Murdoch ME, Reif JS, Mazzoil M, et al: Lobomycosis in bottlenose dolphins (Tursiops truncatus) from the Indian River Lagoon, Florida: estimation of prevalence, temporal trends, and spatial distribution. Eco Health **5**(3):289–297, 2008.
160. Newman SJ, Smith SA: Marine mammal neoplasia: a review. Vet Pathol **43**:865–880, 2006.
161. Nielsen O, Nielsen K, Stewart REA: Serological evidence of Brucella spp. Exposure in Atlantic walruses (Odobenus rosmarus rosmarus) and ringed seals (Phoca hispida) of Arctic Canada. Arctic **49:**383–386, 1996.
162. Nielsen O, Stewart REA, Nielsen K, et al: Serological survey of Brucella spp. antibodies in some marine mammals of North America. J Wildlife Dis **37:**89–100, 2001.
163. Nielsen O, Nielsen K, Braun R, et al: A comparison of four serologic assays in screening for Brucella exposure in Hawaiian monk seals. J Wildl Dis **41**(1):126–133, 2005.
164. Niño-Torres CA, Gardner SC, Zenteno-Savín T, et al: Organochlorine pesticides and polychlorinated biphenyls in California sea lions (Zalophus californianus californianus) from the Gulf of California, México. Arch Environ Contam Toxicol **56**(2):350–359, 2009.
165. Nollens H, Jacobson E, Gulland FMD, et al: Pathology and preliminary characterization of a parapoxvirus isolated from a California sea lion (Zalophus californianus). J Wildl Dis **42**(1):23–32, 2006.
166. Nollens HH, Wellehan JF, Saliki JT, et al: Characterization of a parainfluenza virus isolated from a bottlenose dolphin (Tursiops truncatus). Vet Microbiol **128**(3–4):231–242, 2008.
167. Norman SA, DiGiacomo RF, Gulland FM, et al: Risk factors for an outbreak of leptospirosis in California sea lions (Zalophus

Downloaded from vet.sagepub.com at FLORIDA ATLANTIC UNIV on May 17, 2011

californianus) in California, 2004. J Wildl Dis **44**(4):837–844, 2008.
168. O'Hara TM, Hoekstra PF, Hanns C, et al: Concentrations of selected persistent organochlorine contaminants in store-bought foods from northern Alaska. Int J Circumpolar Health **64:** 303–313, 2005.
169. Ohishi K, Zenitani R, Bando T, et al: Pathological and serological evidence of Brucella infection in baleen whales (Mysticeti) in the western North Pacific. Comp Immunol Microb **26:** 125–136, 2003.
170. Orvos DR, Versteeg DJ, Inauen J, et al: Aquatic toxicity of triclosan. Environ Toxicol Chem **21:**1338–1349, 2002.
171. O'Shea TJ: Environmental contaminants and marine mammals. *In:* Biology of Marine Mammals, ed. Reynolds JE, Rommel SA, pp. 485–563. Smithsonian Institution, Washington, DC, 1999.
172. O'Shea TJ, Bossart GD, Fournier M, et al: Conclusions and perspectives for the future. *In:* Toxicology of Marine Mammals, ed. Vos JG, Bossart GD, Fournier M and O'Shea T, pp. 595–613. Taylor & Francis, London, 2003.
173. O'Shea TJ, Tanabe S: Persistent ocean contaminants and marine mammals: a retrospective overview. *In:* Toxicology of Marine Mammals, ed. Vos JG, Bossart GD, Fournier M and O'Shea T, pp. 99–134. Taylor & Francis, London, 2003.
174. Perrett LL, Brew SD, Stack JA, et al: Experimental assessment of the pathogenicity of Brucella strains from marine mammals for pregnant sheep. Small Rumin Res **51:**221–228, 2004.
175. Porte C, Janer G, Lorusso LC, et al: Endocrine disruptors in marine organisms: approaches and perspectives. Comp Biochem Physiol C Toxicol Pharmacol **143**(3):303–315, 2006.
176. Prenger-Berninghoff E, Siebert U, Stede M, et al: Incidence of Brucella species in marine mammals of the German North Sea. Dis Aquat Organ **81**(1):65–71, 2008;.
177. Raga JA, Banyard A, Domingo M, et al: Dolphin morbillivirus epizootic resurgence, Mediterranean Sea. Emerg Infect Dis **14**(3):471–473, 2008.
178. Ramsdell JS, Muha N: Acute domoic acid poisoning in rats leads to a chronic syndrome of aggressive behavior and epilepsy. Fifth Symposium on Harmful Algae in the U.S. Ocean Shores, Washington, DC, 2009, p. 68.
179. Ramsdell JS: The molecular and integrative basis to domoic acid toxicity. *In:* Phycotoxins: Chemisty and Biochemistry, ed. Botana L, pp. 223–250. Blackwell, Ames, IA, 2007.
180. Ramsdell JS, Zabka TS: In utero domoic acid toxicity: a fetal basis to adult disease in the California sea lion (Zalophus californianus). Mar Drugs **6**(2):262–290, 2008.
181. Randolph SE: Perspectives on climate change impacts on infectious diseases. Ecology **90:**927–931, 2009.
182. Rector A, Bossart GD, Ghim SJ, et al: Characterization of a novel close-to-root papillomavirus from a Florida manatee by using multiply primed rolling-circle amplification: trichechus manatus latirostris papillomavirus type 1. J Virol **78:**12698–12702, 2004.
183. Rector A, Stevens H, Lacave G, et al: Genomic characterization of novel dolphin papillomaviruses provides indications for recombination within the Papillomaviridae. Virology **378:** 151–161, 2008.
184. Reddy ML, Dierauf LA, Gulland FMD: Marine mammals as sentinels of ocean health. *In:* Marine Mammal Medicine, ed. Dierauf L and Gulland F, pp. 3–13. CRC Press, Boca Raton, FL, 2001.
185. Rehtanz M, Ghim S-J, Rector A, et al: Isolation and characterization of the first American bottlenose dolphin papillomavirus: Tursiops truncatus papillomavirus type 2. J Gen Virol **87:**3559–3565, 2006.
186. Rehtanz M, Bossart GD, Doescher B, et al: Bottlenose dolphin (Tursiops truncatus) papillomaviruses: Vaccine antigen candidates and screening test development. Vet Microbiol. 2008. doi:10.1016/j.vetmic.2008.06.017.
187. Rehtanz M, Ghim S, McFee W, et al: Papillomavirus antibody prevalence in free-ranging and captive bottlenose dolphins (Tursiops truncatus). J Wildl Dis **46:**136–145, 2010.
188. Reif JS, Peden-Adams MM, Romano TA, et al: Immune dysfunction in Atlantic bottlenose dolphins (Tursiops truncatus) with lobomycosis. Med Mycol **4:**1–11, 2008.
189. Reif JS, Mazzoil M, McCulloch SD, et al: Lobomycosis in Atlantic bottlenose dolphins (Tursiops truncatus) from the Indian River Lagoon, Florida. J Am Vet Med Assoc **228:** 104–108, 2006.
190. Reijnders PJH: Reproductive failure in common seals feeding on fish from polluted coastal waters. Nature **324:**456–457, 1986.
191. Retamal P, Blank O, Abalos P, et al: Detection of anti-Brucella antibodies in pinnipeds from the Antarctic territory. Vet Rec **146:**166–167, 2000.
192. Rhyan JC, Spraker TR: Emergence of diseases from wildlife reservoirs. Vet Pathol **47**(1):34–39; 2010.
193. Robertson LW, Hansen LJ: PCBs: Recent Advances in Environmental Toxicology and Health Effects. University Press of Kentucky, Lexington, KY, 2001.
194. Ross HM, Foster G, Reid RJ, et al: Brucella species infection in sea-mammals. Vet Rec **134:**359–364, 1994.
195. Ross HM, Jahans KL, MacMillan AP, et al: Brucella species infection in North Sea seal and cetacean populations. Vet Rec **138:**647–648, 1996.
196. Ross P, De Swart RL, Addison R, et al: Contaminant-induced immunotoxicity in harbour seals: wildlife at risk? Toxicology **112:**157–169, 1996.
197. Ross PSR: The role of immunotoxic environmental contaminants in facilitating the emergence of infectious diseases in marine mammals. HERA **8:**277–292, 2002.
198. Rotstein DS, Burdett LG, McLellan W, et al: Lobomycosis in offshore bottlenose dolphins (Tursiops truncatus), North Carolina. Emerg Infect Dis **15**(4):588–590, 2009.
199. Rubin CH, Lanier A, Socha M, et al: Exposure to persistent organochlorines among Alaska Native women. Int J Circumpolar Health **60:**157–169, 2001.
200. Sandau CD, Ayotte P, Dewailly E, et al: Analysis of hydroxylated metabolites of PCBs (OH-PCBs) and other chlorinated phenolic compounds in whole blood from Canadian Inuit. Environ Health Perspect **108:**611–616, 2000.
201. Schaefer AM, Reif JS, Goldstein JD, et al: Serological evidence of exposure to selected pathogens in free-ranging Atlantic bottlenose dolphins (Tursiops truncatus) from the Indian River

Downloaded from vet.sagepub.com at FLORIDA ATLANTIC UNIV on May 17, 2011

Lagoon, Florida and Charleston, South Carolina. Aquatic Mammals **35:**163–170, 2009.
202. Schaefer AM, Goldstein JD, Reif JS, et al: Antibiotic-resistant organisms cultured from Atlantic bottlenose dolphins (Tursiops truncatus) inhabiting estuarine waters of Charleston, SC and Indian River Lagoon, FL. EcoHealth. 2009. doi:10.1007/s10393-009-0221-5.
203. Scholin CA, Gulland F, Doucette GJ, et al: Mortality of sea lions along the central California coast linked to a toxic diatom bloom. Nature **403**(6765):80–84, 2000.
204. Schulman FY, Lipscomb TP, Moffett D, et al: Histologic, immunohistochemical, and polymerase chain reaction studies of bottlenose dolphins from the 1987-1988 United States Atlantic coast epizootic. Vet Pathol **34:**288–295, 1997.
205. Silvagni PA, Lowenstine LJ, Spraker T, et al: Pathology of domoic acid toxicity in California sea lions (Zalophus californianus). Vet Pathol **42**(2):184–191, 2005.
206. Slenning BD: Global climate change and implications for disease emergence. Vet Path. **47:**28–33, 2010.
207. Sohn AH, Probert WS, Glaser CA, et al: Human neurobrucellosis with intracerebral granuloma caused by a marine mammal Brucella spp. Emerg Infect Dis **9:**485–488, 2003.
208. Stavros H-CW, Bossart GD, Hulsey TC, et al: Trace element concentrations in blood of free-ranging bottlenose dolphins (Tursiops truncatus): influence of age, sex and location. Mar Pollut Bull **56:**348–379, 2008.
209. Stavros H-CW, Bossart GD, Hulsey TC, et al: Trace element concentrations in skin of free-ranging bottlenose dolphins (Tursiops truncatus) from the southeast Atlantic coast. Sci Total Environ **388:**300–315, 2007.
210. Stein JE, Tilbury KL, Meador JP, et al: Ecotoxicological investigations of bottlenose dolphin (Tursiops truncatus) strandings: accumulation of persistent organic chemicals and metals. *In:* Toxicology of Marine Mammals, ed. Vos JG, Bossart GD, Fournier M and O'Shea T, pp. 458–85. Taylor & Francis, London, 2003.
211. Stoddard RA, Atwill ER, Gulland FMD, et al: Risk factors for infection with pathogenic and antimicrobial-resistant fecal bacteria in northern elephant seals in California. Public Health Rep **123:**360–370, 2008.
212. Stone DA: Predicted climate changes for the years to come and implications for disease impact studies. Rev Sci Tech **27:**319–330, 2008.
213. Tabuchi M, Veldhoen N, Dangerfield N, et al: PCB-related alteration of thyroid hormones and thyroid hormone receptor gene expression in free-ranging harbor seals (Phoca vitulina). Environ Health Perspect **114**(7):1024–1031, 2006.
214. Tachibana M, Watanabe K, Kim S, et al: Antibodies to Brucella spp. in Pacific bottlenose dolphins from the Solomon Islands. J Wildl Dis **42**(2):412–414, 2006.
215. Tanabe S, Iwata H, Tatsukawa R: Global contamination by persistent organochlorines and their ecotoxicological impact on marine mammals. Sci Total Environ **154:**163–177, 1994.
216. Tanabe S: Contamination and toxic effects of persistent endocrine disrupters in marine mammals and birds. Mar Pollut Bull **45:**69–77, 2002.
217. Taubenberger JK, Tsai MM, Atkin TJ, et al: Molecular genetic evidence of a novel morbillivirus in a long-finned pilot whale (Globicephalus melas). Emerg Infect Dis **6:**42–45, 2000.
218. Taylor LH, Latham SM, Woolhouse MEJ: Risk factors for human disease emergence. Phil Trans R Soc Lond B **356:**983–989, 2001.
219. Tiedeken JA, Ramsdell JS: DDT exposure of zebrafish embryos enhances seizure susceptibility: relationship to fetal p,p′-dde burden and domoic acid exposure of california sea lions. Environ Health Perspect **117:**68–73, 2009.
220. Trainer VL, Baden DE: High affinity binding of red tide neurotoxins to marine mammal brain. Aquatic Toxicol **46**(2):139–148, 1999.
221. Tryland M, Kleivane L, Alfredson A, et al: Evidence of Brucella infection in marine mammals in the North Atlantic Ocean. Vet Rec **144:**588–592, 1999.
222. Tuerk KJS, Kucklick R, Becker PR, et al: Persistent organic pollutants in two dolphin species with focus on toxaphene and polybrominated diphenyl ethers. Environmental Science and Technology **39:**692–698, 2005.
223. Van Bressem M-F, Visser IG, Van De Bildt MG, et al: Morbillivirus infection in Mediterranean striped dolphins (Stenella coeruleoalba). Vet Rec **129:**471–472, 1991.
224. Van Bressem M-F, van Waerebeek K, Raga JA, et al: Serological evidence of Brucella species in odontocetes from the south Pacific and the Mediterranean. Vet Rec **148:**657–661, 2001.
225. Van Bressem M-F, Waerebeek KV, Jepson PD, et al: An insight into the epidemiology of dolphin morbillivirus worldwide. Vet Microbiol **81**(4):287–304, 2001.
226. Van Bressem MF, Raga JA, Di Guardo G, et al: Emerging infectious diseases in cetaceans worldwide and the possible role of environmental stressors. Dis Aquat Organ **86**(2):143–157, 2009.
227. Van Dolah FM, Douchette GJ, Gulland F, et al: Impacts of algal toxins on marine mammals. *In:* Toxicology of Marine Mammals, ed. Vos JG, Bossart GD, Fournier M and O'Shea T, pp. 247–270. Taylor & Francis, London, 2003.
228. Vedros NA, Smith AW, Schonewa J, et al: Leptospirosis epizootic among California sea lions. Science **172:**1250–1251, 1971.
229. Veldhoen N, Skirrow RC, Osachoff H, et al: The bactericidal agent triclosan modulates thyroid-associated gene expression and disrupts postembryonic anuran development. Aquatic Toxicol **80:**217–227, 2006.
230. 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**(3):397–405, 2008.
231. Vetter W, Turek C, Marsh G, et al: Identification and quantification of new polybrominated dimethoxybiphenyls (PBDMBs) in marine mammals from Australia. Chemosphere **73**(4):580–586, 2008.
232. Visser IKG, Van Bressem M-F, de Swart RL, et al: Characterization of morbilliviruses isolated from dolphins and porpoises in Europe. J Gen Virol **74:**631–641, 1993.
233. Walsh CJ, Luer CA, Noyes DR: Effects of environmental stressors on lymphocyte proliferation in Florida manatees,

Downloaded from vet.sagepub.com at FLORIDA ATLANTIC UNIV on May 17, 2011

Trichechus manatus latirostris. Veterinary Immunology and Immunopathology **103:**247–256, 2005.

234. Wells RS, Rhinehart HL, Hansen LJ, et al: Bottlenose dolphins as marine ecosystem sentinels: developing a health monitoring system. EcoHealth **1:**246–254, 2004.
235. Whatmore AM, Dawson C, Groussaud P, et al: A marine mammal Brucella genotype associated with zoonotic infection. Emerg Inf Dis **14**:517–518, 2008.
236. Woshner VM, O'Hara TM, Bratton GR, et al: Concentrations and interactions of selected essential and non-essential elements in ringed seals and polar bears of Arctic Alaska. J Wildl Dis **37:**711–721, 2001.
237. Woshner V, Knott K, Wells R, et al: Mercury and selenium in blood and epidermis of bottlenose dolphins (Tursiops truncatus) from Sarasota Bay, FL: interaction and relevance to life history and hematologic parameters. EcoHealth **5**(3): 360–370, 2008.
238. Ylitalo, GM, Stein JE, Hom T, et al: The role of organochlorines in cancer-associated mortality in California sea lions (Zalophus californianus). Mar Pollut Bull **50:**30–39, 2005.
239. Zabka TS, Goldstein T, Cross C, et al: Characterization of a degenerative cardiomyopathy associated with domoic acid toxicity in California sea lions (Zalophus californianus). Vet Pathol **46**(1):105–119, 2009.
240. Zegers BN, Mets A, Van Bommel R, et al: Levels of hexabromocyclododecane in harbor porpoises and common dolphins from western European seas, with evidence for stereoisomer-specific biotransformation by cytochrome p450. Environ Sci Technol **39**(7):2095–2100, 2005.

Downloaded from vet.sagepub.com at FLORIDA ATLANTIC UNIV on May 17, 2011