BCTOX BC Toxicology News Monthly Bulletin

Dedicated to Toxicological Issues in Population and Environmental Health in British Columbia

Keep Engaged with Toxicology News in BC

Contents

Solve the mystery!

--- Participate in our "solve the mystery" and win a prize!

First, let us congratulate ***Dr M. Madani Civi***, School of Population and Public Health, UBC, Vancouver, who won last month's prize. BCTOX is thankful for his accurate description of the problem.

Second, the reason for the premature death of Alexander the Great is controversial. There are reasons to believe that he was assassinated through poisons.

--- Are you convinced that he was assassinated? What toxicant could be the cause of death?

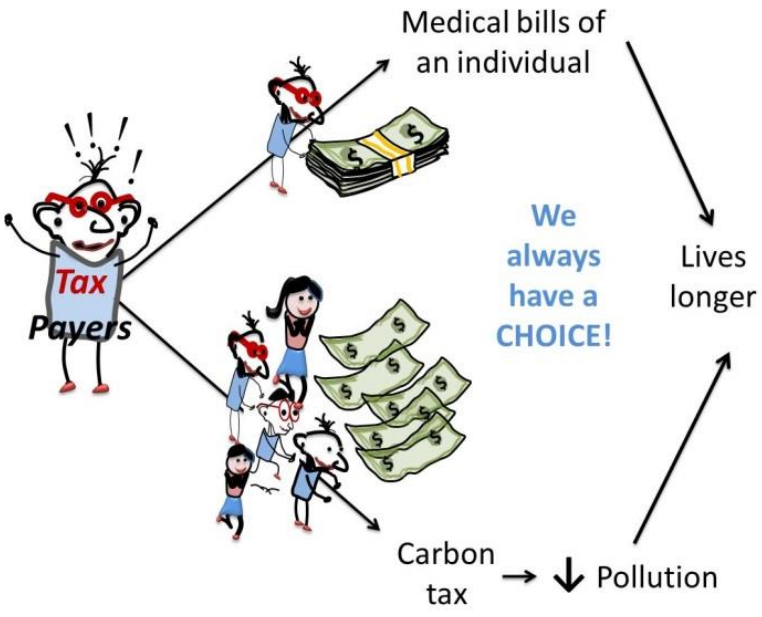
Please read the story. --- Take a guess (or confirm the given manifestations), and email in your response to be entered into the BCTOX drawing for a $20 gift card (Deadline: Feb 15, 2019).

What is BCTOX?

While BCTOX is not official and not liable for reported news and views, it is BC-related, full of concise and inspiring information, handpicked and fun to read. BCTOX keeps you engaged with toxicological issues in population and environmental health in British Columbia.

--- BCTOX is shared with a large number of health and environmental professionals in BC and beyond. It can increase the visibility of your work!

BC Toxicology Figure of the Month



Carbon Tax; drop, drop make an ocean!

Carbon Tax*; drop, drop make an ocean!

Choice of Carbon Tax

--- We have to make the concept of "Carbon Tax" intellectually easy to understand for the public!

Next time expensive medical bills for cancer, heart and lung diseases, etc. come up in a conversation, think of a small amount of carbon tax that could have been paid by each one of us to prevent those diseases!

--- Carbon tax is very cost effective and too cheap to be criticized!

--- The benefits of the Carbon Tax is for OUR generation too, not just for our children.

--- The carbon Tax did not start in 2019! The tax rate based on $35/tonne of emissions [April 1, *2018*] would be 7.78, 8.95 and 6.65 ¢/litre for gasoline, diesel (light fuel oil) and natural gas, respectively.

* A comment from one of our readers, Bret Watson: The word "tax" is the problem in my mind - "carbon pollution fine" makes it more sensible and less emotional!

About Us

Aims and Scope

BC Toxicology News Monthly Bulletin (BCTOX) aims to popularise the knowledge of toxicology and expand the use and awareness of Toxicology News in British Columbia, Canada. It tries to engage health and environmental professionals with online published toxicology news, publicly available information, and by providing short communications. BCTOX mainly focuses on adapting or summarizing relevant toxicology news in BC. The Bulletin accepts and welcomes contributions from professionals and the public as long as they meet BCTOX standards.

How to access the original news items? If you click on the link related to each one of the provided stories, it will take you to the original site.

Publication Frequency: BCTOX is published monthly in English by Reza Afshari.

Provided information in GRAY is not related to the current issue, but could be of interest.

ISSN: 2560-645X

Policies:

Open Access Policy: This bulletin provides open access to all its content.

***Fee*:** BCTOX is free-of-charge for readers, authors and contributors.

Copyright Statement

This bulletin is not official and for the most part is not peer-reviewed. It does not cover all the news, and is not liable for the accuracy of the news from the media. It is, however, BC related, informative, handpicked and fun to read. The provided contents are not necessarily BCTOX's views.

BCTOX has been modified since (BCTOX 2017 June 2(6)) issue. It is now accepting 400 word educational material, commentaries, and research abstracts (with data) as long as they are within the scope of the bulletin and meet our standards.

We are going to publish up to four short or full papers in each issue. This section of the journal is peer reviewed.

Archiving. Digital Archiving: In addition to indexing database this Bulletin utilizes digital archive as well as hard copies to guarantee long-term preservation and restoration.

Publication Ethics

This bulletin follows International Committee of Medical Journal Editors (ICMJE)'s Recommendations. Authors (i) must declare any conflict of interest in a given manuscript, and we utilize COPE workflow to transparently handle it, (ii) follow ICMJE definition of author and contribution, and (iii) accept the ethical policy including regulation and malpractice statement.

Guide for Authors

From June 2017 (BCTOX 2017 2(6)) we publish original research, mini reviews, short communications, letters, case reports, and case series as long as they are limited to 400 words and the content is British Columbia -related. These publications are peer reviewed.

References

References should be given in the Vancouver style and numbered consecutively in the order in which they are first mentioned in the text. Citation in the text should be in line with text in parentheses with Arabic numbering style.

List of contributors of this issue

Reza *Afshari*; Editor-in-Chief
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To contribute to the next issues, provide your opinion or report a mistake, please email us, your feedback is greatly appreciated.

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BCTOX has a professional blog, thanks to the University of British Columbia. https://blogs.ubc.ca/bctox2015/

Google Scholar

https://scholar.google.ca/citations?user=uaHeNh8AAAAJ&hl=en

New subscribers will be added to the mailing list upon their request.

If this bulletin is not of interest to you, let us know please so we do not to fill up your mailbox in the future.

Toxicology news in this month was focused on biomonitoring and climate change.

How to cite BCTOX's articles:

AUTHORS. TITLE, *BCTOX* 2017;2(8): PAGES.

Acknowledgment

BCTOX respectfully acknowledges that it is published on the ancestral homelands of the Coast Salish peoples, including the territories of the xʷməθkwəy̓ əm (Musqueam), Skwxwú7mesh (Squamish), Stó:lō and Səl̓ílwətaʔ/Selilwitulh (Tsleil-Waututh) Nations.

Erratum from the previous issues None.

---- We cordially invite you to contribute to BCTOX by providing 1000- to 2000-word articles and commentaries on a toxicology-related environmental, public health or clinical problem or an initiative that you have taken! These commentaries are peer reviewed and can be referenced. To cite abstracts of the current issue: Authors' surname, Initials, Title. BCTOX 2018;3(1); Pages.

BCTOX is available online: https://blogs.ubc.ca/bctox2015/ and Google Scholar https://bit.ly/2SnZL1n

The challenges to public health of arsenic in well water

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How to site this article? Dummer JDT. The challenges to public health of arsenic in well water. BC Toxicology News Monthly Bulletin 2019; 2(4): 433-434.

Introduction

Arsenic is a naturally occurring toxic metalloid classified by the International Agency for Research on Cancer (IARC) as a class I carcinogen that causes bladder, kidney, lung, and skin cancer.[1] Human exposure to arsenic is through a range of occupational and environmental pathways, including: consumption of arsenic contaminated food and water, cigarette smoking, exposure to smelting by-products and to fossil fuel smoke, and inhalation and ingestion of arsenic contaminated mine tailings, dusts and soils.[2]

Despite the multiple exposure pathways, the primary human exposure is via drinking water that is contaminated with inorganic arsenic naturally present in some types of bedrock.[3]

Arsenic in well water is a worldwide public health hazard.[4-6] Evidence of a dose-response relationship between drinking water arsenic and cancers of the skin, lung, liver, bladder and kidney in areas with high levels of arsenic greater than 100 µg/L in groundwater is well established.[7,8] Chronic exposure to arsenic in drinking water is also associated with increased risk for hypertension, diabetes, coronary artery disease and poor cognition and neuropsychological functioning, even at lower arsenic concentration levels.[9–12]

Although the magnitude of the health risk at low to moderate levels of arsenic has been contested due to mixed epidemiological data, a consistent body of evidence is now accumulating highlighting the increased cancer risk associated with drinking water arsenic concentrations around the current World Health Organization (WHO) maximum acceptable concentration (MAC) of 10 µg/L.[13-16] For example, a recent meta-analysis of studies world-wide reported a doubling of bladder cancer risk at arsenic levels around the current WHO MAC.[17]

Data from Canada also indicate increased cancer risk at lower arsenic concentrations—an analysis in Nova Scotia reported a 16% increased risk of bladder cancer at arsenic concentrations between 2 to 5 µg/L;[18] a finding consistent with a recent case-control study of bladder cancer in New England which also found increased cancer risk at low to moderate arsenic concentrations.[19]

Thus, given the wealth of epidemiological evidence there is a strong argument for lowering the current arsenic drinking water MAC. Indeed, Health Canada acknowledges that the current 10 µg/L MAC is an operational guideline that was set based on municipal and residential treatment achievability and not only health risk.[20]

Health Canada emphasize that for health purposes efforts should be made to reduce arsenic levels to as low as reasonably achievable.

Around 30% of Canadians draw drinking water from groundwater sources which, depending on the local geological conditions, have potential to be contaminated with naturally occurring arsenic.[21] 12% of Canadians overall and around 7% of British Columbians obtain drinking water from a private well, which source groundwater.[22] Elevated levels of arsenic have been found in well water in most provinces and territories, with noted hotspots of elevated arsenic in parts of British Columbia (BC).[21]

The BC Ministry of Environment Water Quality Check Program reported that 4.2% of groundwater samples obtained between 1977 and 1990 had arsenic levels greater than 10 µg/L.[23]

Arsenic concentrations above the current MAC were found in drinking water wells on the Sunshine Coast and the Gulf Islands, 100 Mile House, Bowen Island, Burns Lake, Chase, Kamloops, Quesnel, Vernon, Chilliwack, Langley and Williams Lake.[23]

Some wells on Saltspring Island, parts of the Lower Mainland, and near Nukko Lake have also reported high levels of arsenic and it has been noted that arsenic concentrations above the drinking water guideline may also occur locally in other parts of BC.[23]

A more recent study conducted in the Surrey-Langley area found that 43% of the 98 private wells sampled had arsenic concentrations greater than 10 µg/L and a further 40% had arsenic concentrations between 3-10 µg/L.[24]

The public health challenge

The public health challenge of arsenic in drinking water is compounded in Canada because private wells are unregulated and private well users are responsible for testing and treating their drinking water.[25] Public awareness of the health risks posed by drinking water contaminants in Canada is low and compliance with testing guidelines is poor.[26,27]

A study conducted in Nova Scotia found that few people test or treat their well water in line with Health Canada guidelines.[28] Reasons for this lack of compliance were complex, but included convenience to testing facilities, cost, awareness and access to appropriate treatment technologies and lack of risk awareness.[28]

Even in areas where there has been widespread publicity about arsenic in drinking water, not all well users adhere to guidelines.[29]

Evidence suggests many barriers to effective well user remediation of arsenic, including constraints related to community knowledge of arsenic risk and treatment options, and challenges associated with identifying appropriate treatment technologies.[25,28]

Over a tenth of Canadians source drinking water from a private well and, due to geology, exposure to naturally occurring arsenic is widespread and represents an important public health issue. There exist major challenges related to reducing the health risk associated with arsenic in private well water.

Conclusion

As noted, there is a strong argument for lowering the arsenic MAC to protect public health. However, although this is an important regulatory option, for private well users adherence to safe drinking water guidelines is at the well owner's discretion, which means the resource is essentially unregulated and the guideline limit is advisory and not enforced. Therefore, it is important that community-based interventions and educational and risk awareness campaigns are combined with a guideline limit that adequately reflects health risk.

To reduce the health impact of arsenic in well water there is an urgent need for more comprehensive risk management and public health interventions, combined with regulatory reform and appropriate, effective and affordable treatment options.

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BCTOX's Marine Biotoxins Surveillance System in BC from Jan 2016 - Apr 2019: shifting patterns of biotoxins on the west coast of Canada; Data from CFIA

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Public health surveillance is "the continuous, systematic collection, analysis and interpretation of health-related data needed for the planning, implementation, and evaluation of public health practice" according to WHO.

BCTOX is hopeful that this initiative will draw the attention of public health professionals to the changing patterns of marine biotoxins that may cause shellfish poisoning. The graphs could be predictive indices for what is going to come next month!

Bi-weekly marine bio-toxin monitoring in West Coast BC from Jan 2016to Apr 2019

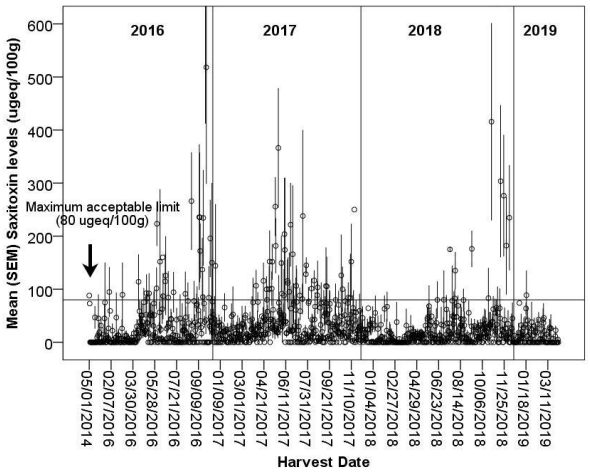
Saxitoxin (STX)

Background Saxitoxin (STX)-group toxins are a group of closely related tetrahydropurines and mainly produced by dinoflagellates belonging to the genus Alexandrium such as Alexandrium tamarensis.

STX cause paralytic shellfish poisoning (PSP) in humans, characterised by a range of symptoms from a slight tingling sensation or numbness around the lips to fatal respiratory paralysis. In fatal cases, respiratory arrest occurs 2 to 12 hours following consumption of contaminated shellfish.[1]

Results Saxitoxin (ug/100g) that may cause Paralytic shellfish poisoning (PSP) among detected shellfish samples in BC (Jan 2017 to Jan 2019)

- Positive cases were always detected (more than 99%)
- Above regulatory limit of 80 ug/100g was frequent
- Below regulatory limit Saxitoxin levels were more common in winters 2016 to 2019. Peaks are mot associated with falls or summers.



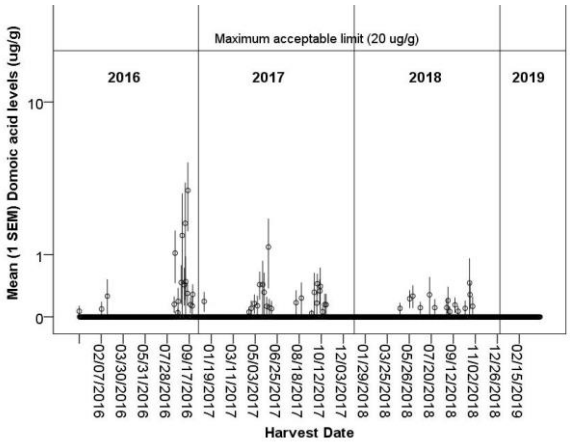
Domoic acid (DA)

Background Domoic acid, an excitatory amino acid is produced by diatoms that called Pseudo-nitzschiae, of which at least 14 strains are toxic;[2] it accumulates in filter-feeding molluscs (as well as certain crustaceans and finfish). Acute exposure to DA is associated with amnesic shellfish poisoning (ASP), a syndrome characterized by both gastrointestinal and neurological manifestations and which led to three deaths in a 1987 Canadian Atlantic Coast outbreak.[3] The U.S. Food and Drug Administration (FDA), the European Food Safety Authority (EFSA), and Health Canada promulgated regulatory limits for DA [4] [5] based on assessment of that outbreak.[3]

Results Domoic acid (ug/g) that may cause Amnesic shellfish poisoning (ASP) among detected shellfish samples in BC (Jan 2017 to Jan 2019):

- Very few positive cases detected (less than 1%)
- No case was above the regulatory limit of 20 ug/100g.

Below regulatory limits Domoic acid levels were observed in falls of 2016, 2017, 2018 and summer of 2017.

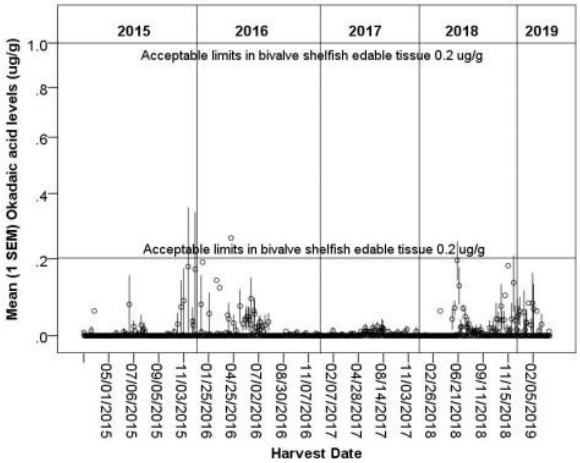


Okadaic acid (OA)

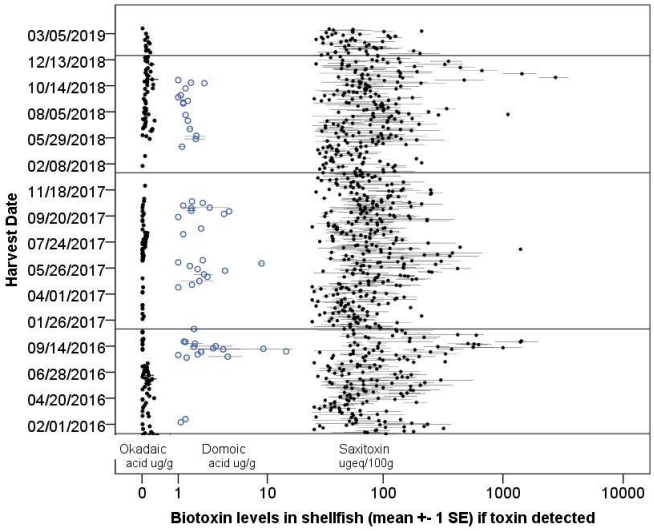
Background OA-group toxins are usually produced by planktons in the sea, and can contaminate shellfish, notably bivalve molluscs such as oysters, mussels, scallops, and clams. Contaminated shellfish may cause diarrhetic shellfish poisoning (DSP). [Note: DSP can also be caused by other toxins, not only OA-toxins.][6]

Results Okadaic acid (sum of okadaic acid and dinophysis toxins (DTX-1, DTX-2 and DTX-3) that may cause Diarrhetic Shellfish Poisoning (DSP) among shellfish samples in BC (Jan 2017 to Jan 2019):

- Very few positive cases detected (less than 1%)
- Very few cases were above the regulatory limit of 0.2 ug/g.
- Higher Okadaic acid levels happened more commonly in falls.



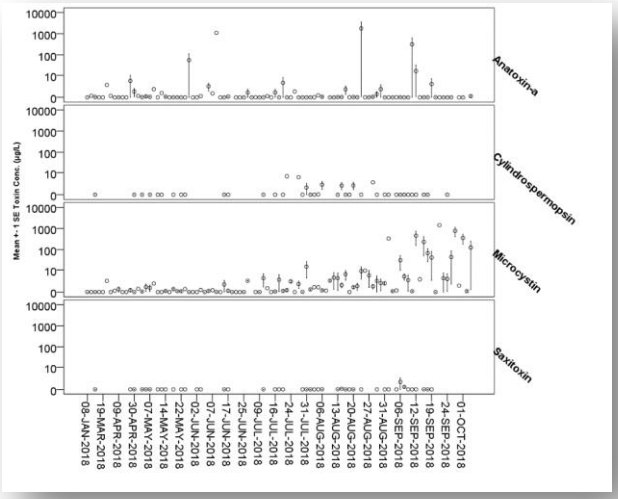
Saxitoxin, Domoic acid and Okadaic acid do not always follow th3 same pattern in west coast BC (Jan 2016 to Apr 2019)



Other biotoxins. Data from WASHINGTON STATE Toxic Algae, Shifting pattern of biotoxins

Regulatory authorities in B.C. do not require routine environmental measurements for other marine biotoxins including Anatoxin-a, Cylindrospermopsin and Microcystin.

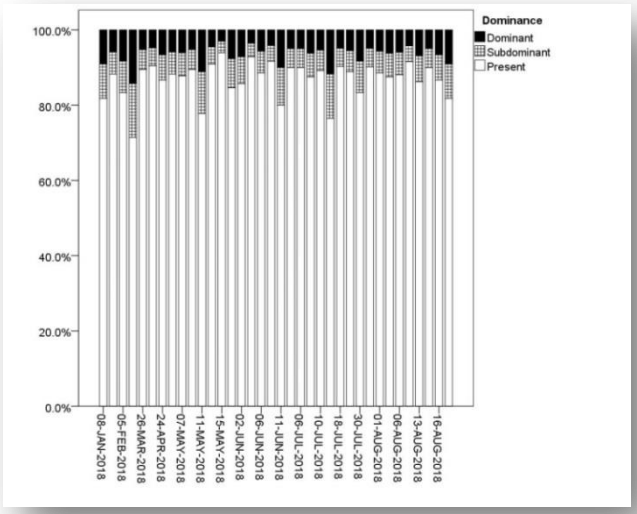
This information, however, is available from Washington State, which is the closest available information. The pattern is shown below (2018 Jan to Sep).

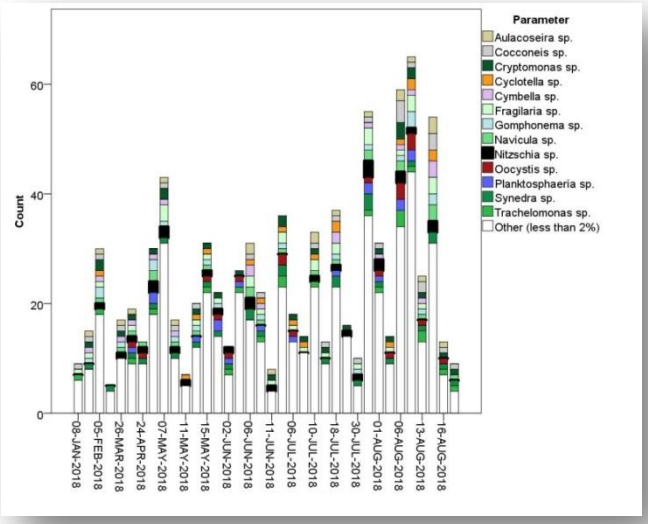


Phytoplankton's - WASHINGTON STATE *(2018 Jan to Sep)*[n= 995]

Regulatory authorities in B.C. do not require routine environmental measurements of Phytoplanktons.

This information; however, is available from Washington State, which is the closest available information. The pattern is shown below (2018 Jan to Sep).





Shifting pattern of biotoxins on the west coast of Canada

1. Other Marine Miotoxins

1- ***Algae bloom*** are simple plants that do not have ordinary leaves or roots. True algae (*green* algae) start to bloom in late spring and early summer in rather colder areas or near water.

--- They are the result of excess nutrients, particularly phosphates originating from fertilizers; other sources include excess carbon and nitrogen and catalyst residual sodium carbonate.

--- Algae are short-lived, and decaying dead organic matter consumes dissolved oxygen in the water, resulting in hypoxia and die off of plants and animals in large numbers.

2- ***Harmful algae bloom*** (or ***red tide***); involves toxic phytoplankton such as dinoflagellates of the genus Alexandrium and Karenia, or diatoms of the genus Pseudo-nitzschia. Such blooms often take on a red or brown hue. They produce natural toxins.

--- Reappearance of blue-green algae at Elk Lake that are lethal to dogs is a constant concern for water quality, prompting a CRD advisory notice (2018-11-20).[7]

2-1- *Saxitoxin*

Dinoflagellate Alexandrium fundyense produces Saxitoxin that causes paralytic shellfish poisoning

2-2- *Domoic acid*

Pseudo-nitzschia diatom produces Domoic acid that causes amnesic shellfish poisoning.

2-3- *Okadaic acid*

--- Dinoflagellates Dinophysis produce Okadaic acid (sum of okadaic acid and dinophysis toxins (DTX-1, DTX-2 and DTX-3) that cause Diarrhetic Shellfish Poisoning (DSP)

2-4- *Azaspiracid*

Dinoflagellate Azadinium spinosum produces Azaspiracid (a phycotoxin) and analogues. Azaspiracid can result in severe acute symptoms that include nausea, vomiting, diarrhea, and stomach cramps.

EU and FDA regulatory limit is 160 µg/kg (reports from Europe).

--- No information is available online from BC

2-5- *Brevetoxin*

Karenia brevis dinoflagellate produces brevetoxin that causes neurotoxic shellfish poisoning (common in Florida and the Gulf of Mexico).

NSP is diagnosed through gastrointestinal and neurological symptoms: nausea and vomiting, paresthesias of the mouth, lips and tongue as well as distal paresthesias, ataxia, slurred speech and dizziness. Neurological symptoms can progress to partial paralysis and respiratory distress.[8]

--- No information is available online from BC

--- Officials in *Florida* say dolphins seem to be red tide's latest victims as more than 20 have washed up dead. Scientists attributed the deaths to brevetoxin (2018-11-27).[9]

2-6- *Cyclic imines*

"The dinoflagellates Karenia selliformis and Alexandrium ostenfeldii / A. peruvianum have been implicated in the biosynthesis of gymnodimines and spirolides, while Vulcanodinium rugosum produces pinnatoxins and portimine."[10 11]

--- No information is available online from BC.

"Most incidents of palytoxin poisoning have manifested after oral intake of contaminated seafood. Poisonings in humans have also been noted after inhalation, cutaneous/systemic exposures with direct contact of aerosolized seawater during Ostreopsis blooms and/or through maintaining aquaria containing Cnidarian zoanthids."[12]

"Common symptoms include numbness, paraesthesia and swelling around the site of exposure (cutaneous exposure), rhinorrhea, cough, dyspnea (inhalational exposure), perioral paraesthesia, dysgeusia (oral exposure) and eye irritation (ocular exposure)"[13]

2-7-1 *Coral*

Toxic coral in aquarium sends Quebec family to hospital - Zoanthid corals can be toxic, be aware when handling them. (Global News)[14]

The green type Zoanthid coral is a common feature of saltwater aquariums, but can contain palytoxin (photo adopted from ([15] [16]))

--- Case report; Seven members of a family exposed to toxic Zoanthid coral (that may contain palytoxin) in their home aquarium. They bought the aquarium second-hand from a business where it had been on display and transported it with its contents to his home in Gatineau, Quebec. They experienced sneezing within minutes followed by chest pains, problems breathing, fever, shaking, and vomiting (2018-04-24).[16] [17]

--- Case report; While cleaning his fish tank in Oxfordshire, U.K. an aquarium owner scraped the coral's surface (pulsing xenia), and inadvertently a particular kind of deadly toxin known as palytoxin was released into the air.

--- The family went to bed, but became deeply sick the following day, experiencing acute breathlessness, coughing and other symptoms. All six people in the house were hospitalized, along with four firefighters and two dogs (2018-04-07).[18]

--- No information is available online from BC.

2-8- *Pectenotoxin*

--- No information is available online from BC

2-10- *Yessotoxin and analogues*

Abalone photo adapted from reference (2014-02-08).[19]

Lingulodinium polyedrum and Gonyaulax spinifera Dinoflagellates produced Yessotoxins that are related to ciguatoxins. Yessotoxins cause diarrhetic shellfish poisoning. [20]

EU regulatory limit is 1 µg of YTXs per g (1 mg/kg).

--- Case report; Thousands of dead red abalone washed up on the beaches of Sonoma County in Northern California in August 2011. Later scientists from the University of California found that a harmful algal bloom was to blame: the causative agent was Yessotoxin (2014-04-17).[21]

--- No information is available online from BC

2-9- *Tetrodotoxin and analogues*

After ingestion of puffer fish. The flesh of the puffer fish (i.e. fugu) is considered a delicacy in Japan.

"Paresthesias initially affect the tongue, lips, and mouth and progress to involvement of the extremities. Gastrointestinal symptoms may be seen and include nausea, vomiting, and less often, diarrhea. Muscle weakness, headache, ataxia, dizziness, urinary retention, floating sensations, and feelings of doom may occur. An ascending flaccid paralysis can also develop.

Other reported effects include diaphoresis, pleuritic chest pain, fixed dilated pupils, dysphagia, aphonia, seizures, bradycardia, hypotension, and heart block. Death can occur within hours secondary to respiratory muscle paralysis or dysrhythmias.

Clinical effects in the mildest of cases resolve within hours, whereas the more severe cases may not resolve for days. Treatment is supportive; there is no specific antitoxin. Patients who have progressed to having generalized paresthesias, extremity weakness, pupillary dilation, or reflex changes should be admitted to the hospital for observation until peak effects have passed. Those with respiratory failure should be intubated and placed on mechanical ventilation.

Vasopressor support may be necessary for hypotension refractory to intravenous fluids. Atropine has been used for symptomatic bradycardia."[22]

Image adapted from MedScape

Ciguatoxin

Ciguatera fish poisoning (CFP)

Ciguatera is caused by eating contaminated reef fish. Symptoms include diarrhea, vomiting, numbness, itchiness, sensitivity to hot and cold, dizziness, and weakness. Onset can occur from half an hour to up to two days. Diarrhea may last four days. Certain symptoms typically remain for a few weeks to months. Heart difficulties such as a slow heart rate and low blood pressure may occur.[23] --- Recreational exposure to cyanobacteria can cause GI, pruritic skin rashes and hay fever. [24]

Scombroid Fish Poisoning: Histamine Poisoning

3- *Cyanobacteria (blue green algae)*

Cyanobacteria are aquatic and photosynthetic bacteria that live in the water, and can manufacture their own food.

Cyanobacterial toxins

Cyanotoxin – not related to cyanide – contains neurotoxins, hepatotoxins, cytotoxins, and endotoxins. It causes rapid death by respiratory failure.

--- No information is available online from BC.

Anatoxin-a

Anatoxin-a is produced by cyanobacters and causes loss of coordination, muscular fasciculations, convulsions and death by respiratory paralysis.

Cylindrospermopsin
Microcystin
BCTOXScope (CYANOscope)

BCTOX publishes your pictures of cyanobacteria samples found in BC with your name.

Email your image(s) to BCTOX@yahoo.com

--- Even if you are not sure that it is cyanobacteria, upload it please!

Make sure to include the date, geographical area and other relevant information.

Examples

Photo

Photo

--- Algae gallery by Washington State. Toxic Alga is publicly accessible!

Decision Tree for Drinking Water: Cyanobacterial Toxins – Step Descriptions (No information is available online from BC)

STEP A: STEP A: Initial screening for suspected blooms: Examine the water for one or more of total nitrogen and phosphorus. Check for bloom formation.

STEP B: If yes to any of: nitrogen (N)>658 µg/L; phosphorus (P)> 26µg/L; an N:P ratio < 23; changes in secchi depth; or blooms observed, go to Step C. If no, return to Step A.

STEP C: Sample the raw water. Use a portable field kit to test for the presence of microcystins.

STEP D: If the presence of microcystins is detected (>1.0µg/L) with a field test kit, go to step E, and alert the health authority of a potential issue. If microcystins are absent, return to step A.

STEP E: Use a portable test kit to test the treated water supply for microcystins.

STEP F: If the portable test kit indicates microcystins are present (>1.0µg/L) in the treated water, send a sample to the lab for confirmation and immediately notify the health authority.

STEP G: If the lab results indicate the seasonal MAC of 1.5µg/L has been exceeded, immediately contact the health authority for consultation and decision making.

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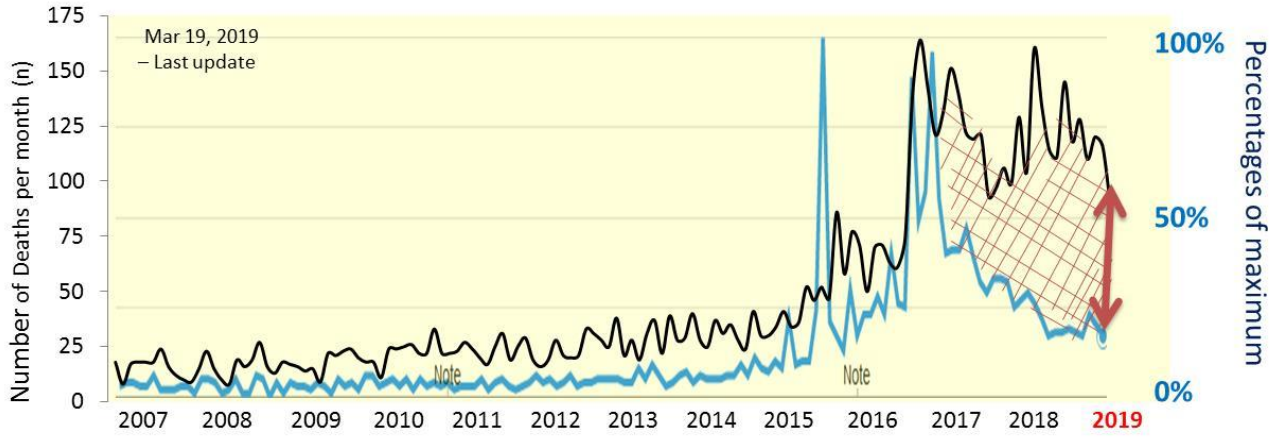
BCTOX's Toxicology Surveillance; Drug Overdose Deaths and Public interest in Fentanyl in BC
Mar 19, 2019

Public interest in fentanyl is declining in BC; opioid overdose deaths are still high. Reza Afshari



Opioid overdose deaths per month as compared to public sentiments from 2007 to Nov 30, 2018 in BC (graphs are superimposed).

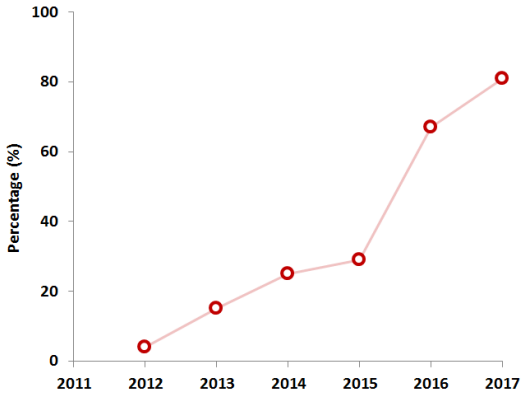
Opioid overdose deaths in BC (Jan 2007 to Jan 2019 [last update 19 March 2019]); suggests a sharp increase that has reached a plateau. Data from BC Coroners Service. --- Is this a new norm?

Public interest in fentanyl in BC's major cities (Jan 2007 to Jan 2019); suggests a sharp increase followed by a sharp decrease. Data from google trends. --- Is this social fatigue?

As can be seen, public are continuously less interested in fentanyl in 2018 that may imply a decline in public outraged with the concept. This decline has happened despite the fact that opioid overdose deaths are still high. --- Intervention should be shifted to keep engaged the public with the dangers of opioid overdoses as a part of risk management.

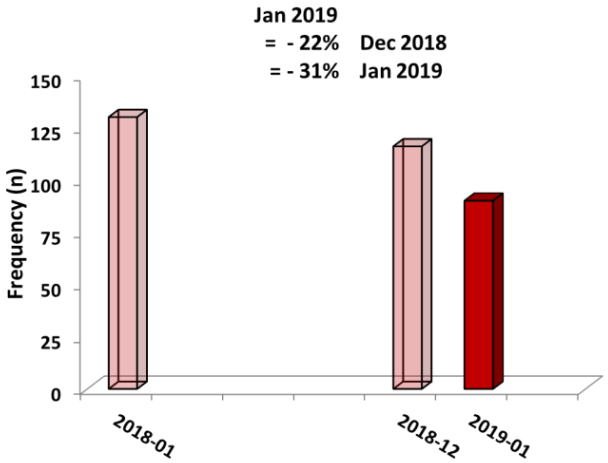
Fentanyl Detected Illicit Drug Overdose Deaths in BC (2012- 2017 July)

Data from (BC Coroners Service 2017-12-31) -] (accessed Feb 20, 2018) [BCTOX graph]



Estimation of Illicit drug overdose attributed deaths in BC in Jan 2010 (Apr 19, 2019)

The number of Illicit drug overdose deaths in Jan 2019 was 90 (Data from the BC Coroners Services (accesed 2019-04-19), which is 31% less than Jan 2018, and 22% less than last month [BCTOX graph]



Public interest in fentanyl in BC's major cities: Cumulative results starting from Aug 2018

Reza Afshari, Environmental Health Services, BC Centre for Disease Control, BC. Reza.Afshari@bccdc.ca

British Columbia as the ground zero of fentanyl overdose tragedy faced increased number of opioid overdose induced deaths in particular since 2015.[1]

Following the increase number of deaths, public health emergency was announced in Apr 14, 2016 in the province. The number of deaths dramatically increased during December 2016.

This short survey was performed to evaluate the public interest in fentanyl from Aug 2015 to August 2017 among different major cities in BC.[2]

Google Trends©(GT), an online tracking system of Internet weekly hit-search volumes (Google Inc.) were utilised to extract the data. GT collects, categorizes and connects data to a topic. Characteristics include real world based on search terms in categories of importance, interest by region, interest over time, removed personal information, eliminated repeated searches from the same person over a short period of time, unbiased random samples, and very low volume searches are counted as zero.[3]

Results are shown in figure 1. As can be seen, following publicizing fentanyl potential to kill among "teenagers" and due to "recreational use" of fentanyl in early August 2015, a dramatic increase in public interest observed. However for 7 months this interest was relatively focused in Vancouver alone (○; figure 1).

Later Surrey, Victoria and Burnaby joined the list of cities in BC in which searches for fentanyl passed 1% of all individual term searches. It is clear by overlapping the number of deaths in BC (----) on the original graph (figure 1) that Kelowna, Kamloops, Richmond and Coquitlam were joined the list of cities coincide with the sharp increase in December 2016.

Fentanyl popularised in searches in Nanaimo, Maple Ridge, Abbotsford, Prince George, North Vancouver and West Minister in the following months.

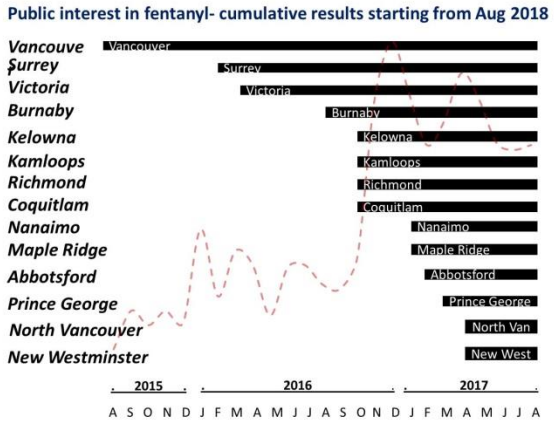


Figure 1. Public interest in fentanyl in BC's major cities: Cumulative results starting from Aug 2018 (data from google trends).

(----) Number of opioid overdose induced deaths in BC,

(▬) Search interests appeared in google trends. Results are relative to the highest point on the chart for the given region and time.

In addition, public interest in fentanyl gradually declined after a few months. Figure 2 compares the rank of searches in different cities. As can be seen, fentanyl popularity in Vancouver (○), Surrey (–) and Burnaby (--) have declined over this period.

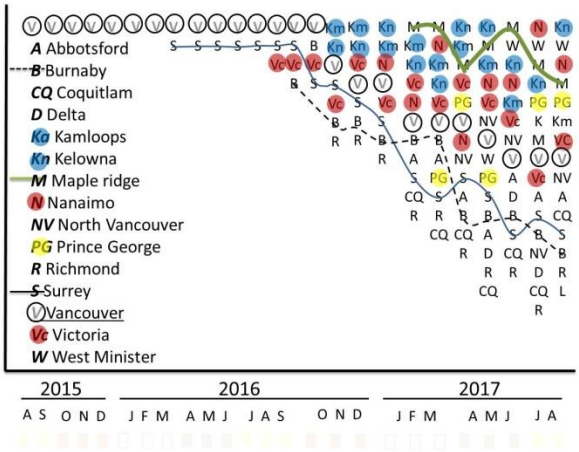


Figure 1. Public interest in fentanyl in BC's major cities: Cumulative results starting from Aug 2018 (data from google trends).

While this pattern may suggest a real sense of security due to declining the number of deaths in a particular geographic area and thus reflective of a real sense of security, it could suggest a diminishing public interest or fatigue in public.

These results have implication for risk management in public health.

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BC Toxicology News Monthly Bulletin
BCTOX 2019 Mar 2(4): 431-455

The Poisonous Lethal Assassination of Alexander the Great

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How to site this article? Afshari R. Poisonous lethal assassination of Alexander the Great. BC Toxicology News Monthly Bulletin (BCTOX) 2019; 2(4): 442-445.

Introduction

Alexander the Great (356 - 323 BCE)

Alexander III of Macedon, or Alexander the Great (356 - 323 BC), came to power as the king of the ancient Greek Macedon kingdom following his father's assassination, who had captured Athens two years earlier. At the time, the court was familiar with both execution and subtle assassinations of enemies!

Alexander's psychology

Alexander's father, Philip, was always away on wars and his beautiful mother, Olympias, was passionate, jealous, arrogant, headstrong, meddlesome and narcissistic in nature. --- At seventeen years old princess Olympias married Phillip as a result of a political union, becoming his third wife. Love was a luxury they could not afford. Once Philip found a serpent lying by Olympias and interpreted it as the deity father of Alexander.

Eventually Phillip broke up with Olympias and married Cleopatra (not the famous Cleopatra of Egypt), after which Olympias and Alexander plotted frequently against Philip. Phillip's assassination has been controversially attributed to them as they had a motive and opportunities.

Olympias was committed to achieve a glorious future for her son, and forged stories surrounding Alexander's birth as a hero; he also had the best tutors, including the magnificent philosopher Aristotle. She committed five documented murders and ordered over 100 executions, including those of Alexander's step mothers and half brothers and sisters following Philip's assassination to guarantee Alexander's succession. Olympia turned out to be a vicious monster that had control of her loyal son. Alexander did not have the chance to separate himself from his unconscious desires for his mother. There would have been a love-hate relationship between the two.

Although it is risky to analyze Alexander's personality after 2200 years, Freudian concepts such as the Oedipus complex [referring to a child's unconscious desire for the opposite-sex parent, according to Sigmund Freud] and related "castration anxiety" [referring to an overwhelming fear of damage to or loss of the penis according to Freud theories] and fear of loss of love can be applied to his personality and childhood. Alexander's childhood seemed to follow a perfect scenario for developing an Oedipus complex.

Alexander's father, Philip, was a genius military strategist and a pragmatic ruler who transformed the Macedonian kingdom out of the imaginable in his reign. He was celebrated at every step of his life because of his frequent and significant victories.

Figure 1. Alexander the Great (356 - 323 BC); Chin up position and face turn to the right

--- Alexander's loyalty to his mother perhaps led to a surreal never-ending competition with his father from his childhood onward. He would have won his mother over at any cost! Alexander's desire to expand the kingdom beyond imagination until he died was probably rooted there.

Once Alexander complained to Philip of having so many children, he responded: "if you have many competitors then prove yourself worthy of your kingdom because of yourself, not me". Apparently, he took his father's advice to heart, going on a mission to become a hero. Olympias was inspiring him, too.[1]

--- Have you ever competed with your father? Is he a hero or a dominant figure in your mind? --- Freudian followers are convinced that the Oedipus complex is an essential stage of psychosexual development that should be resolved as we grow up and take control. Failure to tackle the problem may lead to neurosis. Let's put ourselves in Alexander's shoes, it would have been very difficult for him to grow up to be worthy of Phillip, to win his mother and remain loyal. I am not sure whether he was able to fulfill his unconscious desire; however, it is clear from Alexander who was tutored effectively by Aristotle, he was violent in temper, impulsive in nature and megalomaniac, but entirely calculative. He grew up surrounded by prophecies of his success, his parents' dreams, and believed that he was on a deity mission to conquer the world. On the night that he was born, the temple of Diana at Ephesus burned down to ashes. He was enthusiastic and in love with pursuing glory. He was striving for excellence to fulfill the prophecy of being a hero.

There is evidence suggestive of his boasted self-esteem. His pose was exclusively based on descriptions and his sculptures (Figure 1); his chin positioned upwards and face turned to the right to expresses his pride of youth and the adamantine will of a hero, if his chin position was not due to cervical deformity. [2]

Alexander's death

Alexander was a mastermind strategist of a war that captured Asia by crashing the Achaemenid (Persian) Empire and invading India in a series of battles. His kingdom was extended from Europe to Asia and Africa. Alexander unexpectedly died at the age of 32 in Babylon - Persia in 323 BC, where he was going to lay his capital.

Circumstances justify he was assassinated

Alexander was not short of enemies. There were two distinct groups with motive and opportunity to kill him; the Greek-Macedonians and the Persians. --- Alexander and Olympias ruthlessly executed many members of the Royal family and his army was tired of constant warfare away from home pursuing Alexander's ambitions.

He was short-tempered and egotistical which kept his family and military close circle annoyed. In the last years of his life, he adopted some elements of an adversary nation, Persia, adopting its culture, dress and even used a Persian style of tent as a central element of his court[3] costing him the sympathies of his Greek-Macedonians elites. While his soldiers killed in fierce fights, he created a superior guard, spear-bearers, from distinguished adversary subjects headed by Oxyathres, Darius' brother.[3] He also brutally punished the accused subjects following a few failed attempts against his life. He defeated Darius III, but married his daughter, princess Stateira II.

He was not fond of sex but enjoyed the company of middle aged women such as his mother and Darius' mother Sisygambis, who was allegedly in a theosophical love relationship with him. Reportedly, Sisygambis died upon hearing of Alexander's death! He ignored his beloved wife, the astonishingly beautiful Roxana and got romantically involved in a homosexual relationship with his bodyguard Hephaestion. Alexander was devastated when he died!

From a second angle he was antagonised too. As much as Alexander is celebrated in Greek-Roman literature, history is written by the victorious. He has been portrayed as a negative

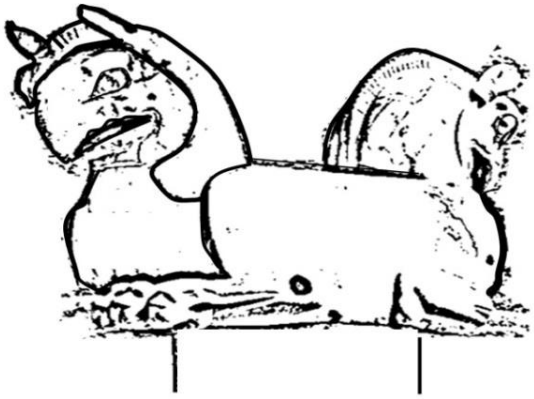

Figure 2. Persepolis.

figure in ancient Persian (Zoroastrian) literature, in which Alexander is titled Gujastak or cursed wizard, who burned the fire temples, sacred texts and the capital Persepolis (Figure 2). He was not short of enemies in his palace!

Was he murdered*?*

Let's look at the facts. You may make your mind up in whatever way you wish, but the indications for a plotted murder are abundant.

Eventually, the power structure of his court became increasingly ambiguous and secretive; friends and enemies were constantly replacing each other. He gradually developed a grandiose paranoid personality turning everyone into potential enemies.

Facts

- Alexander was young and strong and died at the age of 35
- Recorded symptoms support a rather acute disease that includes poisoning
- His enemies resided in his court from both the Greek-Macedonian and the Persian side of his empire
- The assassination of rulers was common among Greek-Macedonian kings, including his father
- Rumors suggested he was poisoned by his closest allies. His cupbearer, Iollas was accused of poisoning his wine

There is circumstantial evidence, and as a toxicologist I tend to genuinely believe that his death was not due to a natural cause.

Clinical findings of his terminal illness

Although the real cause of his death is a mystery, the last twelve days of his life tell a peculiar story under a medical lens. His clinical findings started with a sudden sharp pain in his stomach during a feast and followed by eleven days of weakness, progressive inability to walk, speak or move, followed by his death. Presence of fever in this period was reported but disputed. He was conscious during the whole twelve days.[4]

It is hard to imagine the agonising psychologic process that he had gone through in his last days; at some stage he should have thought of poisoning or got convinced of an assassination plot. But who was the perpetrator? In previous attempts, he killed all accused instantly. He was not strong enough; however, to slaughter suspects this time. He should have been suspected of the crime by someone from his inner circle, and perhaps so close that he could not bring it up! Perpetrators could have been from different nations, all of whom had plenty of legitimate as well as illegitimate reasons.

The symptoms were intensifying and physical and emotional pain was on the rise. I cannot presume at what point he realised that he would die, when he could do nothing.

--- Oh Misery; A* forgotten *captive, A trapped pray whose hunter moved on!

Hazin *Lahiji (1692 -1766)*

A bitter truth for him as well as whoever was loyal to him. Some were scared of the fact that he might survive and massacre everyone, some scared of his death and the anger and revenge of the next king. It was eleven long days of uncertainties, prays, mediations and anxiety. The place should have smelled of death, dark and cold. Let's not go there even in our nightmares!

Non-toxicological reasons

Various attempts have been made to speculate Alexander's death, and these vague symptoms are open to interpretation for all of us. Apparently this ambiguity is not just for us; scientists have also speculated a wide range of diseases that are totally different in nature, including malaria, typhoid fever, parasitic or viral West Nile illness. [5 4 6]

Toxicological reasons

A poisoning or overdose leading to a stomach ulcer or rupture would eventually cause death in a few days! The course of Alexander's clinical finding supports this theory the most. In his last days he was administered mediations by Greek, Persian and Egyptian physicians, presenting further opportunity to poison him.

In my view as a toxicologist, a perfect plot to his assassination would have been to start with lower doses and continue with higher doses to avoid suspicious.

Alcohol (Ethanol)

Alexander was a heavy drinker. Sbarounis has hypothesised that he died as a result of acute pancreatitis secondary to heavy alcohol consumption.[2 7] It could also have been the result of a perforated stomach, an esophageal ulcer, or complication of acute alcoholic excess. [8 9 10]

Alcohol (Methanol)

Nowadays, ethanol production is regulated and toxicologically safe to consume. During Alexander's time, wine could have been produced unsafely that leading to methanol production in addition to ethanol. Methanol is a highly lethal poison; one tea spoon of methanol can kill a child. Secondary fermentation that happens during storage is an important factor increasing the concentration of methanol.

Methanol poisoning leads to gastrointestinal and central nervous system complications that can cause drowsiness and paralysis; this would perfectly explain the course of his death. Methanol poisoning is not a rapid killer, and slays the victim in the duration of a few days!

Toxicologically unsafe produced alcohol that contains ethanol adulterated with methanol is still a major cause of accidental lethal overdose across the globe but is much more common in the Middle East, where industrial alcohol production and use are religiously and legally banned. A few of my colleagues and I described the symptoms of methanol poisoning comparing outbreaks in Christian majority countries of Estonia and Norway with Muslim majority countries of Iran and Tunisia (see Risk factors related to poor outcome after methanol poisoning. Clin Toxicol (Phila). 2012 Nov;50(9):823-31). [11 12]

Poisonous plant Veratrum album

Schep et al., proposed an alternative theory according to which a poisonous plant, Veratrum album (Figure 3), which was recognised at the time, was to blame.[4] There are merits to this theory. However, I am not convinced.

Figure 3. Poisonous plant Veratrum album

Natural hair removal (depilatory) agents

For millennia, naturally occurring depilatory agents were in use in the near- and Middle East. They were also known to be highly lethal. Even today, suicidal attempts with Nooreh, a combination of calcium oxide (CaO) and orpiment (Arsenic sulphide; As_2S_3) happen in that part of the world, and poets have even written about it. It used to be the element of choice for suicide in deprived populations and prisoners. Based on my own experience, severely exposed patients usually die within 4 to 6 days.

Consuming these corrosive agents harm the throat, esophagus and stomach, causing severe pain similar to what happened to Alexander. If these patients eat food or drink water, a burning pain in their throat occurs. They are recommended not to eat or eventually they stop eating due to pain. If a rupture happens, fever will follow due to infection. At that stage, during Alexander's time, the fate of the patient would have been sealed.

The patient remains conscious until the last minute of life. It seems to me deliberate poisoning of Alexander with a combination of calcium oxide and orpiment explains his death the best.

Symptoms of this poisoning that presumably should have consumed mixed into Alexander's alcohol or food start soon after consumption. Hair removal chemical mixture contains arsenic as well, which can explain the rest of the symptoms.

Arsenic poisoning

Attributing Alexander's death to arsenic poisoning has been discussed before.[4] Death due to poisoning, with whatever agent that is considered, straggles behind twelve day late occurrence of his death. The long process lies not only in the nature of the poison but also in how it was ingested. Madam Tufana's death recipe with Arsenic in the 17th century recommended three increasing doses to avoid suspicion; a fact that Alexander's calculative court residents would have been familiar with!

The impact of poisoning on Alexander's legacy

As much as he was adventurous in his life and death, his funeral and burial were even more surprising. His body was prepared and embalmed in Babylon and transferred toward Macedonia, when his corpse was hijacked, and eventually placed in a glass sarcophagus in Alexandria, Egypt. His body was on view for 550 years before it disappeared again. In his glass coffin, his body outlived all his rivals and enemies that were defeated, killed or died of natural causes one by one. Alexander's sculptures are on display in major museums in the 21st century, and even right now we are enjoying discussing his fate. I suppose that there is no similar Emperor whose body remained in glass for display for over five centuries into the modern era, despite the fact that that part of the world has gone through such major cultural changes. There are weakly supported rumors that an early Christian church was built over his last place of rest, where the Mosque of the Nebi Daniel is located in modern era in Alexandria. The truth, however, has remained a mystery even to this day! [5] In my view, he is alive no matter where his bones are. He changed the world, didn't he? He does not need a mausoleum, as he is alive in the minds of all of us. Alexander the Great is still a decisive figure and while an icon of power, pride and glory in the Western World, he remains a cursed wizard in the Persian collective memory.

If he earned being worthy of reigning as his father wished, and he achieved all these success in just 13 years, let's imagine what he would have been capable of doing if he had not been killed so young. He would have invaded perhaps Arabia, Central and South Africa, China and Siberia?! What if he had reached the sea shores everywhere? For an ambitious person like him, it would have been time to overcome the oceans, I suppose. In that case America would have been discovered by the West 1700 years earlier.

Let's visualise that Christianity reached North and South America much earlier, tobacco was introduced to us centuries in advance and the human population had found the space to grow two millennia ago. I dare to go further, our civilisation - our lives today would have been much more advanced. It's a pity that he died soon before he conquered the world! It is not certain whether we lost Alexander to a vicious poisoner in a cruel frame up of his allies, but it is certain that his poisoning, if there was one, and death changed the course of history very dramatically.

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