

Correspondence

To the Editors:

Recently, an International Consortium for Jellyfish Stings was formed with its headquarters at our institution. Your readers might be interested in a meeting summary and additional notes about clinically important developments in the field.

Digest of selected papers presented at the 5th International Conference on Coelenterate Biology held at the University of Southampton:

The fact that nematocyst discharge in *Hydra* is independent of nerve cells was reported by Aerne and colleagues from Zurich.

Bob Endean from Australia reported that the discharge of nematocysts from *Chironex fleckeri* was probably produced by a change in the sol-gel-crystal configuration of the matrix within the nematocysts of the box-jellyfish.

Drs Avian, Del Negro and Rottini-Sandrini of Trieste showed an analysis of nematocysts of *Pelagia noctiluca* and *Rhizostoma pulmo* from the Adriatic and found that there was a greater variety of cnidocytes than had been described in previous studies. These authors recommended a review of the nematocysts in all scyphomedusae.

Dr R.H. Brewer reported that two contiguous populations of *Cyanea capillata* were found in the Connecticut Niantic river estuary. This work was reported in this year's *Biological Bulletin* (176:272, June 1989) and shows a difference between these two populations, which live within two distinct water bodies having different saline concentrations. We have observed this in the Chesapeake Bay; Dr Karen Long from our group reports that *Cyanea* found in the middle of Delaware Bay have a hemolysin in the venom which is absent in species found upon the shoreline.

Dr Burnett of Baltimore reported the clinical manifestations of jellyfish envenomation and stressed that there was a sex predilection for more serious envenomation in human females. A wide variety of symptoms can be found after jellyfish stings. Our group has recently seen a patient with eight days of blurred vision following a sting by *Lanuche* species off Nassau and two patients with single joint arthralgia proximal to a sting.

Drs Del Negro, Kokelj and Tuharo from Trieste reported corroboration of the fact that *Aurelia aurita* can produce pain, urticaria and skin ulcerations. The Trieste investigators pointed out that *Rhizostoma pulmo* may give rise to urticaria or constitutional symptoms. *Pelagia noctiluca* produces itching, pain and an erythematous urticarial eruption. All three of these jellyfish venoms can be dermonecrotic in experimental models. Dr Kokelj also illustrated a patient who had profound postinflammatory hyperpigmentation following a sting by *Chrysaora hysocella*. This abnormality responded to treatment with topical hydroquinone bleach within a few months.

Drs Endean and Rifkin reported a sequel to their work describing the ultramicroscopic morphology of nematocyst discharge in box-jellyfish. They have seen the cnidocyte within the tentacles advance superficially within the epithelium and retreat into a 'silo'-like structure. These firing cells seem to prime or not depending upon the activity of the filamentous basket, which can advance the nematocyst to the tentacle surface.

Drs Fluckiger, Gerke, Weber and Tardent from Zurich reported micromanipulations of *Hydra* nematocysts. They showed spectacular motion pictures of nematocysts whose

walls had been punctured, after which a tremendous release of pressure was apparent when the tubule exited without evaginating. This behavior suggested that the nematocyst must be under considerable intrinsic pressure and that normal discharge of the tubule with its associated structures occurs only when mechanical forces are applied to the operculum. The same investigators showed that isolated nematocysts do not respond to electrical triggering, but do respond to reducing agents such as dithioerythritol. It appears that cyst operculum opening and ejection of the stylets can occur within 10 to 70 msec, depending upon the stimulus. Further observation indicated that discharge of the cyst was associated with an influx of the surrounding medium, contributing to intracapsular pressure of that cyst.

Drs Gerke-Drolet, Zierold, Weber and Tardent found that quick-frozen cells with discharged nematocysts contained the same amount of free potassium ion in the matrix as did nondischarged capsules.

Dr Paul Greenwood of Colby College found that nematocysts contained within the pharyngeal pouches of several nudibranch species were stored differently in different species, and that their discharge rates were different than those of nematocysts isolated independent of the cnidophage.

Drs Ostman, Kim, Paralmo and Pongparyoorn of Sweden and the USA found that there are five morphologically different nematocyst types within *Cyanea*. They succeeded in purifying a muscle-contracting toxin of molecular weight 300000 daltons, which is a basic protein and not cytolytic. Isorhizas of *Cassiopea* and *Catylorhiza* had smaller threads than did those of *Cyanea*.

Drs Rottini-Sandrini and Avian of Trieste reported that there was a difference in the developmental ovocytes stages of *Pelagia noctiluca*. There was evidence to believe that there is a reproductive spurt in the spring and autumn relative to summer. This distribution is likely related to sea temperature, metabolic rate and food availability.

Drs Shanks and Graham of the University of North Carolina, Chapel Hill studied *Stomolophus meleagris* and found that the free-swimming jellyfish were deflected by water turbulence but reoriented themselves to their initial orientation or at 180° to that orientation. They found that the jellyfish orients itself on swimming relative to directional cues in the water column and that swimming direction was correlated with the direction of the wind and surface waves, but not with the sun or local current direction.

Drs Tilbury and Cameron of the University of Queensland, Brisbane, report that the cnidium of *Goniopora* species was found to be consistent with respects to types and proportions of nematocysts present among the colonies of each species. This means that the analysis of these organelles can be used to identify the species.

Bob Hartwick of Townsville, Australia reported more experiments on the life cycle of *Chironex fleckeri*. He found that metamorphosis and the migration of polyps toward certain areas were dependent partially upon light and seasonal rainfall. This jellyfish reproduces sexually, as well as asexually, with a polyp phase. The adult medusae migrate into the tidal estuaries to spawn, fertilize eggs, and produce polyps and planulae. A polyp can reproduce asexually by budding; it lives off various copepods before returning to oceanic waters in the summertime.

The same investigator also studied *Carybdea sivickisi*. This jellyfish swarms, is very small, and is capable of causing nuisance stings. It feeds off polychaetes and does not have a creeping polyp stage. Similar animals have been found along the eastern coast of Australia, as well as off New Zealand and in the Caribbean.

Dale Calder of Toronto enumerated the types of hydroids found in a mangrove area of Belize. Several of these species were venomous.

Additional notes dealing with jellyfish envenomation:

Dr Karen Long refined her Masters thesis from the University of Delaware and detected a low molecular weight hemolysin in the nematocyst venoms of both *Chrysaora quinquecirrha* and *Cyanea capillata*. However, she finds the compound only in the large, more venomous specimens of *Cyanea* found in the middle of the Delaware Bay, rather than in the smaller specimens found along the shoreline.

Dr Iekhsan Othman, a Fulbright Scholar on leave from the University of Malaysia, has studied the venom of *Chironex fleckeri*. He has tried numerous biochemical techniques and found disadvantages with each. However, he has detected a lethal toxic fraction which contains at least two bands on analytical isoelectric focusing. These fractions are antigenically active at higher titers against convalescent serum than against crude venom as antigen. Several purification techniques yielded fractions with a common band of M.W. 24000 daltons.

Other work reported by our group in association with Dr Othman and Drs Endean, Williamson, and Callanan in Australia has shown that verapamil potentiates the life-saving effect of ovoid box-jellyfish antivenom in mice. It appears that verapamil might stabilize the animal long enough for the antivenom to take effect.

Dr Peter Fenner has performed outstanding taxonomic research and found that the species previously identified as *Morbaaka* is probably an unknown *Tamoya*. When he and I visited the British Museum of Natural History, it was apparent that some of their species were misclassified. Peter is now collaborating with other jellyfish experts to prepare a better scheme for *Tamoya* species classification.

JOSEPH W. BURNETT, MD
Division of Dermatology
University of Maryland Hospital
22 S. Greene Street
Baltimore, MD 21201, USA

Pitfalls in prospective research in the rural Third World: some personal cautions

To the Editors:

I would like to offer some words of caution to research workers from the 'developed' world about to embark on a project in the rural Third World for the first time. Indeed, this letter could be entitled 'How NOT to do research in the Third World'!

During a recent tour of duty as surgeon at the British Military Hospital in Nepal, I was struck by the difficulty of choosing the correct procedure to treat the large number of persons with tropical pyomyositis and subcutaneous abscesses that predominate seasonally during the late monsoon. The number of patients who presented with the condition precluded routine admission, yet the sizes of abscess cavities (often in excess of 200 ml) and toxic condition of many of the patients meant that out-patient treatment was less than ideal. Therefore, we designed a prospective trial to determine the optimal method of out-patient treatment, randomly allocating persons into groups for incision and drainage with and without primary closure, with and without antibiotic treatment, and with and

without corrugated drainage of deep abscess cavities. The trial was supported by Beechams Ltd, which generously funded a microbiology technician and supplied the antibiotic (amoxicillin) free of charge.

The first problem arose when our antibiotic supplies were impounded by local customs agents, as our import quota for the year had been exceeded. After three months of intense negotiations, our supplies were released, but by then, the monsoon season was already well advanced. Thus, the peak incidence of pyomyositis had already passed by the time the project began. With the arrival of better weather, we discovered that patients' decisions in the third world are governed by different priorities than those of westerners. When the trial was terminated, only 58/130 patients (45%) returned for follow-up, many disappearing forever with their tube drains in-situ! Five of these patients had active untreated pulmonary tuberculosis (PTB), and one had acute myeloid leukaemia. Once persons were restored to near-normal function, agricultural subsistence activities took precedence over health matters. Because of our failure to satisfactorily follow up on outpatients, none of our results reached statistical significance.

Additionally, we never discovered the degree of patient antibiotic compliance, although our experience with tuberculosis (TB) later showed that a high proportion of the poorest individuals failed to complete a course of medication because their drugs were sold in the marketplace.

In the Third World, avenues of unexpected clinical intrigue may suddenly be revealed during the course of such research if data are carefully analysed. Because of the randomized and blinded nature of our trial, we failed to do this and missed valuable opportunities for parallel research. For instance, of 77 chest radiographs obtained, active PTB was discovered in 14 patients. *Staphylococcus pyogenes* (92/130) and *Streptococcus pyogenes* (15/130) were the predominant pathogens cultured from the abscesses. However, 15 of the 16 abscesses which failed to yield an organism on culture occurred in the neck. Examination of the chest radiographs from these patients showed that 9 of the 15 had active PTB, and presumably, that these cervical abscesses were missed 'collar-stud' infections. I wonder whether all patients from high-risk communities who present with neck abscesses should be more thoroughly investigated (or treated) for TB? In addition, was there a relationship between abscess formation, anaemia (81/130), profound hypoalbuminaemia (15/130), and parasitic bowel infestation (41/78 patients)? Our trial generated interesting questions, but failed to resolve our initial hypothesis!

Beware, then, of some of the pitfalls of Third World research. Pick a patient population that can be properly monitored, and ensure that climate, attitudes and patient economics do not seasonally influence pathology or the outcome of treatment. Make sure you have timely and adequate supplies of trial drugs, and bear in mind the likely lack of patient compliance. When possible by virtue of study design, maintain ongoing analysis of data and results, and always consider opportunities for parallel projects that may arise from such analysis. Above all, when on a limited tour of duty in a fascinating environment, do not underestimate the time required to collect adequate data. To undertake research in the Third World, personal qualities of unbridled enthusiasm and determination may be your most useful assets!

P.J. GUY
British Military Hospital
Hannover, FRG
British Forces Post Office 33