Aerosolized Red-Tide Toxins (Brevetoxins) and Asthma*

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Background: **With the increasing incidence of asthma, there is increasing concern over environmental exposures that may trigger asthma exacerbations. Blooms of the marine microalgae, *Karenia brevis*, cause red tides (or *harmful algal blooms*) annually throughout the Gulf of Mexico. *K brevis* produces highly potent natural polyether toxins, called *brevetoxins*, which are sodium channel blockers, and possibly histamine activators. In experimental animals, brevetoxins cause significant bronchoconstriction. In humans, a significant increase in self-reported respiratory symptoms has been described after recreational and occupational exposures to Florida red-tide aerosols, particularly among individuals with asthma.**

Methods: **Before and after 1 h spent on beaches with and without an active *K brevis* red-tide exposure, 97 persons ≥ 12 years of age with physician-diagnosed asthma were evaluated by questionnaire and spirometry. Concomitant environmental monitoring, water and air sampling, and personal monitoring for brevetoxins were performed.**

Results: **Participants were significantly more likely to report respiratory symptoms after *K brevis* red-tide aerosol exposure than before exposure. Participants demonstrated small, but statistically significant, decreases in FEV_1, midexpiratory phase of forced expiratory flow, and peak expiratory flow after exposure, particularly among those participants regularly using asthma medications. No significant differences were detected when there was no Florida red tide (*ie*, during nonexposure periods).**

Conclusions: **This study demonstrated objectively measurable adverse changes in lung function from exposure to aerosolized Florida red-tide toxins in asthmatic subjects, particularly among those requiring regular therapy with asthma medications. Future studies will assess these susceptible subpopulations in more depth, as well as the possible long-term effects of these toxins.**

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Key words: asthma; brevetoxins; harmful algal blooms; *Karenia brevis*; red tides; sensitive populations; spirometry

Abbreviations: ELISA = enzyme-linked immunosorbent assay; LOD = limit of detection

Asthma in the United States affects 10.6% of noninstitutionalized adults and 12.5% of children.[1] Asthma is a major health disorder causing asthmatic children to miss 14 million school days per year.[2] In 2002, asthma health-care costs totaled $14 billion (in US dollars).[3] A range of environmental exposures (from air pollution to cockroach antigen) is associated with this asthma epidemic.[2,4] Frequent Florida red-tide events in the Gulf of Mexico present a unique environmental exposure for persons with asthma who live or work near the shore. Our research in animals and humans suggests that persons with asthma (including children) may be more sensitive to the aerosols of these red tides.[5–8]

Red tides, an annual events in the heavily populated Gulf of Mexico, are blooms of the marine dinoflagellate *Karenia brevis*.[9,10] The blooms, often lasting for months, can span the Florida coastline, and have been reported in Mexico and on the North Carolina coast. The highly potent natural polyether toxins of *K brevis*, known as *brevetoxins*, activate voltage-sensitive sodium channels and possibly act as

histamine activators. More than 12 brevetoxins have been identified. Studies[7,8,11,12] in experimental animals have shown that brevetoxins can cause respiratory irritation and bronchoconstriction. In humans, brevetoxins produced during *K brevis* red tides can cause both neurotoxic shellfish poisoning, which is an acute gastroenteritis with neurologic symptoms occurring after the ingestion of contaminated shellfish, and upper respiratory distress after the inhalation of the red-tide brevetoxin aerosols.[5,6,12–22] Persons with asthma may be particularly sensitive to adverse health effects from these aerosolized toxins.[5,6,10,23]

Respiratory effects from exposure to aerosolized *K brevis* red tides and from pure brevetoxins have been reported in experimental animals.[7,8,11] In an experimental asthma sheep model, inhalation challenge with aerosolized red tide (as well as pure brevetoxins) at doses less than or equal to those experienced by humans inhaling *K brevis* red-tide aerosols on beaches caused a significant and rapid increase in airway resistance.[7,8] This brevetoxin-induced bronchospasm was effectively blocked by atropine, the mast cell-stabilizing agent cromolyn, the histamine H_1 antagonist chlorpheniramine, and the β_2-agonist albuterol.[7,8] Furthermore, although the acute bronchoconstrictor effects of inhaled brevetoxins can be seen in both asthmatic and normal sheep, the response is more severe in the asthmatic subgroup with previously inflamed lungs due to a recently induced asthma exacerbation.[7]

Human exposure to aerosolized Florida red-tide toxins occurs on or near beaches during an active *K brevis* bloom with onshore winds and surf, which breaks up the cells and releases toxins into the water, creating onshore aerosols.[24] Brevetoxin concentrations in the aerosols ranging from < 0.5 to 108 ng/m^3 have been measured during *K brevis* red-tide episodes associated with reported respiratory symptoms in humans.[5,6,20,21,25–27] With a mass median aerodynamic diameter of 7 to 9 μm, $> 90\%$ of the particulate is believed to be deposited in the nose; however, very fine respirable particulates of red-tide brevetoxin aerosol < 2.5 μm in size have been measured.

In humans, the inhalation of aerosolized *K brevis* red-tide toxins results in conjunctival irritation, rhinorrhea, nonproductive cough, and wheezing.[10,12,15,19,22,28] In the population of healthy individuals, there is reportedly rapid reversal of these symptoms by leaving beach areas or entering an air-conditioned area.[9,19,20,29] Asthmatic persons appear to be more susceptible to *K brevis* red-tide aerosols.[5,6] This study further evaluated the exposures and effects of aerosolized red-tide brevetoxins in 97 asthmatic subjects after 1-h exposure to *K brevis* red tides and after 1-h nonexposure at the beach.

Materials and Methods

This study was part of the ongoing evaluation of aerosolized *K brevis* red-tide brevetoxin exposure, and the possible acute and chronic adverse health effects of brevetoxins in humans and animals by an interdisciplinary team of researchers from federal, state, private, and local organizations.[5] These studies have been approved by the participating institutional review boards. The study location was Siesta Beach (Sarasota, FL), where prolonged Florida red tides lasting months have become an almost annual event.

Asthmatic participants were defined as follows: (1) self-reported diagnosis by a physician; (2) age $\geq$ 12 years; (3) smoking history of $\leq$ 10 years; (4) ability to walk for $\geq$ 30 min continually on the beach; and (5) resident of the Sarasota area for $\geq$ 6 months. They were asked to spend $\geq$ 1 h at the beach in areas with ongoing environmental monitoring; they could return at any time from the beach if they felt symptomatic, and all participants were encouraged to use any personal medications as needed throughout the study period.[6]

Each asthmatic subject participated in at least one evaluation during an active *K brevis* bloom (*ie*, the exposure period), and in one evaluation during a period when there was not a bloom (*ie*, the nonexposure period). Both evaluations included the following before and after the beach visit: questionnaires, nasal swab sampling, and spirometry. Study participants were asked to carry a personal air monitor while at the beach. Detailed baseline information was collected for all subjects (including their medical history and possible confounders) in a baseline questionnaire,

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