# Oceans and Human Health: A New Era of Environmental Opportunities

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> *Because of the broad mission of NIEHS [National Institute of Environmental Health Sciences] to develop public health and clinical strategies to prevent environmentally caused diseases, our science complements that of all the other Institutes in the NIH [National Institutes of Health] that deal with the categorical diseases.*
>
> Kenneth Olden
> (Personal communication, 27 September 2004)

The mission of the NIEHS links it to all human diseases in which the environment plays a role, and increasing evidence links an environmental element to most disease. The NIEHS also complements other agencies within the federal government whose missions include environmental jurisdiction. Throughout the years since the NIEHS was established, and certainly since 1991 when Dr. Kenneth Olden became director of the NIEHS, the NIEHS has considered "environment" in its broadest sense. Examples include the agricultural/farm environment, the inner-city urban environment, the built environment, extreme environments, and the ocean environment. In all these environmental arenas, the NIEHS has addressed the research problems with a combination of regular peer-reviewed research grants, program projects, and centers and consortia. To a greater or lesser degree, the NIEHS has also provided funding opportunities through Small Business Innovative Research (SBIR) and Small Business Technology Transfer programs, translational research programs, the Superfund Basic Research Program (SBRP), and worker training.

The ocean environment is a venue that is no different from the farm environment or the built environment or the industrial environment, but it has always seemed to

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be a less-than-equal setting for traditional research as classified under the NIEHS portfolio. Why is that? Perhaps it is because the NIEHS originated in industrial toxicology. Perhaps the ocean sciences community has not made a credible case for increased research emphasis until recently. Perhaps it is that much less is known about our ocean world, so even crafting the right questions is a challenge. In this last regard, the NIEHS may be mapping out the first scientific expedition to explore the world's oceans and seafloor on a new *HMS Challenger* with a different crew and a revised mission.

Consider, however, that natural and anthropogenic toxicants are abundant in the world's oceans. Ocean environments yield a variety of nutraceuticals, food additives, and animal meal goods that directly or indirectly affect human health. Bacteria, viruses, and other nasty microbes abound in the world's oceans. Products from the sea have long served the human race by accenting industrial products, cosmetics, and scientific microbial media, and by supplying products that fill scientific supply houses. All are common elements of NIEHS programs that address the effects of environmental chemicals on human health and well-being.

Oceans and human health (OHH) research has become one of the most interdisciplinary research endeavors in science. Modern oceanography began as a field of science less than 130 years ago and became sophisticated only during World War II because of the U.S. Navy's interest in tactical ocean superiority. The biomedical disciplines, with expertise acquired at medical schools and basic science departments over the past 200 years, participate in ocean sciences that have reached their current technology fervor in the past two decades. The application of biomedical expertise to problems in ocean science has been a fruitful endeavor, especially since the 1960s. Within the ocean sciences community, the NIEHS has led by example in fostering interdisciplinary science (where disparate disciplines influence one another co-dependently) rather than traditional multidisciplinary science (where venues and ships of opportunity are the sole commonality—each discipline collecting data independently). A cross-agency collaboration between the NIEHS and the U.S. Environmental Protection Agency (U.S. EPA) resulted in the SBRP (NIEHS 2003), a collaboration that has provided many learning opportunities in the development of the current NIEHS/National Science Foundation (NSF) Centers for Oceans and Human Health (NIEHS/NSF 2002). Like SBRP, which combined disparate biomedical science and engineering expertise, the present OHH program combines the dissimilar biomedical and oceanographic sciences (Tyson et al. 2004). The NIEHS has promoted OHH research in more limited ways since inception of the institute. Early biomedical researchers could make enormous scientific advances by applying their expertise to oceanographic (marine) problems or systems. This expertise emphasized physiology predominantly, but technology in the form of analytical techniques and equipment has afforded catalytic contributions to marine science. It was no accident that National Oceanic and Atmospheric Administration (NOAA) borrowed heavily from the NIH/NSF model for subject matter and collaboration in its own oceans and human health programs (Sandifer et al. 2004). Many scientists hope that it was an unfortunate coincidence that NOAA set up an entirely parallel OHH program. Obviously, to maximize synergy, it would seem efficient to have scientists from all agencies on the same ships during these early explorations into OHH.

**Figure 1.** The nudibranch *Hermissenda*, a marine model used in memory and learning. Photo courtesy of A. Kuzirian, Woods Hole Oceanographic Institution (Kuzirian et al. 1998).

Other examples of the intercalation of basic biomedical sciences with ocean sciences exist, and in this treatise I attempt to draw attention to several discoveries and/or models derived from marine science programs that have served the entire biomedical community. Some are entirely addressed by NIEHS programs; others are primary in other institutes of the NIH but serve the NIEHS mission or provide synergy. *Environmental Health Perspectives* has published other articles and editorials on a variety of aspects of OHH (Rose et al. 2001), ocean health (Knowlton 2004), and coastal zone health (Stegeman and Solow 2002) and recently has described the four new Centers for Oceans and Human Health. They will not be duplicated here, nor will tsunamis, hurricanes, and other coastal disasters be discussed, although the terrible personal and community devastation the world has recently witnessed in the Pacific will not soon be forgotten.

In this article I begin by describing the oldest of the OHH sponsorships by the NIEHS, followed by a brief treatment of each of three primary themes of the present NIEHS/NSF Centers for Oceans and Human Health, and conclude by briefly considering a future interaction across agencies that will surely come to pass if the disparate science communities come together and make their wishes known.

## The Marine and Freshwater Biomedical Sciences Centers

The NIEHS, under the direction of its second director, Dr. David Rall, first entered the ocean arena in an interdisciplinary research mode in 1978 with the establishment of the Marine and Freshwater Biomedical Sciences (MFBS) Center program. Envisioned to coordinate research and activities to improve understanding of processes within the ocean that may affect human health, early MFBS Centers exploited marine organisms as model systems for medicine and biomedical research. By the late 1980s, scientific discoveries in the marine environment that directly affected human health were well documented, and thereafter research groups began to explore a variety of ocean environments in the same interdisciplinary manner as did the larger Environmental Health Sciences Centers. Clearly, the availability of biomedical technology and expertise to meet the challenges of ocean-based research has been well served by the MFBS program. Of obvious relevance is the realization by the NIEHS that the MFBS program is bestowed with the most conservative investment that provides the most liberal payoff. Some discoveries along the way were characterized as mere serendipity. But then, serendipity is defined as "always making discoveries, by accidents and sagacity, of things not in quest of . . . ." (Walpole 1754). Otherwise stated, "Luck is the meeting of preparedness with opportunity." The NIEHS continues to provide the opportunity for sagacious minds by funding four centers, strategically located in the Northeast in Bar Harbor, Maine, in the Southeast in Miami, Florida, in the Northwest in Corvallis, Oregon, and on the Great Lakes in Milwaukee, Wisconsin. A fifth opening for an MFBS Center is intimated by the NIEHS Centers web site, which lists four centers in a five-center program.

### Marine Organisms as Models for Biomedical Research

The original focus of the MFBS Centers was on the basic science leading to the development of marine and freshwater models as alternatives to living terrestrial mammal models. Examples include the dogfish shark at Mount Desert Island Biological Laboratory Center in Salisbury Cove, Maine, the rainbow trout model of cancer at the Oregon State University Center in Corvallis, Oregon, and *Aplysia californica* as a model for memory and learning at the University of Miami Coral Gables Center in Miami, Florida. The National Center for Research Resources, through its Comparative Medicine Initial Review Group, funds a program whose mission is the development of alternative models of human disease, and many marine models are funded by that mechanism. Marine and freshwater resources provide zebrafish as an aquatic "mouse" model, swordtail aquarium fish as models for carcinogenesis, the flatworm *Caenorhabditis elegans* for genomics, and a variety of small freshwater species for toxicological pathway elucidation. Some very useful marine animal models also have been developed, one of which resulted in the award of a Nobel Prize to Dr. Eric Kandel for his pioneering work in memory and learning in the *Aplysia* model (Kandel et al. 1995).

Additional research laboratories have supported marine biomedical research over many decades. One of the most influential is the Marine Biological Laboratory in Woods Hole, Massachusetts (Figure 1). Fostering a prosperous tradition of neuroscience for more than six decades, and supporting numerous future Nobel laureates, it was at the Marine Biological Laboratory that much of the basis of neurophysiology was first described—in marine organisms: retinal neurophysiology, the development and use of the voltage-clamp technique in squid by Cole and Moore (1960), the discovery of the squid giant axon, the elegant analysis of the action potential of the squid giant axon by Hodgkin and Huxley (1952), and the squid giant synapse discovery by Bullock and Harigawa (1957) used for elucidating the mechanisms of synaptic transmission. It is noteworthy that the coastal region near the Marine Biological Laboratory provided the study organisms and the unique environment for interaction of neuroscientists from around the world.

Alternatives to living mammalian models will always be an important part of the NIEHS portfolio. The NIH has only scratched the surface of the potential that marine and freshwater model systems hold for biomedical research. Hindsight, it is said, is 20/20. For NIEHS in this arena, foresight was crystal clear.

### Harmful Algal Blooms and Their Bioactive Metabolites

Some of the most deadly and potent natural toxins known are derived from harmful algal blooms—the classic red tides (Figure 2). Yet other marine toxins are thought to arise from microbial "infections" in, or on, other marine creatures. Each of these materials, once they are characterized for specific mechanism of action and chemical structure, move quickly from the strictly academic realm into biomedical scientist's "tool boxes" as exquisitely specific biological probes. The classic toxin, of course, in the marine toxin field is tetrodotoxin. Known as a specific poison since the sixth century, the structure was not elucidated until 1964

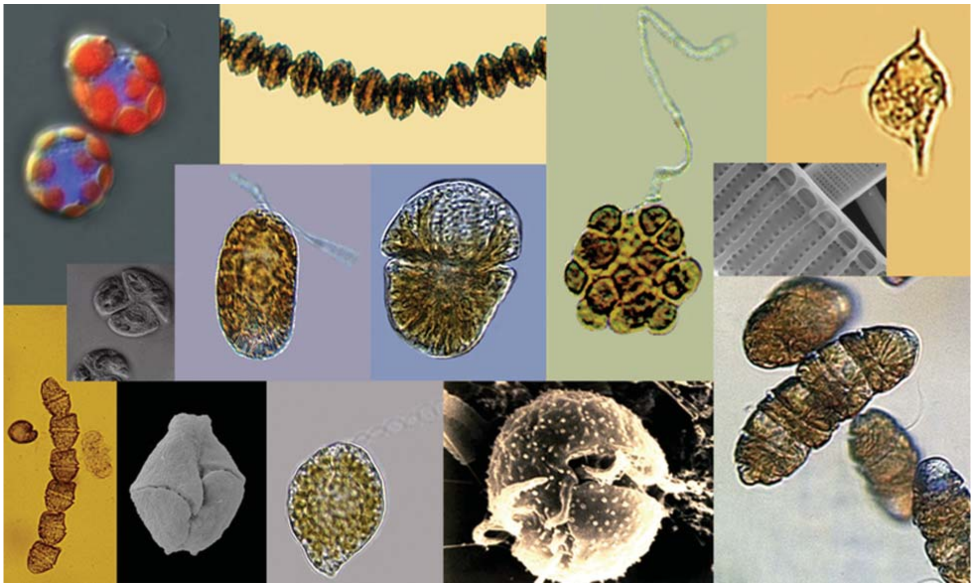

**Figure 2.** Montage of harmful algal bloom organisms.

by Woodward (1972), the Kishi-Goto group, and the Tsuda-Ikuma group simultaneously, and Kishi's group accomplished its total racemic synthesis (Goto et al. 1965). Narahashi described the mechanism of tetrodotoxin's selective blockade of sodium channels in 1964 (history described in Narahashi 2000). Woodward was awarded the Nobel Prize in 1965, in part for his work with tetrodotoxin (Narahashi 2000). The value of this particular toxin in electrophysiological research is so profound that seminars describing any aspect of sodium channel structure or function are often queried at the end with "What effect does the application of tetrodotoxin have on this observed activity?" Models of sodium channel structure have been postulated based on this toxin's channel-blocking characteristics that depend on the presence of a guanidinium moiety. With the description of another toxin from shellfish called saxitoxin (possessing two guanidinium moieties), the molecular modeling work of Lipkind and Fozzard (1994) has led to some still-active debates about the three-dimensional structure of voltage-gated ion channels in excitable membranes. Other toxins, members of the *Conus* snail arsenal of small polypeptide toxins, have a similar sodium channel-blocking activity; the U.S. Food and Drug Administration has recently approved one for use in pain control.

Another group of marine toxins is the brevetoxins. Having activity opposite to the guanidinium toxins, they act as molecular doorstops holding voltage-gated sodium channels in an open configuration. These polyether brevetoxins and a number of synthetic derivatives have had some limited success in dissecting the various molecular allosteric changes thought to occur sequentially during ion channel topographic progression from closed to open to inactivated and back to the closed state. The mechanism by which ion channels carry out these presumably allosterically modulated conformational changes can be perturbed by the brevetoxins. Discovery of a natural polyether antagonist to brevetoxins has recently been reported. Isolated from the same red tide organism, these materials act as toxin antagonists. Further work has revealed a specific modulatory effect that may be important in the treatment of mucociliary diseases such as cystic fibrosis (Abraham et al. 2005).

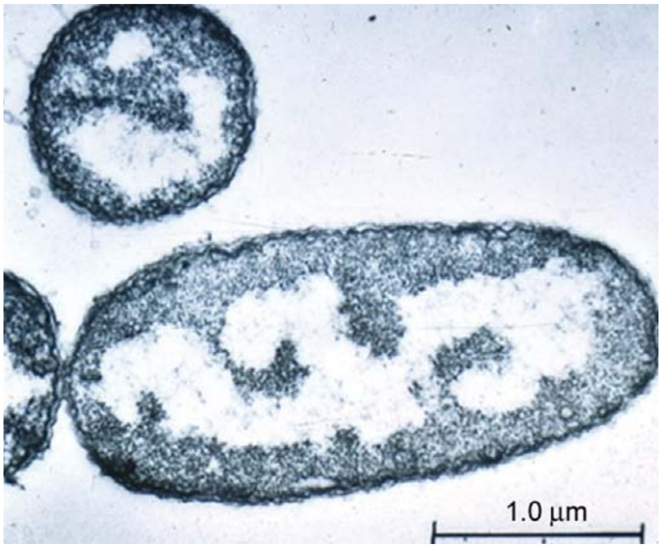


**Figure 3.** Electron micrograph of *Vibrio cholerae*. Photo courtesy of R. Sizemore, University of North Carolina Wilmington.

Similarly, okadaic acid from marine microalgae has been employed as a specific inhibitor of protein phosphatases 1 and 2a. The use of okadaic acid as a specific tool in protein phosphatase research afforded the opportunity to conduct site-directed mutagenesis studies and achieve a cloned protein phosphatase 1 for cascade system investigations. Clinically, one of its specific toxicological actions (the basis for the current mouse bioassay) is that of enhancing water intrusion into the intestine. Intramural NIEHS investigators are exploiting this physiological effect as a treatment for bowel dysfunction in cystic fibrosis patients (Xie et al. 1998). In all these cases, as the basic science surrounding their mechanism of action and their basic chemistry is nearing completion, the toxins (now called "specific molecular probes") have already entered the research arsenals of membrane biologists and physiologists and of neuroscientists and enzymologists. Ultimately, they—or clinical drugs designed on their chemistry—will enter the physician's stockpile of available drugs. Research on the mechanism of action of marine toxins has been funded by the NIEHS since its early days.

## Vector- and Waterborne Human Diseases

It is estimated that human pathogens in the marine environment lead to significant health problems and annual losses of billions of dollars of income worldwide. Jed Fuhrman and others tell us that the seas are full of microorganisms, bacteria and viruses, rhaphidophytes and dinoflagellates, diatoms and coccolithophores (Fuhrman 1999, 2002; Hewson et al. 2003).

Both recreational and oral exposures (through food) are primary routes of exposure to oceanborne pathogens. Bacteria originating from humans and terrestrial animals are present and include native marine organisms (e.g., *Vibrio vulnificus*, *Vibrio parahemolyticus*) (Figure 3). Viruses have a limited host range, and pathogenic viruses of human health concern enter coastal regions from human sources (fecal transmission and possibly blood-borne contaminants in wastewater). Protists such as *Cryptosporidium* and *Giardia* are also prominent. Incomplete sewage treatment, leaking pipes, land runoff, and contaminated rivers and streams all contribute to coastal microbial flora.

Real environmental events were discounted in the past as folklore. But further scientific discovery, supported in part by NIEHS funds, led to description of very real threats to human health. Vectors can be in the form of filter-feeding organisms, biological transporters, and winds and ocean currents. For example, ciguatera fish poison and seven other types of marine toxins in seafood affect more than 60,000 persons annually with short- and long-term neurological illness, often requiring less than 1 mg of toxin to poison humans and many times have effects lasting for weeks to months. Folklore dates ciguatera intoxication back to the early 1600s. The economic loss from seafood intoxication alone is estimated at greater than $49 million annually, of which 45% is public-health related. No specific test exists for detecting contaminated fish, and approved tests for shellfish poisons are only now becoming available. Keep in mind that fisheries products are transported and sold worldwide by seafood distribution systems (Anderson et al. 2000).

The incidence of cholera in India has been linked to marine copepods as disease vectors of the bacterium *Vibrio cholerae* (Figure 3). The nature of the link is uncertain, but the potential exists for global transport of the disease on the backs of marine crustacea. Many of these microbes are presently nonculturable from marine sources (Colwell et al. 2003). Coral diseases and coral reef demise are due in part to fungi and bacteria from terrestrial environments blown into coastal waters during El Niño and La Niña events. During the annual hurricane season in the Southeastern United States, living microbes

**Figure 4.** Cultures of microalgae that produce okadaic acid, a protein phosphatase inhibitor. Photo courtesy of C. Tomas University of North Carolina Wilmington. (Inset) *In situ* cultivation of the soft coral *Pseudopterogorgia elizabethae*, which contains a prostaglandin used in antiwrinkle cream. Photo courtesy of H. Lasker, SUNY Buffalo.

in dust from the Sahara have been detected in the winds of south Florida. The mechanism by which they establish their virulence in marine waters is not understood. Surely human pathogens may also be transported by the world's winds (Griffin et al. 2001) (Figure 4).

We know relatively little about the fates of most pathogens in marine environments, but we know they are present. Survival and persistence of various pathogens are areas of active research, especially in this time of general global warming, when microbes previously circumtropical in geographic prevalence have the opportunity to move north- and southward. In coastal communities, public health officials point to the measurement of "indicator organisms" such as fecal coliform bacteria as microbial safety indicators. Pathogens prevalent in coastal U.S. waters may change, with such organisms as *Vibrio cholerae* becoming a problem. Global distribution patterns, virulence, and antibiotic resistance are all factors that public health scientists will deal with in the years to come. Issues of principal importance for microbial contamination of populated coastal regions include quantification and detection of the pathogenic species (not of indicator species), basic science studies that address the pathogenicity of microbes (including genomics, proteomics, and immunochemical trait deciphering), and dispersal mechanisms (which requires sophisticated physical oceanographic methods of current tracking, partitioning, and dispersal). Epidemiological studies are needed in tandem to evaluate risks of various pathogens. This requires rapid, inexpensive, and accurate tests for the organisms (or, better yet, virulent strains) that affect near-shore environments (Fuhrman 2002).

## Marine-derived Pharmaceuticals

"Drugs from the sea" is a theme of the current NIEHS OHH program. Beneficial products already derived from cultivated marine organisms (Figure 4) include agar-agar from seaweed, the basis of solid support bacterial culture media. Agar also helps keep ice cream together and retards melting. (We tend to forget those marine products that have been in laboratories and the home for more than a few decades.) A popular wrinkle cream contains prostaglandins derived from aquacultured gorgonians (soft corals)—an alternative to the injection of botulinum toxin for controlling wrinkles (so you can still smile; Figure 4). Menhaden fishmeal provides the omega fatty acid supplement in some chicken and hog feeds.

The National Cancer Institute has been investigating the oceans as a source of bioactive compounds for the past 30 years. Logistically the effort has been a search for new organisms that produce potentially valuable bioactive chemicals. Cancer, a major human health problem, was a disease that might logically respond to new chemicals with cytotoxic activity. Natural products effective against certain cancers have been identified: bryostatin from the colonial bryozoan, ecteinascidin from ascidians or sea squirts, and discodermolide from deep-sea sponges. Anti-inflammatory and antiviral/antimicrobial agents have also been described. All arise from marine organisms that are part of the biodiversity of the world's oceans.

The late John Faulkner commented on the preponderance of microbial symbionts in species like sponges and spent the latter part of his career considering the endosymbiotic chemistry in marine microbial communities (Faulkner et al. 1993). Marine microorganisms were highlighted as a novel resource for new drugs by the National Research Council publication *From Monsoons to Microbes: Understanding the Ocean's Role in Human Health* (Fenical et al. 1999). In this treatise, to which NIEHS investigators contributed, cultivation of marine microbes should be a major effort of NIH drug discovery programs in the years to come. According to Bull et al. (2003), novel natural-product chemotypes with interesting structures and biological activities continue to be reported. Without such discoveries, "there would be a significant therapeutic deficit in several important clinical areas, such as neurodegenerative disease, cardiovascular disease, most solid tumors, and immune-inflammatory diseases."

Based on the myriad discoveries of microbially produced drugs useful as antibiotics, immune-suppressive agents, and anticancer compounds from terrestrial sources, the marine and freshwater environment—especially the deep-sea sediments and hydrothermal vents—should provide for unusual small and macromolecules with unique and exploitable functions. Enzymes from marine organisms also possess potentially useful characteristics, unique to the environment in which they live. For example, *Methanococcus jannaschii* produces a specific restriction endonuclease found to be useful in cleavage of small single-stranded DNA "flaps." Called the "flap endonuclease," this particular enzyme, with its thermophilic preference, adds yet another tool to the arsenal of sequencing tools for geneticists (Rao et al. 1998). Strain 121, an archaean (formerly called bacteria) discovered in a "black smoker" thermal vent deep in the Pacific Ocean, holds the record for being the "hottest organism known to man." Isolated in 2003, strain 121 is thought to have possibilities in the treatment of toxic waste as well as high-temperature detergents, based on its heat-resistant degradative enzymes (Kashefi and Lovley 2003).

Historically, upon discovery of potentially active materials, it was then the task of the biomedical marine scientist to relocate the host organism, catalog it, and collect sufficient raw material for work-up. Clearly, marine biomedical scientists and ocean ecologists might end up at cross-purposes if environmental harvesting reached excessive proportions. Difficulties in discovery and harvest were only compounded by the Convention on International Trade in Endangered Species (CITES 2000), which protects the resource while severely limiting massive collection efforts. Thus, the supply of biomass for extraction and purification of potential raw drugs is a limiting element. In this regard, of urgent emphasis is the development of culture methods to enable exploitation of drugs and other biochemicals for commercial uses to cure or treat human disease. The NIEHS can fund novel methods of collection and cultivation of all types of potentially useful organisms; extremophile organisms, molecules, and processes represent only one example of a resource untapped. Recent NIEHS-funded efforts support the cultivation of organisms from the sea to provide a continued source of raw materials without having to resort to continued wild-type collection.

**Figure 5.** EXPO 98 Discovery Amphitheater titled "The Oceans: Our Legacy for the Future." Photo courtesy of F. Adler, Team Administrator for the NIEHS portion of the USA Pavillion.

## Communicating Ideas Precisely: Oceans and Human Health in Our Daily Lives

Terrestrial ecosystems are experiencing resurgence in known but conquered diseases. Ocean environments are also experiencing an increase in incidence of previously rare or unknown diseases or virulent variations of common diseases. Man is witness to marine epizootics due to uncontrolled infections, harmful algal blooms, or reliance on a food source that has inexplicably become tainted or unfit for consumption. Both the human health and oceanographic communities must collaborate more fully in communicating the hazards and benefits of oceans in human health to the general public. With effective communication, encouraged by the NIEHS in all its programs, an accurate recounting of ocean events and relationships can dissuade the public from believing the all-too-common "spin" without proper scientific foundation.

Scientists provide accurate descriptions of episodes of massive marine deaths of fish, birds, and marine mammals, as well as infectious diseases associated with bacteria hitchhiking on the backs of copepods. The popular press and the motion picture industry sometimes paint more sensationalistic scenarios. But, of course, our agendas are different. A popular urban myth, a cult classic movie, and the World Exposition 1998 held in Lisbon, Portugal (EXPO 98; Figure 5) serve as examples of communication of misinformation, a fictionalized accounting of an actual event, and a presentation of compelling scientific facts. To be specific, in the 1950s, the press linked Florida "noxious aerosols" to the leaking 55 gal drums of World War II nerve gas. Decades of study now indicate that the "nerve gas" is the brevetoxin, a natural neurotoxin in seaspray that causes respiratory distress at $1 \times 10^{-15}$ mole per liter air. However, sinister alternative explanations arise from time to time. In the 1960s, Alfred Hitchcock's movie *The Birds* is a recounting of actual events in California coastal communities. The movie fictionalizes the first records

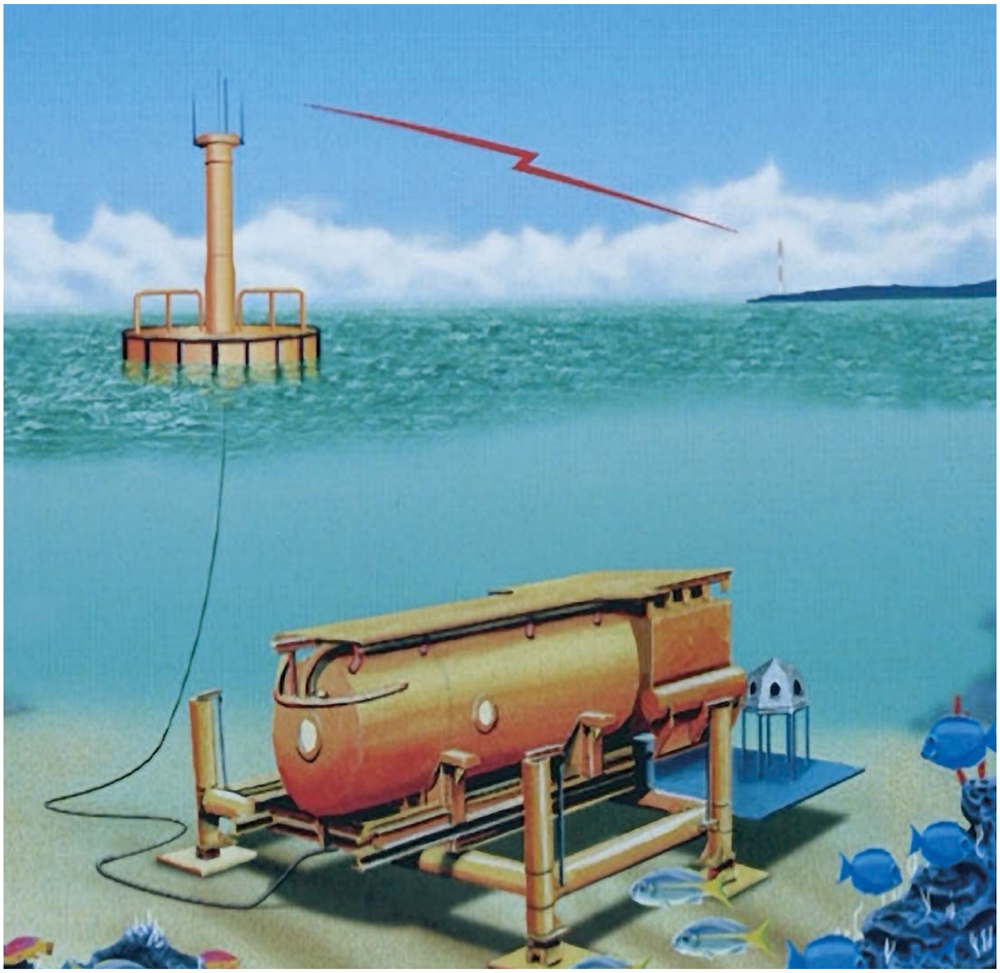

**Figure 6.** The recent development of Aquarius 2000 is an example of a NURP (NOAA's Undersea Research Program) partnership with industry and academia. The Aquarius underwater laboratory has been redesigned to include an autonomous data/telemetry buoy that was developed in cooperation with the Harris Corporation and Harbor Branch Oceanographic Institution. The buoy will supply all the life support and communications capabilities previously provided by a barge manned by up to four technicians. In addition, the new buoy will provide real-time data and video links from the sea floor laboratory back to the shore-based support laboratory and eventually to the world via the World Wide Web. Aquarius is owned by NOAA and is operated by the University of North Carolina at Wilmington. Illustration by Jeffrey Ashwell/Harris Corporation.

of amnesic shellfish poisoning, and some of the first species intoxicated were birds. Similar neurotoxic events involving sea lions and sea otters were scientifically documented in 1998 (Scholin et al. 2000), ironically when the First National Ocean Conference was discussing global ocean environment issues in Santa Barbara.

EXPO 98, titled "The Oceans: A Heritage for the Future," was held in the "Year of the Ocean," and the Office of Naval Research (ONR) and the NIEHS were co-sponsors of the exhibit. The entire NIEHS-sponsored half of the USA Pavilion was devoted to OHH, including marine models of human disease, harmful algal blooms, and neurophysiology of harmful algal blooms. The NIEHS story was told in movie form, children's ocean health issues were presented in cartoon form, and the health of circumpolar human inhabitants was graphically recounted using an iceberg display. The ONR half of the exhibit was devoted to ocean exploration and instrumentation. The pavilion hosted more than two-thirds of Congress, four different Cabinet secretaries, and more than 15 million civilian visitors during its short 4 month run. The two halves of the exhibit underscored, in subliminal fashion, the issues that needed study, and the mechanism by which they could be achieved. The NIEHS and ONR deserve credit for initiation of the present national interest in OHH.

The final section of this article addresses opportunities for global environmental health monitoring, a concept first articulated during EXPO 98.

## Predictive Models Based on Indicators of Public Health—The Need to Partner

Unique opportunities exist that, if missed, will not likely occur again in our lifetimes (Knap et al. 2002). This is related primarily to the state of the art in the disciplines that will interact and collaborate but also to the potential to build upon the work of the Presidential Ocean Commission. The commission, chaired by Admiral James Watkins (USN Ret.), will likely transform ocean sciences over the next 40 years and holds the potential for recommending major additional funding through the White House. What is unique about such a potential? First, the NIEHS has demonstrated the willingness and ability to cross departmental lines within the federal government and address pressing human and environmental health issues. Humans are, after all, only one species on Earth, and environmental episodes that alter human lives also alter animal lives. Second, the naval forces of the United States have been reduced in fiscal stature relative to the other branches of the armed services, primarily because of the perceived increased importance of terrestrial battlefield venues versus ocean-based scenarios. Clearly, the resources of the Navy need to be realigned in part with an expanded mission of research. The research aspect of the Navy's budget has been dwindling, partly because without wars on the oceans there is no pressing need to understand more about the aquatic battlefield. I submit that the opponents in the ocean's battlefields have merely changed because we are no longer fighting a human enemy but instead are battling a much more fearsome opponent—one about which we know very little.

An opportunity exists, then, for the nation to use existing Navy resources to complement those resources of the NIH, NSF, and NOAA to collaboratively address, in tandem, ocean environmental human health factors and the health of the ocean environment. Issues that are particularly timely and that address everyone's agenda include, among many other items, ocean observing and forecasting of harmful events or blooms: coastal monitoring is on the verge of implementation (Figure 6). Multiple large regional efforts in coastal ocean–observing systems will provide opportunities for now-casting and ultimately forecasting and will collect environmental data on time scales never before achieved. This largely NOAA and ONR effort will provide several millions of dollars annually for fixed platforms, buoys, moorings, and ships to implement biomedical detection devices and sampling for the research areas described above. An intensive informatics network is anticipated to archive metadata in a user-friendly way.

Another timely issue involves new analytical technologies, developed by the biomedical community, that are closer than ever to real-time deployment in robust sampling equipment. The opportunity for rosette-style microarray technology deployment for detection, speciation, and quantification of marine organisms and contaminants can be realized, not just imagined. The ONR routinely sponsors tracking and device deployment and optimization. Detection devices are a current SBIR interest for agents or materials/organisms of a harmful nature, to detect and forewarn of impending exposure. Correlating environmental contaminants and human exposure is the mantra of the NIEHS, perhaps in collaboration with the Department of Homeland Security for certain ocean-derived agents.

In general, we have a miniscule baseline of temporal measurements of any contaminants, or other indicators of global change based on anthropogenic inputs. These data require collection, archiving, and analysis. Metadata sets already pose a major challenge to the biomedical and oceanographic communities individually.

With a multiagency interest in OHH, especially the expressed interest of NSF, NIEHS, and NOAA in working on a common agenda, the collaboration across agencies and departments is probably the most unique and exciting development ever to strike the joint OHH community. The subject area is a concern for scientists, regulators, administrators, and the public. Since 1991, the NIEHS has increased its support of marine science research relevant to the human condition. The technologies have transferred rapidly to the ocean science community such that technologies that used to take a decade for transfer now take months or occur simultaneously. We have discovered that continents are not separated by the ocean (yes, it is really only one big body of water!), but that the land merely emerges in places within this large body of water. The story of how closely linked are oceans and human health will continue to unfold in the decades to come (Beck et al. 2000).

## Summary

The National Institute of Environmental Health Sciences (NIEHS) has supported environmental health sciences that overlap with ocean science questions and resources since its inception. The second NIEHS director, David Rall, and NIEHS's third director, Dr. Kenneth Olden, exhibited active interest in the development and funding of oceans and human health–related research, education, and outreach. The institute has provided fiscal support for regular research grants, center grants, and program project grants; for individual and institutional training grants; and for conference and meeting support. During Dr. Olden's tenure, the institute has also demonstrated leadership in working with other institutes within the National Institutes of Health to further ocean-based biomedical research and has reached out to other funding agencies and departments of the federal government. The Marine and Freshwater Biomedical Science Center program is the longest lasting, most productive, and high-profile aspect of NIEHS's funding in the ocean environmental health sciences, and under Dr. Olden's leadership that program has steadily increased in stature. Developed collaboratively with Rita Colwell, immediate past director of the National Science Foundation, the present Centers for Oceans and Human Health are a joint exercise of the two agencies. The Marine and Freshwater Biomedical Science Center program, the three research foci of the present Centers for Oceans and Human Health program, and increased collaborative oceans and human health research will all contribute to the health of the world's oceans and, by co-dependence, the health of humans.
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## Notes

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The National Institute of Environmental Health Sciences (NIEHS) can avow leadership in funding research to understand the relationship between oceans and human health. Kenneth Olden can be identified as both promoter and activist of interdisciplinary research in environmental health sciences and specifically in the ocean sciences related to human health. Numerous staff within the intramural and extramural community of NIEHS continue to serve as guides and advocates of environmental health sciences related to the oceans. To the institute, Dr. Olden, and the NIEHS extramural program staff, we marine biomedical scientists owe a debt of gratitude.

Work from the Baden laboratory has been funded by the NIEHS since 1979. Grants have included a Young Environmental Scientist Award, R01-ES05853 and R01-ES06411 awards, a P30-ES05705, and a current P01-ES10594 award.

The author declares he has competing financial interests. These include recent, present, and future grant support, compensation and receiving payment for expert testimony related to OHH issues. He has been named inventor on one or more patent applications related to ocean-derived drug candidates, and in his present position as director of the Center for Marine Science at the University of North Carolina Wilmington may gain or lose financially through publication of this article.

## References

Abraham WM, Bourdelais AJ, Sabater JR, Ahmed A, Lee TA, Serebriakov I, et al. 2005. Airway responses to aerosolized brevetoxins in an animal model of asthma. Am J Respir Crit Care Med 171:25–34.

Anderson DM, Hoagland P, Kaoru Y, White AW. 2000. Estimates of Economic Impacts from Harmful Algal Blooms in the United States. WHOI Technical Report 2000-11. Woods Hole, MA:Woods Hole Oceanographic Institute.

Beck LR, Lobitz BM, Wood BL. 2000. Remote sensing and human health: new sensors and new opportunities. Emerg Infect Dis 6:217–226.

Bull AT, Ward AC, Goodfellow M. 2003. Search and discovery strategies for biotechnology: the paradigm shift. Microbiol Mol Biol Rev 64:573–606.

Bullock TH, Harigawa S. 1957. Intracellular recording from the giant synapse of the squid. J Gen Physiol 40:565–577.

CITES (Convention on International Trade in Endangered Species). CITES-Listed Species Database. Cambridge, UK:United Nations Environment Programme World Conservation Monitoring Centre. Available: http://www.cites.org/eng/resources/species.html [accessed 14 February 2005].

Cole KS, Moore JW. 1960. Ionic current measurements in the squid giant axon membrane. J Gen Physiol 44:123–167.

Colwell RR, Huq A, Islam MS, Aziz KMA, Yunus M, Khan NH, et al. 2003. Reduction of cholera in Bangladeshi villages by simple filtration. Proc Natl Acad Sci USA 100(3):1051–1055.

Faulkner DJ, He H, Unson MD, Bewley CA, Garson MJ. 1993. New metabolites from marine sponges: are symbionts important? Gazz Chim Ital 123:301–307

Fenical W, Baden D, Burg M, de Ville de Goyet C, Grimes DJ, Katz M, et al. 1999. From Monsoons to Microbes: Understanding the Ocean's Role in Human Health. Washington DC:National Academy Press.

Fuhrman JA. 1999. Marine viruses and their biogeochemical and ecological effects. Nature 399(6736):541–548.

Fuhrman JA. 2002. Community structure and function in prokaryotic marine plankton. Antonie Van Leeuwenhoek 81:521–527.

Goto T, Kishi Y, Takahashi S, Hirate Y. 1965. Tetrodotoxin. Tetrahedron 21:2059–2088.

Griffin DW, Garrison VH, Herman JR, Shinn, EA. 2001. African desert dust in the Caribbean atmosphere: microbiology and public health. Aerobiologica 17:203–213.

Hewson I, Vargo GA, Fuhrman JA. 2003. Bacterial diversity in shallow oligotrophic marine benthos and overlying waters: effects of virus infection, containment, and nutrient enrichment. Microb Ecol 46:322–336.

Hodgkin AL, Huxley AF. 1952. A quantitative description of membrane current and its application to conduction and excitation in nerve. J Physiol 117:500–544.

Kandel ER, Schwartz JH, Jessell TM. 1995. Essentials of Neural Science and Behavior. Norwalk, CT:Appleton & Lange.

Kashefi K, Lovley DR. 2003. Extending the upper temperature limit for life. Science 301:934.

Knap A, Dewailly E, Furgal C, Galvin J, Baden D, Bowen RE, et al. 2002. Indicators of ocean health and human health: developing a research and monitoring framework. Environ Health Perspect 110:839–845.

Knowlton N. 2004. Ocean health and human health [Editorial]. Environ Health Perspect 112:A262.

Kuzirian AM, Epstein HT, Nelson TJ, Rafferty NS, Alkon DL. 1998. Lead, learning, and calexcitin in Hermissenda. Biol Bull 195:198–201.

Lipkind, GM, Fozzard HA. 1994. A structural model of the tetrodotoxin and saxitoxin binding site of the $Na^+$ channel. Biophys J 66:1–13.

Narahashi T. 2000. Neuroreceptors and ion channels as the basis for drug action: past, present, and future. J Pharmacol Exp Ther 294:1–26.

NIEHS. 2003. RFA ES-04-001: Superfund Basic Research and Training Program. Release date: 16 September 2003. Research Triangle Park, NC:National Institute of Environmental Health Sciences. Available: http://grants.nih.gov/grants/guide/rfa-files/RFA-ES-04-001.html [accessed 14 February 2005].

NIEHS/NSF. 2002. RFA ES-03-003: Centers for Oceans and Human Health. Release date 21 November 2002. Research Triangle Park, NC/ Washington, DC:National Institute of Environmental Health Sciences/ National Science Foundation. Available: http://grants.nih.gov/grants/guide/rfa-files/RFA-ES-03-003.html [accessed 14 February 2005].

Rao HGV, Rosenfield A, Wetmur JG. 1998. Methanococcus jannaschii flap endonuclease: expression, purification, and substrate requirements. J Bacteriol 180:5406–5412.

Rose JB, Epstein PR, Lipp EK, Sherman BH, Bernard SM, Patz JA. 2001. Climate variability and change in the United States: potential impacts on water- and foodborne diseases caused by microbiologic agents. Environ Health Perspect 109(suppl 2):211–221.

Sandifer PA, Holland AF, Roles TK. 2004. The oceans and human health. Environ Health Perspect 112:A454–A455.

Scholin CA, Gulland F, Doucette GJ, Benson S, Busman M, Chavez FP, et al. 2000. Mortality of sealions along the California coast linked to a toxic diatom bloom. Nature 403:80–83.

Stegeman JJ, Solow AR. 2002. Environmental health and the coastal zone. Environ Health Perspect 110:A660–A661.

Tyson FL, Rice DL, Dearry A. 2004. Connecting the oceans and human health. Environ Health Perspect 112:A455–A456.

Walpole H. 1754. Letter to Horace Mann, 28 January.

Woodward, RB. Nobel Lecture. 1972. In Nobel Lectures, Chemistry 1963–1970. Amsterdam:Elsevier Publications.

Xie W, Solomons KR, Freeman S, Kaetzel MA, Bruzik KS, Nelson DJ, et al. 1998. Regulation of $Ca^{2+}$-dependent $Cl^-$ conductance in a human colonic epithelial cell line (T84): cross-talk between Ins(3,4,5,6)P4 and protein phosphatases. J Physiol (Lond) 510:661–673.