

S.P.C. 1974-1975
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SOUTH PACIFIC COMMISSION

SEMINAR ON ICHTHYOSARCOTOXISM

Papeete, French Polynesia, 16th - 22nd August, 1968

R E P O R T

South Pacific Commission
Noumea, New Caledonia
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INTRODUCTION

This Seminar on Ichthyosarcotoxism was the first international meeting on the subject to be held in the South Pacific area. It was convened as the result of recommendations from the Seminar on Health Problems of Coral Atoll Populations (Tarawa, May 1967), and a request from French Polynesia.

As ichthyosarcotoxism is widespread and important throughout the area it serves, the South Pacific Commission has aided research and collected material for a period of eighteen years. Recent progress in research into the problem, with all its ramifications, indicated that a conference of specialists involved was very desirable so that each could exchange information and present this in collated form for the benefit of territories involved and for those active in research.

The Seminar was held at the "Ecole Normale de Tipaerui", Papeete, Tahiti, from the 16th to the 22nd of August 1968. After a formal opening by the Secretary-General of French Polynesia at a ceremony in the Council of Government Meeting Hall, Dr E. Poyet, Director of Health of French Polynesia, was elected as Chairman, with Professor A.H. Banner of the University of Hawaii, and Professor Y. Hashimoto of the University of Tokyo as Vice Chairmen; Mr M. Legand and Dr P. Helfrich were elected as French and English rapporteurs.

The purpose of the Seminar was the exchange of current information on all aspects of ichthyosarcotoxism, its clinical manifestations, its epidemiology, the nature, origin and pharmacological actions of toxins involved, its medical treatment and its economic and nutritional implications. In addition, the Seminar aimed at providing a wider understanding of the subject and at providing a stimulus for further research.

Participants represented all the major specialities involved and attended from Australia, Cook Islands, France, French Polynesia, Hawaii, Japan, New Caledonia, United Kingdom, and United States of America. Formal discussions were supplemented by visits to medical and fisheries research centres in Tahiti and Rangiroa as well as visits to reef areas where toxic species exist in Tahiti and Moorea.

Free discussion and the co-operation of participants resulted in a successful and stimulating Seminar which emphasised that, while some progress has been made, there still remains a great deal of research to be undertaken.

PROCEEDINGS

1. Definition

Basically the term ichthyosarcotoxism means fish flesh poisoning. It encompasses many differing varieties of intoxication which have been delineated either on the basis of the clinical picture produced or of the species of causative fish. Many species, many toxins are involved and precise definition or categorisation is not possible in the present state of knowledge. However, there appears to be broad differentiation between characteristic illnesses which appear following ingestion of diverse species of toxic fish and illnesses which occur following ingestion of particular species. In both categories, any portion of the fish may give rise to intoxication and this intoxication is not the result of accidental contamination by bacterial food pathogens. Fishes involved are those which inhabit tropical reef waters.

1.1 Ichthyosarcotoxism as the result of ingestion of diverse species of toxic fish

1.1.1 Ciguatera. Ciguatera is a clinical syndrome characterised by disturbances, in varying proportions, of the neurologic, cardiovascular, gastrointestinal and skeleto-muscular systems. Considerable variation in the syndrome exists but that most constant and characteristic is disturbance of the neurologic system manifested by dysthenia on contact with cold objects, myalgia and pronounced muscle weakness.

Most tropical fish poisoning falls into this category.

1.1.2 Hallucinatory fish poisoning. Hallucinatory fish poisoning is a clinical syndrome characterised by psychologic disturbances of hallucination and depression. Gastrointestinal disturbance may occur.

1.2 Ichthyosarcotoxism found in taxonomic groups

1.2.1 Elasmobranch poisoning. From ingestion of sharks, skates and rays.

1.2.2 Clupeoid poisoning. From ingestion of sardines and sardine-like fishes.

1.2.3 Scombroid poisoning. From ingestion of tuna and mackerel-like fishes.

1.2.4 Tetraodon poisoning. From ingestion of puffers and puffer-like fishes.

As ciguatera is the most commonly occurring form of fish poisoning in tropical areas, discussion will deal with this subject unless otherwise stated.

III - pattern of intoxications at a sustained low level with well-defined geographical limits and species involved.

Ciguatera is known to have occurred in the 16th century in the Indian Ocean and New Caledonia; more recent reports attest to its presence in the South-Central and North-Western Pacific and evidence exists that there has been a gradual spread in a North-Easterly direction. In 1939, it spread to the Linè Islands, and in 1957 the first case was reported from the ingestion of reef fish in Hawaii.

4. Geographical distribution and epidemiological factors in ciguatera

Ciguatoxic fishes are widely distributed among oceanic islands in the tropical Indo-Pacific and in the Caribbean. They generally occur only around islands within 30° of the Equator and rarely along the coasts of continents with the exception of Australia. The large islands of the Philippines and Indonesia appear to be free of ciguateric fishes.

The species involved in ciguatera fish poisoning include a variety of reef fishes normally utilized as food. The most common are the acanthurids (surgeon fishes), the lutjanids (snappers), serranids (groupers), carangids (jacks, pompanos), scarids (parrot fish), and sphyraenids (barracuda). Ciguatera rarely occurs in tutas or other pelagic species.

Ciguatera may be prevalent in fishes from certain islands or certain parts of islands; the geographic range may expand and contract; the number of toxic species may fluctuate and the toxicity of species may vary in intensity but knowledge of the dynamics of these changes is little understood as it is based upon incomplete data from scattered reports. Some evidence exists that cyclical increases in ciguatera occur with a peak of outbreaks and subsequent decline to a low level for a prolonged period. During the periods of increase, more species of fish become toxic, and the level of toxicity of individual fish increases. In the decline, compulsive carnivorous fish show persistence of toxicity for a longer time than other species. This persistence is aggravated by fishing practices in some areas where gut, liver and waste are dumped at the sea where the fishes have been caught, thus producing cyclical transmission of toxins through scavenger fish.

The incidence of ciguatera is most marked in populations dependent on fish protein, thus tending to affect lower socio-economic groups. However, no stratum of society is immune and, where toxic fish species exist, the entire population is considered to be at risk.

5. Clinical picture

Ciguatera presents a polymorphous clinical picture with a few characteristic features which enable ready diagnosis to be made.

The full clinical picture is one of toxic polyneuritis in association, to a greater or lesser extent, with three other types of disturbance: gastrointestinal, cardiovascular and algic. General symptoms of malaise, asthenia and chills frequently appear and there have been reports of oliguria and haematuria. Asthenia may be severe enough to make walking difficult and may persist for a long period. Laboratory investigations are unproductive.

The most complete form with its various syndrome - neurologic digestive, cardiovascular and algic with repercussions on the general condition - is adopted as typical for purposes of description.

5.4 Progress and Prognosis

The condition is rarely fatal but deaths have been reported. Generally, the cardiovascular symptoms subside within a few days but paresthesia, asthenia and pruritus may persist much longer with some residual incapacity over a period of some months.

6. The toxin, its isolation, identity and properties

6.1 Evidence that a multiplicity of toxins are involved in ichthyosarcotoxism has been increasingly accumulated and at least seven different toxins have been demonstrated in toxic fishes.

A fat-soluble toxin, probably identical with ciguatoxin, has been found in the muscle of Lutjanus bohar and L. monostigma. This toxin may be a principal one in ciguatera.

A water-soluble toxin causing transient vomiting in cats has been found and designated as ciguaterin. It has been confirmed to be distributed widely in the liver and occasionally in the muscle of representative ciguatoxic fishes. This toxin, however, may be a less important factor than ciguatoxin in the development of ciguatera.

The skin of a sea bass (Pogonoperca punctata) has been found to contain a toxin, inducing in cats ciguatera-like syndromes when force-fed or injected. This revealed both ichthyotoxic and hemolytic activities with a closer similarity to the ichthyotoxin found in soapfish rather than to the pahutoxin in boxfish.

A water-soluble substance toxic to mice was detected in the viscera and digestive tract contents of a filefish (Alutera scripta). From its chemical properties this could be a new marine toxin. The toxin in the viscera was indistinguishable in chemical and pharmacological properties from that in the ingested materials, which mainly consisted of broken reef corals tentatively identified as Goniopora sp. This may strongly suggest the presence of toxic reef corals which serve as a primary source of toxin in the filefish and perhaps in many other coral feeders.

Further toxins have been isolated from the liver and flesh of Gymnothorax javanicus and from toxic crabs.

6.2 Liver toxin from Gymnothorax javanicus

Although it has been known for some time that livers of ciguaterix fish contain a higher concentration of toxin than does the flesh, early attempts at extraction of toxic shark livers were unsatisfactory. A procedure was devised by which toxin from the livers of the moray eel Gymnothorax javanicus could be extracted and purified.

In the course of this work it was discovered that toxin could be extracted not only from livers of eels with a mongoose rating of +1 to +5, but also from Johnston Island G. javanicus with a zero (i.e., non-toxic) mongoose rating. In fact, livers obtained from eels with mongoose ratings of 0 to +3 contain approximately the same amount of toxin per unit weight of liver. Livers from G. javanicus (Johnston) with mongoose ratings of +4 and +5 possess distinctly larger amounts of toxin per unit weight of liver.

6.5 Pharmacological action

Ciguatoxin extracts from the flesh and liver of moray eels (Gymnothorax javanicus) have been tested by intravenous injection in rats. To show the pharmacologic action, respiratory rate, pulse rate and blood pressure tracings were recorded continuously before and after injection. In the otherwise untreated animal, ciguatoxin produced transient apnoea, hypotension and bradycardia immediately following or during administration, followed shortly by re-establishment of respiration with hypertension and tachycardia. To determine the physiological origin of these reactions, rats were subjected to several procedures such as resection of the ninth and tenth cranial nerves and medication with drugs of known mechanisms of action.

The results of these investigations indicate direct muscarinic and nicotinic cholinomimetic effects which are not the result of anti-cholinesterase action. Atropine has been found to be an antagonist of the peripheral muscarinic actions although it is not effective against the central respiratory failure produced by ciguatoxin; in large dosage, some protection against peripheral nicotinic actions has also been observed. Comparison of toxins at different stages of purification has shown that there is some reduction in the number of cholinergic sites affected by the most purified toxins. On the other hand the pure liver toxin appears to be pharmacologically identical to one of the purified flesh fractions. It is concluded that the crude toxin may contain more than one toxic molecule but that all toxin types have a basically similar "cholinergic" mechanism of action.

7. Bio-assays

Field studies on ciguateric fish have been limited by the lack of a simple test for toxicity. Lack of knowledge of the chemistry of the toxin together with the multiplicity of toxins have not permitted the development of any chemical tests. The only practical tests applicable have been bio-assays using cats, rats, mice, mongooses and chickens. Both the intraperitoneal injection of extracts into mice and the mongoose feeding test have been utilised fairly widely as bio-assays but both have their limitations and difficulties.

A new test has been developed utilizing the stream crayfish of the southern United States (Procambarus clarkii, Girard) and an emulsified homogenate of the liver. The crayfish was chosen as it has twice been reported to be sensitive to toxic fish; extract of fish liver was chosen as it may contain up to 50 times as much toxin per unit weight as flesh.

In the testing technique fish liver is minced and then homogenized mechanically in a solution of 4.5% Tween 60 (Polyoxethelene sorbitan monosterate) in 0.9% NaCl, at the ratio of 1 g liver to 2 ml solution. This homogenate is heated to 60° C for 30 minutes and then centrifuged. The resulting supernatant fluid is used to inject crayfish at 0.33% body weight on the ventral side of the second abdominal segment, lateral to the midline.

If the crayfish is injected with a blank control solution, or with extract from non-toxic fish, there is no reaction. If the crayfish is injected with extract from a toxic fish, it reacts in one of the following ways: transient convulsions with abdominal flexure, loss of aggressive posture with the chela, awkward stance and twitching of appendages, loss of righting reflex or moribundity and death. Of these reactions, the loss of righting reflex is the most convenient for purposes of assessment. This loss of righting reflex is defined as existing when a crayfish which has turned over, or has been turned over on to its back with a rod fails to right itself after two minutes.

The green alga Enteromorpha sp. and the brown Ectocarpus sp. succeeded Chrysonophos on the new surfaces after about a month in the sea. Still later these algae were largely replaced by many species such as the bluegreens Calothrix crustacea and Lynngbya majuscula, the brown Sphacetaria sp., the green Cladophora sp., and the reds Polysiphonia sp., Centroceras clavatum, and Laurencia sp. These algae were tested en masse. The bluegreens Hormothamion enteromorphoides, Lynngbya aestuarii, and Calothrix sp. and assorted diatoms were the principal algae growing on a concrete surface placed on a sand bottom in the lagoon near a toxic reef in Tahiti; this surface was subject to some silting by sand. A new surface placed in the sea on December 23 for twenty days yielded primarily Cladophora, and one in 15 days beginning February 29 mainly Enteromorpha (with some Eryptotrichia, Sphaecelaria, and Cladophora). The bluegreen Phormidium sp., which was found growing naturally at the edge of Teavaraa Pass, Tahiti, was also tested. The two mice injected with extracts of this alga died in 34 minutes at the dosage of 2000 μ /g. Deaths from other algae required at least 3000 μ /g. A test with seawater alone produced death in two mice in 85 minutes at 3500 μ /g.

The following algae were collected at toxic sectors at Ishigaki in the Ryukyu Islands: the green Chlorodesmis sp., the diatom Synedra sp., and the bluegreens Phormidium sp. and Lynngbya sp. None were toxic beyond the level of 3000 μ /g.

Although these results do not suggest that any of the algae tested are the source of ciguatera toxins, it should be remembered that the toxic level in the responsible organism may be very low and thus difficult to demonstrate by direct feeding or injection of extracts into mice. Also it is possible that a precursor of the toxic substance occurs in an alga which exhibits no toxic properties until it is metabolized by animals.

8.2 The rôle of other organisms

A limited number of observations on the stomach contents of fish have shown the presence of two types of yeasts in toxic fish but only one in non-toxic fish. Insufficient work has been performed to draw any conclusions from this and further investigations are required before the possible rôle of yeast as a toxin producer can be elucidated.

8.3 The rôle of newly exposed underwater surfaces

Disturbance of submarine substrata as the result of blasting, underwater construction, ship or aircraft wreck, disposal of war material, etc. have been frequently recorded as being followed by the appearance of toxicity in fish. An example of this effect was reported from the island of Hikueru in the Tuamotu Group. Here a wharf was constructed using reef material but its site was unsuitable for ships working at certain states to tide and sea so that unloading then was necessary at a point two miles distant. Within two years, fish in both areas became toxic and the incidence of toxicity subsequently extended until they fused. Another incident demonstrates equally this effect. Two aircraft crashed into a lagoon. In view of the possibility of development of toxicity in fish, attempts to remove both wrecks were made, but only one was successfully removed. The other remained submerged and, about it, fish developed toxicity. It would appear from such observations that the exposure of new submarine surfaces as well as disturbance of substrata does result in the appearance of toxicity.

Vitamin B complex, colchicine and salicylic acid have been used to reduce neurological disorders; synthetic antihistamines and magnesium hyposulphite for pruritis; antispasmodic drugs, lactic acid bacilli and vegetable charcoal for digestive tract disorders; and analeptics with steroids for cardiovascular shock.

Where dehydration is present, fluid and electrolyte replacement therapy plays an essential part in the initial phase of severe toxicity.

9.2 Specific treatment

9.2.1 Oximes

As the result of recent investigations, oxime-type cholinesterase regenerators have been tried both alone and in association with atropine. Their action appears reasonably effective in relieving the vagal hyper-excitation symptoms of ciguatera, especially when administered early.

9.2.2 Ion chelating agents

Chelating agents act by combining with heavy metallic ions to form stable complexes in which metal is dissimulated, thus losing its toxicity. The structure of the ciguatoxin molecule appears to simulate a heavy metal in this type of action and chelating agents have had some success.

Both oximes and chelating agents require to be administered in hospital at an early stage and their use is thus necessarily limited.

10. Ichthyosarcotoxism and marine protein food resources

10.1 The increasing world population pressures, the urgent need for establishing a solid fishing economy among under-developed countries, the need for low-priced high quality protein food products by almost two-thirds of the world's population, and the rapid advance and expansion of insular shore fisheries all indicate the importance of establishing a better understanding of the marine protein food potential.

The oceans annually produce about 400 million metric tons of animal protein in a variety of species and sizes suitable for harvest and use by man. Since 1850, the world catch of fishes and shellfishes has progressively increased from about 1.5 million tons to about 50 million tons in 1964, less than ten percent of the total catch coming from fresh water. Analysis of the total catch reveals that about 85.9 percent of the organisms were fishes, and the remainder were shellfish (7.6 percent), whales (5.1 percent), and other aquatic animals (1.4 percent).

Despite the fact that ichthyologists recognize about 25,000 species of fishes, less than 13 kinds make up the bulk of the world's fisheries catches. A few kinds of fishes are heavily exploited, some are fished but unexploited, and others are abundant but go unharvested. Recent studies indicate that the rapidly growing fisheries are not in northern or southern latitudes but rather are in tropical seas and it is anticipated that this trend will continue with even greater efforts being directed to tropical insular areas.

RECOMMENDATIONS

1. The Seminar recommends that particular attention be devoted to the epidemiological and ecological aspects of marine biotoxinations (especially ichthyosarcotoxism). This should include the documentation, collation, identification of causative agents, biology, clinical data, incidence of outbreaks, and economic implications. All these data should be coordinated, collected, and distributed by an international agency.
 2. The Seminar recommends that the South Pacific Commission requests the World Health Organization that ichthyosarcotoxism and marine biotoxination be included amongst the reportable diseases, since these represent:
 - (a) an important, world-wide, public health problem on which little is known; and
 - (b) serious impairment of the future development of world food resources of marine origin.
 3. The Seminar recommends that intensive study be given to the problems of marine biotoxinations since they are a limiting factor in the future economic development of marine aquaculture techniques.
 4. The Seminar recommends that the various governments grant every financial and administrative support to any international research programme on marine biotoxination and especially ichthyosarcotoxism that might be established in their territory.
 5. The Seminar recommends that intensive study be given to the development of a more suitable bio-assay method for use in field investigations on marine biotoxination.
 6. The Seminar recommends that periodic meetings be held to exchange information on all aspects of marine toxins and other marine substances with useful biological activity. These meetings should be held approximately every two years starting with participation in the 1970 Twelfth Pacific Science Congress at Canberra, Australia.
 7. The Seminar recommends that the South Pacific Commission publish a regular newsletter at about 3 to 6 monthly intervals providing information on fish poisoning and research activity to public health workers and interested workers.
 8. The Seminar supports the proposal of the Technical Meeting on Fisheries held in Noumea in June 1968 for the establishment of an agency specifically charged with responsibility for initiating and assisting the rational development of the resources of the reef and lagoon and immediate offshore waters, and urges that the Agency support research on ichthyosarcotoxism.
 9. The Seminar recommends that the future economic potential of marine biochemical agents be explored as to their use as new foods and pharmaceutical products.
 10. In view of reliable information on serious and continuing outbreaks of fish poisoning in the Marquesas Islands, and in view of the potential information that can be gained from a study of such a highly toxic area, the Seminar recommends that a coordinated scientific study be undertaken employing those specialists that can most profitably exploit this situation. It further recommends that this endeavour make a special effort to obtain toxic raw material needed for later chemical and pharmacological studies.
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ANNEX I

CONFIDENTIAL

A G E N D A

16th August 1968

9:00 a.m.

Official Opening
Briefing on Seminar Procedure
Election of officials

Afternoon

Field visit to the Marine Biology Laboratory
at Papara.

18th August 1968

All day

Trip to Rangiroa (Tuamotu Islands)

- Visit to Fisheries Department facilities
at Avaatoru (cold storage, fish pond).
- Exhibition of commercial and toxic fish
species by J. Tapu, World Champion of
under-water spear-fishing.
- Description of work being done on sharks
by T.W. Brown, of the British Overseas
Deep Sea Diving & Salvage Service, Australian
Deep Sea Diving and Salvage Service.

19th August 1968

Morning

Actual significance of fish poisoning in general,
and particularly of ciguatera, in the various
participating territories. Geographic distribution.
Public health aspects. Development of ichthyo-
sarcotoxism.

Afternoon

Epidemiological aspects: major ciguatoxic
species, apparent seasonal variations.

Clinical aspects: variations according to
species; the sensitization and summation concepts.

Paraclinical aspects: emphasis in complementary
tests.

20th August 1968

Morning

Present knowledge of marine toxins which may
be a cause of fish poisoning. Pharmacological
and chemical characteristics of the various
toxic fractions.

Afternoon

Problems of experimenting with animals; various
techniques, in particular, the possible use
of invertebrates.

Early diagnosis of fish toxicity: the value
of empirical notions, advances in the development
of a scientific technique.

Experimental induction of toxicity in non-toxic
fishes.

ANNEX II

LIST OF PARTICIPANTS

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LIST OF WORKING PAPERS

- SPC/ICHT/WP. 1 - Recent cases of ichthyosarcotoxism recorded in British Solomon Islands Protectorate.
- SPC/ICHT/WP. 2 - Clinical forms of fish poisoning of the "Ciguatera" type in French Polynesia, by Raymond Bagnis.
- SPC/ICHT/WP. 3 - Ciguatera in Tahiti: An endemic disease, by R. Bagnis, J. Bennett, V. Joutain, and F. Nanai.
- * SPC/ICHT/WP. 4 - The significance of marine biotoxins to marine protein concentrates and food from the sea, by Dr Bruce W. Halstead.
- SPC/ICHT/WP. 5 - Occurrence of toxic crabs in the Ryukyu and Amami Islands and similarity of the crab toxin to Saxitoxin, by Shoji Konosu and Yoshiro Hashimoto .
- SPC/ICHT/WP. 6 - Toxins found in ciguatoxic fishes in the Ryukyu Islands, by Yoshiro Hashimoto.
- SPC/ICHT/WP. 7 - Ciguatera in the Ryukyu and Amami Islands, by Yoshiro Hashimoto, Shoji Konosu and Takeshi Yasumoto.
- SPC/ICHT/WP. 8 - Some cases of ciguatera and cognate ichthyosarcotoxism reported from Tokyo, by Tokiharu Abe.
- SPC/ICHT/WP. 9 - Outline of ichthyosarcotoxism in New Caledonia, by G. Chemier
- SPC/ICHT/WP.10 - Ichthyosarcotoxism (Fish Poisoning) in New Guinea, by A.M. Rapson.
- SPC/ICHT/WP.11 - Comments on some cases of ciguatera observed in American Samoa, by Ernest Thompson.
- SPC/ICHT/WP.12 - Selected list of bibliographical references on ichthyosarcotoxism.
- SPC/ICHT/WP.13 - The biology of Ctenochaetus striatus, a known ciguateric acanthurid fish of Tahiti, by Charles K. Walters.
- SPC/ICHT/WP.14 - Ciguatera in Queensland, by G.D. Broadbent.
- * SPC/ICHT/WP.15 - Cerebellar syndrome in Ciguatera, Notes on two cases, by M. Barbotin and R. Bagnis.
- * SPC/ICHT/WP.16 - Pharmacological reaction of the rat to ciguatoxin, by Martin D. Rayner.
- * SPC/ICHT/WP.17 - Liver toxins from Gymnothorax javanicus, by Takeshi Yasumoto and Paul J. Scheuer.
- * SPC/ICHT/WP.18 - A new field and screening bioassay for ciguatera, by Emile Keene, Helen A. Randall and Albert H. Banner.
- * SPC/ICHT/WP.19 - Ciguatoxin, by Wataru Takahashi and Paul J. Scheuer.
- * SPC/ICHT/WP.20 - Marine algae as a possible source of ciguatera toxins, by John E. Randall.
- * SPC/ICHT/WP.21 - Patterns of development of ciguatera fish poisoning in the Pacific, by Philip Helfrich.

SOUTH PACIFIC COMMISSION

SEMINAR ON ICHTHYOSARCOTOXISM

(Rangiroa, French Polynesia, 16th - 22nd August 1968)

RECENT CASES OF ICHTHYOSARCOTOXISM
RECORDED IN BRITISH SOLOMON ISLANDS PROTECTORATE

Central District : (Guadalcanal, Savo, Nggela, Russell Islands,
Rennel, Bellona, Santa Ysabel)

No cases said to be on record.

Eastern District : (San Cristobal, Ulawa, Santa Cruz, Ugi, Santa Ana,
Vanikoro, etc.)

Red snapper: reported to be 2 varieties around Solomons. One can cause an illness characterised by vomiting, muscular aches and pains (Santa Cruz), no fatalities reported.

From different sources (Ulawa and Ugi) reported that this fish is very toxic to infants - several cases reported of babies having convulsions similar to tetanus - after mother ate supper. Toxin presumably ingested in breast milk.

Grouper: also reported to be toxic to infants of lactating mothers. No cases of fatal poisoning reported.

Barracuda: intolerance to barracuda reported by the Ariki Kafika (Tikopia) who reports that he had an illness consistent with ciguatera poisoning after eating this fish. Vomiting and nausea were followed by muscular pains and weakness lasting several days. Other Tikopians similarly affected.

Puffer fish: cases previously encountered in the Solomons of tetraodon poisoning which, on occasion, has been fatal - 1958, two deaths recorded in Honiara (from Rove) within a few hours of ingesting sharp-backed puffer fish, also 1962, death in Reef Islands from the same fish. Smooth puffer and sharp-backed puffer recognised as poisonous fish in this District and avoided. Spiny puffer only eaten after thorough cleaning and removal of gonads.

Trigger fish, filefish and boxfish: are commonly eaten, although there has been one case of poisoning from boxfish (Dr Beck).

Moray eel (*Gymnothorax flavimarginatus*) : considered poisonous in Tikopia and avoided, but eaten in Santa Cruz and Cristobal. Toxicity encountered in Santa Cruz.

Turtle: some time ago (?1963), two people died, one adult, one child, in Santa Ana after eating turtle. One other man who ate some of the same turtle was admitted to Kira Kira Hospital seriously ill- but survived.

SOUTH PACIFIC COMMISSION

SEMINAR ON ICHTHYOSARCOTOXISM

(Rangiroa, French Polynesia, 16th - 22nd August, 1968)

SUMMARY

CLINICAL FORMS OF FISH POISONING OF THE "CIGUATERA" TYPE
IN FRENCH POLYNESIA

by Raymond BAGNIS
Naval Captain, Medical Officer

Fish toxicity has existed in French Polynesia for a very long time, the majority of cases being of the ciguatera type.

The results of 350 clinical observations recorded over a three-year period have been analysed: detailed description of the complete form with - basically - its four characteristic syndromes: digestive, cardiovascular, neurological, algic, and an associated syndrome the components of which are more or less constant; the course normally followed leads towards recovery without after-effects within a period ranging from three days to one month.

The type of description chosen for the purpose of the exposé is the most characteristic, but a certain number of factors come into play which multiply the number of particular cases. Consequently the author has endeavoured to establish a classification of the clinical forms, bearing in mind the polymorphism of the symptoms, the sensitization phenomena and the rôle of the causal species.

There follows a consideration of the problem of ciguatera diagnosis; this is determined on the basis of three specific symptoms: modification of sensitivity (permanent symptom), bradycardia and mydriasis which appear in the hours following the ingestion of a suspect fish; this clinical association enables ciguatera to be differentiated from the other varieties of fish toxicity encountered in French Polynesia.

Finally, passing rapidly over a pathogeny as yet little known, the author shows that the oximes, cholinesterases regenerators, successfully used in association with large doses of atropine and a vitamin B cocktail in the treatment of severe and complete forms of toxicity, do not appear to constitute the specific treatment eagerly anticipated during the last few years.

Work accomplished in the Medical
Oceanography Section of the
Louis Malardé Research Institute,
in collaboration with J. Bennett,
V. Joutain and F. Nanai,
Papeete, 3rd April, 1968.

SOUTH PACIFIC COMMISSION

SEMINAR ON ICHTHYOSARCOTOXISM

(Rangiroa, French Polynesia, 16th - 22nd August, 1968)

CIGUATERA IN TAHITI: AN ENDEMIC DISEASE

S U M M A R Y

A survey was carried out with a view to ascertaining the true extent of the incidence of poisoning by toxic fish in Tahiti, and its consequences. It covered an actual population of 33,085 persons - i.e. close on 89% of the population of the districts and the two townships of Tahiti.

The year 1966, from January to December inclusive, was chosen as the period of time in which the survey of cases of intoxication was to be made. The incidence of the illness - i.e. the total number of cases which had occurred during that period - was 2,798. The rate of incidence is 8.45%. It can be said, therefore, that this endemic disease is extensive.

This survey has also enabled a count to be made of over 40 species of toxic fish, the majority being carnivorous. This list does not include the species found in the other islands or island groups.

A survey was carried out in respect of the toxic areas and a map drawn up showing the extent of ichthyotoxism in Tahiti. This map will serve as a control instrument in the event of possible changes in the toxic areas and will be placed at the disposal of anyone who may wish to consult it.

Finally, the analysis of the data collected reveals that ichthyotoxism also constitutes a fairly considerable problem in the economic field.

SOUTH PACIFIC COMMISSION

SEMINAR ON ICHTHYOSARCOTOXISM

(Rangiroa, French Polynesia, 16th - 22nd August, 1968)

ABSTRACT

THE SIGNIFICANCE OF MARINE BIOTOXINS TO MARINE PROTEIN CONCENTRATES AND FOOD FROM THE SEA

by Dr. Bruce W. Halstead *

Biotoxicity and Marine Protein Food Resources: The increasing world population pressures, the urgent need for establishing a solid fishing economy among underdeveloped countries, the dire need for low-priced high quality protein food products by almost two-thirds of the world's population, and the rapid advance and expansion of insular shore fisheries all point up the drastic need to establish a better understanding of the edibility of our marine protein food potential.

The oceans annually produce about 400 million metric tons of animal protein in a variety of species and sizes suitable for harvest and use by man. Since 1850, the world catch of fishes and shellfishes has progressively increased from about 1.5 million tons to about 50 million tons in 1964. Less than ten percent of the total catch came from fresh water. The remainder were marine organisms. Analysis of the total catch reveals that about 85.9 percent of the organisms were fishes, and the remainder were shellfish (7.6 percent), whales (5.1 percent), and other aquatic animals (1.4 percent).

Despite the fact that ichthyologists recognize about 25,000 species of fishes, less than 15 kinds make up the bulk of the world's fisheries catches. A few kinds of fishes are heavily exploited, some are fished but unexploited, and others are abundant but go unharvested (Schaefer and Revelle, 1959).

Recent studies indicate that the rapidly growing fisheries are not in northern or southern latitudes but rather are in tropical seas (Chapman, 1965). It is anticipated that this trend will continue with even greater efforts being directed to tropical insular areas.

The old perspective of viewing the ocean as a source of food in the direct form of fish (fresh, frozen, dried or canned) is rapidly expanding to include fish meal, fish protein concentrates, and other protein derivatives. In addition, various other forms of marine organisms, i.e., marine invertebrates and plants, are also being contemplated as potential sources of marine protein concentrates. The use of fish protein concentrates (FPC) from low-priced marine fishes has been strongly recommended by most food economists as one of six possible solutions to the problem of the world protein deficit. FPC is particularly meritorious because it is a high quality protein; it can be cheaply produced; untapped fish resources are abundantly available in many parts of the world; FPC can be easily stored and transported with minimal problems. In general, modern technology is looking to the sea with eager anticipation as to the possible utilization of a broad spectrum of marine animals and plants as new sources of food, pharmaceuticals and biochemical agents having medical, industrial, scientific and military applications.

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SOUTH PACIFIC COMMISSION

SEMINAR ON ICHTHYOSARCOTOXISM
(Rangiroa, French Polynesia, 16th - 22nd August, 1968)

ABSTRACT

OCCURRENCE OF TOXIC CRABS IN THE RYUKYU AND AMAMI ISLANDS
AND SIMILARITY OF THE CRAB TOXIN TO SAXITOXIN
by Shoji Konosu and Yoshiro Hashimoto *

Nineteen cases of illness associated with the ingestion of toxic crabs were traced in the Ryukyu and Amami Islands. The signs were characterized by vomiting, paralysis, and rapid death. In the screening test for toxic crabs, three species, Zosimus aeneus, Platypodia granulosa and Atergatis floridus, were found to contain a paralytic toxin, which killed mice in a few minutes. Specimens of A. floridus caught along the southern coast of the main land of Japan were also poisonous.

A marked individual variation of toxicity was recognized in each species. In general, the appendages were more toxic than the cephalothorax, and the exoskeleton also contained a considerable amount of toxin. The toxin was easily dialyzable, soluble in water and methanol and insoluble in most fat solvents.

For the purification of crab toxin, the ion-exchange column chromatographic method for saxitoxin was found to be applicable without any modification, and a partially purified preparation of toxin having a toxicity as high as 1,760 M.U./mg solid (the minimum lethal dose for mice, 0.028 y/g body weight) was obtained from the water extracts of Z. aeneus.

In paper and thin layer chromatographic behaviors and the dose-death time relationship in mice, the crab toxin was indistinguishable from saxitoxin and apparently different from tetrodotoxin. The crab toxin may be identical with or closely related to saxitoxin.

Original Text: English

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SEMINAR ON ICHTHYOSARCOTOXISM
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ABSTRACT

TOXINS FOUND IN CIGUATOXIC FISHES IN THE RYUKYU ISLANDS

by Yoshiro HASHIMOTO *

Evidence for multiplicity of toxin involved in ciguatera has been increasingly accumulated. At least four different toxins have been demonstrated in ciguatoxic fishes in the Ryukyu Islands.

The fat-soluble toxin probably identical with ciguatoxin was found in the muscle of Lutjanus bohar and L. monostigma. This toxin may be a principal one in ciguatera, as Dr Banner suggested.

A water-soluble toxin causing transient vomiting in cats was found and designated as ciguaterin. It was confirmed to distribute widely in the liver and occasionally in the muscle of representative ciguatoxic fishes. This toxin, however, may be a less important factor than ciguatoxin for development of ciguatera.

The skin of a sea bass (Pogonoperca punctata) was found to contain a toxin inducing in cats ciguatera-like syndromes when force-fed or injected. Besides, it revealed both ichthyotoxic and hemolytic activities and a close similarity to the ichthyotoxin found in soapfish rather than pahutoxin in boxfish.

Finally, a water-soluble substance toxic to mice was detected in the viscera and digestive tract contents of a filefish (aluteres scriptus). From the chemical properties it is supposed to be a new marine toxin. The toxin in the viscera was indistinguishable in chemical and pharmacological properties from that in the ingested materials which were mainly consisted of broken reef corals tentatively identified as Goniopora sp. This may strongly suggest the presence of toxio reef corals which serve as a primary source of toxin in a filefish and presumably many other coral feeders.

Original Text : English

* Laboratory of Marine Biochemistry, Faculty of Agriculture, the University of Tokyo.

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SEMINAR ON ICHTHYOSARCOTOXISM

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ABSTRACT

CIGUATERA IN THE RYUKYU AND AMAMI ISLANDS

by Yoshiro Hashimoto, Shoji Konosu and Takeshi Yasumoto*

In a field investigation, the latent prevalence of ciguatera in the Ryukyu and Amami Islands was ascertained and about 20 species of fish were reported to be toxic, excluding puffers, spoiled scombroid fishes, castor oil fishes and the liver of large-sized fishes such as tunas and sharks. Among them, the following five species were found to be most important as the cause of typical ciguatera, red snapper (Lutjanus bohar), snapper (L. monostigma), moray eels (Gymnothorax spp.), grouper (Epinephelus fuscoguttatus), and sea bass (Variola louti). Symptoms induced by these fishes were quite similar to each other and characterized by joint ache, languor, dry-ice sensation, diarrhea and vomiting. A narrow regionality of toxic fishes was reported, and it is interesting that the areas suspected to be toxic are closely related with well-developed coral reefs.

A rabbitfish (Siganus sp.) was reported to induce occasionally itching, severe headache and flush of face, suggesting the presence of a different toxin. The following species were also reputed to be toxic in a few areas; L. vaigiensis, L. fulviflamma, Plectropomus truncatus, Aluterus scriptus, Pogonoperca punctata, Sphyrnaena picuda, Lutjanus sp., and Cheilinus sp.

Besides these fish poisonings, 4 cases due to toxic turtles, about 20 due to toxic crabs, and 5 due to coconut crabs were located respectively.

Original Text: English

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SOUTH PACIFIC COMMISSION

SEMINAR ON ICHTHYOSARCOTOXISM

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ABSTRACT

SOME CASES OF CIGUATERA AND COGNATE
ICHTHYOSARCOTOXISM REPORTED FROM TOKYO

by Tokiharu ABE*

Despite every effort to stop selling dubious fishes from alien waters, a few cases of ciguatera or cognate poisoning caused by eating fish have been observed in Tokyo and vicinity. The following three cases of fish poisoning are briefly reported here.

- 1) Ciguatera caused by barracuda. In May, 1949, about thirty persons of five families in Tokyo suffered from ciguatera by eating a barracuda, Sphyræna picuda Bloch & Schneider, taken by tuna long line, set somewhere in the tropical region of the Pacific Ocean. Professor Y. Hashimoto found a new type of toxin from the fillet of the fish.
- 2) Ciguatera caused by a lutjanid or another red fish. In July, 1966, eleven persons suffered from ciguatera by eating a red fish measuring ca. 60 cm. in total length. The fish, two in number, were given by fishermen who happened to anchor at the pier of the Central Wholesale Market of Tokyo Prefecture, to boys of a junior high school visiting the market. They asked a fish retailer to make fillets of the fish, and distributed them to their families and friends for supper. All the persons, eleven in number, who ate the fish suffered from vomiting, diarrhea and paralysis within one to seven hours after the supper.
- 3) Poisoning caused by eating dried flesh of a puffer. In March, 1968, two persons in Tokyo were poisoned by dried flesh of a puffer (tetraodontid), Fugu vermicularis radiatus (Abe), taken probably by trawl in East China Sea or adjoining water. Thanks to an ordinance issued by the Metropolitan Government, poisoning by fresh or frozen puffers rarely occur in Tokyo and vicinity, but dried puffers are usually sold to retailers without being passed through the Central Wholesale Market of Tokyo Prefecture. The dried flesh of puffers has long been regarded as nontoxic. The symptoms were slight.

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SOUTH PACIFIC COMMISSIONSEMINAR ON ICHTHYOSARCOTOXISM

(Rangiroa, French Polynesia, 16th - 22nd August, 1968)

OUTLINE OF ICHTHYOSARCOTOXISM IN NEW CALEDONIA

by

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In New Caledonia, ichthyosarcotoxism presents a problem which is both economic and medical.

In fact, the relatively high incidence of this disease in the Territory acts as a brake on the marketing of fish, despite the abundant quantities in which it is found along the New Caledonian coastline.

It is impossible to assess the extent of this disease, for in the absence of a specific therapy, and in view of the generally mild nature of this illness which can be treated at home, most patients do not consult a medical practitioner and use medication, often based on vegetable infusions, for which the "prescription" has been passed on from mouth to mouth.

For this reason, although this disease seems very widespread, no more than a dozen admissions for ciguatera are recorded annually in the Gaston Bourret Hospital of Noumea.

Most of the species of fish caught both in the lagoon and near the reefs are liable to cause this disease. Its incidence, however, seems proportional to the size of the fish ingested, the larger type being more likely to give rise to disorders than the small ones (with the exception of sardines). The species most often affected belong to the Serranidae, Lethrinidae and Scomberomidae families.

The symptoms shown by the patients are variable: the most common are symptoms which affect the nervous system (dysesthesia, various kinds of algesia, asthenia). In other cases, disorders of the alimentary tract (vomiting, diarrhoea) or the cardiovascular system (drop in blood-pressure) predominate.

Bearing in mind the possibility of a metallic origin, an attempt was made at the Gaston Bourret Hospital to treat ichthyosarcotoxism by an ion chelating agent, the calcic disodic salt of ethylene - diamine - tetra - acetic acid (calcic E.D.T.A.)*

* Patented under the name of disodic Calcitetracemate (Laroche Navarron Laboratories).

SOUTH PACIFIC COMMISSION

SEMINAR ON ICHTHYOSARCOTOXISM

(Rangiroa, French Polynesia, 16th - 22nd August, 1968)

ABSTRACT

ICHTHYOSARCOTOXISM (FISH POISONING) IN NEW GUINEA

by A.M. Rapson *

Rossel Island has been most seriously affected by fish poisoning. In New Guinea generally, puffer fish, box fish and Grammistes caused the fatalities and chinaman fish, red bass and pike the most serious cases of illness. Although chinaman fish are poisonous in the Milne Bay district this species caught in deep water off North New Britain is sold in Rabaul. Statistics are a guide to the distribution of ichthyosarcotoxism but there is no way of judging what the real death or sickness rate may be. Cases from Rossel Island describe people suffering from fish poisoning eating the same species caught in the same locality as the fish which made them sick without any affects whatsoever. Rossel Island is surrounded by one of the biggest lagoons in New Guinea, and there appears to be little doubt that toxins are developed mainly in inshore reef or shallow waters. A small fish caught in New Ireland waters and called there talultaman is boiled wrapped in the leaves of beach lilies as soon as it is caught; otherwise it causes stomach cramps and further investigation of this use of beach lily leaves may yield information on the phenomenon of ichthyosarcotoxism. Local remedies for fish poisoning may also on investigation be found to have value in making poisonous fishes fit for food. The feeding of fishes on luminescent organism is a possible cause of toxicity. Case histories are normal and medical remedies and local cures are described. Deaths from eating shellfish and from red tide are included from an open coastal area where few fish poisoning cases are recorded, in an attempt to link biological data with a possible relationship between plankton and bottom feeders. The known cases of red tide poisoning occur off reef areas on open coasts while the principal cases of ichthyotoxism are from lagoon areas.

Original Text: English

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SOUTH PACIFIC COMMISSION

SEMINAR ON ICHTHYOSARCOTOXISM

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ABSTRACT

COMMENTS ON SOME CASES OF CIGUATERA
OBSERVED IN AMERICAN SAMOA

by

Dr. Ernest Thompson*

The author wishes to point out the fact that at this point there is no specific method available to the people of Samoa by which they could recognize which fish is toxic, excepting of course the unfortunate "Try-it-out" test; that the toxin is thermostable and is not water soluble; that an attack of poisoning will not impart immunity; that the toxin is not the result of bacterial action or putrefaction; that the body's adaptive and defensive processes are slow in neutralizing or eliminating the toxin; and, finally, that the seaweed AGA (Samoa term) and the toxin it bears is to be further investigated.

* Department of Medical Services,
Pago Pago, American Samoa.

Original text: English

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SEMINAIRE SUR L'ICHTHYOSARCOTOXISME

(Papeete, Polynésie Française)
16 - 22 août 1968

SELECTED LIST OF BIBLIOGRAPHICAL REFERENCES ON ICHTHYOSARCOTOXISM

This document presented by the South Pacific Commission to the participants attending the Seminar on Ichthyosarcotoxism is not a Bibliography in the strict sense but rather a list of references drawn up from our Library Index Cards, and from titles of articles which were brought to our notice. This list is certainly incomplete; we hope, however, that it will be useful to those who require information which cannot be found in the working papers prepared for the Seminar.

LISTE CHOISIE DE REFERENCES BIBLIOGRAPHIQUES SUR L'ICHTHYOSARCOTOXISME

Ce document présenté par la Commission du Pacifique Sud aux participants du Séminaire sur l'Ichthyosarcotoxisme n'est pas une bibliographie au sens propre du terme mais plutôt une liste de références établie d'après les fiches existant dans notre bibliothèque et les titres d'articles portés à notre connaissance. Elle est certainement incomplète; nous espérons néanmoins qu'elle pourra être utile à ceux qui voudraient rechercher des renseignements qu'ils ne trouveraient pas dans les documents de travail préparés pour le Séminaire.

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SOUTH PACIFIC COMMISSION

SEMINAR ON ICHTHYOSARCOTOXISM

(Papeete, French Polynesia, 16th - 22nd August, 1968)

ABSTRACT

THE BIOLOGY OF CTENOCHAETUS STRIATUS,
A KNOWN CIQUATERIC ACANTHURID FISH OF TAHITI

by Charles K. Walters*

Ctenochaetus striatus, one of the most abundant reef fishes in French Polynesia, is the subject of a study being undertaken by the University of Hawaii (Hawaii Institute of Marine Biology) in conjunction with the Institut de Recherches Médicales Louis Malardé with reference to a number of aspects of the biology of this Acanthurid fish and with emphasis on its ciguateric properties. A field laboratory was constructed and staffed at Atimaono, Tahiti, specifically for this research.

Ctenochaetus striatus, characterized by a single folding spine on each side of the caudal peduncle, faint longitudinal striations, and numerous elongate teeth loosely attached to the jaws, abounds in areas of suitable coral growth up to 35 meters, although it is most abundant in depths above 20 meters. The shallow water habitat is characterized by abundant Acropora coral growth with numerous sheltered surfaces for the species' quiescent night-time period. The fish is generally herbivorous, its fine dentition limiting the diet to fine algae and organic detritus. Feeding nearly ceases during the spawning season from November to March. The spawning process appears to consistently coincide with outgoing currents, understandably, as the egg and larval life of the species are pelagic.

Through SCUBA observations of tagged fish, it has been found that Ctenochaetus striatus undergoes a diurnal migration of 300-400 meters horizontally and 10-15 meters vertically to the reef edge. Some populations are involved in movement from a deep water resting place to a shallow reef feeding grounds, while other populations undergo the opposite migration. Parallel reef migration appears to be within 300 meters for this species of Acanthuridae.

Predation upon Ctenochaetus striatus is extensive, as it is preyed upon in all of its life stages - from egg to adult. While predators feeding upon the eggs and larval stages of Ctenochaetus striatus are normally non-toxic, those feeding on the adult fish are often toxic. The seasonal variation and the distribution of toxicity of Ctenochaetus striatus is being emphasized and will be discussed at the Tahiti Seminar on Ichthyosarcotoxism.

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SEMINAR ON ICHTHYOSARCOTOXISM
(Papeete, French Polynesia, 16 - 22 August, 1968)

CIGUATERA IN QUEENSLAND

[Some notes on the Ciguatera syndrome as observed in Queensland over the last four years, particularly to record some of the features that do not seem to have been emphasised elsewhere.]

by

G.D. Broadbent
Medical Practitioner
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Australia.

"Ciguatera" appears to be as frequently encountered along the Great Barrier Reef as elsewhere in the Pacific. Generally its effects seem less severe, though this may be due to dietary preferences, e.g. the Acanthuroidea, although one of the commonest reef fish, is not generally eaten. Lutjanus nematophorus and L. coatesi have a reputation for toxicity and are usually discarded.

More than half the cases are caused by Plectropomus maculatus, half the remainder by Epinephilus fuscoguttatus and tauvini with cases from Cheilinus undulatus, L. coatesi and nematophorus and Scomberomorus commeson. The average weight of the fish was fourteen pounds (6.4 Kilos).

Eighty cases of Ciguatera caused by Scomberomorus commeson from Cairns, Townsville, Rockhampton and Gladstone have been recorded. No cases resembling "Scombroid" poisoning have been reported.

One case of Ciguatera due to Lates calcifer caught in an estuary south of Townsville was noted. This fish is most commonly found in tidal estuaries and inland freshwater streams, extending occasionally to inshore reef areas. It is not found on the Barrier Reef.

A most striking feature of Ciguatera here is its potentiation and reactivation by the ingestion of alcohol. Usually this causes skin itch, followed by paraesthesia of the hands and mouth as soon as five minutes after ingestion. It has occurred up to six weeks from the last fish meal.

Sensitisation or "memory effect" following Ciguatera is common. Usually for several months afterwards a small amount of similar fish non-toxic to a non-sensitised individual, will reproduce symptoms within a few hours. An extreme example followed severe poisoning from the liver of Epinephilus tauvini. This patient asserts that, seven years later, eating small amounts of Plectropomus maculatus or Epinephilus sp. still brought on recurrence of paraesthesiae and malaise, although Lethrinus chrysostomus from the same reef areas

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(Papeete, French Polynesia, 16 - 22 August 1968)

ABSTRACT

CEREBELLAR SYNDROME IN CIGUATERA

Notes on two cases

by

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and

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Papeete

At the Territorial Hospital in Papeete, the authors observed two cases of ciguatera presenting a new feature: to the usual clinical picture was added a total and severe bilateral cerebellar syndrome which developed slowly but favourably towards complete recovery without any after-effects.

The fish involved in each case belongs to the species Scarus microrrhinus Bleeker, its local name being "Uhu raepuu".

After describing the clinical symptoms, giving the results of the complementary tests that were carried out and outlining the treatment applied, the authors stress how difficult it is to diagnose a cerebellar syndrome which is not well-marked without a thorough neurological examination.

A parallel is then established with the symptoms observed in a series of cases of poisoning by Tridacna maxima on the island of Bora-Bora and it is emphasized that one of the toxic fishes was caught in the same "evil" area of this leeward island.

Finally, an attempt to elucidate the cause of the disease through a clinical approach is made in the light of present knowledge of the feeding habits of both Scarus microrrhinus and Tridacna maxima.

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(Papeete, French Polynesia, 16th - 22nd August, 1968)

ABSTRACT

PHARMACOLOGICAL REACTION OF THE RAT TO CIGUATOXIN

by Martin D. Rayner*

The following ciguatoxin extracts, from flesh and livers of Johnston Island eels, have been tested by intravenous injection in rats:

(a) Flesh toxins

(i)	solvent extracted toxin, toxicity	600	µ/g
(ii)	column purified toxin	5	µ/g
(iii)	TLC purified fraction 1	0.5	µ/g
(iv)	TLC purified fraction 2	0.7	µ/g

(b) Liver toxins

(i)	column purified toxin	0.2	µ/g
(ii)	TLC purified toxin	0.03	µ/g

The effects noted can be classified as follows:

- (a) Indirect or Reflex actions brought about as a result of the stimulation of certain peripheral receptors involved in cardiovascular and respiratory control systems (notably the chemo and baroreceptors and the lung stretch receptors).
- (b) Direct actions of the toxins, in particular
- (i) CNS effects. Transitory excitation of respiration is followed by pronounced depression leading to total respiratory failure. Other systems are presumably also affected but have not yet been studied.
 - (ii) Neuromuscular effects. Increased tone and facilitation are followed by depressed excitability and eventually by complete neuromuscular block.
 - (iii) "Direct" cholinergic effects, e.g. Bradycardia and negative inotropic action;
Stretch and chemoreceptor stimulation;
Stimulation of intestinal smooth muscle;
Weak ganglionic stimulation.
 - (iv) "Indirect" cholinergic effects, e.g. Release of catecholamines from sympathetic nerve endings, resulting in peripheral vasoconstriction, tachycardia and positive inotropic action.

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ABSTRACT

LIVER TOXINS FROM GYMNOTHORAX JAVANICUS

by Takeshi Yasumoto and Paul J. Scheuer*

For the past several years our source of ciguatoxin has been the flesh of moray eels, Gymnothorax javanicus, from Johnston Island. Because of our earlier unsatisfactory experience with the extraction of toxin from shark livers we had concentrated our efforts on the processing of eel flesh. A trial run with some eel livers unexpectedly showed that these livers can be extracted without difficulty and that they yield 2 ppm of toxin based on wet weight with an LD₁₀₀ of about 0.05 mg/kg (IP injection in mice). Furthermore, we have been able to show that eels with a zero mongoose rating bear toxic livers of a toxicity comparable to those derived from eels with a mongoose rating of +3. Gross symptoms in mice injected with Gymnothorax liver toxin parallel those which are caused by injection of toxin derived from Gymnothorax flesh.

Chemically, intact liver toxin differs from flesh toxin by the absence of a glycerol fatty acid ester moiety. Until this point was established we carried out our degradative studies by hydrolytic procedures, which have been successful with flesh toxin. It now appears that hydrolytic methods are not suited to the nature of liver toxin and different approaches will be explored.

The chemical and physical properties of liver toxin essentially parallel those of the nitrogenous moiety of flesh toxin which is obtained by methanolysis followed by chemical reduction and acetylation. The low volatility of the toxin has so far hampered its investigation by mass spectral procedures.

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ABSTRACT

A NEW FIELD AND SCREENING BIOASSAY FOR CIGUATERA

by

Emile Keene, Helen A. Randall and Albert H. Banner*

Field studies on ciguateric fish have been limited by the lack of a simple test for toxicity. To date, our knowledge of the chemistry of the toxin has not permitted us to develop any chemical test; in bioassay, screening tests with cats or mongooses are limited by the scarcity or absence of the animals on most islands while the mouse injection bioassay calls for long and elaborate chemical extraction of the toxin.

We have developed a new test, utilizing the stream crayfish of southern United States (Procambarus clarkii (Girard)) and an emulsified homogenate of the liver. The crayfish was chosen as it has twice been reported to be sensitive to toxic fish; the liver was chosen as it may contain up to 50 times as much toxin per unit weight as the flesh.

In the testing technique:

1. The liver is minced and then homogenized mechanically in a solution of 4.5% Tween 60 (Polyoxethelene sorbitan monosterate) in 0.9% NaCl, at the ratio of 1 g liver to 2 ml solution.
2. Heat homogenate to 60° C for 30 minutes; centrifuge.
3. Inject crayfish at 0.33% body weight on ventral side of second abdominal segment, lateral to midline.

If the crayfish is injected with a blank control solution, or with extract from nontoxic fish, there is no reaction. If the crayfish is injected with extract from a toxic fish, it reacts in the following ways:

1. Transient convulsions with abdominal flexure.
2. Loss of aggressive posture with the chela.
3. Awkward stance and twitching of appendages.
4. Loss of righting reflex.
5. Moribundity and death.

Of these reactions the one easiest to quantify is the loss of righting reflex. The measure of this is when the crayfish turns over or is turned to his back with a rod; if he fails to right himself after two minutes, the reflex is considered lost.

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ABSTRACT

CIGUATOXIN

by Wataru Takahashi and Paul J. Scheuer*

Ciguatoxin as isolated from the flesh of Gymnothorax javanicus is a labile yellowish oil with an LD_{100} of 0.1 - 0.5 mg/kg (intraperitoneal injection in mice). It lacks distinctive ultraviolet absorption, but its infrared spectrum reveals the presence of hydroxyl and carbonyl moieties. Functionality tests fail to detect the presence of primary amino groups but indicate the presence of a quaternary amine moiety. Elemental analyses suggest an approximate empirical formula of $C_{35}H_{65}NO_8$ thus indicating a highly oxygenated molecule.

Mild acid or base hydrolysis liberates glycerol, fatty acids, water-soluble and organic soluble amine products. Gas-liquid chromatography reveals that the fatty acids are mixtures of which the major components are myristic, palmitic, palmitoleic, stearic, and oleic acids. High resolution mass spectral measurements of the water-soluble products indicate a large molecule with three nitrogen atoms. The organic soluble degradation product contains a quaternary amine function.

Oxidation followed by vigorous acid hydrolysis resulted in additional products. One of the fragments is non-nitrogenous and contains a linear hydro-carbon chain of about thirty carbon atoms. Another degradation product contains a quaternary amine moiety attached to a large alkyl group. A number of water-soluble amine fragments were also isolated. Chemical degradations and mass spectral measurements indicate that ciguatoxin is a large complex molecule in which the nature and exact number of nitrogen atoms are not yet known.

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ABSTRACT

MARINE ALGAE AS A POSSIBLE SOURCE OF CIGUATERA TOXINS

by John E. Randall*

Several authors have suggested that benthic marine algae may be the source of the toxin which causes ciguatera. Knowledge of the food habits of fishes provides us with the strongest evidence of this. Some fishes which feed only on benthic algae may produce ciguatera when eaten. This does not constitute proof of an algal origin of the toxin, however, for herbivorous fishes often ingest detrital material of sundry origin and some fragments of animals incidentally with their plant food. Thus some other organisms such as a sponge or a fungus might be the causal agent. Or it might be an organism such as a bacterium growing in association with an alga. Another reason to suspect algae is that toxic substances have been isolated from them (although none yet resemble ciguatoxin).

Algae were collected from reefs where poisonous fishes are found in the Society Islands, especially those which grow early on new surfaces, for testing of toxicity, but none displayed any significant quantity of toxin. The first alga tested was the chrysophyte Chrysonephos lewisii; it was clearly the dominant organism on surfaces of concrete, coral rock, and durotex placed on three toxic reefs in Tahiti and one in Moorea during the southern winter after a period of two to three weeks. The green alga Enteromorpha sp. and the brown Ectocarpus sp. succeeded Chrysonephos on the new surfaces after about a month in the sea. Still later these algae were largely replaced by many species such as the bluegreens Calothrix crustacea and Lynxbya majuscula, the brown Sphacetaria sp., the green Cladophora sp., and the reds Polysiphonia sp., Centroceras clavatum, and Laurencia sp. These algae were tested en masse. The bluegreens Hormothamnion enteromorphoides, Lynxbya aestuarii, and Calothrix sp. and assorted diatoms were the principal algae growing on a concrete surface placed on a sand bottom in the lagoon near a toxic reef in Tahiti; this surface was subject to some silting by sand. A new surface placed in the sea on December 23 for twenty days yielded primarily Cladophora, and one in 15 days beginning February 29 mainly Enteromorpha (with some Erythrotrichia, Sphacelaria, and Cladophora). The bluegreen Phormidium sp., which was found growing naturally at the edge of Teavaraa Pass, Tahiti, was also tested. The two mice injected with extracts of this alga died in 34 minutes at the dosage of 2000 μ /g. Deaths from other algae required at least 3000 μ /g. A test with seawater alone produced death in two mice in 85 minutes at 3500 μ /g.

The following algae were collected at toxic sectors at Ishigaki in the Ryukyu Islands: the green Chlorodesmis sp., the diatom Synedra sp., and the bluegreens Phormidium sp. and Lynxbya sp. None were toxic beyond the level of 300 μ /g.

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SEMINAR ON ICHTHYOSARCOTOXISM

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ABSTRACT

PATTERNS OF DEVELOPMENT OF CIGUATERA FISH POISONING
IN THE PACIFIC

by Philip Helfrich*

The classification of fishes that are toxic to eat have been grouped in various ways and, for the purposes of this discussion, a modification of the classification of Halstead (1967) is followed. It should be noted that ciguatoxic fish or those which cause the disease "ciguatera" when ingested by humans may be the result of more than a single toxin; at least four toxins have been implicated in ciguatera outbreaks described by Banner (1967). In this discussion of the patterns of development of ciguatera no attempt will be made to distinguish the various toxins that might be involved in outbreaks of the disease.

Fluctuations in the geographical distribution and intensity of ciguatera fish poisoning have been experienced in several areas in the Pacific, as reported by Jones (1956), Cooper (1964), Bartsch, *et al.* (1959), Helfrich and Banner (1964), and Helfrich, *et al.* (1968). An examination of the available information suggests a sequence of events that typify an outbreak or marked increase in cases of ciguatera in a given area. The phenomena triggering such outbreaks are largely unknown, however the hypothesis developed by Randall (1958) suggests mechanisms whereby the sequence of events in fluctuations in ciguatera might be explained. Randall, expanding on the work of earlier researchers, hypothesized that the toxin was produced by a benthic organism, probably an alga or organisms living on an alga, which underwent exponential type growth under certain conditions. He suggested that at least one of these conditions was the exposure of new surfaces on the submarine substrata.

Based upon Randall's hypothesis and upon the information available on outbreaks, although such information is quite inadequate, a scheme of trophodynamics of the toxin in an ecosystem is proposed.

Examination of data on fluctuations of ciguatera from islands and archipelagoes of the Indo-Pacific appear to fall into three categories: I - Pattern of intoxications observed in areas with no previous history of ciguatera; II - Pattern of intoxications in areas with a continuous history of ciguatera at a low level, with periodic marked increases in ciguatera; III - Pattern of intoxications at a sustained low level with well defined geographical limits and species involved.

The dynamics of these three patterns is proposed.

The patterns of ciguatera development hypothesized are based upon incomplete evidence from personal observations and various scattered sources. The evidence for their existence is somewhat tenuous and conjectural, however it is presented as a possible framework to which further evidence can be added to aid us in understanding the dynamics of ciguatoxin in marine communities. It is hoped that at least it will stimulate fruitful discussions that will open up previously unexplored areas of research.

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ABSTRACT

CIGUATERA-TYPE FOOD POISONING ON THE ISLAND OF REUNION (1966-67)
AND J. MORICE'S THEORY REGARDING THE ORIGIN OF THE TOXICITY
OF SOME TROPICAL FISH SPECIES

by

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Scientific and Technical Institute
of Marine Fisheries
St Denis, Reunion Island

1. On the Indian Ocean island of Reunion, the consumption of tropical fish caught either locally (by small fishermen) or on the banks of Saya de Malha, some 700 nautical miles to the north, caused several cases of ciguatera-type poisoning. The species involved are named; they are mainly Serranidae, Lutjanidae and Carangidae. The actual incidence of fish poisoning has not yet been estimated.

2. A possible explanation of the toxicity of some tropical fish species is given. Although no systematic testing of this hypothesis has yet been undertaken, the author deems it worthwhile to summarize the observations made from 1961 to 1964 by Morice on St Bartholomew Island (French West Indies). These suggest that the toxicity of some of the fish might be connected with the presence of skull lesions, severe in some cases. Such lesions may be caused by a micro-organism carried by isopodous crustacea which are parasites of the branchial cavity and nostrils and are frequently encountered in many species. We believe we have found such lesions in fishes in the Indian Ocean and on the coast of Tahiti.

Original text: French

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SEMINAR ON ICHTHYOSARCOTOXISM

(Papeete, French Polynesia, 16th - 22nd August, 1968)

NOTE ON THE USE OF OXIMES IN THE TREATMENT OF CIGUATERA

by Raymond Bagnis

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The use of oximes in the treatment of ciguatera was envisaged in 1965 following pharmacological investigations which had been carried out at the Hawaii Marine Institute and which had revealed, in the course of laboratory experiments on rats, that there was an analogy between the effect of "ciguatoxins" and that of organophosphorous products contained in certain insecticides.

The experimental product used was Protopam^(R) chloride distributed by "Campbell Pharmaceutical Inc., New York", the chemical formula of which is as follows: 2-formyl-1 methyl pyridinium chloride oxime. This patent drug is regarded as having no serious secondary effect.

When administered in conjunction with atropine, "Protopam" keeps alive rats who had been given twice the normal lethal dose of impure ciguatoxin.

It was used in the treatment of humans for the first time in September 1964 in Honolulu, in the case of one of the victims of an extremely serious intoxication which had already caused the death of two people. Whilst the results could not be described as conclusive, the way was open to further experiments. Unfortunately in view of the absence of other acute forms of ciguatera, American research-workers were unable to use this product more extensively in Hawaii itself.

In the light of these data and for a period of approximately six months during 1966 ciguatera was being treated experimentally in Tahiti by means of "Protopam" - a procedure carried out side by side with the symptomatic treatment which was still the only one applied in most cases. Analysed below are our results bearing on 48 patients:

Means of administration: intravenous or intramuscular.

Method of application: on its own or in conjunction with atropine.

Doses: Adults : 1 gramme injection which may be repeated.

Children: 25 mg injection per kg of body weight.

Number of patients treated: 48

Form of procedure used in experiments on adults:

Method 1 : Very serious cases of immediate urgency, accompanied by a state of shock.

- 1 gramme of Protopam in an intravenous perfusion of 250 cc of salt serum to be given in the course of 30 minutes.
- $\frac{1}{4}$ milligrammes of atropine to be given subcutaneously and repeated within the following half-hour.
- These doses may be repeated once after two hours if the state of shock remains unchanged.

CONCLUSIONS

Being a drug with a particularly favourable effect on the symptoms provoked by the excessive vagal stimulation characteristic of the muscarine-type phase of ciguatera, Protopam becomes more potent when used in conjunction with atropine.

Its action is the more effective if administered early and, in serious cases, immediately.

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Original Text: French

ANNEX IV a

Message from the Secretary-General of the South Pacific Commission

It is with pleasure that I send a message, through Dr A. Guinea, the Commission's Medical Officer, to welcome the participants to this Seminar on Ichthyosarcotoxism. Dr Guy Loison, the Commission's Programme Director for Health, joins me in expressing warm appreciation to Tahiti for extending its traditional hospitality so that the Seminar could be held here. It is appropriate that this is so as there has been a considerable amount of research in this area. The subject of fish poisoning is an important one and it is almost certain that some of you here have had personal experience of it. I am sure, therefore, that your discussions will be followed closely and with great interest.

The fact that toxic effects can result from eating fish has been known for a very long time by the inhabitants of the islands in the Pacific. The people who live from the sea have acquired considerable knowledge on poisonous fish and have evolved certain procedures to judge whether or not a certain fish was poisonous. But this has not, any more than it does not today, prevent widespread illness and even death as the result of fish poisoning.

It is only recently that the scientist has caught up with the indigene in his observations and that there has been any attempt to investigate the phenomenon of toxicity as the result of eating fish. Interest, however, has been increasing in recent years as it became obvious that this problem involved much more than individual illness or death. Some populations in the Pacific area are growing at an estimated rate of up to 4.6% per year. With limited land area and limited land utilisation, the protein assets available in surrounding seas become increasingly important. Changing cultures, changing economics bring changed pattern on nutrition but the desire and the need for fish protein remains. If this need is to be met, it is of the utmost importance that the nature of fish poisoning be understood in an effort to find some solution. The Commission has been interested in and aware of the problem since 1950. From that time it has aided in research and the accumulation and distribution of as much relevant information as possible on the subject by the provision of technical services and financial assistance. In the same period, many individual scientists from numerous disciplines have maintained research in an attempt to find rational answers to a problem that seems essentially irrational. With so many variables, this multi-disciplinary approach is essential; the doctor does not always know a great deal about marine plants, or the involved chemistry of toxins isolated. If success can be attained it is necessary that the information obtained by medical officers, marine biologists, chemists, ecologists, oceanographers and other specialists be correlated and discussed. This, of course, is the object of the Seminar and the Commission is proud that it has been of assistance in organizing this, the first such Seminar in the South Pacific.

It is hoped that the meeting will produce some recommendations which will be of value to the great many people living in the area and I hope that the discussions will also assist each member of the Seminar in his own endeavours.

Opening Address by the Secretary-General of French Polynesia

Sir, (to the South Pacific Commission Representative)

Ladies and Gentlemen,

Governor Sicurani has been detained with the Minister for Scientific, Space and Atomic Research who arrived in Tahiti this morning, and he has accordingly asked me to represent him and to tell you that he is extremely sorry to be unable to preside in person over this Opening Session of the Seminar on Ichthyosarcotoxism.

In his name I bid you welcome to French Polynesia.

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A little over a year ago, in May 1967, a Conference was held in Tarawa under the auspices of the South Pacific Commission on the special aspect of food and health problems of coral atoll populations.

In accordance with the discussions a recommendation was adopted emphasizing the need to develop and co-ordinate research into the intoxications caused by the ingestion of certain marine organisms.

This meant stressing once again a very old peculiarity of certain fish species, confirmed by many a ship's crew, often at the members' own cost, and recorded in their log-books by all the great navigators who followed Cook, Wallis, Bougainville and La Pérouse.

I should like in particular to quote Moerenhout who was travelling to the Great Ocean Islands between 1829 and 1834, and who reports that, when calling in Hood Island - probably the island known to-day under the name of South Marutea, in the Tuamotu Group - he and his schooner's Captain and crew became the victims of poisoning after eating some fish, albeit perfectly fresh fish. "When I tried to get up", he writes, "I felt strangely unwell. A headache and pains in every part of my body scarcely allowed me to get out of bed."

I leave it to you to decide, Gentlemen, whether this excellent observer of Polynesian manners and customs has managed to give an accurate description of the symptoms of an illness which, having carefully considered all kinds of hypotheses, he attributes to the fact that "Certain fish which we thought wholesome, were poison".

What cannot be disputed is that this illness did exist and that the islanders knew and feared it, since Moerenhout further records, in connection with Waterland Island - doubtless the present Ahe Island - that "the Indians do not want to live there and even claim that, during various seasons of the year, all the fish in that area represent a poison pervasive enough to cause death within a few days."

Since the days of Moerenhout, we have scarcely progressed in our knowledge of this mysterious sickness, and the fear of poisoning to-day deprives the peoples of the Pacific Islands, the West Indies and some of the Far Eastern and Indian Ocean Island Groups of food resources which could be drawn in abundance from the surrounding Ocean.

Thus to the name of Tahiti, in addition to the renown for its traditional charms, will be attached all the prestige of the Science of Humanity and of Disinterestedness.

Gentlemen, I wish you a pleasant stay amongst us, and I declare open the Seminar on Ichthyosarcotoxism.

Original Text: French