Human Exposure to Cyanotoxins and their effects on Health

"At this time, available data are insufficient to develop quantitative recreational values for cyanobacterial cell density related to inflammatory health endpoints" [1]

This literature review is to analyze articles on recreational exposure to human health from Cyanotoxins. Currently the Environmental Protection Agency (EPA) and the Utah Division of Water Quality (UDWQ) are setting water quality standards for algae. The EPA recently released a draft "Human Health Recreational Ambient Water Quality Criteria or Swimming Advisories for Microcystins and Cylindrospermopsin" on recommended concentration for Microcystin and Cylindrospermopsin. In the draft the EPA suggest states adopt recreational guidelines of 4 µg/L and 8µg/L, for Microcystin and Cylindrospermopsin, respectively. The guidelines are based on exposure to children at the 90th percentile. The EPA goes on to say "At this time, available data are insufficient to develop quantitative recreational values for cyanobacterial cell density related to inflammatory health endpoints. The reported epidemiological relationships in the literature are not consistent for specific health outcomes or those health outcomes associated with specific cyanobacterial cell densities."[1]

Figure 1: Great Salt Lake

A vast amount of uncertainty exists when it comes to cyanobacteria and Cyanotoxins. Some types of cyanobacteria produce certain types of Cyanotoxins, however not all cyanobacteria produce toxins.

When ingested in large quantities over duration, Cyanotoxins can be lethal to humans. Nevertheless to date there have only been a few case where Cyanotoxins might have been fatal. One of the most talked about cases is where "an outbreak of acute liver failure occurred at a dialysis center in Caruaru, Brazil"[2]. The dialysis center had used contaminated water for dialysis, and only after analyzing the victim's symptoms and pathology it was concluded that the major contributing factor of death of the dialysis patients was intravenous exposure to Microcystins. The estimated concentration of Microcystin was 19.5 µg/L. The pathology consisted of animal studies of two Cyanotoxins (Microcystin and Cylindrospermopsin). The study also indicates due to the prolonged outbreak, victims might have had multiple exposures.

Harmful Algal Blooms are publicized in the water world every day; the reaction to these blooms is that they pose an immediate threat to humans. Studies indicate that exposure of Cyanotoxins can occur through multiple pathways such as: inhalation, contact with the nasal mucous membrane, dermally, consumption, oral intake through supplements and intravenously through dialysis[2]. The World Health Organization has set a tolerable daily intake of 0.04 µg/kg per day by body weight for Microcystin-LR, this number was based on histopathology and serum enzyme level changes where no observed adverse effect level of 40 µg per kilogram was determined; a factor of 1000 for uncertainty of intra-species variability was applied to obtain the 0.04 µg/kg by body weight.

Many studies explore recreational exposure to microcystin or Cyanotoxins, with correlation to health effects, however in the case of aerosol there has been no indication of direct causation.

Summaries of literature are provided through out this article.

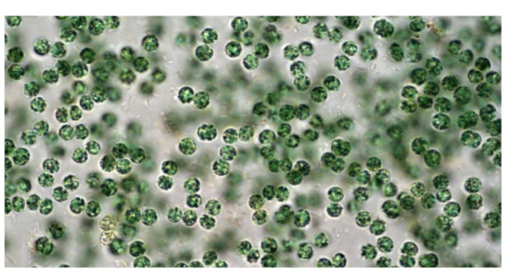

Figure 2: Microcystin[a]

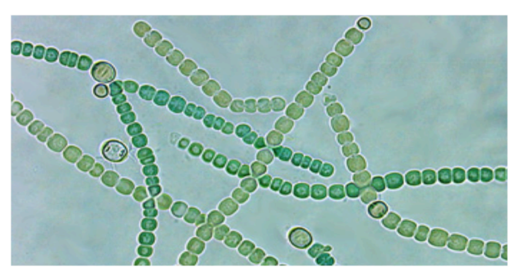

Figure 3: Cylindrospermum[b]

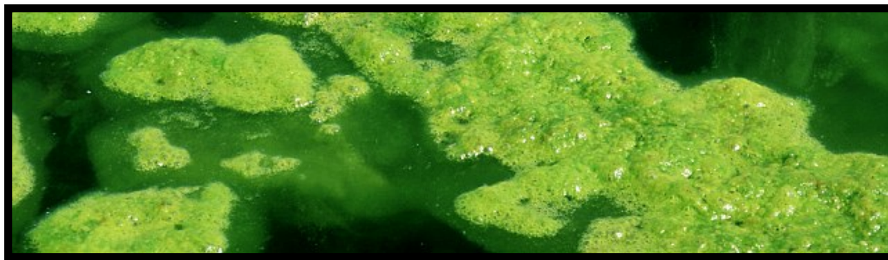

Figure 4: Algae[c]

Recreational exposure to microcystin during algal blooms in two California Lakes[3]

"Recreation exposure to microcystin during algal blooms in two California lakes explores a study conducted among 81 children and adults planning recreational activities on either of three California reservoirs, two with significant ongoing blooms of toxin-producing cyanobacteria (Referred to Blooms Lake 1 & 2) and one without a toxin producing algal bloom (Referred to Control Lake)"[3]. Control Lake was setup as a lake to monitor non-cyanobacterial blooms; the control lake did not have cyanobacterial due to the characteristics of the lake being deeper and cooler. Water samples were collected from the lakes twice a day; in the morning and the evening. The samples were then sent to Green Waters Laboratories. The samples were evaluated using both ELISA methods and LC/MS. Air samples were collected using air-samplers worn by selected participants in the study. Only seven individuals from the Control Lake agreed to participate while in the Bloom Lakes 81 individuals agreed to participate. In the end it was indicated "that the study was not able to determine whether sufficient aerosolized Microcycstin reached the lower respiratory tract for it to be absorbed through the lungs and appear in the blood." In other words no toxin was found in the blood samples.

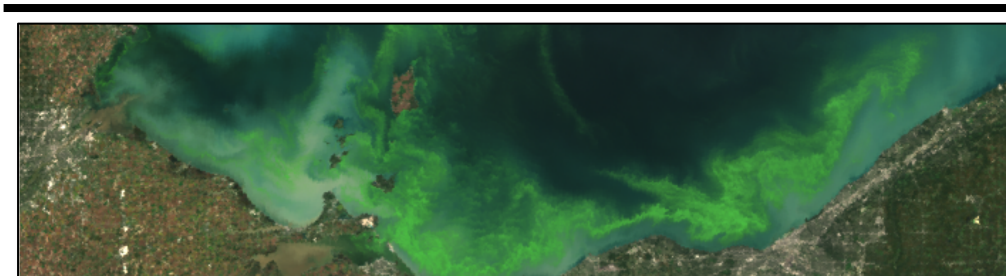

Figure 5: Algal Bloom via Satellite[d]

Recreational exposure to aerosolized brevetoxins during Florida red tide events[4]

The next study "Recreational exposure to aerosolized brevetoxins during Florida red tide events", the individuals used spirograms to perform pulmonary function tests on 129 participants before and after a red tide event. Nasal swabs were also performed on individuals with moderate to high exposure based on symptoms. The study was conducted on participants that visited two separate Florida red tide events; the first study was conducted during February 1999 and the second study was conducted during October 1999. Due to the large gap in time the study indicates a possibility of individuals visiting the beach during both events. The results of spirograms test found no clinically significant changes in pulmonary function; the swab tests were also not definitive.

Figure 6: Great Salt Lake

Health Effects of Exposure to Cyanobacteria during Recreational water-related activities [5]

An Australian study "Health effects of exposure to cyanobacteria during recreational water-related activities", conducted phone surveys of 852 participants after they visited a body of water that was expected to have algal blooms. 777 out of the 852 participants were considered exposed and 75 were considered non-exposed since they did not have contact with water. The water related recreation activities included: jet-skiing, water skiing, swimming and wind-surfing. The results for the study when considering the complete data set did not reflect a significant difference between the exposed and unexposed participants (odds ratio = 1.12), however once exclusion factors were applied the odds ratio increased to 1.87. The exclusion factors included the following: an individual who had water contact or symptoms in the five days prior to the initial interview. The study indicated in their methods that toxicity tests were conducted, however they were not presented in results or data other than the indication of whether or not they were present.

The study also indicated two days after exposure there was no significant difference in the occurrence of symptoms between the exposed and non-exposed individuals.

Figure 7: Utah Lake Algal Bloom[e]

Cyanotoxins in desert environments may present risk to human health[6]

Cyanotoxins are not only present in water but can also be present in the desert. The study explores the possibility of inhalation of cyanotoxins during a dustbowl. Samples were gathered in the desert of Qatar on the supertidal salt flats, the samples showed presence of Microcystin. Microcystin concentrations via ELISA method were between 1.5 and 6.5 ng/g in the crust. The findings were then applied to a mice study on Microcystin inhalation spray, the study quantified a no observed adverse effect limit (NOAEL) and a lowest observable adverse effect limit (LOAEL). The NOAEL and LOAEL in mice were determined to be 3 µg/kg and 31.3 µg/kg for Microcystin-LR, respectively. The study indicated that microcystin present in inhaled dust from the desert crust is unknown, however based on inhalation toxicity data the study concluded that a 60 kg adult could inhale approximately 60-120 ng of microcystin-LR equivalent per day assuming that unfiltered air was being breathed in a desert dust storm.

Figure 8: Algal Scum[f]

Recreational Exposure to low Concentrations of Microcystins during an Algal Bloom in a Small Lake[7]

The next study examined 97 participants planning recreational activities during a visible algal bloom. Analysis consisted of water samples, air samples, and human blood samples. The water samples were analyzed for potential respiratory viruses, in order to eliminate confounding of respiratory illnesses that might be caused by factors other than Microcystin. Although no respiratory viruses were detected, Escherichia coli were found in water sample in low concentrations, indicating fecal contamination. Microcystin was also detected in low concentrations from 2 μg/L to 5 μg/L in the water samples. Through LC/MS methods Microcystin was detected in only one blood sample, where the amount was quantified as 1μg/L, however the results of this sample was denoted as a either a false positive or as exposure of microcystin was not identified as microcystin-LR, -RR or –YR. Samples for the study were gathered at four stations over 3days. The study indicates that although a visible bloom was present they did not find many toxins in the water; this is because of the nature of the microcystin cells. "Microcystins are endotoxins stored and isolated inside algal cells"[7], only when lysis occurs will toxins be present. "95-98% of the algal blooms toxins are intracellular"[7]. The potentially toxic cell counts observed in the study were from 45,199 cells/mL to 143,958 cells/mL. Self-reported symptoms were also gathered from participants, which showed greater indication of symptoms prior to the recreational activity.

Figure 9: Benthic Algae

Characterization of Aerosols Containing Microcystin [8]

A study was conducted in order to analyze the quantity of microcystin produced through aerosolization. Aerosol droplets containing Microcystin were produced in the laboratory and sampling instruments were deployed in the field to measure the microcystin. The study concluded that detection of low quantities of microcystin is possible. A field study was conducted on Bear Lake in Michigan during an algal bloom from August 4, 2006 to August 6, 2006. One high volume filter and impactor sample were obtained each day. While the purpose of the high volume filter was to measure the quantity of the Microcycstin the purpose of the impactor was to measure the particle diameter of the aerosolized Microcycstin particles. The resulting concentrations of the high volume filter samples were the following: 0.05, 0.023, and 0.057 ng/m^3 from August 4-6, 2006, respectively. As for the impactor results the particle sizes were only measured on August 4 and August 6. The fine particle mode was at 0.4 μm and the course particle mode was at 6.5 μm. Personal samplers were also given to participants over the 3 day period. A total of 24 personal samplers were obtained, the data can be seen in the figures below. The personal samplers for the first and second day detected small quantities of Microcycstin, however the third day the samplers did not detect any Microcycstin.

Date	Temperature (C)	Humidity (%)	Average Wind Speed (m/s)
8/4/2006	31.1 ± 1.4	38.4 ± 8.4	3.4± 0.9
8/5/2006	29.7 ± 2.7	46.3 ± 8.0	1.5± 1.1
8/6/2006	26. 0± 2.3	71.7 ± 10.0	3.2± 1.6

Figure 10: Bear Lake Data [g]

Date	Microcystin Concentration (ng/m^3)	Sample Number
8/4/2006	0.08 ± 0.09	10
8/5/2006	0.07 ± 0.14	10
8/6/2006	0.0 ± 0.0	4

Figure 11: Bear Lake Microcystin Personal Samplers Concentrations [h]

Identification of Microcystin in benthic cyanobacteria linked to cattle deaths on alpine pastures in Switzerland[9]

Many animal studies have also been conducted to analyze the effects of Cyanotoxins present in livestock habitats. The study "Identification of Microcystin in benthic cyanobacteria linked to cattle deaths on alpine pastures in Switzerland" explores the death of cattle in the pastures of Switzerland. A total of 105 cattle died in the last two decades due to acute liver necrosis. The study also discusses the death of four calves; water samples were collected during the same time period. A total of 165 samples were collected. Out of the samples that did test positive for cyanobacteria the quantity present was less than 2µg of cyanobacterial proteins. The proteins themselves contained up to 31µmol of microcystin-LR equivalent g^{-1} protein. The calves were autopsied, neither cyanobacterial cells nor toxins could be found in the rumens contents and liver of the four calves. Even with the absence of cyanobacteria in the liver, at the end the study still concluded cyanotoxins as the death of the animals due to the elimination of other toxins.

Human Exposure to Cyanotoxins and their effects on Health[2]

Cyanotoxins can have a variety of health effects, which can drastically vary anywhere from a mild headache to serious health conditions. Routes of exposure of cyanotoxins also vary from: inhalation, contact with the nasal mucous membrane, and dermal exposures. Cyanotoxins can also be found in dietary supplements known as blue green algae supplements (BGAS). According to the suppliers BGAS are rich in protein and provide health benefits such as: detoxification, weight loss, elevated mood, energy and increased alertness and therapy for Attention Deficit Hyperactivity Disorder. Some of the supplements have greater microcystin content than the recommended World Health Organization value of 1µg d.w. The conclusion of the article states "The precise doses of these toxins are still an open issue which should be solved in order to prevent possible health risks.

Conclusion

A great of amount of uncertainty exist when trying to quantify appropriate cyanotoxins concentrations for recreational activities via aerosol. All studies in this analysis hypothesized a potential harm but found no definitive results to prove otherwise. Even the Environmental Protection Agency stated “available data are insufficient to develop quantitative recreational values for cyanobacterial cell density related to inflammatory health endpoints”. Additional research needs to be conducted to analyze the effects of aerosol cyanotoxins.

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