Chapter 1

Introduction

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CONTENTS

Safe drinking-water is of paramount importance for human health. Throughout history, access to drinking-water has been a prerequisite for the development of civilisations – and the loss of access often a key factor for their decline. Recognising the vital role of drinking-water for public health, the World Health Organization (WHO) dedicates a significant share of its efforts to promote the safety of water for today and for the future (Onda et al., 2012). With a human population reaching 10 billion by the mid of this century, the pressure on global drinking-water resources will not cease, and ongoing efforts in research, management and governance are needed to recognise, understand and mitigate health risks associated with water use. This includes further uses of water involving human exposure, particularly for recreation, and, depending on specific local or regional circumstances, also for irrigating crops, cooling water or dust suppression, for example.

Health hazards recognised in water today comprise infectious microorganisms (e.g., bacteria, viruses and protozoa causing gastrointestinal diseases), geogenic substances (e.g., arsenic, fluoride, uranium), industrial and agricultural chemicals (e.g., perfluorinated chemicals [PFCs], pesticides) and toxins produced by cyanobacteria – the subject of the first edition of "Toxic Cyanobacteria in Water" (Chorus & Bartram, 1999) and of the present volume.

Among the hazards considered in the Guidelines for Drinking Water Quality (GDWQ; WHO, 2017), infectious microorganisms are the most significant causes of mortality on a global scale, causing a substantial burden of disease via diarrhoeal illnesses such as cholera, cryptosporidiosis or retroviral enteritis (James et al., 2018; Roth et al., 2018; Prüss-Ustün et al., 2019). In contrast, the contribution of toxic chemicals in water to morbidity and mortality is rarely acute, and aside from a few geogenic chemicals, the impacts on health are less visible and less clearly attributable to chemicals. This applies particularly for carcinogenic compounds, the impacts of which accumulate over time. Thus, considering global causes of mortality and morbidity, data to estimate the disease burden through exposure to chemicals in water are typically lacking.

This is also true for cyanobacterial toxins: only a relatively low number of recorded cases of acute human intoxication are clearly attributable to these toxins (Wood, 2016). Nonetheless, like with other toxins potentially found in drinking-water, exposure to low, subacute concentrations is possible because drinking-water is an indispensable part of the human diet, and hence, exposure is difficult to avoid – abstinence or replacement from alternative sources for longer periods is not a feasible option in most settings.

Compared to other agents that may occur in water and that are covered in the GDWQ, the occurrence and behaviour of cyanotoxins is fundamentally different and consequently requires different management approaches. On the one hand, the producing cyanobacteria need to be addressed as microorganisms that can proliferate in surface waters – but which are not in themselves infectious – requiring measures to reduce their occurrence that shift management from microbiology to ecology. On the other hand, their toxins are chemicals and need to be addressed as such, including the derivation of values for maximally tolerable concentrations and the development of technical methods to reduce their concentration through drinking-water treatment.

Other unique characteristics include:

- Cyanotoxins are among the most toxic naturally occurring compounds: lethal doses are in the same range as some toxins from mushrooms (amanitin, phaloidin) or plants (aconitine, strychnine, atropine).
- Cyanotoxins occur worldwide in many lakes, reservoirs and rivers used as sources of drinking-water or for recreational activity.
- Contact with toxic cyanobacteria is difficult to avoid without implementing severe restrictions: most people who enjoy swimming in natural waters most likely have been in contact with toxic cyanobacteria.
- The occurrence of toxic cyanobacterial blooms is often not perceived as a danger by the public in the same way as a spill of an industrial toxin or chemical with the same hazard potential would be, because it may be regarded as “natural” and hence innocuous.
- Cyanotoxins are produced naturally within surface waters and are not, like most chemicals for which guideline values have been set or proposed, directly introduced by human activity. For many of the anthropogenic contaminants, legislation regulating their use and release into the environment has successfully reduced concentrations

in ground or surface waters an approach that is not practicable for cyanobacterial toxins.
- The control of toxigenic cyanobacteria is complex and typically requires efforts on scales beyond the water supply and waterbody with its immediate environment, potentially including the management of entire catchments and requiring longer-term investments (e.g., in sewage management) as well as political decisions with wider impact (e.g., on fertiliser use).

Thus, cyanobacteria and their toxins pose specific challenges, and guidance with respect to their management warrants a dedicated WHO publication.

Cyanobacteria have been present in natural ecosystems since the Precambrian Era, some 2 billion years ago (Wilmotte, 1994), and the production of cyanotoxins is probably an equally ancient characteristic (Rantala et al., 2004). The first scientific report on toxic cyanobacteria dates from the late 19th century (Francis, 1878), but earlier historical records have been interpreted as similar poisoning events (Codd et al., 2015). Studies on cyanobacterial toxins in lake sediments found microcystins (Zastepa et al., 2017) and cylindrospermopsin (Waters, 2016) in layers deposited well before the 20th century. In comparison with more recent sediments, in most cases, the assumed historic concentrations were, however, much lower than those found in today's eutrophic lakes.

In large parts of the world, waterbody eutrophication started accelerating in the middle of the 20th century, in the wake of urbanisation and industrialisation. Since that time, massive cyanobacterial blooms have occurred in many lakes and reservoirs in which this phenomenon was not known before. Therefore, it is not the biosynthesis of toxins itself that created a new health hazard, but the more recent significant proliferation of toxic cyanobacteria in waterbodies as a result of human activities. This health hazard most probably will gain growing importance as cyanobacterial blooms are expected to increase at the scale at which eutrophication is expected to increasingly occur in many regions of the world (Huisman et al., 2018).

Whether or not global warming is likely to increase cyanobacterial proliferation depends on specific conditions in a particular waterbody. In order to support the inclusion of climate change scenarios in risk assessment and management (e.g., water safety planning), this book includes information on how these conditions may influence cyanobacterial growth and bloom formation.

Cyanobacteria can produce a huge diversity of secondary metabolites, the biosynthetic pathways of which are known for a number of individual compounds or compound classes, respectively. Only a small share of the known metabolites shows toxic effects, but these cyanotoxins have caused numerous cases of poisoning of farm or wild animals, which demonstrate their toxic potential (Wood, 2016; Svirčev et al., 2019) and which suggests that animal illnesses and deaths are sentinel events for human health risks (Hilborn & Beasley, 2015). A large body of evidence from experimental studies with laboratory animals has elucidated their mode of action: some cyanotoxins are highly neurotoxic and others can damage the liver, kidney or other organs when ingested.

Epidemiological studies have looked for chronic effects in human populations exposed to toxic cyanobacteria, and indeed, a number of studies since the mid-19th century associate symptoms with cyanotoxin exposure. The key caveat of several of these anterior studies is the lack of data on the dose to which the population might have been exposed and a lack of analytical tools for detecting other hazards at that time, such as molecular techniques for the detection of pathogenic viruses. However, although our current knowledge may question some of the epidemiological evidence frequently quoted to highlight the cyanotoxin hazard, the evidence from animal experiments is clear and sufficient to derive guideline values for a range of cyanotoxins.

In this respect, cyanotoxins are in line with most other substances for which World Health Organization (WHO) has set guideline values: this is not typically done because a substance has been widely shown to cause human illness or result in fatalities through water consumption, but rather because a substance has significant toxic properties and water is recognised as a relevant pathway for exposure. Given the widespread occurrence of cyanobacteria – as compared to the occurrence of many purely anthropogenic contaminants in water – cyanotoxins are likely to occur more widely and more often in concentrations of potential concern than many of the other chemicals considered in the Guidelines for Drinking Water Quality (WHO, 2017).

1.1 DOCUMENT PURPOSE AND SCOPE

The second edition of "Toxic Cyanobacteria in Water" presents the state of knowledge regarding the impact of cyanobacterial toxins on health through the use of water and provides guidance on assessing and managing the risks of cyanobacteria and their toxins in order to protect drinking-water sources and recreational waterbodies. It further provides an overview of exposure through other important sources, including food, use of dietary supplements and through dialysis.

This edition is an update of the first edition of this publication, which was published 20 years ago (Chorus & Bartram, 1999). In addition to updating the state of knowledge specifically related to cyanobacteria and their toxins, this updated edition accounts for developments in and best practices for water supply management, namely, water safety planning, as well as the broader state of knowledge on climate change, eutrophication and others.

Water safety planning (see Box 1.1) is a comprehensive preventive risk assessment and risk management approach, and is a critical component of WHO's Framework for Safe Drinking-Water, to most effectively ensure drinking-water safety. Most importantly, the Water Safety Plan (WSP) approach systematically addresses all steps in a water supply from catchment to consumer (Bartram et al., 2009).

While the concept of WSP development is tailored to drinking-water supplies, many of its elements can be applied to the assessment and management of other potential exposure routes. For food safety – fish and shellfish in the context of this volume – the related concept of HACCP (Hazard Analysis Critical Control Points; from which WSPs were developed) applies and can readily be linked to WSP elements. The WSP approach is currently being developed for application to other areas of water management, that is, as Sanitation Safety Plans and Recreational Water Safety Plans. Among the hazards relevant to water, cyanobacteria are often likely to expose people through multiple pathways, and adopting a WSP approach will provide the most effective approach to protecting their health.

BOX 1.1: DEVELOPING A WATER SAFETY PLAN (WSP)

Drinking-water safety often relies heavily on the verification of compliance to water quality standards. However, by the time laboratory results show non-compliance, the population served will already have consumed the water and become exposed – and in the case of pathogens, many people may thus become ill. Therefore, "end-of-pipe" monitoring alone is insufficient to guide management decisions. The WSP approach shifts the emphasis of drinking-water quality management to a holistic risk-based approach that covers all processes from catchment to consumer which are crucial for maintaining drinking-water quality.

A WSP is specifically developed for the individual water supply. The process of developing it means

1. describing the system to identify and **analyse the hazards** and the **hazardous events** that are likely to cause the hazard to occur, and to **assess the health risks** they may present, as well as the **system's performance** in controlling these hazards and hazardous events;
2. to identify which additional barriers – the **control measures** – could be implemented to control these risks at different levels: the catchment, in the waterbody and at the offtake, in drinking-water treatment, in distribution networks and in households. Further, to **validate**

that **control measures** are appropriate for the intended purpose and achieve their respective contribution to mitigate the risks;

3. to ensure that control measures are working as intended by implementing a **monitoring system** that effectively indicates whether the **system's performance** is within the operational limits set for the respective measure. This requires the definition of **critical limits** for monitoring results, as well as setting up **corrective actions** to take immediately if values were outside these critical limits;
4. to **document** these steps and **revise** the whole system at regular intervals, that is, to assess whether the risk assessment is still adequate, the system's design takes account of the control of all relevant risks, and performance of the whole system is satisfactory;
5. to **verify** the outcome – that is, that drinking-water quality actually meets the targets set – in respect to the topic of this book, by targeted analysis of cyanotoxin concentrations in finished drinking-water.

Going through these steps effectively requires preparation, particularly forming a **team** including the technical expertise needed for the assessments and the stakeholders needed for making decisions. Preparation also includes **describing the supply system** from catchment to consumer, identifying **who will be exposed** to the water (particularly with respect to sensitive subpopulations) and obtaining the full endorsement and support from senior management for developing the WSP.

The WSP concept focuses attention on **risk assessment** and on **process control**. It is an operational system of quality management. This structured, systematic approach to process control is particularly useful for managing cyanotoxin risks, as it provides a platform for including expertise for the management of the catchment and waterbody, as well as interests of stakeholders involved in source water management.

World Health Organization (WHO) describes the WSP concept in Chapter 4 of Guidelines for Drinking Water Quality (GDWQ):

https://www.who.int/publications/i/item/9789241549950

and provides a WSP manual with practical guidance for individual settings:

https://apps.who.int/iris/handle/10665/75141

More WHO resource materials on water safety planning are available at https://www.who.int/teams/environment-climate-change-and-health/water-sanitation-and-health/water-safety-and-quality/water-safety-planning

1.2 TARGET AUDIENCE

"Toxic Cyanobacteria in Water" is intended for use by all those working on toxic cyanobacteria, with a specific focus on public health protection. It intends to empower professionals from different disciplines to communicate and cooperate for sustainable management of toxic cyanobacteria, for example:

- for public health professionals, including those in the fields of water supply and the management of recreational water, by providing detailed information on cyanobacteria and their ecology as well as on the management of catchments, waterbodies and water supplies;
- for ecologists and catchment and waterbody managers, by providing information on the public health impacts of cyanobacteria and their toxins.

This publication may also be useful to academia for a basic understanding of the current state of knowledge – and its gaps – and thus of possible research needs. This volume is not intended to replace textbooks on limnology, taxonomy, bacteriology or physiology that provide much more detail on issues such as eutrophication control, cyanobacterial diversity, toxin biosynthesis or toxicity mechanisms, and for further information, readers are referred to other sources quoted in the respective chapters, as well as to the WHO guidance on "Protecting Surface Water for Health" (Rickert et al., 2016) and "Guidelines for Safe Recreational Water Environments" (WHO, 2003).

1.3 DOCUMENT STRUCTURE AND OVERVIEW

This volume includes five key sections:

- introduction to cyanobacteria and their toxins (Chapters 2–4);
- understanding and assessing potential exposure routes (Chapter 5);
- guidance on control measures for cyanotoxin hazards (Chapters 6–10);
- overview of methods for sampling and analysis (Chapters 11–14);
- guidance on cyanotoxin-specific aspects of public surveillance, incident management and communicating cyanotoxin risks to the public (Chapter 15).

Chapter 2 includes detailed descriptions of the cyanotoxin groups that are relevant to human health. Although the chemically diverse cyanotoxins share the feature of being toxic to mammals, their respective modes of action are quite diverse. Each of the sections on a group of cyanotoxins in Chapter 2 summarises the state of knowledge on chemical structure, toxicity and mode of action, producing cyanobacteria and biosynthesis, occurrence and environmental fate. For those cyanotoxins for which WHO proposes Guideline Values or “Health-Based Reference Values” (i.e., for microcystins, cylindrospermopsin, anatoxin-A and saxitoxin), the respective section summarises the considerations for the derivation of these values, referring to the respective WHO background documents for more detailed information.

Chapter 3 introduces cyanobacteria as organisms which occur naturally in a large variety of habitats, from ultraoligotrophic oceans to deserts – and in a broad diversity of freshwaters. It further briefly describes the limited number of taxa known to contain metabolites of relevance to human health.

Chapter 4 describes the main environmental conditions that may lead to blooms of cyanobacteria, among which elevated nutrients concentrations are a key precondition which is important to understand when developing management strategies to control blooms. It includes further environmental conditions that determine the dominance of specific cyanobacterial taxa, their temporal dynamics and their spatial heterogeneity.

Chapter 5 reviews the available scientific and epidemiological evidence for each relevant route for human exposure to hazardous concentrations of cyanotoxins: drinking-water (section 5.1), recreational and occupational activity (section 5.2), food (section 5.3), renal dialysis (section 5.4) and cyanobacteria as food supplements (section 5.5). For exposure through drinking-water or recreation, it proposes Alert Level Frameworks to guide timely management responses to elevated concentrations of either cyanobacteria or their toxins. These frameworks help focus operational monitoring for two purposes – to minimise the risk of unnoticed exposure, but also to avoid inefficient monitoring efforts where risks are likely to be low.

A prerequisite to choosing the locally most effective approach is to understand and characterise the individual water-use system. Cyanotoxin occurrence and exposure can be reduced and managed by measures that act at different levels. Chapter 6 therefore describes the steps to take for assessing the given conditions and developing the locally most effective management approach, aligned with the water safety planning framework. Cyanotoxins are most effectively and sustainably controlled by avoiding conditions which lead to cyanobacterial proliferation. Figure 1.1 illustrates the conditions that lead to elevated concentrations of cyanotoxins, and the subsequent chapters describe control measures that can be taken to minimise the cyanotoxin hazard at different levels: nutrient loads from the catchment (Chapter 7), nutrient concentrations and other conditions in the waterbody (Chapter 8), the selection of sites for drinking-water offtake or of recreational areas (Chapter 9) and the treatment of raw water to produce drinking-water (Chapter 10).

The guidance given in Chapters 6–10 intends to support developing a locally specific approach to controlling cyanotoxin occurrence. This is

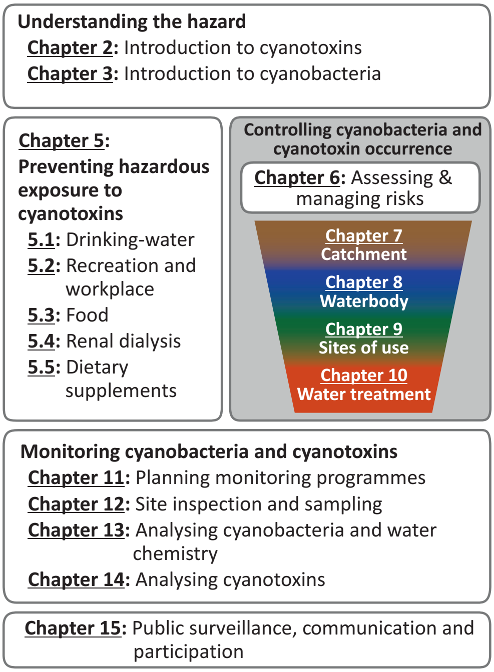

Figure 1.1 Overview of the structure of "Toxic Cyanobacteria in Water" 2nd edition.

supported by monitoring cyanobacteria and cyanotoxin occurrence. Chapter 11 outlines the planning of monitoring programmes. This includes a section on remote sensing, a technology that is becoming increasingly accessible, and, although it will likely not replace field work, offers opportunities to optimise targeted monitoring. Chapter 12 gives guidance for on-site field work. Laboratory analytical methods for cyanobacteria and associated water chemistry are presented in Chapter 13, from microscopic determination of cyanobacterial biomass to nutrient analyses and recently developed molecular methods. The analysis of cyanotoxins themselves is discussed in Chapter 14, from chemical and biochemical methods to a critical assessment of bioassays that have been applied in cyanotoxin research and their role in future cyanotoxin research. These chapters are not intended to replace specialised textbooks and standards by giving details on how to perform specific analytical methods; rather, in order to support the development of efficient monitoring programmes, they provide an overview of widely used methods and techniques, together with their respective laboratory requirements, specific advantages and shortcomings.

Chapter 15 discusses public health surveillance, incident planning and response, as well as public communication and participation to develop awareness and support appropriate personal decisions on water use. As the public becomes increasingly aware of the cyanotoxin risk through the media and their own experience, a well-planned communication strategy can prevent undue unsettledness of the public and help sustain public confidence in health institutions, water authorities and drinking-water supplies.

Due to space limitations, only a relatively small share of the many valuable studies on various aspects of cyanobacteria and their toxins can be cited in this volume. We hope our colleagues accept our apologies for the selection we had to make.

Despite several decades of intensive study of cyanotoxins, questions remain open: the current understanding of health risks is still sketchy – as is in part reflected by uncertainty factors in the derivation of guideline values for some cyanotoxins and a lack of such values for many of their structural variants. Also, our understanding of the ecological and evolutionary value of toxic and bioactive cyanobacterial metabolites is still very limited – there is still no satisfactory answer to the obvious question: why do cyanobacteria produce toxins? Hence, toxic cyanobacteria in water will remain an important subject for future research.

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