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Oceans and human health: Emerging public health risks n the marine environment

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Abstract

There has been an increasing recognition of the inter-relationship between human health and the oceans. Traditionally, the focus of research and concern has been on the impact of human activities on the oceans, particularly through anthropogenic pollution and the exploitation of marine resources. More recently, there has been recognition of the potential direct impact of the oceans on human health, both detrimental and beneficial. Areas identified include: global change, harmful algal blooms (HABs), microbial and chemical contamination of marine waters and seafood, and marine models and natural products from the seas. It is hoped that through the recognition of the inter-dependence of the health of both humans and the oceans, efforts will be made to restore and preserve the oceans.

Keywords

Harmful algal bloom (HAB); Microbial pollution; Global climate change; Anthropogenic pollution; Natural products; Marine models

1. Brief introduction

In the past, the most obvious human health issues, associated with the oceans have been those of deaths and injury among the marine occupations such as fishing (NIOSH, 2003). However, there is an increasing recognition of the inter-relationships, between more global issues of

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human health and the oceans. The 1999 National Research Council book “From Monsoons to Microbes: Understanding the Oceans Role in Human Health” first laid out specific focus areas of scientific interest and data gaps. These included: global change, harmful algal blooms (HABs), microbial and chemical contamination of marine waters and seafood, and marine models and natural products from the seas (Knap et al., 2002; Dewailly et al., 2002; NRC, 1999; Anon, 2001; Pew Report, 2003; Stegeman et al., 2002; Kovats et al., 1998; Tyson et al., 2004; Fleming and Laws, 2006)

Climate is inextricably linked to many human health issues, playing a central role in driving environmental variations in temperature, precipitation and winds. All of these physical factors may interact with biological, socioeconomic and cultural factors to result in impacts on human ceans morbidity and mortality. It is increasingly important to understand the environmental and societal phenomena that lead to health impacts in order to design policy strategies to minimize the negative impacts (Rayner and Malone, 1998; NRC, 1999; Knap et al., 2002; Wolff, 2002). The interactions between oceans and human health are increasing, in part, due to the increasing numbers of humans living within close proximity of the world’s oceans. A significant proportion of the world’s population live within 75 miles of an ocean coast and this density of human coastal populations is increasing daily, particularly in subtropical and tropical areas (Knap et al., 2002; Tibbetts, 2002). In the last two years, two major Ocean Commissions in the United States, the US Ocean Commission and the private Pew Ocean Commission, have warned that coastal development and population pressures along coasts are responsible to a significant degree for the dramatic degradation of US ocean and coastal environments (Pew, 2003; Ocean Commission, 2004). The significant consequences of this increased population density, particularly in subtropical coastal regions, can be seen in the horrific results of recent weather events: Hurricane Mitch (October 1998) caused over 9000 deaths with another 9200 people missing in Honduras, Nicaragua, Guatemala and El Salvador, while an earthquake and tsunami in Papua, New Guinea (July 1998) caused over 2000 deaths and the earthquake and tsunami in Indonesia and beyond in December 2005 caused the deaths of at least 175,000 people. Due to severe poverty and limited resources of these human populations in subtropical areas, the oceans remain an important source of protein for local subsistence, quality of life and are an integral part of other economic activities such as tourism.

Human populations, particularly coastal dwellers, rely heavily on the use of unpolluted coastal marine waters for both food and recreational purposes. However, microbial contamination by bacteria, viruses and protists, related directly and indirectly to human and animal activity, increasingly is affecting the safety of the seafood supply, as well as the commercial and recreational use of coastal marine waters. In addition to microbial contamination, predominantly anthropogenic chemical contamination of marine waters has lead to the increasing threat of high levels of heavy metals, polyaromatic hydrocarbons, and other environmentally persistent substances entering the marine foodchain (Dewailly et al., 2000). Food poisoning and recreational/occupational exposure to contaminated marine waters have been estimated to cost millions of dollars in health costs and loss of income worldwide (NRC, 1999; DeLong, 2001; Pruss, 1998; Lipp and Rose, 1997; Anderson et al., 2000). At the same time, in some cases possibly due to the increased nutrient loading from human activities and/or global change, the number, geographic ranges, and variety of harmful algal blooms (HABs) and their toxins appear to be increasing, with impacts on human health indirectly through the food chain as well as directly for coastal marine dwellers (Van Dolah, 2000; Anderson,1994; Backer et al., 2003a,b; Backer et al., 2005; Fleming et al., 2002; Anderson et al., 2000).

Finally, there has been the realization that, similar to, or perhaps even more than the endangered tropical rainforests, the earth’s oceans are a source of great biological diversity with an almost unexplored potential to provide significant therapeutic, as well as nutritional, benefits for humans and other animals (NRC, 1999; Faulkner, 2001). Current successful examples include:

Bryostatin 1, a potent anticancer agent from a marine invertebrate; Ecteinascidin 743, a potent anticancer drug from the Caribbean sea squirt; and Discodermolide, a potential anticancer drug from a marine sponge in clinical trials. In addition to the marine organisms and coral reefs, even the HAB toxins themselves may be of future therapeutic value for humans (Burja et al., 2001; Abraham et al., 2005). Finally, the marine animals themselves may serve as alternative models of human diseases and human physiology (such as the sea slug, aplysia, and the elucidation of the processes of memory). Therefore, the exploration and preservation of the earth's marine environment have significant worldwide public health implications for current and future generations.

2. Human health and climate uncertainty

The ocean plays a vital role in climate via its capacity to store and transport heat around the globe. Ocean currents and atmospheric winds together produce the climate as we know it. Climate is distinct from weather: "weather" is the daily to weekly fluctuations in temperature, winds, precipitation, etc.; "climate" is what is expected on a season-to-season basis, and relates quite closely to the Sun's radiation (e.g., it snows and is 'cold' in northern North America in winter). Year to year fluctuations in climate are what is known as "inter-annual variability". A dramatic example of inter-annual variability is the El Ninño/Southern Oscillation (ENSO). ENSO events are periodic warming (El Niño) and cooling (La Niña) in the eastern equatorial Pacific Ocean which arise approximately every 2–10 years with varying degrees of intensity. The physical impacts of ENSO are not confined to the Pacific Ocean, but are felt throughout much of the globe via changes in atmospheric circulation patterns which affect temperature and precipitation patterns worldwide. Although there is no single identifiable cause, or trigger, for ENSO events, it is possible to predict this phenomenon 3–6 months in advance using computer models (Glantz, 2001; International Research Institute for Climate Prediction, 2003).

Beyond inter-annual variability, there are well known trends in climate patterns that have taken place over the last few decades, even going back an entire century. The mean temperature of the entire globe has increased by 0.6–1.6 °F (0.4–0.8 °C), and the sea level has risen by 10–20 cm since the beginning of the 20th century. These trends are commonly referred to as "global warming" or "global climate change". The specific causes of these trends are difficult to prove, but there is increasing consensus in the scientific community that human activity over the 20th century, in particular the addition of very significant amounts of carbon dioxide (CO_2) due to fossil fuel burning, have had a measurable effect on the climate. The Intergovernmental Panel on Climate Change (IPCC) has produced three comprehensive reports (in 1992, 1995, 2001) which included a summary of the state of scientific understanding of the impacts of human activities on climate and projections about how the climate may change under these so-called "anthropogenic forcings" in the future (a fourth report is scheduled to come out in 2007). Those studies suggested that global warming and sea level rise will continue for many decades, even with the most optimistic scenarios for cut-backs in fossil fuel burning.

However, there remain very significant uncertainties about how the physical climate will change. Much of this uncertainty arises because of the incomplete understanding of how all of the different parts of the climate system interact, and in particular, what role the ocean will play in the climate's response to these anthropogenic forcings. Some scientists believe that in addition to the slow and steady changes in temperature and sea level, global warming could impact the frequency, severity and spatial patterns of climate events such as ENSO seasonal weather patterns (IPCC, 2001). With the ocean playing an important role in affecting and being affected by climate change, its linkages to human health must be viewed in the context of climate variability and climate change. Some of the known impacts of climate on human health on different timescales are discussed below.

2.1. Extreme events

Hurricanes (typhoons) and tornadoes are examples of extreme events that have both immediate and medium term impacts on large groups of people. Powerful winds and tidal surges physically impact dwellings and persons who have not been evacuated. Post-hurricane problems (such as tainted drinking water supplies resulting in diarrheal diseases, and vector-borne disease outbreaks resulting from standing water) can inflict much more human suffering than the storm itself, if relief measures are not quickly implemented. Thus, hurricanes of the same magnitude and with similar characteristics will impact groups differently depending on their levels of vulnerability (e.g., relevant and enforced building codes), capability of the particular society to respond (e.g., communication and transportation infrastructure), and other socioeconomic factors (e.g., availability of insurance) (Diaz and Pulwarty, 1997). There is evidence of ENSO’s influence on the number of Atlantic hurricanes, and there are also multi-decadal trends in the number of the most intense Atlantic storms (Goldenberg et al., 2001). As coastal populations continue to grow, these climate related fluctuations in hurricane number may lead to even greater impacts, particularly in poorer subtropical coastal areas (Pielke and Landsea, 1998).

2.2. Seasonal to inter-annual climate variability

Seasonal changes are linked to a range of well known health impacts (e.g., ‘the flu season’, pollen outbreaks, ozone and UV exposure damaging skin cells, etc.). Outside of the seasonal cycle, ENSO has the greatest impact on climate, especially in the tropics and subtropics. Increases in ocean temperature in the Pacific by themselves can lead to ecosystem responses, such as increased occurrence of algal blooms. These blooms may concentrate toxins that can be transported via wind to land and vice versa (Backer et al., 2003a). In other cases, the temperature change may trigger changes in the dormant stages of diseases such as cholera (Colwell, 1996). The cholera may then be transmitted to humans through the handling of seafood products and more direct exposure. The warm water off the coast of Peru during a relatively mild El Niño is attributed with triggering a cholera outbreak that in turn triggered a panepidemic that swept throughout Latin America in the early 1990s (Epstein et al., 1994).

The secondary impacts of ENSO include changes in the patterns of precipitation (space and time distribution, in addition to total quantity). In the case of increased precipitation, for example, increases in mosquito and other insect vector populations that carry a range of diseases due to more areas with stagnant water (i.e., malaria, dengue, etc.) might be expected (Kovats, 2000). ENSO-related precipitation changes also affect the habitats of animals that can host and transmit diseases (Shaman et al., 2004). As the ability to predict such epidemiological outbreaks increases (Bouma et al., 1997; Hopp and Foley, 2001; Myers et al., 2000), some proactive steps (e.g., education campaigns, spraying, stockpiling medicines) can be taken.

Changes in ocean characteristics that contribute to drought can result in many other types of impacts. The fires in Indonesia during the 1997–98 El Niño led to extremely poor air quality throughout much of Asia, impacting those vulnerable to respiratory problems. Droughts can also change predator–prey relationships in ecosystems, leading to dominant species that may host pathogens such as viruses harmful to humans (e.g., rodents carrying Han-tavirus) (Epstein, 1995).

2.3. Climate change

As on inter-annual timescales, trends in climate occurring over decades to centuries can have both direct, as well as rather indirect, impacts on human health. As Colwell (1996) noted, the incidence of some cholera outbreaks appears to be related to ocean temperatures. With temperature changes projected to be as large as 8 °F in coming decades, it is difficult to predict how such large, global changes will further impact waterborne disease outbreaks. Compounding these temperature changes are changes in sea level. As the level of the sea rises, salt water can intrude into freshwater systems on land, which may have significant impacts on the quality and availability of drinking water (Meehl, 1996). There are also potential health impacts associated with temperature changes over land. For example, growing seasons in some areas may become shorter and the temperature and precipitation extremes more erratic, leading to poorer harvests for subsistence farmers, that in turn can impact nutrition of large populations already vulnerable to disease (e.g., much of sub-Saharan Africa). Because of the large range of possible physical climate changes over both ocean and land that may occur in the future, and the complexity of the biological and sociological responses, it is difficult to fathom the range of potential impacts on human health in the decades to come. Some, in fact, may be positive for some areas or sectors (for example, extended growing seasons in some higher latitude areas), but there exists great uncertainty in specifying future winners and losers.

2.4. Final points: prediction and policy relevance

Uncertainty in the projections of climatic change precludes predicting how the specific characteristics of impacts in different regions will be manifested. Put simply, the predictive models are still too crude to allow targeted actions related to health to be taken at local levels. Due to the uncertainty associated with global warming scenarios and impacts, special attention should be paid to health impacts associated with seasonal to inter-annual climate phenomenon and extreme events, as they can serve as proxies for anticipating both physical–biological impacts and human responses that may occur in the future. These events occur on timescales more amenable to political reactions. Furthermore, it is already known that basic advances in developmental factors such as access to clean water, sewage systems, and vaccination programs make human populations much less vulnerable to climate-health hazards (Kates, 2000). Perfect predictions of the future are not needed, however to take common sense steps toward reducing societal vulnerability to the inevitable surprises that await us.

3. Harmful algal blooms (HABS)

Harmful algal blooms (HABs) are caused by blooms of single-celled algae known as phytoplankton, such as dinoflagellates, diatoms and cyanobacteria (NRC, 1999). HABs can occur in all aquatic environments; in marine environments, they are also known as “red tides” since the organisms discolor the water a range of different colors (including red). HABs cause harm to the environment and other organisms either through such severe overgrowth that the HAB organisms eliminate the growth of other species and/or by the elaboration of extremely potent natural toxins.

A number of human illnesses are caused by ingesting seafood contaminated with the natural toxins produced by the HAB organisms (Backer et al., 2005; Backer et al., 2003b; Baden et al., 1995; Fleming et al., 2001). Phytoplankton are the base of the marine food web, and toxins they produce can bio-accumulate and concentrate in organisms higher in the food chain. In addition to exposure through seafood ingestion, environmental exposures can occur when the HAB organisms are broken up by waves. For example, human exposure to water and aerosols containing toxins during the break-up of Florida red tides have been associated with reports of respiratory distress (Backer et al., 2003a; Fleming et al., 2005; Kirkpatrick et al., 2004).

Some toxins elaborated by marine phytoplankton can be acutely lethal. The toxins, small non-peptides, are some of the most powerful natural substances known; for example, ciguatoxin associated with ciguatera fish poisoning is toxic to humans in a total body dose of 70 ng. Because these toxins are tasteless, odorless, and heat and acid stable, normal screening and food preparation procedures will not prevent intoxication if the fish or shellfish is contaminated (Baden et al., 1995).

3.1. Human diseases

The primary diseases associated with marine phytoplankton result from eating toxin-contaminated seafood (primarily shellfish). These illnesses include: amnesic shellfish poisoning (ASP), diarrheic shellfish poisoning (DSP), neurotoxic shellfish poisoning (NSP), azaspiracid shellfish poisoning (AZP), and paralytic shellfish poisoning (PSP). Other human illnesses are caused by ingesting toxins from marine phytoplankton, but are not necessarily associated with a free floating bloom. For example, ciguatera fish poisoning results from consuming fish contaminated with ciguatoxins elaborated by phytoplankton (e.g., *Gambierdiscus toxicus*) blooming on coral reefs (Backer et al., 2003b, 2005; Baden et al., 1995; Fleming et al., 2001, 2002; Lehane and Lewis, 2000). In addition to these diseases, human exposure to blooms of HAB organism may result in other health complaints. For example, as noted above, investigators have reported both upper and lower respiratory symptoms and decreased respiratory function among persons (particularly asthmatics) visiting beaches with active blooms of the Florida red tide organism, *Karenia brevis* (Backer et al., 2003a; Kirkpatrick et al., 2004; Fleming and Laws, 2006). The symptoms are caused by exposure to marine aerosols containing brevetoxins (the natural toxins elaborated by the organism) that have been driven onshore by the wind.

The primary target of many HAB toxins is the neurologic system, although affected individuals usually present a wide range of symptoms, resulting in confusing clinical pictures. Gastrointestinal symptoms may begin minutes to hours after eating contaminated seafood. In the case of paralytic shellfish poisoning (PSP), amnesiac shellfish poisoning (ASP), and ciguatera fish poisoning, accompanying acute respiratory distress may be fatal within minutes to hours. Ciguatera and amnesic shellfish poisoning (ASP) may also produce debilitating chronic neurologic symptoms lasting months to years. Other toxins, for example those from the blue green algae (cyanobacteria), can cause dermatotoxicity, hepatotoxicity, immunotoxicity, and respiratory toxicity, and they can be carcinogenic (Backer et al., 2003b, 2005; Baden et al., 1995; Fleming et al., 2001). Chronic disease (neurologic, immunologic, etc.) associated with the HAB toxins is an area of active scientific research. For example, Landsberg and others (Van Beneden, 1997; Landsberg, 1996) have reported the increased incidence of gonadal tumors in shellfish exposed to HAB toxins with carcinogenic properties, while Cordier et al. (2000) found increased digestive cancers among humans living in areas with DSP poisonings in France. The long-term health of the human populations who consume these potentially carcinogenic and neurotoxic organisms should be considered an important priority in terms of their potential public health impact.

Under-diagnosis and under-reporting, especially in endemic areas, make it difficult to know the true worldwide incidence of the marine toxin diseases; ciguatera affects at least 50,000–100,000 people per year who live in or visit tropical and subtropical areas, but there is significant under-reporting of this relatively common marine toxin disease even in endemic areas (CDC, 1996; McKee et al., 2001; Lehane and Lewis, 2000). Furthermore, it is not clear if the incidence of these diseases is increasing worldwide, given the lack of appropriate diagnosis and surveillance (Fleming et al., 2002). However, greater numbers of human–marine interactions, as well as the apparent increased frequency of HABs, suggest growing incidence of HAB-associated human illness (Van Dolah, 2000; Hallegraeff, 1992).

Incidence and prevalence rates for these illnesses, particularly in areas where seafood is a critical part of a subsistence diet and where the diseases are endemic, can also be high. Human populations most likely to be exposed to, and thus affected by, HAB toxins include: those occupationally involved in seafood harvesting, shipping and processing; seafood consumers; environmental workers; and individuals who live, work and play on or near the water and coastal communities, especially indigenous peoples who rely on seafood for a substantial proportion of their diet (Backer et al., 2003b, 2005).

3.2. Economic impact

As noted above, in the past many of these illnesses have been highly localized to island and coastal communities as endemic diseases. With increasing worldwide seafood consumption and trade, as well as international tourism, these diseases are expanding beyond their traditional geographic boundaries. One side effect has been the high costs of diagnosis and treatment of disease in traditionally non-endemic areas (Todd, 1990; Lange et al., 1992). Anderson et al. (2000) estimated that at least US$449,291,987 were spent on dealing with the known HABs from 1987 to 1992 in public health, commercial fishery, recreation/tourism and monitoring/management in the US alone, with an average cost of approximately US$50 million/yr (Hoaglund et al., 2002). Lewis (1986) found that ciguatera in the South Pacific caused depression of both the local and exporting fishing industries and tourism, and had an indirect affect on human health due to avoidance of consumption of fresh fish. Accurate estimates of the human costs of these diseases necessitate adequate knowledge of their prevalence and incidence, as well as the understanding of their acute and chronic human health effects.

3.3. Causes

In addition to increased worldwide seafood consumption, other anthropogenic factors may have helped spread the dinoflagellates and their toxins. Human-assisted transportation of the dinoflagellates or their cysts occurs in spat cultivation (e.g., young bivalve shellfish sold commercially to global markets for aquaculture) and through the dumping of ship ballast water. In response, new international regulations will require ships to purge ballast water in the open ocean prior to docking (Hallegraeff and Bolch, 1992b). Human-generated environmental changes, such as reef destruction and eutrophication, also may help explain the apparent increase in human marine toxin disease as well as the increase in red tides reported worldwide (Todd, 1994; Viviani, 1992; Epstein et al., 1994; Tester, 1994; Stegeman et al., 2002; Van Dolah, 2000).

As discussed above, global climate changes, which some suggest are linked to human activities, also may help explain the apparent global increase of algal blooms as well as the appearance of new marine toxin diseases (Todd, 1994; Viviani, 1992; Epstein et al., 1994; Tester, 1994; Stegeman et al., 2002; Van Dolah, 2000). For example, cholera outbreaks have been linked to HABs since copepods carrying the bacteria, *Vibrio cholerae*, feed on marine algal blooms; thus, these algal blooms can lead to cholera dissemination and outbreaks associated with increasingly frequent monsoon flooding and global warming (Epstein et al., 1994).

3.4. Prevention

The prevention of the HAB-related diseases in human populations is based on monitoring and preventing exposures, as well as surveillance of disease in human populations (Fleming et al., 1995; Todd, 1997; Backer et al., 2003b, 2005). For example, in the case of the diseases such as PSP, primary prevention is comprised of shellfish bed monitoring; when saxitoxin levels in the shellfish become dangerously high, beds are closed to harvesting. Continued monitoring allows reopening of the shellfish beds when toxin levels drop to levels that make the shellfish safe for human consumption. Secondary prevention activities are developed to decrease the prevalence of disease by reducing the duration of clinical illness and by instituting early detection. Secondary prevention of the HAB-related illnesses could involve the surveillance of biomarkers of both exposure and sub-clinical effects in target populations. Additional activities would include the development of educational and monitoring systems (including environmental and human health monitoring) for future primary prevention. The goal of tertiary prevention is to reduce complications resulting from actual HAB-related illness and disease. This would involve the early diagnosis and treatment of clinical disease.

All forms of public health prevention require the existence of an infrastructure including knowledgeable public health personnel who are able to work in the field collecting surveillance information and exposure samples. Also important is the education of healthcare and public health personnel concerning the diagnosis, treatment, and reporting of HAB-related illnesses. At-risk populations should be informed about how to recognize HAB-related illnesses as well as measures to prevent exposure to HAB toxins (such as not consuming shellfish during times of red tides and/or fish kills or avoiding drinking from fresh water with toxic blue, green blooms). Finally, the cooperation of the seafood industry and other industries will be required to implement successful prevention programs (Fleming et al., 2001; Backer et al., 2003b, 2005; Fleming et al., 2002).

4. Microbial contamination

Microbial contamination by marine bacteria (and their toxins), viruses, parasites and other organisms is an increasing worldwide problem. Microbial contamination occurs secondary to point source sewage dumping, as well as from indirect contaminated run off; it is predominantly an issue in coastal areas. Humans are exposed to microbial contamination by consuming contaminated seafood, and through recreational and occupational exposure to contaminated marine waters.

5. Microbial water contamination

As with shellfish beds, water quality for coastal waters used for recreational purposes has been regulated by measuring concentrations of indicator microbes. Microbes so used are those typically found in human feces in high concentrations. An elevated concentration of these indicator microbes within coastal waters and habitats should indicate that the water has been contaminated by human waste, and is unsafe for recreational use. There have been many studies conducted in areas of known point sources of sewage contamination where the use of these indicators has been found to be reliable (Haile et al., 1999; USEPA, 1976; USEPA, 1986). A few studies have found “indicators” to be reliable in areas where non-point sources of sewage contamination were identified (Lipp et al., 2001).

Recently, however the use of indicator microbes to regulate the recreational use of coastal waters has come into question, particularly in the subtropical and tropical marine environments in areas where there are no known point sources of contamination. The US Environmental Protection Agency (USEPA, 1986) recommends that the indicator microbe enterococci be utilized for marine waters, and *Escherichia coli* or enterococci for fresh waters, to determine whether health advisories or closures should be issued. The USEPA/Beaches Environmental Assessment and Coastal Health (BEACH) Act of 2000 requires that in the US by 10 April 2004, coastal states and territories adopt beach water quality criteria at least as protective as the USEPA’s (1986) criteria. Many states are in the process of accepting the USEPA (1986) criteria. However, as of 2006, many monitoring agencies worldwide did not adopt USEPA’s (1986) criteria, and still use USEPA’s (1976) recommendation of fecal and/or total coliforms as the indicator microbes of choice.

Studies have shown that total coliforms proliferate naturally in soil (Toranzos, 1991), particularly in subtropical environments. Studies conducted in Hawaii, Guam, Puerto Rico, Sierra Leone and Florida (Fujioka and Byappanahalli, 1998; Fujioka and Byappanahalli, 2001; Rivera et al., 1998; Hazen and Bermudez, 1988; Wright, 1989; Solo-Gabriele et al., 2000; Desmarais et al., 2002) have shown that in the absence of any known sources of human/animal waste, fecal indicators are consistently present and recovered in high concentrations in the environment (streams, vegetation, soil/sediment, and storm drains). Both enterococci and *E. coli* have been found in the environment in areas where no point sources of sewage contamination are apparent. These indicator microbes multiply in warm tropical environments outside of the human intestinal tract, thereby calling into question the use of these indicator microbes as indicators of sewage (Roll and Fujioka, 1997; Solo-Gabriele et al., 2000; Desmarais et al., 2002). Furthermore, Griffin et al. (1999) found elevated levels of enteric viruses in waters within the Florida Keys which did not correlate with the levels of indicator microbes within those waters.

To make matters even more complicated, there have been documented cases where coastal waters monitored for both sets of microbial indicators (enterococci and members of the coliform group) have passed regulatory limits for enterococci but not for fecal coliforms, and vice versa (S. Elmir, Department of Health, personal communication). So a regulator is left with a perplexing situation: which indicator microbe(s) should be used, and once data are obtained, how should these be interpreted?

The USEPA guidelines (i.e. using *E. coli* and enterococci) for coastal waters were established based on three water quality and epidemiological studies performed in the 1980s in temperate regions; furthermore, all had a known point source of contamination potentially impacting the study site (USEPA, 1986). As discussed above, questions have been raised about whether or not the results of such studies are applicable to the tropical coastal ecosystems, in particular in areas where there are no known point sources of sewage, given differences in hydro-climatologic and microbiologic conditions.

The USEPA’s (1999) Action Plan for Beaches and Recreational Waters (USEPA, 1999) acknowledged that the current indicators can be found in subtropical environments where there was no apparent warm-blooded animal source of contamination. The document emphasized the need to establish the conditions under which the microbes proliferate and potentially develop new tropics-specific indicators. The US Environmental Protection Agency 2001 Workshop (Fujioka and Byappanahalli, 2001) concluded that: (a) soil, sediments, and plants may be significant indigenous sources of indicator bacteria in subtropical waters; (b) the inherent environmental characteristics of the tropics affect the relationships between indicators of fecal contamination (*E. coli*, fecal coliforms, enterococci) and health effects observed in bathers, which may compromise the effcacy of EPA guidelines; and (c) fecal indicator bacteria (fecal coliforms, *E. coli*, enterococci) can multiply and persist in soil, sediment, and water in some subtropical environments.

Several epidemiologic studies have found that, compared with bathing in uncontaminated waters, bathing in temperate recreational waters contaminated with domestic sewage or storm drain runoff has been associated with an increased risk for transmission of infectious diseases, including gastroenteritis, febrile respiratory illness, eye and ear infections, and skin infections and rashes. However, there were weaknesses in the designs of many of these studies, including the absence of data describing microorganism levels in the water that could be used to describe an individual’s exposure, and a failure to account for other risk factors for the illnesses of interest (Fleisher et al., 1998). Pruss (1998) reviewed all the significant existing epidemiologic studies on the health effects from exposure to recreational water. She found that most studies reported a dose-related increase in swimming-related illnesses associated with increases in recreational water indicator bacteria counts. The indicator organisms that reportedly correlated best with the health outcomes were enterococci/fecal streptococci for marine and freshwater, and *E. coli* for freshwater. The majority of these studies were conducted in the northern US and UK and often with known point sources of pollution, with few studies evaluated in subtropical marine recreational waters without known point sources of pollution (Haile et al., 1999; Kueh et al., 1995; Fujioka et al., 1994; Prieto et al., 2001; Fleisher et al., 1998).

These results, coupled with the evidence that infectious microorganisms can occur in subtropical waters in the absence of specific contamination events and the dearth of information describing the impact of these illnesses (i.e., the severity of the illness or need for medical care), indicate that the actual public health risk associated with bathing in subtropical waters containing microorganisms, including those from EPA’s list of microbial indicators, is still unknown.

6. Microbial seafood contamination

Seafood poisoning, particularly secondary to microbial contamination, accounts for a large and growing proportion of all food poisoning incidents. In the United States, fish, shellfish, and other marine organisms are responsible for at least one of six food poisoning outbreaks with a known etiology, and for 15% of the deaths associated with these particular outbreaks (CDC, 1996; Lipp and Rose, 1997; Anon, 1995; Fleming et al., 2001). From 1971 to 1990, seafood was the single most important vehicle in food poisoning outbreaks in Korea (32%) and Japan (22%), where seafood was responsible for 43% and 62%, respectively, of outbreak-related fatalities (Lee et al., 1996b; Chan, 1995). Of note, persons with compromised immune systems, such as the elderly or persons with HIV/AIDS, are at particular risk from microbial seafood poisonings.

Shellfish, especially the filter feeding bivalve mollusks (oysters, scallops, mussels, clams, cockles) live in estuarine areas and obtain their food by filtering large amounts of water. A wide variety of organisms and toxins pathogenic to humans can accumulate in the shellfish alimentary tract, especially if the filtered water is contaminated by sewage and/or chemical pollutants. Shellfish harvested in contaminated marine waters are extremely efficient transvectors of seafood pathogens because by filtering the water as they feed, the shellfish are concentrating the pathogens (CDC, 1996; Todd and Harwig, 1996; Cliver, 1994). The other commonly consumed group of shellfish is the crustaceans (e.g., shrimp, crab, and lobsters). Although not filter feeders, they can acquire surface contamination from contaminated water. Refrigeration paradoxically increases the pathogens’ geographic range, permitting transport of apparently healthy seafood to many geographic areas, thus extending and prolonging outbreaks. Inadequate procedures for tracing and recall of contaminated seafood also serve to extend outbreaks (Dowell et al., 1995; Sugieda et al., 1996).

Traditionally, the most frequently reported seafood poisoning outbreaks have been associated with bacteria. Although increased sophistication of laboratory testing now implicates viral origins as well, new bacteria-associated seafood poisonings are appearing due to increasing worldwide seafood consumption by sensitive subpopulations, as well as parasitic infections among less-well known ethnic groups (Fleming et al., 2001).

6.1. Bacteria

Vibrios are natural inhabitants of marine environments. Pathogenic marine Vibrio species, especially *V. cholerae*, *V. parahaemolyticus*, and *V. vulnificus*, most commonly cause disease when they are ingested in raw shellfish and, less commonly, in fish (Lee et al., 1996a; Matte et al., 1994). As discussed above, many Vibrio species are not associated with fecal contamination, so the use of fecal coliform counts as clean water indicators does not ensure that water or seafood beds are free of pathogenic vibrios (Lipp and Rose, 1997). Cholera, caused by the toxin-producing *V. cholerae*, can be a severe infection with mortality rates as high as 50%, although it is more commonly an asymptomatic infection (Weber et al., 1994; Albert et al., 1997). *Listeria monocytogenes*, Salmonella and Aeromonas species are frequent contaminants of raw fish and shellfish, especially if the seafood has had prolonged exposure to elevated temperatures. The risk of transmission is higher for shellfish than for fish, because shellfish often are refrigerated for many days without obvious spoilage then eaten raw (Fleming et al., 2001).

A wide spectrum of bacterial species has been cultured from shellfish and fish without definitive etiologic connections to seafood poisoning outbreaks (Ben Embarek, 1994; Merino et al., 1995; Chen, 1995; Romero et al., 1994). Some of these organisms, like Aeromonas, are part of the normal flora of the seafood. Others are more likely introduced by unhygienic human handling. The seafood diseases caused by bacterial toxins generally are associated with improper food preparation, handling and storage. Scombroid fish poisoning, due to bacterial growth from inadequate refrigeration and handling resulting in the production of histamine-like substances, is probably the most commonly reported bacterial toxin fish-associated illness in US (Saavedra-Delgado and Metcalfe, 1993; Fleming et al., 2001). The bacteria *Clostridium botulinum*, type E, is most prevalent in fresh water and marine environments. The bacteria produce botulism toxin E on smoked fish, fish eggs, and uneviscerated and salted whitefish, often associated with inadequate canning procedures (Watters, 1995; Saavedra-Delgado and Metcalfe, 1993). Enterotoxigenic *E. coli*, the common pathogen of travelers’ diarrhea, and toxigenic *Staphylococcus aureus* have been detected on seafood (Fleming et al., 2001).

International trade in feral-harvested seafood, and increasingly in aquaculture seafood products, has facilitated the introduction of pathogens into new geographic areas, as well as into seafood and human communities (Todd, 1994). For example, *Salmonella agona* was first introduced to Europe following the importation of Peruvian fishmeal, with subsequent rapid spread into other food products, producing an increase in human outbreaks. Furthermore, the intensive use of antibiotics in the aquaculture industry, leading to antibiotic accumulation in seafood tissues, increases the potential for development of multiply-resistant bacteria (D’Aoust, 1994; Park et al., 1994).

6.2. Viruses

The small round structured viruses (SRSVs) (Matte et al., 1994) or Norwalk-like viruses, are classified as caliciviruses and are common causes of outbreaks of gastrointestinal illness. Because the infectious dose is small, cooking the shellfish does not reliably eliminate the risk of contracting gastroenteritis. Outbreaks of Norwalk-like gastroenteritis have been reported after grilling, stewing, steaming, and frying shellfish (McDonnell et al., 1997; Kirkland et al., 1996). Routine water quality tests from the areas of contaminated shellfish collection were within normal limits, demonstrating once again that fecal coliform monitoring is inadequate protection for SRSV contamination (Gunn et al., 1982).

As with other seafood-related pathogens such as *V. cholerae*, seafood poisoning with hepatitis A has been associated with significant geographic spread due to seafood export patterns. For example, an outbreak of hepatitis A after consumption of raw oysters from Florida resulted in human cases in five different states, including Hawaii (Desenclos et al., 1991). The most common cause of these outbreaks is the consumption of raw or inadequately prepared shellfish from sewage contaminated waters (Sagliocca et al., 1995).

6.3. Parasites

Consumption of raw and inadequately cooked seafood, especially in certain ethnic subpopulations, is associated with parasitic infections, particularly with anisakids and cestodes (Ahmed, 1993). Recent reports have found increased parasitic contamination in shellfish subjected to human sewage having organisms such as cryptosporidium (Fayer et al., 2003).

6.4. Prevention

Elimination of point source sewage and indirect contaminated run-off into coastal waters, as well as correct food preparation and handling, with appropriate water and seafood monitoring will eliminate the majority of microbial diseases acquired from either contaminated marine waters or contaminated seafood. This implies however, the existence of sanitary and public health infrastructure that may be a distant goal, particularly in many developing nations.

7. Anthropogenic chemicals

Over two billion people worldwide rely on seafood as a major source of protein in their diet, and seafood consumption continues to increase worldwide (FAO, 1999). Additionally, the sustainability of remote coastal populations depends on a source of uncontaminated seafood. Many types of manmade contaminants threaten the marine system, brought to the oceans by contaminated freshwater and run off, direct industrial and solid waste dumping, and even by atmospheric transport (Kaufman et al., 2002). These anthropogenic contaminates include synthetic organic chemicals and specific heavy metals.

7.1. Synthetic organic chemicals

Synthetic organic chemicals are a loosely defined group of substances that include all synthetic substances that result from industrial activities, most infamously the petroleum hydrocarbons and polycyclic aromatic hydrocarbons (PAHs). Their introduction to the marine environment arises from direct discharge (point sources), discharge to municipal sewage systems or rivers, and venting to the atmosphere. These compounds are best classified in terms of their source functions (size and nature of the land-based sources), persistence, bioavailability, tendency to bioaccumulate, and toxicity.

Substances of particular concern are chlorobiphenyls, chlorinated dioxins, and some industrial solvents. Current scientific knowledge of these compounds is extensive, but still not complete, and new compounds continue to be identified in animal tissue. For example, the flame retardants polybrominated biphenyls and polybrominated diphenyl ethers have been reported recently in sperm whales, which feed in deep waters. Along with tetrabromo-bisphenol-A and hexabromocyclododecane, global production of these compounds is approximately 150,000 tons per year (DeBoer et al., 1998).

Some pesticides and herbicides also pose potential hazards to human health. Some synthetic organic chemicals have been linked to possible endocrine-disrupting functions. Herbicide and pesticide exposure seen in wildlife, including marine and freshwater organisms, may be linked with reproductive and developmental problems seen in humans (Heindel et al., 1998; Aguilar et al., 2002). Dichlorodiphenyltrichloroethane (DDT) was banned in the United States and Europe in 1972 but is still being used in tropical and subtropical countries for malaria control. The International Agency for Research on Cancer (IARC) considers DDT to be “possibly” carcinogenic. DDT is regarded as an estrogen mimic, and dichlorodiphenyldi-chloroethylene (DDE) is an androgen receptor antagonist. Subacute levels of exposure show effects on the central nervous system of humans (AMAP, 1998).

PAHs are derived from the thermal transformation of fossil fuel, primarily petroleum. Some PAHs are formed by naturally occurring, low-temperature metamorphic processes. They enter the marine system through municipal or industrial effluents, via atmospheric pathways from industrial emissions, or through exhaust fumes of internal combustion engines and domestic heating systems. The known carcinogenic effects of some PAHs are of primary concern for human health. PAHs enter humans primarily through food consumption. For example, among non-smokers, 99% of total benzo[*a*]pyrene levels come from ingestion (Kennish, 1997). PAHs bioaccumulate in marine organisms such as bivalves, and are regarded as animal carcinogens. They can be absorbed by the human body, metabolized by the liver and kidney, and eliminated via feces and urine. The health outcomes associated with PAH exposure include lung cancer, low birth rates, and decreased fecundity (AMAP, 1998).

Human exposure to synthetic organic substances occurs primarily from eating contaminated foods. A large number of studies (e.g., AMAP, 1998) related to this issue have been performed in remote fishing communities in the Arctic, because these lipophilic contaminants are transported by the atmosphere, deposited in the land and water, ingested by wildlife, and biomagnified up the marine food web, ultimately being consumed by humans living in these regions. Unfortunately, because the “environmental soup” has many different contaminants, relating a deleterious effect in specific marine organisms to the action of a specific compound is very difficult. Studies suggest that polychlorinated biphenyls (PCBs) do have a variety of effects on human reproduction, neurobehavioral development, liver function, birth weight, immune response, and tumorigenesis (Dewailly et al., 2000; Heindel et al., 1998). In particular, studies in Arctic populations have linked fetal cord blood PCB concentrations with low birth weight, small head circumference, and immunosuppression (AMAP, 1998).

7.2. Metals

The metals group is composed of all metals and metalloids in the marine environment. It is important to distinguish between the introduction of metals from anthropogenic activities and those from natural weathering processes. Although sources of metals in the marine environment are numerous and diverse (elevated metal levels accompany almost every type of effluent), little evidence of widespread adverse biologic effects exists other than risks to human health posed by metals in seafood. Elevated metal levels in seawater are unlikely (other than in the immediate vicinity of point sources), due in most cases to their rapid removal by adsorption to suspended particulate materials. Tributyl-tin (used as a constituent in antifouling paints on boats) and methyl mercury (formed by the microbial methylation of inorganic mercury) are two highly toxic compounds that have been shown to be responsible for well-recorded marine pollution incidents. The basis of bioaccumulation and toxicity for these substances lies in their forms of speciation. Thus, special attention may be required to identify specific forms of other metals in the future.

Mercury is used in a wide range of industrial processes and mining practices. Once it is released into anoxic environments, bacteria can rapidly methylate this metal. Methyl mercury is biomagnified in the environment (Dewailly et al., 2001). Its half-life is 60–120 days in humans, up to 2 years in fish. Methyl mercury causes cytotoxic, kidney, and brain damage, with concentrations of 1–2 mg/kg in brain tissue producing neurotoxic effects. Fetal exposure to methyl mercury is of great concern since the rapidly growing neurologic tissue of the fetus is especially vulnerable to the effects of methyl mercury.

As expected, individuals who consume seafood have the highest concentrations of methyl mercury in their tissues. Average hair concentrations of humans eating 10–20 g/day are less than 1 ppm; however, among individuals poisoned by methyl mercury in Japan and Iraq, concentrations of 50–100 ppm were found in hair samples (Harada, 1995). Environmentally chronic exposures have been reported in populations dependent on fishing in Amazonia, Coastal Peru, Seychelles, Faroe Islands, the Arctic, and New Zealand (Davidson et al., 1998; Grandjean et al., 1997; Kjellstrom et al., 1986; Marsh et al., 1995; Myers et al., 1995).

Cadmium can bioaccumulate in the environment, including the ocean environment, and its uptake by humans is affected by the uptake of lead. IARC has designated cadmium as a Group I carcinogen (i.e. known human carcinogen), although the major human health risk associated with cadmium is nephrotoxicity (proteinuria and renal failure) (AMAP, 2004). Environmental exposures to lead have been linked to poor neural development in children, but no cases of lead poisoning related to a marine source have been documented. The use of leaded gasoline in the developed world has decreased but remains an issue in less developed areas of the world. Arsenic is also a highly toxic metal, but, as with lead, no known arsenic poisonings have occurred as a result of marine exposures or consumption of seafood. Both arsenic and lead occur in marine sediments as a result of industrial discharge. Like mercury, arsenic can be converted to more lipophilic and toxic methyl forms. Although the effects of these metals on marine ecologic health are known, the specific mechanisms of transfer to humans merit more attention.

7.3. Other issues

Specific clinical effects related to contaminants have been the subject of numerous epidemiologic studies. In populations exposed to low doses, only subtle effects are expected to occur. For lead and cadmium, epidemiologic studies and animal experiments provide sufficient data to set thresholds for human exposure. The general consensus is that 10 μg/dl is the maximum blood lead concentration acceptable for children. In this case, measuring blood lead in a group of children is a relatively easy, cheap, valid, and manageable biomarker to assess both exposure and risk in children. However, for most ocean-related contaminants such as methyl mercury and persistent organic pollutants, results from epidemiologic studies are more contradictory. Cohort studies in Michigan (Jacobson and Jacobson, 1996) and North Carolina (Rogan et al., 1986) have provided conflicting results on neurobehavioral changes in children who were exposed prenatally to PCBs. Conflicting results were also reported on neurologic impairments in children who were exposed to methyl mercury during fetal development: a study in the Seychelles did not report any deleterious effects (Davidson et al., 1998), whereas a cohort study in the Faroe Islands found significant neurotoxic effects (Grandjean et al., 1997). There may be many reasons for these discrepancies, including differences in methods, exposure mixtures, nutritional interactions, and genetic susceptibility. Nevertheless, it is clear that increasing levels and distribution of anthropogenic substances in seafood and marine waters have potentially significant human health implications.

8. Remedies from the seas

The ocean is not only a source of risks to health, but also the source of novel marine animal systems and bioproducts with important applications as: pharmaceuticals, molecular probes, diagnostics, cosmetic and nutritional supplements, and biomaterials for prosthetic use as well as marine models of human disease. The rich biodiversity in the oceans forms the basis for an equally rich chemical diversity from which many bioproducts have already been discovered, and some are commercially available (see Table 1) (Pomponi, 1999).

9. Marine natural products

Based on the success of Bergmann and colleagues in the late 1950s (Bergmann and Burke, 1955), which led to the development of two drugs based on marine sponge nucleosides (Ara-A for herpes infections and Ara-C for leukemia) (Baker and Murphy, 1981), as well as the pioneering research in marine natural products drug discovery by the Roche Research Institute of Marine Pharmacology during the mid-1970s (McConnell et al., 1994), scientists began to explore marine biodiversity and its potential for discovery of new bioactive compounds. An intense effort in marine natural products drug discovery by academic, government, and industry laboratories, especially in the past two decades, is based on a number of facts. The oceans are a rich source of both biological and chemical diversity, with hundreds of thousands, perhaps even millions, of new species yet to be discovered. Marine microorganisms, in particular, represent the greatest opportunity for discovery of new species and new chemicals (Colwell, 1997; Jensen et al., 2005). A relatively small number of marine organisms, primarily algae and invertebrates, has already yielded thousands of novel chemical compounds (Ireland et al., 1993; Newman and Cragg, 2004a,b), yet only a small percentage of these chemicals has been studied for their potential as useful products. Finally, although there is a major effort by pharmaceutical companies in the design of synthetic chemicals for drug discovery, marine natural products still provide unusual chemical structures upon which molecular modeling and chemical synthesis of new drugs can be based.

A major emphasis has been on the discovery of marine-derived anticancer compounds, due in large part to the availability of funding to support marine-derived cancer drug discovery. Two examples of promising marine-derived compounds in clinical trials for the treatment of cancer are Yondelis® (ecteinascidin 743) and discodermolide. Yondelis® is a complex alkaloid derived from the mangrove tunicate *Ecteinascidia turbinata* and licensed by the University of Illinois to PharmaMar S.A (Wright et al., 1990; Rinehart et al., 1990). Discodermolide, a polyketide isolated from deep-water sponges of the genus *Discodermia*, inhibits the proliferation of cancer cells by interfering with the cell’s microtubule network (ter Haar et al., 1996). This compound is licensed by Harbor Branch Oceanographic Institution to Novartis Pharmaceutical Corporation.

Despite the emphasis on the part of the US and other government funding agencies, as well as the pharmaceutical industry, on identifying new marine-derived anticancer compounds, marine natural products have also been found to have other biological activities. Marine natural products have other potential biological activities, including the mediation of the inflammatory response. The pseudopterosins are glycosides derived from the Caribbean soft coral, *Pseudopterogorgia elisabethae* (Roussis et al., 1990). These are in advanced preclinical trials as anti-inflammatory and analgesic drugs, and purified extracts of this soft coral are available commercially as additives in skin care products. The topsentins are a class of alkaloids with potent topical anti-inflammatory activities. Evaluation of the compounds suggests that they may offer a unique opportunity for medicinal use as anti-inflammatory drugs or as additives to skin-care products, such as sunscreens (McConnell et al., 1994).

A number of marine-derived compounds also have been discovered with antiviral and antifungal activity. Like their terrestrial counterparts, chemicals produced by marine microorganisms have shown potent activity against some infectious diseases (Fuoco et al., 1997; Rowley et al., 2004), and the potential for development of marine-derived anti-infective drugs is high. Fenical and his colleagues have discovered more than 2500 species of a new genus of actinomycete, Salinospora, the majority of which show anticancer activity (Mincer et al., 2002; Feling et al., 2003).

Several marine-derived compounds, discovered initially as potential pharmaceuticals and subsequently abandoned as drug candidates for a variety of reasons (such as *in vivo* toxicity or lack of suitable patent protection to enable exclusive pharmaceutical development) are available commercially as molecular probes, non-drug substances that can be used to study the basis of important biochemical events. For example, many of the commercially available, marine-derived, molecular probes inhibit enzymes or other receptors involved in normal or pathologic molecular processes. Their use as research tools often allows scientists to study the mechanisms by which other drugs act to treat or cure a disease. Some examples are marine-derived neurotoxins (such as tetrodotoxin, saxitoxin, conotoxin, and lophotoxin) that have been instrumental in defining the structure and function of membrane channels that facilitate nerve transmission. Understanding the function of these neurotoxins has allowed drugs to be designed and targeted to those sites of nerve transmission. Research in this area has led to the development of a drug that has been recently approved by the FDA for use in pain management. Prialt® (Elan Corporation plc) is a synthetic equivalent of a cono-peptide produced by the piscivorous snail, *Conus magus*, to paralyze its prey (Olivera, 1997; McIntosh et al., 1999). Finally, the discovery of a natural antagonist (brevenal) to the potent neurotoxins called brevetoxins (both groups of chemicals produced naturally by the marine dinoflagellate, *Karenia brevis*) has lead to the patenting of brevenal and similar synthetic compounds for possible use in the treatment of cystic fibrosis and similar lung diseases (Abraham et al., 2005).

9.1. Marine models

The use of model systems as surrogates for the study of pathological states related to the environment arises from several advantages that complement the direct use of mammalian systems. Because aquatic species often have unique biological characteristics, many of them can offer the researcher a distinct experimental advantage over a mammalian system. Importantly, fish and invertebrates represent a vast phylogenetic diversity that far exceeds that of mammals. A comparative experimental approach drawing on this diversity ultimately can lead to the use of the "best" model species for a given pathology.

Since aquatic species often have different susceptibilities to environmental agents than mammals, these differences can be exploited to discover the underlying unifying mechanisms of toxicity and effect. Often the aquatic model is simpler and can give the scientist a "stripped-down" version of a more complicated mammalian system. Sometimes fish are more sensitive to critical toxins than mammals, and in particular may be more sensitive to the carcinogenic and less to the toxic effects.

In applying a comparative toxicological approach, aquatic species offer a simpler, natural, intensive exposure system because respiratory surfaces, skin, and fin surfaces (which lack keratinization) can be bathed directly in water with the toxicant of interest. Since fish and invertebrates naturally experience body temperature changes, the effects of temperature on environmental-health related processes can be directly and realistically studied in these species. Finally marine models represent enhanced opportunities for genetic research and manipulations, where developing embryos can often be directly observed, as well as convenient models for sentinel species of environmental effects.

Successful examples of marine models include: neurophysiological models (*Aplysia*, Squid, Damselfish, Turtles), developmental models (Sea Urchins, Tunicates, Zebrafish), cell and embryo preservation (Artemia, Fish Eggs), carcinogenesis models (Rainbow Trout, Medaka, *Ziphophorus*), genomics (Pufferfish), and physiologic models (Dogfish Shark, Toadfish, Killifish). Notably, beyond the initial characterization of the vertebrate genome with pufferfish that foreshadowed the human genome project, many of the above model species are now subjects of genome and transcriptome (EST) sequencing projects that will further enhance their comparative utility.

Most of the world's oceans remains to be explored. With rare exceptions (e.g., the analysis of deep sea cores to identify unusual microbes), the deep sea bottom, mid-water habitats, and most of the oceans at depths greater than those accessible by scuba, have not yet been explored for novel chemicals and marine organisms with applications to human health. The National Research Council (1999), in its review of the ocean's role in human health, recommended a greater focus on marine organisms, both as marine model systems of human diseases and as sources of new pharmaceuticals. New funding initiatives are needed to support this effort in all therapeutic areas (not just cancer), and new interdisciplinary research and education programs to provide innovative approaches to marine-based drug discovery.

10. Conclusions

This brief overview demonstrates that the interactions between the oceans and human health are complex, global and apparently increasing. Furthermore, through microbial and chemical contamination as well as global change, humans are indirectly and directly affecting the health of the oceans. This in turn has significant implications for human health, particularly if future potential remedies and models from the seas, as well as important sources of protein in seafood, are lost due to anthropogenic contamination and change. Although it is clear that challenges remain to developing a better understanding of the connection between the marine environment and human health, we now have an opportunity to mitigate and prevent further destruction of the ocean environment, and in turn, protect the health of current and future generations of humans and other organisms.

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Table 1

Some examples of commercially available marine bioproducts

Product	Application	Original source
Pharmaceuticals		
Prialt® (Elan Corporation, Dublin, Ireland)	Pain management drug	Snail, *Conus magus*
Ara-A (Acyclovir)	Antiviral drug (herpes infections)	Sponge, *Cryptotethya crypta*
Ara-C (Cytosar-U, Cytarabine)	Anticancer drug (leukemia and non-Hodgkin's lymphoma)	Sponge, *Cryptotethya crypta*
(Brevenal)	Cystic fibrosis	Dinoflagellate, *Karenia brevis*
Molecular probes		
Okadaic acid	Phosphatase inhibitor	Dinoflagellate
Manoalide	Phospholipase A_2 inhibitor	Sponge, *Luffariella variabilis*
Aequorin	Bioluminescent calcium indicator	Bioluminescent jellyfish, *Aequora Victoria*
Green fluorescent protein (GFP)	Reporter gene	Bioluminescent jellyfish, *Aequora Victoria*
Medical devices		
ProOsteon®, Biocoral® (Interpore)	Orthopedic and cosmetic surgical implants	Coral, mollusc, and echinoderm skeletons
Diagnostics		
LALF (Limulus antilipopolysaccharide factor)	Detection of endotoxins (LPS)	Horseshoe crab
Enzymes		
Vent™ and DeepVent™ DNA polymerase (New England BioLabs, Inc.)	Polymerase chain reaction enzyme	Deep sea hydrothermal vent bacterium
Nutritional supplements		
Formulaid® (Martek Biosciences, Columbia, MD)	Polyunsaturated fatty acids used as additive in infant formula nutritional supplement	Microalgae
Pigments		
Phycoerythrin	Conjugated antibodies used in ELISAs and flow cytometry	Red algae
Cosmetic additives		
"Marine extract" in Resilience® line of cosmetics (Estée Lauder)	Cosmetic (anti-inflammatory)	Caribbean gorgonian, *Pseudopterogorgia elisabethae*

[1] Adapted from Pomponi (1999)