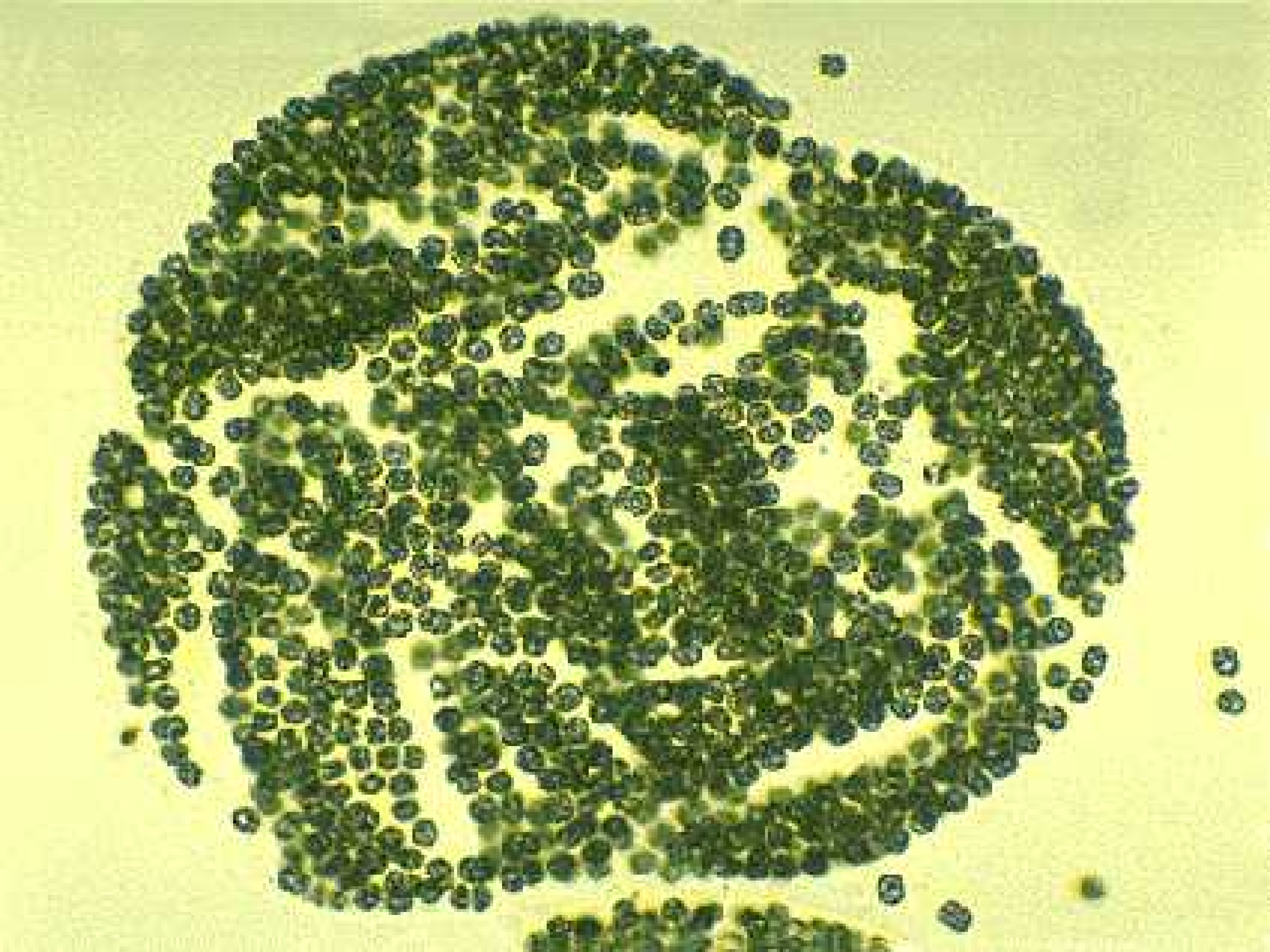
CYANOBACTERIA EXPOSURE RISKS FROM RECREATION

HYPE OR HAZARD?

TOPICS TO OUTLINE

1. Current situation in Oklahoma
2. What do we know about recreational exposure?
3. Exposures of concern
4. The historical record
5. What should we do with the information?



CURRENT SITUATION

- Recreational exposures to cyanobacteria have become an increasing concern as blooms have become more frequent.
  - Nationwide issue
- Many states are working to develop plans/procedures to deal with blooms.
- In the absence of federal guidance, states have adopted a number of approaches to address the problem.

CURRENT SITUATION IN OKLAHOMA

- Oklahoma is also trying to figure out what to do when blooms happen;

however.....

- this is proving to be a difficult issue to resolve.
  - A little bit of scientific uncertainty
  - A lot of politics

SCIENTIFIC UNCERTAINTY

- There are uncertainties about the levels of exposure and effect (this is true for ***all*** compounds).
  - Some of the public is hesitant to make conclusions in the presence of uncertainties.
  - Some of the public use the presence of uncertainties as a tactic to block implementation of controls (common strategy)
  - Current wave of general distrust of government and scientists.

POLITICS

- Politics
  - The posting of warning signs scares away customers.
    - Economic costs are often a driver of political decisions.

THE SITUATION WE ARE FACING

- Opinions (as expressed at recent public meetings):
  - This is a potentially serious public health issue.
  - This is not really a big deal.
  - This is just all hype – no one has ever gotten sick.
  - Advisories hurt the economy.
  - Swimming is inherently risky. People drown all the time so there is no reason to tell them about this relatively minor risk.

2. WHAT DO WE KNOW ABOUT RECREATIONAL EXPOSURE?

WHAT DO WE KNOW ABOUT RECREATIONAL EXPOSURE?

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

CAN WE QUANTIFY RECREATIONAL EXPOSURE?

- Yes!!!!!!!!!!
- All exposures are a product of contact time and dose.
  - Exposure is the amount of cyanobacteria or toxin(s) present.
  - Contact time can be estimated as the time spent in the water.
  - Dose = amount of cyanobacteria/toxin(s) present * contact time

INGESTION EXPOSURE

- Studies have shown that the average swimmer ingests between 100-200 mL of water.
  - The effects of ingestion are based on toxins and/or biomass present and the relative ability of the body (mostly the liver) to biotransform (activate/deactivate) toxic compounds.

STANDARD CHEMICAL DAILY INTAKE (CDI) CALCULATION FOR INGESTION EXPOSURE

- I = (C x CR x AF x EF) /BW
  - I = intake (mg/kg/d)
  - C = chemical concentration (mg/L)
  - CR = contact (exposure) rate (L/d)
  - AF = adsorption factor (unitless)
    - assumed to be 1 unless other data is available
  - EF = exposure factor (unitless)
    - product of the exposure frequency and years/total days over which the exposure is averaged)
  - BW = body weight (Kg)

CALCULATIONS AND ASSUMPTIONS MADE BY WHO FOR MICROCYSTIN EXPOSURE

- 20,000 cells/mL of microcystin-producing species can produce 2 - 10 ug/L of microcystin .
  - Shown experimentally
- Consumption of 100 mL would result in a dose of 0.2 - 1 ug of microcystin/day
  - This is below the Tolerable Daily Intake for microcystin
    - 2.4 ug/day for adults; 0.4 ug/day for children
  - Assumed to represent a low risk

TOLERABLE DAILY INTAKE (TDI) FOR MICROCYSTIN

- Based on animal experimentation in mice
  - Liver changes were seen at 40 ug/kg body wt./day
  - This number was divided by 1000 (safety factors*)to produce a TDI of 0.04 ug/kg/day

    * safety factors considered factors such as interspecies variability. This is standard methodology in toxicology.

  - Average adult = 60 kg*0.04 = 2.4 ug/day = TDI
  - Average child = 10 kg*0.04 = 0.4 ug/day = TDI

CALCULATIONS AND ASSUMPTIONS MADE BY WHO FOR MICROCYSTIN EXPOSURE

- At 100,000 cells/mL of ***Microcystis…***
  - Experimentation has shown that individual cells of *Microcystis* can produce 0.2 pg/cell.
    - 100,000 x 0.2 = 20,000 pg/mL = 20 ng/mL = ***20 ug/L***

- Assuming ingestion of 100 mL while swimming….
  - 0.1 L * 20 ug/L = 2.0 ug
- Approaches the TDI for adults
- Exceeds the TDI for children
- Assumed to represent a moderate risk

DERMAL EXPOSURE

- The average adult has approximately 19400 cm^2 of body surface area.
  - The skin's ability to absorb toxins varies by area.
- Exposure is directly related to contact time.
- A very important factor is the sensitivity of the individual to cyanobacteria (or any other compound) which can vary greatly.
  - Individuals can become sensitized with repeated exposure.

CHEMICAL DAILY INTAKE (CDI) CALCULATION FOR DERMAL EXPOSURE

- Water dermal intake =
  - (C x P x SA x ET x EF x ED) x (1 liter/1000 cm^3)/BW
    - C = contaminant concentration in water (mg/L)
    - P = permeability constant (cm/hr)
    - SA = exposed body surface area (cm^2)
    - ET = exposure time (hours/day)
    - EF = exposure frequency (days/year)
    - ED = exposure duration (years/total days exposed)
    - BW = body weight (Kg)

INHALATION EXPOSURE

- Inhalation of aerosols is likely to occur due to the nature of recreational activity and our climate.
  - Frolicking (don't get to use that word much) agitates the water and generates aerosols.
  - Wind action generates aerosols
- Inhaled aerosols can have various effects depending upon the nature of the aerosol.
  - Dermatotoxins versus cell toxins versus irritants.

CHEMICAL DAILY INTAKE (CDI) CALCULATION FOR INHALATION EXPOSURE

- Air inhalation intake =
  - (C x IR x AF x EF)/BW
    - C = contamination concentration (mg/M^3)
    - IR = inhalation rate (M^3/day)
    - AF = absorption factor (unitless)
      - assumed to be 1 unless data indicate less
    - EF = exposure factor (unitless)
      - product of exposure frequency (events/year) and exposure duration (years/lifetime)
    - BW = body weight (Kg)

INHALATION EXPOSURE

- Many reports list respiratory symptoms with swimming exposure to cyanobacteria.
- This is probably an under-appreciate route of exposure, especially to lipopolysaccharides.
  - Likely important for other toxins as well
- OUHSC will be conducting experiments this summer to quantify LPS aerosolization rates.

3. EXPOSURES OF CONCERN

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

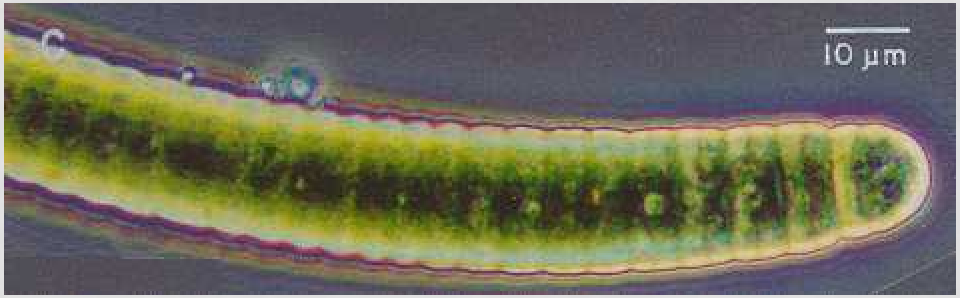
A WORD ABOUT OTHER TOXINS….

- Many compounds with toxic effects produced by cyanobacteria have been identified; however,……
- Toxic effects in swimmers occur even when none of these are present (or when they are so low that they shouldn’t produce effects)
- We do not know if this is due to the presence of unknown compounds or if cyanobacteria as a mass protein source may trigger effects, independent of individual toxic compounds.
    - Probably a little of both…

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				


100 µm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HEALTH EFFECTS DATA FOR CYANOTOXINS

- The best data available is based on animal models.
- There is a well-developed literature characterizing the effects of individual toxins including:
  - LD_{50}
  - Toxicological mechanisms
  - Pharmacodynamics

TOXICITY OF CYANOTOXINS

Toxin	LD_{50} (ug/kg)
Microcystin	60
Anatoxin-a	200
Cylidrospermopsin	2
Saxitoxin	10

POTENCY OF VARIOUS TOXINS

Toxin	Amount (mg) needed to kill a 220 pound person*
Microcystin	5-10
Cylindrospermopsin	200-600
Nicotine	100
Copperhead	1100
King Cobra	130-160
Diamondback Rattlesnake	270-560
Botulinum toxin	0.0001

*Based on the LD50 which is the amount of toxin that it takes to kill 50% of a test population. The smaller the number, the more potent the toxin.

4. THE HISTORICAL RECORD

THE HISTORICAL RECORD

- Three types of evidence for recreational impacts:
  - Incident 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 (numbers of people and amount of cyanobacteria) 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 INCIDENT REPORTS

- Hayfever-like
  - Conjunctivitis
  - Rhinitis
  - Sneezing
- Dermatologic
  - Rash
  - Irritation
  - Blotches
- Gastrointestinal
  - Nausea
  - Vomiting
  - Diarrhea
  - Abdominal pain
- Mixed symptoms
- ***Death***

SYMPTOMS REPORTED FROM INCIDENT REPORTS

Hayfever-like	Dermatologic	Gastrointestinal	Mixed Symptoms	Death
Conjunctivitis	Rash	Diarrhea	Most common	Animals
Rhinitis	Irritation	Vomiting		Human?
Sneezing	Blotching	Nausea		
	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.

ANIMAL DEATHS

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

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
       - Microcystin – 2 hits – (1 ug/L and 12 ug/L)
       - Cylindrospermopsin – 7 hits (1-2 ug/L)
       - Saxitoxin – not found
       - Anatoxin-a – one hit (1 ug/L)*

       * Symptoms were significantly associated.

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)
   - No correlation with hepatotoxins
   - Symptoms were reported at cells = 5,000/mL
   - High cell counts were considered to be >80,000/mL

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

RESULTS OF EPI STUDIES

- Other studies (4) have not found statistically significant results.
  - 3 were cross-sectional design
  - 1 was case-control

WHAT CAN WE CONCLUDE ABOUT RECREATIONAL RISKS?

- Risk is elevated when toxins are present.
  - High levels of toxins represent a serious health risk.
- There is a significant risk of symptoms when toxins are at low levels or even absent.
  - 20-30% of exposed have shown symptoms.
    - This may reflect the general level of sensitive members in the population.

DO WE KNOW ENOUGH ABOUT RISK TO SAY THIS?

OTHER IMPORTANT CONSIDERATIONS

- Potential to produce toxins is a very important concept.
  - Populations can very rapidly (hours) move from producing no toxin to producing lots of toxin.
- Risks from most toxins have not been adequately assessed.

5. WHAT SHOULD WE DO WITH THE INFORMATION?

WHAT SHOULD WE DO WITH THIS INFORMATION?

- Most jurisdictions set public health advisory policies based on cell counts and/or levels of toxins (usually microcystin)
- These are usually some variation of the guidelines set by WHO
  - WHO guidelines are based on potential of cells to produce microcystin
  - Potential dose received by stated toxin levels (usually microcystin)

WHAT IS AN ADVISORY?

- An advisory is merely a tool to inform the public of potential risks presented by the presence of cyanobacteria.

THE IMPORTANCE OF A TWO-PRONGED APPROACH

- Cell counts provide the best estimate of risk.
  - Health effects are seen in the absence of toxins
  - Populations can rapidly switch on toxin production.
  - Most cost-effective measure.
- Toxin measurement identifies the most hazardous compounds.
  - Toxins can be present long(weeks) after populations crash.
  - Toxin analysis can be very expensive.
    - ELISA kits are available for some toxins
    - LC/MS is needed for some toxins or variants of common toxins.
      - Microcystin has ~70 variants

WHO GUIDELINES FOR BLUE-GREEN ALGAE LEVELS AT BEACHES

Risk of Adverse Health Effects	Cyanobacteria (cells/mL)	Microcystin-LR (ug/L)	Recommended Action
Low	<20,000	<10	?
Moderate	20,000-100,000	10-20	?
High	100,000-10,000,000s	20-2,000	?
Very High	>10,000,000	>2,000	?

WHAT ARE THE "RECOMMENDED ACTIONS"

- Varies by jurisdictions from advisories to warnings to beach closures.
- Oklahoma has followed the WHO guidelines and issued a number of advisories last year.
  - Some park managers closed beaches

ACTIONS THIS YEAR IN OKLAHOMA

- A number of people were called to the Capitol this spring to discuss Oklahoma's policy.
- Several groups prepared reports:
  - Monitoring
  - Health Effects
  - Public Outreach
- This information is being used (?) to develop legislation.

STATUS OF CURRENT POLICY IN OKLAHOMA

- Legislature working on language to amend Oklahoma’s “policy” for cyanobacteria
- Economic interests are pushing for a policy stating that ***both*** cell counts and toxin levels must be present at some level before an advisory can be issued.
  - 100,000 cells/mL ***and*** microcystin >20 ug/L before an advisory can be issued.
  - If this policy had been in effect last year, advisories would have been issued on only one reservoir.

WHAT WILL THE NEW POLICY MEAN?

- No other toxin can be considered in determining whether to issue an advisory.
- No cell/count, no matter how high, will be enough to prompt issuance of an advisory (in the absence of microcystin >20 ug/L)

POSSIBLE INFLUENCES ON LEGISLATIVE DECISION-MAKING

- The legislature performed an independent risk evaluation and derived their numbers from this.
- The legislature does not believe the published literature and has its own ideas.
- The legislature thinks that we shouldn't inform the public of risk unless it is severe.
- The legislature does not accept the report of the Health Effects of Cyanobacteria Committee.

other possibilities?

THE SAD TRUTH

- The sad truth is that some decision-makers in this state are putting economic interests before public health.
  - Of course this ignores the economic interests of those who become ill.
- The current legislation being considered will not provide adequate public health protection.

WHAT *SHOULD* WE DO?

- Some of the public has expressed the opinion that this is no big deal since "no one is dying from this stuff"
  - This is generally a true statement.
  - Typical symptoms are not severe: diarrhea, rash, respiratory distress, vomiting - but may require medical treatment.
- If you went to the lake and you had any of these symptoms would it be a big deal to you?
  - How about your children?

WHAT WOULD THE AVERAGE CITIZEN WANT TO KNOW?

- Would the average citizen want to know that their child has a 1 in 5 chance of becoming ill if they swim in a lake? (1 in 10?) (1 in 100?)
- Should we inform them of this risk?