Seafood Toxins

P. R. G. VARMA

Poisoning caused by the ingestion of toxin-containing seafood has been a part of man's concern for centuries. These toxins are either naturally present in the seafood or formed in the seafood due to some bacterial action on some natural compounds present in the seafood or accumulated in them due to aquatic pollution. The seafood toxins include Paralytic Shellfish Poison (PSP), Ciguatera toxins, Tetrodotoxin (Puffer fish), Ptychodiscus brevis toxins and Scombroid related toxins. Of these, except Scombroid toxins, all other toxins are naturally present in the seafood whereas Scombroid poisoning results from improper handling and/or processing of seafoods.

1. Ciguatera toxins

Ciguatera poisoning is an important and serious cause of morbidity in humans that result from the consumption of a large variety of reef associated fishes throughout the world. The term ciguatera is of Spanish origin and is used to refer to intoxications caused by the ingestion of a marine snail, *Turbo livona pica* known in Spanish by the Cuban name 'Cigua'. It is estimated that well over 50,000 people are afflicted by the disease yearly. Ciguatera is separate and distinct from other human illnesses (botulism and scombroid poisoning) and results from eating seafood that has spoiled because of improper handling and/or processing. Cooking (eg. frying, baking, broiling, boiling) smoking, drying, salting or freezing does not appear to destroy the toxin in the fish flesh and one cannot tell from the smell or appearance whether or not a fish is ciguatoxic. The victims usually recover from the illness within a few days. However, the symptoms may last for several weeks, months or possibly years. Death seldom occurs.

Well over 400 species of fishes have been listed as causing Ciguatera poisoning. Ciguatera species are limited to those fishes that feed on algae

or detritus on coral reefs and larger reef carnivores that prey on these herbivores. Barracuda, grouper and snapper are the fish most often implicated in the disease.

Ciguatoxin is the principal toxin caused by Ciguatera throughout the world. Certain dinoflagellate are the causative agents. The responsible species are *Gramblerdiscus toxicus* which produces Ciguatoxin and maitotoxin and *Prorocentrum concavum* which produces scaritoxin like toxin, maitotoxin like toxin and one very potent unnamed fast acting toxin. All these toxins contribute to the Ciguatera Syndrome.

Symptoms of Ciguatera poisoning are complex involving the digestive, cardiovascular and neurological systems. Usually, the illness begins with gastrointestinal inflammation, which causes severe dehydration and weakness, followed by cardiovascular and neurological Syndromes. The distinctive features of the poisoning are severe pruritus, temperature reversal and paresthesia-tingling and numbness of the extremities. The neurological symptoms may persist for months or years. Treatment for Ciguatera is symptomatic with no proven antidote known. However, Protamide has been used successfully in treating Ciguatera cases on Grand Bahama Island. Protamide is approved in 15 countries (eg. Belgium, Spain, U.K., Portugal) but is not approved for use in the U.S. Ciguatoxin has not been obtained in a pure form yet, but the most purified preparation showed a toxicity of 8 µg/kg in mice.

The difficulties to develop anti-ciguatera measures are (1) no simple and reliable bioassay method has been developed (2) variability of toxicity in Ciguateric fishes and (3) narrow and spotty geographic distribution of toxic fishes (fishes would be toxic at one reef and not at another a short distance away).

2. Paralytic shellfish poisoning (PSP)

Shellfish have become an important item on the world's food supply. Shellfish such as mussels and clams that feed on microscopic organisms concentrate and retain bacteria, viruses, toxins and poisons associated with

the organisms they feed on. One important hazard associated with shellfish consumption is Paralytic shellfish poisoning (PSP), caused by a highly lethal neurotoxin which the shellfish retain from feeding on certain poisonous dinoflagellates. Out of about 1200 species of dinoflagellates only a few produce the paralytic poison and they occur sporadically along many seacoasts throughout the world. Molluscs feed on the dinoflagellates and absorb toxic principle without themselves being affected. The toxin is not destroyed by cooking or steaming. Shortly after eating a contaminated shellfish, the consumer experiences a tingling sensation on the lips followed by progressive paralysis of the limbs and finally death due to respiratory paralysis (within 2-24 hrs) depending upon the dose. No antidote is known but artificial respiration administered soon after the symptoms appear are known to have saved lives.

The scientists of the University of California observed a particular dinoflagellate upon which the molluscs were feeding. The dinoflagellate was identified as *Gonyaulax catenella.* The *G. catenella,* like most other dinoflagellates, blooms over a period of 2 to 3 weeks and gradually dies off as other organisms bloom. In the natural state, mussels become poisonous soon after poisoning dinoflagellates bloom and excrete or destroy the poison within 2 to 3 weeks after the bloom has disappeared. However, the mussels will remain poisonous for a few weeks more. About 95% of the poison in mussel is seen in the dark gland or hepato-pancreas. Poisonous shellfish neither look nor taste different from normal ones. Although heavy blooms of dinoflagellates cause a 'red tide' (red discoloration) in water, concentrations as low as 400 or 500 cells/ml are sufficient to make the mussels too poisonous for human consumption. It would be advisable not to eat shellfish if a red tide bloom is apparent.

Further investigation on PSP showed that *Gonyaulax tarnarensis (car. excavate)* caused clams and scallops along the north east coast of North America and England to become poisonous. Death of humans resulted from the consumption of 5000 to 20000 Mu (A mouse unit (Mu) was defined as the minimum amount of poison that would kill a 20 gm mouse in 15 minutes when 1 ml of an extract of shellfish was injected intraperitoneally. Higher amounts than the minimum kill in shorter time).

The toxic principle named Saxitoxin was isolated from Alaskan butter clam *Saxidomas giganteus*. It was later found to be identical to the toxin obtained from the axenic culture of *G. catenella* and to the toxin obtained from the mussel *Mytilus californianis*.

Saxitoxin was found to be a white hygroscopic solid, highly soluble in water. The molecular formula is $C_{10}H_{17}N_7O_4$. The poison can be reduced with hydrogen at room temperature and pressure to produce a non-toxic derivative.

After a number of mouse bioassay tests, the FDA has set up a top limit of 80 µg of poison per 100 gm of shellfish meat as marketable for human consumption. The limit is well below the 1 to 4 mg deemed necessary in foods to cause sickness and death of humans.

3. Diarrhetic shellfish poisoning (DSP)

Diarrhetic shellfish poisoning (DSP) is a term given to a type of shellfish poisoning distinctly different from the paralytic shellfish poisoning (PSP) in both symptomatology and etiology. Unlike PSP, the predominant human symptoms of DSP are gastro-intestinal disturbance; no fatal cases have so far been reported. Nevertheless, the high morbidity rate and the worldwide distribution of DSP make it a serious threat to both public health and shellfish industries. The origin of this toxin is the dinoflagellate, *Dinophysis fortii*. The toxin is named as Dinophysis toxins (DTX S) and is structurally related to *okadaic acid*. During 1976-82, more than 1300 people were officially diagonised as DSP cases in Japan. Frequency of signs and symptoms include diarrhoea (92%) nausea (80%), vomiting (79%), abdominal pain (53%) and chill (10%). Incubation period ranged from 30 minutes to few hours. Suffering may last for 3 days. Cooking did not destroy the toxin, but intoxication could be avoided if the digestive gland (where the toxin is concentrated) is removed beforehand. Maximum limit of the toxin is 5 mouse unit/100 gm meat.

4. Pufferfish toxin

It is common knowledge that many species of pufferfish are toxic to man. In spite of such recognition, a great number of persons have

been intoxicated by ingesting pufferfish in Japan. The pufferfish toxin, *Tetrodotoxin* (TTX) is named after the family Tetradontidae into which most pufferfish are classified. This is a very serious poison in that the mortality rate is over 50%. In Japan, where pufferfish is a delicacy, despite all precautions, about 100 persons die every year from this affliction. However, the flesh of these fishes is non-toxic or, less toxic but the toxin is mainly present in the viscera The risk normally arises from contamination of the flesh by the viscera. In Japan, only certain trained persons are allowed to prepare the fish for public consumption. The origin of the toxin is not known. The lethal dose of TTX in humans is about *10,000 MU*. In Japan, pufferfishes are toxified up to a level of several hundred mouse units per gram.

5. Neurotoxic shellfish poisoning (NSP)

This poisoning has been detected in people who consumed bivalves that have been exposed to "red tides" of the dinoflagellate *(Ptychodiscus breve)*. The disease has been limited to the Gulf of Mexico and areas off the coast of Florida. Toxins are highly lethal to fish and red tides of this dinoflagellate are also associated with massive fish kills.

The symptoms of NSP resemble those of PSP except that paralysis does not occur. NSP is seldom fatal.

6. Amnesic shellfish poisoning (ASP)

This has only recently been identified. The intoxication is due to domoic acid, an amino acid produced by the diatom *Nitshia pungens*. The first reported incidence of ASP occurred in the winter of 1987/88 in eastern Canada, where over 150 people were affected and 4 deaths occurred after consumption of cultured blue mussels.

The symptoms of ASP vary greatly from slight nausea and vomiting to loss of equilibrium and central neural deficits including confusion and memory loss. The short term memory loss may be permanent in surviving victims, thus the term Amnesic Shellfish Poisoning.

The control of marine biotoxins is difficult and the disease cannot be entirely prevented. The toxins are all of non-protein nature and extremely stable. Thus, cooking, smoking, drying or salting does not destroy them, and one cannot tell from the appearance of fish or shellfish flesh whether it is toxic.

The major preventive measure is inspection and sampling from fishing areas and shellfish beds and analysis for toxins. The mouse bioassay is often used for this purpose and if high levels of toxin are found, commercial harvesting is halted. No other method is currently available for control of the disease. It seems unlikely that it will ever be possible to control phytoplankton composition in growing areas, eliminating toxigenic species, and there is no reliable way to forecast when a particular phytoplankton will grow and thus no way to predict blooming of toxigenic species.

Removal of toxin by depuration techniques may have some potential, but the process is very slow and costly. There is also a risk that a small number of individuals decline to open and pump clean water through the system thereby retaining their original level of toxicity.

To be effective, monitoring requires reliable sampling plans and efficient means of detection of the toxins. The sampling plan must take into consideration that toxicity of shellfish can increase from negligible to lethal levels in less than one week. Also, the toxicity can vary within a growing locality for shellfish according to geography, water currents and tidal activity.

7. Scombroid poisoning

Scombroid poisoning is caused by ingestion of foods containing unusually high levels of histamine. Scombroid poisoning occurs world wide in all countries where fish is consumed. The evidence supporting the role of histamine as the causative agent in scombroid poisoning is compelling. However, histamine ingested with spoiled fish is much more toxic than histamine ingested in an aqueous solution. This paradox may be explained by the presence of potentiators of histamine toxicity in

spoiled fish. Several substances including Cadeverine and Putrescine have been identified as possible potentiators of histamine toxicity that would be expected to be present in spoiled fish. The mechanism of action of these potentiators has not been completely elucidated, but they appear to act by inhibition of intestinal histamine-metabolizing enzymes. This enzyme-inhibition increases the intestinal uptake of unmetabolized histamine.

Scombroid poisoning is a chemical intoxication occurring after the ingeston of foods containing unusually high levels of histamine. The incubation period for this food-borne disease is short, ranging from several minutes to several hours following ingestion. The duration of the illness is typically only a few hours, but symptoms lasting up to several days have been reported.

A variety of symptoms can occur in cases of scombroid poisoning. The symptoms can be cutaneous (rash, urticaria, edema, localized inflammation), gastrointestinal (nausea, vomiting, diarrhoea), hemodynamic (hypotension) and neurological (headache, palpitation, tingling, flushing or burning). Most individuals suffering from scombroid poisoning will experience only a few of these symptoms.

The fish most commonly implicated in these outbreaks are the so called scombroid fish belonging to the families Scomberesocidae and Scombridae. These fish would include the many varieties of tuna, skipjack, bonito, albacore, mackerel, spanish mackerel, bluefish, saury, butterfly kingfish and seerfish. Tuna, skipjack and mackerel are the most commonly involved scombroid fish.

Several types of non-scombroid fish can also be incriminated in outbreaks of scombroid poisoning. Thus, scombroid poisoning is a misnomer. A more appropriate name for this foodborne disease would be histamine poisoning. The non-scombroid fish that have been involved in outbreaks of histamine poisoning are mahi-mahi, sardines, pilchards, anchovies, herring and black marlin.

spoiled fish. Several substances including Cadeverine and Putrescine have been identified as possible potentiators of histamine toxicity that would be expected to be present in spoiled fish. The mechanism of action of these potentiators has not been completely elucidated, but they appear to act by inhibition of intestinal histamine-metabolizing enzymes. This enzyme-inhibition increases the intestinal uptake of unmetabolized histamine.

Scombroid poisoning is a chemical intoxication occurring after the ingeston of foods containing unusually high levels of histamine. The incubation period for this food-borne disease is short, ranging from several minutes to several hours following ingestion. The duration of the illness is typically only a few hours, but symptoms lasting up to several days have been reported.

A variety of symptoms can occur in cases of scombroid poisoning. The symptoms can be cutaneous (rash, urticaria, edema, localized inflammation), gastrointestinal (nausea, vomiting, diarrhoea), hemodynamic (hypotension) and neurological (headache, palpitation, tingling, flushing or burning). Most individuals suffering from scombroid poisoning will experience only a few of these symptoms.

The fish most commonly implicated in these outbreaks are the so called scombroid fish belonging to the families Scomberesocidae and Scombridae. These fish would include the many varieties of tuna, skipjack, bonito, albacore, mackerel, spanish mackerel, bluefish, saury, butterfly kingfish and seerfish. Tuna, skipjack and mackerel are the most commonly involved scombroid fish.

Several types of non-scombroid fish can also be incriminated in outbreaks of scombroid poisoning. Thus, scombroid poisoning is a misnomer. A more appropriate name for this foodborne disease would be histamine poisoning. The non-scombroid fish that have been involved in outbreaks of histamine poisoning are mahi-mahi, sardines, pilchards, anchovies, herring and black marlin.

be the highest near the gut cavity of the anterior section and decreased in the sections approaching the tail. Seasonal variations in histidine content were also observed. The highest content was during summer when the fish had highest fat content.

Factors contributing to histamine production

Icing plays an important role in minimising the production of histamine. Icing the fish immediately after catch and keeping the ice to fish ratio low (1:2) will substantially lower the histamine production in landed fish. Proper icing is required especially in tropical countries with high temperature and relative humidity which favour the growth of most microorganisms. In Indonesia, skipjack tuna caught by artisanal fishermen often caused histamine poisoning. The fish caught by artisanal fishermen were held without chilling (icing) for up to 8 hrs under direct sunlight at relatively high temperature and humidity. This may be one of the reasons for high histamine content. Histamine content of delayed iced skipjack was significantly higher than those immediately iced on board the fishing vessel. With storage of tuna, herring and mackerel at 4°C for 3-4 days, the histamine content exceeded 100 mg/kg. On the fifth day, histamine content reached 596 ppm. in mackerel, 978 ppm. in herring and 3720 ppm. in tuna. Therefore, the storage temperature should be 0°C or below.

Histamine is not produced in frozen storage. High levels of histamine occurred sporadically in commercial canned scombroid fish products sampled from different parts of the world. A good percentage of the samples had histamine content more than 100 ppm. In good products, histamine content varied between 0.28 to 4.02 ppm. Histamine content in canned products is mainly related to the raw material quality.

Based on the experience acquired in the investigation of hundreds of scombroid poisoning incidents, the U.S. FDA recently established 50 mg/100 gm as the hazard action level for histamine in tuna.