Exposure and Effect Assessment of Aerosolized Red Tide Toxins (Brevetoxins) and Asthma

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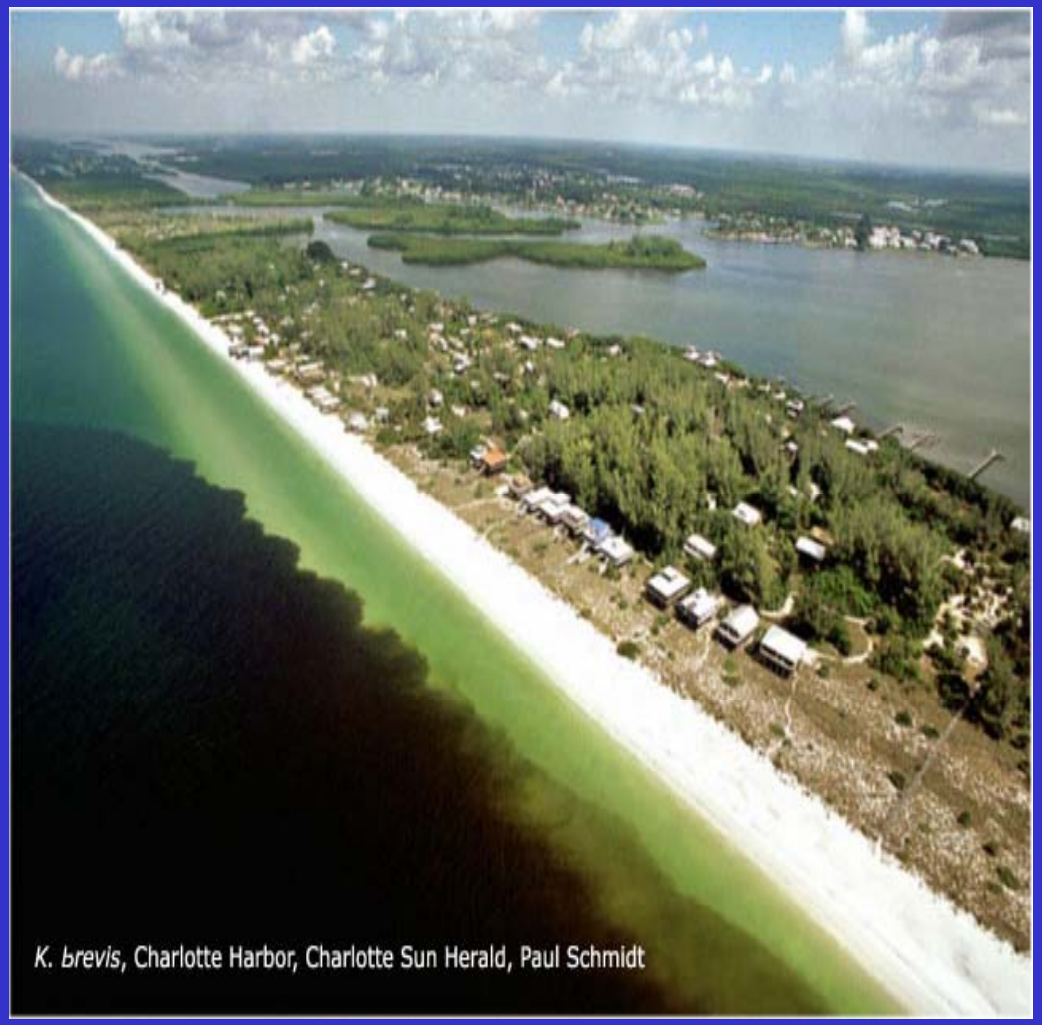
Florida Red Tide Research: Background



Florida Red Tide

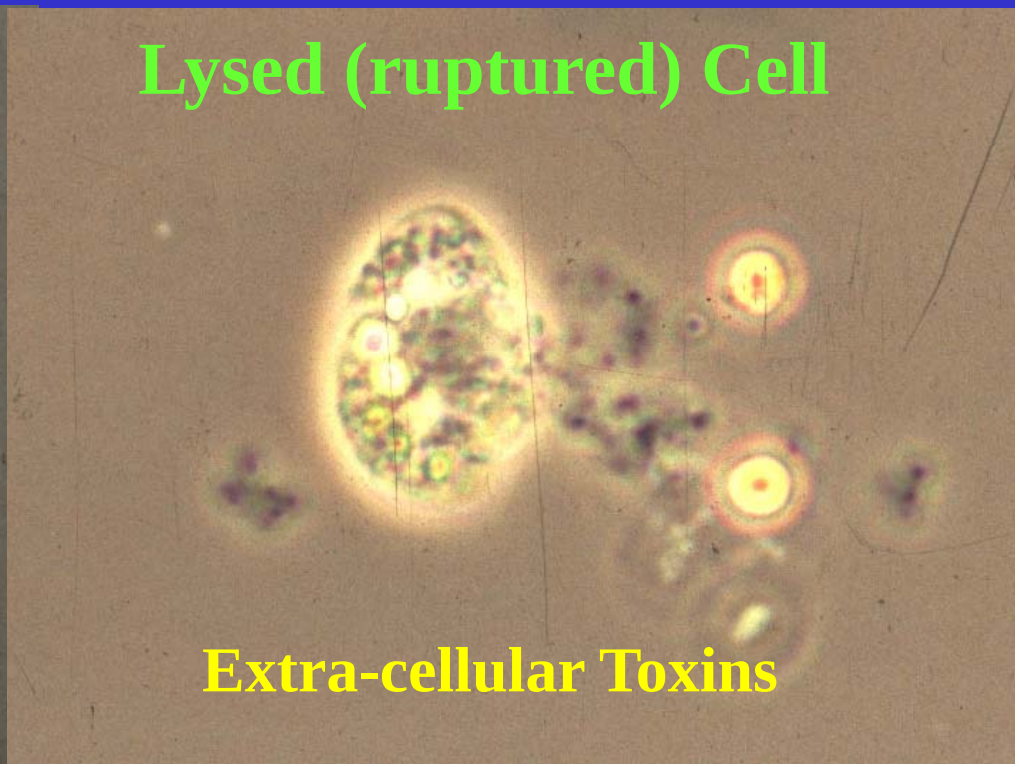
Karenia brevis

(formerly *Gymnodinium breve, Ptychodiscus brevis*)

Whole (live) Cell

Intra-cellular Toxins

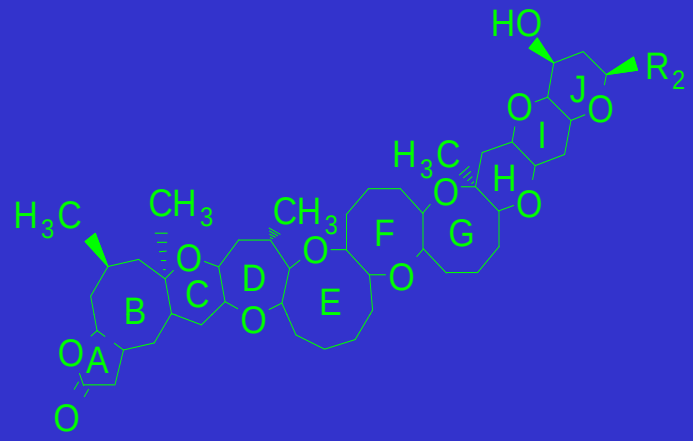
Lysed (ruptured) Cell



Extra-cellular Toxins

Brevetoxins

PbTx Type-2



PbTx Type-1

	R1	R2
PbTx-2:	H	$CH_2C(=CH_2)CHO$
PbTx-3:	H	$CH_2C(=CH_2)CH_2OH$
PbTx-5:	CH_3CO	$CH_2C(=CH_2)CHO$
PbTx-6:	H	$CH_2C(=CH_2)CHO$ 27,28 peroxide
PbTx-8:	H	$CH_2C(=CH_2)COCH_2Cl$
PbTx-9:	H	$CH_2CH(CH_3)CH_2OH$

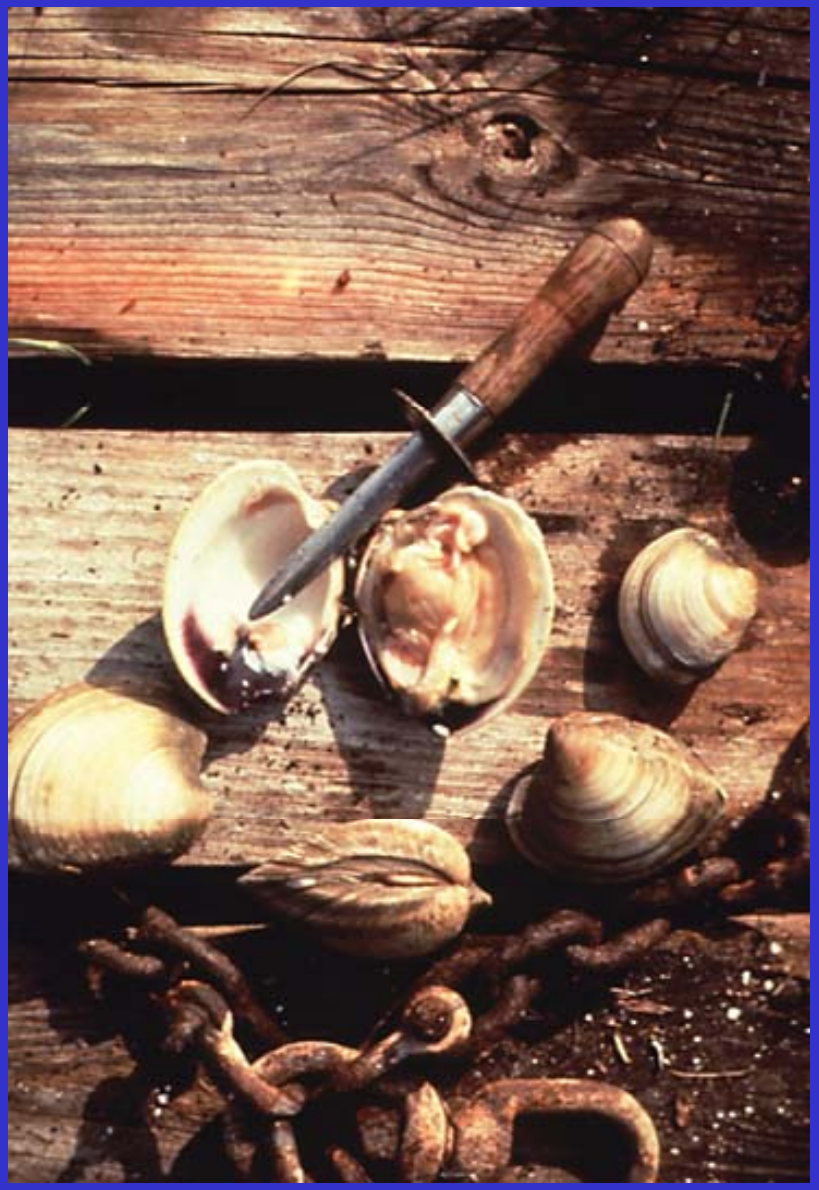
	R1	R2
PbTx-1:	H	$CH_2CH(CH=CH_2)CHO$
PbTx-7:	H	$CH_2CH(CH=CH_2)CH_2OH$
PbTx-10:	H	$CH_2CH(CH_3)CH_2OH$

Red Tides & Fish Kills

Endangered Florida Manatee

Florida Red Tide (Brevetoxins) Environmental Impact

Neurotoxic Shellfish Poisoning




Welcome to SIESTA BEACH
STAND NO. 7
WATER TEMP: 88 °F
29 °C
TIDES: HIGH 5:18 PM
LOW 11:32 AM
COMMENTS: RED TIDE IS STILL IN OUR AREA, SORRY
THE GOOD NEW IS YOU DON'T HAVE TO WORRY ABOUT THE SHARKS
GUARD:
FLAGS
SURF & BEACH CONDITIONS
GOOD
CAUTION
DANGER
HAZARDOUS MARINE LIFE

Aerosolized Florida Red Tide (Brevetoxins) & Recreational Exposure

Aerosolized Florida Red Tide (Brevetoxins) & Occupational Exposure

Prior Research Results

- **Non-exposure**
  - No significant changes for symptoms & spirometry
    - Asthmatics & Healthy Occupational Populations
- **1 Hour Acute Exposure**
  - Significant upper & lower airway symptoms in Both
  - Significant changes in air flow as measured by spirometry in Asthmatics
- **Acute/Chronic Red Tide Toxin Exposure**
  - Increased Emergency Room Respiratory Admission Rates
    - Exposure > Non Exposure
    - Coastal > Inland

Florida Red Tide Research: Methods


Whitfield Estates
MANATEE
Matoaka
789
Sarasota/Bradenton International Airport
Parmalee
HARDEE
Myakka City
Sarasota
780
B Vista St
Miakka
Edgeville
Sarasota Heights
Tatum Ridge
Lido Beach
Bee Ridge
Hidden River
Grey Gully Rd
70
758
Sandy
Pine Level
Sunrise
Honore
Beneva Rd
White Beach
Venice
72
Siesta Key
FLORIDA
Osprey
Shiney Town
SARASOTA
681
Nokomis Beach
Laurel
North Jetty
Sidell
761
Venice
Eastgate
75
Venice Gardens
Warm Mineral Springs
South Venice
US Hwy 41
Venice Groves
41
North Port
Woodmere
Murdock
Tarpon Point
Manasota
777
776
CHARLOTTE
Englewood
El Jobean
Charlotte Harbor
Port Charlotte
Charlotte Beach
New Point Comfort
17
Grove City
Punta Gorda
Punta Gorda Beach
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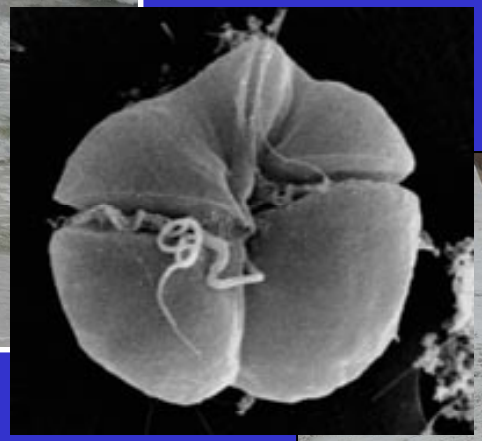
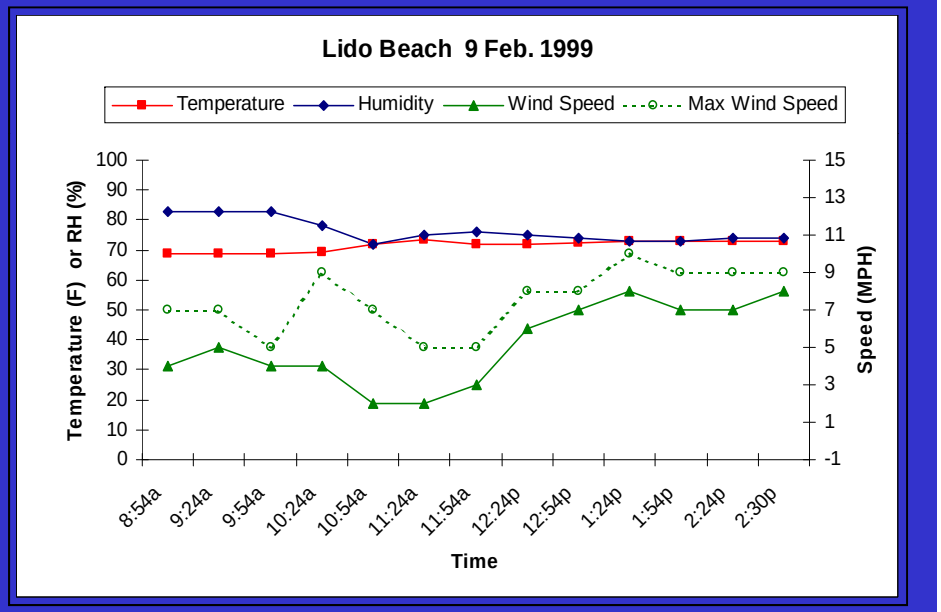
Florida Red Tide (Brevetoxin) & Organism & Toxin Monitoring



Florida Red Tide (Brevetoxin) Air Monitoring & Environmental Conditions

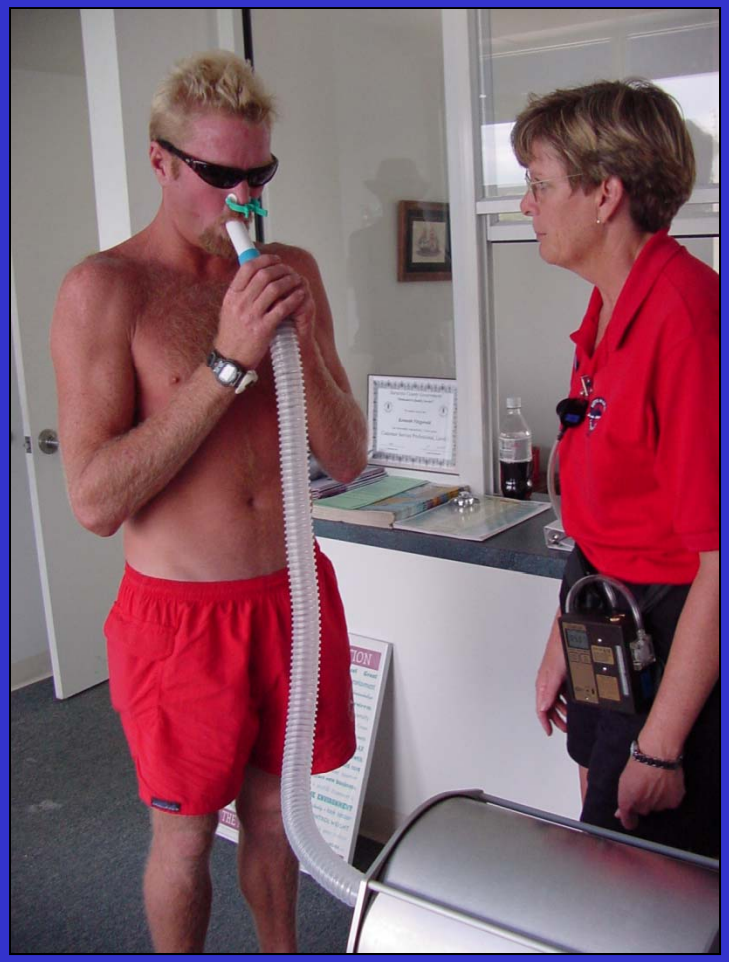


Florida Red Tide (Brevetoxin) & Personal Monitoring

Brevetoxin Extraction from Air Filters

Florida Red Tide (Brevetoxins) & Baseline and Pre/Post Exposure Interviews

Florida Red Tide (Brevetoxins) & Baseline & Pre/Post Exposure Spirometry



Symptoms

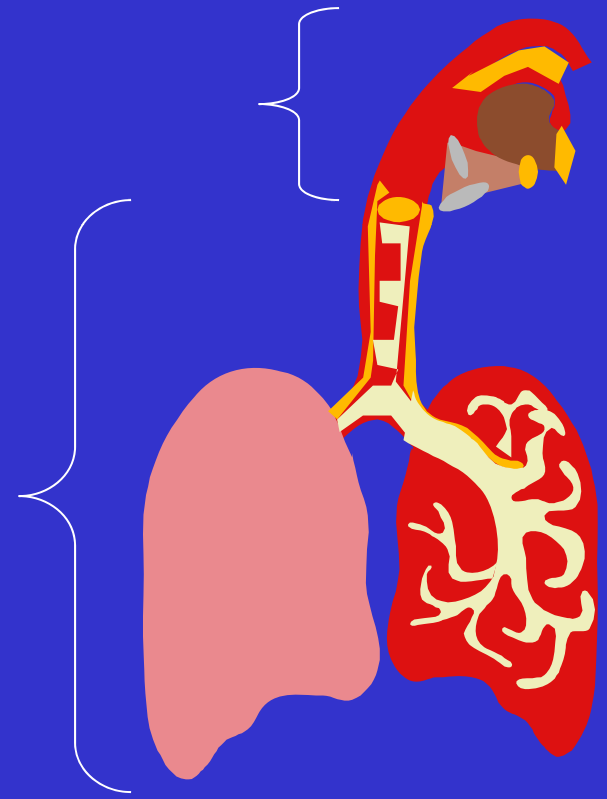
- ✓ Throat irritation
- ✓ Nasal congestion
- ✓ Eye irritation

Upper Airway

- ✓ Cough
- ✓ Wheezing
- ✓ Shortness of Breath
- ✓ Chest tightness
- ✓ Headache

Lower Airway

- ✓ Itchy skin
- ✓ Diarrhea



Florida Red Tide Research: Results

- **Exposure vs Non Exposure: 1 hour**
- **Water & Air Brevetoxin Monitoring**
  - Water: Cells & Toxin
    - Cell Count; ELISA & LCMS
  - **Air: Toxin**
    - Personal sampler by ELISA
    - Hourly Environmental Sampler by ELISA & LCMS
- **Human Subject Pre/Post Exposure**
  - Symptoms: Yes/No, Symptom Score
  - Pulmonary Function Tests
    - FEV_1, FVC, FEF_{25-75}, PEF

Brevetoxin Air Monitoring Results

Environmental Measure	Mean +/- SD (ng/m^3)	Range (ng/m^3)	Median (ng/m^3)
Personal sample ELISA	73.3±78.9	0 - 366.2	45.7
Ambient hourly sample ELISA	161.5±96.3	0 - 375.4	141.0
Ambient hourly sample LCMS	**53.4±32.9**	**0 -117.5**	**56.8**

Asthma Study Population

Variable	Asthmatics [N (%)]
N	87
Age ± Standard Deviation (Range in years)	44.9 ±19.2 (12.0-79.0)
Female (%)	52 (59.8)
White (%)	85 (97.7)
Hispanic (%)	1 (1.2)
Years with diagnosis ±SD	16.5 ± 25.2
Using asthma medications currently (%)[a]	68 (88.3)
Positive History Florida Red Tide Symptoms w/ exposure (%)	77 (90.6)
Current smoker (%)	8 (12.3)
Hospitalized ≥1 in past year from Respiratory Causes (%)	11 (13.1)
Used medications[a] within 12 hours before study exposure (%)[b]	30 (34.5)
Living > 1 mile from Coast (%)[b]	55 (63.2)

[a]Asthma medications predominantly beta$_2$ agonists; [b]at time of ambient LCMS brevetoxin measurement

Symptoms Yes/No vs Ambient Monitoring (LCMS)

Symptoms	Overall (N=87)		Ambient LCMS Brevetoxin Level				Ambient LCMS Brevetoxin Level			
			Below Median		Above Median		Lowest 25th Percentile		Highest 25th Percentile	
	Pre/Post (N)	p value[a]	Pre/Post (N)	p value[a]	Pre/Post (N)	p value[a]	Pre/Post (N)	p value[a]	Pre/Post (N)	p value[a]
Cough	41	0.0001	11	0.13	**30**	**0.0001**	5	0.26	**15**	**0.0001**
Wheezing	17	0.01	2	0.26	**15**	**0.0001**	1	0.56	**6**	**0.01**
Throat irritation	34	0.0001	12	0.37	**22**	**0.0001**	4	0.41	**13**	**0.0003**
Shortness of Breath	21	0.02	5	0.56	**16**	**0.0003**	3	1.00	**9**	**0.01**
Chest tightness	28	0.0001	12	0.02	**16**	**0.0003**	6	0.16	**7**	**0.03**
Nasal irritation	28	0.02	11	0.84	**17**	**0.0002**	8	0.80	**8**	**0.02**
Eye	11	0.23	3	0.71	8	0.058	3	0.32	3	0.93
Headache	16	0.10	8	0.59	8	0.058	3	1.00	3	0.66
Itchy Skin	7	0.37	2	0.41	5	**0.03**	1	0.56	2	0.16
Diarrhea	0	----	0	----	0	----	0	---	0	----
Other	6	0.16	3	0.66	3	0.08	3	0.32	2	----

Pre/Post (N) = persons who came to beach with no symptom and left with that symptom; [a]significance testing by McNemar's test

Symptoms Yes/No vs Ambient Monitoring (LCMS)

Significant Changes All Sx:

- No Asthma Rx 12 hours within Exposure
- Residence > 1 mile from Coast

Significant Changes Cough & Chest Sx only:

- Asthma Rx 12 hours within Exposure
- Residence ≤ 1 mile from Coast

Symptom Score vs Ambient Monitoring (LCMS)

	Below Median Brevetoxin Level		Above Median Brevetoxin Level	
	Pre/post Mean Difference in the Symptom Score (± SD)	**p value[a]**	**Pre/post Mean Difference in the Symptom Score (± SD)**	**p value[a]**
All participants	0.32±3.51	0.57	**4.14±3.46**	**0.0001**
Used asthma medications within 12 hours before study exposure				
Medication	0.67±3.10	0.34	**5.11±5.06**	**0.02**
No Medication	1.35±3.68	0.11	**3.89±2.97**	**0.0001**
Distance of Residence from Coast				
Close	0.06±4.12	0.95	**2.89±2.32**	**0.006**
Far	0.64±3.03	0.33	**4.44±3.71**	**0.0001**

"Medication" = used asthma medication within 12 hours of beach exposure; "No medication"= did not use asthma medication within 12 hours of beach exposure; Close" = ≤ 1 mile from coast; "Far" = > 1 mile from Coast; [a]significance testing by paired ttest (significant values <0.05 are bolded)

Pulmonary Function vs Ambient Monitoring (LCMS)

PFT	Exposure Level	PFT Mean Difference (ml) +/- SD	p value[a]
FEV1	Above Median	27.3±123.0	0.62
	Below Median	39.8±113.8	
FVC	Above Median	10.0±128.5	0.10
	Below Median	61.4±159.4	
FEF 25 75	Above Median	-22.3±333.97	0.32
	Below Median	40.2±234.9	
PEF	Above Median	224.3±500.1	0.95
	Below Median	217.9±560.2	

[a]*significance testing by ttest of difference in mean differences*

Conclusions

1 hour brevetoxin exposure > 57 ng/m^3

- Asthmatics statistically significant increases self-reported respiratory symptoms & total symptom scores
  - All asthmatics
  - No Rx < Rx
  - Inland > Closer
- No changes in pulmonary function test
- Low aerosolized brevetoxin exposures associated with biologic response in humans

Limitations

- Self-reported Sx data
  - Consistent with asthma literature
- Disconnect PFT with exposure
  - Prior studies demonstrate exposure effect in asthmatics
  - PFT relatively insensitive at very low exposures

Inter-disciplinary Collaborators

- CDC
- Florida Department of Health
- Florida Department of Environmental Protection
- Florida Marine Research Institute
- Harbor Branch
- Lovelace Institute
- Mote Marine Lab
- NIEHS
- S. Florida Poison Information
- Univ Miami School of Medicine/RSMAS
- Univ North Carolina (Wilmington)

Aerosolized Florida Red Tide Toxins

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[No other relationships to disclose]