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Aerosolized Red Tide Toxins (Brevetoxins) and Asthma: Continued health effects after 1 hour beach exposure

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Abstract

Blooms of the toxic dinoflagellate, *Karenia brevis*, produce potent neurotoxins in marine aerosols. Recent studies have demonstrated acute changes in both symptoms and pulmonary function in asthmatics after only 1 hour of beach exposure to these aerosols. This study investigated if there were latent and/or sustained effects in asthmatics in the days following the initial beach exposure during periods with and without an active Florida red tide.

Symptom data and spirometry data were collected before and after 1 hour of beach exposure. Subjects kept daily symptom diaries and measured their peak flow each morning for 5 days following beach exposure. During non-exposure periods, there were no significant changes in symptoms or pulmonary function either acutely or over 5 days of follow-up. After the beach exposure during an active Florida red tide, subjects had elevated mean symptoms which did not return to the pre-exposure baseline for at least 4 days. The peak flow measurements decreased after the initial beach exposure, decreased further within 24 hours, and continued to be suppressed even after 5 days. Asthmatics may continue to have increased symptoms and delayed respiratory function suppression for several days after 1 hour of exposure to the Florida red tide toxin aerosols.

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Keywords

Harmful Algal Blooms (HABs); inhalation toxicity; Karenia brevis; coastal

1.0. Introduction

Over the past decade, an interdisciplinary and inter-institutional team of researchers have been evaluating aerosolized Florida red tide toxin exposures, and their possible acute and chronic adverse health effects in humans and animals. Our research in animals and humans strongly suggests that asthmatics may be more sensitive to the aerosols from the harmful algal blooms (HAB) known as “Florida red tides” (Backer et al. 2003; Fleming et al. 2005, 2007, 2009; Kirkpatrick et al. 2005; Milian et al. 2007). These aerosols contain the potent natural toxins, brevetoxins, which are produced by the HAB organism, *Karenia brevis*, in the Gulf of Mexico and elsewhere.

Respiratory effects from exposure to either aerosolized *K. brevis* red tides or pure brevetoxins have been reported in experimental animals (Abraham et al. 2005a, 2005b; Asai et al. 1982; Benson et al. 2005). In an experimental sheep model of asthma, inhalation challenge with aerosolized red tide culture and pure brevetoxins at doses less than or equal to environmental levels caused significant and rapid increases in airway resistance, as well as prolonged increases in airway hyper-responsiveness on the days following exposure (Abraham et al. 2005a, 2005b, 2009; Zaias et al. 2004). In this animal model, brevetoxin-induced bronchospasm can be effectively blocked by pre-treating with commonly used asthma medications (e.g. albuterol) as well as by anti-histamines (e.g. chlorpheniramine), as well as treated after brevetoxin exposure by albuterol (Abraham et al. 2005a, 2005b).

In a cohort of human asthmatics, we have demonstrated that environmental exposure to the Florida red tide aerosols causes a significant increase in reported symptoms and a significant decrease in pulmonary function after a 1 hour beach exposure (Fleming et al. 2005, 2007, 2009; Milian et al. 2007). In addition, we found that persons calling the Poison Control Aquatic Toxins Hotline (tel: 888 232 8635) to report exposure to Florida red tide were more likely to report respiratory symptoms lasting several days to weeks and increased use of medications and visits to doctors (Quirino et al. 2004). We have also observed increased emergency room admissions for respiratory diseases (including pneumonia, bronchitis, and asthma) during active Florida red tides, particularly for coastal residents (Kirkpatrick et al. 2006). Finally, an initial analysis indicated that respiratory symptoms may last for several days after exposure to Florida red tide aerosols at the beach (Kirkpatrick et al. 2009).

These data may have important implications for asthmatics who live and/or work in coastal areas. First, Florida red tide aerosols may cause health effects that last beyond an acute exposure. Second, as US coastal populations continue to grow, more people (including asthmatics and other persons with chronic respiratory diseases) are potentially being impacted by ocean-borne threats, such as toxin-containing aerosols. Finally, evidence is accumulating that Florida red tides may be increasing in intensity and duration (Brand et al. 2007). In this study, we explored further the possible sub-acute effects in asthmatics from exposure to Florida red tide aerosols at the beach.

2.0. Methods

2.1. Study location & participants

The study location was Siesta Beach (Sarasota, Florida). Since 2003, we have followed an open cohort of 120 asthmatics with the following characteristics: self-report of physician-

diagnosed asthma; ≥ 12 years of age; history of smoking ≤10 years; able to walk on the beach continuously > 30 minutes; and > 6-month residence in the Sarasota area (Fleming et al. 2005, 2007, 2009; Milian et al. 2007). The participants in the present follow-up study were a subgroup of 52 asthmatics from the primary beach study who agreed to do study activities over a 5 additional days after the day of their 1 hour beach exposure (i.e. a total of 6 days of data collection). The study was approved by the participating entities' Institutional Review Boards.

2.2. Study Activities

The activities for the main beach study have been described in detail previously (Fleming et al. 2005, 2007, 2009; Milian et al. 2007). Briefly, all participants completed questionnaires, collected nasal swabs, and completed spirometry tests before and after the exposure (i.e. a 1-hour walk on the beach). The pre- and post-beach questionnaires collected information on recent medical history and medication use, as well as symptoms and possible confounders (e.g. smoking). They were asked to walk 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 (including asthma medications) as needed throughout the study period. Each study participant also carried an IOM personal air monitor (SKC Inc., Eight Four, PA) during their 1 hour of beach exposure.

Study personnel trained according to National Institute of Occupational Safety and Health (NIOSH) standards administered spirometry using a portable OMI2000 10-liter dry rolling seal volume spirometer to all study participants before and after 1 hour beach exposure (Occupational Marketing, Inc., Houston, Texas) (NIOSH 1997). The spirometry values included the peak expiratory flow (PEF). Only data conforming to the standard guidelines for collection and interpretation of spirometry measurements were accepted, and all study participants had ≥ 3 reproducible spirograms before and after visiting the beach.

In addition to the spirometry, the 52 follow-up participants also received individual instruction on using a handheld peak flow meter (Spiroflow© Adult Peak Flowmeter). They measured and recorded their own peak flow directly after participating in the main beach study, and at three times each morning for the next 5 days. The best of three measurements were used in the analyses. Study participants also filled out a simple symptom and medication diary every morning. At the conclusion of the 5 days of follow-up, the subjects mailed back the symptom/peak flow diary in a pre-addressed, stamped envelope. To encourage compliance, they also were interviewed on the phone on the first and last day of the follow-up study concerning their symptoms and medication use. The activities were performed during a time when there was an active Florida red tide, and during a time when there was no active bloom.

2.3. Ambient monitoring

As described previously, water samples were collected twice daily in 1-liter glass bottles from the surf zone at Siesta Key beach during the main beach study and throughout the 5 day follow-up study (Fleming et al. 2005, 2007, 2009; Milian et al. 2007; Naar et al. 2002; Pierce et al. 2005). The water samples were analyzed for *K. brevis* cell counts and for brevetoxin concentrations, using both the brevetoxin ELISA and liquid chromatography mass spectroscopy (LCMS) analysis (Naar et al. 2002; Pierce et al. 2005). During the primary beach study, air samples for toxin and aerosol particle size were collected using two types of high-volume samplers and a personal sampler of the subjects' breathing zones. Brevetoxin concentrations were measured in samples from the high volume sampler and the personal sampler (Cheng et al. 2005; Fleming et al. 2009; Kirkpatrick et al. 2010).

2.4. Health Assessment

Questions about the presence and severity of symptoms established as relevant to brevetoxin exposure in past studies (i.e., cough, wheeze, throat irritation, shortness of breath, chest tightness, nasal congestion, eye irritation, and headache) were asked before and after spending 1 hour on the beach, as well as in the follow-up interviews and symptom diaries (Fleming et al. 2005, 2007, 2009; Kirkpatrick et al. 2009; Milian et al. 2007). Since brevetoxins have been measured up to 1.6 km inshore from the coast during active *K. brevis* bloom aerosols when there are strong enough onshore winds, “coastal residence” was defined as residence on a barrier island or along Sarasota Bay within 1.6 km of a coast (Kirkpatrick et al. 2010). As in prior studies, the use of asthma medications within 12 hours before going to the beach was used as a surrogate for increased asthma severity or lack of control (Fleming et al. 2005, 2007, 2009; Milian et al. 2007).

2.5. Statistical Analysis

The study database was created in Microsoft ACCESS with direct entry during participant interviews. Descriptive and other statistical analyses were performed using SAS statistical software Version 9.1 (SAS, Cary, NC), including ttests for the spirometry data before and after the 1 hour beach exposure. The mean number of symptoms reported and the mean peak flow (measured by handheld peak flow meter), a measure of pulmonary effect, were the two dependent variables that were compared for the time points: pre-beach walk (i.e. prior to the 1 hour of beach exposure), the post-beach walk (i.e. just after the 1 hour of beach exposure), and the subsequent five days following the 1 hour of exposure on the beach.

The hypotheses tested were: 1) The dependent variables were the same across the pre-beach walk and the following 5 days; 2) The dependent variables were the same across the post-beach walk and the follow-up days; 3) The dependent variables were the same when the participants lived within 1.6 km of the coast; 4) The dependent variables were the same when the participants lived more than 1.6 km of the coast; 5) The dependent variables were the same when the participants used medicines in the last 12 hours (i.e. less controlled more severe asthmatics); and 6) The dependent variables were the same when the participants did not use medicines in the prior 12 hours (i.e. more controlled asthmatics). Given these hypotheses, mixed modeling was used. The model was examined separately for each of the hypotheses listed above. The factors were: 1) individual subject; 2) time point (i.e. pre/post beach exposure, 5 subsequent days of follow up); and 3) exposure (Florida red tide exposure or not), with the variance estimated by compound symmetry as the algorithm did not converge using other methods of variance structures.

When examining the hypotheses concerning the distance from residence to the beach, the data were stratified by residential proximity with the model containing the same factors listed above. The use of medications could not be analyzed using the method described for proximity as the use varied depending upon the day of the field day; and medication use during the five days of follow up after the beach exposure was not collected. Two individuals, one during exposure study and one during non-exposed study, did not record their usage of drugs so the “n” is smaller. Therefore, these analyses were performed on the exposed studies and non-exposed studies stratified by medication use. Finally, the number of participants was too small to evaluate the subgroups created by using both medication and location together with mixed models.

3.0. Results

There was 100% compliance in returning the completed symptom diaries for both the exposed and unexposed studies for the 5 day follow-up study. Of the 52 asthmatic

participants, 33 (64%) were female; the mean age was 41.1+/-19.6 years (Table 1). Of these asthmatics, 22 (43%) were considered more severe asthmatics at the time of the study since they used their medications within 12 hours of coming to the beach for the primary study. Seventeen (33%) lived in coastal areas <1.6 km of the coast, while 35 (67%) lived inland ≥1.6 km from the coast.

Brevetoxins were detected in the seawater (2.25-69.26 μg/L) and air (21.2-74.7 ng/m^3), and high concentrations of *K. brevis* cells (from 200,000 to >1 million cells/L) were found in seawater during the March 2005 and September 2006 exposure studies (Fleming et al., 2005, 2007, 2009). Non-detectable to very low levels of brevetoxins and *K. brevis* cells were found during the non-exposure studies in May 2004 and June 2006 (Fleming et al. 2005, 2007, 2009; Milian et al. 2007).

3.1. Symptoms

For the entire subcohort, the highest number of mean symptoms (3.09+/-2.14) was seen after 1 hour acute Florida red tide exposure at the beach during the active Florida red tide exposure periods (Table 2). The mean number of symptoms for the subsequent 5 days after the 1 hour beach exposure did not show any delayed onset of increased symptoms after the initial beach exposure, however the mean number of symptoms did not return to the pre-beach exposure mean (1.33+/-1.54) until day 4 of follow-up (1.35+/-1.74). The analyses comparing the follow-up days to the pre-exposure mean number of symptoms were statistically significant for the exposure period ($p<0.0001$) and the study days ($p=0.02$); the interaction of exposure and days was not statistically significant. The least squares mean number of symptoms for the exposure studies was 1.54 as compared to a mean of 1.13 for the non-exposed walks. When comparing the mean number of symptoms for the post-beach walk and the five days of follow-up, the interaction of exposure and days was highly significant ($p<0.0001$), as were the effects of exposure and days. The mean number of symptoms was statistically significantly different from the 1 hour post-beach exposure (3.09+/- 2.14) for all 5 days of follow-up. Therefore, the greatest increase in the mean number of symptoms was directly after the 1 hour of beach exposure and there was no delay in the onset of these increased symptoms; however, it took several days for the mean number of symptoms to return to the pre-exposure baseline.

The cohort was examined for those living near coast. When comparing the pre-beach mean number of symptoms to the means for the 5 follow-up days, only exposure was statistically significant ($p<0.01$) (data not shown). The observed mean number of symptoms for the non-exposure period was 1.65 (+/-1.73) prior to the 1 hour of beach exposure as compared to a mean of 0.59 (+/-1.12) prior to the 1 hour of beach exposure during a Florida red tide exposure; however, the means after 1 hour of beach exposure were 1.18 (+/-1.67) for the non-exposure period and 2.24 (+/-2.24) during a Florida red tide exposure. There was no evidence of a further increase in symptoms (i.e. a delayed effect) after this initial 1 hour beach exposure, however the means for the follow-ups during the exposure period were never below 0.59, even by the fifth day; in contrast, for the non-exposure time period, the means ranged from 1.24 to 1.06.

The individuals who lived inland had a different pattern. When comparing the mean number of symptoms for the pre-beach exposure to the follow-up days, both exposure and day effects were statistically significant ($p<0.0004$ and $p<0.02$, respectively). However, the interaction between exposure and non-exposure was statistically significant ($p<0.0001$) when comparing the mean number of symptoms among the post-beach exposure and the follow-ups days. The mean for post-beach was statistically significant from all the days of follow-up when the Florida red tide was present, as well as different from all the mean non-exposure post-beach and follow-ups day ($p<0.0001$). The mean number of symptoms

reported for those living inland had an observed mean of 3.49 (+/- 2.05) after walking on the beach during a Florida red tide bloom as compared to the a mean of 2.24 (+/-2.24) for those living within 1 mile of the coast. These results indicate that those subjects living inland may not be as exposed to the Florida red tide prior to their study exposure as those subjects who live within a mile of the coast; therefore, the inland subjects come to the beach with fewer symptoms, but leave the beach with a greater number of symptoms. Neither the inland nor the coastal residents demonstrated any delayed increased effect after the initial 1 hour beach exposure, and neither inland nor coastal residents returned to their pre-walk mean until the fifth day.

The data were stratified by medication use in the 12 hours prior to the beach exposure (i.e., more severe vs. more controlled asthma), and evaluated with and without Florida red tide exposure (data not shown). For the more severe asthmatics during Florida red tide exposure, the effect of day was almost statistically significant ($p=0.06$) comparing the mean number of symptoms pre-beach exposure (0.36+/-0.90) to the subsequent 5 follow up days; the effect of day was statistically significant ($p=0.001$) comparing the mean number of symptoms post-beach exposure (2.77+/-1.77) to the subsequent 5 follow up days. During the non Florida red tide exposure for the severe asthmatics, the pre-beach exposure mean number of symptoms was 2.04+/-2.0 (higher than during the pre-beach exposure during a Florida red tide bloom), but the mean number of symptoms decreased after the 1 hour of beach exposure (1.50+/-1.59); the effect of day was not statistically significant for either pre-beach or post beach exposure mean number of symptoms compared to the subsequent 5 days of follow-up. The severe asthmatics did not show any delayed increased effect after the 1 hour of beach exposure but they did not return to the pre-beach exposure baseline until day 5 of follow up during Florida red tide exposure; no differences in the mean number of symptoms were seen during the non Florida red tide exposure period.

For the more controlled asthmatics during Florida red tide exposure, the results showed the mean number of symptoms pre-beach exposure (0.72+/-1.25) was statistically significant ($p=0.05$) compared to the subsequent 5 follow up days; the effect of day was highly statistically significant ($p<0.0001$) comparing the mean number of symptoms post-beach exposure (3.17+/-2.38) to the subsequent 5 follow up days, but there was no increase in the mean number of symptoms beyond that seen after 1 hour of beach exposure. During the non Florida red tide exposure for the more controlled asthmatics, the pre-beach exposure mean number of symptoms was 0.77+/-1.12 with a slight increase in the mean number of symptoms after the 1 hour of beach exposure (1.07+/-1.38); neither pre-beach or post beach exposure mean number of symptoms when compared to the subsequent 5 days of follow-up were statistically different. The more controlled asthmatics returned to the pre-beach exposure baseline by day 5 of follow up during Florida red tide exposure; no differences in the mean number of symptoms were seen during the non Florida red tide exposure period.

3.2. Peak Flow measurements

The PEF measurements using the spirometry before and after the 1 hour of beach exposure demonstrated statistically significant changes in PEF for the entire subpopulation (255.4+/-385.2 ml/sec; $p<0.0001$) comparing each individual's post exposure to their pre-exposure PEF (Table 3). Similarly for the other subgroups of use of asthma medications and residence, there were statistically significant changes in the PEF. Thus, 1 hour of exposure at the beach during a Florida red tide significantly decreased the respiratory function of this group of asthmatics from prior to exposure as measured by spirometry.

The peak flow measurements using the hand-held peak flow meter were only collected at 1 hour post-beach exposure, but not before exposure (and the peak flow data collected by the NIOSH approved spirometry before and after the 1 hour of beach exposure were not

comparable due to the different collection methods). Interestingly, for the entire sub cohort, the highest mean peak flow measurement as measured by the hand-held peak flow meter was seen at the 1 hour post-beach exposure (0.424+/-0.127 L/sec), with a further decrease in the peak flow at 24 hours after initial exposure (0.404+/-119), and the lowest peak flow (0.401+/-0.130 L/sec) at 5 day of follow-up; there was no return to the post-exposure mean peak flow level even after 5 days of follow-up (Table 2). The analyses comparing the 5 subsequent follow-up days to the post-exposure mean peak flows were statistically significant for the exposure period ($p<0.02$) and the study days ($p=0.03$); the interaction of exposure and days was not statistically significant.

During the Florida red tide exposure, the highest mean peak flow measurements were seen at the 1 hour post-beach exposure for coastal asthmatics (0.444+/-0.138) and for inland asthmatics (0.414+/-0.122), with the inland asthmatics more severely effected (data not shown). There was a subsequent delayed decrease in peak flow on the first day of follow up, with no return to this mean peak flow level even after 5 days of follow-up for either group. For the inland asthmatics, the analyses comparing the 5 subsequent follow-up days to the post-exposure mean peak flows were statistically significant for the exposure period ($p<0.006$) and almost statistically significant for the study days ($p=0.07$); the interaction of exposure and days was not statistically significant; for the coastal asthmatics, there were no statistically significant effects or interaction.

During the Florida red tide exposure, the highest mean peak flow measurements were seen at the 1 hour post-beach exposure for more severe asthmatics (0.422+/-0.138) and for more controlled asthmatics (0.440+/-0.123), with the more severe asthmatics more severely effected (data not shown). There was a subsequent delayed decrease in peak flow on the first day of follow up, with no return to this mean peak flow level even after 5 days of follow-up for either group. For both the more severe asthmatics and the more controlled asthmatics, the analyses comparing the 5 subsequent follow-up days to the post-exposure mean peak flows were statistically significant for the study days ($p=0.02$ and $p=0.03$, respectively).

4.0. Discussion

This 5 day follow-up study was initiated based on the anecdotal reports of our asthmatic study participants of delayed and/or prolonged effects after their 1-hour exposure to Florida red tide toxin at the beach during our primary study. Previous studies have reported the delayed onset of asthma from occupational and environmental exposures (Mapp et al. 2006; Reed et al. 1981), and our own animal studies have suggested that acute exposures can lead to prolonged abnormalities in airway function (Abraham et al. 2005a,2005c; Fleming et al. 2005, 2007, 2009; Kirkpatrick et al., 2006; Milian et al. 2007).

This study demonstrated that just 1 hour of Florida red tide toxin exposure caused the greatest effect in the mean number of reported symptoms, but that these symptoms lasted for at least 5 days after this one hour of exposure. Of interest, there was no evidence of any delayed onset of increased reported symptoms within days of the 1 hour beach exposure.

However, peak flow measurements worsened even after the 1 hour of exposure measurement, with the worst peak flow levels at day 1 of follow-up as measured by the handheld peak flow meter; furthermore, the peak flow measurements did not return to the post exposure level even after the 5 days of follow-up. Thus, although asthma is a diagnosis based on the combination of reported symptoms and more objective measures (such as peak flow), there may be a disconnect between what the asthmatic experiences in terms of symptoms and their physiologic state in terms of pulmonary function (Stemple and Fuhlbrigge 2008). This apparent delay in and prolongation of both symptoms and pulmonary

function impact after only 1 hour of beach exposure to Florida red tide toxins is important asthma treatment and management information for the healthcare providers and asthmatics living in coastal areas impacted by this harmful algal bloom and its aerosolized toxins.

We also found that the more controlled asthmatics reported increased mean symptom levels right after their 1 hour of beach exposure, they returned to normal after 5 days; the more severe asthmatics reported higher mean symptom level after their 1 hour of beach exposure and continued to experience elevated symptoms for up to 5 days of follow-up. Although the mean post-exposure peak flow measurements were similar between the more severe and more controlled asthmatics, by day one of follow-up, the mean peak flow measurements of the more severe asthmatics were more severely impacted than the more controlled asthmatics; and there was no return to the post-exposure mean peak flow level even after 5 days of follow-up for either group. Of note, the bronchoconstriction response is more severe in the asthmatic subgroup of the brevetoxin sheep model which has previously inflamed lungs due to recently induced asthma exacerbation compared to normal or even asthmatic sheep without prior asthma exacerbation (Abraham et al. 2005a, 2005b). It is also interesting to consider that the more severe asthmatics who had used asthma medications (such as the $beta_2$ agonist, albuterol) which have been shown to both prevent and treat the bronchoconstriction associated with exposure to Florida red tide might actually have experienced an even greater health impact from their brevetoxin exposure if they had not taken these medications within 12 hours of their beach exposure (Abraham et al. 2005a, 2005b). These human and animal data identify the more severe, less well controlled asthmatics as a particularly vulnerable group to the impacts of the aerosolized Florida red tide toxins.

Asthmatics with an inland residence reported more mean symptoms and experienced greater decline in their peak flow measurements compared to coastal residents over the 5 days after 1 hour of beach exposure to Florida red tide aerosols. This may be due to their relative lack of environmental exposure to Florida aerosols prior to their study beach exposure; our prior work has demonstrated the transport of Florida red tide aerosols as much as 1.6 km inland (Kirkpatrick et al. 2010). Overall, this information has important health implications for asthmatic tourists, as well as inland residents with asthma, of coastal areas impacted by Florida red tide blooms and their aerosolized toxins.

4.1. Limitations

There were a number of limitations to this study. Although we added self-administered peak flow measurement as a more objective measure of pulmonary function to the self report of symptoms for the 5 day follow-up study, these peak flow meters are relatively inaccurate and the study population was relatively small. We did not measure the peak flow using these meters prior to the 1 hour of exposure (this measurement will be added in future studies). Nevertheless, the peak flow as measured by the NIOSH-approved spirometry before and after the 1 hour of exposure at the beach in which we compared each individual participant to themselves clearly demonstrated the significant impact on peak flow (and other pulmonary measures) from the brevetoxin aerosols of Florida red tides (Table 3) (Fleming et al. 2005,2007,2009). Finally, since brevetoxins have been measured inland, it is possible that the study participants were exposed after the 1 hour beach study exposure to the Florida red tide toxins due to occupation and other activities, not just through coastal residence location (Kirkpatrick et al. 2010). And we do not yet know what the impacts of repeated aerosolized brevetoxin exposures are on asthmatics over time.

5.0. Conclusions

This study provides unique and important information for people with asthma and their healthcare providers living near coastal areas with regular Florida red tide events. In conjunction with the other acute 1 hour beach exposure studies performed by these investigators, this study suggested that even 1 hour of aerosol exposure during an active red tide for asthmatics may result in increased reported symptoms and pulmonary function depression that can last for up to or beyond 5 days. These effects were most pronounced for the more severe asthmatics and those living inland; these effects might also be severe for those without prior Florida red tide exposure such as asthmatic tourists. The delayed onset by 24 hours of augmented pulmonary function depression from the 1 hour beach exposure is important information in terms of the clinical care and treatment of asthmatics with Florida red tide toxin exposures, particularly since it was preceded by, but not concomitant with, an increase in reported symptoms. Finally, given that we have also demonstrated increased admissions to the emergency room for pneumonia, bronchitis, asthma and upper airway complaints during active Florida red tides (Kirkpatrick et al., 2006), it would seem that asthmatics should avoid beach areas during onshore winds with active Florida red tides, as well as monitor themselves carefully for asthma exacerbations by both peak flow and symptom evaluation over a considerable time period following any exposure to aerosolized Florida red tide toxins.

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Abbreviations

CDC	Centers for Disease Control and Prevention
ELISA	Enzyme linked immunosorbent assay
HAB	Harmful algal bloom
K. brevis	*Karenia brevis*
L	Liter
LCMS	Liquid chromatography mass spectroscopy
LOD	Limit of detection
mL	Milliliters
NIEHS	National Institute of Environmental Health Sciences
NIOSH	National Institute of Occupational Safety and Health
NSP	Neurotoxic shellfish poisoning
PEF	Peak expiratory flow

Table 1
Demographics of 52 physician-diagnosed asthmatic study participants

Variable	N (%)
N	52
Age ± Standard Deviation (Range in years)	41.1+/-19.6 (15-71 years)
Female (%)	33 (64%)
White (%)	50 (95%)
Hispanic (%)	0
Years with diagnosis ±SD	22.9+/-16.9
History of using asthma medications at time of baseline survey (%)[a]	44 (85%)
Positive History of Florida Red Tide Symptoms with exposure (%)	48 (90%)
Current smoker (%)	3 (6%)
Hospitalized ≥1 in past year from Respiratory Causes (%)	8 (15.4%)
Used medications [a] **within 12 hours before study exposure (%)**[b]	22 (42%)
Living > 1.6 km from Coast (%)[b]	33 (64%)

[a] Asthma medications predominantly beta$_2$ agonists;

[b] at time of exposure studies

Table 2
Analysis of Respiratory Symptoms and Peak Flow measured by Peak Flow Meter by Study Day

Table 2. Report of Symptoms and Peak Flow: Entire Subpopulation							
Study Day	**N**	**Non-exposure**		**Exposure**			
		Mean +/- Standard Deviation	**Range**	**Mean +/- Standard Deviation**	**Range**	**Difference from Pre-beach Exposure (p value)**	**Difference from Post-beach Exposure (p value)**
Number of Symptoms							
Pre-beach exposure	51	1.37+/-1.71	0-6.00	1.33+/-1.54	0-6.00	NS	N/A
1 hour Post-beach Exposure	52	1.28+/-1.48	0-6.00	3.08+/-2.18	0-8.00	N/A	*
Follow-up Day 1	52	1.19+/-1.24	0-4.00	2.02+/-2.01	0-7.00	NS	**<0.0001**
Follow-up Day 2	52	1.15+/-1.36	0-4.00	1.64+/-1.97	0-8.00	NS	**<0.0001**
Follow-up Day 3	52	1.09+/-1.56	0-6.00	1.53+/-1.85	0-8.00	NS	**<0.0001**
Follow-up Day 4	52	0.94+/-1.31	0-6.00	1.35+/-1.75	0-8.00	NS	**<0.0001**
Follow-up Day 5	52	1.02+/-1.43	0-6.00	1.28+/-1.67	0-8.00	NS	**<0.0001**

Table 2. Report of Symptoms and Peak Flow: Entire Subpopulation							
Study Day	**N**	**Non-exposure**		**Exposure**			
		Mean +/- Standard Deviation	**Range**	**Mean +/- Standard Deviation**	**Range**	**Difference from Pre-beach Exposure (p value)**	**Difference from Post-beach Exposure (p value)**
Peak Flow (L/second) measured by peak flow meter							
1 hour Post-beach Exposure	52	0.422+/-0.118	0.230-0.750	0.424+/-0.127	0.169-0.800	N/A**	*
Follow-up Day 1	52	0.409+/-0.118	0.200-0.700	0.404+/-0.119	0.144-0.750	N/A**	**<0.0001**
Follow-up Day 2	52	0.415+/-0.125	0.225-0.770	0.407+/-0.135	0.168-0.871	N/A**	**<0.0001**
Follow-up Day 3	52	0.411+/-0.125	0.200+/-0.740	0.397+/-0.128	0.184-0.800	N/A**	**<0.0001**
Follow-up Day 4	52	0.413+/-0.126	0.210-0.800	0.402+/-0.130	0.154-0.800	N/A**	**<0.0001**
Follow-up Day 5	52	0.415+/-0.132	0.230-0.850	0.401+/-0.130	0.118-0.800	N/A**	**<0.0001**

[3] **N/A**= not applicable; **NS**= not statistically significant;

* = Statistically significant model for both Day and Exposure (p<0.0001);

** =Pre-beach exposure peak flow not available (only through spirometry)

Table 3

Peak expiratory flow (PEF) measured by Spirometry before and after 1 hour beach exposure for follow-up subcohort (N=52)

		Unexposed			Exposed		
Spirometry Value	**N**	**Pre-Beach Mean [L/sec] ± SD**	**Mean Difference [ml/sec] ± SD after beach**	**Significance (p value)****	**Pre-Beach Mean [L/sec] ± SD**	**Mean difference [ml/sec] ± SD after beach**	**Significance (p value)***
Entire Subpopulation	52	7.535±1.964	126.7±582.5	0.12	7.774±2.039	255.4±385.2	**<0.0001**
Use of Asthma Medications							
More Severe Asthma (Rx+)	22	7.643±1.940	979.2±740.4	0.52	7.477±2.036	268.6±504.1	**0.02**
More Controlled Asthma (Rx-)	29	7.557±1.959	147.8±423.1	0.08	7.969±2.081	240.0±280.1	**<0.0001**
Residence							
Coastal (Close)	17	7.912±2.303	312.3±508.2	**0.02**	7.960±2.055	265.9±359.3	**0.008**
Inland (Far)	35	7.352±1.785	365.7±601.6	0.72	7.684±2.056	250.2±402.2	**0.0008**

* paired ttest comparing each individual's post exposure to their pre-exposure PEF