

Report to the Florida Harmful Algal Bloom Taskforce

Blue Green Algae, Their Toxins and Public Health Issues

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Introduction

The Cyanobacteria or blue green algae are an ancient and ubiquitous family of photosynthetic organisms (Chorus 1999, Carmichael 1994, Falconer 1989, NHMRC 1994). Many of these organisms are able to fix nitrogen, and are therefore an important part of the food chain. The cyanobacteria frequently are found growing in marine, brackish and fresh waters, including freshwater surface drinking sources, such as lakes and drinking water reservoirs. Similar to the marine algal blooms, cyanobacteria periodically will grow exuberantly, known as “blooms.” The reasons for these blooms are not completely understood, but in some cases they may be related to nutrients added naturally and through man-made sources such as fertilizer runoff or sewage (Philipp 1991, Carmichael 1993, Rapala 1997, Ling 2000). These blooms can cause significant environmental impact due to the decrease in oxygen in the water, resulting in the die-off of fish and other organisms. Furthermore, again similar to marine algal blooms or red tides, these blue green algal blooms can produce significant quantities of natural toxins, for reasons as yet unknown. When they produce these highly active natural biotoxins, these blue green algal blooms are known as a “harmful algal bloom (HAB).” To date at least 12 different species of Cyanobacteria have been shown to produce toxins, often several different toxins per species (Carmichael 1994). The main toxic cyanobacterial genera include *Anabaena*, *Aphanizomenon*, *Nodularia*, *Oscillatoria*, and *Microcystis* (Carmichael 1993, NHMRC 1994, Chorus 1999).

Toxins

These toxins, along with those produced by the marine organisms such as dinoflagellates and diatoms, are extremely toxic to many species. There is a wide spectrum of blue green algal toxins, predominantly affecting the nervous, hepatic and dermatologic systems (ie. Neurotoxic, hepatotoxic and dermatotoxic).

The dermatotoxins include aplysiatoxins and lyngbyatoxin, and are often reported from marine cyanobacteria blooms. These are potent tumor promoters and protein kinase C activators. These toxins can cause severe dermatitis with only skin contact, as well as gastrointestinal inflammation with oral exposure (Chorus 1999).

The neurotoxins include: anatoxin a and anatoxin a (S) (both unique to the cyanobacteria), as well as saxitoxin and neosaxitoxin (also elaborated by marine dinoflagellates and associated with the human disease paralytic shellfish poisoning or PSP). Anatoxin a acts like the neurotransmitter acetylcholine except that it cannot be degraded by acetylcholinesterase; anatoxin a (S) is a natural organophosphate, binding to the acetylcholinesterase enzymes; the saxitoxins are sodium channel blockers. Singly or in mixtures, these cyanobacterial neurotoxins can cause death within minutes secondary to respiratory paralysis (Codd 1997, Carmichael 1994, Carmichael 1993).

The hepatotoxins are cyclic peptides, predominantly microcystins, nodularins, and cylindrospermopsin. Of note, these toxins are particularly toxic to the liver in part due to selective transport mechanisms that concentrate these toxins from the gut and blood into the liver cells; they damage the liver by deranging the cytoskeletal architecture of the hepatocytes. Microcystin is also believed to cause damage to cells' DNA by the activation of endonucleases (Jochimsen 1998). Cylindrospermopsin is a protein synthesis inhibitor, resulting in wide spread necrosis of the tissues of many organs. The microcystins and the nodularins are protein phosphatase inhibitors, as well as being potent tumor promoters in animals (similar to the carcinogen, okadaic acid, elaborated by marine dinoflagellates and associated with the human disease diarrhetic shellfish poisoning or DSP). The microcystins cause liver necrosis leading to death within hours to days (Elder 1993, Carmichael 1994, Humpage 1999, Yu 1995, Ohtani 1992, MacKintosh 1990, Repavich 1990, NHMRC 1994, Chorus 1999). At lower doses, enteritis and hepatitis are seen shortly after ingestion of these toxins.

The same cyanobacteria species can produce both neurotoxins and hepatotoxins, even during the same bloom; often the presence of the hepatotoxin is masked by the premature death of the animal due to the neurotoxin. In addition, there exist other toxins (including lipopolysaccharides, endotoxins and additional neurotoxins), as well as yet undescribed cyanobacterial toxins including additional tumor promoters (Falconer 1989, Codd 1997, Falconer 1994, Falconer 1996, Chorus et al.,2000).

Animals

Domestic

There have been frequent reports of thirsty domestic animals and wildlife consuming freshwater contaminated with toxic blue green algal blooms, and dying within minutes to days from acute neurotoxicity and/or hepatotoxicity (Jochimsen 1998, Elder 1993, Carmichael 1994, Codd 1997, Mahmood 1988, Carbis 1995, Negri 1995, Repavich 1990). Toxic blooms of cyanobacteria with associated animal poisonings have been reported in all continents except Antarctica (NHMRC 1994). Mammals and birds appear to be more susceptible to the blue green algal toxins than aquatic invertebrates and fish, with some species variability. Prolonged morbidity and mortality have also been reported in animals exposed to blue green algae in the wild. For example, Carbis et al (1995) followed sheep exposed to *Microcystis aeruginosa* in a lake in Australia for 6 months; there was a 34% mortality over this period among the exposed sheep without clear etiology even after resolution of the initial liver toxicity observed during the first 3 weeks.

Laboratory

Experimentally, acute high dose administration of microcystin can lead to death from hepatoencephalopathy within hours, and chronic administration to mice of sublethal amounts of *Microcystis* extracts in drinking water results in increased mortality with chronic active liver disease, even at fairly low doses and in relatively short time periods (Heinze 1999). Falconer et al (1992) gave intra peritoneal (ip) injections to mice of the gut and gut contents of boiled edible mussels from a water bloom of *Nodularia* in Western Australia. The cell density of the bloom in the water had been up to 100,000 cells/mL. The ip injections were lethal secondary to acute (within 24 hours) hepatotoxicity to 1 kg mice at 89 mg dry weight/kg; the *Nodularia* bloom LD₅₀ was 24.4 mg dry weight/kg. Based on this research, Falconer et al (1992) concluded that edible mussels should not be collected for human consumption during a toxic blue green algal bloom.

In laboratory experimental animals, teratogenic activity has been demonstrated with oral administration of *Microcystis* extracts; approximately 10% of otherwise normal neonatal mice had small brains with extensive hippocampal neuronal damage (Carmichael 1993, Astrachan 1980).

Studies in cultured cells have also shown tumor promotion, and microcystins are preferentially taken up by hepatic cells, so that hepatic tumor promotion is likely (Falconer 1996, Carmichael 1994, Carmichael 1993, Sugimura 1986, Humpage 1999, Ito 1997). As noted above, the microcystins can cause tumor promotion in animals exposed to chronic low level non-lethal doses. Nishikawa et al (1992) showed that microcystins are powerful tumor promoters of hepatic liver tumors in rats mediated through the inhibition of protein phosphatase type 1 and type 2A activity (Hong-Bing 1996). Lyngbyatoxin A has been shown to be a potent tumor promoter in a two stage mouse skin carcinogenesis study by Fujiki et al (1984).

Humans

There are relatively few case reports and even fewer epidemiologic studies of the human health effects of the blue green algal toxins (Carmichael 1993, Jalaludin 1992, Falconer 1999, Chorus 1999, Ransom 1994). Humans can be exposed to the cyanobacteria and their toxins through direct skin contact or by drinking contaminated waters; other possible routes of exposure include inhalation of aerosol,

consumption of contaminated food, and even through dialysis (Codd 1997, Chorus 1999). Occupational exposures for fishermen, watermen, and scientists, as well as recreational exposures for the general public, are both possible (Codd 1997, Baxter 1991, Philipp 1991).

Seasonal gastroenteritis has been reported worldwide and may be related to the consumption of contaminated drinking water (Carmichael 1993, Volterra 1993, Codd 1984, Falconer 1999). Algal blooms are known to occur mainly in the late summer and early Fall because light intensity and temperature are known to play a role in their formation (Duy 2000).

There are individual case reports of persons exposed through swimming to blue green algal blooms with skin irritation and allergic reactions (both dermatologic and respiratory) with continued positive reaction on skin testing (Falconer 1989, Carmichael 1993, Falconer 1999, Hashimoto 1974, NHMRC 1994, Chorus 1999). In particular, urticaria (hives), blistering and even deep desquamation of skin in sensitive areas like the lips and under swimsuits has been reported, especially with *Lyngbya majuscula* in tropical areas. Consumption of or swimming in cyanobacterial toxin-contaminated waters has also yielded increased case reports of gastrointestinal symptoms, especially diarrhea (Billings 1981, Probert 1995). Turner et al (1990) reported 2 cases of pneumonia in healthy army recruits following probable inhalation from a canoe on waters with a blue green algal bloom of *Microcystis aeruginosa*; 16 other exposed recruits reported of a variety of gastrointestinal (hepatoenteritis), dermatologic and respiratory complaints (Turner 1990).

In addition to gastrointestinal and dermatologic symptoms, eye irritation, asthma, and “hay fever symptoms” have been reported repeatedly with contaminated recreational water exposure in the US, Canada, UK, and Australia. Actual Type I hypersensitivity to cyanobacteria (as detected via skin patch testing and bronchial provocation testing) has also been reported. Airborne cyanobacteria and cyanobacteria present in house dust have been investigated as causes of naso-bronchial allergies (NHMRC 1994).

Known Human Outbreaks

In general, the few epidemiologic studies available have been performed after a significant community exposure event.

Some of the first reports of adverse health effects from exposure to the blue green algae were by Veldee (1931) when an estimated 9000 persons out of a population of 60,000 in Charleston (West Virginia) reported acute gastroenteritis after a period of low rain fall and reportedly contaminated drinking water; other outbreaks were seen along the Ohio River in the same year (Tisdale 1931). Lipp and Erb (1976) reported that 62% of the population of 8000 of Sewickley (Pennsylvania) suffered from acute gastroenteritis; the reservoir was found to be contaminated by *Schizothrix calcicola*. In 1988, severe gastroenteritis was reported in Brazil after the flooding of a newly constructed dam and reservoir with 2000 cases and 88 deaths (particularly children) over a 42 day period; cases were restricted to the areas supplied by drinking water from the reservoir and those ill had only consumed boiled water with negative bacterial and viral cultures. *Anabaena* and *Microcystis* blooms were present in the reservoir at the time of the flood (Chorus 1999, Teixeira 1993).

With a long history of episodes of possible adverse health effects in animals and humans in Australia, Pilotto et al (1997) studied the effects in South Australia of exposure to blue green algae as a result of recreational water activities. They used a serial symptom questionnaire on a large sample (777 “exposed” and 75 “unexposed”), as well as water sampling for cyanobacteria and toxin. Although there was no difference in the type and quantity of symptoms reported acutely, the Investigators found a significant trend to increasing symptom occurrence with duration of exposure, and a symptom dose response that correlated with exposure to 5000 cells per ml for more than one hour; however, symptoms did not

correlate with the presence of hepatotoxins in the water. The Investigators suggested that the current safety threshold for exposure of 20,000 cells per mL may be too high. El Saadi et al (1995) performed a case control study in 11 South Australian towns along the Murray River, a cyanobacterial historic epicenter, using gastrointestinal and dermatologic cases and controls with similar town distributions. Persons who drank the river water, even after chlorination, were significantly more likely to have gastrointestinal symptoms, while those using river water for domestic purposes were significantly more likely to have both gastrointestinal and dermatologic symptoms, compared with persons using rainwater. Furthermore, there was a correlation with report of symptoms and mean log cyanobacterial cell counts.

Liver enzymes, especially GGT, have also been found to be increased after consumption of drinking water contaminated with Microcystis toxins in Australia. Other Australian episodes have included a severe outbreak of hepatoenteritis after drinking water with a novel cyanobacterial toxin contamination on Palm Island in Queensland (Australia) (Falconer 1983, Carmichael 1993, Bourke 1983, Probert 1995, El Saadi 1995, Chorus 1999). In this particular episode, the drinking water reservoir had been dosed with copper sulphate to remove a persistent cyanobacteria bloom of *Cylindrospermopsis raciborskii*, leading to lysis of the algal cells and substantial release of toxins into the drinking water. Reportedly some of the children were critically ill with severe hepatoenteritis and kidney failure, and 150 persons (140 children) were ultimately hospitalized. Subsequent research identified the cytotoxic cylindrospermopsin as well as other toxins as the probable cause of the outbreak. In another study by Falconer (1994) in different area of Australia with a similar situation of cyanobacterial toxin contamination of a drinking water supply after the use of copper sulfate, clinical liver function data were examined. There was a statistically significant increase in the liver enzyme GGT in persons drinking from the contaminated reservoir only during the period of bloom and cell lysis compared to all others in the same area with different water supplies. GGT has also been used as an effective marker for liver injury in experimental animal studies with microcystin exposure (Falconer 1994a, Chorus 1999).

A recent and infamous outbreak occurred in Brazil when over 100 patients on kidney dialysis developed visual disturbances, nausea and vomiting, followed by 50 deaths from acute liver failure. Apparently the dialysis water had been contaminated with blue green algal toxins from the reservoir supplying the clinic; microcystins produced by cyanobacteria were subsequently identified in the water and in the human tissues. Inadequate water treatment procedures and the failure of the clinic staff to change filters usually used in preparation of the local water for the dialysis procedure were two factors leading to the contamination and the subsequent deaths (Jochimsen 1998). There is some disagreement between studies over whether the water the clinic received had been chlorinated prior to its being trucked to the clinic (Pouria 1998, Jochimsen 1998); as far as can be determined, it seems that the water had not been chlorinated, only flocculated. A second dialysis clinic supplied by the same reservoir received water which went through the entire process of treatment including chlorination; no illness was reported at the second clinic.

The following is a table showing dates and studies of a list of known human exposures to cyanobacterial toxins.

Table 1. Reported Human Outbreaks associated with Cyanobacteria.

Study Year	Location	Population Affected	Exposure Route	References
1930-31	West Virginia	9000/60,000	Unknown	Veldee 1931 Tisdale 1931
1959	Saskatchewan	12 people	Swimming	Dillenberg 1960
1960-65	Harare, Zimbabwe	Children	Drinking water	Zilberg 1966
1975	Sewickey, PA	62% of 8000	Drinking water	Lippy 1976

1979	Palm Island, Aust.	139 children	Drinking water	Byth 1980
1980-81	Pennsylvania/Nevada	>100 people	Swimming, water skiing	Carmichael 1985
1989	Staffordshire,UK	18 recruits ill	Swimming, canoeing	Turner 1990
1992	Outback Aust.	Unknown	Drinking	Hayman 1992
1992	River Murray, Aust.	26 people	Drinking	El Saadi 1993
1994	China	High rates liver cancer	Drinking	Yu 1994
1996	Caruaru, Brazil	63 deaths	Dialysis	Jochimsen 1998

(adapted from Duy 2000)

Perinatal Effects

Pilotto et al (1999) attempted to look at perinatal outcome and the possible relationship with cyanobacterial contamination of drinking water in an ecological study. The investigators examined the perinatal outcome (prematurity, low birth weight and very low birth weight, and congenital defects detected at birth) for 32,700 singleton live newborns of non-Aboriginal mothers from 1992-94 in South Eastern Australia; exposure data was based on weekly cell counts from 29 drinking water storage sites for the 156 towns in the same area (percentage of time occurrence and average cell counts), and the mother's address at the time of the newborn's birth. This work was based on the concern raised by laboratory animal studies showing impaired fetal development (especially neurologic) and low birth weight after exposure to untreated reservoir water sampled during a bloom, as well as fetal mortality, small fetuses, and congenital malformation with injection of microcystins into pregnant rats. Although there were statistically significant associations with particular exposure levels and particular birth outcomes (especially the very low birth weight category and exposure during the first trimester with percentage of time occurrence, and congenital malformations with average cell counts), there was an overall lack of dose response; similar results were seen for the whole gestation and the last 12 weeks of gestation. The authors concluded that their ecological study did not provide clear evidence for an association. However, as they pointed out, there were no individual drinking water exposure data and in areas with frequent known cyanobacterial contamination, systematic avoidance of drinking water can be common.

Cyanobacteria-like Bodies and Traveler's Diarrhea

There have been a host of articles concerning cyanobacteria as a source of chronic relapsing diarrhea, especially in travelers (both immunocompromised and not) to developing nations; the illness seems to be associated with the organisms rather than the toxins, and furthermore may actually be a separate group of organisms that are cyanobacterium-like (Soave 1986, Anon 1991, Hale 1994, Long 1990, Shlim 1991). These may, in fact, be a separate class of organisms referred to as *Cyclospora* (Bendall 1993). Some researchers have even postulated a role for the blue green algae as a carrier or reservoir of the bacteria *Vibrio cholera*, the latter responsible for the human bacterial disease cholera (Islam 1994, Chorus 1999).

Cancer

Yu et al and others (1989a, 1989b, 1995, Junshi 1990, Chorus 1999) have studied the possible relationship between the consumption of surface drinking water (pond, ditch, river vs well water or deep well) and an increased risk for primary hepatic cancer (as well as chronic gastrointestinal diseases) in China. China has an extremely high rate of primary liver cancer, previously associated with hepatitis B and aflatoxin exposures (Yu 1995). However, reportedly large epidemiologic studies in 1973 and in 1983 were performed in Haimen, Quidong and Nanhui Counties (Guangxi province, China) to evaluate drinking water source, exposure and risk of primary hepatic cancer. These studies found not only a significantly increased risk of primary liver cancer in areas of high surface drinking water consumption

(SIR=2.6) compared with areas of non-surface drinking water consumption (SIR=0.34), but also a strong dose response relationship. Reportedly, changing from pond/ditch to deep well (at least 200 m) water in Quidong lead to a stabilization with subsequent decrease of the mortality rate from primary hepatic cancer, while in Haimen where there was no change, the liver cancer mortality rates continued to increase during the same time period; in an area where there was a mixture of well and river water, there was no significant change in the mortality rate during this time period. Monitoring studies using a sensitive ELISA test from microcystins revealed high levels of microcystins, as well as the presence of blue green algae, in the surface as opposed to other drinking water sources (Ueno 1996). On average the surface water sources contained 130 pg/ml of microcystins compared to the well samples (the vast majority less than 49 pg/ml) (Falconer 1996).

Ito et al (1997) was able to induce neoplastic nodular formation in mouse liver by repeated ip injections of sublethal dose (20 ug/kg) microcystin LR without the use of an initiator; however, repeated oral administration of a sublethal dose (80 ug/kg) did not result in nodular formation. Ueno et al (1996) postulated that the combined effects of a potent hepatocarcinogen such as aflatoxin from the diet with intermittent microcystin intake through drinking water could explain the high rates of primary liver cancer associated with surface drinking water source in this area. Yu (1995) reported on the results of experiments with male F-344 rat exposed to different mixtures of aflatoxin, deep well water, and pond/ditch water after partial hepatectomy. The results showed significant increase in the gamma-glutamyl transferase (GGT) liver enzyme in rats exposed to aflatoxins and pond/ditch water compared to the other groups including control. Yu (1995) postulated that microcystins are promoters with a synergistic effect between microcystins and aflatoxins for primary hepatocellular carcinoma. As a result of this work, the Chinese government has reportedly urged their people to use deep water wells or minimally granular activated carbon filtration for their drinking water, as well as other interventions (ie. hepatitis B vaccine and shifting to rice instead of corn to avoid aflatoxins), to prevent primary liver cancer in China.

Fleming et al.(2000) performed an ecological study of Florida using Geographic Information Systems to examine the risk of primary liver cancer as related to proximity to a surface water treatment plant. Residence within the service area of a surface water treatment plant was found to be a significant risk factor for primary liver cancer as compared with those living adjacent to surface treatment plant areas, i.e. areas served with water from deep wells. This study had no way of assessing individual exposure to cyanobacteria and the increased risk was not beyond the normal range of liver cancer rates for the state as a whole.

In addition to liver cancer, there is recent research suggesting a possible role for the blue green algal toxins and colon cancer. Humpage (2000) examined the formation of aberrant crypt foci (ACF) in mice as modified by exposure to microcystins. He found while the number of crypts did not increase the depth (or total area) of each crypt was increased and two overt colonic tumors were observed in the treated mice. Because ACF's are a known precursor to colon cancer in humans this study indicates that microcystins could potentially "stimulate preneoplastic colon tumour growth.

Treatment

In general, the only treatment available for exposure to the blue green algal toxins is supportive medical treatment after complete removal from exposure (Chorus 1999). If the exposure was oral, administration of activated carbon to decrease gut absorption may be efficacious if given within hours of exposure. Artificial respiration with exposure to the neurotoxins (such as saxitoxin) should also be considered (NHMRC 1994). Based on past outbreaks, monitoring of volume, electrolytes, liver and kidney function should all be considered in the case of acute gastroenteritis associated with some of the blue green algal toxins.

Although no specific treatments exist for the cyanobacterial toxins, Nagata et al (1995) have created at least 6 monoclonal antibodies (Mabs) to microcystin LR isolated from *Microcystis aeruginosa*. These MABs showed a protective effect on the hepatotoxicity and inhibition of protein phosphatase of microcystin LR *in vitro* and *in vivo* in a dose dependent manner.

Of note, activated carbon given to experimental animals pre-treatment was not an effective antidote for preventing effects from subsequent microcystin administration (Mereish 1989, Beasley 1989). Hermansky et al (1991) used a variety of chemoprotectants in pre treatment prior to exposure of experimental mice to a lethal dose of microcystin LR (100 ug/kg); phenobarbital (but not the calcium channel blockers or water soluble anti-oxidants) provided partial protection, while the hydrophobic anti-oxidants (such as Vitamin E and silymarin), glutathione active compounds (such as glutathione), and immunosuppressive agents (such as rifampin and cyclosporin A) provided significant protection if given 48 hours prior to exposure to microcystin in laboratory animals.

Prevention and Control

Monitoring

Due to their significant potential toxicity and the lack of specific treatment modalities available, the best treatment for the health effects of the blue green algae is the prevention of exposure to the blue green algal toxins. Therefore, monitoring for these toxins in surface drinking and recreational waters, as well as other exposure venues, is crucial in the prevention of human health effects from the blue green algal toxins (NHMRC 1994, Chorus 1999). For example, recent monitoring studies in Florida (SJRWMD 2000) of recreational and surface drinking water supplies with algal blooms, have found 87/167 samples (75 individual water bodies) with significant levels of toxin producing blue green algae. All of these samples had positive identification of blue green algal toxins with 80% lethal in mice. Monitoring should include visual monitoring for blooms, cell counts and identification, and toxin identification and toxicity testing; other monitoring indices have also been used, including phosphorus levels in the water, as well as surveillance of health effects in human and animal populations (Chorus 1999).

Falconer (1994a) recommended 20,000 cells/ml sampled in the top meter of open water as the maximum safe level of cyanobacteria in recreational waters. Nevertheless, Falconer warned that if the bloom is toxic, swallowing or bathing in these waters should be considered hazardous. Chorus et al (1999) used data from Pilotto et al (1997) to derive a guideline for acute non-cumulative health effects resulting in discomfort, not serious health outcomes. Significantly increased odds ratios for eye irritation, rash and gastrointestinal symptoms were associated with water contact for more than 1 hour above 5000 cyanobacterial cells/mL and for persons bathing in water with 5000-20,000 cells/mL. Pilotto et al (1997) suggested that the current safety threshold for exposure of 20,000 cells per mL might be too high based on their results.

With monitoring programs, response programs must be established based on the results of regular monitoring. Australia and the UK have attempted to develop such monitoring and response programs for surface drinking water sources (NHMRC 1994, Jones 1993, Burch 1993) with alert levels and corresponding responses based on the number of cyanobacterial cells per ml in routine sampling. For example, Burch et al (1993) and Chorus et al (1999) propose Alert Levels 1 (cells 500-2000 cells/mL or offensive odor or taste), Level 2 (potentially toxic cells 2000-15,000 cells/mL for 2-3 consecutive samples or confirmed toxic bloom, persistent odor/taste, and obvious bloom), and Level 3 (persistent high numbers widespread, toxic, cells >15,000 cell/mL for toxic species, persistent bloom, and only partial success of control measures). Level 1 is associated with increased monitoring; Level 2 results in media information release and consultation with health authorities as well as control measures (such as booms, activated carbon); and Level 3 results in the same actions as Level 2 as well as possible declaration of

water as unsafe for consumption and provision of safe drinking water alternatives after consultation with health authorities. Subsequent health surveillance and evaluation may be necessary, especially if exposure is suspected. Separate guidelines should be developed for recreational and occupational use of potentially contaminated surface waters based on the probability and severity of potential health effect development from exposure to cyanobacterial toxins (Bartram and Rees 1999, Chorus 1999). In areas of endemic toxic blue algal blooms, public education and awareness plans should be considered (Chorus 1999), including issues such as avoidance of occupational and recreational exposure, description of possible health effects, and warnings that boiling water will not destroy the cyanobacterial toxins.

Standards

In general, the information available is considered inadequate for the calculation of a tolerable daily intake (TDI) for the majority of the cyanobacterial toxins (Chorus 1999). In particular, data are not available on metabolic disposition, acute and subacute toxicity, repeated administration, developmental effects, and carcinogenicity and genotoxicity. In such cases, a TDI can be derived using the LOEL or NOAEL divided by appropriate safety and uncertainty factors, as described in the Addendum to the World Health Organization Guidelines for Drinking Water Quality (WHO 1998).

A study by Fawell et al (1994, Chorus 1999) derived a NOAEL of 40 ug/kg body weight per day in a mice gavage study with a 1000 fold uncertainty factor (intra-species, inter-species, limitations of database) resulting in a provisional TDI of 0.04 ug/kg body weight per day of microcystin LR. Falconer (1994a, 1994b) used the following 10 fold safety factors: use of subchronic data applied to lifetime risk, use of pig data applied to humans, use of intra-human variation, and tumor promotion risk; therefore he applied a 10,000 overall safety factor. He used subchronic exposure data in pigs that showed a lowest observed effect level of 280 ug/kg/day, and an assumption of 2 liters water intake per day by a 60 kg adult. This led him to a provisional TDI of 0.067ug/kg body weight per day. The WHO (1998) adopted a provisional guideline (TDI x body weight x proportion of total daily intake of the contaminant ingested from drinking water divided by the daily water intake in liters) for microcystin LR of 1.0 ug/L. Special exposure circumstances (such as dialysis water) may necessitate even stricter control levels (Chorus 1999).

Drinking Water

Barriers that reduce exposure of drinking water to cyanobacterial blooms at “critical control points” are the first step in prevention, especially for surface drinking water sources (Chorus 1999, Hitzfeld, 2000). Of note, algacides, especially copper sulfate, can be added to water supplies to control toxic blooms, but acutely this leads to cell lysis and substantial release of the toxins into the water, as well as the possibility of copper toxicity, thus exacerbating the potential for health effects (Chorus 1999, Carmichael 1993, Falconer 1999, NHMRC 1994). Therefore, removal of intact cells is recommended (Chorus 1999). Activated carbon, chlorination and ozonation in conjunction with other water treatment practices have all been used in the treatment of drinking water supplies with potential blue green algal contamination with results varying based on concentration and time (NHMRC 1994, Jones 1993, Chorus 1999). Chlorine has been found to oxidize cylindrospermopsin, but not microcystins (Hitzfeld, 2000). The use of activated carbon treatment during active blooms will decrease but not necessarily eliminate levels of cyanobacterial toxins in drinking water (Chorus 1999; J Burns SJRWMD, FL, verbal communication). This is of particular concern when the toxin is a potential carcinogen, since low level chronic exposure may predispose to the development of cancer (Chorus 1999, Carmichael 1993, NHMRC 1994). Changing drinking water sources to groundwater sources should be explored (Chorus 1999). Future possible treatments involve ultraviolet light, titanium dioxide and filtration with an ultrafine membrane to remove whole algal cells Hitzfeld, 2000).

Recreational Water

The recreational use of water bodies experiencing an algal bloom is becoming an increasing concern as intranasal exposure to toxins has been found to be similar to intraperitoneal exposure (Chorus, 2000). Because unattractive "scums" and foul smells are not always present during toxic algal blooms, people, especially children and infants, are at risk of acute exposure to toxins while swimming, water skiing and even showering or cleaning with untreated water. Chorus notes that dogs in particular can consume large quantities of water while playing and grooming themselves after water contact. She recommends that organized water events be cancelled when blooms occur and that people shower with treated water after swimming in water not known to be safe. Because toxins degrade naturally after their release, the presence of a known toxin in water is not necessarily a problem. In fact, some 75% of all cyanobacteria sampled contain toxins. It is the huge conglomerations of cells that present a concern for recreational water use, i.e. the formation of large blooms in late summer and early fall (Chorus 2000).

Food and Supplements

There is a possibility of exposure to these toxins also through the consumption of contaminated food (Prepas 1997, Falconer 1992, Vasconcelos 1999). Microcystin has been shown to be toxic to a range of zooplankton (Duy et. al., 2000), and there has been concern that the toxin may accumulate in the bodies of fish destined for consumption by humans. For example, based on examination of the gut contents of mussels during a bloom of *Microcystis* in Australia, Falconer et al (1992) concluded that edible mussels should not be collected for human consumption during a toxic blue green algal bloom. Vasconcelos (1999) studied fish and shellfish in Portugal, looking particularly for the toxin microcystin-LR. The author found that mussels and clams concentrated the toxin in their gut, but seemed unaffected by the toxin themselves. Both carp and crayfish were also found to have detectable levels of toxin in their muscle as well as in the viscera. The fact that toxin was found in fish not associated with a specific bloom event indicates that human diets rich in fish and shellfish may pose a threat of chronic low level exposure.

Use of potentially contaminated water for irrigation is controversial since not only can the irrigation aerosol cause potential harm through skin and respiratory contact, but there is limited evidence that terrestrial plants, including food crops, can take up microcystins (MacKintosh 1990, Chorus 1999, Codd, 1999). Codd (1999) hypothesized that washing produce would not be sufficient to remove toxins, but did not in fact evaluate the effects of any control measures on the contaminated produce.

Cyanobacteria (particularly *Spirulina* and *Aphanizomenon flos-aquae*) have been used as food and possible therapeutic agent in the US, Canada, Mexico, and India (NHMRC 1994, Chorus 1999). Although most cyanobacteria species are nontoxic, the etiology and conditions for toxicity are not well understood, nor have the health risks and benefits of long term consumption of cyanobacteria been studied. Gilroy (2000) conducted a study of commercially sold blue green algae supplements after a documented bloom in a lake in Oregon where algae is routinely gathered for sale. He found that 85/87 of the samples tested positive for toxins, most notably microcystins. The toxins were heterogeneously distributed through the products, indicating a wide variation in consumer exposure. The study concluded that some form of monitoring is needed to ensure the safety of these products, perhaps encouraging also the use of cultured algae as opposed to that gathered from the "wild".

Summary

In summary, blue green algae are ubiquitous in surface waters throughout the year in subtropical climates such as Florida, and they are associated with frequent toxic blooms. Both occupationally and recreationally humans can be exposed via dermal and aerosol routes, as well as through consumption of drinking water and possibly contaminated foods. The human health effects associated with the blue green algal toxins are predominantly by inference from their known health effects in a wide variety of organisms, especially neurotoxicity, hepatotoxicity and tumor promotion.

Short term and long term health effects have not been thoroughly evaluated in persons with occupational, recreational and consumption exposure to blue green algae and their toxins (NHMRC 1994). Countries which do not have adequate supplies of treated water for their populations are at particular public health risk associated with blue green algal toxins, as are also children infants and animals. Current drinking water treatment practices in the US do not regularly monitor , or necessarily remove these toxins from the drinking water since this would involve extremely expensive measures (J Burns, SFWMD, verbal communication, Falconer 1989, Volterra 1993, Falconer 1999, Heinze 1999). Even with treatment, low level chronic exposure to the carcinogenic hepatotoxins are possible in persons consuming drinking water derived from surface water drinking plants in Florida and other parts of the US.

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