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Mannitol: the treatment of choice in the acute phase of ciguatera

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Until the introduction of intravenous mannitol therapy, treatment for ciguatera was only symptomatic and supportive. Mannitol was first used in the Marshall Islands (Palafox et al., 1988) and soon after in Australia (Pearn et al., 1989). These studies both reported dramatic and sustained improvement in many of the victims of ciguatera. Specifically mannitol appeared to reduce the duration and severity of ciguatera. Several recent experiences with mannitol and ciguatera lend further support to these earlier studies. Mannitol is now the treatment of choice in the acute phase of ciguatera in Australia (Figure 1). Mannitol is most effective at reversing the neurological disturbances, particularly in the more severe cases of ciguatera.

The mannitol treatment regimen for ciguatera is shown in Table 1. Ciguatera is diagnosed when symptoms typical of ciguatera appear within 24 hr of eating a suspect fish (see *Ciguatera Information Bulletin* no. 1 for details). The most important contra-

indication to the use of mannitol is dehydration. Patients must be adequately hydrated prior to the infusion of mannitol. The response of patients to mannitol infusion is often dramatic, with some symptoms abating during the infusion.

Table 1. Mannitol therapy for confirmed ciguatera

- Intravenous infusion of 20% mannitol solution over 30
- 1 g mannitol given per kg body weight (i.e. 5ml/kg)
- Adequate hydration must be established prior to mannitol
- Mannitol is most useful during the acute phase of ciguatera

Other patients report slower improvement, with some having a relapse about a day after treatment. In these latter cases, a second infusion of mannitol often has further beneficial effects. In Australia, not all ciguatera sufferers (<25%) respond to the mannitol treatment. The reasons for poor response of some people have not been determined. However,

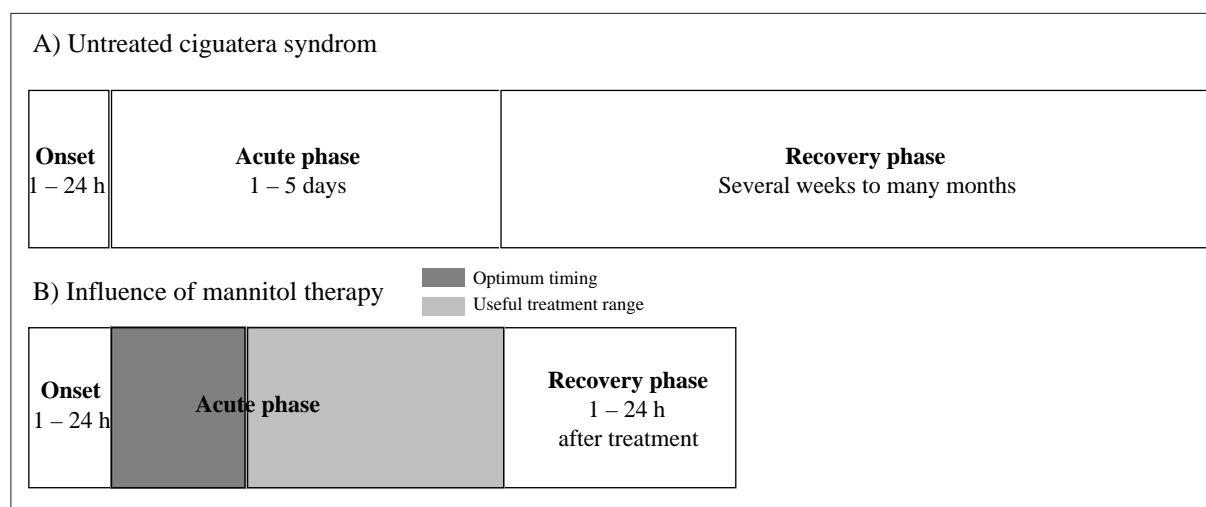


Figure 1. Mannitol therapy for ciguatera. (A) shows the normal course of the disease and (B) the influence of intravenous mannitol. The apparent optimum timing for the treatment is early in the acute phase.

the Australian experience indicates that mannitol is most useful when given early in the acute phase of the illness (Fig.1), and may be of less benefit when given during the normal recovery phase of ciguatera. A double-blind clinical trial of the mannitol therapy has not been reported to date.

The mechanism of mannitol's beneficial action in cases of ciguatera has been studied by the Ciguatera Research Group at the Southern Fisheries Centre, Deception Bay. These studies indicate that mannitol does not displace ciguatoxin from its site of binding, nor does it chelate ciguatoxin. The appearance of an oedema (swelling) of the cells (Schwann cells) surrounding myelinated peripheral nerves (and possibly similar cells in the central nervous system) in cases of ciguatera may provide the explanation. Hyperosmotic mannitol, through its water drawing action would reduce this cell swelling and thereby effectively reverse the course of this often distressing and debilitating disease.

To explain the long term effectiveness of mannitol, I hypothesise that (i) mannitol prevents long-term nerve damage (eg. lesions, anoxic zones) that probably develops from the oedema (ii) ciguatoxin normally remains bound to its receptors in the body

only for a few days (not weeks), and the longer-term effects of ciguatera relate to nerve damage.

These hypotheses also explain why mannitol would be most effective when given early in the disease. Interestingly, it has been repeatedly observed in Australia that the diuresis that would normally follow an infusion of mannitol does not appear when mannitol is used to treat ciguatera (all patients were adequately hydrated). The explanation for this observation is not apparent, but it does suggest that mannitol does not act to flush ciguatoxin from the body by increasing urine output. Further studies are required to define more precisely why mannitol is useful in the treatment of ciguatera.

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Fourth International Conference on Ciguatera Fish Poisoning in Tahiti

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Researchers studying ciguatera presented the latest research developments and exchanged information at the Fourth International Ciguatera Conference in Papeete from 4 to 7 May. Inshore Fisheries Scientist Paul Dalzell represented SPC.

Topics ranged from general country statements about ciguatera and the ecology of the dinoflagellate, *Gambierdiscus toxicus*, to the results of highly specialised physiological research on the mechanism by which ciguatoxins affect nerve and muscle cells.

Paul Dalzell and Richard Lewis of the Queensland Department of Primary Industry jointly chaired the session on the socio-economic impact of ciguatera. Paul presented summaries of data on fish landings in the Pacific Islands and incidence of ciguatera. He also introduced the new SPC Fisheries Programme/Health Programme Ciguatera Database and gave some preliminary results. Participants were also given a chance to see the new commercially produced ciguatera kits produced by Hawaii Chemtect International. These are based on the monoclonal antibody test devised by Dr Y. Hokama of the Hawaii University Medical School.

Two forms of test kit were demonstrated to the meeting: a small disposable kit containing a single test, and a larger more elaborate kit containing equipment and reagents for multiple testing. The single test comes in card form, contains all the reagents, and is designed to be used to test one fish. The larger kit, which can be used for up to 50 tests, is designed for multiple testing on one fish or testing several fish.

About 100 persons attended the meeting. The Pacific Islands were well represented, with people attending from the Cook Islands, the Federated States of Micronesia, Fiji, French Polynesia, Guam, Kiribati, New Caledonia and Solomon Islands. Participants also came from Australia, France, Germany, Japan, Mayotte, Martinique, Puerto Rico, Réunion and the United States.

The Inshore Fisheries Research Project supported the attendance of Edwin Oreihaka from the Solomon Islands Fisheries Division and Ahser Edwards from the Community College of Micronesia in the Federated States of Micronesia.