Neurotoxicology of Red Tide Poisoning

Received: April 29, 2016; Accepted: April 30, 2016; Published: May 08, 2016

Editorial

Red Tide poisoning is a result of toxins released from marine dinoflagellates (various algae) and received its name from the discolored (reddish) water created by an algal bloom. It appears this event has occurred for centuries in many locations even before the occurrence of pollution, agricultural run-off and current observations of global warming. There were reports of the Red Tide in Florida during the 1800’s [1, 2]. However, historical reports indicate that the Red Tide occurred throughout history with an observation noted as early as 1528 in the Gulf of Mexico; although, the first “verifiable” event was in 1648 [2, 3]. The Red Tide occurs throughout tropical waters of the world [4]. In the United States the predominant region is Florida, mostly in the Gulf of Mexico; but events have been noted in the Atlantic and Pacific Oceans. Periodically, there have also been occurrences off the Texas coast [2]. Other locations of notable interest where events occur include Scotland and the South Pacific (e.g. Australia), indicating harmful algal events can occur in northern locations and are likely experiencing an expanding geography due to global warming. There is an increasing frequency of Red Tide phenomena throughout the world with temperature and pollution being indicated as the contributing factors [2].

The most common dinoflagellate responsible for the Red Tide is Karenia brevis; although, there are a number of other species of algae (e.g. Karenia papillorionacea, Chattonella species, Fibrocapsa japonica) having been reported to produce toxins associated with this event [4-6]. These toxins generated by the marine dinoflagellates are brevetoxins (PbTx’s), with two primary structural forms (backbone A and B) [4]. Fundamentally, these toxins result in three different types of events (a) fish kills (harm to wildlife), (b) toxicity from ingestion of an organism accumulating the toxin and (c) inhalation toxicity [2, 4]. For man, Red Tide events are due to harmful algal blooms (HAB) that result from high numbers of a species of algae producing a toxin that usually accumulates in another organism (filter feeders), which is frequently shellfish. It has been estimated that 60,000 human toxicity cases occur a year worldwide with a mortality rate of about 0.15% for PbTx [7]. Generally, toxins from these dinoflagellates functions as either neurotoxins or hemolytic agents [6, 8]. There have been reports of this alga also producing immune-toxicity, cardiotoxic and anti-cholinesterase phosphorus-containing agents [8, 9]. Brevetoxins have been implicated in harmful effects to various marine organisms (e.g. fish, dolphins, manatees) as well as wide-spread inhalation toxicity to humans near the seashore [10-12].

Brevetoxins are tasteless, lipid soluble, and both heat and acid stable that cause (depolarization) opening of sodium voltage gated ion channels. These toxins have a molecular weight of about 900 [8]. Due to their lipid solubility, brevetoxins can cross the blood-brain barrier, are easily absorbed into the body, and exhibit wide spread distribution with primary metabolism in the liver. These characteristics suggest a one-compartment model. Excretion occurs through bile and to minor extent urine [4]. Disruption of sodium channels causes an inward flow of sodium ions and is the primary cause for neurotoxic shellfish poisoning (NSP). Disruption of sodium channels cause dysfunction of the respiratory and cardiac system due to spontaneous firing (uncontrolled sodium influx) [8]. There may also be inhibition of calcium related pathways in neurons resulting in disruption of calcium homeostasis [13]. For respiratory effects, there appears to be involvement of mast cells (degranulation) which can result in the release of histamine causing bronchoconstriction. These findings are supported by animal studies (e.g. sheep, guinea pigs) where increased airway resistance has been observed yet could be blocked by cromolyn and a histamine H1 antagonist [6, 8]. This, in part, explains respiratory symptoms associated with exposure to this alga. As for many toxins, brevetoxin metabolites...
may have greater potency than the parent product with likely biotransformation occurring through the P450 system [8]. Brevetoxins are difficult to detect in the laboratory and cannot be removed from food products.

Over 10 different brevetoxins have been isolated along with an antagonist, brevenal [14, 15]. Brevenal may be the first antagonist produced by an organism directed toward its own toxin. It has been reported that the concentration of brevetoxin in water during a Red Tide event is 5-10 µg/L with particles of toxin being 6.7 µm (mass median aerodynamic diameter) [16]. Respiratory symptoms have been reported for airborne brevetoxins in the range of 3-4 ng/m³; although, much higher concentrations have been observed (21-39 mg/m³) [15-17]. However, even when there was no Red Tide event occurring, airborne levels in the range of 1 to 49 ng/m³ have been recorded, with some reporting respiratory symptoms [15]. Since K. brevis is an unarmored dinoflagellate wave action can fracture the organism releasing toxins. This results in sea spray, droplets and salt particles containing toxins, especially during blooms [16, 17].

Human exposure to brevetoxin occurs either through inhalation or ingestion of contaminated shellfish (molluscs) which results in NSF [1, 4, 17]. Characteristics of NSF include gastrointestinal issues, diarrhea, nausea, abdominal distress loss of motor control, ataxia, paresthesia, vertigo, and muscle pain [4, 6, 8]. Symptoms occur in about 3 h; although a range of 15 min to 18 h have been reported [4]. In severe cases, seizures, convulsions, tachycardia and partial paralysis have been observed [4]. In general, symptoms are usually mild and either not reported or misdiagnosed. A NSF event can last a few days from consumption of contaminated sources (e.g. clams, mussels, coquinas or other types of filter feeders) [8]. In most cases multiple symptoms are reported.

The first report of an association with respiratory disease and the Red Tide was made in 1917. However, there are other algae that can cause similar symptoms (Trichodesmium), but are generally not observed in the Gulf of Mexico [2]. Commonly inhalation can result in rapid occurrence of chest tightening, bronchoconstriction, congestion, eye and respiratory irritation, but usually wains when leaving the seashore area [8, 18].

There is a report of respiratory effects occurring from the Red Tide by personnel conducting dredging of a marine channel in Florida [19]. Around this time period a fish kill was observed along with a high level of K. brevis (≥ 1,000,000 cells/L). A study by Mendoza et al. [20] reported brevetoxin exists in sediment and these levels may increase after blooms occur. From this information, it is possible that sediment and sand could be a potential source of brevetoxins with exposure occurring from contact along with aerosolization of particles. This investigation supports another occupational concern involving Lifeguards where a decreased respiratory function (upper airway) was observed in those exposed to aerosolized brevetoxins [21]. In a study of asthmatics, decreased airway function was observed after exposure to K. brevis [22]. A case study [23] indicated those with chronic pulmonary problems may be at an increased risk from exposure to brevetoxins resulting in significant changes in spirometry. Such reports indicate these toxins, and possibly others from HAB, may have stronger immunological consequences than indicated in the literature. These studies together indicate that recreational beachgoers may experience respiratory problems when exposed to aerosols containing brevetoxin or K. brevis [8]. During Red Tide events there has been a report of increased rates of pneumonia among coastal residents [24]. Reports of this nature suggest Red Tide events, and toxins associated with them, may have a much greater health effect on local populations than previously considered. This makes brevetoxin not only an important issue related to food poisoning but an environmental and occupational hazard as well.
References

1 Fleming LE, Kirkpatrick B, Backer LC, Walsh CJ, Nierenberg K, et al. (2011) Review of Florida Red Tide and Human Health Effects. Harmful Algae 10: 224-233.

2 Magana HA, Contreras C, Villareal TA (2003) A historical assessment of Karenia brevis in the western Gulf of Mexico. Harmful Algae 2: 163-171.

3 Baden DG, Bourdelais AJ, Jacocks H, Michelliza S, Naar J (2005) Natural and derivative brevetoxins: historical background, multiplicity and effects. Environ Health Perspect 113: 621-625.

4 Watkins SM, Reich A, Fleming LE, Hammond R (2008) Neurotoxic Shellfish Poisoning. Mar Drugs 6: 431-455.

5 Fowler N, Tomas C, Baden D, Campbell L, Bourdelais A (2015) Natural and derivative brevetoxins: historical background, multiplicity and effects. Environ Health Perspect 113: 621-625.

6 Wang DZ (2008) Neurotoxins from marine dinoflagellates: a brief review. Mar Drugs 6: 349-371.

7 Bibak M, Hosseini SA (2013) Investigation Red Tide effects on human health. World Journal of Fish and Marine Sciences 5: 96-99.

8 Kirkpatrick B, Fleming LE, Squicciarini D, Backer LC, Clark R, et al. (2004) Literature Review of Florida Red Tide: Implications for Human Health Effects. Harmful Algae 3: 99-115.

9 Turner AD, Higgins C, Davidson K, Veszelovszki A, Payne D, et al. (2015) Potential threats posed by new or emerging marine biotoxins in UK waters and examination of detection methodology used in their control: brevetoxins. Mar Drugs 13: 1224-1254.

10 Walsh CJ, Butawan M, Yordy J, Ball R, Fiewel judging L, et al. (2015) Sublethal red tide toxin exposure in free-ranging manatees (Trichechus manatus) affects the immune system through reduced lymphocyte proliferation responses, inflammation, and oxidative stress. Aquat Toxicol 161: 73-84.

11 Pierce RH, Henry MS (2008) Harmful algal toxins of the Florida red tide (Karenia brevis): natural chemical stressors in South Florida coastal ecosystems. Ecotoxicology 17: 623-631.

12 Twiner MJ, Fiewel judging L, Fire SE, Bowen-Stevens SR, Gaydos JK, et al. (2012) Comparative analysis of three brevetoxin-associated bottlenose dolphin (Tursiops truncatus) mortality events in the Florida Panhandle region (USA). PLoS One 7: e42974.

13 Berman FW, Murray TF (2000) Brevetoxin-induced autocrine excitotoxicity is associated with manifold routes of Ca²⁺ influx. J Neurochem 74: 1443-1451.

14 Hoagland P, Jin D, Beet A, Kirkpatrick B, Reich A, et al. (2014) The human health effects of Florida red tide (FRT) blooms: an expanded analysis. Environ Int 68: 144-153.

15 Bourdelais AJ, Campbell S, Jacocks H, Naar J, Wright JL, et al. (2004) Brevenal is a natural inhibitor of brevetoxin action in sodium channel receptor binding assays. Cell Mol Neurobiol 24: 553-563.

16 Cheng YS, Zhou Y, Pierce RH, Henry M, Baden DG (2010) Characterization of Florida red tide aerosol and the temporal profile of aerosol concentration. Toxicon 55: 922-929.

17 Cheng YS, McDonald JD, Kracko D, Irvin CM, Zhou Y, et al. (2005) Concentration and particle size of airborne toxic algae (brevetoxin) derived from ocean red tide events. Environ Sci Technol 39: 3443-3449.

18 Benson JM, Hahn FF, Tibbetts BM, Bowen LE, March TF, et al. (2004) Florida Red Tide: Inhalation Toxicity of Karenia brevis Extract in Rats. Harmful Algae 10: 502-504.

19 Centers for Disease Control and Prevention (CDC) (2008) Illness associated with red tide--Nassau County, Florida, 2007. MMWR Morb Mortal Wkly Rep 57: 717-720.

20 Mendoza WG, Mead RN, Brand LE, Shea D (2008) Determination of brevetoxin in recent marine sediments. Chemosphere 73: 1373-1377.

21 Backer LC, Kirkpatrick B, Fleming LE, Cheng YS, Pierce R, et al. (2005) Occupational exposure to aerosolized brevetoxins during Florida red tide events: effects on a healthy worker population. Environ Health Perspect 113: 644-649.

22 Fleming LE, Kirkpatrick B, Backer LC, Bean JA, Wanner A, et al. (2007) Aerosolized red-tide toxins (brevetoxins) and asthma. Chest 131: 187-194.

23 Steensma DP (2007) Exacerbation of asthma by Florida "red tide" during an ocean sailing trip. Mayo Clin Proc 82: 1128-1130.

24 Kirkpatrick B, Fleming LE, Backer LC, Bean JA, Tamer R, et al. (2006) Environmental exposures to Florida red tides: Effects on emergency room respiratory diagnoses admissions. Harmful Algae 5: 526-533.