International Workshop on Ciguatera Management

Joondoburri Conference Centre
Bribie Island Australia
13 - 16 April 1993

Major Sponsors:

DPI
QUEENSLAND DEPARTMENT OF PRIMARY INDUSTRIES

Fisheries Research and Development Corporation

FINAL REPORT

"INTERNATIONAL WORKSHOP ON CIGUATERA MANAGEMENT"

project number 91/91

Principal investigator:

Dr Richard J. Lewis

Southern Fisheries Centre

PO Box 76, Deception Bay, Q4508

(Phone: 07 203 1444, Fax: 07 203 3517)

a project of:

QUEENSLAND DEPARTMENT OF PRIMARY INDUSTRIES

(QDPI)

funded by:

FISHERIES RESEARCH AND DEVELOPMENT CORPORATION

(FRDC)

1. PROJECT SUMMARY

An International Workshop on Ciguatera Management was held at QDPI's Joondoburri Conference Centre on Bribie Island, 13-16 April 1993. This meeting provided the first opportunity for discussion of issues related to ciguatera at an international forum in Australia. Fifty-six registrants participated in the scientific programme which included 41 contributions (either oral or poster presentations) from local and overseas researchers. The latest research on ciguatera was discussed, especially research with implications for the management of ciguatera. The Workshop covered a broad range of topics through presentations from invited speakers and included two workshop sessions that addressed the clinical management of ciguatera and the detection of ciguateric fish. The proceedings of the Workshop will be published as a special issue of *Memoirs of the Queensland Museum*. We anticipate approximately 30 papers will be published in early 1994 following peer review. The Workshop reinforced the need for further research on (i) the detection of ciguateric fish and (ii) the environmental factors contributing to outbreaks of ciguatera.

2. BACKGROUND TO PROJECT

Ciguatera remains a problem for a number of fisheries in Australia. An International Workshop on Ciguatera Management was planned that specifically addressed management issues and established the current status of the field in a published proceedings.

Research on ciguatera in Australia has been supported by FRDC (formerly FIRTA and FIRDC) for over 12 years. This research has achieved a number of important objectives. Specifically this research has: (i) identified and characterised the problem of ciguatera in Australia; (ii) established the general aspects of the pharmacology of the poisoning; (iii) established a means to treat ciguatera; (iv) determined the origin of ciguatera in Australia; (v) determination of the chemistry of several ciguatoxins

found in fishes; (vi) established that fishes may excrete ciguatoxin and that some fishes are susceptible to the toxin; (vii) established techniques for production of antibodies to ciguatoxin; (viii) accumulated the largest single sample of pure ciguatoxin presently available in the world and (ix) assessed the effects of ciguatera on nerves *in vivo* in humans and rats. Despite this research in Australia and additional research conducted overseas, we still do not have a rapid test for routine screening of potentially toxic species before sale to the consumer. In addition, little is known of the environmental factors contributing to ciguatera outbreaks. A precise understanding of these areas is required if ciguatera is to be effectively managed.

Research on ciguatera is presently underway in mainland France, mainland USA, Japan, French Polynesia, Hawaii and the Marshall Islands. An international meeting on ciguatera would provide a forum for the consolidation of the field which has recently been through a period of rapid advance. A major outcome of the Workshop will be the establishment of clear directions for future ciguatera research in Australia and overseas.

3. PROJECT OBJECTIVES

(a) Organise and hold an international workshop on ciguatera that specifically addresses management issues.

(b) Attract key workers in ciguatera and related fields to present on selected topics related to the management of ciguatera.

(c) Conduct workshops on detection, treatment and control of ciguatera to be recorded and included in published proceedings.

(d) Establish the current status of the field in a published proceedings.

4. PROJECT METHODS

A Workshop on Ciguatera was held at the Joondoburri Conference Centre, Bribie Island, 13-16 April 1993. Much of the success of the meeting is attributable to the dedication and careful preparation by the Organising Committee. Particularly noteworthy were the efforts of Michelle Sellin and Michael Holmes. The Organising Committee comprised:

Richard J. Lewis (Chairman)
Michael J. Holmes
Michelle Sellin
Barry Pollock
Mike Dredge
Noel Gillespie.

A total of 26 invited speakers presented 31 talks at the meeting. The invited speakers included 16 international leaders in the field. Four main areas of ciguatera management were covered by the Workshop:

- Detection of ciguateric fish
- Pharmacology and treatment of ciguatera
- Clinical aspects and epidemiology of ciguatera
- Origin of the toxins involved in ciguatera

The Workshop covered a broad range of topics through presentations from invited speakers and two workshop sessions that addressed the clinical management of ciguatera and the detection of ciguateric fish. The full proceedings of the Workshop, which should comprise ~30 papers, will be published as a special issue of *Memoirs of the Queensland Museum*.

Each article will be peer reviewed by two referees in accordance with the procedures of the journal. Much of the review process will be handled by the Scientific Committee which comprises:

Richard J. Lewis (Australia, Chairman)
Michael J. Holmes (Australia)
John H. Pearn (Australia)
Milani Y. Chaloupka (Australia)
Anne-Marie Legrand (French Polynesia)
Takeshi Yasumoto (Japan).

The success of the project could be assessed on several bases including: (i) the number and talent of delegates attracted to the conference (ii) quality and timeliness of the published proceedings (iii) the extent to which the conference will consolidate research in the field (iv) the appropriateness and incisiveness of management/research directions forthcoming from the conference.

5. PROJECT RESULTS

The Workshop brought together scientists, medical practitioners and fisheries managers with an interest in ciguatera and focussed on current research having implications for the management of ciguatera. Participation by those directly involved in the fishing industry was unfortunately below expectation.

A total of 56 registrants from Japan, mainland USA, Hawaii, France, French Polynesia, New Caledonia, Germany and each of the eastern sea-board states of Australia attended the Workshop. The Workshop comprised oral and poster presentations and included two discussion sessions which specifically addressed (i) the detection of ciguateric fishes and (ii) the management of ciguatera cases. At this meeting it was determined that the next ciguatera meeting would be in mid-1994 in Hawaii.

Details of the brochures produced for the Workshop are given in **Appendix I** (Programme and Abstracts), **Appendix II** (Second Notice), **Appendix III** (List of Registrants) and **Appendix IV** (Opening Speech). Below is an overview of the Workshop, discussing the outcomes of each of the four major areas covered, is presented in sections 4.1 - 4.4.

4.1 *Detection of ciguateric fish*

At the meeting a cost-effective screen for ciguateric fish was widely recognised as perhaps the single most effective management tool able to directly reduce the adverse effects of ciguatera on public health, fisheries, trade and tourism (R. Lewis). Several different approaches to the detection of toxic fish were presented. Two approaches measured the interaction between ciguatoxin and the sodium channel through (i) the inhibition of brevetoxin binding to sodium channels in a rat brain synaptosome preparation (A-M. Legrand) (ii) the cytotoxic effects of ciguatoxin on sodium channel-containing cell lines pre-exposed to ouabain and veratridine (R. Manger). Both assays were more sensitive than the mouse bioassay and may replace ***in vivo*** assays in laboratories possessing the specialised equipment required. These approaches require further development before they can be used as cost-effective screens.

Antibody-based screens or related assays still hold most promise for the cost-effective detection of ciguateric fish. This approach is the basis of a potential commercial test to detect ciguateric fish being developed by HawaiiChemtect. D. Park presented a summary of the performance of the solid-phase immunobead assay (Ciguatect™) which was claimed to be able to detect ciguateric fish. The test was reported to be unsuitable for detecting toxins in slightly acidic fish flesh (pH = ~6.5), a factor that may considerably limit the usefulness of the test. Y. Hokama commented that the test may not work because the solid-phase used in the Ciguatect™ test may not be as efficient at extracting ciguatoxins from fish as the "correction fluid" used for the solid-phase by Hokama (with the same antibody used for both tests). This explanation does not account for the high number of positive results obtained by the

Ciguatect™ test. Predictive indices from 5% to 75% (compared with carefully conducted mouse bioassay results) were obtained when this test was used in an independent study of ciguateric fish from the Caribbean by R. Dickey (Food and Drug Administration, USA). Lack of available pure ciguatoxin and an inability to independently validate the levels of ciguatoxins present in test fish samples hamper attempts to validate the Ciguatect™ test. Further Australian research in this area is expected to result in significant advances.

4.2 *Pharmacology and treatment of ciguatera*

Major advances are being made into how ciguatoxins cause poisoning (P. Hamblin, J. Brock, J. Molgo, M. Capra, F. Vogalis, C. Purcell, E. Benoit, K. Terao) but the precise mechanism of action of mannitol to relieve the symptoms of ciguatera is still a matter of debate. A double-blind clinical study of the mannitol treatment is being conducted but the results of this study are being acquired slowly and were not available at the time of the meeting (N. Palafox). Clinical experiences with the mannitol therapy continue to be positive and mannitol should remain the treatment of choice for ciguatera in Australia, especially for the acute phase of the disease (N. Palafox, D. G. Blythe). Full acceptance by medical practitioners of the therapy will come about slowly until the treatment is confirmed by clinical studies, preferably with the support of an animal model for ciguatera that responds to mannitol. Further studies investigating new animal models for ciguatera may provide confirmation for mannitol's efficacy and indicate how mannitol acts.

4.3 *Clinical aspects and epidemiology of ciguatera*

While most of the clinical features of ciguatera are well documented, the long-term effects of ciguatera and how frequently these occur are poorly understood. Follow-up research on victims is required to establish the true extent of long-term effects, especially the allergy-like reactions that can last after a single exposure to toxic fish (T. Ruff). Problems of misdiagnosis and non-reporting were discussed by J. Pearn. Australia is considered well placed to conduct research in these areas which. Such

research is expected to produce significant advances our understanding of the long-term effects of ciguatera and should improve the treatment of ciguatera.

The ciguatera database maintained by QDPI represents the best (anywhere) long-term (27 years) database on ciguatera cases that is accessible by computer. Analysis of this database using the most recently developed statistical modelling approaches reveals major shifts over time in the nature of the poisoning in Queensland and the in the species of fish involved (M. Chaloupka). The high incidence of ciguatera in the Pacific and how these countries address the problem was discussed by P. Dalzell.

The legal situation with regard to ciguatera in Queensland was also discussed at the Workshop (J. Payne). Duty of care issues and the Queensland Workplace Health and Safety Act could be pursued for a successful court action against suppliers of toxic fish. The "ban" on red bass and chinaman fish but not on other species known to be intermittently toxic, especially coral trout and Spanish mackerel, may weaken the industry arguments that it is satisfying duty of care issues with regard to ciguatera. Legal opinion was that consumption of warm water fish in Australia had associated with it a greater than negligible risk of contracting ciguatera. It was further considered that duty of care issues would not be adequately addressed if the problem of ciguatera was not continually monitored and if management options to reduce the risk were not being sought on an ongoing basis.

4.4 *Origin of the toxins involved in ciguatera*

Gambierdiscus toxicus is now widely accepted as the organism that produces the toxins involved in ciguatera (T. Yasumoto, M. Holmes). Indeed this organism may be the only source of toxins involved in ciguatera. Structure for GTX-4A (52 epi-GTX-4B), the major gambiertoxin produced by a Rangiroa Atoll strain of *G. toxicus* grown in culture, was presented at the meeting (T. Yasumoto). This toxin is likely to be the precursor of CTX-2 and could undergo acid-catalysed spiroisomerisation to the other ciguatoxins found in fish (ie GTX-4B, CTX-1 and -3). From this understanding we now have a much clearer picture of how the ciguatera toxins arise.

The structure of maitotoxin was also presented. This maitotoxin consists of numerous trans-fused polyether rings as do the ciguatoxins.

At the present time little is known of the environmental factors that cause the upsurges of ciguatera (M. Holmes, J-P. Vernoux, U. Kaly, S. Hahn, J. Babinchak, R. Bagnis, G. Hallegraeff, Y. Hokama, P. Scheuer). Further Australian research in this area is expected to result in significant advances. The ciguatera "hot spot" in Platypus Bay experiences periodic upsurges in ciguatera and is an ideal study site to examine factors contributing to these upsurges (M. Holmes).

Also discussed at the meeting was the potential for a range of other toxic algae to be introduced into Australia with resultant outbreaks of diarrhetic, paralytic, neurotoxic and amnesic shellfish poisoning (G. Hallegraeff). Such outbreaks may arise through ballast water introduction and/or environmental degradation. These biotoxins have the potential to severely damage a number of fisheries in Australia. Timely Australian research in this area would minimise any adverse impacts of such outbreaks to the local fishing industry.

5. DISCUSSION

The FRDC supported "International Workshop on Ciguatera Management" was a successful meeting. Objectives (a)-(c) have been achieved and objective (d), which is to publish the current status of the field in a published proceedings in the *Memoirs of the Queensland Museum*, is proceeding as planned.

The Workshop highlighted the need for the development of a cost-effective screen for ciguatera, especially if the legal issues surrounding ciguatera in Australia are considered. Deficiencies in our understanding of the environmental factors involved in outbreaks of ciguatera also need to be addressed through further research.

The project can also be judged a success in terms of the projects predefined performance indicators (shown in italics).

(a) *the number and talent of delegates attracted to the conference.* A total of 56 registrants attended, including 16 international leaders in the field.

(b) *quality and timeliness of the published proceedings.* We anticipate producing by early 1994 a proceedings comprised of ~30 full papers. All papers will be peer reviewed prior to publication to ensure a consistent high standard is achieved.

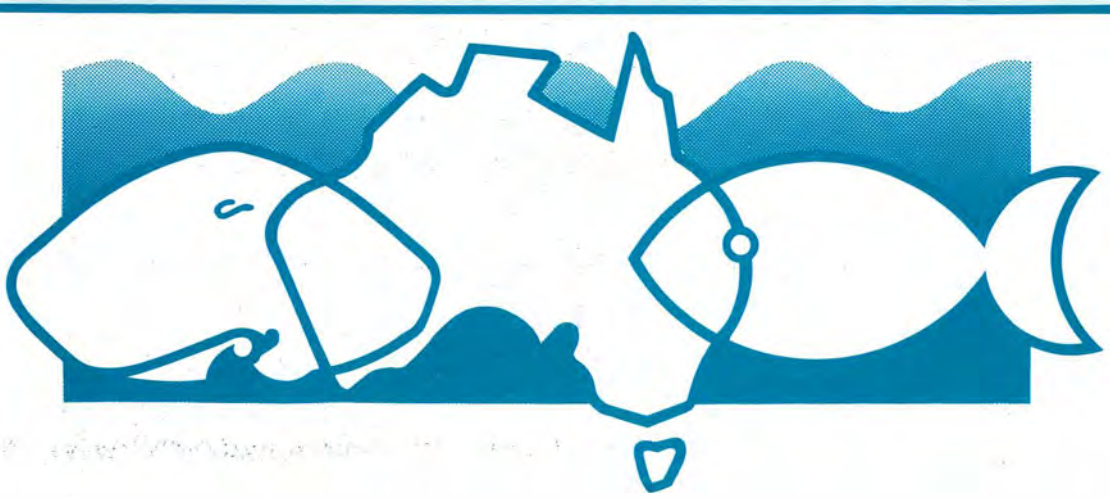
(c) *the extent to which the conference will consolidate research in the field.* The high calibre of the participants and the well organised programme ensured the major research initiatives on ciguatera were discussed and the current status of the field clearly was clearly defined.

(d) *the appropriateness and incisiveness of management/research directions forthcoming from the conference.* By focussing on research related to the management of ciguatera, this Workshop provides sound guidelines for future management/research of ciguatera in Australia. The major outcomes are discussed in sections 4.1 - 4.4 above.

APPENDIX I

Programme and Abstracts

International Workshop on Ciguatera Management



Programme and Abstracts

Joondoburri Conference Centre
Bribie Island Australia
13 - 16 April 1993

Hosted by:

DPI
QUEENSLAND
DEPARTMENT OF
PRIMARY INDUSTRIES

WELCOME

We would like to welcome you to Bribie Island for our International Workshop on Ciguatera Management. We have delegates attending from all over the world for what promises to be a stimulating scientific forum. Please ask one of the organising committee should you require any assistance during your stay.

ORGANISING COMMITTEE

Richard Lewis (Chairman)
Michael Holmes
Michelle Sellin
Barry Pollock
Mike Dredge
Noel Gillespie

SCIENTIFIC COMMITTEE

Milani Chaloupka (Australia)
Michael Holmes (Australia)
Anne-Marie Legrand (French Polynesia)
Richard Lewis (Australia, Chairman)
John Pearn (Australia)
Takeshi Yasumoto (Japan)

MAJOR SPONSORS

Fisheries Research and Development Corporation
Queensland Department of Primary Industries

SPONSOR

Queensland Museum

We gratefully acknowledge the support of these organisations.

INFORMATION

- *Registration Desk*

  The Registration desk is located adjacent to the Joondoburri Conference Centre reception area. The desk will be open during the following hours.

Monday 12 April	4.00 pm - 6.00 pm
Tuesday 13 April	9.00 am - 11.00 am
Wednesday 14 April	8.30 am - 9.00 am
Thursday 15 April	8.00 am - 9.00 am
Friday 16 April	8.30 am - 9.00 am

  Outside callers can contact the Workshop Secretariat during the meeting by telephone (07) 408 3777 or facsimile (07) 408 3435. Cash (not traveller's cheques) should be used to cover any additional expenses on checking out from Joondoburri.

- *Transfers*

  A daily bus transfer between Koolamara Beach Resort and Joondoburri will be provided. The first bus will leave Koolamara 45 minutes before the first scientific session each day. Please meet buses outside Joondoburri at the times indicated for tour commencement.

- *Name Badges*

  A name badge will be issued at registration - please ensure that you wear this at <u>all</u> conference sessions and social events. A second name badge is issued for easy identification of your satchel.

- *Slides*

  Slides should be placed into the labelled carousel(s) provided and should be made available to the projectionist 15 min before each session commences.

- *Posters*

  Those presenting posters are asked to hang their posters in the poster room using the velcro fasteners provided. Please mount your poster on Tuesday between 9 and 11 am. On Tuesday evening between 7.30 - 9.30 pm poster authors are asked to stand beside their poster(s) to answer questions.

- *Meal Tickets*
  Lunch (green) and dinner (black) tickets will be issued to all guests staying at Joondoburri or Koolamara. During the Workshop (13-16 April) lunch and dinner should be taken at Joondoburri. Guests staying outside the 13-16 April should take lunch or dinner at their accommodation. During your stay, breakfast will be supplied at either Joondoburri or at Koolamara Beach Resort Motel, depending on where you are accommodated.

  For participants not staying at the arranged accommodation, lunch tickets (A$10.00) and dinner tickets (A$13.50) can be purchased on registration. Tickets for these meals are limited.

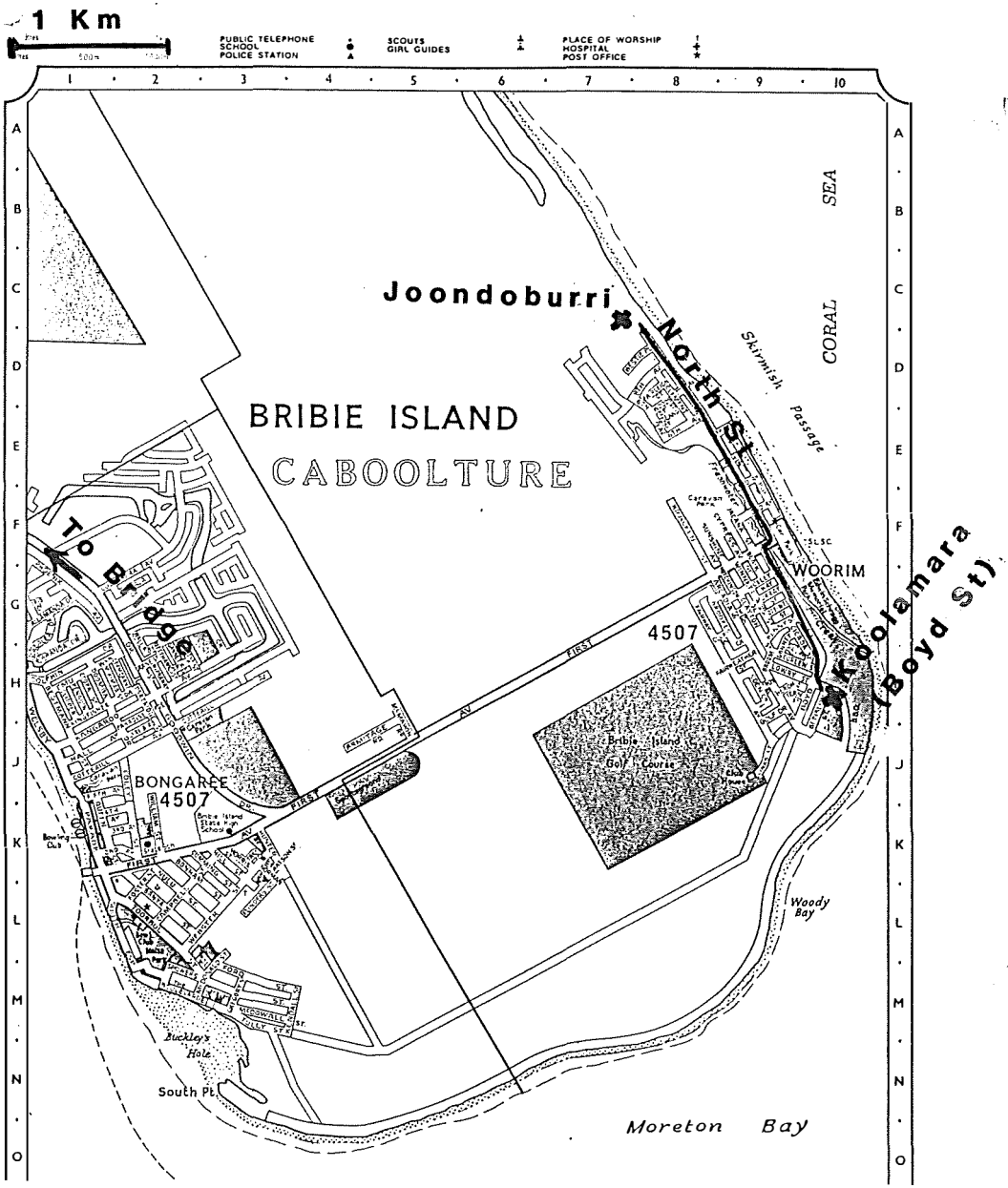
- *Welcoming BBQ*
  All guests are invited to attend the "ice-breaker" on Monday evening. The BBQ commences at 6.30 pm.

- *Workshop Dinner*
  The Workshop Dinner will be held at Morgan's Seafood Restaurant, Bird of Passage Parade, Scarborough. Cost is $55 per person. Coaches will depart from Joondoburri at 4.30 pm, visiting the Southern Fisheries Centre *en route* to the Restaurant. We will arrive at the restaurant at 6.30 pm and return at approximately 10.00 pm.

- *Tours*
  Tours to Sunshine Plantation (Wednesday) Pumicestone Passage (Thursday) are included with registration. These tours depart Joondoburri at 1.45 pm, with both tours returning to Joondoburri by 5.30 pm. The Bribie Passage boat cruise includes a devonshire tea served mid-afternoon.

- *The Beach*
  The beach adjacent to Joondoburri is regarded as a safe swimming beach. Those not familiar with surf or rips should consult reception for an update on swimming conditions prior to swimming. It is recommended for your safety that you swim in a group.

- The organisers reserve the right to make last minute changes to the timing or running order of this programme. Changes will be posted on the symposium notice board in the lecture theatre foyer.


1 Km
PUBLIC TELEPHONE
SCHOOL
POLICE STATION
SCOUTS
GIRL GUIDES
PLACE OF WORSHIP
HOSPITAL
POST OFFICE
1 2 3 4 5 6 7 8 9 10
A B C D E F G H J K L M N O
Joondoburri
North St
SEA
CORAL
Skirmish Passage
BRIBIE ISLAND
CABOOLTURE
To Bribie
WOORIM
SLSC
Kooiamara
(Boyd St)
4507
First Av
Bribie Island Golf Course
BONGAREE
4507
Woody Bay
Buckley's Hole
South Pt
Moreton Bay

PROGRAMME SUMMARY

(Please consult full programme for daily details)

MONDAY	TUESDAY	WEDNESDAY	THURSDAY	FRIDAY
FREE	Registration Posters mounted	Pharmacology (9.00 am start)	Clinical (8.30 am start)	Origin (9.00 am start)
	MORNING TEA (10.30 - 11.10 am)			
	Official Opening (11.30 - 12.00 pm)	Pharmacology	Clinical	Origin
	LUNCH (12.40 - 1.30 pm)			
	Detection (2.00 pm start)	Visit to Sunshine Plantation (1.45 - 5.30 pm)	Boat cruise of Pumicestone Passage (1.45 - 5.30 pm)	Tour of QDPI's Bribie Island Aquaculture facilities (2.00 - 3.00 pm)
AFTERNOON TEA (3.30 - 4.10 pm)				
Registration (4.00 - 6.00 pm)	Detection	Sunshine Plantation	Boat Cruise	Visit to QDPI's ciguatera laboratory (4.30 - 6.00 pm) en route to Dinner
Welcoming BBQ dinner at Joondoburri (6.30 - 10.00 pm)	*DINNER (6.00 - 7.00 pm)*			Workshop dinner at Morgan's Seafood Restaurant (6.30 - 11.00 pm)
	7.30 - 9.30 pm Poster session with authors in attendance	7.30 - 9.30 pm "Detection" Workshop session	7.30 - 9.30 pm "Clinical" Workshop session	

PROGRAMME

MONDAY, APRIL 12, 1993

3.30 - 4.00 pm	Afternoon tea
4.00 - 6.00 pm	Registration at Joondoburri
6.30 - 10.00 pm	Welcoming BBQ Dinner (Registrants and accompanying person welcome)

TUESDAY, APRIL 13, 1993

9.00 - 11 am	Registration, Posters mounted for display
10.30 - 11.30 am	Morning tea
11.30 - 12.00 noon	Official Opening
12.00 - 1.30 pm	Lunch
1:30 pm	Group photograph

DETECTION SESSIONS:

Chair: Y. Hokama

2.00 - 2.30 pm	**Ciguatera research - an historical perspective** Scheuer PJ (Honolulu, USA)
2.30 - 3.00 pm	**Structures of maitotoxin and ciguatoxin congeners isolated from cultured *Gambierdiscus toxicus*** Yasumoto T Satake M Murata M Naoki H Amamiyamachi T (Sendai, JAPAN)
3.00 - 3.30 pm	**Immunological, biochemical and chemical features of the ciguatoxins: implications for detection of ciguateric fish** Lewis RJ (Deception Bay, AUSTRALIA)
3.30 - 4.10 pm	Afternoon tea

Chair: T. Yasumoto

4.10 - 4.40 pm	**On the global increase of harmful algal blooms** Hallegraeff GM (Hobart, AUSTRALIA)

4.40 - 5.10 pm **Reef management and seafood safety monitoring programs for ciguatera**
Park DL Goldsmith CH (Arizona, USA)

5.10 - 5.40 pm **Evaluation of the ciguatect^{TM} immunoassay for the detection of ciguatera-related biotoxins in Caribbean finfish**
Dickey RW Granade HR McClure FD (Dauphin Island, USA)

6.00 - 7.00 pm Dinner

POSTER PRESENTATIONS: (authors in attendance)

7.30 - 9.30 pm **Recent progress on the ciguatera-related biotoxins of the Caribbean**
Dickey RW Shen J Granade HR Bencsath FA (Dauphin Island, USA)

Distribution of ciguateric dinoflagellates in Mayotte Island (S.W. Indian Ocean)
Grzebyk D Berland B Thomassin BA Arnoux A (Marseille, FRANCE)

A profile of hydrogeological parameters, *G. toxicus* substrate occupation and endemic toxicity at Wathumba Creek lagoon and Platypus Bay, Fraser Island
Hahn ST Capra MF (Brisbane, AUSTRALIA)

The origin of ciguatera in Platypus Bay, Australia
Holmes MJ Lewis RJ Sellin M Street R (Deception Bay, AUSTRALIA)

A survey for ciguatera fish poisoning in West Hawaii
Ichinotsubo D Asahina Y Titis E Hokama Y (Hawaii, USA)

Short and long range inverse detected NMR of Ciguatoxin-1
Lewis RJ Brereton IM (Deception Bay, AUSTRALIA)

Invertebrates implicated in the transfer of gambiertoxins to the benthic carnivore *Pomadasys maculatus*
Lewis RJ Holmes MJ Sellin M (Deception Bay, AUSTRALIA)

Ciguatera and herbivores: uptake and accumulation of ciguatoxins in *Ctenochaetus striatus* on the Great Barrier Reef
Lewis RJ Sellin M Gillespie NC Holmes MJ Keys A Street R Smythe H Thaggard H Bryce S (Deception Bay, AUSTRALIA)

Modification of nerve conduction in the rat by brevetoxin (PbTx-3)
Purcell CE Cameron J Capra MF (Brisbane, AUSTRALIA)

Pathologic changes in murine hearts induced by intermittent administrations of ciguatoxin
Terao K Ito E Ohkusu M Yasumoto T (Chiba, JAPAN)

WEDNESDAY, APRIL 14, 1993

PHARMACOLOGY SESSIONS:

Chair: E. M. McLachlan

9.00 - 9.30 am — **Ciguatoxin-1 induces spontaneous synaptic activity in isolated sympathetic ganglia of guinea pigs**
Hamblin P McLachlan EM Lewis RJ (Brisbane, AUSTRALIA)

9.30 - 10.00 am — **Effects of ciguatoxin-1 on electrical activity recorded intracellularly from rat tail artery in vitro.**
Brock JA Jobling P McLachlan EM Lewis RJ (Newcastle, AUSTRALIA)

10.00 - 10.30 am — **Detection of ciguatoxic fish by using the binding property of ciguatoxins to voltage-dependant sodium channels**
Legrand A-MF Lotte CJ (Tahiti, FRENCH POLYNESIA)

10.30 - 11.10 am Morning tea

Chair: A-M. F. Legrand

11.10 - 11.40 am **Studies on the mode of action of ciguatoxins on motor nerve terminals, cholinergic synaptosomes and nerve cells**
Molgo J Juzans P Morot-Gaudry Y Shimahara T Comella JX Meunier F Moulian N Legrand AM (Paris, FRANCE)

11.40 - 12.10 pm **Maitotoxin induces muscle contraction and a non-selective cationic current in single smooth muscle cells of the guinea-pig proximal colon**
Lang RJ Vogalis F Holmes MJ Lewis RJ (Melbourne, AUSTRALIA)

12.10 - 12.40 pm **Effects of gambiertoxin in biophysical and pharmacological properties of ionic channels in the peripheral nervous system**
Benoit E Legrand A-M (Orsay, FRANCE)

12.40 - 1.30 pm Lunch

1.45 - 5.30 pm Tour

6.00 - 7.00 pm Dinner

DETECTION WORKSHOP:

Co-Chairman: R. J. Lewis and M. F. Capra

7.30 - 9.30 pm **Impact of a validated, cost effective screen for ciguateric fish**
Lewis RJ (Deception Bay, AUSTRALIA)

Ciguatect-H^{TM}, a clinical diagnostic tool for ciguatera poisoning
Park DL Gamboa M (Tucson, USA)

Detection of ciguatoxin, brevetoxin, and saxitoxin by cell bioassay
Manger R Leja L Lee S Hungerford J Wekell M (Bothell, USA)

The mouse ciguatoxin bioassay: directions for use
Vernoux J-P (Caen, FRANCE)

THURSDAY, APRIL 15, 1993

CLINICAL SESSIONS:

Chair: R. A. Bagnis

8.30 - 9.00 am	**Duties of care: legal aspects in relation to ciguatera** Payne J (Brisbane, AUSTRALIA)
9.00 - 9.30 am	**Clinical aspects of ciguatera: an overview** Ruff TA (Melbourne, AUSTRALIA)
9.30 - 10.00 am	**Design, methods and rationale in the evaluation of intravenous mannitol for the treatment of acute ciguatera fish poisoning** Palafox N (Baltimore, USA)
10.00 - 10.30 am	**Ciguatera - dilemmas in clinical recognition, presentation and management** Pearn JH (Brisbane, AUSTRALIA)
10.30 - 11.10 am	Morning tea

Chair: J. H. Pearn

11.10 - 11.40 am	**The responses of vertebrate nerves to ciguatoxin** Capra MF Cameron J Flowers AE Purcell CE (Brisbane, AUSTRALIA)
11.40 - 12.10 pm	**Natural versus anthropogenic disturbances to coral reefs: comparison in epidemiological patterns of ciguatera** Bagnis RA (Tahiti, FRENCH POLYNESIA)
12.10 - 12.40	**The changing face of ciguatera prevalence** Chaloupka MY Lewis RJ Sellin M (Brisbane, AUSTRALIA)
12.40 - 1.30 pm	Lunch

1.45 - 5.30 pm Tour

6.00 - 7.00 pm Dinner

CLINICAL WORKSHOP:

Co-Chairman: J. H. Pearn and N. Palafox

7.30 - 9.30 pm **Evaluation of intravenous (IV) mannitol therapy for the treatment of the marine toxin disease, acute and chronic ciguatera poisoning**
Blythe DG (Coral Gables, USA)

Management of ciguatera fish poisoning in the South Pacific
Dalzell P (Noumea, NEW CALEDONIA)

FRIDAY, APRIL 16, 1993

ORIGIN SESSIONS:

Chair: N. C. Gillespie

9.00 - 9.30 am **The origin of ciguatera**
Holmes MJ Lewis RJ (Deception Bay, AUSTRALIA)

9.30 - 10.00 am **Ciguatera in the French West Indies**
Vernoux J-P (Caen, FRANCE)

10.00 - 10.30 am **Assessment of ciguateric fish in Hawaii by immunological, mouse toxicity and guinea pig atrial assays**
Hokama Y Asahina AY Titus E Ichinotsubo D Miyahara JT (Honolulu, USA)

10.30 - 11.10 am Morning tea

Chair: M. J. Holmes

11.10 - 11.40 am	**Development of a single step purification method for screening production of ciguatoxins in *Gambierdiscus toxicus*** Babinchak JA Moeller PDR Van Dolah FM Ramsdell JS (Charleston, USA)
11.40 - 12.10 pm	**Test of the effect of disturbance on ciguatera in Tuvalu** Kaly UL Jones GP (Townsville, AUSTRALIA)
12.10 - 12.40 pm	**Oral and intraperitoneal administration studies of toxins derived from fish tissues and extracts of cultured *G. toxicus* in the humbug (*D. aruanus*) damsel-fish (*P. wardi*) and the stripey (*L. carponotatus*).** Hahn ST Capra MF Miller DM (Brisbane, AUSTRALIA)
12.40 - 1.30 pm	Lunch
2.00 - 3.00 pm	Tour of QDPI's Aquaculture facility
4.30 - 6.00 pm	Tour of QDPI's Ciguatera Laboratory at Southern Fisheries Centre
6.30 - 10.00 pm	Workshop Dinner at Morgan's Seafood Restaurant

- END OF MEETING -

TUESDAY

13 th APRIL

DETECTION SESSIONS:

(invited speakers)

CIGUATERA RESEARCH - AN HISTORICAL PERSPECTIVE

Paul J. Scheuer

Department of Chemistry, University of Hawaii at Manoa
Honolulu, HI 96822, U.S.A.

Spanish speakers in the Caribbean coined the name ciguatera, but the Pacific has been the principal venue of ciguatera research during the past thirty-five years. The late A.H. (Hank) Banner's effort provided much of the stimulus and inspiration that have led to substantial advances in our knowledge, and hence the management, of ciguatera. Coincidentally, this research generated valuable leads for marine research far removed from its roots.

Beginning with Banner's original premises, this lecture will track ciguatera research, its successes and its failures, and recount forays into fertile and barren ground. Despite impressive advances, ciguatera has not faded away. Indeed, challenges remain for a new generation of researchers.

STRUCTURES OF MAITOTOXIN AND CIGUATOXIN CONGENERS ISOLATED FROM CULTURED GAMBIERDISCUS TOXICUS

*Takeshi Yasumoto, *Masayuki Satake, *Michio Murata, **Hideo Naoki:* Faculty of Agriculture, Tohoku University, Tsutsumi-dori Amamiyamachi, Aoba-ku, Sendai, 981 Japan; **Suntory Insti-tute for Bioorganic Research, Wakayamadai, Shimamoto-cho, Osaka 618, Japan

Maitotoxin (MTX) was isolated from cultured cells of Gambierdiscus toxicus collected in the Gambier Islands (GII1 strain). In order to determin the structure, the toxin was cleaved into three fragments (A, B, C) by sodium periodate oxidation, followed by sodium borohydride reduction. Structures of fragments A and B were determined by 2D NMR experiments. The structure of fragment B, the largest fragment of 2306 Dalton, was negative FAB MS/MS experiments. Comparison of the spectra between the fragments and intact MTX allowed us to assemble the whole structure of MTX. MTX has molecular weight 3422 (nominal, as disodium salt) and is constructed from 142 carbon chain, comprising 32 ether rings, 21 methyls, one exomethylene, 28 hydroxyl groups, and two sulfate esters.

Two ciguatoxin (CTX) congeners, CTX3C and CTX4A, and a new polyether toxin named gambierol were isolated from the culture of G. toxicus collected at Rangiroa Atoll (GRI1 strain). CTX4A is 52-epiCTX4B and CTX3C is 1,2,3,4-nor-E-homo-CTX4B. The ladder-shaped polyether skeleton of gambierol differs from the other two. Production of CTX4A and CTX3C, by cultured G. toxicus unambiguously confirmed the generic origin of ciguatera toxins.

IMMUNOLOGICAL, BIOCHEMICAL AND CHEMICAL FEATURES OF THE CIGUATOXINS: IMPLICATION FOR DETECTION OF CIGUATERIC FISH.

Richard J. Lewis. Southern Fisheries Centre, QDPI, Deception Bay, Qld 4508, Australia.

The development of a validate, cost-effective screening assay for ciguatoxins contaminating fish will provide a major management tool to minimise the adverse impacts of ciguatera. In this review, the history of progress towards such a goal is summarised and the implications for detection of recent advances in our understanding of ciguatera are discussed. Ciguatera results predominantly from the effects of the most potent ciguatoxin (ciguatoxin-1) which is present at >0.1 ppb (10^{-10} M/kg) in the flesh of carnivorous fish. Consequently, CTX-1 should be the principal target of any assay for ciguateric fish. Significant levels of the less potent ciguatoxins, including ciguatoxin -2 and -3, (eg CTX-2, -3) also accumulate in fish and could potentially interfere with the response of an assay. The role in human poisoning of other toxins in ciguateric fish has not been substantial. The ciguatoxins have a high affinity for voltage-dependant sodium channels (ED_{50} = 0.2 - 0.8 nm) that is proportional to their i.p. LD_{50}s in mice. Assays (biosensors) taking advantage of this binding and perhaps the sodium channel opening that results may provide a sensitive assay for ciguatoxins with a response proportional to potency. The ciguatoxins may also bind to a range of proteins, an interaction that may interfere with the assay response or that could perhaps be utilised in the development of novel assays. Ciguatoxin-1, -2 and -3 do not possess a useful chromophor for selective detection; however, each possess a relatively reactive primary hydroxyl through which a label could be attached (after appropriate clean-up) prior to detection. Detectors (eg fluorescence or mass spectrometic) coupled to optimised HPLC may provide the required sensitivity for detection of derivatised ciguatoxins in crude extracts of fish.

ON THE GLOBAL INCREASE OF HARMFUL ALGAL BLOOMS

Gustaaf M. Hallegraeff

Department of Plant Science, University of Tasmania,
GPO Box 252 C, Hobart, Tasmania 7001, Australia

Harmful algal blooms have occurred throughout recorded history but during the past two decades the effects on human health and economic impacts of such events have increased in frequency, intensity, and geographic distribution. To some extent, this simply reflects our increased awareness of toxic species and the enormous expansion in aquaculture efforts. Evidence is accumulating, however, that human activities contribute significantly to this increase through the stimulation of exceptional blooms by cultural eutrophication (e.g. from domestic, industrial and agricultural wastes; acid precipitation, deforestation and increased land run-off) and by the spreading of nuisance organisms in ships' ballast water. The global nature of these phenomena is illustrated with examples drawn from Japan, North America, Europe, South-East Asia and Australia, and involving species of dinoflagellates, diatoms, prymnesiophytes, raphidophytes and cyanobacteria.

REEF MANAGEMENT AND SEAFOOD SAFETY MONITORING PROGRAMS FOR CIGUATERA

Douglas L. Park, U. of AZ, & Catherine H. Goldsmith, HCI, Pasadena, CA

Programs designed to provide assurance that foods susceptible to ciguatera are safe to eat require several facets. These include a marketplace screening of suspect foods, separation of adulterated product to less risk uses, and development of systems designed to predict hazardous food production/collection areas. The analytical methods needed for screening/monitoring programs must meet the following criteria to be practical: (a) facile use and interpretation; (b) rapid; (c) accurately differentiate between toxic and nontoxic samples; (d) low cost; (e) sufficient quantities to meet private, industrial, and regulatory agency testing demands; and (f) where feasible, provide for a means of confirmation of identity.

The solid-phase immunobead assay (Ciguatect™) for the detection of ciguatera-related toxins, available from HawaiiChemtect International, has the highest potential for application to screening marketplace fish for ciguatera toxicity. The kit can be used at several points along the marketing plan, including on-board vessels, dockside, in processing plants, distribution organizations, retail outlets, regulatory agencies, and by consumers. To minimize potential economic losses to industry, testing fish early in the plan is recommended.

In conclusion, a seafood safety monitoring program would entail a testing program including: monitoring fish harvesting areas; development of a sampling plan; screening fish at various points; re-analysis of positive testing fish; and diverting toxic fish to lower risk uses. Ciguatect™ can be used to monitor reef fishing areas for ciguatera potential and screen for toxic fish in the marketplace.

EVALUATION OF THE CIGUATECT™ IMMUNOASSAY FOR THE DETECTION OF CIGUATERA-RELATED BIOTOXINS IN CARIBBEAN FINFISH

Robert W. Dickey, H. Ray Granade and Foster D. McClure
Gulf Coast Seafood Laboratory, Office of Seafood, U.S. Food and Drug Administration, Dauphin Island, AL 36528, USA

The Ciguatect™ solid-phase immunobead assay for the detection of ciguatera-related polyether biotoxins in finfish was evaluated for consistency with mouse bioassay results. Fifty finfish specimens collected from ciguatera endemic waters of St. Thomas, U.S.V.I., and one fish remnant from a confirmed case of human ciguatera poisoning were bioassayed. Mouse bioassays were performed in duplicate on chromatographic eluate fractions from silica gel corresponding to that of ciguatoxins. The dosage range was 45 to 180 grams of muscle tissue equivalent from each finfish specimen. The specimens were classified as either ciguatoxic or non-ciguatoxic on the basis of observable signs of ciguatoxicity and death within 48 hours. The 51 specimens were then assayed by three variations of the Ciguatect™ procedure, which differed in the method of tissue sampling: i.e. single exposure, triple exposure and single exposure to solvent extract from flesh (REM™: rapid extract method). Statistical analyses were performed after the method of McClure, 1990. The Ciguatect™ sensitivity rates (positive matches) for the single, triple and REM™ exposure procedures were 58%, 85% and 97%, respectively. Specificity rates (negative matches) were 17%, 22% and 6%, respectively. Corresponding false negative rates were 82%, 55% and 50%, and false positive rates were 44%, 33% and 33%. Predictive indices for Ciguatect™ performance under ciguatoxin contamination rates ranging from 5% to 75% project that high false negative and false positive values might be expected in market situations.

WEDNESDAY

14 th APRIL

PHARMACOLOGY SESSIONS:

(invited speakers)

CIGUATOXIN-1 INDUCES SPONTANEOUS SYNAPTIC ACTIVITY IN ISOLATED SYMPATHETIC GANGLIA OF GUINEA PIGS

Hamblin, Paul*, McLachlan, Elspeth M. and Lewis, Richard J.
Department of Physiology & Pharmacology, University of Queensland, and Southern Fisheries Centre, Deception Bay, Qld.

An electrophysiological study has been undertaken of the actions of purified ciguatoxin-1 (CTX-1) on the neurones of guinea pig sympathetic ganglia isolated *in vitro*, using conventional intracellular microelectrode techniques. Low concentrations of CTX-1 (0.2-0.8 nM) applied even briefly (<15 min) via the perfusing solution induced a dramatic increase in the spontaneous occurrence of excitatory synaptic potentials (ESPs) which persisted for many hours. The amount and pattern of activity varied between neurones and occurred in the absence of any change in either the passive or active electrical properties of the neurones themselves. Single supramaximal preganglionic stimuli evoked a summed response which was unaltered after exposure to CTX-1, but was followed by a variable duration high frequency burst of ESPs. These bursts resembled in form those occurring spontaneously in the same cell, and apparently arose from individual preganglionic axons. The effects were abolished by reduced Ca^{++}, Ω-conotoxin, low doses of TTX or raised divalent cation concentrations. The results indicate that some preganglionic axons have CTX-binding sites that open Na^{+} channels causing spontaneous depolarization and initiating repetitive discharges.

*supported by a travel grant from the British Council.

EFFECTS OF CIGUATOXIN-1 ON ELECTRICAL ACTIVITY RECORDED INTRACELLULARLY FROM RAT TAIL ARTERY IN VITRO.

James A. Brock*, Phillip Jobling, Elspeth M. McLachlan, and Richard J. Lewis#.
Department of Physiology and Pharmacology, University of Queensland, Qld 4072, Australia. *Medical Faculty, University of Newcastle, NSW 2308, Australia. #Southern Fisheries Centre, Department of Primary Industries, Deception Bay, Qld 4508, Australia.

Ciguatoxin-1 (CTX-1) is a lipid soluble toxin arising from the benthic dinoflagellate, *Gambierdiscus toxicus*, which is responsible for the disease *ciguatera*. This disease is characterised by a range of symptoms involving the peripheral nervous system. CTX-1 has been suggested to have a selective action on tetrodotoxin (TTX)-sensitive Na^+ channels and induces spontaneous nerve action potentials due to opening of sodium channels at normal resting potential. In this study the effects of CTX-1 on the rat tail artery have been investigated. Intracellular recordings were made from isolated sections of rat tail artery. Application of 0.002 - 0.2 nM CTX-1 increased the rate of occurrence of spontaneous excitatory junction potentials (SEJPs) and increased the duration of the evoked excitatory junction potential (EJP), the decay phase no longer being fitted by a single exponential function. At 0.2 nM CTX-1 also produced a large (25 - 30 mV) maintained depolarization. The effects of CTX-1 were abolished by tetrodotoxin (0.3 µM) and were calcium dependent. In addition EJPs and SEJPs were blocked by the purinoceptor antagonist suramin (1 mM) and the maintained depolarization was blocked by the α-adrenoceptor antagonist phentolamine (1 µM). These data suggest the actions of CTX-1 are due solely to activation of the sympathetic nerves innervating the rat tail artery.

DETECTION OF CIGUATOXIC FISH BY USING THE BINDING PROPERTY OF CIGUATOXINS TO VOLTAGE-DEPENDANT SODIUM CHANNELS.

Anne-Marie F. Legrand and Catherine J. Lotte.
Institut Territorial de Recherches Médicales Louis Malardé, PO Box 30 Papeete, Tahiti, French Polynesia

Binding studies indicate that CTX (coded -1B), the principal toxin isolated from moray eel viscera and CTX-4B (or GT-4B) isolated from wild dinoflagellate *Gambierdiscus toxicus*, Adachi and Fukuyo, competitively inhibit the binding of the brevetoxin (3H)-PbTx-3 to rat brain membranes. The affinity of CTX-1B is around 30 times higher than that of PbTx-3 while CTX-4B has around the same affinity as the brevetoxin. The results confirm that the two toxins act at the voltage-dependant sodium channel of rat brain membranes. Experiments on minor toxins isolated from ciguatoxic material are under way. Preliminary results indicate a common property of the compounds to inhibit the binding of PbTx-3. This property is used to evaluate the ciguatoxicity of hazardous fish. A rapid extraction procedure and a routine binding assay have been established.

STUDIES ON THE MODE OF ACTION OF CIGUATOXINS ON MOTOR NERVE TERMINALS, CHOLINERGIC SYNAPTOSOMES AND NERVE CELLS.

Molgo, J., Juzans, P., Morot-Gaudry, Y., Shimahara, T., Comella, J.X., Meunier, F., Moulian, N. and * Legrand, A.M.

Laboratoire de Neurobiologie Cellulaire et Moléculaire,* C.N.R.S., *91198-Gif sur Yvette, France and * Institut Territorial de Recherches Médicales Louis Malardé, Papeete, French Polynesia.

The main emphasis of this presentation is given to detail the mode of action of ciguatoxin (CTX-1b) and gambiertoxin4b (CTX-4b) on Ca^{2+}-dependent and external Ca^{2+}-independent acetylcholine (ACh) release from pure cholinergic synaptosomes and motor nerve terminals using chemiluminescent and electrophysiological techniques for continuous ACh detection. In addition, using confocal laser scanning microscopy, which allows optical sectioning of *living* vertebrate neuromuscular junctions at a desired thickness and a subsequent 3-dimensional reconstitution of the structures, we have followed the changes in surface area of motor nerve terminals during the massive ACh release caused by CTX-1b. We also will detail the effects of mannitol, an agent that has been used for treatment of ciguatera fish poisoning. Finally, the use of cell-permeable Ca^{2+} chelators, intracellular Ca^{2+} antagonist as well as fura-2 based microfluorometrical techniques allowed to obtain new informations about Na^{+}-dependent Ca^{2+} mobilization and intracellular Ca^{2+} stores stimulated by CTX-1b.

This study was supported by a grant (91/090 to J.M.) from Direction des Recherches Etudes et Techniques .

MAITOTOXIN INDUCES MUSCLE CONTRACTION AND A NON-SELECTIVE CATIONIC CURRENT IN SINGLE SMOOTH MUSCLE CELLS OF THE GUINEA-PIG PROXIMAL COLON.

Richard J. Lang*, Fivos Vogalis*, Michael J. Holmes+ and Richard J. Lewis+ .
*Department of Physiology, Monash University, Clayton, Vic.
+Southern Fisheries Centre, Deception Bay, Qld. Australia.

We have investigated the mechanisms of action of maitotoxin-2 (MTX) a marine toxin isolated from the toxic dinoflagellate *Gambierdiscus toxicus* on the contractility of the intact circular smooth muscle of guinea-pig proximal colon and on the membrane currents recorded in its' enzymatically-dispersed single cells, using standard contraction and patch clamp techniques. MTX (0.005-5.0 nM) induced an initial phasic contraction, sensitive to atropine (2 μM) blockade, followed by a cessation of all spontaneous contractile activity. Contractions to acetylcholine (0.5 μM) were irreversibly reduced $\approx$ 75% by MTX (0.5 nM) (n=5). MTX (5 nM) completely abolished the contractions to acetylcholine, but reduced contractions to raised K^+ saline (40 mM) only 54 $\pm$ 9% (n=4). The blockade of the acetylcholine contractions was mimicked, in part, by the Na^+ ionophore, monensin (0.1-10 μM). Single colonic smooth muscle cells were perfused with K^+-filled patch pipettes and voltage clamped at a holding potential of -80 mV. MTX (5nM) induced a large inward current (I_{MTX})(1-3 nA) after a delay of 15-45 minutes. This current was not prevented by the K^+ channel blockers: tetraethylammonium (TEA; 2-126 mM), 4-aminopyridine (5 mM), quinidine (5 mM), glibenclamide (10 μM); or when the Ca^{2+} was removed. This current was blocked by Cd^{2+} (0.1-1 mM) and reduced by nifedipine (10 μM) and La^{3+} (1 mM). I_{MTX} had a linear current-voltage relationship with a reversal potential near -30 and 0 mV when cells were filled respectively with K^+ or Cs^+. When most of the extracellular Na^+ (126 mM) was replaced with TEA^+, this current reversed near -60 mV. These results suggest that MTX induces the opening of Cd^{2+}-sensitive channels which allow the flow of Na^+, K^+ and Cs^+, but not TEA^+.

EFFECTS OF GAMBIERTOXIN IN BIOPHYSICAL AND PHARMACOLOGICAL PROPERTIES OF IONIC CHANNELS IN THE PERIPHERAL NERVOUS SYSTEM

Evelyne Benoit and Anne-Marie Legrand, Laboratoire de Physiologie cellulaire, URA CNRS 1121, bât 443, Université de Paris XI, 91405 Orsay Cedex, France and U.R. Océanographie Médicale, Institut Louis Malardé, BP 31, Papeete, Tahiti, Polynésie Française

Ciguatoxin and more recently gambiertoxin have been shown to interact with Na channels in various preparations. In particular, the toxins have been reported to induce modifications of either a fraction of or all Na channels in the peripheral nervous system. We analysed the effects of gambiertoxin on the ionic currents of myelinated nerve fibres, in order to investigate the biophysical and pharmacological properties of toxin-modified Na and K channels.

The effects of external applications of 1.2-24 nM of gambiertoxin (CTX-4B) extracted from the dinoflagellate *Gambierdiscus toxicus*, Adachi and Fukuyo, were studied of ionic currents of the frog myelinated nerve fibre under voltage clamp conditions.

No effect of CTX-4B was observed for toxin concentrations varying from 1.2 to 6 nM. In contrast, the addition of 12-24 nM of CTX-4B to the control solution induced the appearance of spontaneous action potentials at a frequency of 30-100 Hz, due to modifications in the voltage characteristics of Na current which, in particular, was activated at the resting membrane potential. In addition, the voltage characteristics of K current were also modified by the toxin and, in the presence of 24nM of CTX-4B, both Na and K currents were reduced to about 20-30% of their control value. In contrast to control action potentials elicited by stimuli, toxin-induced spontaneous action potentials were suppressed by lidocaine, mannitol or an increase in external Ca concentration. However, unmodified and toxin-modified Na currents were similarly sensitive to each of the above substances.

It is concluded that gambiertoxin, at low concentrations, modifies the biophysical properties of K and Na channels and in addition, at high concentrations, blocks ionic channels. However, the pharmalogical properties of ionic channels are not modified by the toxin.

WEDNESDAY EVENING

14 th APRIL

DETECTION WORKSHOP SESSION:

IMPACT OF A VALIDATED, COST EFFECTIVE SCREEN FOR CIGUATERIC FISH.

Richard J. Lewis, Southern Fisheries Centre, QDPI, Deception Bay, Qld 4508, Australia.

Ciguatoxins contaminating ciguateric fish may be detected by a range of *in vivo* (eg mouse, cat, mosquito or chicken), *in vitro* (eg antibody, sodium channel binding or biosensor) and chemical assays. Research continues on the development of simple, inexpensive screens for ciguateric fish. Such screens for ciguateric fish should selectively detect low levels of ciguatoxin-1 (0.1-5.0 ppb) either directly in fish flesh or in an easy to prepare extract. An "acceptable" cost for such testing has not been established. Implementation of a screen for ciguateric fish will reduce the adverse health impacts of ciguatera. An attendant benefit will be the improved marketability of reef fish, especially for species presently considered unsuitable for consumption eg red bass, chinaman fish and paddletail in Queensland. It is unclear when in the marketing chain reef fish should be screened for ciguatoxins.

CIGUATECT-H™, A CLINICAL DIAGNOSTIC TOOL FOR CIGUATERA POISONING

Douglas L. Park & Pedro M. Gamboa, U. of AZ

Ciguatera, a human disease that has been reported since the arrival of the Spanish over 500 years ago, still remains as the most important natural seafood poisoning illness in many parts of the world, including the USA. Up to now the diagnosis for this disease has been strictly epidemiological, primarily due to the unavailability of a sound chemical method with the selectivity and sensitivity required for detecting minute amounts of the responsible toxins. With the emergence of immunoassay-based techniques, and particularly the use of monoclonal antibodies, new avenues have been opened. A novel approach to analytical separations has been developed, immuno-affinity chromatography, where the toxin separation process is based on the ability of biological substances to bind specifically to complementary ligands which have been chemically attached to an inert matrix. The current method involves the coupling of an immuno-affinity column to an ELISA format, resulting in a clinical quantitative diagnostic tool for marine polyether toxins responsible for ciguatera fish poisoning. An alternative method utilizing a rapid extraction procedure to remove and partially purify the toxins from the serum and detection using a solid-phase immunobead assay (S-PIA, Ciguatect™) has also been developed. This paper addresses the applicability of immuno-affinity chromatography, coupled with ELISA quantitation and the extraction/S-PIA methods, on the clinical diagnosis of ciguatera. Preliminary results from serum of symptomatologically diagnosticated patients are presented; and the potential for implementing monitoring programs, on suspected trasvectors in endemic areas, is discussed.

DETECTION OF CIGUATOXIN, BREVETOXIN, AND SAXITOXIN BY CELL BIOASSAY

Ron Manger, Linda Leja, Sue Lee, James Hungerford and Marleen Wekell. U.S. Food and Drug Administration, Seafood Products Research Center, Bothell, WA 98041-3012

Monitoring programs for marine toxins have depended in large part on the mouse bioassay, however, there is mounting pressure to develop alternative assays to reduce the reliance on animal testing. Significant initial progress has been made towards this end for the detection of agents that block sodium channels, such as the saxitoxins, by Kogure *et al* (Toxicon, 1988) and Jellet *et al* (Toxicon, 1992). In the present study we have augmented the utility and simplified these earlier methods by determining the effect that specific marine toxins have upon mitochondrial dehydrogenase activity. Furthermore, we have extended the application of the assay to allow the characteristic detection of either agents that block sodium channels, such as saxitoxins, or sodium channel enhancers such as brevetoxins and ciguatoxins. The assay responds in a dose dependent manner and identifies the toxic activity as either sodium channel blocking or enhancing. In addition, the assay is highly sensitive, with present detection limits of 2 ng/ml for either saxitoxins or brevetoxins (PbTx-1 and PbTx-3). Assay response to ciguatoxins and brevetoxins is rapid allowing dose dependent detection within 4 to 6 hr. The method is simple, utilizes readily available reagents, and is well within the scope of even modest tissue culture facilities. This cell-based protocol has the potential to serve as an alternate and complementary method to the standard mouse bioassay.

TITLE : THE MOUSE CIGUATOXIN BIOASSAY : DIRECTIONS FOR USE.

VERNOUX, J.P., ILVENUC - UNIVERSITY OF CAEN - FRANCE

Ciguatera fish poisoning is a widespread and causes serious health problem in the world. Nevertheless diversity and heterogeneity of ciguatoxins delay the use of chemical and immunological methods. However realistic methods useful for ciguatoxin screening in fish are needed for public health studies. In this view the mouse bioassay could be very useful since it is simple and not too expensive. Qualitative and semi-quantitative methods for analysis of ciguatoxins from 50, 100 or 200 g of fish tissue are precisely described and some results are shown.

THURSDAY

15 th APRIL

CLINICAL SESSIONS:

(invited speakers)

DUTIES OF CARE: LEGAL ASPECTS IN RELATION TO CIGUATERA.

John Payne, Estwick and White Solicitors, Toowong, Qld 4066, Australia.

Implications of the Queensland Workplace Health and Safety Act and Common Law Duties of Care to the management of ciguatera for Industry participants; consideration of aspects of the Trade Practices Act, Fair Trading Act and Sales of Goods Act, what rights and obligations exist, and what changes should be made.

CLINICAL ASPECTS OF CIGUATERA: AN OVERVIEW

Tilman A Ruff Dept. of Social & Preventive Medicine, Monash Medical School, Alfred Hospital, Melbourne.

Ciguatera is a polymorphous disease posing important health, nutrition, economic and social problems for inhabitants of endemic areas, and occasionally for those in non-endemic areas. Limited progress has been made in understanding the pathophysiology of the disease and in developing effective treatment.

The clinical features of the disease are reviewed, and incidence, morbidity and mortality data are outlined. Progress in treatment of ciguatera is discussed, and key issues and needs for future research are described. These include:

- consistent epidemiologic data, using a consistent case definition;
- the human immune response to ciguatoxins;
- the pathophysiological mechanisms underlying human disease, potentiation of disease by alcohol, and the phenomenon of sensitisation;
- better tests for ciguatoxins; and
- effective and safe treatment for affected patients.

DESIGN, METHODS AND RATIONALE IN THE EVALUATION OF INTRAVENOUS MANNITOL FOR THE TREATMENT OF ACUTE CIGUATERA FISH POISONING

Neal Palafox, Box 686, John Hopkins School of Public Health, U.S.A.

The Ciguatera Double Blind Study is an investigator initiated, grant supported, multicenter, randomized, controlled trial which is designed to: 1) investigate the efficacy of intravenous 20% mannitol in comparison to a placebo (intravenous 5% dextrose in water) for treatment of acute ciguatera fish poisoning; 2) determine the response time to treatment; and 3) determine relapse rate 48 hours post treatment. Mannitol and the 5% dextrose were randomly assigned to patients who presented with ciguatera fish poisoning to one of four hospitals. Medical treatment was provided through a protocol. Patients response was monitored at 10 min, 30 min and 2½ hours after therapy was begun. Patient followup was done for 48 hours after the treatment was given. This paper will describe the design and methods of the trial and a discussion for the underlying rationale for key design decisions.

CIGUATERA - DILEMMAS IN CLINICAL RECOGNITION, PRESENTATION AND MANAGEMENT

John Pearn, Department of Child Health, Royal Children's Hospital, Brisbane, Qld, 4029

Both the clinician and the consulting scientist are confronted with several key problems in the recognition and management of the ciguatoxic victim. Currently, failure to consider the possibility of ciguatera, in a patient presenting with any one or more of the pleomorphic constellation of symptoms and signs which are the hallmark of the disease, remains the most important ongoing dilemma of management. The concept of differential diagnosis is "the formulation of a list of diseases, commensurate with the elicited history and the observed signs, arranged in decreasing order of likelihood". All familiar with ciguatera are aware of the multiplicity of other different diagnoses which are included in the list of possibilities generated by the perplexed victim and his or her family, by an attending first-aider, or by the admitting doctor in the emergency room of the referral hospital. In single cases, the difficulty of raising a differential diagnosis is compounded, especially in milder cases where more characteristic features of the florid neurological symptoms and some of the characteristic signs such as bradycardia, are not manifest. Differential diagnosis, over recent decades, has included a broad range of diseases including hysteria, psychosis and neurosis, malingering, viral illnesses, metal and insecticide poisoning and auto-immune disease. Another of the unresolved dilemmas in managing the ciguatoxic patient is to interpret the chronicity of symptoms correctly. Although numerous anecdotal reports remain, doubt persists about the persistence of symptoms for more than a year or so. At this point of scientific endeavour, no cumulative frequency histograms have been generated, by symptom, for proven cases followed prospectively. Such remains an important clinical research challenge for the future.

A third dilemma concerns the use of Mannitol, and the timing of its introduction. Collaborative clinical research undertaken in Queensland, Australia, has indicated that there is little benefit to be obtained if Mannitol is not given within 48 hours of the onset of symptoms. This is a perplexing dilemma because a considerable number of victims first present for medical review later than this time in the course of their disease. This workshop session will consider these and related clinical points, in the context of the collective experience of an international ciguatera meeting.

THE RESPONSES OF VERTEBRATE NERVES TO CIGUATOXIN.

Michael F Capra, John Cameron, Andrew E Flowers and Christine E Purcell. School of Life Science, Queensland University of Technology, Brisbane, Australia.

Electrophysiological studies were performed on a variety of nerve preparations from both mammals (rats and humans) and fish. The responses of the peripheral nerves of humans to ingested ciguatoxin were assessed in the Sural nerves of fifteen victims of acute ciguatera poisoning. In rats the responses of the ventral coccygeal nerve in anaesthetised animals were studied after intoxication was induced by intraperitoneal injection of sub-lethal doses of ciguatoxin. In fish, isolated segments of the spinal nerves and the lateral line branch of the Vagus nerve of both "carriers" and "non carriers" of ciguatoxin were exposed to solutions of ciguatoxin in fish Ringer.

In all nerve preparations there were significant changes in a range of nerve conduction parameters including conduction velocity, amplitude, and the duration of refractory periods and the supernormal period. In all preparations there was a significant prolongation of and increase in the magnitude of the supernormal period. These changes conform with studies on isolated cells that suggest a fundamental action of ciguatoxin on Na^+ gating mechanisms.

Both rat and fish preparations have been used to assess the efficacy of a range of potential antagonists of the ciguatoxin response. In rats, the ciguatoxin induced changes in supernormality are unaffected by mannitol but significantly antagonised by lignocaine. In fish lignocaine and tetrodotoxin antagonise the responses induced by ciguatoxin.

It has also been established that the nerves of fish respond to ciguatoxin in a similar manner to those of mammals and it is suggested that fish may have evolved some degree of protection against ciguatoxin by mechanisms that do not involve the Na^+ channel.

NATURAL VERSUS ANTHROPOGENIC DISTURBANCES TO CORAL REEFS : COMPARISON IN EPIDEMIOLOGICAL PATTERNS OF CIGUATERA.

Raymond A. BAGNIS. Institut Territorial de Recherches Médicales Louis Malardé, B.P. 30 Papeete, Tahiti, French Polynesia and Université Française du Pacifique, B.P. 4635 Papeete, Tahiti, French Polynesia.

The patterns of evolution of ciguatera fish poisoning vary from place to place over the world. From many surveys in endemic areas carried on to point out the succession of events associated to outbreaks of the disease, has emerged the role of the disturbances on coral reefs.

Seasonal natural disturbances like storms, heavy rains with freshwater drainage, red tides... seem to result in a pattern of poisoning in which the overall picture of ciguatera is quite stable with the same fish species (most of the time large predators) exhibiting the same level of toxicity in well defined geographical areas.

Cyclic natural catastrophes like hurricanes, tsunami, coral bleaching... could be related to a pattern of diffuse continuous poisoning at a low level with periodic marked increases of outbreaks among the local populations, caused by fish of various trophic levels.

Anthropogenic disturbances like undersea works, crashing of ship anchors, ship wreckages, dumping of wastes, building of piers or wharfs and any other damage to alive corals may result in a flare up of poisonings in areas with quite no previous history of ciguatera. In this pattern, most of the herbivorous fish (mainly grazers and browsers) and the predaceous carnivores, as well as certain invertebrates of localized areas, may be toxic during a few years.

THE CHANGING FACE OF CIGUATERA PREVALENCE

M.Y. Chaloupka[1], R.J. Lewis[2] and M. Sellin[2]
[1]Queensland Department of Environment and Heritage, Brisbane, Qld, 4002, Australia
[2]Southern Fisheries Centre, QDPI, Deception Bay, Qld, 4508, Australia

Ciguatera cases in Queensland (recorded mostly by the Queensland Health Department) from 1965 to 1992 have been complied into a comprehensive database - the database comprises 920 cases attributable to 343 outbreaks.

PELAGIC fish (mainly mackerel species) account for 65% of all recorded cases while REEF fish account for 35% of cases. PELAGIC fish were found to have a significantly higher prevalence of 8 of the 27 surveyed symptoms than REEF fish, these being temperature reversal, diarrhoea, nausea, vomiting, abdominal pain, joint pain, dental pain and ataxia. NORTHERN fish ($\leq 24^{\circ}$ catch location) accounted for 33% of recorded cases while SOUTHERN fish accounted for 67% of the recorded cases. NORTHERN fish were more likely than SOUTHERN fish to be associated with a NEUROLOGICAL symptom profile (odds ratio = 2.0; 95% CI [1.38, 2.82]). NEUROLOGICAL profiles (neurological symptoms only) accounted for 18.2% of all recorded cases. Interestingly, this symptom profile has become more prevalent over the last decade, reflecting a significant shift in toxic fish consumption from SOUTHERN PELAGIC to both NORTHERN and REEF fish.

A subset of the 920 cases (N=657) were used to model temporal and geographical shifts from 1976-1992 in major responses such as time to onset of first symptom (ONSET) and prevalence of a NEUROLOGICAL profile. Statistical modelling methods used included recent advances in robust regression modelling (generalised additive modelling) and statistical graphics. Significant and complex shifts in temporal and spatial prevalence were found. The results and implications of this modelling exercise will be discussed.

THURSDAY EVENING

15 th APRIL

CLINICAL WORKSHOP SESSION:

EVALUATION OF INTRAVENOUS (IV) MANNITOL THERAPY FOR THE TREATMENT OF THE MARINE TOXIN DISEASE, ACUTE AND CHRONIC CIGUATERA POISONING.

Donna Glad Blythe, University of Miami, Miami, Florida 33146, U.S.A.

Design: Case Series
Setting: Two clinical practises in South Florida
Patients: 107 patients over a 7 year period with the clinical diagnosis of acute and chronic Ciguatera Poisoning from the South Florida-Caribbean area
Interventions: 70 patients with Ciguatera Poisoning received IV Mannitol treatment (1 g/kg) within hours to 1000 days from exposure; 37 patients with Ciguatera Poisoning received only supportive therapy, if any
Main Outcome Measures: Subjective report of acute response to Mannitol treatment was rated on a scale of 0-4+ by the patient; 4+ denoted complete recovery from symptoms.
Results: The treated and non-treated groups were comparable except for a significantly increased time from exposure to presentation in the untreated group. 29 out of 32 (91%) patients treated within the first 48 hours from exposure had complete reversal of symptoms.
Conclusions: Although not a formal randomized clinical trial, this case series does provide valuable information and support for the use of intravenous Mannitol in the treatment of acute and chronic Ciguatera poisoning.

MANAGEMENT OF CIGUATERA FISH POISONING IN THE SOUTH PACIFIC

P. Dalzell, Inshore Fisheries Research Project, South Pacific Commission, BP D5 Noumea Cedex, New Caladonia

Catches of near-shore or coastal fish continue to be a major source of animal protein for the nations of the South Pacific region. Nominal landings of near-shore fishes amount to about 90,000 t/yr, about half of which is reef fish. Ciguatoxic fishes are found throughout much of the region but and in some locations, such as the island of Niutao in Tuvalu, there is a very high risk of intoxication associated with eating reef fish. However, even in high risk areas, species known to cause ciguatera continue to be consumed due to the reliance of the populace on fish for food and because ciguatera is not generally considered to be a significant health problem, even where it is widespread. This low level of concern with ciguatera is reflected in the attitude of general practitioners and other medical staff, who are reluctant to see ciguatera given priority to more serious (and treatable) maladies.

In view of its relative insignificance as a medical problem in the region, it would seem appropriate that fisheries development initiatives should aim to improve supplies of non-toxic deep reef slope species and pelagic species caught in the open sea away from the reef. Elsewhere, ciguatera management is probably best focussed on limiting the impact of fish poisonings on tourism and reef fish exports. Initiatives to improve the management of ciguatera such as the South Pacific Commission's seafood poisoning database are discussed.

FRIDAY

16 th APRIL

ORIGIN SESSIONS:

(invited speakers)

THE ORIGIN OF CIGUATERA.

Michael J. Holmes and Richard J. Lewis. Southern Fisheries Centre, QDPI, Deception Bay, Qld 4508, Australia.

Ciguatera is caused by eating the flesh of fishes contaminated with ciguatoxins. Ciguatoxins-1, -2 and -3 are the major ciguatoxins found in the flesh and liver of ciguateric fishes with ciguatoxin-1 being the major toxin in terms of both quantity and toxicity. Gambiertoxin-4b is the likely precursor of ciguatoxin-3 which is in turn oxidatively metabolised in fishes to ciguatoxin-1. Consequently, gambiertoxin-4b is responsible for more than 90% of the toxicity of ciguateric fishes. Gambiertoxin-4b has been extracted from biodetritus containing large numbers of the benthic dinoflagellate *Gambierdiscus toxicus*, indicating *G. toxicus* as the primary source of toxins involved in ciguatera. Putative gambiertoxins have also been detected from certain strains of cultured *G. toxicus*. We have suggested that ciguatera occurs when *G. toxicus* strains genetically capable of producing gambiertoxins enter the food chain of fishes. However, the link between *G. toxicus* and the major toxins that cause ciguatera remains circumstantial since gambiertoxin-4b has not yet been unambiguously identified from cultures of this dinoflagellate. Toxins from other sources, mainly other benthic dinoflagellate species, have been suggested as being involved in ciguatera but there is little evidence to support these claims.

TITLE : CIGUATERA IN THE FRENCH WEST INDIES.

VERNOUX, J.P., ILVENUC - UNIVERSITY OF CAEN - FRANCE

Ciguatera fish poisoning was studied on the island of Saint-Barthelemy, Leeward islands, in the Caribbean sea from 1979 to 1989. Clinical features of the illness include gastrointestinal and neurological disorders such as neuromuscular and neurosensory manifestations, visual disturbances and persistent itching. The incidence of ciguatera was 0,3 to 1 % per year. 429 specimens of fish caught in fish-pots or by hook and line were checked for ciguatoxin by mouse and chicken bioassay. It was found that jacks and barracudas were highly ciguatoxic species. Small carnivorous fishes classified as invertebrate feeders play an important role in the transmission of ciguatoxin in the food chain since their toxin content was not negligible. Herbivorous fishes such as surgeonfishes or parrotfishes which are not implicated in ciguatera transmission by local population were not ciguatoxin carriers unless exception at an extremely low level. The presence of G. toxicus in coastal waters of St Barth's was established. So G. toxicus could be assumed to be the principal elaborator of ciguatoxin. Nevertheless puzzling results obtained from previous experiments realized in Tahiti with G. toxicus could accredit another interpretation which is presented here.

ASSESSMENT OF CIGUATERIC FISH IN HAWAII BY IMMUNOLOGICAL, MOUSE TOXICITY AND GUINEA PIG ATRIAL ASSAYS.

Yoshitsugi Hokama, Audrey Y. Asahina, Eric Titus, Dana Ichinotsubo and James T. Miyahara, John A. Burns School of Medicine, University of Hawaii, Honolulu, Hawaii, 96822.

Ciguatera studies were determined at the Waianae Boat Harbor following a large outbreak of fish poisoning due to Migul cephalus (mullet, ama ama) in January-March of 1991. A dozen or more individuals became ill after eating freshly caught mullet. Typical clinical manifestations of gastro-intestinal, neurological and aches and pains of ciguatera were shown by the patients. The immunological assay for ciguatoxin and polyethers with monoclonal anti-ciguatoxin (MAb-CTX) showed 80% of the mullet to be in the borderline and positive categories. The herbivores, Ctenochaetus strigosus, Acanthurus sandvicensis and other Acanthurus sp. all showed high levels of toxins. The mackerels showed little or no toxic levels, while the carnivores (jack, amberjack) showed borderline to positive levels of toxicity. Abundant growth of algae 1-2 feet below the the sea water surface was present. This algae species was identified as a Bryopsis sp. (green alga). All five sites examined had algae growth and contained Gambierdiscus toxicus in moderate numbers. In two areas (sites 1 and 2) when the Bryopsis disappeared (summer-early winter), no Gambierdiscus toxicus was found. Fish extracts of mullet and other herbivores (palani, manini, kole-surgeonfishes) were highly toxic for mouse. Guinea pig atrium analysis of the wild Gambierdiscus toxicus and fish extracts showed typical ciguatoxin-like inotropic response strongly inhibited by tetrodotoxin. Data presented in this abstract were obtained from the leeward region of the island of Oahu and confined to Waianae Boat Harbor. (Supported in part by the Department of Health, State of Hawaii and NIH-GMO 8125-19).

DEVELOPMENT OF A SINGLE STEP PURIFICATION METHOD FOR SCREENING PRODUCTION OF CIGUATOXINS IN GAMBIERDISCUSTOXICUS.

John A. Babinchak, Peter D.R. Moeller, Fran M. Van Dolah and John S. Ramsdell. National Marine Fisheries Service, P. O. Box 12607, Charleston, SC 29412 USA

Production of ciguatoxin congeners (CTXs) from mass cultured dinoflagellates appears to be the only source of CTXs that has the potential of providing sufficient quantities of purified toxins for studies on biosynthesis, structural analysis, pharmacology, biotransformation and detection. Recent isolates from Tahiti, Guam and Grand Cayman Island were cultured in micro-carriers flasks. All except dense mucoid producers adapted well to the parameters of the mass culture system. After sonicating the cells in MeOH, the crude MeOH extract was prepared for high performance, low pressure liquid chromatography and introduced to a Michel-Miller column packed with Iatrobeads, a porous, beaded silica. A solvent scheme using 100% $CHCl_3$, MeOH/$CHCl_3$ and H_2O/MeOH was used to completely separate CTXs from MTXs. The CTXs were analyzed using a battery of bioassays including mouse bioassay and a rapid cytotoxicity assay for total toxicity, $^{45}Ca^{++}$ flux assays in cultured cells to distinguish MTX from CTX, and RIA and receptor binding displacement of ^{3}H-brevetoxin for quantification of CTX. A sample of purified CTXs from G. toxicus clone MQ2 was used as a standard for evaluating the assays.

TEST OF THE EFFECT OF DISTURBANCE ON CIGUATERA IN TUVALU

Ursula L. Kaly and Geoffrey P. Jones
Marine Biology, James Cook University, Townsville,Q 4811, Australia.

This paper describes a field study on the potential link between the occurrence and intensity of ciguatera outbreaks and human disturbance of coral reefs. We focused on three islands in the Tuvalu Group of atolls, Niutao, Nui and Nanumea, each with different histories of ciguatera outbreak. Two forms of human disturbance were examined. These were the relatively small-scale disturbances associated with ship wrecks, and meso-scale disturbances associated with the construction of boat channels by blasting. Densities of *Gambierdiscus toxicus* and toxin levels in an indicator species of fish (*Ctenochaetus strigosus*, Acanthuridae) were examined using a variation of Yasumoto's field sampling method, and Hokama's Stick Test, respectively. At Nui and Nanumea, sites in and around boat channels of known age and controls were surveyed. At Niutao, we were able to survey cell abundances and/or fish toxicity before and after the construction of two channels, at two existing wrecks and at several controls. There was some suggestion of increased levels of cell abundances around channels at Nanumea and Niutao (the islands with current, or a history of outbreak), but not at Nui (historically ciguatera free). However, at Niutao, the overriding pattern of *G. toxicus* density around the island was independent of either form of human disturbance. Fish toxicity data were harder to interpret, but appear to suggest a similar broad pattern, unrelated to human disturbance. We suggest that some forms of human disturbance may affect (or even precipiate) outbreaks of ciguatera, but that other factors are likely to play a larger role.

ORAL AND INTRAPERITONEAL ADMINISTRATION STUDIES OF TOXINS DERIVED FROM FISH TISSUES AND EXTRACTS OF CULTURED *G. TOXICUS* IN THE HUMBUG (*D. ARUANUS*), DAMSEL-FISH (*P. WARDI*) AND THE STRIPEY (*L. CARPONOTATUS*).

Scott T. Hahn[1], Michael F. Capra[1] and Donald M. Miller[2]

[1]Centre for Biological Population Management, Queensland University of Technology, GPO Box 2434, Brisbane, 4001, Australia, [2]Southern Illinois University School of Medicine, IL, USA.

Toxin administration experiments were designed to compare effects of ciguatoxin(s) (CTX) and toxin(s) in extracts of *G. toxicus* (GDT) between teleost fish, and between species of teleosts; to quantify bioaccumulation of toxins in fish skeletal muscle; and to obtain evidence of bioconversion of GDT to CTX in treated fish.

Based on interpretation of signs and death-times, CTX and GDT administered i.p. are potent teleost neurotoxins. A comparison of dose effect of *G. toxicus* extract in *D. aruanus* and *P. wardi* shows variable susceptibility to *G. toxicus*-related toxins in fish that may be related to trophic niche.

Feeding and subsequent extraction and quantification of CTX in *L. carponotatus* defined approximate oral effective dosages and rates of incorporation in skeletal muscle. Feeding experiments in *L. carponotatus* indicated that the potency of GDT is at least half that of CTX. *L. carponotatus*, *D. aruanus* and *P. wardi* were unable to bioaccumulate or bioconvert GDT to CTX under these experimental conditions in quantities sufficient for detection in the mouse bioassay of residues derived from the skeletal muscle of experimental fish.

POSTER

PRESENTATIONS:

RECENT PROGRESS ON THE CIGUATERA-RELATED BIOTOXINS OF THE CARIBBEAN

Robert W. Dickey, Jinlin Shen, H. Ray Granade and F. Aladar Bencsath, Gulf Coast Seafood Laboratory, Office of Seafood, U.S. food and Drug Administration, Dauphin Island, AL 36528, USA

Maitotoxin (MTX) is the largest and most toxic of the marine polyethers. Approximately 30% of this complex 3424 DA molecule has been elucidated from a Pacific strain of Gambierdiscus toxicus (Murata, et al., 1992). Efforts to purify MTX from a Caribbean strain of the dinoflagellate yielded a chromatographically pure isolate which appears to closely resemble Pacific MTX in structure. In general, the proton spectrum corresponds well with that of the Pacific isolate. Specifically, multiplets at 5.75 and 5.65 ppm and two singlets at 5.25 and 5.15 ppm correlate strongly with those of Pacific MTX; a dense cluster of signals between 3.0 and 4.5 indicate the presence of many -CH-O- units; three broad multiplets between 2.0 and 2.4 ppm, a singlet at 1.8, and a series of doublets upfield of 1.0 ppm also correlate well with available data. However, signals at 5.35 and 5.5 ppm which are not present in spectra from Pacific MTX may indicate that the Caribbean isolate differs slightly in olefinic portions of the molecule.

Derivatization experiments with the chromophore-poor ciguatoxin-1 (CTX-1: Lewis, et al., 1991) yielded a fluorescent coumarin-carbamic acid ester of the biotoxin. HPLC with fluorometric detection produced a moderately intense detector response to two nanograms of the CTX-1 derivative. The derivative shows potential for the detection of ciguatoxins from finfish. Mass spectrometric verification of peak identity and matrix effects on the separation were investigated.

DISTRIBUTION OF CIGUATERIC DINOFLAGELLATES IN MAYOTTE ISLAND (S.W. INDIAN OCEAN)

Daniel Grzebyk, Brigette Berland and Bernard A. Thomassin, Centre d'Océanologie de Marseille (CNRS - URA 41) 13007 Marseille and Andrè Arnoux LHMA Faculté de Pharmacie 13005 Marseille France

Spatial distribution of ciguateric dinoflagellates are analysed at the end of the 1992 dry season in the coral reef lagoon of Mayotte high island. Different substrates have been considered (algae, algal turfs and dead corals), along a transect in the N.E. lagoon, going from the back of an alluvial bay to the outer barrier reef, through lagoonal patch reefs.

Lagoonal and oceanic waters at this time were oligotrophic.

Dinoflagellates population (*Gambierdiscus toxicus, Ostreopsis* spp. and *Prorocentrum* spp.) reveal that the main reef biota affected are neither the back of the bay nor the barrier reef outer slope. Highest densities of all species of dinoflagellates are recorded on the inner slope of the barrier reef and on lagoonal patch-reefs; these areas receive low influence of terrigenous inlets and are under influences of megatidal and passage currents.

On nearly all the substrates, dinoflagellate densities are generally *Ostreopsis* spp. > *Prorocentrum* spp. > *G. toxicus*. But some substrates, specially several red algae, bear noticeably higher densities suggesting a stimulation processes. Experimental bioassays, comparing growth on incubated seawaters with algae, prove significant effects of the pre-conditional seawaters tested: a red algae *Halymenia floresia* inhibits the growth of *G. toxicus* while a second one *Portoeroa hornemanii* and a mixture of brown algae *Turbinaria ornata* and *Sargassum* sp. stimulate it; the two red algae stimulate equally the growth of *Ostreopsis* sp.

Notable quantities of *G. toxicus* are observed on dead corals, but the standardized estimation of real densities *in situ* on this substrate are difficult. This makes difficult the estimation of the toxigenic reservoir in the most contaminated zones: if algal densities (per g of algae) appear lower (< 140 cell.g^{-1} for *G. toxicus*) than in other regions in the world, the scatter of the macrooalgae at this season is low relatively with the extention of dead coral surfaces.

A PROFILE OF HYDROGEOLOGICAL PARAMETERS, *G. TOXICUS* SUBSTRATE OCCUPATION AND ENDEMIC TOXICITY AT WATHUMBA CREEK LAGOON AND PLATYPUS BAY, FRASER ISLAND.

Scott T. Hahn and Michael F. Capra

Centre for Biological Population Management, Queensland University of Technology, GPO Box 2434, Brisbane, 4001, Australia.

A 14 month etiological study of ciguatera at Wathumba Creek Lagoon and adjacent Platypus Bay included evaluation of lagoon and bay waters in terms of ciguatoxigenic dinoflagellate growth conditions, benthic dinoflagellate substrate occupation estimates and the assessment of ciguatoxin(s) (CTX) and toxin(s) in extracts of *G. toxicus* (GDT) present in a broad sample of local food-web participants. Microscopic and macroscopic gut contents of organisms representative of biological samples were also described.

The physicochemical nature of the Platypus Bay bight appears to influence positively the numbers of certain genera of dinoflagellates in this region. Positive correlations between *G. toxicus* cell densities and toxicity were not obvious in the context of CTX and GDT present in organisms collected concurrent with dinoflagellate substrate occupation maxima. CTX and GDT were observed in animal tissues throughout the study, although interpretation of the data is complicated by sporadic occurrence in some species and not in others, temporal variation within species showing toxicity, and intraspecies variability of the toxin type present in their tissues. Specific relationships between benthic consumers and elaboration and bioconversion of GDT to CTX are discussed.

THE ORIGIN OF CIGUATERA IN PLATYPUS BAY, AUSTRALIA.

Michael J. Holmes, Richard J. Lewis, Michelle Sellin and Raewyn Street. Southern Fisheries Centre, QDPI, Deception Bay, Qld 4508, Australia.

Platypus Bay on the north-western side of Fraser Island is the only site in Queensland known to frequently harbour ciguateric fishes. Platypus Bay is not typical of areas normally associated with ciguateric fishes as it contains no corals but has a sandy bottom covered with an unattached green macroalgae (*Cladophora* sp.). Benthic biodetritus samples sieved from the *Cladophora* during seven sampling trips between May 1988 and February 1990 contained *Gambierdiscus toxicus* with mean population densities ranging from 4 to 556 cells per gram of *Cladophora*. Biodetritus samples collected from six of these sampling trips were extracted for toxins. Putative major and minor gambiertoxins (precursors of the ciguatoxins) were detected, suggesting that these *G. toxicus* populations in Platypus Bay are the origin of the toxins found in the ciguateric fishes caught in Platypus Bay. However, gambiertoxins were detected from only one of the six samples. This indicates that not all strains of *G. toxicus* produce these toxins in the wild. The concentrations of major and minor gambiertoxins produced by these wild *G. toxicus* were considerably greater than the highest levels found from cultured *G. toxicus* clones isolated from Platypus Bay. The presence of "super-producing" strains of *G. toxicus* is hypothesised to explain the high concentrations of these toxins.

A SURVEY FOR CIGUATERA FISH POISONING IN WEST HAWAII

Dana Ichinotsubo, Audrey Y. Asahina, Eric Titus and Yoshitsugi Hokama, John A. Burns School of Medicine, University of Hawaii, 96822.

Approximately 25-30 fishes have caused ciguatera fish poisoning involving more than 100 individuals in the State of Hawaii, as reported annually by the State Department of Health (DOH). Generally, about 6-10 species are involved including herbivores and carnivores. In this study, a specific site on the island of Hawaii was selected because of a persistent outbreak of fish poisoning in the first few months of nearly every year due to Cheilinus rhodochrous, (wrasse, po'ou). The survey of the site (Puako, Hawaii) consisted of (1) algae and Gambierdiscus toxicus assessment; (2) fish analysis by immunological assay; (3) following fish extraction testing in mouse toxicity assay; and (4) analysis with guinea pig atrium for the effect on the Na^+ channels. The immunological assay showed borderline and positive in more than 50% of the fish species examined. The species examined included herbivores and carnivores. Several species of algae was found, including Jania sp. and Turbinaria ornata previously shown to be associated with Gambierdiscus toxicus blooms. In five sections within a two mile shoreline area, Gambierdiscus toxicus was noted in two sections in small to moderate numbers 9-291/gm algae. Most of the mouse toxicity and guinea pig data showed presence of ciguatoxin-like and an undefined sodium channel inhibitor toxin in some of the herbivores examined. These herbivores include Ctenochaetus strigosus, (kole) and Acanthurus sandvicensis (manini). Organic solvent extracts from some of these two species showed inhibition of the Na^+ channel in the guinea pig atrium assay. The inhibition appears to be very similar in action to tetrodotoxin (Supported in part by the Asian-Pacific Research Foundation and the DOH, State of Hawaii.)

SHORT AND LONG RANGE INVERSE DETECTED NMR OF CIGUATOXIN-1.

Richard J. Lewis[1] and Ian M. Brereton[2]. [1]Southern Fisheries Centre, QDPI, Deception Bay, Qld 4508, Australia and; [2]Centre for Magnetic Resonance, University of Queensland, Qld 4072, Australia.

Short range (HMQC, $^{1}J_{CH}$) and long range (HMBC, $^{2,3}J_{CH}$) 2-dimensional inverse detected heteronuclear NMR spectra of 0.45 mg of ciguatoxin-1 are shown. These spectra support the structure proposed for ciguatoxin-1 and confirm the ^{13}C assignments and location of the two quarternary carbons in ciguatoxin-1. The location of four ether linkages was also confirmed from the HMBC experiment.

INVERTEBRATES IMPLICATED IN THE TRANSFER OF GAMBIERTOXINS TO THE BENTHIC CARNIVORE *Pomadasys maculatus*.

Richard J. Lewis, Michael J. Holmes and Michelle Sellin. Southern Fisheries Centre, QDPI,
Deception Bay, Qld 4508, Australia.

The food chain hypothesis for the transfer of ciguatoxins (CTX) to carnivorous fish has gained widespread acceptance. *P. maculatus* in Platypus Bay, Queensland cause ciguatera and have been shown to be contaminated with ciguatoxins-1, -2 and -3. *P. maculatus* is a benthic carnivore that apparently feeds predominately on the shrimps and crabs that live in *Cladophora* sp. that harbours the *Gambierdiscus toxicus* in Platypus Bay. Of the potential prey of *P. maculatus* in Platypus Bay, only the shrimps (mostly *Alpheus* sp.) contained detectable levels of ciguatoxin-like toxins, implicating shrimps (and perhaps crabs) as an important vector in the transfer of gambiertoxins to carnivorous fish. Any toxic effects of *G. toxicus* on shrimps may facilitate the selective feeding of fish on shrimps containing the highest toxin levels. Such selective feeding provides a mechanism for the funnelling of the *G. toxicus* produced gambiertoxins to *P. maculatus*. It remains to be determined if shrimps are capable of biotransforming the gambiertoxins to ciguatoxins or whether biotransformation of the gambiertoxins is accomplished exclusively by fish. Given that *P. maculatus* is at times highly toxic (Lewis and Sellin, 1992) and within a year can be non-toxic, it is likely that the gambiertoxins enter the food chain as intense bursts that perhaps last for only several weeks. At these times the shrimps would presumably be highly toxic. Depuration and/or detoxification are likely to account for the apparently rapid loss of gambiertoxins and ciguatoxins from shrimps, crabs and *P. maculatus*.

CIGUATERA AND HERBIVORES: UPTAKE AND ACCUMULATION OF CIGUATOXINS IN *Ctenochaetus striatus* ON THE GREAT BARRIER REEF.

Richard J. Lewis, Michelle Sellin, Noel C. Gillespie, Michael J. Holmes, Annie Keys, Raewyn Street, Heather Smythe, Hazra Thaggard and Sarah Bryce. Southern Fisheries Centre, QDPI, Deception Bay, Qld 4508, Australia.

The benthic herbivore *Ctenochaetus striatus* is a common detritivorous grazer likely to be a key species transfering ciguatoxin precursors (gambiertoxins) to carnivorous reef fish. Toxins in *C. striatus* were extracted and the toxins present characterised by mouse bioassay and chromatography. The biodetritus on which it feeds were collected by a specially designed sampling devise and the toxins present compared with those in *C. striatus*. Gambiertoxin-like and ciguatoxin-like toxins predominated in these samples. Lesser amounts of fast acting and unidentified toxins were also detected but no maitotoxin was detected. Similar levels of ciguatoxin-like toxins were found in *C. striatus* collected from John Brewer or Davies Reefs, despite the former reef still displaying major damage as a result of a crown of thorns starfish infestation. Levels of ciguatoxins in *C. striatus* from these reefs were considered below levels that would constitute a ciguatera problem. This conclusion is consistent with the low risk of contracting ciguatera from carnivorous fish captured at these reefs.

We were unable to detect low-polarity gambiertoxins in the liver of *C. striatus*, suggesting that these toxins were biotransformed to the more polar ciguatoxins (ciguatoxin-1, -2 and/or -3) in the liver of herbivorous fish. The levels of ciguatoxin-like toxicity in the visceral contents of *C. striatus* were 3- to 6- fold less than the levels of such toxins in the biodetritus, perhaps as a result of bacterial degradation associated with the active fermentation/digestive strategy used by this species. Alternatively, gambiertoxins may be rapidly assimilated in the intestine of *C. striatus*.

MODIFICATION OF NERVE CONDUCTION IN THE RAT BY BREVETOXIN (PBTX-3).

Christine E. Purcell, John Cameron and Michael F. Capra, School of Life Science, Queensland University of Technology, Brisbane.

Brevetoxins are lipid-soluble polycyclic ether toxins isolated from the marine dinoflagellate *Ptychodiscus brevis*. The toxins PbTx-2 and PbTx-3 bind to a specific receptor site (site 5) on the voltage-dependent sodium channel, a site shared with ciguatoxin. This study set out to examine the effects of PbTx-3 and a possible antagonist on the parameters of nerve conduction.

Electrophysiological studies were carried out on the ventral coccygeal nerve of male Wistar rats. Prior to experimentation each animal was anaesthetised with intramuscular Leptan (420*u*l/kg). A Medelec MS92a electromyography unit was used for recordings. PbTx-3 (15*u*g/kg) was administered intravenously over 15 minutes. In antagonist experiments lignocaine (500*u*g/kg) was delivered intravenously, over 30 minutes.

PbTx-3 produced a significant increase in both the magnitude and duration of supernormality to that of control nerves. This toxin also increased the absolute and relative refractory periods and decreased the conduction velocity. Lignocaine returned these parameters towards control values.

These results demonstrate that PbTx-3 alters nerve conduction parameters of rats in a similar way to ciguatoxin (Cameron et al., 1991). It is suggested that brevetoxin may provide a suitable model in further studies pertaining to possible therapeutic agents for ciguatera poisoning.

Cameron, J., Flowers, A.E. & Capra, M.F. (1991) Journal of the Neurological Sciences, 101, 87-92.

PATHOLOGIC CHANGES IN MURINE HEARTS INDUCED BY INTERMITTANT ADMINISTRATIONS OF CIGUATOXIN

Kiyoshi Terao(1), Emiks Ito(1), Misako Ohkusu(1) and Takeshi Yasumoto(2)

1) Research Institute for Pathogenic Fungi and Microbial Toxicoses, Chiba University, 1-8-1 Inohana, Chuo-ku, 260 Chiba, Japan

2) Faculty of Agriculture, Tohoku University, 1-1 Tsutsmidori Amemiya, Aoba-ku 980 Sendai, Japan

Ciguatoxin (CTX) at doses of either 0.1 or 0.05 μg/kg were given orally by intubation into male ICR mice once a week for 6 months. Until about 8 weeks after the beginning of the experiments the mice in both groups showed no abnormal clinical signs and pathological findings in the hearts. After about 10 weeks from the beginning, mice treated with 0.1 μg/kg showed marked hypertrophy of the hearts, whereas no pathological changes were seen in the hearts of the mice given CTX at the low dose. By TEM, there were swelling or rupture of the endothelium of the capillaries and widening caused by exudation or collagen fibres in the interstitial space. Occasionally, degenerated or swollen mitochondria were prominent in the myocardium. Accumulation of platelets in the capillaries was frequently observed. In contrast, the mice treated with CTX at the low dose showed no pathological changes even at the ultrastructural level until 6 months. The present study confirmed that CTX has a potent cumulative effects on the cardiac tissue.

SUMMARY INDEX

Workshop Address:

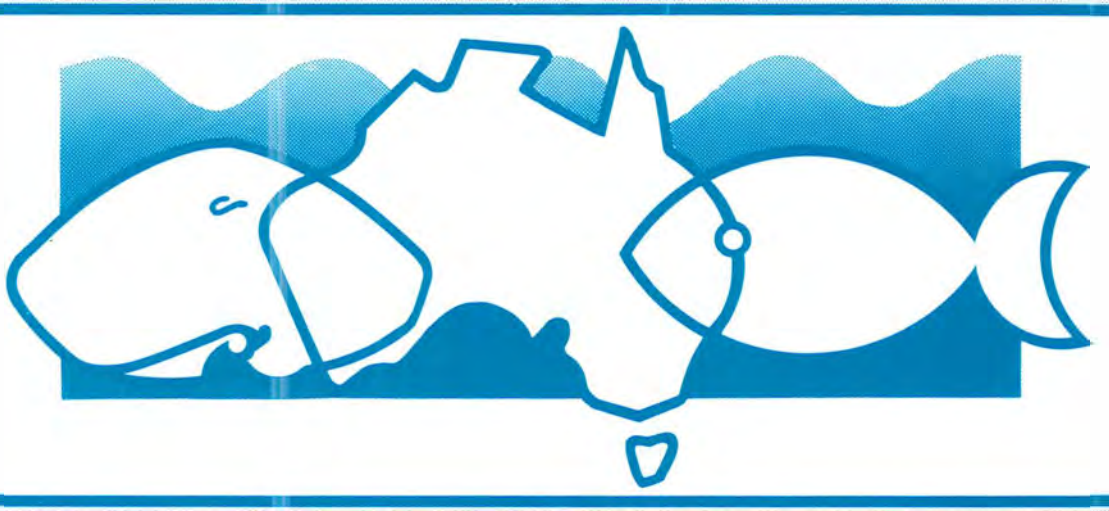
Joondoburri Conference Centre
North Street Woorim
PO Box 270
Bribie Island Queensland 4507

Telephone (617) 408 3777
Facsimile (617) 408 3435

APPENDIX II

Second Notice

International Workshop on Ciguatera Management



Second Notice

Registration Brochure and Call for Papers

Bribie Island, Australia 13-16 April 1993

CONTENTS

INVITATION

Greetings to Co-Workers,

The International Workshop on the Management of Ciguatera will be held 13-16 April 1993 at Joondoburri Conference Centre, Bribie Island, Australia (see enclosed brochure for details).

The Organising Committee is delighted that a meeting to discuss research on ciguatera will be held for the first time in Australia. Participants will be able to take advantage of the relaxed atmosphere on Bribie Island. The warm weather at this time of year will allow full advantage to be taken of the long sandy beaches within a few minutes walk of Joondoburri.

The scientific program will advance on the substantial achievements of earlier ciguatera meetings and will focus on research that has implications for the management of ciguatera. This workshop will introduce to you much of the research activity underway on ciguatera around the world.

I warmly welcome you to the Workshop and look forward to meeting you at Bribie Island in mid-April 1993.

Richard J. Lewis
Chairman
Organising Committee

SPONSORS

Fisheries Research and Development Corporation
Queensland Department of Primary Industries (QDPI)

ORGANISING COMMITTEE

Richard Lewis (Chairman)
Michael Holmes
Michelle Sellin
Barry Pollock
Mike Dredge
Noel Gillespie

SCIENTIFIC COMMITTEE

Milani Chaloupka (Australia)
Michael Holmes (Australia)
Anne-Marie Legrand (French Polynesia)
Richard Lewis (Australia, Chairman)
John Pearn (Australia)
Takeshi Yasumoto (Japan)

TIMETABLE AND DEADLINES

Post Workshop Tours Deposit	10 January 1993
Receipt of Abstracts	28 February 1993
Post Workshop Tours Full Payment	28 February 1993
Receipt of Papers	13 April 1993

ADDRESS FOR CORRESPONDENCE

Ciguatera Management Workshop Secretariat
Southern Fisheries Centre
PO Box 76, Deception Bay
Queensland 4508
AUSTRALIA
Telephone: 617 203 1444
Facsimile: 617 203 3517

SCIENTIFIC PROGRAM

This international meeting will bring together world experts to examine new developments in ciguatera, especially research that has implications for the management of ciguatera. The program will include talks by **Invited Speakers**, and a continuous **Poster session**. Two evening **Workshop Sessions** will be structured around short oral presentations (15 min each). The preliminary schedule is as indicated below:

TUESDAY, 13 APRIL 1993	morning	Opening Ceremony
	afternoon	Chemistry (invited speakers)
	evening	Formal Poster session
WEDNESDAY, 14 APRIL 1993	morning	Pharmacology (invited speakers)
	evening	Workshop on "Detection of ciguateric fish"
THURSDAY, 15 APRIL 1993	morning	Clinical aspects (invited speakers)
	evening	Workshop on "Management for ciguatera cases"
FRIDAY, 16 APRIL 1993	morning	Origin (invited speakers)

CALL FOR PAPERS

You are invited to submit abstracts (Abstract Form enclosed) describing original research in areas including:

- Chemistry of ciguatoxins
- Clinical aspects
- Diagnosis
- Risk assessment
- Treatment
- Origin
- Risk minimisation
- Environmental considerations
- Detection
- Pharmacology
- Duty of care issues

Each abstract must be accompanied by a completed Abstract Form. Abstracts are required by 28 February 1993 and should be accompanied by your Registration Form.

PUBLICATION OF PROCEEDINGS

A record of the meeting will be published in the "Memoirs of the Queensland Museum" series. Manuscripts offered for inclusion [which must be presented on arrival to the meeting] will be peer reviewed prior to publication.

Three double-spaced, hard-copies of Manuscripts are required. A copy of each manuscript should also be provided on floppy disk, preferably in WordPerfect 5.1 (or similar) on a 3½" disk, to assist with the publication proceedings. Manuscripts could be structured into an Abstract, Introduction, Materials and Methods, Results, Discussion, References, Tables and Figure Legends. Invited speakers will be allocated ~8 journal pages (~750 words/page) for the typeset manuscript. Authors presenting poster(s) or giving oral presentations at the evening workshop sessions will be allocated ~4 journal pages for each presentation. Figures and black and white photographs of high quality can be included. Send each original on a separate page. Colour photographs will be included only if colour is essential for clarity of information. References should be given in name and date form in text, with the term *et al.* being used if there are more than two authors. Examples of citations are: (Jones, 1976); (Jones and Smith, 1975); (Jones *et al.*, 1976)...as reported by Jones and Smith (1975); ....as described by Jones *et al.* (1976). References should be listed alphabetically at the end of the Manuscript. If there is more than one reference with the same author(s) and the same year of publication, the references should be differentiated by *a*, *b*, etc. (e.g. 1964 *a*, *b*). Please cite references in the following manner, including full titles for journals.

LEGRAND, A.M., LITAUDON, M., GENTHON, J.N., BAGNIS, R. AND YASUMOTO, T. 1989. Isolation and some properties of ciguatoxin. Journal of Applied Phycology. 1: 183-188.

YASUMOTO, T., NAKAJIMA, I., OSHIMA, Y. AND BAGNIS, R. 1979. A new toxic dinoflagellate found in association with ciguatera. 65-70. In D.L. Taylor and H.H. Seliger (eds) 'Toxic dinoflagellate blooms'. (Elsevier: North-Holland).

REGISTRATION

Participation is open to all persons interested in ciguatera and related diseases. Those who wish to attend the Workshop should complete the enclosed Registration Form and return it to the Secretariat. Each registrant must fill out a separate form. Additional forms are available from the Secretariat on request or a photocopy may be used. Please read this booklet carefully before completing your form. Overseas delegates please ensure your form is sent by AIRMAIL.

REGISTRATION FEE

Full Delegate	A$250
Day Registration	A$100
Accompanying person	A$ 80

ENTITLEMENTS

The registration fee entitles delegates to the following:

- Attendance at all scientific sessions
- Program, abstract book and list of delegates
- Copy of the published proceedings (Full & Day registrants)
- Welcoming BBQ
- Visit to Sunshine Plantation
- Ferryman Cruise of Pumicestone Passage

Accompanying persons are entitled to the following:

- Welcoming BBQ
- Visit to Sunshine Plantation
- Ferryman Cruise of Pumicestone Passage

PAYMENT OF FEES

Payment of fees must accompany each registration form. Payments from overseas must be made by bank cheque in Australian dollars (A$) drawn on an Australian bank in Brisbane. Please print your name and full address on the back of the bank cheque which must be made payable to "Qld Department of Primary Industries".

Australian delegates can also pay by personal cheque made payable to "Qld Department of Primary Industries". Payment **cannot** be made by credit card or direct transfer.

ACKNOWLEDGEMENTS

Your registration will be acknowledged in writing on receipt of Registration Forms accompanied by payment.

CANCELLATIONS

Cancellation of registration must be notified in writing to the Secretariat.
Cancellations received before;

28 February 1993	A$50.00 cancellation fee
13 April 1993	50% refund of registration fees, and full refund of accommodation less one night.

OFFICIAL LANGUAGE

English will be the official language for the Workshop.

REGISTRATION TIMES

Monday, 12 April 1993	1400-1800 hrs
Tuesday, 13 April 1993	0800-1100 hrs
Wednesday to Friday, 14-16 April 1993	0730-0830 hrs

A representative from Harvey World Travel will be in attendance on Tuesday morning to discuss post Workshop tours.

ACCOMMODATION

Motel-style accommodation has been reserved on Bribie Island. The flat rate of $90 per person twin share or $120 single for each night, includes all meals (except the Workshop dinner). Please consider twin share accommodation where possible. To book your accommodation full payment is requested. Late cancellation will result in the cost of one night's accommodation not being refunded. Bookings for accommodation are made on the Registration Form.

INSURANCE

Registration fees do not include insurance of any kind. The Organising Committee strongly recommends that you take out insurance of your choice at the time you book your travel. The Workshop Secretariat will not take any responsibility for any participant failing to insure. This travel insurance is to be purchased in your country of origin.

PARKING

Parking is available at the Joondoburri Conference Centre.

SOCIAL PROGRAM

- WELCOMING BBQ
  Monday, 12 April 1993, 1800-2300 hrs

  An invitation is extended to all delegates and registered accompanying persons to attend an informal BBQ at the Joondoburri Conference Centre. A family of kangaroos may entertain us on the lawns of the Centre.
  Please be aware that this Monday is a public holiday in Australia.

- SUNSHINE PLANTATION VISIT
  Wednesday, 14 April, 1400-1700 hrs

  Take the opportunity to visit one of Queensland's top tourist destinations. A wide-range of interesting foods and rides are available at modest cost. Transport to and from Sunshine Plantation will be by bus.

FERRYMAN CRUISE
Thursday, 15 April, 1400-1730 hrs

A highlight of your stay on Bribie Island will be a few hours spent cruising the beautiful waters of Pumicestone Passage which separate Bribie Island from the mainland. We may be lucky to sight dugong feeding on the seagrass beds before sunset. Devonshire tea will be provided.

- ## BRIBIE ISLAND AQUACULTURE CENTRE
Friday, 16 April, 1400-1530 hrs

There will be an opportunity to take a guided tour of this world class facility, specialising in prawn and dolphin fish aquaculture.

- ## SOUTHERN FISHERIES CENTRE
Friday, 16 April, 1700-1830 hrs

On route to the Workshop dinner, we will visit QDPI's ciguatera research facilities at Deception Bay.

- ## WORKSHOP DINNER
Friday, 16 April, 1830-2200 hrs

The dinner will be held at one of Brisbane's best seafood restaurants. Please register early for this event. A selection of Australian wines will be included with the meal.

- ## THE BEACH

The Joondoburri Conference Centre is within a few minutes walk of the ocean beach of Bribie Island. This white sandy beach stretches for miles in either direction. Fishing may be arranged if there is sufficient interest. Please consult the enclosed pamphlet on Joondoburri Conference Centre for further details on the attractions of Bribie Island.

REGISTRATION FORM

INTERNATIONAL WORKSHOP ON CIGUATERA

13-16 April 1993

Joondoburri, Queensland

Please print clearly or type and keep a photocopy of this form for your records.

A. DELEGATE

Name: . . . .
Mr/Ms/Dr etc First Name (for badge) Surname

Position: . . . .

Organisation: . . . .

Postal Address: . . . .

. . . .
City/Suburb State Postcode/Zip Country

Telephone: . . . .

Facsimile: . . . .

Accompanying Person(s):

. . . .
Title/Surname First Name Title/Surname First Name

B. ACCOMMODATION

Prepaid Accommodation during Workshop (includes all meals except "Workshop Dinner").
Twin/Double Room @ $90 per person per night
Single Room @ $120 per person per night

IMPORTANT - PLEASE COMPLETE THIS SECTION

Check in date: . . . . Check out date: . . . .

Accommodation required: Twin Share ☐ Double ☐ Single ☐

Number of nights required: . . . .

I wish to share a room with: . . . .

Please match me with a roommate:

Smoking ☐ Non-Smoking ☐ Male ☐ Female ☐

Special requirements: . . . .

Prepaid Accommodation A$ ☐

C. WORKSHOP REGISTRATION FEES

☐ Full Delegate $250

☐ Day Registration $100 ☐ Tues ☐ Wed ☐ Thurs ☐ Fri

☐☐ Accompanying persons $ 80 per person

Registration Fee $A ____

D. SOCIAL PROGRAMME

I wish to reserve my place at the following:

☐ "Workshop" Seafood Dinner (Friday 16) @ $55 per person (No. of persons)

☐ Welcoming (Monday 12) **free** (No. of persons)

☐ Sunshine Plantation Visit (Wednesday 14) **free** (No. of persons)

☐ Ferryman Cruise (Thursday 15) **free** (No. of persons)

Conference Dinner(s) A$ ____

E. I am planning to join a post Workshop tour Yes ☐ No ☐

F. PAYMENT

Section B (Full Accommodation) A$.....

Section C (Registration) A$.....

Section D (Social Programme) A$.....

GRAND TOTAL A$ ____

I enclose Bank Cheque (drawn on an Australian Bank in Brisbane) for A$ . . . . . .

I enclose personal cheque (Australian Residents only) . . . . . .

Signature. . . . . Date. . . . . .

Please make cheques payable to: **Qld Department of Primary Industries**

Forward this form and payment to: **Ciguatera Management Workshop Secretariat**
Southern Fisheries Centre (QDPI), PO Box 76,
Deception Bay Q4508, AUSTRALIA

POST WORKSHOP TOURS

TOUR-A
The Great Barrier Reef-Island Resort

Heron Island, situated 72 km off the Queensland coast on the Great Barrier Reef, is a true coral cay. The island has been declared a marine National Park because of its abundant bird and marine life.

Day 1-Saturday, 17 April 1993 (L,D)
Transfer to Brisbane airport for your morning flight to Gladstone. You will be met at Gladstone by a representative from Heron Island and transfered to the Marina for your sea trip to Heron Island. Launch departs for Heron Island at 1100 hrs. Accommodation in Reef Suites.

Days 2,3,4 and 5-Sunday 18 to Wednesday 21 April 1993 (B,L,D, Daily)
Days at leisure to enjoy swimming, scuba diving, snorkelling, coral reef walking, reef viewing in a semi-submersible boat, fishing, bird watching or tennis. (Additional charges/hire fees apply for some of these activities).

Day 6-Thursday 22 April 1993 (B,L)
Transfered by launch across to Gladstone, arriving at the Gladstone Marina at 1530 hrs. Transfer to Gladstone airport for your flight back to Brisbane domestic airport.

END OF TOUR ARRANGEMENTS

TOUR COST: A$ 1,425.00 per person twin share; A$ 1,725.00 per person single use accommodation.
A deposit of A$ 150.00 per person is required by **10 January 1993.**
Tour includes economy class flights Brisbane/Gladstone/Brisbane, Launch trips to and from Heron Island, accommodation, all transfers and most meals.

TOUR-B
Top End Discovery-Northern Territory (Air/Coach/Air Tour)

NOTE: A minimum of 10 people (maximum 18) required for this tour to commence.
This is a guided tour with travel in an air-conditioned 19 seater Mini Coach.

Day 1-Saturday 17 April 1993
Transfer to Brisbane airport for your flight to Darwin. On arrival you will be met by an Australian Pacific Tours Representative and transfered to your overnight accommodation at the Darwin Travelodge.

Day 2-Sunday 18 April 1993 Darwin-Crocodile Farm-Kakadu National Park (D)
Depart Darwin at 0800 hrs for tours of the northern capital and a crocodile farm. Overnight at Kakadu Holiday Village (2 nights), located in Kakadu National Park.

Day 3-Monday 19 April 1993 Yellow Waters Cruise-Ubirr Rock-Kakadu National Park (B,D)
Kakadu National Park, some 20,000 square kms, is rich in flora, wildlife and natural scenic features. Opportunity to see a myriad of waterbirds and crocodiles in their natural habitat as we cruise Yellow Waters Billabong. Explore around Ubirr Rock, rich in Aboriginal rock art dating back 20,000 years. Opportunity to take an optional scenic flight over Arnhem Land (not included in tour price).

Day 4-Tuesday 20 April 1993 Katherine Gorge Cruise (B,D)
See giant anthills on the way to the tiny settlement of Pine Creek, then on to Katherine for the spectacular cruise on Katherine Gorge, now called Nitmiluk, a word taken from the Aboriginal Dreamtime. Watchout for the odd freshwater crocodile. Overnight at the Frontier Motor Inn, Katherine.

Day 5-Wednesday 21 April 1993 Thermal Pool, Mataranka (B,D)
Travel south to Mataranka and visit the famous thermal pool, a tropical oasis. Swim in the clear turquoise thermal pool, sparkling under the tropical rainforest. Our route takes us to the quaint township of Batchelor, once the base of the Rum Jungle Uranium Mines. At dusk the surrounding bush comes alive with the cries of hundreds of parrots. Overnight at Batchelor, Rum Jungle Motor Inn (Share accommodation may occur in this remote area).

Day 6-Thursday 22 April 1993 Litchfield Park-Darwin (B)
This morning discover the beauty of Litchfield Park, a huge sandstone plateau. Creeks tumble over rapids and cascading waterfalls descend into crystal-clear rock pools. Return to Darwin where the coach tour concludes. Overnight at Darwin Travelodge.

Day 7-Friday 23 April 1993
You will be transfered from your hotel to the airport by a representative from Australian Pacific Tours. Depart Darwin for Brisbane domestic airport.

END OF TOUR ARRANGEMENTS

TOUR COST: A$ 1,875.00 per person twin share; A$ 2,165.00 per person single use accommodation.
A deposit of A$ 150.00 per person is required by **10 January 1993.**
Tour includes economy class flights Brisbane/Darwin/Brisbane, accommodation, coach tour, cruises, all transfers and some meals.

INFORMATION REGARDING POST WORKSHOP TOURS

HARVEY WORLD TRAVEL (THE GAP) (License Number 968) have arranged these tours.

Reservations
Reservations must reach Harvey World Travel (The Gap) not later than **10 January 1993** and must be accompanied by a deposit of A$ 150.00 per person payable by International Bank Cheque in Australian dollars drawn on an Australian Bank in Brisbane to "Harvey World Travel (The Gap)" at the address below. Participants will be notified by airmail/fax and advised of fine details. If minimum numbers are not achieved for the Top End Discovery-Northern Territory tour (and if you do not wish to change to the Heron Island tour) a complete refund of the published tour price will be made.

Tour Inclusions
- Economy class airfares
- Accommodation with private facilities
- Sightseeing as per itineraries
- Meals as specified: (B=Breakfast, L=Lunch, D=Dinner)
- Transfers where specified

Not Included
- Meals other than specified
- Personal expenses
- Drinks and anything not specifically mentioned

Full Payment for Post Workshop Tours
Full payment for tours must be received not later than **28 February 1993** and should be made by International Bank Cheque in Australian Dollars drawn on an Australian Bank in Brisbane and made payable to and sent to:

HARVEY WORLD TRAVEL (THE GAP)
Shop 11, 1000 Waterworks Road, The Gap,
Queensland 4061
Australia
Telephone: 61-7-300 5300, Fax: 61-7-300 5681
PLEASE DO NOT MAKE PAYMENTS BY INTERNATIONAL BANK TRANSFER

Cancellation

Before 28 February 1993 full refund less deposit.
After 28 February 1993 only 40 to 50% of Full Payment will be refunded.
In the event of minimum numbers not achieved for the Top-End Discovery Northern Territory tour, a complete refund of the published price will be made (unless you decide to switch to The Great Barrier Reef-Island Resort tour, in which case the difference in cost will be refunded).

Insurance

Post Workshop Tour fees do not include insurance of any kind. It is strongly recommended that at the time you register for the Workshop and book your travel you take out an insurance policy of your choice. The policy should include loss of fees/deposit through cancellation of your participation in the Workshop, or through cancellation of the Workshop, loss of international/domestic air fares through cancellation for any reason, loss of tour monies through cancellation for any reason including airline or related services strikes within Australia, failure to utilise tours or pre-booked arrangements due to airline delay, Force Majeure or any other reason, medical expenses, loss or damage to personal property, additional expenses and repatriation should travel arrangements have to be altered.

The Workshop Secretariat will not take any responsibility for any participant failing to insure. This travel insurance should be purchased in your country of origin.

Disclaimer

The services specified in these itineraries are available at the time of writing. In the event that any (or all) service(s) become unavailable for any reason, Harvey World Travel (The Gap) will make every effort to supply alternate services of equal standard and value. However, the Workshop Secretariat and Organisers cannot accept any responsibility for failure to provide the specified services.

GENERAL INFORMATION FOR OVERSEAS DELEGATES

Brisbane

Brisbane, Australia's gateway to tropical Australia and the capital of Queensland, is adjacent to some of the world's best surf beaches which stretch north and south of the city on the shores of the Pacific Ocean. Bribie Island has one such beach.

Planning your Travel

Because of time change and jet lag, the organising committee strongly recommends that you arrive in Australia by Monday, 12 April. This will enable participation in the first Workshop event in the evening of Monday 12 April 1993.

Airport Transportation

Transportation for delegates will be provided from the Brisbane Domestic and International Airports to your accommodation at Bribie Island (~1 hour journey). The cost of a taxi would be ~A$60.

Passports and Visas

A valid passport is required. The majority of overseas visitors require a visa for entry into Australia. Check this matter carefully with your airline or travel agent as immigration laws are strictly enforced. An A$20 departure tax is payable at the airport prior to departure.

Vaccinations

A current valid international certificate of inoculation against yellow fever is required if passengers come from, or travel through, infected areas. Check this carefully with your airline or travel agent.

Quarantine

Australia is free from many plant and animal diseases prevalent in other countries. Very strict quarantine rules apply to the import of animals and plants, which cannot be brought into the country without prior application. Animal and plant products are also restricted. Prior written approval is required before biological samples may be imported.

Language

English is the official language.

Climate and Clothing

April is autumn in Australia. In south Queensland it is usually warm with an average temperature of 21°C. We suggest you bring light cotton clothing, with something warmer for evenings.

Dress for social functions is smart casual. Generally Australians are informal dressers. For special occasions like dining at better class hotels or restaurants, a tie and jacket are recommended.

Time

Brisbane is 10 hours ahead in respect of Greenwich Mean Time.

Currency

Decimal currency is used in Australia and Australian dollars (A$) are the legal tender. Travellers cheques in foreign currencies will be cashed by banks and hotels but are not usually accepted in shops. Notes are distinguished by different colours in values of $100, $50, $20, $10 and $5. Coins are for $2, $1 and lesser amounts.

Banking

Banks are generally open 0930 to 1600 hours Monday to Thursday and 0930 to 1700 hours Friday. Exchange facilities are also available at the airport.

Credit Cards

Most hotels, larger restaurants and shops will accept international credit cards, the most widely recognised being Diners Club, American express, Mastercard and Visa. Credit cards are not accepted at Joondoburri Conference Centre.

Tipping

Tipping is not as widespread or regulated in Australia as it is in other parts of the world. Tipping is your prerogative, a reward for service. A gratuity of about 10 per cent is usual in restaurants if good service is received.

Electricity

Electrical current is 240 volts, 50 Hz. Connections for appliances is a flat 3 pin plug.

Shopping

Shopping hours vary from state to state in Australia. Shops in Queensland open from 0900 to 1730 during the week with late night shopping on Thursday in the suburbs and Friday in the central business district of Brisbane. On Saturdays, most shops open from 0900 to 1600.

INSTRUCTIONS AND ADVICE FOR POSTER PRESENTATIONS

Posters should be no larger than 1 metre x 1 metre. Larger posters will be accepted if agreement is reached with the organisers at least one month before the meeting.

The poster should be easily readable at a distance of 2 metres. Use lower and upper case, ie, do not use only capitals because all-capital text is often difficult to read. Avoid using mixtures of type styles. Suggested minimum heights of characters are as follows:

Title:	25 mm
Headings:	15 mm
Text:	6-8 mm

A matt finish on photographs reduces glare and gives better visibility.

The message that your poster contains should be clear and understandable without oral explanation. At the top of the poster include its title, the name of the authors, the institution(s) where the work was completed, and preferably a photograph of the authors. The text should be brief throughout. Any description of methods should be very simple and concise. Results should be presented graphically if possible. Use pictures, symbols and colour. Figure legends are essential and should be short but informative.

Handouts providing either a summary or more detail of poster presentations are permissible.

At least one of the authors must be with the poster on Tuesday evening (April 13) to discuss the work. Posters will remain on display for the duration of the meeting.

- NOTES -

Workshop Secretariat

Southern Fisheries Centre
PO Box 76, Deception Bay
Queensland 4508
AUSTRALIA

Telephone: 617 203 1444
Facsimile: 617 203 3517

APPENDIX III

LIST OF

REGISTRANTS:

INTERNATIONAL WORKSHOP ON CIGUATERA MANAGEMENT

BRIBIE ISLAND, AUSTRALIA 13 - 16 APRIL, 1993

Dr John Babinchak
National Marine Fisheries Service
PO Box 12607
Charleston
SOUTH CAROLINA USA 29422-2607

Dr Raymond Bagnis
Université Française du Pacifique
Centre Universitaire de Polynésie
Française, BP 4635, Papeete, Tahiti
POLYNESIE FRANCAISE

Mr Paul Bird
4 Spiceley Crescent
HEATLEY QLD 4814

Dr Donna Glad Blythe
Rosenstiel Medical Marine Biology
4950 Le Jeune Road
Suite A, Córal Gables
Florida 33146 **USA**

Mr Alan Bremner
International Food Institute of
Queensland
19 Hercules Street
HAMILTON QLD 4007

Dr James Brock
Medical Faculty
UNIVERSITY OF NEWCASTLE NSW 2308

Mr John Burke
Southern Fisheries Centre
PO Box 76
DECEPTION BAY QLD 4508

Dr Bruce Campbell
Sullivan and Nicolaides
134 Whitmore Street
TARINGA QLD 4068

Mr Kevin Campbell
Line Committee Chairman
Queensland Commercial Fishermen's
Organisation
17 Hume Parade
PARADISE POINT QLD 4216

Dr Mike Capra
Centre for Biological Population Management
Queensland University of Technology
BRISBANE QLD 4000

Mr Milani Chaloupka
Department of Environment & Heritage
160 Ann Street
BRISBANE QLD 4001

Mr Richard Cormick
Department of Chemistry
Monash University
CLAYTON VIC 3168

Mr Paul Dalzell
South Pacific Commission
BP D5
NOUMEA NEW CALEDONIA

Dr David Davies
South Pacific Underwater Medicine Society
Suite 6 Killowen House
St Anne's Hospital
MT LAWLEY WA 6050

Mr Richard Dewis
School of Life Science
Biochemistry Section
Queensland University of Technology
George Street
BRISBANE QLD 4000

Dr Robert Dickey
Food & Drug Administration
Fishery Research Branch, FDA
PO Box 158
DAUPHIN ISLAND ALABAMA 36528

Mr Mike Dredge
Southern Fisheries Centre
PO Box 76
DECEPTION BAY QLD 4508

Mr Andrew Flowers
Centre for Biological Population Management
Queensland University of Technology
BRISBANE QLD 4000

Dr Noel Gillespie
Bribie Island Aquaculture Centre
Department of Primary Industries
PO Box 191
Bellara
BRIBIE ISLAND QLD 4507

Mr Daniel Grzebyk
Centre d'Océanologie De Marseille
(CNRS - URA 41)
13007 Marseille
FRANCE

Ms Sharon Guy
Department of Chemistry
Monash University
CLAYTON VIC 3168

Dr Scott Hahn
School of Life Science
Biochemistry Section
Queensland University of Technology
George Street
BRISBANE QLD 4000.

Dr Gustaaf Hallegraeff
CSIRO Division of Fisheries
GPO Box 1538
HOBART TAS 7001

Mr Paul Hamblin
C/- Department of Physiology
& Pharmacology
UNIVERSITY OF QLD QLD 4072

Professor Yoshitsugi Hokama
Department of Pathology
John A. Burns School of Medicine
University of Hawaii
1960 East-West Rd **HONOLULU HI 96822 USA**

Dr Mike Holmes
Southern Fisheries Centre
PO Box 76
DECEPTION BAY QLD 4508

Mr Dana Ichinotsubo
Department of Pathology
John A. Burns School of Medicine
University of Hawaii
1960 East-West Rd **HONOLULU HI 96822 USA**

Mr Phillip Jobling
Department of Physiology & Pharmacology
University of Queensland
ST LUCIA QLD 4067

Dr Ursula Kaly
AIMS
PMB No 3
TOWNSVILLE QLD 4810

Dr Geoff King
Medical Superintendent
Mossman Hospitals Board
PO Box 332
MOSSMAN QLD 4873

Dr Richard Lang
Department of Physiology
Monash University
CLAYTON VIC 3168

Mr Dan Lee
Department of Pathology
John A. Burns School of Medicine
University of Hawaii
1960 East-West Rd **HONOLULU HI 96822 USA**

Dr Anne-Marie Legrand
Institut Louis Malardé
PO Box 30
PAPEETE TAHITI
FRENCH POLYNESIA

Dr Richard Lewis
Southern Fisheries Centre
PO Box 76
DECEPTION BAY QLD 4508

Dr Ronald Manger
US Food and Drug Administration
22201 23rd Dr. S.E.
PO Box 3012
BOTHELL WA 98041-3012 USA

Professor Elspeth McLachlan
Department of Physiology & Pharmacology
University of Queensland
ST LUCIA QLD 4067

Dr Dietrich Mebs
Zentrum der Rechtsmedizin
University of Frankfurt
Kennedyallee 104
D-6000 Frankfurt/Main 70
RFA

Dr Jordi Molgo
CNRS
Laboratoire de Neurobiologie
Cellulaire et Moléculaire
91190 Gif-sur-Yvette **FRANCE**

Dr Neal Palafox
5711 Oakshire Road
Baltimore
MARYLAND 21209 USA

Dr Douglas Park
University of Arizona
Department of Nutrition & Food Science
309 SHANTZ TUCSON ARIZONA 85718

Mr John Payne
Solicitor
PO Box 286
TOOWONG QLD 4066

Professor John Pearn
Department of Child Health
University of Queensland
Royal Children's Hospital
BRISBANE QLD 4029

Dr Patrick Perlmutter
Department of Chemistry
Monash University
CLAYTON VIC 3168

Dr Barry Pollock
Fisherics Services
Department of Primary Industries
GPO Box 46
BRISBANE QLD 4001

Ms Christinc Purcell
Centre for Biological Population Management
Queensland University of Technology
BRISBANE QLD 4000

Dr Tilman Ruff
Social & Preventive Medicine
Monash Medical School
Alfred Hospital, Commercial Road
PRAHRAN VIC 3181

Professor Paul Scheuer
University of Hawaii
Department of Chemistry
2545 The Mall
HONOLULU HAWAII 96822

Ms Michelle Sellin
Southern Fisheries Centre
PO Box 76
DECEPTION BAY QLD 4508

Dr John Sheridan
Health and Welfare Building
63-79 George Street
BRISBANE QLD 4000

Mrs Raewyn Street
Southern Fisheries Centre
PO Box 76
DECEPTION BAY QLD 4508

Prof Kiyoshi Terao
Chiba University
Research Center for Pathogenic Fungi &
Microbial Toxicoses
1-8-1 Inohana Chuo-Ku
Chiba 260 **JAPAN**

Dr Jim Tibbals
Deputy Director
Intensivc Care Unit
Royal Children's Hospital
PARKVILLE VIC 3052

Dr Peter Tuxworth
3 Whitc Strcet
INGHAM QLD 4850

Dr Jean-Paul Vernoux
Physiologie Animale & Bioinformatique
Université de Caen
Esplanade de la Paix
14032-Caen **CEDEX FRANCE**

Dr Fivos Vogalis
Department of Physiology
Monash University
CLAYTON VIC 3168

Professor Takeshi Yasumoto
Tohoku University
1-1 Tsutsumidori-amemiya
AOBA-KU SENDAI 981 JAPAN

APPENDIX IV

SPEECH NOTES FOR
JON SULLIVAN MLA ON BEHALF OF
THE MINISTER FOR PRIMARY INDUSTRIES

OPENING OF THE INTERNATIONAL
WORKSHOP ON CIGUATERA MANAGEMENT

JOONDOBURRI CONFERENCE CENTRE
BRIBIE ISLAND
11.30am - 13 April 1993

INTRODUCTION

- Ciguatera is a disease caused by eating poisonous individuals of normally edible warm-water fishes. It is a rarely fatal disease that causes a range of often debilitating and distressing symptoms in people.

IMPORTANCE OF CIGUATERA RESEARCH TO THE FISHING INDUSTRY

- Several important commercial species eg. coral trout and Spanish mackerel cause most of the ciguatera problem in Queensland. These are multi million dollar fisheries.

- Ciguatera outbreaks attract publicity with attendant negative effects on the sale of seafood.

- Victims may seek compensation through the courts. This could have widespread effects on seafood trade and could result in the cost of insurance cover increasing.

- Victims can take weeks or even longer to recover. The loss of productivity is an additional cost associated with the disease.

- The significance of ciguatera research to the Fishing Industry is reflected in the major support given by the Fisheries Research and Development Corporation and the Queensland Department of Primary Industries to hold this International Workshop on Ciguatera Management.

IMPORTANCE OF INTERNATIONAL COOPERATION

- Ciguatera research involves chemical, biochemical, ecological, pharmacological, clinical, immunological and epidemiological studies. This diverse range of disciplines neccessitates a wide-range of skills usually not available to any one research group.

- Despite a history of continuous research on ciguatera since the late 1950's, progress in several important areas, notably the detection and origin of ciguatera, are not sufficiently advanced to allow the introduction of effective management programmes.

- A spirit of international cooperation can only serve to accellerate progress in these and other areas of ciguatera research.

- Countries and Pacific Island Regions represented at this workshop include: Japan, French Polynesia, New Caledonia, mainland France, Germany, United Kingdom, Hawaii and mainland USA. Scientists from Victoria, Tasmania and New South Wales, as well as Queensland are also in attendance.

- The list of speakers for the workshop reads like a Who's who of ciguatera research and includes the names of Paul Scheuer, Takeshi Yasumoto, Hoagi Hokama, Raymonds Bagnis, Jean-Paul Vernoux and Anne-Marie Legrand, names familiar to all in ciguatera research. We are delighted these and the other contributors made the effort to travel to this Workshop in Queensland.

QDPI'S INVOLVEMENT IN CIGUATERA RESEARCH

- Ciguatera research in QDPI commenced in 1980 when Dr Noel Gillespie initiated studies on the origin of ciguatera in Queensland.

- Since then QDPI's research on ciguatera has broadened to include chemical, biochemical, pharmacological, ecological and epidemiological studies, often in collaboration with other research groups.

- The group is proud of its achievement in the field. Results achieved by the group include:

    - the finding that ciguatoxin and maitotoxin production by *Gambierdiscus toxicus* is a strain-dependent phenomena.
    - the elucidation of the structure for two new ciguatoxins found in the flesh and viscera of ciguateric fish.
    - the successful trial of the mannitol therapy for ciguatera in Queensland in collaboration with medical practitioners.

WORKSHOP AIMS

- The Workshop brings together scientists involved in research related to ciguatera to discuss the latest advances in the field.

- Particular emphasis is placed on the discussion of research that has implications for the improved management of ciguatera.

- Areas where progress is still required include; the treatment of ciguatera; the detection of toxic fish; and the factors contributing to the genesis of ciguatera. I note that many of the talks will be addressing these very issues.

- Record the contributions at the Workshop in a published proceedings in cooperation with the Queensland Museum.

- I believe that the workshop will provide clear pointers to the direction for future ciguatera research, given the participation at this Workshop of most of the key researchers in the field.

OFFICIALLY OPEN THE WORKSHOP