Additional Q&A for **Freshwater Science: Health Impacts of Algal Toxins in the Context of Chronic Illnesses**

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1. **We know that phosphorus and nitrogen are major contributors to HABs and the major source of P and N comes from agricultural runoff. In your work with HABs, have you discovered any other sources of phosphorus and nitrogen other than agriculture?**

   Our work is focused on the potential adverse health effects following exposure to environmental toxins such as those produced by HAB's. For sources of phosphorus and nitrogen, there is excellent ongoing research at the University of Toledo Lake Erie Center (Dr. Thomas Bridgeman), The Ohio State University Stone Laboratory (Dr. Justin Chaffin) and Bowling Green State University (Dr. George Bullerjahn) among others.

2. **Is there any study now complete with specific health risk factors that consider exposures and long-term risks?**

   We are not aware of any long-term human health studies completed to date, but this is a very important area of investigation.

3. **Do you have any thoughts on the health impact of algal toxins on progressive neurological disease, specifically those tied to inflammatory disease such as multiple sclerosis?**

   Members of the organic anion transporting polypeptide (OATP) family that participate in the uptake of HAB toxin's such as microcystin are expressed in cells of the blood-brain barrier and have been shown to transport microcystin and there are some limited in vitro (i.e. cell based) neural cell line studies in this area. While it is possible that microcystins could potentially cross the blood brain barrier, to our knowledge there are no thorough studies that have directly linked these toxins to diseases such as multiple sclerosis, however this is an important area that requires further investigation.

4. **When the factsheets that were shown at the end of the presentation are ready, where will those be posted?**

   The fact sheets will be posted on the Great Lakes Commission HABs Collaborative website at [glc.org/work/habs/publications](http://glc.org/work/habs/publications). The fact sheets are undergoing a final round of revisions and approvals and we hope to have these posted on the website soon.
5. I've heard that some other compounds/substances in HABs (aside from the actual toxins), such as lipopolysaccharides, can induce allergic and other reactions in some people. Are you aware of any research into or evidence of this?

While lipopolysaccharides from various bacteria are capable of inducing a variety of immune responses, whether the lipopolysaccharides contained in the cyanobacteria that form HABs can induce allergic reactions in humans has not been firmly established or refuted.

6. Different MC congeners have different toxicity and natural HABs have a mix of congeners. How different would the results be if you used MC-RR or MC-LA or a mix of congeners?

Excellent question. Our studies have focused on MC-LR as a prototypical and abundant HAB toxin. We are in the process of investigating additional congeners such as MC-RR and MC-LA and will share the results as soon as we have completed these studies.

7. One way we try to account for the variability in susceptibility from person to person is to apply an uncertainty factor of 10 to the NOAEL or LOAEL. Are the doses that you used within that factor of 10 designed to account for inter-individual variability?

Yes, in order to keep studies comparable with others in the literature, we follow the published NOAEL and LOAEL guidelines for microcystin-LR which were established in normal healthy animal models. We have found that in models of pre-existing nonalcoholic fatty liver disease, even microcystin exposures below the NOAEL and LOAEL are capable of inducing further liver injury.

8. Did your study compare annual repeat exposure by healthy people versus people with preexisting conditions?

No, our data from human exposure events is only from retrospective analysis of national emergency room data, so additional work is needed to understand the health effects in healthy and those with pre-existing conditions after long term or low dose exposures.

9. Can the histology methods you used with dosed mice be applied to wildlife (ex: fish, water snakes, eagles) to determine if they are being impacted by MCs? Would you expect similar results depending on if the animal had healthy vs unhealthy liver?

We recently reported that healthy Lithobates catesbeiana (American bullfrog) tadpoles exposed to HAB toxins containing 1 μg/L (1 nmol/L) of total microcystins for only 7 days results in significant liver and intestinal toxicity using a combination of techniques including Hematoxylin and eosin (H&E) histology staining (Su RC, et al.. Harmful algal bloom toxicity in lithobates catesbeiana tadpoles. Toxins. 2020. 12(6), 378; doi.org/10.3390/toxins12060378). Our results using models of pre-existing disease (liver and inflammatory bowel disease) suggest that these diseases may increase susceptibility to the adverse health effects of MC-LR exposure.

10. Student Question: How does the algae get into the water?

Algal blooms can result from the transfer of algae spores and excess nutrients (particularly phosphorus and nitrogen) spilling into water bodies creating an abundant food source for the cyanobacteria (blue-green algae) to grow given the right conditions such as a warm climate.
11. Student Question: How long do HABs last?
The time length of a HAB is dependent on several factors including the amount of nutrients present and the climate. HABs typically occur during late summer and early fall lasting 3-5 months.

12. Student Question: What makes the HABs so toxic and deadly?
Harmful algal blooms composed of cyanobacteria (blue-green algae) can be dangerous due to the release of cyanotoxins such as microcystin-LR. In addition to microcystin-LR, there are over 200 variants of cyanotoxins that can be released by cyanobacteria. These toxins are deadly because they stop a very important biological process (called “dephosphorylation”) that is needed for cells to function properly.

13. Student Question: Are HABs invasive?
HABs can become invasive under certain conditions such as a high nutrient load (particularly phosphorus and nitrogen) and a warm climate. HABs have been reported to occur not just in the Great Lakes, but globally.

14. Student Question: How often can these conditions occur? HABs and the effects?
Many environmental factors such as excess nutrient load and warm temperatures contribute to the frequency of HABs. HABs typically occur during late summer and early fall lasting 3-5 months.

15. Student Question: What about measuring with a breath test to detect the HABs?
Studies are under active investigation to collect breath samples in order to determine the presence of HAB toxins and the response of the lungs to HAB toxins.

16. Student Question: How long did it take to learn all of this?
Scientists have been working on studying HABs and their effects for many years, although as HAB’s have been more common throughout the world, research has intensified.