Pilot Pathogen Prioritization Survey Results for Cetaceans

Stephanie Venn-Watson, DVM, MPH[1], Andy Stamper, DVM[2], Working Group on Marine Mammal Unusual Mortality Events[3], and Teri Rowles, DVM, PhD[4]

1 Epitracker, San Diego CA
2 Disney, Orlando Florida
3 Appointed working group of external experts
4 NOAA, National Marine Fisheries Service

EXECUTIVE SUMMARY

Numerous microbes have been isolated from and reported in cetaceans. These reports have varied from the isolation of a bacterial species once in one animal to the association of a virus to numerous mass mortality events. During 2009-2010, the Working Group for Marine Mammal Unusual Mortality Events undertook the task of prioritizing cetacean pathogens with respect to the following factors:

- Likelihood of marine mammal exposure to the pathogen
- If exposed, likelihood of marine mammal illness
- If exposed, likelihood of marine mammal death
- If exposed, likelihood of marine mammal epizootic Public health implications: zoonotic, reportable in the U.S., or emerging/reemerging diseases among humans

A total of 76 pathogens had been identified and published in marine mammals. Raw risk scores and weighted risk scores (incorporating survey participants' confidence in their risk ratings), were used to prioritize pathogens by large cetaceans and small cetaceans. Adequate data were only available to prioritize pathogens for small cetaceans. The ten highest priority pathogens among small cetaceans were morbillivirus, parapoxvirus, *Brucella* spp. anisakis, calicivirus, herpesvirus, nasitrema, *Clostridium* spp., and toxigenic *Escherichia coli.*

Of the 76 pathogens included in the survey, 27 (35.5%) were zoonotic, and 12 (15.8%) and 20 (26.3%) were associated with reportable and emerging/reemerging human diseases in the United States, respectively.

We conclude that marine mammals, including cetaceans, are important and underutilized sentinels of zoonotic, reportable, and emerging diseases among humans. Routine surveillance of baselines and changes in infectious diseases among marine mammals may facilitate conservation efforts, target medical treatments for rehabilitation facilities, reveal movement of terrestrial pathogens to the marine environment, and enable prediction of ocean-based emerging diseases among humans. As such, marine mammals should be included as important wildlife species to monitor under the growing One Health movement.

BACKGROUND

Numerous microbes have been isolated from and reported in marine mammals. These reports have varied from the isolation of a bacterial species once in one animal to the association of a virus to numerous mass mortality events. During 2009-2010, the Working Group for Marine Mammal Unusual Mortality Events (WGMMUME) undertook the task of prioritizing marine mammal pathogens.

METHODOLOGY

Literature Review

The WGMMUME reviewed journal publications and conference abstracts related to pathogens isolated from marine mammals. Information from these publications was categorized by pathogen category (bacterium, fungus, parasite, protozoan, or virus) and large cetacean or small cetacean. Further, information about each pathogen and marine

mammal group was divided into evidence of marine mammal exposure, morbidity (illness), mortality (death), and epizootics (outbreaks). To assess the relevance of marine mammal pathogens to public health, the pathogen list was compared to the Centers for Disease Control's lists of important zoonoses, U.S. reportable diseases, and emerging/reemerging infectious diseases.

Prioritization of Pathogens

Questionnaires focusing on a specific pathogen were developed. Each questionnaire had general information (pathogen, marine mammal group, pathogen category, and documented location) and existing evidence related to marine mammal exposure, morbidity, mortality, and epizootics associated with the pathogen (Appendix B).

Subject matter experts (SMEs) in pathogens and cetaceans were identified and sent an electronic packet of questionnaires. After reviewing the evidence provided, SMEs rated each pathogen-marine mammal pair by the risk of exposure of marine mammals to the pathogen. SMEs then rated the risk of morbidity, mortality, and epizootic if the given marine mammal group were exposed to the pathogen. Risks were rated as 'none', 'low', 'moderate', and 'high'.

There was great variation in the amount of evidence available by pathogen and large and small cetaceans. As such, SMEs provided confidence ratings (none, low, moderate, and high) to each of their risk scores. For example, if an SME rated the risk of small cetacean exposure to morbillivirus as 'High', but felt that more evidence was needed for U.S. West coast animals, they may have rated their confidence in their risk score as 'Moderate'.

Risk scores were translated as follows: None=0, Low=1, Moderate=2, High=3. Due to the importance of exposure to a given pathogen before it could be associated with morbidity, mortality, or an epizootic, exposure risk ratings were doubled. Confidence scores were translated as follows: None=0.25, Low=0.5, Moderate=0.75, High=1.0. Thus, the *Raw Risk Score (RRS) = (Risk of Exposure x 2) + Risk of Morbidity + Risk of Mortality + Risk of Epizootic*. The *Weighted Risk Score (WRS), incorporating confidence levels = (Risk of Exposure x Exposure Confidence) + (Risk of Morbidity x Exposure Confidence) + (Risk of Mortality x Exposure Confidence) + (Risk of Epizootic x Exposure Confidence)*. Given these algorithms, the highest possible score for either the RRS or WRS was 15. The lowest was 0.

RESULTS

Literature Review
A total of 76 pathogens isolated from marine mammals were identified in the literature and included in the prioritization process (Tables 1-5). This list included 26 (34.2%) bacteria, 12 (15.8%) fungi, 15 (19.7%) parasites, 7 (9.2%) protozoa, and 16 (21.1%) viruses (Appendix A). Nineteen (25%) pathogens were identified in large cetaceans, 40 (52.6%) in small cetaceans, 40 (52.6%) in otariids, 53 (69.7%) in phocids, and 17 (22.4%) in lutrinae.

Prioritization of Pathogens
Only small cetaceans had enough evidence for SMEs to comfortably assign risk and confidence ratings. The ten highest prioritized pathogens of small cetaceans, in order from highest to lowest, were morbillivirus, parapoxvirus, *Brucella* spp. anisakis, calicivirus, herpesvirus, nasitrema, *Clostridium* spp., and toxigenic *Escherichia coli*.

Relevance to Public Health
Of 76 pathogens included in the survey, 27 (35.5%) were zoonotic, and 12 (15.8%) and 20 (26.3%) were associated with reportable and emerging/reemerging human diseases in the United States, respectively. Marine mammal pathogens that were both reportable and emerging/reemerging human diseases in the United States were *Listeria monocytogenes*, *Mycobacterium tuberculosis*, *Salmonella* spp., *Shigella* spp., Group B *Streptococcus*, *Vibrio cholera*, *Cryptococcus* spp., rhabdovirus, and West Nile virus.

DISCUSSION

We report 76 pathogens associated with marine mammals, including cetaceans. Most of these pathogens have been reported in terrestrial animals, including humans. Our prioritized list of marine mammal pathogens demonstrates that the ocean and land indeed share common bacteria, fungi, parasites, and viruses. Further, many of these pathogens are associated with common diseases in marine and terrestrial mammals. While molecular diagnostics

have greatly improved the ability to find microbes in marine mammal samples, there continues to be difficulties in assessing the impact of pathogens on both individual animal health and population stability.

One barrier to better understanding cetacean pathogens is the difficulty of diagnosing the cause of disease in marine mammals. The following three general marine mammal populations have been used to detect pathogens: stranded wild animals found dead, found alive, and/or temporarily housed in rehabilitation facilities; free-ranging wild animals involved in health assessment projects; and managed marine mammal collections housed at academic institutions, marine mammal parks and aquaria, or the U.S. Navy. Dead, stranded animals are rarely found fresh, and natural decay often hinders the ability to conduct useful microbiological or histopathological workup. When pathogens are detected in tissues, it is often unknown if the pathogen was associated with a chronic or acute infection, underlying or immediate cause of death, or simply an incidental finding. Thus, there is a need to better identify pathogens from live or fresh marine mammals, and to pair these results with health or illness. Population baseline exposures to and infections with would greatly aid investigators to interpret diagnostic findings during unusual mortality events. There is also a need for the greater community studying cetacean populations to recognize infectious disease as a possible significant cause of mortality. To date, most efforts investigating cetacean population health have not included the role of infectious disease. Finally, if opportunistic or secondary infections are identified in cetaceans, they can be helpful indicators that underlying causes are present (e.g., contaminants or primary viral disease)

Pathogens may have greater negative impact on specific cetacean populations, including areas in which there are isolated, small populations of animals, limited gene pool s; crowding of animals which can lead to a higher risk of infectious disease spread; nutritional challenges; and any other factor that may increase the chance of disease transmission or host susceptibility.

There has been difficulty identifying pathogens while epizootics are occurring. As such, the community may benefit from syndrome-based surveillance to track syndromes in cetaceans over time. Given the high prevalence of cetacean pathogens that are zoonotic, rehabilitation centers should have infection disease control plans. Further, there may be a need to discuss whether or not a rehabilitated animal with an infectious pathogen should be released back to the wild population.

Finally, common pathogens reported among cetaceans and humans indicate that cetaceans can be important sentinels of changes in pathogens globally. Monitoring baselines and changes in pathogens and associated cetacean health over long periods of time may provide important clues for emerging diseases in humans, serve a role in the One Health initiative, and be an indicator of the impact of human and agricultural waste into the ocean.

Table 1. Bacterial Species Reported in Marine Mammals

Pathogen	**Zoonotic**	**Large Cetacean**	**Small Cetacean**	**Otariid**	**Phocid**	**Sea Otter**
Arcanobacterium phocae			x	x	x	x
Bartonella henselae	x		x			
Brucella spp.	x*	x	x	x		
Campylobacter spp.	x+				x	
Chlamydiophilia psittaciae	x				x	
Clostridium spp.			x	x	x	
Coxiella burnetii	x*				x	
Dermatophilus congolensis			x	x		
Edwardsiella tarda		x	x	x		
Eryseipelothrix rhusiopathiae	x	x	x		x	
Escherichia coli (toxigenic)	x+		x	x	x	
Helicobacter spp.			x	x	x	
Klebsiella spp.				x	x	
Leptospira interrogans serovars	x+			x	x	x
Listeria spp.	x*+			x	x	
Mycobacterium spp.	x*+			x	x	
Mycoplasma spp.				x	x	
Mollicutes (*Mycoplasma*, *Ureoplasma*, *Acholeplasma*)		x	x		x	
Nocardia spp.		x	x		x	
Pasteurella spp.	x			X	x	x
Pseudomonas aeruginosa			x	X		
Salmonella spp.	x*+		x	X	x	x
Shigella spp.	x*+				x	
Staphylococcus aureus	x+		x		x	
Streptococcus spp.	x*+	x	x		x	x
Vibrio spp.	x*+		x		x	x

* = reportable human pathogen in the United States. Source: CDC, 2010
+ = emerging or reemerging human pathogen in the United States. Source: CDC, 2010

Table 2. Fungal Species Isolated from Marine Mammals

Fungal Species	**Zoonotic**	**Large Cetacean**	**Small Cetacean**	**Otariid**	**Phocid**	**Sea Otter**
Aspergillus spp.			x	x	x	
Blastomyces dermatitidis				x		
Candida spp.		x	x	x	x	
Coccidiodes immitis	x		x	x		x
Cryptococcus spp.	x*+		x			x
Fusarium spp.		x	x	x	x	
Histoplasma capsulatum	x+		x	x	x	x
Lacazia loboi			x			
Malassezia spp.				x	x	
Microsporum spp.					x	
Trichophyton spp.			x	x	x	
Zygomyces spp.		x	x		x	

* = reportable human pathogen in the United States. Source: CDC, 2010
+ = emerging or reemerging human pathogen in the United States. Source: CDC, 2010

Table 3. Parasite Species Isolated from Marine Mammals

Parasite Species	**Zoonotic**	**Large Cetacean**	**Small Cetacean**	**Otariid**	**Phocid**	**Sea Otter**
Acanthocephalans spp., *Cornysoma* spp., *Bolbosoma* spp., *Falsifilicollis* spp.					x	x
Anisakids, Anisakis, Pseudoterranova, Contracaecum	x		x	x	x	
Cestodes, Diphylobothrium			x			
Crassicauda spp.		x	x			
Dipetalonma spirocauda, Dirofilaria immitis					x	
Lice, *Anoplura* spp.		x		x	x	
Mites, *Demodex* spp., *Sarcoptes* spp.				x	x	x
Nasal mites, *Halarachne, Orthohalarachne*				x	x	x
Nasitrema spp.		x	x			
Otostrongylus circumlitis				x	x	
Parafilaroides decorus				x	x	
Stenurus spp.			x			
Trichonella native	x*				x	
Uncinaria spp.				x	x	
Zalophotrema				X		

* = reportable human pathogen in the United States. Source: CDC, 2010
+ = emerging or reemerging human pathogen in the United States. Source: CDC, 2010

Table 4. Protozoa Species Isolated from Marine Mammals

Protozoa Species	**Zoonotic**	**Large Cetacean**	**Small Cetacean**	**Otariid**	**Phocid**	**Sea Otter**
Cryptospordium parvum	x+			x	x	
Eimeria phocae					x	
Giardia lamblia	x			x	x	
Karyoikes cetarius		x	x			
Neospora caninum						
Sarcocystis spp.		x	x	x	x	x
Toxoplasma gondii	x	x	x	x	x	x

* = reportable human pathogen in the United States. Source: CDC, 2010
+ = emerging or reemerging human pathogen in the United States. Source: CDC, 2010

Table 5. Virus Species Isolated from Marine Mammals

Virus Species	**Zoonotic**	**Large Cetacean**	**Small Cetacean**	**Otariid**	**Phocid**	**Sea Otter**
Adenovirus				x		
Calicivirus		x	x	x	x	
Coronavirus						
Eastern Equine Encephalitis virus	x*					
Hepadenovirus		x	x			
Hepatitis A					x	
Herpesvirus		x	x	x	x	x
Influenza A and B	x+				x	
Morbillivirus		x	x		x	x
Papillomavirus			x		x	
Parapoxvirus			x	x	x	
Rabies (rhabdovirus)	x*				x	
Rhabdinovirus	x*+			x		
St. Louis Encephalitis virus						
West Nile virus	x*+				X	
Western Equine Encephalitis	x*					

* = reportable human pathogen in the United States. Source: CDC, 2010
+ = emerging or reemerging human pathogen in the United States. Source: CDC, 2010

Table 6. Prioritized List of Small Cetacean Pathogens. Mean pathogen risk scores incorporating risk of exposure, morbidity, mortality, and epizootic potential, as determined by a panel of subject matter experts.

Pathogen	Raw Risk Score	Raw Confidence Score	Weighted Risk Score
Morbillivirus	11.7	3.5	10.3
Parapoxvirus	11	3.8	10.6
Brucella spp.	9.8	3.6	8.8
Anisakis	9.2	3.5	7.9
Calicivirus	9	3.7	8.2
Herpesvirus	9	3.4	7.8
Nasitrema	8.8	3.4	7.6
Clostridium spp.	8.7	3.8	8.4
Stenurus spp.	8.6	3.4	7.6
Escherichia coli	8.3	3.5	7.4
Papillomavirus	8.3	3.6	7.4
Cestodes	7.6	3.6	6.8
Aspergillus spp.	7.6	3.6	6.6
Vibrio spp.	7.5	3.8	7.1
Candida spp.	7.4	3.8	6.9
Cryptocooccus spp.	7.4	3.6	6.8
Crassicauda spp.	7.4	3.4	6.2
Toxoplasma gondii	7.3	3.6	6.4
Pseudomonas spp.	7.3	3.4	6
Zygomyces	7.2	3.2	5.3
Lacazia loboi	6.8	3.7	6.2
Edwardsiella tarda	6.5	3.6	5.9
Erysipelothrix rhusiopathiae	6.5	3.6	5.8
Staphylococcus spp.	6.5	3.6	5.7
Helicobacter spp.	6.5	3.6	5.5
Mycoplasma	6.3	3.3	5.2
Salmonella spp.	6.3	3.3	4.9
Hepadenovirus	6.3	3	4.4
Histoplasma capsulaturm	6	3.5	5.1
Karyoikes cetarius	6	3.6	5.1
Arcanobacterium spp.	6	3.2	4.5
Coccidiodes immitis	5.8	3.4	4.8
Sarcocystis spp.	5.8	3.4	4.8
Nocardia spp.	5.8	3.4	4.6
Fusarium spp.	5.8	3.3	4.5
Bartonella henselae	4.7	3.3	3.7
Trichophyton	4.6	3.6	3.9
Dermatophilus congolensis	4	3.3	3

HIGH PRIORITY PATHOGENS: SYNDROMES, LABORATORY DIAGNOSIS, TREATMENT, AND INFECTION CONTROL – Next Steps

Pathogen	**Pathogen category**	**Marine mammal groups**	**Geographic locations**	**Organ systems affected**	**Zoonotic**	**Laboratory diagnosis**	**Treatment**	**Disinfection**
Adenovirus	Virus			G +/-B,C,D	Unknown			
Brucella species	Bacterium			F +/- A,D,G	Yes			
Calicivirus	Virus			B, C	Yes			
*Coccidioides immitis**	Fungus			F, G	Yes			
*Coxiella burnetii**	Bacterium			A,C,F,G	Yes			
*Cryptococcus gatii**	Fungus			G	Yes			
Eastern equine encephalitis virus	Virus			C,D	Yes			
Herpesvirus	Virus			B	No			
Influenza A or B	Virus			G, C	Yes			
Klebsiella species	Bacterium			B, D, G	Yes			
Leptospira interrogans	Bacterium			E +/- B, C, D, F, G	Yes			
Morbillivirus	Virus		Global	G +/- D	No			
Mycobacterium species	Bacterium			G	Yes			
Otostrongylus	Parasite			G	No			
Parapoxvirus	Virus			B	No			
Pasteurella species	Bacterium			G	Yes			
Pseudomonas species	Bacterium			G, B	Yes			
Rhabdovirus	Virus			D	Yes			
Salmonella species	Bacterium			C	Yes			
Sarcocystis	Protozoan			C, D, G				
Streptococcus species	Bacterium				Yes			
Toxoplasma gondii	Protozoan			D	Yes			
Uncinaria	Parasite			C	No			
West nile virus*	Virus			D+/-B,C	Yes			

Organ systems typically affected in terrestrial mammals: A=Cardiac, B=Cutaneous, C=Gastrointestinal, D=Neurological, E=Renal, F=Respiratory