

## MARINE SEAFOOD TOXIN DISEASES: ISSUES IN EPIDEMIOLOGY & COMMUNITY OUTREACH

Lora E. Fleming MD PhD\*+, Daniel G. Baden PhD\*, Judy A. Bean PhD\*+, Richard Weisman PharmD\*+, Donna G. Blythe MD\*+.

\*NIEHS Marine and Freshwater Biomedical Sciences Center, University of Miami Rosenstiel School, Miami, FL 33149 USA;

+University of Miami School of Medicine, Miami, FL 33136 USA.

### ABSTRACT

In addition to increased seafood consumption and tourism, recent studies link global climate change with an apparent increasing incidence of the Marine Seafood Toxin diseases. However, the epidemiology of the human diseases caused by the harmful marine phytoplankton is still in its infancy. In general, the epidemiology of these diseases has consisted of case reports of acute illness, sometimes as epidemic outbreaks, associated with the ingestion of suspicious seafood. Furthermore, even these outbreaks are highly under-reported, especially in poorer countries and in traditionally non-endemic areas. True incidence data are not available due to the lack of disease and exposure biomarkers in humans, as well as the global lack of routine exposure and disease surveillance. Without true incidence data to establish background population rates, it is impossible to evaluate the impact of Global Change or the apparent increasing incidence [1,2].

Using Ciguatera as an example, general principles of the epidemiology of these diseases will be presented. The issue of disease surveillance as an essential component in the epidemiologic study and public health control of the marine seafood toxin diseases in human populations will be discussed. Recommendations will be made for epidemiologic study and public health control of the marine seafood toxin diseases in human populations.

### Background

Seafood consumption is increasing worldwide [3]. The average annual US per capita consumption of commercial seafood increased from 12.5 to 14.8 lbs during 1980-1992; there was an additional 3 to 4 lbs of recreationally caught fish and shellfish consumed per capita annually in the US. Degner et al (1994) studied of a random sample of 8,000 resident Florida households by telephone survey and found that the average annual seafood consumption was 16.80 lbs (with finfish consumption of 13.20 lbs) [3]. Of note, all the consumption figures are based on all participants as the denominator, not just seafood consumers. In the 1 week recall, 33% of 1071 people from Dade County (FL) consumed marine finfish [4].

### General Epidemiology

The geographic distribution of the Marine Seafood Toxin diseases historically has followed the transvector sources, thus occurring primarily in island and coastal communities. However, increasing international seafood export and tourism

have extended case reports inland and around the world [2,5].

Using Medline computer database, a search was performed for human case reports and disease outbreaks of the Marine Toxin Diseases by geographic locations (see Table 1). The year of the first reported outbreak for each Disease was also noted.

Table 1. **Marine Seafood Toxin Diseases in Humans**

#### *Shellfish Transvector:*

PSP:(1793)

N. America: Alaska, Massachusetts, British Columbia, California, Quebec Province; S. America: Guatemala, Venezuela, Chile, Costa Rica, Argentina; Europe: Spain, France, England, Norway, Denmark (Atlantic Coast); Africa: South Africa, Brunei, Darussalam; Far East: Japan, Malaysia, Thailand; Pacific: New Zealand, Tasmania, Philippines

NSP:(1844)

N. America: Florida, North Carolina, Gulf of Mexico; South America: Brazil; Europe: Spain; Far East: Japan; Pacific: Solomon Islands, New Zealand

DSP:(1960s)

S. America: Chile, Uruguay; Europe: Netherlands, Spain, France, Scandinavia, Denmark; Far East: Japan

ASP:(1987)

N. America: Eastern Canada

#### *Fish Transvector:*

Ciguatera:(1606)

N. America: Canada, USA (Hawaii, Maryland, Vermont, Florida, California, North Carolina), Mexico; Caribbean: Cuba, Dominican Republic, Virgin Islands, Bahamas, Puerto Rico, Guadeloupe, Jamaica, Nevis; Europe: England, Italy; Far East: Hong Kong, Thailand; Pacific: Australia, Samoa, Tahiti, Marquesas, Fiji, Marshall Islands; [+Crew members of various Ships in the Pacific and Caribbean]

Fugu (Tetrodotoxin):(2500 BC Egyptian Tomb)

N. America: New Jersey, New York; Caribbean: Puerto Rico; Europe: Italy; Africa: South Africa, Guyana; Far East: Japan, Philippines, Singapore, Thailand; Pacific: Australia

The worldwide, centuries-old distributions of these Marine Toxin Diseases are evident. Less obvious are their increasing geographic spread, the increasing number of reported human cases over time, and the emergence of new Marine Toxin

Diseases in human populations. Furthermore, this does not take into account the increasing geographic distribution of the actual algal blooms and the marine toxins over time; for example, domoic acid, the toxin which causes ASP, has been found in anchovies after killing pelicans in Monterey (CA), even though no human cases have been reported from that area as yet [6,7].

*Epidemiology: Ciguatera*

In the case of Ciguatera, at least 50,000 to 500,000 people per year who live in or visit tropical and subtropical areas suffer from Ciguatera [2,8]. However, the total number of people suffering from Ciguatera annually is unknown for a variety of reasons. As discussed above, although there exist tests for identification of the marine toxins in the fish, these are rarely available especially in endemic areas; biomarkers in humans for Ciguatera are experimental. Therefore, the diagnosis of Ciguatera is largely clinical [1,9-12]. There is a lack of significant formal Ciguatera surveillance. As part of general disease surveillance, the South Pacific Countries participate in a voluntary reporting system known as the South Pacific Epidemiology Information System (SEPHIS), and "fish poisoning" is one of the reportable illnesses; similarly, in the United States, Ciguatera is a reportable disease to the US Centers for Disease Control (CDC)[1,9,10]. However, the CDC and others estimate that only 2-10% of Ciguatera cases are actually [9-14].

Under-diagnosis and under-reporting make it difficult to know the true worldwide incidence of Ciguatera. In endemic areas, there is under-reporting due to lack of treatment (until recently) so that many patients never seek medical attention, while in non-endemic areas, healthcare workers and patients do not recognize the diagnosis [1,11,12]. Furthermore, the majority of Ciguatera studies in the medical literature consist of case reports and case series by clinicians, with an emphasis on clinical rather than epidemiologic description [1,11,12,15].

In Table 2, the reported incidence and prevalence of Ciguatera must be seen in the context of overall significant under-estimation. For example, in Dade County (FL), Lawrence (1980) estimated that the true annual incidence of Ciguatera could be as great as 50/10,000 [14]. Furthermore, although the incidence rates are probably most accurate in endemic island or reef areas with relatively complete surveillance, even these estimates do not reflect exported cases (such as tourists or through consumption of exported contaminated fish) outside of the endemic areas.

**Table 2. Reported Incidence and Prevalence of Ciguatera**

<u>Rate</u>	<u>Location (Yrs)</u>	<u>Citation</u>
<i>Annual Incidence:</i>		
0.78/10,000/yr	Reunion I. (1986-94)	[16]

0.87/10,000/yr	Hawaii (1985-89)	[17]
3/10,000/yr	Queensland (1965-84)	[18]
5/10,000/yr	Dade, FL (1974-76)	[14]
7.6/10,000/yr	US Virgin I. (1982)	[19]
30/10,000/yr	Guadeloupe (1984)	[20]
100/10,000/yr	South Pac. (1985-90)	[9]
970/10,000/yr	South Pac. (1973-83)	[21]
5850/10,000/yr	French Polyn. (1979-83)	[21]

*Annual or Lifetime Prevalence:*

4.4%	St Thomas, VI (1980)	[22]
7%	Puerto Rico (Lifetime)	[23]
8.45%	Tahiti (1966)	[15]
10%	Niutao, Tuvalu (1990)	[10]
43%	Hao, Tuamotos (1978)	[21]
70%	Polynesian I. (Lifetime)	[21]

An additional issue of great importance to the interpretation of these rates, is that they are calculated based on a denominator of the entire population, not the population at risk. The population at risk would be those who actually consume seafood; in Dade County (FL) this is 33% of the population based on a 7 day recall [4]. Therefore, these rates are further underestimated.

Due to the sharing of fish among family and friends, as well as potentially wide distribution by fish markets and restaurant of large fish, Ciguatera often occurs in disease clusters. For example, Gillespie et al (1986) reported 166 outbreaks involving a minimum of 479 people in Australia [18]; Lawrence et al (1980) reported 43 outbreaks with 129 people in Dade County (FL) [14]; 159 outbreaks involving 447 individuals were reported by Quod and Turquet (1996) in Reunion Island (southwest Indian Ocean) [16] (see Table 2). For accurate surveillance, all cases in these clusters must be followed up [1].

*Social & Economic Impact*

The social and economic impact in endemic regions has been explored for Ciguatera [12,21,24]. In several endemic areas, the local fish are completely avoided as a food source. In Florida, the sale of barracuda (a major source of Ciguatera poisoning) is banned [14]; in the Virgin Islands, many restaurants import fish due to the abundance of Ciguatera contamination [25]. Lewis (1986) in extensive anthropologic studies found that Ciguatera Poisoning in the South Pacific caused depression of both the local and exporting fishing industries and tourism, and had an indirect affect on human health due to avoidance of fresh fish consumption despite its nutritional value [12,21]. In French Polynesia, estimates costs were based on the loss of activity due to illness (>1 million US\$) as well as the loss of earnings due to banned fish (>1 million US\$) [12].

Local and regional seafood distribution systems can spread Ciguatera rapidly. For example, Hammond and Dickey (1993)

reported on a Ciguatera cluster in Florida which ended up involving over 20 people in Alabama and northern Florida [26]. The original fish (amberjack) came from Key West (FL), then was distributed through a dealer in north Florida, who subsequently sold it to a restaurant in Alabama; a third dealer sold the fish to two grocery stores in Alabama and north Florida.

As discussed above, many recent cases of Ciguatera reported in the medical literature have concerned imported cases in more distant non-endemic areas, through tourism and fish importation [5,12,19,26]. These cases can be particularly expensive, both monetarily and psychologically, because extensive and unnecessary medical evaluations are performed by clinicians who do not recognize the particular Marine Seafood Toxin Diseases. In Canada, with an estimated 1000 reported cases per year due to tourism and food importation in 1990, the average medical cost was \$2470/case of Ciguatera [27]. This does not take into account the legal and economic losses from loss of catch and from numerous lawsuits filed after contraction of Ciguatera from store or restaurant acquired fish [8]. For example, in 1991 in Florida, the finfish and shellfish landings amounted to 163 million pounds worth 162 million dollars; in 1990, Florida had 482 seafood processors and wholesalers, which is more than any other state [3].

#### *Global Etiologies*

In addition to increasing seafood consumption and seafood import, anthropogenic causes may have furthered the spread of the dinoflagellates and their toxins. There is a body of evidence to indicate that man-induced transportation of cysts of toxic marine dinoflagellates or of the dinoflagellates themselves occurs in 'spat' and ship ballast [2]. Although controversial, it is hypothesized that human-generated environmental changes such as reef destruction (eg. Ciguatera) and eutrophication or pollution (eg. the red tides), may be responsible for apparent increased reporting in cases of human disease as well as increased incidence of red tides reported worldwide [7,12,28-30].

There is even evidence connecting the apparent global increase of algal blooms with Global Climate Change; this is most vividly illustrated by the connection between Cholera, the red tide transvector and the el Nino climate phenomenon, discussed elsewhere extensively [7,27,28,29].

#### *Environmental Disease Surveillance & GIS*

Disease surveillance, in particular public health surveillance, has been defined as "the ongoing systematic collection, analysis and interpretation of data on specific health events affecting a population, closely integrated with the timely dissemination of these data to those responsible for prevention and control" [31,32]. More traditional environmental disease surveillance systems have been established for populations with known or probable toxic exposures, such as around

hazardous waste sites or areas of massive industrial pollution. Although it could be argued that humans are not the most sensitive sentinel species, such systems are important not only for disease surveillance and prevention, but also to reassure affected communities. Such systems are also relatively easy to establish since the exposures are usually easily defined and measured due to localized sources [32].

Thacker et al (1996) delineate three types of complimentary surveillance for environmental public health: hazard, exposure and outcome surveillance [31]. Hazard surveillance involves source monitoring (such as at a hazardous waste site or coral reef); exposure surveillance involves the use of biomarker monitoring; and, outcome surveillance monitors the disease (or other) health endpoint. In particular, outcome surveillance can be used to establish disease burden in a population and can facilitate epidemiologic research [31]. Intrinsic to the success of an environmental outcome surveillance program are an identified target population, a fairly restrictive case definition, a method of case identification, and possibilities of treatment and prevention of the disease outcome [32]. Herz-Picciotto (1996) notes that "maps of disease patterns serve as a surveillance tool and constitute the first descriptive step" which indicates the crucial role that GIS could play in environmental surveillance [33]. All these key ingredients exist for the Marine Seafood Toxin Diseases, especially Ciguatera.

There is a growing use of GIS to analyze disease ecology in time and space. GIS has been defined as "a computer system that stores and links non-graphic attributes or geographically referenced data with graphic map features to allow a wide range of information processing and display operations, as well as map production, analysis and modeling [34].? There are three basic reasons for using GIS to study Marine Seafood Toxin Diseases. First, the spatial and temporal dimensions are crucial aspects in understanding the etiologic environmental and anthropomorphic factors surrounding these diseases. Second, these diseases are both local and regional, as well as global phenomena. Better understanding and preventive measures cannot be achieved from isolated studies on an individual scale. Third, these diseases are products of complex processes involving environmental, cultural, social and economic elements. GIS combines spatial and temporal analyses, database management and visualization functions into a single computer environment, providing the ideal platform for studying, monitoring and preventing Marine Seafood Toxin Diseases [29,35,36].

#### *An On-going Surveillance Program*

In a collaborative effort, the National Institute of Environmental Health Sciences (NIEHS) Marine and Freshwater Biomedical Sciences Center at the University of Miami and the South Florida Poison Control Center have established one form of outcome surveillance in Dade County (FL). They have recently initiated a Marine Seafood Toxin

Hotline "800" number (tel: 888-232-8635), free to persons calling within the continental United States. All cases fitting a clinical diagnosis of Marine Seafood Toxin disease are reported to the state of Florida Health Department and ultimately to the US Centers for Disease Control and Prevention (CDC). In addition, the Poison Control Information Specialists give treatment recommendations and referrals. In just 3 months with only local publicity and target population education concerning the Marine Seafood Toxin diseases and the Poison Control Hotline, there was a 2.7x increase in the actual number of Ciguatera cases reported in the context of a 1.7x increase in all reported marine-related cases compared to the prior 3 months. This service will provide increased surveillance and appropriate treatment through easy case reporting; in addition, these data can be incorporated into GIS systems for disease modeling and prevention.

#### *The Problem*

The major issues for the study of the Marine Seafood Toxin Diseases, especially their epidemiology and their impact on human health worldwide, are the lack of reliable data on disease burden and the possibility of their increasing incidence and emerging new diseases. In some countries, such as the US, with significant resources, the shellfish-associated Marine Seafood Toxin Diseases have primary prevention through dinoflagellate/toxin monitoring of the shellfish beds; this type of primary prevention is not available in areas of emerging Marine Seafood Toxin Diseases nor in many poorer countries where the lack of data on human burden means that scarce resources are not allocated for primary prevention. In the case of Ciguatera, due to the more mobile fish transvector, primary prevention is currently not practiced even in countries with significant resources. In addition, there is a lack of knowledge concerning the possible chronic health effects of these diseases.

Therefore, increased surveillance using new technologies (such as GIS), combined with education and outreach such as the NIEHS-Poison Control Center collaboration, is essential to understand and prevent the global impact of the Marine Seafood Toxin diseases in the future.

#### **BIBLIOGRAPHY**

1. L. Fleming, J. Bean, D. Baden, in: Manual on Harmful Marine Microalgae. Hallegraeff GM, et al eds. (UNESCO, Denmark), pp. 475-486 (1995).
2. D. Baden, L. Fleming, J. Bean, in: Handbook of Clinical Neurology: Intoxications of the Nervous System. FA deWolff (Ed). (Elsevier Press, Amsterdam), pp. 141-175 (1885).
3. R. Degner, C. Adams, S. Moss, S. Mack, Per Capita Fish and Shellfish Consumption in Florida. Gainesville: Florida Agricultural Market Research Center Industry Report 94-2, (August 1994).
4. K. Portier, U. Yonghwan, R. Degner, S. Mack, Statistical Analysis of Florida per Capita Fish and Shellfish Consumption

Data. Gainesville: Florida Agricultural Market Research Center Industry Report 95-1, (December 1995).

5. W. Lange, F. Snyder, P. Fudala., Arch. Int. Med.. 152, 2049-53 (1992).
6. P. Epstein, Am. J. Public Health. 85, 168-172 (1995).
7. P. Tester, Ann. N.Y. Acad. Sci. 740, 69-77 (1994).
8. D. Miller (ed), Ciguatera Seafood Toxins. (CRC Press, Boca Raton) (1991).
9. A. Tilman, R. Lewis, Mem. Queensland Museum 34, 609-619 (1994).
10. P. Dalzell, Mem. Queensland Museum 34, 471-479 (1994).
11. J. Pearn, Mem. Queensland Museum 34, 601-604 (1994).
12. P. Glaziou, A-M. Legrand, Toxicon 32, 863-873 (1994).
13. R. Bagnis, in: IR Falconer (ed), Algal Toxins in Seafood and Drinking Water. (Academic Press, London) pp.105-115 (1993).
14. D. Lawrence, M. Enriquez, R. Lumish, A. Maceo, J.A.M.A. 244, 254-8 (1980).
15. R. Bagnis, T. Kuberski, S. Laugier., Am. J. Trop. Med. Hyg. 28, 1067-1073 (1979).
16. J. Quod, J. Turquet, Toxicon. 34, 779-785 (1996).
17. J. Gollup, E. Pon, Hawaii Med J. 51, 91-99 (1992).
18. N. Gillespie, R. Lewis, J. Pearn et al, Med. J. Australia. 145, 84-558 (1986).
19. J. Morris, R. Lewis, C. Smith, P. Blake, R. Schneider, Am. J. Trop. Med. Hyg. 31, 574-8 (1982).
20. P. Czernichow, J. Droy, F. Ezelin, J. Leroy, Rev. Epidem. Sante Publique. 32, 315-321 (1984).
21. N. Lewis, Soc. Sci. Med. - Australia. 23, 983-93 (1986).
22. J. McMillan, H. Granade, P. Hoffman, J. Coll. Virgin Is. 6, 84-107, 1980.
23. R. Holt, G. Miro, A. Del Valle, J. Tox.-Clin. Tox. 22, 177-85 (1984).
24. E. Todd, Ann. N.Y. Acad. Sci. 740, 77-94 (1994).
25. C.A. Payne, S. N. Payne, N.E.J.M. 296, 949-50 (1977).
26. R. Hammond, R. Dickey, M.M.W.R. 42, 417 (1993).
27. E. Todd, In: T.R. Tosteson (ed), Proceedings of the Third International Conference. Puerto Rico, pp. 181-196 (1990).
28. R. Viviani., Sci. Total Env. Supplement 1, 631-62 (1992).
29. P. Epstein, T. Ford, R. Colwell, in: Health and Climate Change. (The Lancet Ltd, London), pp. 14-17 (1994).
30. U. Kaly, G. Jones, A. Tilman, R. Lewis, Mem. Queensland Museum 34, 523-532 (1994).
31. S. Thacker, D. Stroup, R. Parrish, H. Anderson, A.J.P.H. 86, 633-638 (1996).
32. T. Aldrich, P. Leaverton, Ann. Rev. Pub. Health. 14, 205-217 (1993).
33. I. Herz-Piccio, Am. J. Pub. Health. 86, 638-641 (1996).
34. J. Antenucci, K. Brown, P. Crosswell, M. Kevany, H. Archer, Geographic Information Systems: a Guide to the Technology. Van Nostrand Reinhold, NY, (1991).
35. D. Briggs, P. Elliott, Wid. Hlth. Stat. Quart. 48, 85-94 (1995).
36. C. Croner, J. Sperling, F. Broome, Stat. Med. 15, 1961-1977 (1996).

