CYANOBACTERIA

AKA *BLUE-GREEN ALGAE*

WHAT WE KNOW ABOUT EXPOSURES AND HEALTH EFFECTS

Topics to Discuss

1. Who/what are the main players?
2. Cyanobacteria Exposure and Effects: Incidents and Studies
3. Risk assessment for exposure to cyanobacteria toxins

1. Who/What are the Main Players?

- Most taxa are not a problem…
  - They occur in all lakes and streams and are a natural part of the environment.
  - Some are used as food supplements (*Spirulina*)

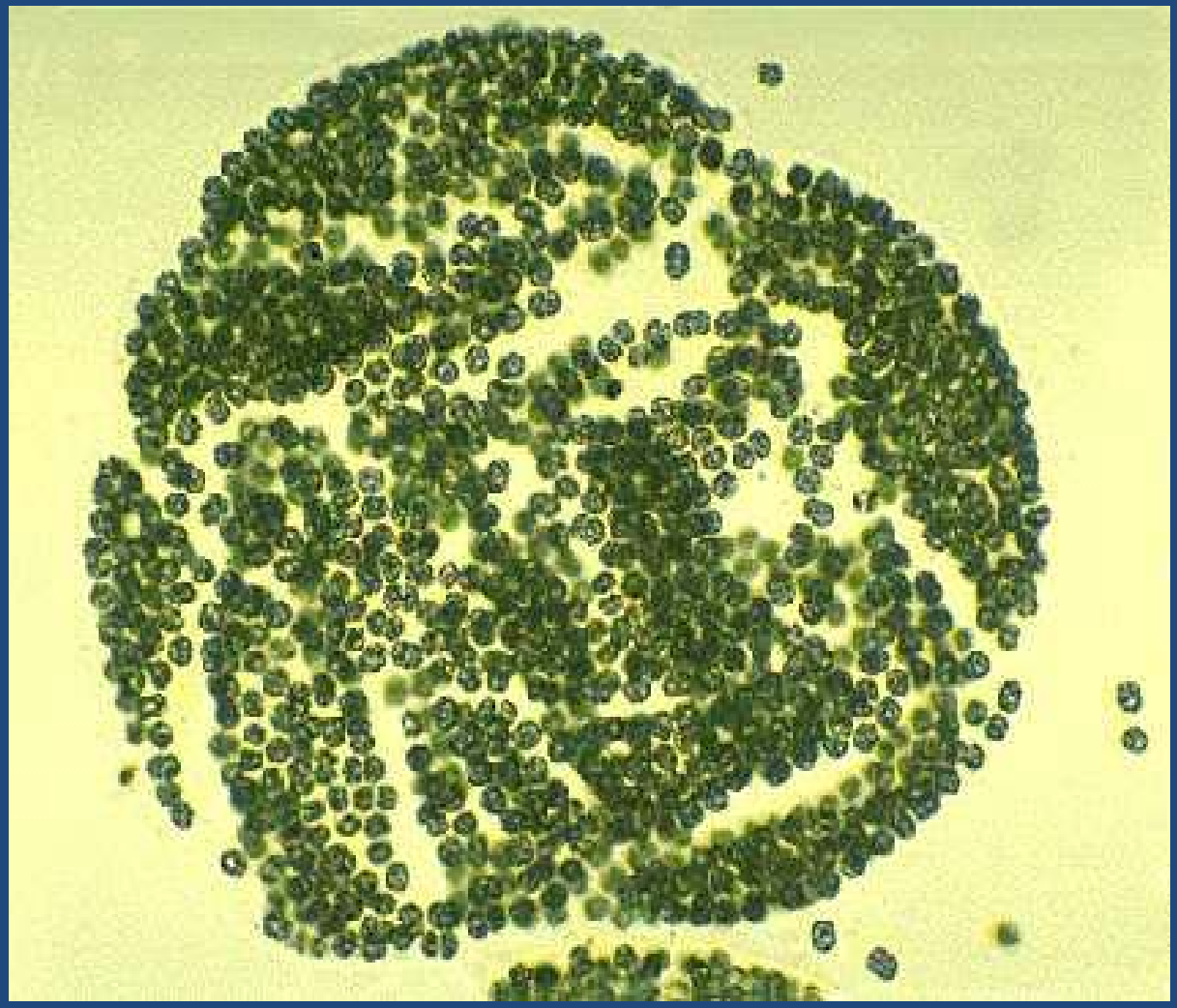
but *… … … … … … … … … … … … … ….*

Cyanobacteria* known to produce toxins

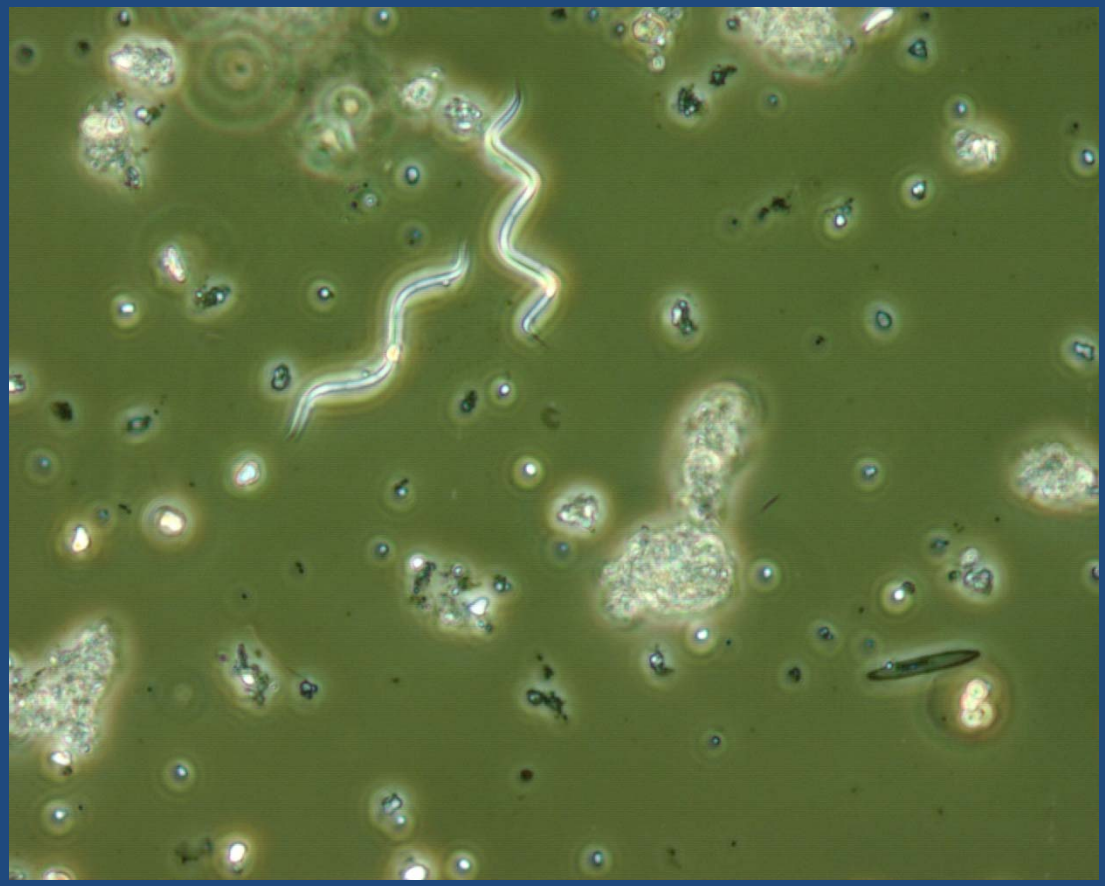
Neurotoxins	Hepatotoxins	Dermatotoxins	General Cell Toxin	Irritant
Anabaena	Microcystis	Lyngbya	Cylindrospermopsis	Most species
Aphanizomenon	Anabaena	Planktothrix	Raphidiopsis	
Oscillatoria	Cylindrospermopsis	Schizothrix	Aphanizomenon	
Cylindrospermopsis	Oscillatoria		Anabaena	
Synechocystis	Nostoc			
Pseudanabaena				
Lyngbya				
Nodularia				
Nostoc				

*partial list

Microcystis



Cylindrospermopsis




10 µm

Compounds of potential concern for cyanobacteria exposure*

Neurotoxins	Hepatotoxins	Dermatotoxins	General Cell Toxin	Irritants
Anatoxins	Microcystins**	Lyngbyatoxins	Cylindrospermopsins	LPS
Saxitoxins	Cylindrospermopsins	Aplysiatoxins		
BMAA	Nodularins			

* Partial list

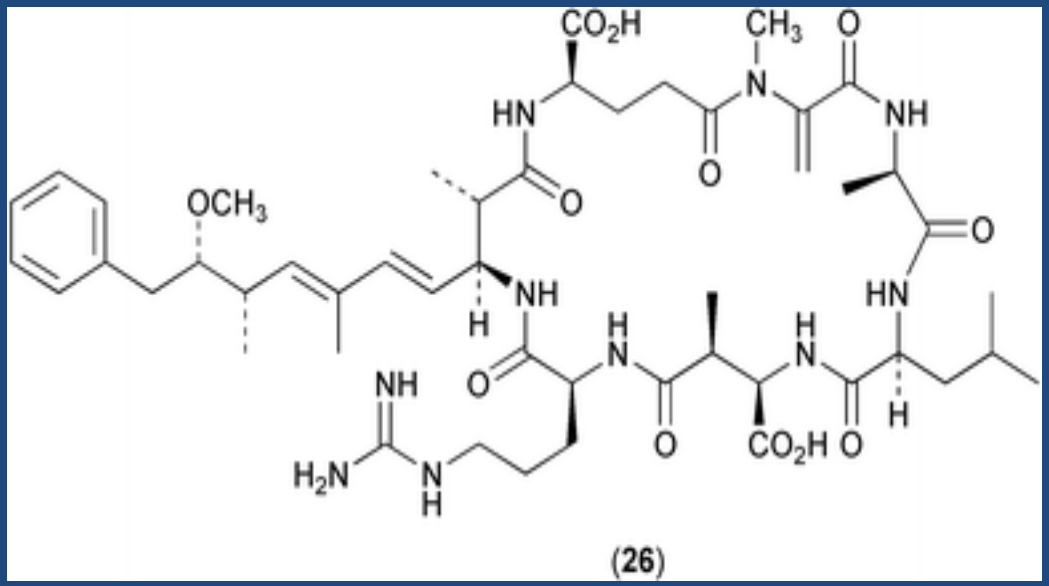
**more than 60 varieties

Potency of Various Toxins

Toxin	LD_{50} (ug/Kg)*
Microcystin	**20 - >1500**
Cylindrospermopsin	**200**
Nodularins	**30-60**
Anatoxin-a(s)	**20-40**
Anatoxin-a	**200-250**
Lyngbyatoxin	**250**
Saxitoxin	**6**
Strychnine	1500-2000
Ricin	2-30
Dioxin	22,000
Western Diamondback	2,000 - 18,500

*<50 ug/Kg is considered "highly toxic"

Microcystin



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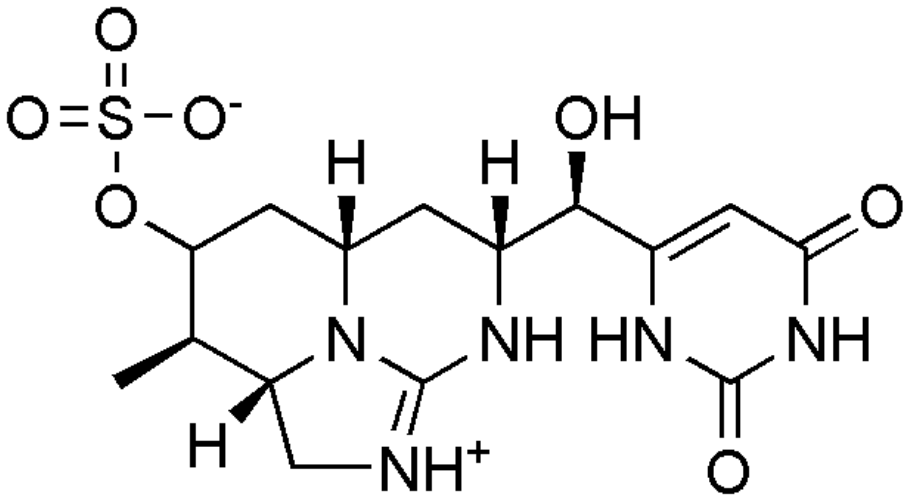
Cylindrospermopsin



2. Cyanobacteria Exposure & Effects:

Incidents and Studies

Some notable reports……

Case Report – Exposure to Cyanobacterial Toxins

- Carauaru, Brazil
  - Hemodialysis reagent prepared with water from a reservoir contaminated with toxic cyanobacteria
    - *Microcystis, Anabaena, Anabaenopsis, Aphanizomenon, Oscillatoria*
  - 126 patients treated
  - 126 patients became ill
  - 108 patients with liver injury
  - 60 died (mostly from liver injury)

Case Report – Exposure to Cyanobacterial Toxins

- Paulo Alfonso, Brazil
  - High levels of *Anabaena* and *Microcystis* in drinking water reservoir
  - Hundreds of hospital admissions
  - ~6 deaths/month from gastroenteritis

- Many other studies have linked illness with drinking HAB contaminated water.

Canadian Study of Health Effects from Cyanobacteria Exposure

Levesque (2009)

Variables			
Drink ***Treated*** Water from Lake with HAB		RR	95% CI
No		**1.00**	
Yes	Ear symptoms	**6.10**	2.5-15.0
	Skin symptoms	**2.65**	1.1-6.4
	Muscle pain	**5.16**	2.9-9.1

What do we know about recreational exposure?

- Swimmer, skier, boaters, etc. can be exposed to water by:
  - Dermal contact
  - Ingestion
  - Inhalation

Recreational Exposure
The Historical Record

- Three types of evidence for recreational impacts:
  - Incident/case reports
  - Epidemiologic studies
  - Controlled studies

The Historical Record Incident Reports

- A number of reports have attributed human illness and exposure to cyanobacteria.
  - Fairly well documented (large number of reports)
- Most of these are anecdotal, however,….
  - rates of exposure have been high enough to make sound conclusions about exposure:effect relationships.
- Confounding problems are:
  - there is no good biomarker for exposure
  - symptoms are similar to many other causes of illness

Symptoms Reported from Case/Incident Reports

Hayfever-like	Dermatologic	Gastrointestinal	Mixed Symptoms	Death
Conjunctivitis	Rash	Diarrhea	Most common	Animals
Rhinitis	Irritation	Vomiting		Human?
Sneezing	Blotching	Nausea		
Respiratory distress	Itching	Abdominal Pain		

A reported death from recreational exposure

- Wisconsin, 2002
- 5 teenagers swam in golf course pond.
  - 3 developed minor symptoms.
  - 2 had their head under water for some time and developed major symptoms.
    - One developed diarrhea and abdominal pain
    - The other developed nausea and vomiting that progressed to shock, seizure, and heart failure.
      - Deceased was found to have acute heart damage (no evidence of pesticides, pathogens, or parasites)
      - Anatoxin-a found in blood and stool of both teens.

Argentina Incident Report

- Jet Skier in lake with cyanobacteria bloom for 2 hours.
  - *Microcystis* - ~35,000 cells/mL
  - Microcystin – 48.6 ug/L
- With a few hours developed:
  - Nausea, vomiting, muscle weakness
- Within a few days:
  - Respiratory distress, renal failure, increase in liver enzymes, increase in leukocytes
- Patient discharged from hospital after 20 days.

Epidemiologic Studies

- Limited in numbers
  - Difficult to set up a study beforehand
    - Crystal balls hard to find (non grant-eligible expenditure)
  - Typical design:
    - interviewing lake visitors after a visit
    - quantify cyanobacteria
      - Toxins
      - Biomass estimation

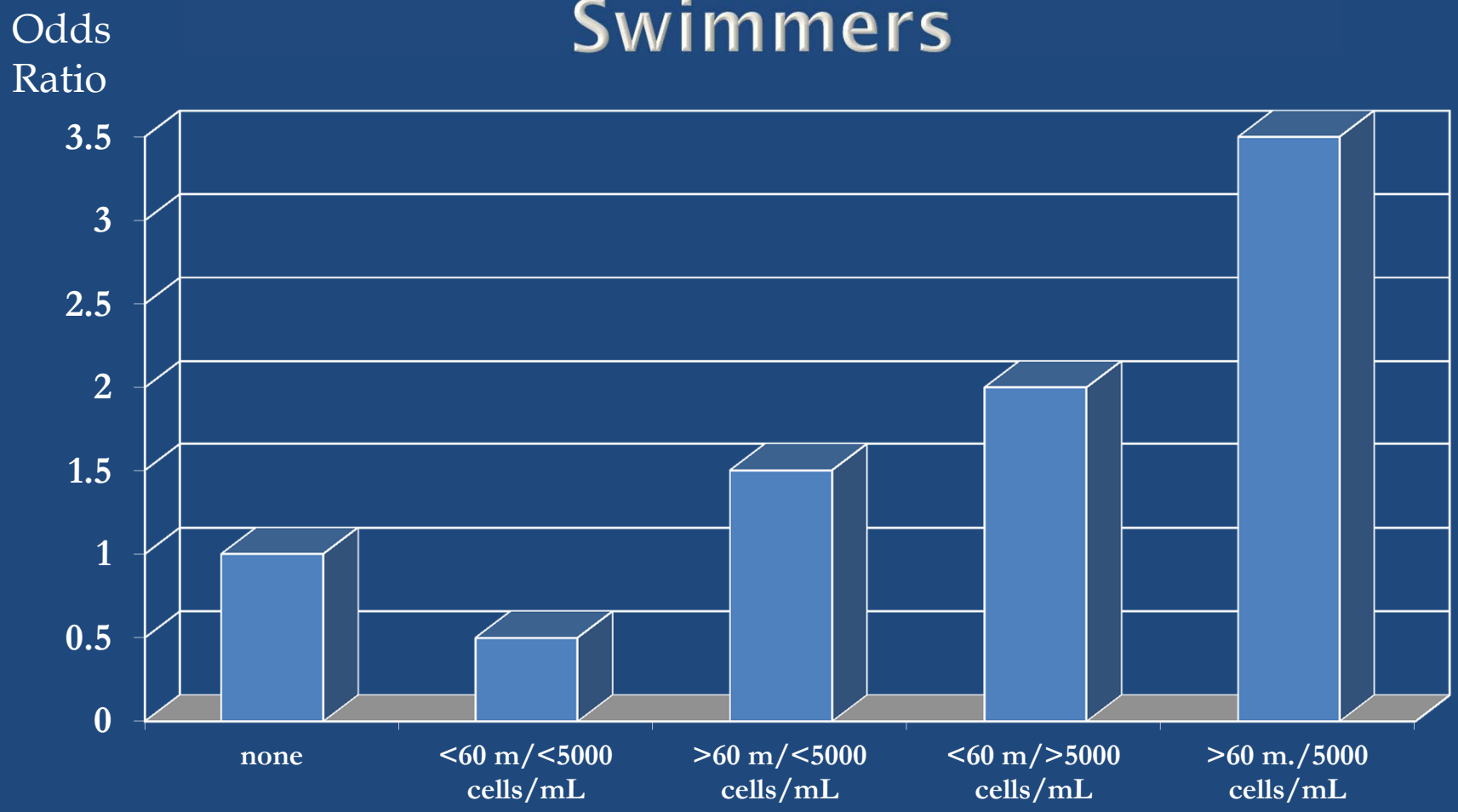
Results of Epi Studies

1. Australia and U.S. (Stewart et al, 2006)
   - Interviewed 3,193 lake visitors
   - Visitors exposed to high levels of cyanobacteria were:
     - More likely (OR=1.7) to report a symptom.
     - More likely (OR=2.1) to report ***respiratory*** symptoms.
     - Toxin levels were very low

Results of Epi Studies

2. Australia (Pilotto et al, 1997)
   - 295 participants exposed to cyanobacteria
     - Several genera present
   - Symptoms were more likely if:
     - Higher number of cells (OR=2.9)
     - Higher contact time (OR=2.7)
     - High contact time and high cells (OR=3.4)
     - Cold and flu symptoms most common
   - No correlation with hepatotoxins

Australian Swimming Study
Occurrence of Symptoms in Swimmers



Canadian Study of Health Effects from Cyanobacteria Exposure

Levesque (2009)

Variables		Symptoms	
Recreational contact with cyanobacteria		RR	95% CI
No		**1.00**	-
	Cyanobacteria counts		
Yes	<20,000 cells/mL	**1.52**	0.7-3.5
	20,000- 100,000 cells/mL	**2.71**	1.0-7.2
	>100,000 cells/mL	**3.28**	1.7-6.4

*G I symptoms plus respiratory, eye, skin muscle, etc.
Most common complaint = respiratory symptoms
Microcystin levels very low.

Controlled studies

- Several studies have examined the effects of directly placing cyanobacteria on skin in volunteers.
- Australia – (Pilotto et al, 2003)
  - Patches with cyanobacteria were applied to healthy volunteers
    - *Anabaena, Microcystis, Cylindrospermopsis, Nodularia, Aphanocapsa*
    - ~20% of subjects developed a rash
      - No difference between toxin and non-toxin producing strains.
      - Reactions were seen at <10,000 cells/mL

Animal deaths

- There have been numerous reports of pets and livestock dying after drinking cyanobacteria-contaminated water.

Suspected/Confirmed Dog Deaths – U.S. 2007–2011

Description	Number
Number of events associated with HAB reported	55
Number of dogs	63
Number attributed to anatoxin (a & a(s)	12
Number attributed to microcystin	3
Number of cases where HAB was biochemically confirmed	8(13%)
Number/% cases reported in literature*	0

* Peer reviewed

3. Risk Assessment

Can we quantify recreational exposure?

- Yes!!!!!!!!!!
  - Using standard exposure calculations
- After measuring dose, we can compare this to Tolerable Daily Intake (TDI) values.
  - TDI is the amount of a substance that can be consumed without appreciable risk.

Tolerable Daily Intake (TDI) for microcystin

- Based on animal experimentation in mice looking at liver changes after exposure to microcystin:
  - It was determined that the TDI should be:
  - TDI Average adult (60 kg) = 2.4 ug/day
  - TDI Average child (10 kg) = 0.4 ug/day

Ingestion Exposure

- We know that:
  - the average swimmer ingests between 100-200 mL of water.
  - 100,000 cells/mL of ***Microcystis*** is capable of producing **20** ug/L of microcystin.

Ingestion Exposure

- Therefore……
  - Ingestion of 100 mL of water (100,000 cells/mL) while swimming =
    - 0.1 L * 20 ug/L = **2.0** ug dose of microcystin
  - Approaches the TDI (2.4) for adults
  - Exceeds the TDI (0.4) for children
  - Assumed to represent a *moderate* risk of health effects.

What can we conclude about recreational risks?

- Exposure to cyanobacteria from recreation presents a health risk.
  - Children are likely to be more exposed than adults.
- There is a significant risk of symptoms when toxins are at low levels or even absent.
- The presence/absence of multiple species and toxins makes standard setting very difficult.

Conclusions

- We have a problem in Oklahoma.
  - Large blooms are certain to happen again.
  - The situation is likely to get worse unless we take measures to fix it.
    - Reducing nutrient loading
- We have a very inadequate monitoring system to detect and report problems.

A Few Big Questions

- Are the frequency and types of reported symptoms enough to prompt warnings?
- Are there any reasons to think that the environmental conditions in Oklahoma produce different types of cyanobacteria blooms?
- Are there any reasons to think that users of Oklahoma lakes respond differently to cyanobacteria than other populations?

Summer 2011 Microcystin Values From Grand Lake

Site	Type of Sample	Microcystin (ug/L)
Duck Creek	Grab	9.9
"	Tow	358
"	Grab	2.6
"	Tow	210
Horse Creek	Grab	49
"	Tow	125
"	Grab	1.2
"	Tow	98
Argentina Case Report		***49***

Do we know enough about risk to say this?