

EuroCigua II



SURVEILLANCE
PROTOCOL FOR
CIGUATERA
POISONING IN THE
EU

March 2024

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Foreword

According to Regulation (EU) 2022/2371, epidemiological surveillance means the systematic collection, recording, analysis, interpretation and dissemination of data and analysis on communicable diseases and related special health issues.

According to Regulation (EU) 2022/2371 of the European Parliament and of the Council of 23 November 2022 on serious cross-border threats to health, the European Centre for Disease Prevention and Control (ECDC) shall ensure the integrated operation of the network for epidemiological surveillance of communicable diseases. Whenever relevant, the network for epidemiological surveillance shall work in close cooperation with the competent bodies of the organisations operating in the field of epidemiological surveillance of communicable diseases and of related special health issues, from the Union, third countries, the WHO, and other international organisations. The Member States (MS) should communicate comparable data of a list of communicable diseases, according to established case definitions, included in the Commission Implementing Decision (EU) 2018/945. Ciguatera poisoning (CP) is not included in this list. However the reporting of investigated food-borne outbreaks has been mandatory for the European Union (EU) MS since 2003. The zoonoses directive 2003/99/EC states that Member States' Competent Authorities shall investigate food-borne outbreaks and transmit to the European Commission every year a summary report of the results of the investigations carried out. Based on an agreement with the European Commission, CP outbreaks data must be reported to the European Food Safety Authority (EFSA) annually.

The EFSA, through a Framework Partnership Agreement (FPA), supports a multiannual and multinational project (EuroCigua II) to provide the basis for an integrated approach to assess the human health risks of ciguatoxins in fish in Europe. It aims at the epidemiological characterization of CP cases, the full characterization of the ciguatoxins (CTXs) profiles involved in CP contamination, the establishment of training programs for the laboratory detection of CTXs in fish, the production of reference materials, the risk characterization of the CP due to imported fish and the initiation of the work for predictive modelling on ciguatera in Europe.

<https://www.sanidad.gob.es/en/areas/sanidadExterior/euroCiguaII/home.htm>

Scope and purpose

This protocol is a guide for EU MS and European Economic Area (EEA) countries in order to carry out retrospective and prospective surveillance of CP in the EU/EEA¹ from 2020 to 2024 in a harmonized manner and on a voluntary basis for the duration of the FPA. The purpose of the surveillance is to characterize the epidemiological pattern of the CP in the EU/EEA.

The protocol is addressed to public health authorities dealing with epidemiological surveillance. The protocol will provide information on the disease, the reporting requirements and recommended public health actions. Public health authorities may consider disseminating the information to the health care system in order to raise awareness among health care professionals. This protocol is not intended to be a guide for outbreak investigation. Responsibility on outbreak investigation and measures implementation fall on the MS.

Disease Description

Introduction

CP is a clinical syndrome caused by eating fish contaminated with CTXs. The number of people suffering of the disease annually was estimated from 10,000-50,000 to 50.000-500.000 individuals, but true incidence

¹ Tropical overseas territories are excluded.

is difficult to know due to under ascertainment and under reporting. Ciguatoxic fish are usually distributed between latitudes 35° north and 35° south, mainly in the Caribbean, Indo-Pacific islands and the Indian Ocean. Occasionally, CP has been reported outside endemic areas, such as the Bahamas, Canada or Chile. In Europe, CP outbreaks due to consumption of fish from Europe (Canary Islands or Madeira) have been reported from Spain and Portugal. Cases of CP may also occur in non-endemic regions because of increasing consumption of imported contaminated fish.

Symptoms

CP patients may have gastrointestinal, neurological and cardiovascular symptoms. Symptoms presentation varies according to the individual characteristics and the geographical origin of the CTXs. Gastrointestinal symptoms precede or accompany the neurological symptoms. Neurologic symptoms usually appear two to 48 hours after eating the contaminated fish. Symptoms reported may include: nausea, vomiting, diarrhoea, abdominal cramps, paraesthesia of lips, tongue and extremities, cold allodynia (burning pain caused by a normally innocuous cold stimulus), a metallic taste, arthralgia, myalgia, pruritus without urticarial or erythema, muscle weakness, blurred vision, hypotension and bradycardia. Cold allodynia is considered characteristic of CP, although it is not suffered by all patients; consumption of shellfish contaminated with brevetoxin may also produce allodynia. Neurological symptoms usually resolve in weeks, although some symptoms can last months. Recurrent symptoms may occur following the ingestion of food or beverages, mainly: alcohol, nuts or non-toxic fish. CP is rarely fatal. However, death may occur in severe cases due to severe dehydration, cardiovascular shock or respiratory failure.

Agent

CTXs are lipid-soluble, heat-stable and acid-resistance neurotoxins. CTXs activate the voltage-dependent sodium channels in cell membranes, which increases sodium ion permeability and depolarizes the nerve cell. The preferred classification is according to their structure, but they have also been classified as Pacific, Caribbean and Indian Ocean CTXs.

CTXs are produced by dinoflagellates of the genera *Gambierdiscus* or *Fukuyoa* that grow on and around reefs. Accumulation of CTXs in the marine food webs results from the ingestion of toxin-producing dinoflagellates by herbivorous fish, which are in turn preyed upon by larger carnivorous fish. The toxins are metabolised to more toxic forms as they move up the food webs. CTXs accumulate in higher concentrations in the visceral organs, roe (fish eggs), and carcasses (e.g. fish heads, eyes and bones).

Reservoirs

Over 400 known fish species from tropical and subtropical waters have been classified as potential CTXs carriers. Examples of the fish most frequently associated with ciguatera cases include: barracuda, grouper, amberjack, snapper, moray eel, hogfish, mackerel, surgeonfish, and parrotfish.

Modes of transmission

CP is due to the consumption of fish contaminated with CTXs. Person to person transmission of CTXs is extremely rare, but transmission from mother to child during breastfeeding or across the placenta and sexual transmission have been described.

Incubation period

The incubation period goes from 2 to 48 hours.

Period of communicability

The period of communicability from mother to child or through sexual transmission is unknown.

Laboratory testing for fish

Laboratory testing to detect CTXs in clinical samples is a challenge since their presence may be in very low amounts, while detection of CTXs in the fish is possible. Fish should be kept frozen at -20°C. This includes fish meal remnants. Fish samples should be double-bagged and securely sealed. In vitro cytotoxicity and receptor binding assays provide sufficient detection capability and they can detect all active toxin analogues. Immunoassays are presently available for some CTXs. Although these assays do not provide information on toxin profiles, they could be applied as screening methods for CTXs. Liquid chromatography-tandem mass spectrometry (LC-MS/MS) methods allow specific detection of individual analogues of Pacific, Caribbean and Indian Ocean CTXs and they may provide CTXs quantification in fish extracts. None of the current methods of analysis to determine CTXs in fish has been formally validated.

If any country does not have the lab capacity for detection of CTXs during the investigation of a CP case or outbreak, testing of fish samples may be possible for research purposes within the project. The feasibility of the request would be assessed case by case contacting the email: eurocigua2@sanidad.gob.es

Disease Reporting

Objective

1. To characterize the epidemiological pattern of ciguatera food poisoning in the EU/EEA.

Case definition

Clinical Criteria

Any person having neurologic symptoms, if other causes have been excluded. Most frequent symptoms are: paraesthesia, cold allodynia, dysesthesia, pruritus without urticarial or erythema, diffuses pain and muscle weakness.

Gastrointestinal symptoms (nausea, vomiting, and diarrhoea) often precede or accompany the neurological symptoms. Cardiovascular symptoms and signs (hypotension and bradycardia) may also be present.

Epidemiological Criteria

Epidemiological criteria for a confirmed case:

Consumption of fish with laboratory confirmed contamination of ciguatoxins in 48 hours prior to disease onset.

Epidemiological criteria for a probable case:

Consumption of fish (species, common name or type) previously associated with ciguatera poisoning (e.g., moray eel, amberjack, barracuda, snapper, or grouper) (Annex 1)² in 48 hours prior to disease onset.

OR

Exposure to the same common source as a confirmed case in 48 hours prior to disease onset.

Epidemiological criteria for a possible case:

Consumption of fish (species, common name or type) either NOT previously associated with ciguatera poisoning or of unknown type, in 48 hours prior to disease onset.

Case Classification

² It is an incomplete list. It can be updated.

A. *Possible case*

Any person meeting the clinical criteria and the epidemiological criterion for a possible case.

B. *Probable case*

Any person meeting the clinical criteria and the epidemiological criterion for a probable case.

C. *Confirmed case*

Any person meeting the clinical criteria and the epidemiological criterion for a confirmed case.

Other definitions

Outbreak definition

Two or more cases with an epidemiological link.

Case/outbreak associated with consumption of autochthonous fish

Case or outbreak associated with consumption of a fish harvested within the EU/EEA³.

Case/outbreak associated with consumption of imported fish

Case or outbreak associated with consumption of a fish harvested outside the EU/EEA³.

Travel associated case/outbreak

Case/outbreak associated with consumption of fish in a tropical endemic area.

Reporting flow

The National Centre of Epidemiology (CNE), belonging to the Spanish Public Health Institute and leader of the epidemiological part of the EuroCigua II project, will collate and analyse the data on CP cases and outbreaks received from the MSs that voluntarily agree to participate in the collection of CP cases and outbreaks. Specific questionnaires (Annex 2 and 3) have been prepared to collect homogenous information. Every case, including outbreak related cases, should be reported through the case report form (Annex 2).

Moreover the CNE will collect information on ciguatera cases and outbreaks from any other available source.

Legal reporting requirements

According to the zoonoses directive 2003/99/EC, competent authorities shall investigate food-borne outbreaks and transmit to the Commission (on the basis of an agreement between EFSA and the EC, this data is reported in an electronic reporting system and a database managed by EFSA) a summary report of the results of the investigations carried out. Requirements for the summary reports to be submitted by the Member States' competent authorities pursuant to Article 9 (1) of that directive are;

- (a) total number of outbreaks over a year;
- (b) number of human deaths and illnesses in these outbreaks;
- (c) the causative agents of the outbreaks, including, where possible, serotype or other definitive description of the agents. Where the identification of the causative agent is not possible, the reason for such unidentifiability should be stated
- (d) foodstuffs implicated in the outbreak and other potential vehicles;

³ Tropical overseas territories are excluded.

- (e) identification of the type of place where the foodstuff incriminated was produced/purchased/acquired/consumed;
- (f) contributory factors, for example, deficiencies in food processing hygiene.

Guidance for the reporting of annual food-borne outbreaks monitoring data can be found on the EFSA website.

Regulation (UE) 2022/2371 on serious cross-border threats to health mention that national competent authorities or the Commission shall notify an alert when the event is unusual or unexpected, it affects or may affect more than one Member State, and it requires or may require a coordinated response at Union level.

Each State Party shall notify World Health Organization of all events which may constitute a public health emergency of international concern within its territory, according to International Health Regulations.

CP cases may be reported to the competent authorities in some countries or regions within the EU/EEA. In the Canary Islands (Spain) reporting of CP from health care practitioners is mandatory.

Public Health Measures

Preventive measures

Avoiding consuming large predatory reef fish from affected areas could help preventing CP. Greater illness severity is associated with eating the fish head or organs. Thus, it is also advisable to avoid consuming visceral organs, roe (fish eggs), and carcasses (e.g. fish heads, eyes and bones).

CTXs are heat-stable toxins and cooking or freezing of the fish will not destroy them. Moreover, CTXs are odourless and tasteless and toxic fish cannot be identified by appearance or behaviour.

It is important to raise awareness among the public and health professionals. Travellers to affected areas should receive educational information about symptoms, transmission mode and prevention and control measures.

Since CP may be transmitted through breastfeeding and unprotected sexual intercourse, advised on refrain from breastfeeding and sexual intercourse (unprotected) while patient is symptomatic should be considered.

Measures for single cases

Cases

Per case, information should be gathered about the illness and consumption of fish in the two days before illness (Annex 2). Samples of the suspected fish or meal should be collected for CTXs testing. Identification and removal of the toxic fish to prevent further cases it is a priority. Information about the fish should be obtained, if possible.

Inform patient that ingestion of some substances (mainly alcohol, fish and nuts) may cause recurrent CP symptoms.

Treatment

There is no specific treatment: symptomatic and supportive treatments may be necessary.

Intravenous mannitol infusion is the most studied therapy for CP. It is suggested that it should be given within 48-72 hours of eating the toxic fish, although beneficial effects have been observed even up to several weeks after onset of symptoms. The results of a double-blind randomized study of mannitol treatment indicate that mannitol and normal saline were associated with clinical improvement and mannitol was not superior to saline. Hazards of mannitol treatment include loss of further fluids in patients suffering from

acute diarrhoea and vomiting and that patients experiencing bradycardia and hypotension are at higher risk of cardiac failure if infused with high doses of mannitol.

Measures for outbreaks

Any case of CP should be investigated as a possible outbreak. For outbreaks (two or more cases with an epidemiological link) an outbreak questionnaire should be completed (Annex 3).

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