

Indicators of Ocean Health and Human Health: Developing a Research and Monitoring Framework

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We need to critically assess the present quality of the marine ecosystem, especially the connection between ecosystem change and threats to human health. In this article we review the current state of indicators to link changes in marine organisms with eventual effects to human health, identify research opportunities in the use of indicators of ocean and human health, and discuss how to establish collaborations between national and international governmental and private sector groups. We present a synthesis of the present state of understanding of the connection between ocean health and human health, a discussion of areas where resources are required, and a discussion of critical research needs and a template for future work in this field. To understand fully the interactions between ocean health and human health, programs should be organized around a "models-based" approach focusing on critical themes and attributes of marine environmental and public health risks. Given the extent and complex nature of ocean and human health issues, a program networking across geographic and disciplinary boundaries is essential. The overall goal of this approach would be the early detection of potential marine-based contaminants, the protection of marine ecosystems, the prevention of associated human illness, and by implication, the development of products to enhance human well-being. The tight connection between research and monitoring is essential to develop such an indicator-based effort. *Key words:* biologic effects, biomarkers, contamination, human health, indicators, ocean health. *Environ Health Perspect* 110:839–845 (2002). [Online 17 July 2002] <http://ehpnet1.niehs.nih.gov/docs/2002/110p839-845knap/abstract.html>

The interactions between humans and the ocean are significant and necessitate more comprehensive study on an international scale. The world's oceans provide great health benefits to humans, ranging from food and nutritional resources, to recreational opportunities, to new treatments for disease. The rising human population and trends in migration to the world's coastal zones continue to increase pressure on this ocean/land interface. Coastal degradation, climate variability, and increased industrialization may pose human health risks from mobilization and transport of anthropogenically derived and natural toxic agents in the environment (Harvell et al. 1999). A National Research Council report on the interactions between ocean and public health, *From Monsoons to Microbes: Understanding the Ocean's Role in Human Health*, has recently been published (National Research Council 1999). International efforts to focus on ocean health and human health issues have been made by the Health of the Ocean panel of the Global Ocean Observing System (UNESCO 1996) as well as a meeting held in Bermuda, 15–19 November 1999 (Knap 2000). These programs have built on

the National Research Council report but have focused specifically on indicators of the effects of anthropogenic agents as well as natural toxins, and on questions targeting the development of biologic markers linking exposure with human and ecologic health end points.

For our purposes, the term "ocean" is all encompassing, ranging from brackish to open ocean conditions. We have defined ocean health in the broadest sense as adopted from the Health of the Ocean panel of UNESCO (1996) as a "reflection of the condition of the marine environment from the perspective of adverse effects caused by anthropogenic activities, in particular habitat destruction, changed sedimentation rates and the mobilization of contaminants" (p. 3). Such conditions refer to the contemporary state of the ocean, prevailing trends, and the prognosis for improvement or deterioration in its quality. Most contamination is concentrated in the coastal zone from a variety of sources; however, long-range transport can deliver contaminants great distances (Knap 1990) and can affect the health of remote human populations (Dewailly et al. 2000). Finally,

human health is defined as "a state of complete physical, social and mental well being, and not merely the absence of disease or infirmity; health is a resource for everyday life, not the object of living. It is a positive concept emphasizing social and personal resources as well as physical capabilities" (World Health Organization 1946: p. 100).

Background

Presently, 60% of the world's population is estimated to live in coastal areas (GESAMP 2001). In fact, the present population of coastal areas exceeds the global population of just 50 years ago (Bowen and Crumbley 1999). This settlement pattern has exacerbated the rate of change in coastal systems and has already placed the goal of "sustainable development"—the balanced socioeconomic benefit of the marine environment—out of reach for some regions. The world population is estimated to increase from about 6 billion currently to 8.3 billion by 2025, with 90% of this growth occurring in subtropical and tropical countries. 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. Natural stocks of seafood have been supplemented by the aquaculture industry. However, marine aquaculture may cause habitat destruction and pollution of the local environment through the production of waste products (National Research Council 1999).

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Many types of contaminants threaten the marine system. Figure 1, adapted from the Global Ocean Observing System's Health of the Ocean Report (UNESCO 2002), provides an overview of the general types of variables measured under various international programs and relates these to measures of ecosystem integrity. It also shows the relationship between sustainable development and human health. Only a subset of these are of specific concern to the issue of ocean and human health. These include synthetic organic chemicals, specific heavy metals, algal toxins, pathogens, pharmaceuticals, and possibly genetically modified organisms. Many of the other contaminants in Figure 1 do not have a specific pathway from the ocean to people, or if they do, the consensus of the recent conference in Bermuda (Knap 2000)

was that evidence was insufficient to warrant their special consideration here.

Recently, human health effects from exposure to the marine food chain have been highlighted by a number of studies (Grandjean et al. 1997; Marsh et al. 1995; Mulvad et al. 1996). Routes of exposure include eating, skin contact, and breathing. A major concern for public health is the ingestion of contaminated seafood, putting those humans who eat contaminated seafood over time at the greatest risk.

Synthetic organic chemicals. Synthetic organic chemicals are a loosely defined group of substances that, aside from petroleum hydrocarbons and polycyclic aromatic hydrocarbons (PAHs), include all synthetic substances that result from industrial activities. 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 tetrabromobisphenol-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).

Human exposure to synthetic organics 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. However, studies suggest that polychlorinated biphenyls (PCBs) 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). Studies in Arctic populations have linked fetal cord blood PCB concentrations with low birth weight, small head circumference, and immunosuppression (AMAP 1998).

Other organic contaminants are also of concern. For example, human exposure to dioxins is a concern for public health. 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

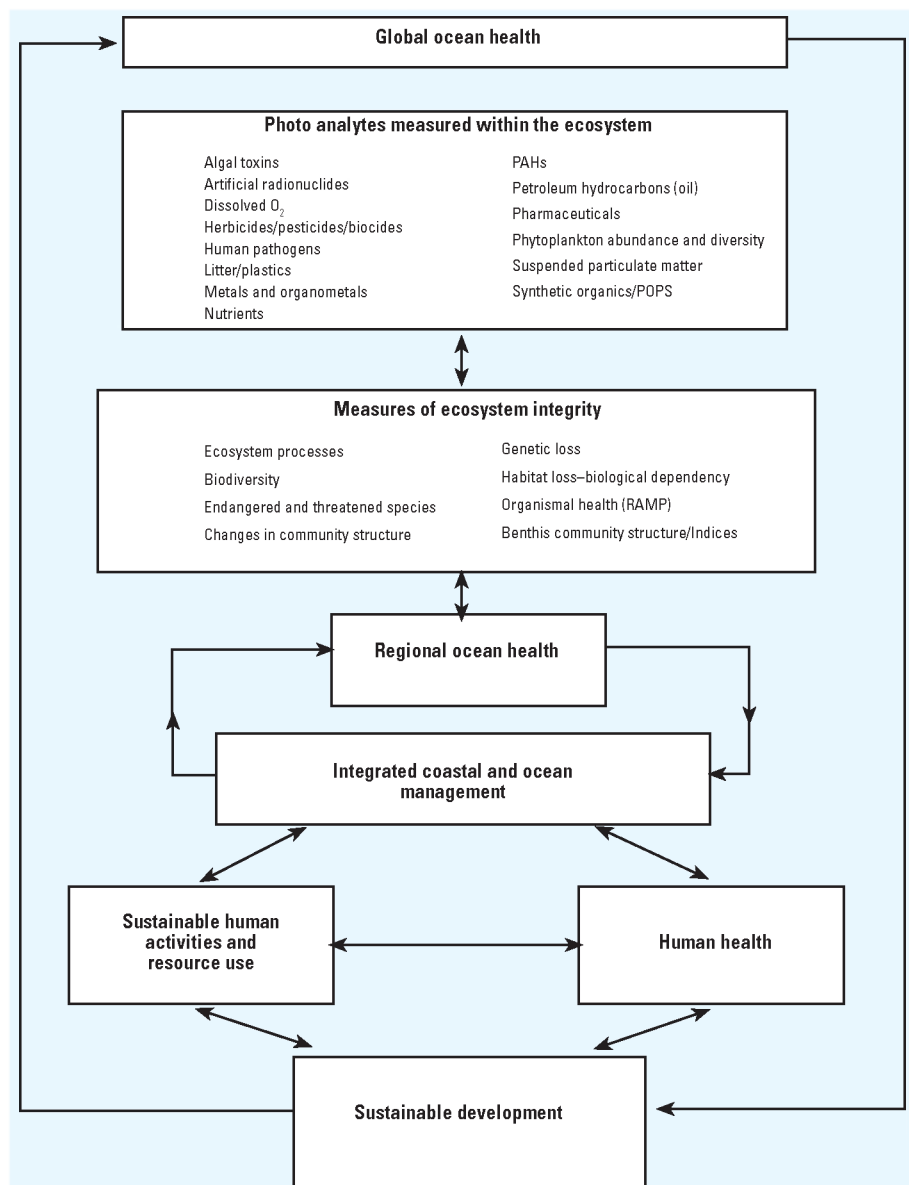


Figure 1. Relationship between global ocean health and sustainable development. Adapted from UNESCO 2002.

mimic, and dichlorodiphenyldichloroethylene (DDE) is an androgen receptor antagonist. Subacute levels of exposure show effects on the central nervous system of humans. Studies continue on the effects of neonatal synthetic organic exposure in the Arctic (AMAP 1998).

Although we have much information on the transfer of organochlorine residues through the marine food web, our knowledge on the transfer to humans through this pathway has been limited to a few classes of contaminants. However, evidence suggests that the organochlorine pesticide dieldrin (the epoxide of aldrin) affects the central nervous system and liver in humans. Generally, how to discern specific compounds and their effects in a large pool of contaminants present in the ocean environment is unclear.

PAHs. PAHs are derived from thermal transformations 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).

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 species (Brouwer et al. 1998). 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 anti-fouling paints on boats) and methyl mercury (formed by the microbial methylation of mercury) are two highly toxic compounds that have been 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 highly lipophilic and is biomagnified in the environment (Dewailly et al. 2001). Its half-life is 60–120 days in humans and 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. 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; McKeown-Eyssen et al. 1983; 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. The IARC has labeled cadmium as a Group I carcinogen (known human carcinogen). The major health risk associated with cadmium is nephrotoxicity (proteinuria and renal failure).

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. Some studies (e.g., Hansen et al. 1991) on human lead blood levels in Greenland have indicated concentrations similar to those of people in Western Europe. Whether this is a direct effect of atmospheric transport or from seafood ingestion is not yet clear (Dewailly et al. 1999). 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 needs more attention.

Marine toxins. Although many definitions of marine toxins exist, the Health of the Ocean panel for the Global Ocean Observing System has defined algal toxins as compounds that are produced by marine organisms on a scale large enough to induce adverse effects on communities of higher marine organisms (National Research Council 1999). In turn, humans may be exposed through the consumption of seafood or through dermal contact from occupational or recreational exposure to a toxin. In the case of *Gymnodinium breve* (Florida red tide), blue-green algae (cyanobacteria), and possibly *Pfiesteria piscicida*, transfer of toxins to humans may also occur through inhalation of aerosols containing the toxin.

Algal toxin outbreaks are mainly associated with dinoflagellates, of which approximately 60 species cause red tides and about 30 produce biotoxins. Of the 5,000 known species of phytoplankton, approximately 80 are toxic (Hackney and Pierson 1994). An increase in documented illness from exposure to marine biotoxins may be due to an increasingly stressed marine environment, an increase in reporting because of greater vigilance, increased seafood distribution worldwide, and a larger range of worldwide tourist travel (Hallegraeef 1993). Accurately assessing overall health risks from exposure to marine toxins is virtually impossible, because few data exist on their transfer through the coastal food web, primarily because many of the milder cases go unreported and thus are not recorded in databases. Different toxins have different effects. Occupational exposure to the dinoflagellate *Pfiesteria* has reportedly been linked to nausea, respiratory problems, and severe memory loss (Grattan et al. 1998). However, *Pfiesteria* is difficult to assess because samples of this single organism are hard to collect, its toxins have yet to be characterized, and the inhalation exposure is difficult to measure (Fleming et al. 1999).

Currently, 20 types of paralytic shellfish poisons (PSPs) have been identified, of which saxitoxin is the major toxin (Table 1), a sodium channel blocker, with primary symptoms of paresthesias and paralysis. The neurotoxic shellfish poison (NSP) toxin brevetoxin acts in the opposite manner, opening sodium channels rather than blocking them. Brevetoxins have less neurotoxic effect than do PSP toxins, but they are easily aerosolized and when inhaled can lead to respiratory infection, coughing, and bronchospasms. Exposure to the amnesic shellfish poison (ASP) toxin domoic acid can lead to seizures, coma, amnesia, and formation of lesions in the brain. The diarrhetic shellfish poison (DSP) toxin okadaic acid leads to self-limiting gastrointestinal symptoms, and cases of poisonings from this toxin are probably dramatically underreported (Baden et al.

1995). The ciguatera fish poison (CFP) toxin ciguatoxin has been documented in up to 400 species of fish, remaining in fish for over 2 years, and is responsible for more than half of all reported seafood-related illnesses (~50,000 reported cases/year).

Like other types of seafood poisoning, many cases of ciguatera poisoning likely go unreported. Symptoms from exposure vary geographically. In Polynesia CFP symptoms are usually neurologic, whereas in the Caribbean the initial symptoms include gastroenteritis and cardiovascular problems.

Microbial risks. Pathogens in the marine environment are a significant human health concern. Exposure can occur by eating contaminated seafood and through occupational and recreational exposures (HEED 1998). The primary sources of human pathogens are untreated human and animal wastes, although transmission can occur between swimmers or, potentially, from seabirds or other wildlife. One of the major causes of reported seafood illnesses is the consumption of raw shellfish contaminated by sewage. A large amount of quantitative epidemiologic and toxicologic information exists on human risks of infectious disease from contaminated seafood consumption and other routes of exposure from seawater. Routes of human exposure include eating contaminated seafood, direct ingestion of seawater, and dermal exposure to both water and sediments (Clark et al. 1997). A recent study has estimated that wastewater-related sickness causes

economic losses of approximately \$8.8 billion per year (GESAMP 2001).

Among the microbial agents related to seafood-borne illnesses, viruses are the most common form of infection, followed by bacteria and then protozoa. The major vectors of viral infection are marine bivalves such as oysters and clams, and the effects are numerous and vary by virus. For example, the Norwalk virus is responsible for 23% of reported waterborne gastroenteritis outbreaks (General Accounting Office 1984). Among the bacteria, *Vibrio vulnificus* has been implicated in a number of shellfish poisonings and wound infections. Other *Vibrio* spp. such as toxigenic *Escherichia coli*, *Shigella* spp., and *Salmonella* spp. can also be contracted from ingesting contaminated foods and water. Information on survival of these pathogens in seawater is limited.

Very little information exists for the protozoa and their potential impact on ocean and human health. *Cryptosporidium* spp. accumulates in shellfish, but to date no outbreaks related to this protozoan associated with seafood consumption have been reported. Gastrointestinal illnesses have been epidemiologically linked to scuba diving in sewage-contaminated waters (MMWR 1983). Anasikiasis is a rare nematode (roundworm) infection acquired through consumption of raw fish and cephalopods (Deardoff and Overstreet 1991); a similar disease associated with the helminthes *Gnathostoma* has been reported in Southeast Asia and the Middle East (Anantaphruti

2001). Diphyllorhynchiasis, or fish tapeworm disease, was traditionally associated with gefilte fish preparation by Jewish women; approximately 10% of people in Scandinavia are reportedly infected with *Diphyllorhynchium* (Fleming et al. 2000).

In general, infections appear to have increased among individuals recreationally and occupationally exposed to seawater (Henrickson et al. 2001), including gastrointestinal, dermal, respiratory, eye, ear, nose and throat infections. Furthermore, children are at greater risk to greater exposures and are uniquely susceptible because of their physiology and development (Landrigan et al. 1998). Also, a child's potential long-term health problems from a variety of exposures could have significant economic consequences.

Environmental and Human Health Indicators

The marine environment. The key objectives in any assessment of marine environmental health on a regional or global scale are to provide information necessary to ensure the maintenance of biodiversity and the integrity of marine communities, minimize the loss of species, limit human influences on living resources (including genetic richness), protect critical habitats, and safeguard human health. All of these objectives are vital to ensuring sustainable development of coastal and marine resources.

Changes in community structure and measures of chemical contamination have

Table 1. Human intoxication syndromes caused by marine toxins.

Disease	PSP	NSP	ASP	DSP	Ciguatera	Puffer fish
Causative organism	Red tide dinoflagellate	Red tide dinoflagellate ^a	Red tide diatom	Red tide dinoflagellate	Epibenthic dinoflagellate	Bacteria?
Major transvector	Shellfish	Shellfish, aerosols	Shellfish	Shellfish	Fish	Fish
Geographic distribution	Temperate to tropical worldwide	Gulf of Mexico, Japan, New Zealand	Canada, NW United States	Temperate worldwide	Subtropical to tropical worldwide	Japan, worldwide
Major toxin (no.)	Saxitoxin (≥ 18) ^b	Brevetoxin (≥ 10) ^b	Domoic acid (3) ^b	Okadaic acid (4) ^b	Ciguatoxin (≥ 8) ^b scartoxin, maitotoxin	Tetrodotoxin (≥ 3) ^b
Neuromechanism	Na ⁺ channel blocker	Na ⁺ channel activator	Glutamate receptor agonist	Phosphorylase phosphatase inhibitor	Na ⁺ , Ca ²⁺ channel activators	Na ⁺ channel blocker
Incubation time	5–30 min	30 min to 3 hr	Hours	Hours	Hours	5–30 min
Duration	Days	Days	Years	Days	Years	Days
Acute symptoms	n,v,d,p,r	n,v,d,b*,t*,p	n,v,d,a*,p,r	d*,n,v	n,v,d,t*,p	n,v,d,p*,r*,↓bp*
Chronic symptoms	None	None	Amnesia	None	Paresthesias	None
Fatality rate (%)	1–14	0	3	0	< 1 (0.1–12)	60
Chronic effects	None observed	Hypersensitivity, immune depression	Memory loss	Tumor promotion	Recurrent symptoms	None observed
Diagnosis	Clinical, mouse bioassay of food, HPLC	Clinical, mouse bioassay of food, ELISA	Clinical, mouse bioassay of food, HPLC	Clinical, mouse bioassay, HPLC, ELISA	Clinical, mouse bioassay, immunoassay	Clinical, mouse bioassay, fluorescence
Therapy	Supportive (respiratory)	Supportive	Supportive (respiratory)	Supportive	Mannitol, TCA?, supportive	Supportive (respiratory)
Prevention	Red tide and seafood surveillance, report cases	Red tide, then seafood surveillance, report cases	Seafood surveillance, report cases	Seafood surveillance, some red tide, report cases	Seafood surveillance, report cases (clusters)	Regulated food preparation, report cases

Abbreviations: a, amnesia; b, bronchoconstriction; ↓bp, decreased blood pressure; d, diarrhea; ELISA, enzyme-linked immunosorbent assay; HPLC, high-performance liquid chromatography; n, nausea; NW, northwest; p, paresthesias; r, respiratory depression; t, reversal of temperature sensation; TCA, tricyclic antidepressant; v, vomiting.

**Chattonella raphidophyte* from Delaware implicated in 2000. *Numbers in parentheses indicate number of natural derivatives. Data from Baden et al. (1995), with updates from Bourdelais et al. (2002). *Pathognomonic symptoms.

generally been used to indicate the state of ecosystem health. However, such high-level responses are generally too complex and far removed from causative events because they are manifestations of damage rather than predictive indices. Detection of lower-level changes (molecular, cellular, physiologic, and behavioral responses) that underlie higher-level effects and for which causality can be established may provide the desired early warning of impending environmental damage. Individual and subindividual responses may also be amenable to detection by automated monitoring systems. Four approaches to gathering information on indicators are biomarkers, cellular pathology, physiologic and behavioral responses, and changes in populations. All hold the potential to enhance our understanding of marine environmental quality and far-reaching effects on human health.

Our knowledge of distress signals has grown substantially in the past decade, often drawing on our reservoir of knowledge of humans and rodents. The use of biomarkers (indicators) in marine environmental toxicology is increasing, and their potential power is significant. They may be not only diagnostic predictors of pathologic change but also biomarkers of exposure for specific classes of toxic chemicals (xenobiotics) and certain trace metals. This latter type of biomarker has the potential to provide rapid and less costly alternatives to routine chemical analytical screening. Chemical analytical efforts could then be focused on more specific fingerprinting work, thereby helping to elucidate the link between cause and effect.

Potential marine biomarkers (indicators) include alterations in intracellular membranes (e.g., endoplasmic reticulum, lysosomes, endosomes, transport vesicles), genotoxicity (e.g., oxidative adducts, micronuclei), specific proteins or enzymes (e.g., metal-binding proteins, stress proteins, oncoproteins, cytochrome P-450, multidrug-resistant proteins), and inhibition of cholinesterase by neurotoxins (e.g., organophosphates, carbamates). Some of these biomarkers, such as membrane changes and stress proteins, indicate cell injury and potential damage to health, whereas others, such as DNA adducts, cytochrome P-450 (e.g., CYP1A and ethoxyresorufin α -deethylase), multidrug-resistant protein, and metal-binding proteins, indicate exposure to certain classes of xenobiotics and metals (Intergovernmental Oceanographic Commission 2001).

The use of molecular and cellular biomarkers coupled with cellular pathology (histopathology) provides further clues to the source of the specific environmental problem. Histopathologic change can be easily and accurately quantified using microstereologic procedures applied to tissue sections. These

data can then be correlated with both cell injury processes and abnormalities in physiology. Linking these measurements with physiologic and behavioral responses, and more traditional population and community monitoring, will provide a set of early and long-term warning systems for the environment.

Recent developments have led to new methods, which have been tested in the field (Wedderburn et al. 2000). Studies have investigated a neutral red retention assay (Lowe et al. 1995) with histopathologic measurements, as well as determining the physiologic state of mussels using a heart beat monitor in the field (Aagaard et al. 1995). The neutral red retention assay involves sampling the fluid from mussels, staining the fluid, and timing how long the cells retain the stain. Healthy animals retain stain for hours, and those less healthy can lose the stain in minutes. The use of these nondestructive techniques should be encouraged and are already part of a field monitoring assessment program for coastal Brazil.

A recent article comparing U.S. Environmental Protection Agency Environmental Monitoring and Assessment Program Estuaries Program data with National Oceanic and Atmospheric Agency bioeffects data on sediment chemistry and toxicity identified no apparent chemical measurement that successfully predicted toxicity (O'Connor and Paul 2000). This result challenges many theories on the use of sediments as monitors of contamination and deserves further investigation. Metabolites and breakdown products of contaminants may be the primary sources of toxicity long after the concentration of the parent compound is no longer detected (Ehrhardt and Knap 1989). Despite these challenges, indicators continue to play an important role in our understanding of marine environmental health. Efforts are underway to develop microbial biomarkers of contaminant exposure because microorganisms adapt rapidly to changing environments and can be probed for expression of genes that convey resistance to toxic chemicals or catabolic potential for organic pollutants (Ford 2000).

Human health. It is clear that challenges remain to developing a better understanding of the connection between the marine environment and human health. Environmental changes do affect human health, and it is important to identify which indicators have enough sensitivity and specificity to detect these changes. Human mortality and morbidity registries alone are not likely to help monitor environmental changes, because most chronic human diseases are multifactorial and involve genetic, lifestyle, and environmental factors. It is therefore also unlikely that cancer registries or mortality rates will provide a useful indication of changes for ocean-related

illnesses because of issues regarding specificity and the long delay (10–20 years) between exposure to environmental risk factors and detection of cancer. However, morbidity registries on acute diseases such as marine toxin poisoning and other seafood-borne diseases, reporting of which is mandatory in most countries, could provide useful information on any changes in incidence over time. Because these diseases are largely underreported, we urgently need to improve and validate these surveillance systems. Health registries are also very useful for monitoring shorter latency events such as pregnancy complications (low birth weight, congenital malformations, and the like).

Specific clinical effects related to contaminants have been the subject of numerous epidemiologic studies. In general 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 $\mu\text{g}/\text{dL}$ is the maximum blood lead concentration accepted 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.

Unfortunately, cohort studies are extremely expensive in both time and resources and require large multidisciplinary scientific groups. In addition, new xenobiotics or metabolites are regularly identified by analytical chemists, and health officials may not be able to react in a timely manner. To complement standard disease registries and epidemiologic cohort studies, scientists have tried to develop early response biomarkers to detect any reversible or irreversible biologic effects. Potential early warning signal markers deal with the immune system (cytokines, cell markers, antibody response to immunization,

and the like), endocrine activity (hormones such as sexual or thyroid), genotoxicity (DNA and protein adducts for POPs), and enzyme induction (CYP1A2 and ethoxyresorufin *o*-deethylase activity using caffeine breath tests for POPs). Some biomarkers are already in use (aminolevulinic acid dehydratase for lead, β_2 -microglobulin for cadmium), but most still need to be validated. The major challenges to their use are lack of sensitivity and specificity, and thus more work is needed to link the health of the marine environment to that of humans.

Recommendations

Monitoring systems that include the rapid assessment of contaminants in the ecosystem and subsequent risk to human populations, with appropriate internationally distributed databases, need to be developed and validated. Such tools would provide early detection of potential environmental threats and enhance the ability to prevent human illness. Because analyses of contaminants are sometimes expensive and time-consuming, we need to use appropriate markers and indicators, develop new ones, and rigorously validate them all.

Research on oceans and human health needs to be interdisciplinary and structured around a "models-based" approach, focusing on critical themes and attributes of marine environmental and public health risks. Given the extent and complex nature of ocean and human health issues, a program networking across geographic and disciplinary boundaries is essential. The overall goal of such a program would be the early detection of potential marine-based contaminants, with the ultimate outcome being the preservation of natural resources and the prevention of associated human illness.

Such a program could contain four components: a basic mechanistic research component, a biomarkers developmental resource component, an informatics component, and a training component. Within this context, research problems would be proposed and work conducted to find feasible solutions. Biomarker assessment could be modified, expanded, and refined to fit specific situations with dynamic paradigms, and new ocean and human health interactions could be addressed. As the research themes are explored, a training component would be integrated, resulting in the production of the next generation of ocean and human health scientists. Informatics would be continually developed, providing essential feedback and information to a broad range of stakeholders, including those of the international community.

We suggest five initial "models" of human exposure resulting from ocean/human interactions: polar regions/native peoples

food-borne risk exposure; marine toxin aerosols and human health; urban harbors and exposure; seafood consumption and health benefits and risks; and tropical coastal areas and small island states.

This integrative suite of models would allow a more effective understanding of the problems presented by the various sources of anthropogenic and natural contaminants and their effects on humans by oral, dermal, and inhalation exposure. They would also allow an assessment of such critical factors as chronic versus acute exposures, local versus distant sources of contaminant risks, and the degree to which each individual risk is reversible or irreversible. Further, a models-based approach to ocean and human health would allow for an extrapolation of the results and techniques to different environments.

The success of this suite of models depends partly on establishing a comprehensive suite of biomarkers, first by identification and development of new markers, followed by their validation within an ocean and human health context. The translation of biomarkers that are fast, reliable, easy, inexpensive, and internationally available will enhance the abilities to assess, measure, and predict both ecosystem stresses and potential human exposures/health effects.

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