HHS Public Access

Author manuscript

Harmful Algae 2002 (2002). Author manuscript; available in PMC 2015 October 02.

Published in final edited form as:

Harmful Algae 2002 (2002). 2004 ; 10: 508–510.

An Epidemiologic Approach to the Study of Aerosolized Florida Red Tides

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Abstract

Very little has been published in the scientific literature on the human health effects of Florida red tide, either as human clinical case reports or formal epidemiologic studies. In addition to the health effects associated with the ingestion of contaminated shellfish, there have been multiple anecdotal reports of respiratory irritation and possible immunologic effects associated with the inhalation of aerosolized Florida red tide. To investigate the human health effects from environmental exposure to red tide toxins, we have formed an interdisciplinary team of scientists. We have created a network of public and environmental health workers who periodically report local conditions as a red tide develops. In addition, we have access to environmental monitoring data as well as data from a surveillance program supported through the Florida Poison Information Network. When a red tide moves onshore where people might be exposed, the team rapidly assembles at the site to collect environmental samples and epidemiologic data. To assess the more long-term effects from environmental exposure to red tide toxins, we are conducting epidemiologic studies involving occupational and sensitive populations who live in areas that are regularly impacted by red tides. Other scientists are evaluating the acute and chronic respiratory effects of red tides and

brevetoxins in both rat and sheep models as well as refinement of toxin measurement methodology. These models are being used to refine and validate the biomarkers of brevetoxins exposure as well as explore the pathophysiology of health effects from brevetoxins respiratory exposure. Bolstered by the additional research in rat and sheep models, this interdisciplinary scientific team is exploring the acute and chronic exposures and health effects of aerosolized Florida red tides in animal models and various human populations. In the future, this research can be applied to the understanding of exposure and effects of other aerosolized natural toxins such as cyanobacterial toxins.

Introduction

Florida red tide is an almost annual event caused by the dinoflagellate, *Karenia brevis.* This organism produces brevetoxins which cause significant fish kills as well as neurotoxic shellfish poisoning (NSP) if contaminated shellfish are consumed. There have been anecdotal reports of respiratory irritation and possibly immunologic effects associated with the inhalation of aerosolized Florida red tide. Recent die-offs of the endangered Florida manatee were associated with the inhalation of the Florida red tide toxins, and research in sheep and other laboratory animals has confirmed the ability of aerosolized red tide toxins to cause reversible bronchospasm (Kirkpatrick *et al.*, in press; red tide Group, 2002; Cheng *et al.*, in press; Backer *et al.*, 2003).

The traditional public health approach has been quite successful in preventing human cases of NSP in Florida red tide through active environmental monitoring for toxin and organisms with subsequent closure of shellfish beds, in addition to passive public health surveillance. However, faced with an intermittent annual aerosolized exposure with possible acute and chronic respiratory effects, particularly in sensitive subpopulations, in a state highly dependent on tourism and other coastal industries, a new public health and research approach must be instituted. This paper briefly describes an ongoing interdisciplinary research study of the exposure and health effects of aerosolized Florida red tide toxins on humans and animal models.

Methods

To investigate the human health effects from environmental exposure to red tide toxins, we formed an interdisciplinary team of scientists. We created a network of public and environmental health workers who periodically report local conditions as a red tide develops. We have access to environmental monitoring data (*e.g.*, cell concentrations in water samples, satellite imagery) as well as data from a surveillance program supported through the Florida Poison Information Network. When a red tide moves onshore where people might be exposed, the team assembles at the study site to collect environmental samples (air and seawater) and epidemiologic data (including pre- and post-exposure questionnaires, pulmonary function tests, and personal breathing zone monitoring). To assess the chronic effects from environmental exposure to red tide toxins, we are conducting epidemiologic studies involving occupational (including lifeguards and scientists) and sensitive populations (including elderly people with underlying respiratory disease and

children with asthma) who live in areas that are regularly impacted by red tides. Members of the interdisciplinary team are also evaluating the acute and chronic respiratory effects of red tides and brevetoxins in both rat and sheep models as well as refinement of toxin measurement methodology.

Results

The aerosolized Florida red tide toxin research group is performing research integrated between human and animal models as well as between environmental and personal sampling. The measurement in humans and animals of both exposure (*i.e.*, brevetoxins, sea water and other substances) and effects (*i.e.*, respiratory, immunologic, neurologic, and other) is the core objective of this research program.

Exposure Measurement

We have examined samples of sea spray aerosol collected during red tide events and have found that the particles are predominantly large (>2.5 microns). An ELISA test for brevetoxins has been developed and used to measure brevetoxin concentrations in seawater and air (personal and environmental) samples as well as in samples of biological fluids from rats and sheep exposed to brevetoxins under laboratory conditions. Attempts to use the ELISA to measure brevetoxins in human fluids to date have not been successful except in throat swabs. An immunohistochemical stain for brevetoxins, originating from earlier research in highly exposed manatees (Bossart *et al.*, 1998), has also been successfully applied to demonstrate the presence of brevetoxins in samples from exposed laboratory rats and sheep, but not humans. In part, this may reflect the significantly lower concentrations of brevetoxins in humans exposed under natural conditions when compared with laboratory animals.

Effect Measurement

Studies reveal that rats are relatively resistant to brevetoxins (*i.e.*, they demonstrate responses after being exposed to microgram levels of brevetoxins, compared with the picogram exposures in other species). Health effects being evaluated include the respiratory, immunologic, and neurologic systems. Studies in asthmatic sheep have demonstrated significant bronchoconstriction following inhalation challenge with picogram levels of brevetoxins or contaminated sea spray; furthermore, this response can be blocked by pre-treatment with a mast cell inhibitor and by antihistamines (Abraham 2001, Cheng in press). A pilot study of human recreational beachgoers (Backer 2003) found a relationship between the amount of brevetoxins in the air and seawater, with the symptoms reported by study participants. The results indicated that when the cell counts and the brevetoxin levels were higher in water and air samples, and were accompanied by strong onshore winds, people reported an increase in lower respiratory symptoms (*e.g.*, wheezing and chest tightness) after visiting the beach, compared to the symptoms reported before going to the beach. On the moderate exposure day with lower brevetoxin levels in the air and water, fewer people reported lower respiratory symptoms, and were significantly more likely to report upper respiratory symptoms (e.g.. nasal and throat irritation) after being on the beach. We also conducted spirometry tests of pulmonary function using methods and standards approved by

the National Institute for Occupational Safety and Health; however, these tests did not identify any decreases in pulmonary function following exposure to aerosolized brevetoxins. We are now conducting two additional epidemiologic studies using more precise spirometry equipment. A cohort of lifeguards has been assembled as well as additional cohorts of people with asthma (>11 years) and people with Chronic Obstructive Pulmonary Disease (>44 years). The occupational cohort is being evaluated throughout several workdays, while the sensitive cohorts are evaluated during several years by conducting pulmonary function testing and requesting information about symptoms during a red tide and when there is not a red tide in the area.

In addition to the subjective symptom reporting and the spirometry data, we are developing biological markers of the effects of brevetoxins. These markers include swabs of the nose and throat to examine the inflammatory response to exposure. We are also examining other potential markers of biological effect, *e.g.*, neuropsychological testing (including auditory evoked responses) (Lu *et al.*, 2002) and other cellular markers (including epithelial cell factors and immunologic markers). If we are able to demonstrate effects in the animal models at doses comparable to human exposure, then these effect biomarkers will be evaluated in the epidemiologic cohort studies.

Discussion

The strength of our research program to evaluate human exposure to and effects from aerosolized red tide toxins is its integrated interdisciplinary approach. Animal models are being used to refine and validate potential markers of exposure and biological activity as well as to explore the pathophysiology of health effects from respiratory exposure to brevetoxins. We anticipate applying what we learn about human exposure to aerosolized brevetoxins in additional studies of the health effects associated with exposure to aerosols containing other potent natural toxins, such as those produced by cyanobacteria (blue-green algae). In addition, a number of outreach and educational materials that have been created in parallel with this research will be used as models for future materials developed to educate the public about naturally occurring toxins in their environments (www.rsmas.miami.edu/groups/niehs/redtide/; Kirkpatrick *et al.*, in press).

Acknowledgments

Funding for this research was provided by the Centers for Disease Control and Prevention, the State of Florida Dept of Health, the Florida Harmful Algal Bloom Task Force, and the National Institute of Environmental Health Sciences (P01 ES 10594). The researchers would like to thank Dr. Karen Steidinger and the Florida Marine Research Institute (www.floridamarine.org) for their consistent support of this research effort.

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