



Toxic fish

Tropical fish can contain substances which, when consumed, can cause serious health effects. The BfR wants to facilitate the detection of these substances and to raise awareness of this problem in the public.



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Northern Germany, November 2012: within a few days, patients with similar unusual symptoms visit hospitals and emergency departments. They complain of diarrhoea and vomiting as well as pain in their arms and legs and abnormal temperature sensations. Some feel cold as heat and vice versa, and experience the feeling of an electric shock when they come into contact with cold water. In some cases symptoms last for several months; in the majority of cases at least a few weeks. Further cases are registered in Hesse, Rhineland-Palatinate and Bavaria.

Poison Centres provide the first clues of the cause when responding to calls from the public. Several consumers enquire about poisoning from “red snapper fish fillets”. The local food control authorities then collect samples throughout Germany. A total of 23 reports of poisoning from fish fillets reached the National Reference Laboratory (NRL) for the Monitoring of Marine Biotoxins and the Poisoning and Product Documentation Centre at the BfR.

Triggered by ciguatoxins

“Due to the unusual, rarely occurring symptoms here, it quickly became clear to us that we were most likely dealing with ciguatera, the ciguatoxin fish poisoning,” recalls Dr. Herbert Desel, who was Head of the Poison Centre GIZ-Nord at the time and is now Head of the

Poisoning and Product Documentation Centre at the BfR. This unit assesses poisoning reports from doctors and the eight German Poison Centres as an important contribution to the risk assessments of the BfR.

Ciguatoxin, a tongue twister! The word is pronounced “ci-gua-toxin” and refers to a harmful substance that can be taken up into the body when tropical fish is consumed. “Cigua” comes from the Cuban Spanish. The people there call the sea snail *Cittarium pica* “cigua”. They have been familiar with the aforementioned symptoms for centuries and gave the disease the name “ciguatera” because it is said to occur after eating that particular sea snail.

Today, we know that there is not just one ciguatoxin, but several ciguatoxins (CTX) having similar chemical structures. CTX are marine biotoxins (algae toxins). They are mainly produced by microalgae (phytoplankton) that marine animals feed from. More than 20,000 phytoplankton species are known worldwide, but only a few produce marine biotoxins. Humans can ingest them through fish, mussels and other seafood. Algae that produce CTX prefer warm water temperatures, which is why these algae – and, therefore, the contaminated fish – are found in tropical and subtropical regions. Accordingly, fish such as various species of snapper, barracuda or tropical types of mackerel in particular may contain the toxins.



The English sailor James Cook was one of the first Europeans to describe the symptoms of ciguatoxin poisoning. He recorded an incident in his diary on 24 July 1774:

“The night before we came out of Port Sandwich, two red fish the size of a large bream were caught using a hook and line. [...] The following night, everyone who had eaten the fish was seized by violent pains in head and bones, together with scorching heat all over the skin and a feeling of numbness in their joints. There was no doubt that this was caused by the fact that the fish was of a poisonous nature [...] and it took a week or ten days for all the men to recover.”

Contaminated fish not detectable

It is still unclear how ciguatoxins are digested in the human body. “What is certain, however, is that these toxins are very potent. Very low doses are enough to trigger symptoms,” Desel says. However, the probability of dying from the poison is very low. Ciguatoxins cannot be destroyed by frying or cooking, nor by stomach acid. They are preserved for a long time in frozen fish. A particular problem arises for both retail and consumers: fish containing ciguatoxins cannot be distinguished from fish that are not contaminated. The poisons do not alter the appearance, smell or taste.

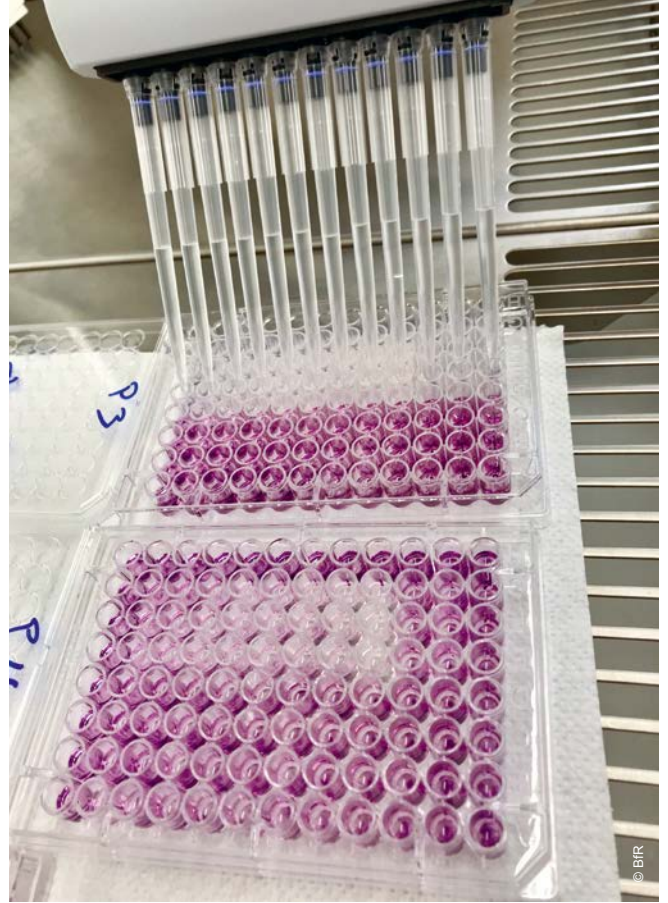
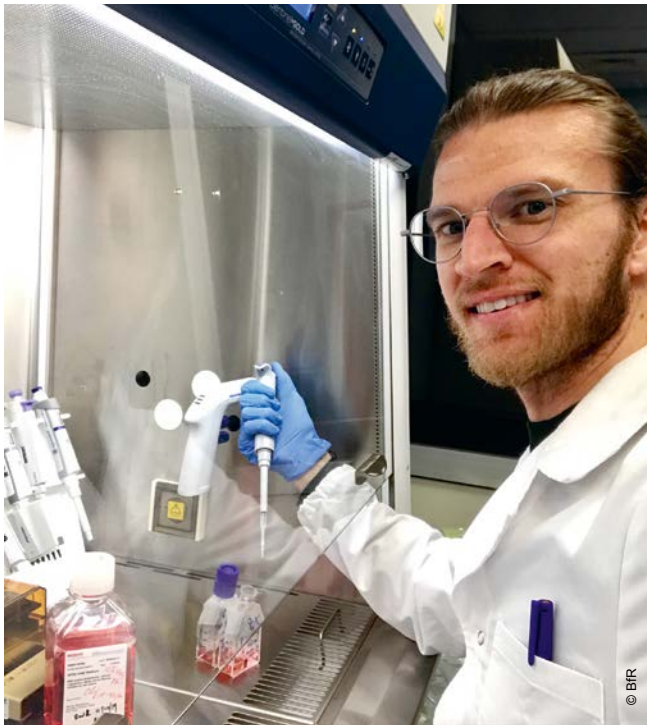
July 2016. Several ciguatera cases in Germany, again. Red snapper fillets, again. All of those affected have eaten fish imported from India. “Ciguatoxins are very similar in structure. Depending on the region, there are minimal differences in the structure of the poison with different effects,” Desel says. CTX are divided into three groups according to their geographical occurrence: P-CTX (Pacific), I-CTX (Indian Ocean) and C-CTX (Caribbean Sea). Ciguatera is the most common fish poisoning in the world. There are an estimated 50,000 to 500,000 cases every year around the world, most of them in the tropics. However, fish imports also lead to ciguatera outbreaks outside of these regions – as a result

of global trade and maybe climate change. Consumers in Germany are, therefore, also affected. This is why the BfR will continue to address this topic in the future.

Detection without animal tests

It is difficult to detect ciguatoxins in fish. “Ciguatera symptoms may develop after a typical fish meal containing a CTX level of only 0.01 nanograms per gram of fish. This corresponds to the weight ratio of an ant to a full-grown blue whale,” Dr. Astrid Spielmeier says, who is, among other things, responsible for CTX analysis at the NRL.

Initially, animal tests were used to detect CTX. It is now possible to detect them using mouse cell lines – without animal experiments. The BfR treats cells with extracts from fish samples to determine the amount of ciguatoxin contained in them. If these samples contain no CTX, a dye added to the cells changes colour. If CTX are present no colour change is observed (see box). The so-called “mouse neuroblastoma cell assay” (N2a) allows numerous samples to be examined within a short time. However, the assay does not allow any assertion about CTX structures. These must be confirmed by mass spectrometry after liquid chromatographic separation.



Mouse cells plus fish extracts: scientists at the National Reference Laboratory for the Monitoring of Marine Biotoxins at the BfR are investigating whether fish samples contain ciguatoxins.

One of the challenges of ciguatoxins analysis is that many of the toxins are not available as reference substances but necessary to unequivocally identify ciguatoxins. Currently, about 40 different ciguatoxin subtypes are known. Those from the Pacific are most extensively investigated. According to Spielmeyer, no official methods for routine testing of fish for ciguatoxins are available. Furthermore, fish contains a lot of protein and some species also contain a lot of fat. Both components are an obstacle for the CTX analysis.

“They interfere considerably with detection and this can become a problem in samples with low concentrations of ciguatoxins,” chemist Spielmeyer says. In addition, CTX attach to proteins and are fat-soluble. “Here, we are dealing with the figurative squaring of the circle. But we hope to be able to establish an analytical method at the BfR soon.”

The BfR is actively involved in the EuroCigua Project: a group of European scientists that have joined forces. Under the umbrella of the European Food Safety Authority (EFSA), it involves 15 European organisations from six EU member states. Two of the aims are to characterise the risks of ciguatoxin poisoning in Europe and to develop and establish new reliable detection methods. Improved analytical methods are necessary because researchers at the BfR expect that the frequency of ciguatera poisonings will rise in Germany. People are increasingly eating exotic dishes, which include fish from the tropics. If symptoms occur, consumers should seek medical advice and store the fish leftovers, if possible, to make them available for laboratory analysis. ■

Ciguatoxins cause certain ion channels (“locks”) of cell membranes to remain permanently open. This impairs the cells’ functions and can lead to cell death. “This effect is used in the N2a assay,” Dr. Dorina Bodi, head of the responsible NRL, says. If sufficient amounts of ciguatoxins are added, e.g. from a fish sample, the cells are not or only partly able to chemically convert a specific dye which is also added during the analytical process. Living cells convert the dye from a colourless to a purple compound. “We can determine how much ciguatoxin is present in a sample based on the colour intensity of the newly formed compound.”

More information:
www.bfr.bund.de/en > A-Z-Index: ciguatera