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Review

Harmful algal blooms and public health

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ABSTRACT

The five most commonly recognized Harmful Algal Bloom-related illnesses are ciguatera poisoning, paralytic shellfish poisoning, neurotoxic shellfish poisoning (NSP), amnesic shellfish poisoning, and diarrhetic shellfish poisoning. Although these exposures result from exposure to different toxins or toxin congeners, these clinical syndromes have much in common. Exposure occurs through the consumption of fish, shellfish, or through exposure to aerosolized NSP toxins. Routine clinical tests are not available for the diagnosis of harmful algal bloom related illnesses, there is no known antidote for exposure, and the risk of these illnesses can negatively impact local fishing and tourism industries. The absence of exposure risk or diagnostic certainty can also precipitate a chain of events that results in considerable psychological distress for coastal populations. Thus, illness prevention is of paramount importance to minimize human and public health risks. To accomplish this, further transdisciplinary research, close communication and collaboration are needed among HAB scientists, public health researchers, and local, state and tribal health departments at academic, community outreach, and policy levels.

Contents

1. Introduction

There is a growing appreciation of the importance of Harmful Algal Blooms (HABs) and HAB-related illnesses to public health. With the dramatic increase in the number of harmful algal blooms, as well as their frequency and intensity in coastal regions throughout the world (Glibert et al., 2005), there are more toxic algal species, more algal toxins, and more geographic areas affected than ever before. Often attributed to natural environmental factors (hurricanes, earthquakes, or sequences of ideal growth and transport conditions), anthropomorphic activity (increased eutrophication, marine transport and aquaculture) and climate change, the proliferation of these species may cause massive fish kills, destroy or poison shellfish beds, contribute to wildlife mortality, human illness and death (Lehane and Lewis, 2000; Pratchett et al., 2008; Badjeck et al., 2010). The risk of HAB-related illnesses is further amplified by shifting preferences to heart-healthy diets, increased travel to coastal destinations, increased consumption of imported fish, the growth of coastal urban communities, and growing segments of the population involved in marine recreation (Jensen, 2006; Ralston et al., 2011). Thus, in

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the absence of ongoing public health surveillance, research, and outreach into HAB-related exposures and illnesses, it is anticipated that the number of cases of HAB-related illnesses will continue to rise over the next decade. With this in mind, this Special Issue of Harmful Algae is devoted to HABs and public health.

With the exception of aerosolization of the toxins produced by "Florida Red Tide" (*Karenia brevis* blooms), the primary vector for HAB-related human health concerns is the consumption of fish and shellfish. Often due to the activity of HAB-related toxins, seafood consumption has become the leading cause of food-borne illness with known etiology. Seafood is responsible for 10–20% of outbreaks and about 5% of all individual illnesses among all food types (Huss et al., 2004; CSPI, 2007). The annual acute care costs of seafood-borne disease are estimated at approximately two-thirds of a billion dollars (Ralston et al., 2011). Persistent symptoms are seen in about 2–3% of cases, and the costs of medical care, lost productivity, and functional disability associated with chronic sequelae are thought to exceed those of acute care. These are conservative estimates as there is considerable diagnostic uncertainty and underreporting of seafood-related illnesses (Sobel and Painter, 2005; Fleming et al., 2011).

To orient the reader to the diverse scientific papers to follow, this article is organized around the five most commonly recognized HAB-related illnesses. This will include a general description of ciguatera fish poisoning (CFP), paralytic shellfish poisoning (PSP), neurotoxic shellfish poisoning (NSP), amnesic shellfish poisoning (ASP) and diarrhetic shellfish poisoning (DSP) with a quick reference table (Table 1). An overview of HABs from a public health perspective will follow, as well as highlights of important areas for future research.

1.1. Ciguatera fish poisoning (CFP)

It is generally well-accepted that ciguatera fish poisoning (CFP) is the most frequently reported seafood-related disease in the United States and most common foodborne illness related to finfish consumption in the world (Isbister and Kiernan, 2005; Lynch et al., 2006; Friedman et al., 2008; Kumar-Roiné et al., 2011). It is endemic in areas where consumption of reef fish is common. These areas include the Caribbean, southern Florida, Hawai'i, the South Pacific and Australia. Additionally, emerging data suggest expansion of the biogeographical range of ciguatoxic fish (Villareal et al., 2007; Bienfang et al., 2008; Dickey and Plakas, 2010) with recent reports of CFP from fish originating in South Carolina and the Northwestern Gulf of Mexico (CDC, 2006).

CFP is caused by the consumption of reef fish that have accumulated potent neurotoxins (ciguatoxin) in their flesh and viscera. The toxins are produced by the marine dinoflagellate *Gambierdiscus* spp., which live on various macroalgal hosts or other substrates in coral reef ecosystems. Herbivorous fish consume these dinoflagellates and, through bioaccumulation and magnification, the toxin advances through the food web through ingestion by carnivorous species. More than 400 fish species are thought to have the potential for ciguatera toxicity (Halstead, 1978; Lehane and Lewis, 2000). The risk is greatest for carnivorous, predatory fish, such as barracuda (of which >70% may be toxic). Other high-risk fish include snapper, grouper, and amberjack (Langley et al., 2009).

The diagnosis of ciguatera fish poisoning (CFP), or "ciguatera," is typically based upon clinical symptoms within the context of a carefully elicited history of recent predatory reef fish consumption. Symptoms of CFP arise within 12 h of eating the toxic fish. The initial symptoms begin with severe gastrointestinal problems (nausea, vomiting, diarrhea, abdominal pain), which usually abate within 24 h (Hokama, 1988). Cardiovascular problems (generally a combination of bradycardia with hypotension) and/or neurologic symptoms may also accompany this acute episode. In the Caribbean and Southern Florida, cardiovascular disorders often reverse within 48–72 h (Hokama, 1988; Butera et al., 2000), yet in Pacific regions, outcomes may be less favorable, as there have been reports of rapid progression to respiratory distress, coma and death (Lange, 1987; Defusco et al., 1993; Habermehl et al., 1994). From a few hours to two weeks after exposure, a diverse range of subjective neurological complaints have been reported in about 70% of cases (Lawrence et al., 1980). These may include pain and lower extremity weakness; painful tingling around the mouth, teeth, nose and throat; peripheral paresthesia, headache, metallic taste, hyporeflexia, and/or dysphagia. The hallmark of CFP neurological symptoms is an unusual paradoxical disturbance of thermal sensation, i.e., cold objects feeling hot and sometimes hot objects feeling cold (Pearn, 2001; Achaibar et al., 2007). Although detailed case reports document a wide range of neurologic symptoms, the full symptom complex of CFP remains to be fully characterized or understood.

While gastrointestinal or cardiac symptoms are generally short-lived, recovery from acute neurologic symptoms is longer and less predictable, as these symptoms can persist from approximately one week to six months (Lange et al., 1992; Butera et al., 2000; Achaibar et al., 2007). In addition, there are many patients who report symptom persistence for several years. The chronic ciguatera syndrome is typically characterized by intractable fatigue, weakness and/or paresthesias, and is accompanied by depression. Chronic symptoms may be present continuously or reappear after a period of presumed recovery. This recurrence may also be triggered by alcohol use or by repeated consumption of fish with low levels of ciguatoxin. This suggests that persons who have had one episode of ciguatera are at increased risk for repeated illness (Morris et al., 1982). In this special issue, Lopez et al. (2016) report their efforts toward developing a conceivable biomarker for chronic and recurrent ciguatera.

1.2. Paralytic shellfish poisoning (PSP)

Paralytic shellfish poisoning (PSP) is a potentially lethal clinical syndrome. It is caused by eating bivalve mollusks (mussels, scallops clams) contaminated with a group of structurally related marine toxins collectively referred to as saxitoxins (STX; Shumway, 1990; James et al., 2010). PSP toxins are concentrated in shellfish as a result of the filtration of toxic algae produced by several dinoflagellates (including *Alexandrium*, *Gymnodinium* and *Pyrodinium*) during "red tide" blooms. Predators of bivalve shellfish (scavenging shellfish, lobsters, crabs and fish) may also be vectors for saxitoxins, thus expanding the potential for human exposure (Halstead and Schantz, 1984). Geographically, the most risky regions for PSP are temperate and tropical marine coasts. In North America, this includes Alaska, the Pacific Northwest, and the St. Lawrence region of Canada; however, incidents of PSP regularly occur in the Philippines and other tropical regions. Toxic shellfish have also been found in temperate regions of southern Chile, England, Japan, and the North Sea.

The initial symptoms of PSP are numbness or tingling around the mouth and lips within 10 min to two hours after shellfish consumption. The timing of symptom onset is thought to be dose-dependent (Gessner et al., 1997a; McLaughlin et al., 2011). In mild cases, this may be the only symptom; however, in more severe cases, the numbness and tingling spread to the neck and face, and may be accompanied by headache, abdominal pain, nausea, vomiting, diarrhea, and a wide range of neurologic symptoms. These neurologic symptoms may include weakness, dizziness, dysarthria, paresthesia, double vision, loss of coordination, vertigo or dizziness, and/or a "floating" sensation. Relatively recent data reported in this special issue (Knaack et al., 2016) suggest that dysphagia and dysarthria are most likely the strongest indicators

Table 1
Seafood intoxications.

Syndrome (major toxin)	Vectors (known and potential)	Onset time and duration	Major symptoms	Treatment	Prevention	Table references (by syndrome)
Ciguatera fish poisoning[a] (Ciguatoxin)	Large, predatory tropical reef fish (barracuda, grouper, red snapper, amberjack); some types of eels; farm-raised fish that feed on contaminated fish.[b]	12–24 h; neurological symptoms can last months to years	**n**, **v**, **d**, **ab**, **p** (especially hands and feet), **t**, **bp**. Also: metallic taste, itching, dizziness. Possible recurrence of neurological symptoms during times of stress, after ingesting alcohol, or low-level fish. Low mortality in the US.[c,d,e]	Supportive. Mannitol therapy is recommended for neurological symptoms.[f] Brevenal has also been indicated.[g]	Avoid consuming risky fish; education on avoiding consumption of viscera especially where reef fish are a key subsistence source[h]; surveillance.[i]	[a] Barbier and Diaz, 2003 [b] DiNubile and Hokama, 1995 [c] Hokama, 1988 [d] Kumar-Roiné et al., 2011 [e] Morris et al., 1982 [f] Dickey and Plakas, 2010; see also for treatment for specific symptoms [g] Nguyen-Huu et al., 2010 [h] Copeland et al., 2014 [i] Tester et al., 2013
Diarrhetic shellfish poisoning[j,k,l] (Okadaic Acid)	Mussels, oysters, scallops, clams, cockles, some species of crabs [m,n,o]	30 min to 15 h; full recovery, within 3 days[m]	**d** (incapacitating), **n**, **v**, **ab**. Headache, fever. No reported mortality.	Supportive. Most people do not seek treatment.	Monitoring seafood and water; regulated in European countries, though outbreaks still occur.[dd]	[j] Hossen et al., 2011 [k] Taylor et al., 2013 [l] Valdiglesias et al., 2013 [m] James et al., 2010 [n] Manerio et al., 2008 [o] Vale and Sampayo, 2002 [p] see[j] and Cordier et al., 2000
Neurotoxic shellfish poisoning[q] (Brevetoxins)	Mussels, clams, whelks, conch, coquinas, oysters, scallops; liver and stomach contents of some planktivarous fish; inhalation of toxin aerosolized by coastal wind and waves. [q,r]	*Consumption:* a few minutes up to 18 h often within 3–4 h *Inhalation:* Minutes to hours (<24 h)	*Consumption*: **p** (perioral, face, extremities), **ab**, **t**, **d**, **b**, **r** (most severe cases). May appear disori-ented or intoxicated (slurred speech, pupil dilation, overall fatigue, involuntary muscle spasms). *Inhalation*: **a**, **b**, **r**. Throat irritation, sneezing, coughing, itchy and watery eyes, burning of upper respiratory tract. No reported mortality for either pathway.	*Consumption*: Supportive. *Inhalation:* Leave the beach and go to an air-conditioned area.	Coastal and seafood monitoring and quarantine; clear, easily available information on recreational closures [s,t]; persons with asthma or other respiratory problems should avoid beaches during "red tides."	[q] see for examples:[j,o,] and Hinder et al., 2011 [r] Hoagland et al., 2014 [s] Plakas and Dickey, 2010. See Terzagian, 2006 for examples [t] Reich et al., 2015
Paralytic shellfish poisoning[u,v,w]	Scallops, mussels, clams, geoducks, cockles, puffer fish, some fish, gastropods, crustaceans [x]	30 min to 3 h; a few hours to a few days	**p** (perioral, often spreading to neck and extremities), **n**, **v**, **r** (severe doses: respiratory paralysis and death). Muscular weakness, drowsiness, incoherent speech. No mortalities in recent US and European outbreaks.	Supportive. Artificial ventilation in severe cases.	Coastal monitoring; quarantine of seafood and region; rapid case reporting; beach clsosures to recreational harvesters.[y]	[u] Etheridge, 2009 [v] Cusick and Sayler, 2013 [w] Hurley et al., 2014 [x] Deeds et al., 2008 [y] for examples, see [c] and McLaughlin et al., 2011
Amnesic shellfish poisoning[z,aa] (Domoic acid)	Razor clams, mussels, oysters, squid. Viscera (not muscle) of scallops, sardines, anchovies, crab, and lobster.[bb]	Within 48 h; months to years with permanent amnesia.	**ab**, **n**, **v**, **r**, disorientation, seizures, permanent short-term memory loss, possible neurodevelopmental delay. Excessive respiratory secretions.[cc] Coma and death only among the most severe cases[y] or elderly.[bb]	Supportive.	Coastal monitoring of water and shellfish; harvesting beach closures; rapid illness reporting.	[z] Grant et al., 2010 [aa] Pérez-Gómez and Tasker, 2014 [bb] Lefebvre and Robertson, 2010 [cc] Teitelbaum, 1990; Teitelbaum et al., 1990; Perl et al., 1990a,b [dd] Trainer et al., 2012

Abbreviated symptoms: **a**, allergic-like; **ab**, abdominal cramps; **b**, bronchoconstriction; **bp**, decrease in blood pressure; **d**, diarrhea; **n**, nausea; **p**, parathesias; **r**, respiratory distress; **t**, reversal of temperature sensation; **v**, vomiting.

of PSP. In the most severe cases, symptoms rapidly progress to severe respiratory problems in a person who otherwise exhibits no evidence of respiratory difficulty (Gessner et al., 1997b) and death may result. In most cases, recovery is rapid and complete with most symptoms resolving within 24–72 h, with 14 days representing the maximum recovery window (Rodrigue et al., 1990; Gessner et al., 1997a). Given the potential severity of the illness, early diagnosis is essential. Toward this end, data regarding the potential utility of a new laboratory test to confirm the diagnosis of STX-PSP is presented by Knaack and colleagues in this special issue (Knaack et al., 2016).

1.3. Neurotoxic shellfish poisoning (NSP)

Neurotoxic shellfish poisoning (NSP) is typically caused by ingesting bivalve shellfish (e.g., clams, oysters and mussels) that are contaminated with brevetoxins. The risk for NSP toxins in shellfish is associated with HABs or "red tides" along the Gulf of Mexico. The greatest number of cases appears to come from the west coast of Florida, although this may be due to differences in surveillance rather than actual differences in occurrence (Daranas et al., 2001; Watkins et al., 2008). Due to careful monitoring, most cases of NSP that occur in the U.S.A. are associated with recreationally-harvested shellfish collected during or post "red tide" blooms (Fleming et al., 2011). Similarly to other HAB-related illnesses, there is an ongoing threat of new NSP cases as HABs may be transported to new regions. In fact, the largest number of reported U.S. cases came from a single outbreak of 48 persons in North Carolina whereby brevetoxin-producing organisms were transported up the eastern seaboard (Morris et al., 1991). Harmful algal blooms and associated outbreaks of NSP have also been reported in New Zealand and Mexico (Ishida et al., 1996; Sim and Wilson, 1997; Hernández-Becerril et al., 2007).

The diagnosis of NSP is based upon clinical presentation and history of bivalve shellfish consumption from a risky area. Symptom onset may range from a few minutes to 18 h after consuming contaminated shellfish; however, in most cases, time to illness is about three to four hours (Morris et al., 1991; Poli et al., 2000). The symptoms of NSP include both gastrointestinal and neurological problems. The most frequently reported symptoms are nausea, vomiting, abdominal pain, and diarrhea; however, these are not often the primary presenting complaint. Of greater concern to most individuals are the neurological symptoms which may include paresthesia of the mouth, lips, and tongue; peripheral tingling, partial limb paralysis, slurred speech, dizziness, ataxia, and a general loss of coordination. Reversal of hot/cold sensation, similar to ciguatera poisoning, has also been reported (Arnold, 2011). The most common symptoms from the North Carolina outbreak were paresthesias (81%), vertigo (60%), malaise (50%), abdominal pain (48%), nausea (44%), diarrhea (33%), weakness (31%), ataxia (27%), chills (21%), headache (15%), myalgia (13%), and vomiting (10%; Morris et al., 1991). Albeit rare, a few subjects have reported respiratory discomfort and distress, with some requiring ventilator support (Watkins et al., 2008). Although hospitalization is sometimes necessary, no fatalities have been reported as a result of NSP (Arnold, 2011). Most patients recover within two to three days without long term or chronic effects (Baden, 1983; Morris et al., 1991; Watkins et al., 2008).

Recent studies suggest that aerosolization of the toxin from sea water produces a transient, self-resolving, inhalational syndrome characterized by respiratory problems and eye irritation (Fleming et al., 2005, 2011). Exposure has been associated with wave action and aerosolized sprays along Florida beaches during "red tide" events. Adverse respiratory effects include upper airway irritation and discomfort, decreases in pulmonary function, and exacerbation of symptoms in people with asthma.

1.4. Amnesic shellfish poisoning (ASP)

The potential risk of domoic acid (DA) to human health was discovered in 1987 in eastern Canada (Perl et al., 1990a,b; Teitelbaum, 1990; Teitelbaum et al., 1990). Persons who ate affected blue mussels harvested from the Prince Edward Island region suffered serious gastrointestinal distress and, in some cases, death. Some survivors were left with a permanent and profound memory disorder, called amnesic shellfish poisoning (ASP). The rapid work of scientists, largely dependent on animal models, led to establishing safety standards for DA for shellfish harvesting and consumption both in the U.S. and Canada. Aggressive monitoring by national and state public health entities (including agencies overseeing human health, fisheries, and food and drug quality) appears to have been effective in preventing further deaths by closing shellfish beds if DA levels exceeded 20 ppm. Within the past 15–20 years, measured DA levels have been significantly elevated on the U.S Pacific coast (Walz et al., 1994; Wekell et al., 1994; Trainer et al., 1998; Grant et al., 2010).

DA is a naturally occurring toxin produced by blooms of *Pseudo-nitzschia*. Shellfish and other marine organisms feed on *Pseudo-nitzschia* and concentrate the toxin within them. Hence, the shellfish become harmful to wildlife and humans that consume them. Although DA has been found in the viscera of Dungeness crab and other organisms, razor clams are one of the most significant vectors, as they can hold the toxin for up to one year in the natural environment, or several years after being processed, canned, or frozen (Wekell et al., 1994).

In some coastal areas, persistent, low-levels have been interspersed with dangerously high levels, leading to increases in toxicity affecting fish, shellfish, shorebirds and sea lions in California, and shellfish in Washington and Oregon (Wekell et al., 1994; Sierra-Beltrán et al., 1997; Scholin et al., 2000; Gulland et al., 2002; Beasley, 2003; Trainer et al., 2007; Goldstein et al., 2008). The extent to which chronic low level exposure impacts human health remains to be determined. Preliminary findings from Grattan et al. (2016), raise the possibility that milder memory problems may be associated with lower level, chronic exposures in adults who are heavy consumers of razor clams. Thus, domoic acid neurotoxicity potentially may be associated with a non-amnesic syndrome.

Clinical diagnosis is largely based upon symptom complaints and eliciting a detailed history of recent shellfish consumption. Acute symptomatology of high-level exposures include vomiting, abdominal cramps, diarrhea, headache, seizures, respiratory excretions, confusion coma and, in some cases, death (Perl et al., 1990a,b; Teitelbaum, 1990; Teitelbaum et al., 1990). In the Prince Edward Island outbreak, the most severe neurological sequelae were found in males over 60 years of age with symptom onset within 48 h of ingestion. In the younger age groups, the most vulnerable individuals were those with preexisting illnesses such as renal disease, hypertension, or diabetes. A few individuals completely recovered; severe memory problems (amnesia) persisted in others, and, in one case, the delayed onset of temporal lobe epilepsy was observed (Cendes et al., 1995).

1.5. Diarrhetic shellfish poisoning (DSP)

Diarrhetic shellfish poisoning is characterized by acute gastrointestinal symptoms triggered by the ingestion of shellfish contaminated with okadaic acid and related toxins. Mussels, clams, scallops and oysters are the most common vectors for the DSP toxins which are produced by a community of dinoflagellates, most notably, *Dinophysis* spp and *Prorocentrum* spp (James et al., 2010; Valdiglesias et al., 2011). Outbreaks of DSP have been reported in the U.S., Japan, France and other parts of Europe, Canada, New

Zealand, United Kingdom, and South America (Yasumoto et al., 1978; Kawabata, 1989; Belin, 1991; van Egmond et al., 1993; Hinder et al., 2011; Trainer et al., 2013). The first confirmed cases of DSP in the United States occurred in 2011 when three people became ill after consuming contaminated mussels harvested from Sequim Bay, Washington State (Trainer et al., 2013). The responsible organisms (*Dinophysis* spp) also have been identified in Texas Gulf coastal waters and oysters in that region reportedly tested positive for okadaic acid (Barbier and Diaz, 2003; Deeds et al., 2010). High concentrations of diarrhetic shellfish toxins recently have been measured for the first time in New York shellfish (Hattenrath-Lehmann et al., 2013), suggesting that a "tipping point" was exceeded across the U.S., allowing these toxins to affect several coastal regions that historically have not been impacted by them.

Similar to other shellfish illnesses, the diagnosis of DSP is largely made by dietary history and symptoms. Symptom onset typically occurs within 30 min to 4 h after eating contaminated shellfish. The main symptom is incapacitating diarrhea, followed by nausea, vomiting, and abdominal cramps (James et al., 2010). The symptoms may be severe and lead to dehydration, but are usually self-limiting and continue for about three days. Although DSP poisoning is traditionally believed to result in full recovery, preliminary data raises the possibility that DSP toxins, due to their lipophilic nature, may be associated with more significant medical problems over time (Cordier et al., 2000; Manerio et al., 2008; Valdiglesias et al., 2011, 2013).

2. Public health implications and future directions

There are five commonly recognized HAB-related illnesses: ciguatera fish poisoning, paralytic shellfish poisoning, neurotoxic shellfish poisoning, amnesic shellfish poisoning and diarrheic shellfish poisoning. At this time, routine, clinical diagnostic tests are not available for any of these syndromes. Thus, there is a substantial diagnostic uncertainty of many HAB-related illnesses, as well as the significant degree of underreporting (Sobel and Painter, 2005; Fleming et al., 2011; Knaack et al., 2016). When diagnoses are made, they are largely based upon symptom presentation and history of seafood consumption.

Since there is no antidote for any of the HAB-related toxin exposures, symptom management and supportive care are the only available treatments, once one has been diagnosed. With this in mind, illness prevention is of paramount importance to manage HAB-related human health risks. Public health intervention, including case identification or surveillance, as well as health promotion to protect at-risk communities is a challenging, albeit necessary activity. An important new direction for HAB related public health research and interventions is managing the uncertainty associated with the presence of a known or suspected HAB related toxin. A wide range of psychological reactivity may accompany threats of a toxin exposure or exposure related illnesses.

Concerns are often amplified if the event is unpredictable, persistent, involves a novel toxin or leads to economic loss in the coastal community. These environmental worries may trigger a chain of events that impinges on the well-being of the coastal community as a whole. Financial resource loss, socioeconomic adversity, or losses of job opportunities are significant stressors that have been associated with the onset and course of anxiety, depression and problems with substance abuse. Similar to other unanticipated coastal events (e.g. hurricanes, floods, oil spill), the capacity of individuals and communities to be resilient in the face of expanding HAB-related threats and potential illnesses should be closely monitored.

At this time, effective public health intervention necessitates active and close communication between HAB scientists; local, state and tribe health and natural resources entities; local physicians, clinics and hospitals; academic communities; and public health practitioners and researchers. Meanwhile, transdisciplinary laboratory, oceanographic, epidemiological, economic, public health, risk perception, and social-psychological research are needed to promote science that could lead to the prevention and early detection of HAB-related illnesses. This would include, but not be limited to, enhancing capacities for toxin detection and environmental monitoring, identifying specific biomarkers for human illness, further characterizing HAB-related syndromes, identifying at-risk individuals and communities, developing interventions at individual and community levels, strengthening outreach effectiveness, improving illness reporting and surveillance programs, and contributing to policy development.

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