Indicators of Ocean and Human Health

Eric Dewailly, MD, PhD¹

Chris Furgal, PhD¹

Anthony Knap, PhD²

Jennifer Galvin, BS, MPH²

Dan Baden, PhD³

Bob Bowen, PhD⁴

Michael Depledge, PhD, DSc⁵

Linda Duguay, PhD⁶

Lora Fleming, MD, PhD, MPH⁷

Tim Ford, PhD⁸

Fredricka Moser, PhD⁹

Richard Owen, PhD¹

William A. Suk, PhD, MPH¹⁰

Umit Unluata, PhD¹¹

ABSTRACT

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 and new treatments for human disease. However, recently, human health effects from exposure to substances present in the marine ecosystem such as synthetic organic chemicals (e.g., chlorobiphenyls, chlorinated dioxins and some industrial solvents), polycyclic aromatic hydrocarbons (PAHs), metals (both introduced and anthropogenic), marine toxins, and pathogens have been recorded and are of great concern. This paper reviews our state of knowledge of the interactions between oceans and human health and proposes indicators and a research strategy to investigate and monitor these relationships more closely. Four approaches to gathering information on indicators included here are: biomarkers; cellular pathology; physiological and behavioural responses; and changes in populations. All hold the potential to enhance our understanding of marine environmental quality and far-reaching effects on human health. Monitoring systems that include the rapid assessment of contaminants in the ecosystem and subsequent risk to human populations, with appropriate internationally distributed data bases, need to be developed and validated. Such tools would provide early detection of potential environmental threats, and enhance the ability to prevent human illness.

RÉSUMÉ

Les interactions entre les humains et les océans sont importantes, et il faut en faire une étude plus approfondie à l'échelle mondiale. Sur le plan de la santé, les humains tirent grandement profit des océans, que ce soit de la nourriture et des ressources nutritionnelles, des activités récréatives et de nouveaux traitements contre les maladies. Cependant, on a signalé récemment, et on se préoccupe beaucoup, des effets sur la santé liés à l'exposition aux substances toxiques présentes dans l'écosystème marin comme les produits chimiques organiques de synthèse (p. ex. les chlorobiphényles, les dioxines chlorées et certains solvants industriels), les hydrocarbures aromatiques polycycliques (HAP), les métaux (d'origine naturelle et anthropique), les toxines marines et les agents pathogènes. Les auteurs examinent l'état des connaissances sur ces interactions et proposent des indicateurs et une stratégie de recherche pour les étudier et les surveiller de plus près. Ils mentionnent quatre approches pour la cueillette de renseignements sur les indicateurs : les biomarqueurs, la cytopathologie, les réactions physiologiques et comportementales ainsi que les changements dans les populations. Ces approches peuvent améliorer la compréhension de la qualité de l'environnement marin et des effets lourds de conséquence pour la santé humaine. Il faut construire et valider des réseaux de surveillance qui permettent de mesurer rapidement les contaminants dans un écosystème et d'en évaluer les risques pour la santé humaine; ces réseaux doivent être reliés à des bases de données à l'échelle mondiale. De tels outils faciliteraient la détection précoce de menaces potentielles pour l'environnement et amélioreraient la prévention des maladies chez les humains.

This paper is the result of a NIEHS-funded conference held in Bermuda in November, 2000 to discuss indicators of ocean and human health. The conference brought together international experts in the areas of marine ecosystem and human health. The result was a list of indicators for aspects of ocean and human health, identification of research needs and the development of an approach to deal with these issues. What is presented here is the discussion relating to environmental health indicators relevant to marine environments.

At present, it is estimated that 60% of the world's population lives in coastal areas and human population growth in coastal zones is about twice that of the global rate. This settlement pattern has exacerbated the rate of change in coastal systems and has already placed the goal of "sustainable development" out of reach for some regions. The

1. Laval University, Quebec

2. Bermuda Biological Station for Research, Inc., St. Georges, Bermuda

3. University of North Carolina, Wilmington, NC

4. University of Massachusetts, Boston, MA

5. University of Plymouth, Plymouth, UK

6. Wrigley Institute, University of Southern California

7. NIEHS Marine and Freshwater Biomedical Sciences Center, University of Miami, Miami, FL

8. Harvard School of Public Health, Boston, MA

9. US State Department, Washington, DC

10. National Institutes of Health, Research Triangle Park, NC

11. Intergovernmental Oceanographic Commission, UNESCO, Paris, France

Much of the text of this paper forms the basis for another paper published in *Environmental Health Perspectives*.¹ The focus of the current paper is on the meeting discussions and conclusions regarding indicators for ocean and human health.

Correspondence: Chris Furgal, Public Health Research Unit, CHUQ - Pavillon CHUL, 2400 rue d'Estimauville, Beauport, QC G1E 7G9, Tel: 418-666-7000 ext. 555, Fax: 418-666-2776, E-mail: christopher.furgal@crchul.ulaval.ca

world population is estimated to increase from about 5 billion (at present) to 8.3 billion by 2025, with 90% of this growth occurring in subtropical and tropical countries. At the same time, over 2 billion people world-wide rely on seafood as a major source of protein in their diet and global seafood consumption continues to increase.²

There are many potential sources of contamination of the marine system. Only a subset of these are of specific concern to the issue of Ocean and Human Health. As determined by the conference participants, priority issues include: persistent organic pollutants (POPs), a few specific heavy metals, algal toxins, pathogens, pharmaceuticals and possibly genetically modified organisms. Routes of human exposure to marine products include ingestion, dermal exposure and inhalation. The largest concern for public health is the ingestion of contaminated seafood, putting those humans who ingest large quantities of seafood at greatest risk.

Persistent organic pollutants (POPs)

POPs are a loosely defined group of substances which, aside from petroleum hydrocarbons and polyaromatic hydrocarbons, include all synthetic substances that result from industrial activities. The introduction of POPs 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 a) toxicity, b) persistence, c) tendency to bioaccumulate, d) bioavailability, and e) source functions (size and nature of the land-based sources). Current scientific knowledge of these compounds is still limited and new compounds continue to be identified. Polynuclear aromatic hydrocarbons (PAHs) are derived from thermal transformations of fossil fuel, primarily petroleum. Some are formed by natural low temperature metamorphic processes. The primary human health concerns related to these substances deal with their carcinogenicity.³ They enter the marine system through municipal or industrial effluents or via atmospheric pathways from industrial emissions, through exhaust fumes of internal combustion engines or from domestic heating systems and humans are exposed to these substances primarily through food chain consumption.

Most POPs have been linked to possible endocrine-disrupting functions and there are links between herbicide exposure and reduced sperm counts in males living in agricultural regions. Human exposure to POPs occurs primarily through ingestion of contaminated foods, often procured directly from the environment (e.g., small traditional fishing communities, etc.) and results in a variety of effects. PCBs, for example, have a variety of effects on human reproduction, neurobehavioural development, liver function, birthweight, immune response, as well as having carcinogenic properties. Studies in Arctic populations have linked fetal cord blood PCB concentrations with low birthweight, small head circumference, and immunosuppression.

Despite the fact that the POP "DDT" was banned in the U.S. and Europe in 1972, it is still being used worldwide for malaria control and is of concern for human health. The International Agency for Research on Cancer (IARC) considers DDT to be "possibly" carcinogenic. DDT is regarded as an estrogen mimic and DDE as an androgen receptor antagonist. Subacute levels of exposure show effects on the central nervous system (CNS) of humans while studies continue on the effects of neonatal POPs exposure in the Arctic.⁴ There is little information on the transfer through the marine food web of other organochlorine pesticides and their effects on humans.

Metals

Trace metals comprise all metals and metalloids in the marine environment. It is important to distinguish between the introduction of trace metals from anthropogenic activities and those from natural weathering processes. Although sources of trace metals in the marine environment are numerous and diverse (elevated trace metal levels accompany almost every type of effluent), there is little evidence of widespread adverse biological effects posed by metals in seafood other than risks to human health.⁵ Elevated metal levels in seawater are unlikely (other than in the immediate vicinity of sources) due, in most cases, to their rapid removal by adsorption to suspended particulate material. In the case of certain organo-metallic complexes/compounds, the situation is quite different.

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 which have been responsible for well-recorded marine pollution incidents. The basis of toxicity for these substances lies in their forms of speciation. Thus, special attention may be required to identify specific forms of other trace metals in the future. Mercury is used in a wide range of industrial processes and mining practices. Once released into anoxic environments, it can be rapidly methylated by bacteria. Methyl mercury (MeHg) is highly lipophilic and is biomagnified in the environment.⁶ The half life of MeHg is 60-120 days in humans and up to 2 years in fish. MeHg causes cytotoxic, kidney and brain damage, with concentrations of 1-2 mg/kg in brain tissue producing neurotoxic effects. Fetal exposure to MeHg is of great concern and as expected, individuals who consume seafood have the highest concentration of MeHg in their tissues. Environmentally chronic exposures have been reported in fishing populations in Amazonia, Coastal Peru, Seychelles, Faroe Islands, the Arctic and in New Zealand.

Cadmium (Cd) can also bioaccumulate in the environment, however its uptake by humans is affected by the uptake of lead (Pb). IARC has labelled Cd as a group 1 carcinogen. The major health risk associated with cadmium is nephrotoxicity (proteinuria and renal failure). Environmental exposures to Pb have been linked to poor neural development in children, however there are no documented cases of lead poisoning related to a marine source. Arsenic is also a highly toxic metal, however, as with Pb, no known arsenic poisonings have occurred as a result of marine exposures or consumption of seafood. Both lead and arsenic occur in marine sediments as a result of industrial discharge. Like mercury, arsenic can be converted to more lipophilic and toxic methyl forms. The effects of these metals on the ecological health of the marine environment are not yet well known.

Harmful algae blooms

Algal toxins are compounds that are produced by marine organisms on a large-enough scale to induce adverse effects on communities of higher marine organisms.

In turn, humans may be exposed through consumption of seafood or through occupational or recreational exposure to the toxins, primarily through dermal contact. In the case of *Gymnodinium breve* (Florida Red Tide) and *Pfiesteria*, transfer to humans can occur through inhalation of aerosols containing the toxin. Algal toxin outbreaks are mainly confined through transfer from dinoflagellates and marine phytoplankton. Currently, there are about 2,000 species of dinoflagellates identified, of which about 60 species cause red tides and about 30 produce biotoxins. Of the 5,000 known species of phytoplankton, approximately 80 are toxic.⁷ There is strong evidence that certain blooms of phytoplankton-producing toxins are induced or sustained as a result of anthropogenic destabilization of the marine ecosystems (e.g., eutrophication).

It is virtually impossible to accurately assess health risks from exposure to marine toxins as very little data exist on their transfer through the coastal food web. Different toxins have different effects. Exposure to the aerosolized neurotoxin of *Phytheria* has been linked to nausea, respiratory problems and severe memory loss.⁸ Twenty types of paralytic shellfish poison (PSP) toxins are currently identified, of which saxitoxin is the major toxin. Primary symptoms of exposure are paresthesias and paralysis. The neurotoxic shellfish poison (NSP) toxin – brevetoxin – is easily aerosolized and inhalation by humans can lead to respiratory infection, coughing and bronchospasms. Exposure to the asptoxin – domoic acid – can lead to seizures, coma, amnesia and formation of lesions in the brain. The diarrhetic shellfish poison (DSP) toxin – Okadaic acid – is probably the most widespread marine toxin illness attributable to seafood consumption⁹ and exposure to the toxin leads to gastrointestinal symptoms. The ciguatera fish poison (CFP) toxin – Ciguatoxin – has been documented in up to 400 species of fish and is responsible for more than half of all reported seafood-related illnesses (~50,000 reported cases/year). Like other types of seafood poisoning, it is felt that many cases go unreported. Variations in symptoms from exposure to ciguatoxin occur geographically. In Polynesia, CFP symptoms are usually neurologic, while in the Caribbean the initial symptoms include

gastroenteritis and cardiovascular problems. Ciguatera toxin has also been linked to premature labour and spontaneous abortions.

Microbial risks

Pathogens in the marine environment are a significant human health concern, both because of exposure through consumption of contaminated seafood and through occupational and recreational exposures. 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. Routes of human exposure to pathogens include consumption of seafood, direct ingestion of seawater, and dermal exposure to both water and sediments.¹⁰ Among the microbial agents related to seafood-borne illnesses, viruses are the most common form of infection, followed by bacteria and finally the protozoa. The major vectors of viral infection are marine bivalves such as oysters and clams. The potential human health effects are numerous and dependent upon the specific virus.

In contrast to our understanding of microbial agents in the marine environment, there is very little known about the protozoa. *Cryptosporidium sp.* have been found to accumulate in shellfish, but to date there are no reports of outbreaks associated with seafood consumption. *Giardia* and *Entamoeba* gastritis have been epidemiologically linked to scuba diving in sewage-contaminated waters. In general, there appears to be an increase in infections (e.g., gastrointestinal, dermal, respiratory, eye, ear, nose and throat infections) among individuals recreationally and occupationally exposed to seawater. Children are at greater risk of contracting these infections and the potential economic consequences are significant.

Pharmaceuticals include all substances used in preventing and treating human and animal diseases. The major conduit of pharmaceuticals into the marine environment is via the municipal sewage system, or in the specific case of aquaculture, by their direct and intentional introduction into fish enclosures. The concerns regarding these substances in the marine environ-

ment are considerable as the use of aquaculture increases worldwide, with a consequent reduction in genetic diversity among fish. This in turn results in an increased need for more pharmaceutical use in the future. There is no conclusive evidence of significant adverse effects in coastal waters, but research in this area is continuing, with some limited information on potential endocrine-disrupting effects.

ENVIRONMENTAL AND HUMAN HEALTH INDICATORS

The marine environment

In the past, measures of concentrations of contaminants and changes in community structure were used to indicate the state of ecosystem health. However, such high-level responses are generally too complex and far removed from causative events and are manifestations of damage rather than predictive indices. Detection of lower-level changes (molecular, cellular, physiological and behavioural responses) which underlie higher-level effects and for which causality can be established, may provide a better early warning of impending environmental damage. Individual and sub-individual responses may also be amenable to detection by automated monitoring systems. Four approaches to gathering information on indicators are suggested: biomarkers, cellular pathology, physiological and behavioural responses, and changes in populations. All hold the potential to enhance our understanding of both marine environmental quality and consequential effects on human health. Tables I to V outline available and needed indicators and data for each of the 5 following priority issues for ocean and human health interactions: seafood consumption, POPs, heavy metals, pathogens and harmful algae blooms.

Our knowledge of distress signals has grown substantially in the past decade, often drawing from the reservoir of our knowledge of humans and rodents. The use of biomarkers (indicators) in marine environmental toxicology is increasing and their potential power is significant: they hold the prospect of being not only diagnostic predictors of pathological 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

TABLE I**Priority Issue: Seafood Consumption**

	External Exposure	Internal Exposure	Early Human Response	Disease	Death	Action
Available Data	Levels of priority chemicals in consumed fish spp.	Fish fatty acid profile (N-3/N-6) among consumers				
Research Needed	*			Seafood eaters disease profile		

* For all indicators, need cheap, fast, easy and transportable testing methods

TABLE II**Priority Issue: POPs (Pesticides, PCBs/PCDD/HCB)**

	External Exposure	Internal Exposure	Early Human Response	Disease	Death	Action
Available Data	<ul style="list-style-type: none"> • Levels of priority chemicals in consumed pelagic and deep sea fish spp. • Levels of priority chemicals in seafood spp consumed 	<ul style="list-style-type: none"> • Measurement in lipophilic tissue and fluids of consumers (fat, milk, plasma, maternal cord blood) 	<ul style="list-style-type: none"> • Endocrine markers • Immune markers • Neurotoxicity markers • Genotoxicity markers 	• Birth defects registry		
Research Needed	<ul style="list-style-type: none"> * Emphasis on predator and fatty spp. • Standard seafood consumption questionnaire • Identification of new contaminants • Biological activity assessment (in vitro receptor assay) 			<ul style="list-style-type: none"> • Childhood infection • Reproduction problems • Cancer 	• Death certificate (cancer)	

TABLE III**Priority Issue: Heavy Metals**

	External Exposure	Internal Exposure	Early Human Response	Disease	Death	Action
Available Data	<ul style="list-style-type: none"> • Hg levels in tuna (global) • Metal levels in bivalve spp. 	<ul style="list-style-type: none"> • MeHg in consumers (hair, blood) • Cd in consumers (24 hr. urine) 	<ul style="list-style-type: none"> • Cd in consumers (beta2 microglob) 			
Research Needed	<ul style="list-style-type: none"> • Se levels in seafood 		<ul style="list-style-type: none"> • Hg effects measurements 	<ul style="list-style-type: none"> • Cd, Hg (blood pressure) 		

TABLE IV**Priority Issue: Pathogens**

	External Exposure	Internal Exposure	Early Human Response	Disease	Death	Action
Available Data	<ul style="list-style-type: none"> • Coliform counts (water, seafood) • Bivalve data on pathogen incidence 			<ul style="list-style-type: none"> • Registry • Cholera incidence • Salmonella incidence • Shigella incidence 	<ul style="list-style-type: none"> • Death certificate review 	
Research Needed		<ul style="list-style-type: none"> • Identify pathogens for marine environment 		<ul style="list-style-type: none"> • Increase registry • Rapid test pathogens 	<ul style="list-style-type: none"> • Increase registry 	

TABLE V**Priority Issue: Harmful Algae Blooms**

	External Exposure	Internal Exposure	Early Human Response	Disease	Death	Action
Available Data	<ul style="list-style-type: none"> • Shellfish poisonings incidences • Dinoflagellates incidences 			<ul style="list-style-type: none"> • Reportable disease incidence (specific, U.S., Canada, Japan) 		<ul style="list-style-type: none"> • Outbreak investigation
Research Needed	*	<ul style="list-style-type: none"> • Compound and metabolites indicators 	<ul style="list-style-type: none"> • Biomarkers of effects (cigu., NSP, ASP) 	<ul style="list-style-type: none"> • Improve surveillance • Follow up chronic diseases 		

and less costly alternatives to routine chemical analytical screening. Chemical analytical efforts can 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 intercellular membranes (e.g., endoplasmic reticulum, lyso-

somes, endosomes, transport vesicles), genotoxicity (e.g., oxidative adducts, micronuclei), specific proteins or enzymes (e.g., metal-binding proteins, stress proteins, oncoproteins, cytochrome P-450s, multi-drug resistance proteins) and inhibition of cholinesterase by neurotoxins (e.g., organophosphates, carbamates). Some of these biomarkers, such as membrane changes and stress proteins, are indicative of cell injury and potential damage to health while others, such as DNA adducts, cytochrome-P450 (e.g., CYP1A and Ethoxyresorufin O-Deethylase (EROD), multi-drug resistance (MDR) protein and metal-binding proteins), can be indicative of exposure to certain classes of xenobiotics and metals.

The use of molecular and cellular biomarkers coupled with cellular pathology (histopathology) provides another clue as to the source of the specific environmental problem. Histopathological change can be easily and accurately quantified using microstereological procedures applied to tissue sections. These data can then be correlated with both cell injury processes and abnormalities in physiology. Linking these measurements with physiological and behavioural responses, and the more traditional population and community monitoring, will provide a set of early and long-term warning systems for the environment.

Human health

It is clear that challenges remain in order to develop a better understanding of the connection between the marine environment and human health. Environmental changes do have an impact on human health and it is important to identify which indicators have enough sensitivity and specificity to be able to detect these changes. It is unlikely that human mortality and morbidity registries alone could help to monitor environmental changes, as 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 as there are issues regarding specificity, and the delay between the exposure to environmental risk factors and cancer is long (10-20 years). However, morbidity registries on acute diseases such as marine toxin poison-

ings and other seafood-borne diseases, which are mandatorily declared in most countries, could provide useful information on any incidence changes over time. As there is acceptance that these diseases are largely under-declared, there is an urgent need to improve and validate these surveillance systems. Health registries are also very useful to monitor short-term events such as pregnancy, and pregnancy complications such as low birthweight, congenital malformations, etc.

Specific clinical effects related to contaminants have been the subject of numerous and recent epidemiologic studies. In low-dose exposed general populations, only subtle effects are expected to occur. For Pb and Cd, epidemiologic studies and animal experiments provide sufficient data to set thresholds for human exposure. There is a general consensus that 10 mg/dl is the maximum Pb blood concentration accepted for children. In this case, measuring blood Pb in a group of children is a relatively easy, cheap, validated and manageable biomarker to assess both exposure and risk in children. However, for most ocean-related contaminants such as MeHg and POPs, results from epidemiological studies are more contradictory. Cohort studies in Michigan¹¹ and North Carolina¹² provided some discrepancies on neurobehavioural changes in children who were prenatally exposed to PCBs. Conflicting results were also reported on neurological impairments in children who were exposed to MeHg during their fetal life. A study in the Seychelles did not report any deleterious effects,¹³ whereas a cohort study in the Faroe Islands did.¹⁴ 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 and require large multidisciplinary scientific groups. In addition, new xenobiotics or metabolites are regularly identified by analytical chemists and it is unlikely that epidemiologists will be able to react in a timely manner. To complement standard disease registries and epidemiological cohort studies, scientists have tried to develop early response biomarkers to detect any reversible or irreversible biological effects. Potential early warning signal markers deal with the immune system (cytokines, cell markers, antibody response

to immunization, etc.), endocrine activity (hormones such as sexual or thyroid), genotoxicity (DNA and protein adducts for POPs), and enzyme induction (CYP-450 1A2 and EROD activity using Caffeine Breath Tests for POPs). Some biomarkers are already in use (ALAD for Pb, b2-microglobuline for Cd) but most still need to be validated. Major challenges to their applicability are a lack of sensitivity and specificity. A great deal more work needs to be done to link the health of the marine environment to human health, and to identify and select the best indicators of this relationship.

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