# Cyanobacterial toxins: a growing health concern

Cyanobacteria first appeared on Earth over 3.5 billion years ago. Over time, they invaded many ecosystems and are now widely distributed geographically. These microorganisms were long considered as plants, since they combine bacterial properties with some of the characteristics specific to algae.

Eutrophic freshwater (i.e. water that is rich in nutrients such as nitrogen and phosphorus) provides the ideal breeding ground for cyanobacteria. Although climate change is thought to play a role in the nature and intensity of cyanobacterial proliferation, human activity is also a contributing factor, in both the urban and rural environments. The input of nutrients associated with the pollution of surface water – as a result of manure or slurry spreading, agricultural fertilisers used near waterways, industrial effluent, insufficiently treated wastewater or sewage sludge – causes the level of eutrophication to rise. When this happens, we talk about algal blooms.

This type of proliferation can be seen primarily in hot, sunny weather with no wind, between late summer and early autumn, when waterways stagnate or flow more slowly and when nutrients are abundant.
The cyanobacteria present in algal blooms can release toxins that are highly dangerous to humans in some cases. These toxins fall into three groups according to their mechanisms of action and their toxicity: dermatoxins, hepatotoxins and neurotoxins.

The main circumstances and routes of exposure to these toxins are swallowing contaminated water, inhalation, or dermal contact during recreational water activities (swimming, water sports). Consuming fruit or vegetables irrigated with contaminated water, or eating aquatic organisms (fish and shellfish) [1] are also possible routes of exposure.

Cyanotoxins have many harmful effects on human health. Gastrointestinal disorders (nausea, vomiting) and a high temperature are the most frequently reported reactions. However, eye or skin irritation and rashes are also common, as are myalgia, and liver or kidney damage. However, the role of these toxins in the development of chronic – particularly neurological – disorders remains controversial from a scientific standpoint [2].
In France, regulations have been put in place for drinking water and recreational activities. The tresholds for acceptable cyanobacteria and/or cyanotoxins concentrations are set by different recommendations or regulations, depending on usage.

In the case of water intended for human consumption, regulations set a limit of 1 µg/L for microcystin-LR[1] [3] in water following treatment at a drinking water plant. This value corresponds to the highest post-treatment concentration that is not considered to carry a risk of acute toxicity.

Concerning the risks linked to swimming and water sports, the regional health agencies (ARS) are responsible for the health monitoring of water bodies declared as bathing sites in France. Based on the sampling results received, the ARS draft recommendations for the local authorities on the advisability of maintaining or suspending activities. It is then up to the mayors to decide whether or not to follow the suggestions of the ARS and to pass on the information to the players concerned. A decision tree has been put in place for the local entities managing water bodies. In the event of persistently high concentrations of cyanobacteria, a strict system of control is implemented, based on a visual inspection of the water (presence of bloom or scum, colour) together with microscopic observations. Three levels of management measures have been established, based on the quantity of cyanobacteria and toxins in the water. Depending on the level, measures will be put in place to limit or prohibit use of the water [4].

As part of its work, ANSES has developed two new toxicological reference values[2]: one for microcystin-LR [5] and one for cylindrospermopsin [6]. More broadly, these TRVs will be used by ANSES to study the health risks associated with the presence of cyanobacteria and their toxins in water intended for human consumption, swimming and other leisure activities[3].

1. Most common cyanobacterial toxin
2. A toxicity reference value (TRV) is a toxicological indicator used to qualify or quantify a risk to human health. It establishes a link between exposure to a toxic substance and the occurrence of an adverse health effect. It is specific to a duration (acute, subchronic or chronic) and route of exposure (oral or respiratory).
3. Request 2016-SA-0165

Last, fishery products must also be considered as a possible source of exposure. ANSES is currently engaged in studies that will seek to suggest the maximum acceptable concentrations in fish based on consumption data[4].

In the early 2000s, several rivers in France were severely affected by the spread of toxic cyanobacteria. Around thirty dogs were reported to have died, primarily in the Tarn (south-west France) and the Loue (eastern France) [7-8]. In summer 2017, almost twenty new cases of suspected canine poisoning were reported along the Loire, in which the dogs had swallowed water contaminated by cyanobacteria and/or cyanotoxins. The fatality rate was seen to be very high in these animals, at almost 50%. The dogs were observed to develop neurological symptoms, frequently associated with respiratory difficulties and a deterioration in their overall condition. The same occurred in summer 2018 [9]. Similar case series have been published in other countries. In one of the recent cases described, 12 dogs died after swimming in a lake near Berlin. All of them showed neurotoxic signs and toxins were detected in all cases [10]. This high rate of canine mortality suggests possible health risks for humans exposed to the same water. Yet few cases of human poisoning have been described in France.

To study the question in greater detail, ANSES and the French Poison control centres (PCCs) analysed the cases of human exposure to cyanobacteria reported to the PPCs between 1 January 2006 and 31 December 2018. Overall, 95 cases of exposure to cyanobacteria were identified, of which 58 were symptomatic.
The vast majority of intoxications observed took place during the last three years, mainly over the summer, in June, July or August. Most cases of exposure (27.6%) were located north of the Loire in Brittany, primarily in the Ille-et-Vilaine *département* (15.5%). The location of these cases is the same as for the cases of canine poisoning in France.
The male-female ratio was 1.15. The population concerned was relatively young, with an average age of 18.2 years and a median age of 12. Overall, ages varied from 2 to 59 years, with people over 40 accounting for just 12% of cases.

The symptoms observed were gastrointestinal in 75.9% of cases (diarrhoea, vomiting, nausea, stomach pain), dermal in 34.5% of cases (rashes, itching), neurological or muscular in 25.9% of cases (headaches, dizziness, myalgia) and general in 24.1% of cases (hyperthermia in particular). Neurosensorial or respiratory symptoms were observed in 5.2% of cases.
Symptoms were benign in 75.9% of cases and moderate in 24.1% of cases. There were no serious cases requiring admission to hospital.

Fifty-five people were exposed to cyanobacteria while practicing a water activity. The main exposure context was toxic algae bloom in bathing and/or water sports areas. Forty-nine people (84.5%) were exposed while swimming in a lake, pond or river, and four while practicing a water sport (canoeing, windsurfing, etc.). Two people were exposed while river fishing. Only three people were exposed as a result of consuming food or water. One person had consumed some water in a lake where swimming was forbidden owing to the presence of cyanobacteria. The second person had eaten a fish from a lake contaminated by cyanobacteria, while the third had consumed tap water in which cyanobacteria were detected.

In the vast majority of cases, the poison control centres did not have metrological data (number of cyanobacteria, types, levels of cyanotoxins). These data were available in only four cases, where the presence of cyanobacteria was confirmed at the bathing site. Moreover, most of the analyses confirming the presence of cyanobacteria were conducted after exposure and the appearance of symptoms.
Several cases stated that the people exposed had not seen the no-swimming signs.
However, four of those exposed were aware of the presence of cyanobacteria.

4. Request 2015-SA-0207

Further, regulations on bathing water require management of the health risk linked to cyanobacteria, based on analytical monitoring by cell counts[5]. It is interesting to note that several cases mentioned that "swimming was banned a few days after exposure owing to the presence of cyanobacteria at the bathing site". This could be explained by the time inevitably taken to collect the sample, send it to the laboratory and analyse the results. The site manager cannot otherwise take prompt enough action if the site is in fact polluted by toxic cyanobacteria. On the other hand, the analyses may have been conducted as a direct result of these cases of human poisoning.

The presence of cyanobacteria across all the world's continents is a growing source of concern, in view of the health risks for both humans and animals. Few studies to date have looked at human exposure to cyanobacteria, hence this first appraisal based on data from the French Poison control centres. The increase in the number of cases of exposure reported over the past three years may reflect a better understanding of this environmental issue, attributable in part to the media coverage of the many animal deaths, particularly in the Loire region. It may also indicate changes to the ecosystems causing the blooms.
The relatively low number of cases of poisoning in humans compared with other mammals [11] could be explained by the fact that spreading cyanobacteria sometimes form algal blooms, making the water look and smell unpleasant. As a result, people are unlikely to swim in the contaminated water and even less likely to swallow it.

The number of cases listed by the poison control centres is likely to be significantly underestimated. Given the non-specific symptoms and the lack of awareness concerning these intoxications, the diagnosis is rarely made, particularly as the symptoms tend to disappear quickly. Moreover, even when a diagnosis is made, it is rarely confirmed, owing to a lack of investigation (few samples taken, tests not widely available, etc.). As a result, most cases of exposure to cyanobacteria are probably never reported to the poison control centres.

Last, it is clearly necessary to issue wider recommendations for the general public, particularly in areas close to water bodies, where the problem is known, and at sites popular with tourists, at the time of year when cyanobacteria are likely to develop.

Efforts to increase awareness and to inform the population will involve putting up clearly visible signs on the risks associated with the presence of cyanobacteria in water used for swimming and other leisure activities. These signs will enable the population to recognise cyanobacteria and to avoid exposure.
Simple, visual signs illustrating a ban on swimming, fishing or water sports, similar to those already found in the Loire region and in Brittany, will serve to warn the population.

**Chloé GREILLET**

5. Number of cyanobacteria cells per ml

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