Emerging Diseases in Marine Mammals: from Dolphins to Manatees

Exposures to viruses, pollutants may lead to diseases, sometimes involving immune dysfunctions, among marine mammals

Gregory D. Bossart

During the past two decades, 30 diseases that were all new to human medicine emerged, while other long-recognized diseases such as malaria, cholera, and tuberculosis resurged at a magnitude not seen in developed countries since the 1850s. Similarly, apparently emerging and resurging diseases are also affecting marine mammals, often showing complex pathogenesis patterns and sometimes involving immunologic dysfunction.

These trends carry important zoonotic implications, according to those veterinarians who are helping to evaluate disease impact on individual marine mammals, populations, and the ecosystems in which they reside. Importantly, these phenomena could signify a broad environmental distress syndrome, whereby human activities trigger ecologic and climatic changes that foster new and reemerging, opportunistic pathogens affecting both terrestrial and marine mammals. Newly described or reemerging disease agents or diseases affecting marine mammals include various papillomaviruses, dolphin poxvirus, and other viral infections; lobomycosis; various neoplastic diseases; algal bloom biointoxications; manatee cold stress syndrome; and the idiopathic cardiomyopathy of pygmy and dwarf sperm whales.

A Range of Infectious and Neoplastic Diseases Affecting Marine Mammals

Rates of neoplasia, particularly malignant neoplasia, steadily increased among several marine mammal species during the past two decades. In this same period, investigators also documented several complex diseases involving emerging infectious agents, some with neoplastic components. For example, approximately 17% of sexually mature stranded California sea lions (*Zalophus californianus*) have a recently described urogenital cancer, which is associated with a novel herpesvirus along with exposure to persistent chemical contaminants such as polychlorinated biphenyls (PCBs) and DDT. Inbred sea lions and those with a specific MHC genotype are more likely to develop this form of urogenital cancer.

Similarly, investigators are finding lingual papillomas (Fig. 1), squamous cell carcinomas, and genital papillomas (Fig. 2) in both free-ranging and captive Atlantic bottlenose dolphins (*Tursiops truncatus*). In some cases, individual dolphins have multiple tumors of mixed histologic type, consisting of papillomas and squamous cell carcinomas, consistent with malignant transformation of the benign papillomatous lesions. Pathologic evidence suggests that these tumors are associated with a novel gammaherpesvirus and newly sequenced dolphin papillomavirus (TtPV-2). Moreover, this disease,

Summary

- Newly described and resurging diseases suggest a broad environmental distress syndrome, triggered in part by human activities.
- Prevalence of neoplastic disease among marine mammals rose during the past two decades along with the emergence of infectious agents that may be associated with these neoplasms.
- Increases in anthropogenic or natural toxins (from algal blooms) in coastal habitats are of concern not only for marine mammals but also for humans.
- Tracking marine organisms provides a way of evaluating aquatic ecosystems and identifying damaging environmental trends.

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which might be sexually transmitted, is associated with immunologic dysfunction. Along parts of the Florida coast, these tumors are occurring at epidemic rates.

The Florida manatee (*Trichechus manatus latirostris*) is one of the most endangered marine mammals in American coastal waters. Naturally resistant to infectious disease, the manatee immune system appears highly developed to protect it against the harsh marine environment and the effects of human-related injury. The first viral disease associated with cutaneous papillomatosis was recently described in Florida manatees. Intriguingly, the cutaneous tumors were also associated with a novel, newly sequenced manatee papillomavirus (TmPV-1) (Fig. 3). Several observations suggest that papillomatosis is associated with immunologic dysfunction.

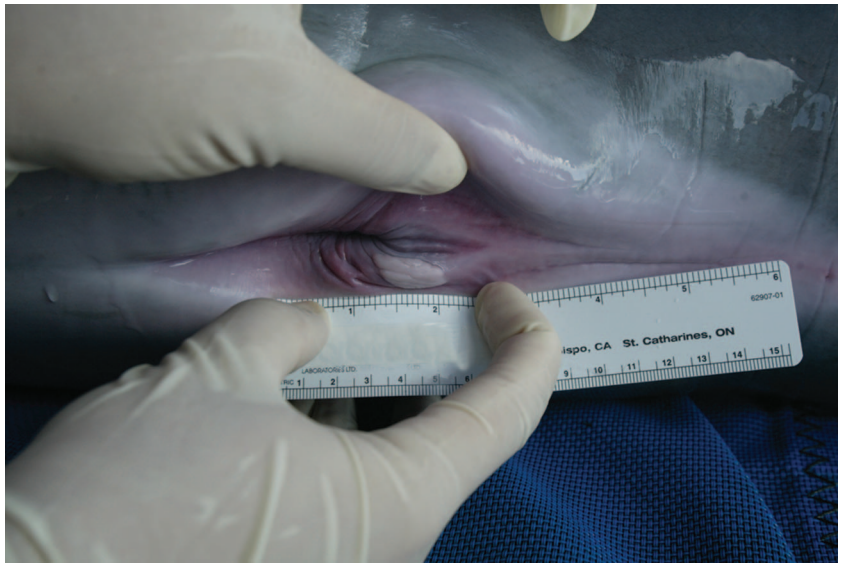
Meanwhile, toxoplasmosis, which sometimes is fatal for humans, is now a major cause of mortality among southern sea otters *(Enhydra lutris nereis*). As predators that consume some of the same foods as do humans, otters are sentinels for pathogenic protozoans, providing crucial information about the flow of this terrestrial parasite through the coastal ecosystem and the emergence of disease at the interface between wildlife, domestic animals, and humans. The protozoal disease causes convulsions, severe depression, and death in otters. Although many animals, including birds and rodents, can serve as intermediate hosts for *Toxoplasma gondii*, cats are the only animals known to shed eggs of this parasite in their feces. *T. gondii* infects about 52% of beach-cast sea otters and 38% of live sea otters, according to a recent seroprevalence analysis along the California coast.

We recently reported the emergence of lobomycosis in epidemic proportions among free-ranging bottlenose dolphins along the Atlantic coast of Florida (Fig. 4). Lobomycosis is a rare chronic mycotic disease affecting the skin and subcutaneous tissues that is caused by the yeast-like organism *Lacazia loboi* (formerly *Loboa loboi*), whose only other known host is humans. Because this organism has not been cultured, diagnosis depends

FIGURE 1

A newly documented oral sessile papilloma in a free-ranging Atlantic bottlenose dolphin discovered as part of a dolphin health assessment program in Florida.

FIGURE 2



A novel genital sessile papilloma in a free-ranging Atlantic bottlenose dolphin discovered as part of a dolphin health assessment program in Florida.

Love of the Sea Leads to a Lifelong Interest in the Health of Its Creatures

Gregory Bossart grew up near Pittsburgh, Pa., an area crisscrossed by rivers. Despite the rivers, he became fascinated with the ocean and its creatures, sometime after his first glimpse, when four years old, of a Delaware beach. He remembers climbing over sand dunes and seeing the great expanse of water. "I got hooked on the ocean when I was little," he says. "The oceans are a mystery. They are one of the last unexplored areas of this planet." He also developed a passion for wildlife during his childhood. He brought home one exotic "pet" after another. "My poor mother endured all of these wild animals in our home—raccoons, all kinds of snakes, including a boa constrictor," he recalls. "You name it, we had it."

Now a wildlife veterinarian and pathologist, Bossart, 55, spent the past 28 years working in marine mammal and avian medicine, focusing on wildlife pathology. "It was the animal connection that steered me to veterinary medicine, and once I got into veterinary medicine, that steered me to the oceans again," he says.

Currently, he is senior scientist, marine mammal veterinarian, and head of pathology at Harbor Branch Oceanographic Institution in Ft. Pierce, Fla. He also is an adjunct professor in the department of pathology at the University of Miami School of Medicine, affiliate professor at Florida Atlantic University, and a member of the graduate faculty at the Medical University of South Carolina.

Bossart received his doctorate in veterinary medicine from the University of Pennsylvania in 1978. From 1981–1985, he was a comparative pathology resident and National Institutes of Health fellow in the department of pathology at the University of Miami School of Medicine. In 1995, he completed his Ph.D. in immunology at Florida International University. His recent research has documented resurging and emerging diseases in manatees, whales, dolphins, and birds. He helped to characterize the first viral disease in manatees, and developed the first immunohistochemical technique for diagnosing brevetoxicosis in marine mammals and birds. He is intensely interested in the concept of emerging diseases.

"We have a good template in human medicine," Bossart says. "Now we are seeing the same pattern in the oceans, particularly in marine mammals. I think it reflects part of the environmental distress syndrome. Man has created opportunities for pathogens

on identifying characteristic yeast-like cells in tissue or exudates from affected dolphins. The reasons for the emergence of this rare disorder are unclear, but data indicate that the disease may be associated with an immunosuppressive co-factor. Emerging diseases of marine mammals are particularly sensitive to environmental perturbations, whether of anthropogenic or natural origins. Thus these dolphins may serve as a sentinel species for a broader public health hazard. Available evidence suggests that lobomycosis may be transferred from infected animals to people. The high prevalence of lobomycosis in a dolphin population in a localized Florida coastal region, which is used extensively for recreational purposes, raises concerns for zoonotic or common source transmission.

Synthetic Toxins, Pollutants May Damage the Health of Coastal Marine Mammals

Coastal ecosystem pollutants affect several species directly, including bottlenose dolphins, polar bears (*Ursus maritimus*), and bowhead whales (*Balaena mysticetus*). Further, when organohalogens and heavy metals accumulate in tissues of polar bears and bowhead whales, contaminant tissue levels may reflect Arctic Ocean health problems more broadly, including among human residents of Alaska, many of whom depend upon and consume local marine products.

Similar trends are observed in other coastal habitats. For instance, bottlenose dolphins along the eastern United States and Gulf of Mexico often are year-round residents in coastal waters where human industrial, agricultural, and recreational activities are plentiful. Elevated organohalogen compounds are found in such dolphins, including PCBs, organochlorine pesticides, and polybrominated diphenyl ethers (PBDEs) in blubber, and perfluoroalkyl compounds (PFCs) in liver. Between 2003 and 2005, PFC levels in free-ranging dolphin tissues from a health assessment study increased by 1.3- to 2.3-fold.

The fat stores of apex predators such as dolphins can accumulate high levels of organic li-

to emerge. Ecologic and climactic changes associated with human activities are encouraging the selection of new pathogens. We use these animals as sentinels for human health."

Bossart, a medical consultant to marine mammal facilities all over the world, also serves as medical director of the Falcon Batchelor Bird of Prey Center at the Miami Museum of Science, where injured birds of prey are sometimes rehabilitated and released. "That's where I got my education in releasing wild animals," he says. However, this topic evokes a strong reaction in him. "We need to understand what our actions mean to the animal—not to ourselves," he says. "Releasing a wild animal back to the wild is a very complex process. First of all, the animal needs to be healthy. Also, the animal has to be behaviorally acceptable as a release candidate."

For example, release criteria were never acceptable for Keiko, the orca whale featured in the 1993 film *Free Willy*. Public clamor and organizational agendas led to Keiko being released, but the animal died alone in the wild after seeking the attention of humans to whom he had become so accustomed. Bossart, who opposed Keiko's release from the beginning, was studying a newly described papilloma virus that afflicted the whale. "Every little kid who believes in Hollywood thought he was releasable, and he was not," Bossart says. "A killer whale is a very social animal. He has to be accepted by other killer whales. Other whales didn't want him. Keiko was like a big golden retriever puppy. He would come over, put his head in your lap, and want his tongue scratched. He was not a candidate for release."

Bossart cites another case involving an orphaned manatee that was raised by humans and then released in Florida. "We put a radio transmitter in her and let her go," he recalls. Manatees typically live in coastal waterways or rivers, not in the ocean. But the device tracked the manatee in several ocean locations, not moving toward the coast. Experts had her recaptured and sent to an oceanarium in Florida. "She was in the Gulf Stream," Bossart says. "She had no clue what she was supposed to do. We owe it to animals to be sure that our agendas don't get in the way of what is best for them."

Bossart and his wife, a former trainer of killer whales, live in Vero Beach with their two daughters, one age four and one six months, a dog, four geese, three cats and two macaws. Despite having "no time for hobbies," he says, "I like to take my family to the beach."

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pophilic toxins. During periods of physiologic or pathologic demands, including fasting, starvation, lactation, or other metabolically intensive activity, stored blubber lipids are mobilized, potentially redistributing chemicals such as PCBs and PFCs. Any increases in these environmental toxins are of concern not only for dolphin populations but also for humans living in coastal regions who may become exposed to those toxins.

Harmful Algal Blooms

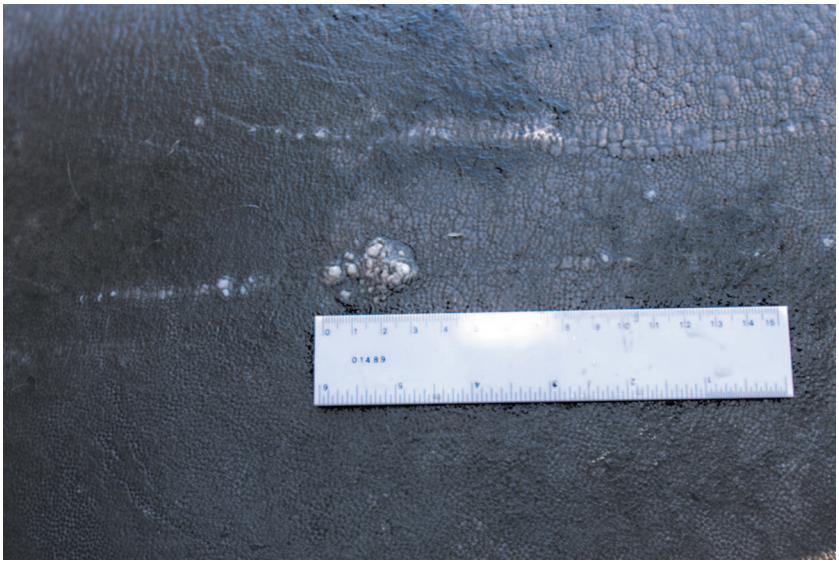
Harmful algal blooms (HABs) produce potent neurotoxins that may lead to mass die-offs of marine mammals such as dolphins, sea lions, and manatees. Moreover, some HAB-associated biotoxins affect human health, including brevetoxins that cause neurotoxic shellfish poisoning, saxitoxins that cause paralytic shellfish poisoning, okadaic acid that causes diarrhea, and domoic acid that is an amnesic agent.

Some marine mammal species prove to be good sentinels for the public health effects of HABs. For instance, several recent epizootics involving endangered Florida manatees and Atlantic bottlenose dolphins were associated with brevetoxins, which are produced by the dinoflagellate *Karenia brevis* that gives rise to Florida red tides. Brevetoxins kill large numbers of fish and cause intoxication in humans who ingest brevetoxin-contaminated, filter-feeding shellfish or inhale toxic aerosols.

In marine mammals, the pathogenesis of brevetoxicosis is suspected to involve inhalation of toxins by manatees or ingestion of toxin-containing foods by both manatees and bottlenose dolphins. Recent data indicate that manatees and bottlenose dolphins may also encounter brevetoxins carried in seagrasses or by fish species, thus delaying that exposure or distancing it from the initial source. Thus, intoxication may occur long after exposure to or far away from a dinoflagellate bloom.

The diagnosis of brevetoxicosis is typically by exclusion and may be based on detecting toxins in fluids and tissues and by pathologic findings,

FIGURE 3



Multiple cutaneous sessile maculopapular papillomas on the dorsum of a manatee associated with a papillomavirus (TmPV-1), whose genome was recently sequenced. The linear distribution of the tumors suggests traumatic self-inoculation.

such as immunohistochemical staining to verify the presence, abundance, and distribution of brevetoxins in tissues. Brevetoxicosis in manatees may occur after chronic inhalation and ingestion, and the subsequent release of inflammatory mediators may lead to fatal toxic shock. Only manatees among marine mammals and humans appear to be susceptible to brevetoxin through inhalation. Indeed, emergency room diagnoses of this pulmonary condition increase during Florida red tides.

FIGURE 4

Cutaneous lobomycosis in a free-ranging Atlantic bottlenose dolphin from Florida.

Marine Mammals as Sentinels for Oceans and Human Health

As such diseases emerge and the effects of global climate change are better understood, some investigators are raising concerns about deteriorating aquatic ecosystems. Such matters are of particular concern in the United States, where more than half the human population inhabits coastal freshwater or marine ecosystems.

Tracking marine organisms as sentinels provides a valuable way of evaluating the well-being of aquatic ecosystems and identifying damaging environmental trends. In turn, these warnings can help experts in characterizing and managing the effects of these trends on oceans or other waterways and on human health. Doing so is especially important since much of the present emerging disease data suggest that complex interactions occur among anthropogenic toxins, immunologic and genetic factors, and infectious organisms in the marine mammals that share coastal environments with humans.

Marine mammals not only are important sentinels for health. They also are charismatic, and thus can help to trigger helpful behavioral responses among humans, including paying closer attention to ocean health issues. In a report from 2004, the U.S. Marine Mammal Commission concluded that threats to marine mammals are ultimately related to the size, growth rate, consumption patterns, and behaviors of humans. It is in our own best interest to pay heed to marine mammal health patterns that could affect us.

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