Paralytic Shellfish Poisoning
A Report of 17 Cases in Cape Town

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SUMMARY

An outbreak of 17 cases of paralytic shellfish poisoning in humans occurred in Cape Town during May 1978. The clinical features were typical and no deaths occurred. Efforts to correlate the severity of disease with the amount of toxin ingested, to demonstrate a protective effect of alcohol, and to demonstrate the immunogenicity of the toxin proved unsuccessful. The regional ecological effects are described. Continued monitoring for the presence of toxic dinoflagellates must be conducted, and the dangers of the consumption of mussels from the Cape west coast should be widely publicized.


Wherever shellfish are consumed the possibility of contracting a disease such as typhoid fever or infective hepatitis is usually widely appreciated, but the danger of paralytic shellfish poisoning (PSP) has received little publicity locally since the 1969 account by Grindley and Sapeika. This report serves as a reminder that despite the undeniable gastronomic delights afforded by some shellfish of the Cape coast, their consumption carries a real risk of disease or even death.

Sporadic dinoflagellate or ciliate blooms causing 'red tides' or 'red water' are common in coastal waters around the world, particularly in temperate and subtropical regions. They are well known on the east and west coasts of North America and the first recorded epidemic of PSP in England was reported in detail in 1968. When conditions in the sea are optimal for the growth and aggregation of dinoflagellates, populations increase rapidly by several orders of magnitude. If they are of a toxic type, the resulting concentrations of associated toxins can reach levels that are hazardous for marine life and for man.

The majority of these organisms are non-toxic (although dense concentrations can be indirectly responsible for huge mass mortalities of marine life), but toxin-producing spe-

Investigation of the Outbreak

The first cases to be brought to the attention of the City Health Department were in 3 White men who had lunched together on 10 May 1978 and who all developed circumoral numbness and paraesthesia before leaving the restaurant. Within hours of the luncheon, all 3 had deve-
loped paraesthesia of the fingers and hands and a floating sensation, and had become ataxic. Two of these patients were attended by private medical practitioners and given antihistaminic drugs, without effect. They were hospitalized on 11 May 1978 because of the generally increased severity of their symptoms, plus headache and/or vomiting.

At this stage the Medical Officer of Health became aware of the situation and forthwith issued statements to the press and radio with the intention of warning the public not to consume mussels. Simultaneously a search for supplies of fresh mussels at City restaurants was commenced. Ten out of 168 restaurants inspected had fresh mussels on their premises, which shellfish were seized and destroyed after samples had been despatched for toxicological analysis.

Further cases were reported to the City Health Department and efforts to trace the source of the mussels were launched in respect of each restaurant found to have stocked them. These efforts were fruitless, as in each case it was claimed that the mussels had been hawked by an unidentified vendor. Suspicion fell on an individual who was warned by a health inspector, and it is of interest that subsequent to this step various restaurants received anonymous telephone calls advising them to destroy their stocks of mussels.

From the start the Health Department established liaison with the Sea Fisheries Branch, who rapidly established the presence of dangerous dinoflagellates in both sea water and in mussels on the coast.

**METHODS**

**Epidemiological Data Collection**

All patients were immediately interviewed by members of the Cape Town Municipal Health inspectorate. Additional data in respect of 12 patients were obtained from their medical practitioners by means of a questionnaire. Telephonic communication or personal interview by one of the authors (M.E.E.P.) provided further medical data in respect of 5 cases.

**Shellfish and Water Sample Collection**

Samples of shellfish were collected from littoral regions as near to the low water mark as possible at various sites along the coast (Fig. 1). In addition black mussels were collected at various hotels and restaurants in and around Cape Town. Phytoplankton samples were taken at Bloubergstrand (N50V net and bucket being used) and the surface temperature was recorded.

**Toxicological Analysis**

Black mussel extracts were prepared (by the Sea Fisheries Branch) and assayed for the content of saxitoxin (by the State Vaccine Institute) according to the methods described by Prakash *et al.* Acid extracts of shellfish were prepared and 1 ml volumes, suitably diluted to cause death within 5 - 7 minutes, were injected intraperitoneally into female white mice of 19 - 21 g. Median death times were recorded and converted to mouse units per 100 g of shellfish according to mouse unit tables. Assays were standardized by the use of a paralytic shellfish poison standard obtained from the US Food and Drug Administration and results were expressed in μg toxin per 100 g of shellfish. (Concentrations of toxin expressed in MU/100 g mussel tissue are usually of the order of 4 times the figures in μg/100 g mussel tissue.)

**Calculation of the Quantity of Toxin Ingested**

As the mussels actually eaten by the patients were obviously not available for assay, this calculation is based on mussels seized from restaurants or collected at appropriate sites.

Cooking reduces the toxicity by more than 70%, unless the cooking liquid is consumed, when up to 50% of the toxicity may remain.* In calculating the quantity of toxin
ingested from steamed or boiled mussels the following formula was used:

\[ A = C \times \frac{W}{100} \times \frac{N}{100} \times \frac{30}{100} \]

where \( A \) = amount of toxin ingested in MU, \( C \) = the concentration of toxin in MU per 100 g raw mussel meat, \( W \) = average weight of a mussel in g, \( N \) = number of mussels eaten, and 30% represents the presumed amount of toxin remaining after cooking.

Similarly the calculation of toxin ingested in mussel soup employed the formula:

\[ A = C \times \frac{W}{100} \times \frac{N}{100} \times \frac{50}{100} \]

where \( A, C, W \) and \( N \) are as described above and 50% represents the presumed amount of toxin remaining in the soup.

Grading of the Severity of Reaction

Severity of reaction was difficult to quantify but a 5-point ordinal scale (0 - 4) was eventually devised, where grade of severity equals the basic rating (0 - 2) plus the subgroup rating (0 - 2).

The basic rating was: 0 = ambulatory, 1 = bedridden, 2 = hospitalized.

The subgroup rating was: 0 = ± circumoral paraesthesia ± paraesthesia of fingers or hands ± paraesthesia of toes or feet ± a feeling of floating, 1 = ± vertigo ± ataxia ± headache ± nystagmus, 2 = ± weakness of upper limbs ± weakness of lower limbs ± dysarthria ± dysphagia ± respiratory difficulty.

Before grading a case in a higher category a score of 50% of the clinical features in the next lowest category had first to be obtained. Gastro-intestinal symptoms were not considered.

Immunogenicity Studies

Paired sera taken 14 days apart were obtained from 2 patients and investigated for evidence of neutralizing antibody formation. Samples of these sera were mixed with equal volumes of saxitoxin to a final toxin concentration of 0.35 µg/ml. Serum/toxin mixtures were incubated at 37°C for 1 hour and centrifuged at 10,000 rpm for 15 minutes, and toxicity levels were monitored. Three mice were inoculated with 1 ml volumes of each sample and mean death times were recorded. Controls included pooled normal human serum and a toxin control.

Estimation of Alcohol Intake

The amount of alcohol ingested with the meal of mussels (Table 1) was estimated from the number of persons consuming a particular number of 750 ml bottles of wine. Hence two persons sharing such a bottle were estimated to have drunk half each, i.e. 375 ml. In 1 case the wine was drunk by the glass and the amount calculated in this instance is probably less accurate (this was patient 9 who also had one tot of whisky).

RESULTS

Epidemiological Features

Of the 17 patients 10 were male and 7 female; all were White. Six had eaten fewer than 6 mussels, 6 had eaten 6 - 11 mussels, 2 had eaten between 12 and 17 mussels and 3 had managed 18 mussels or more. Four patients ate at one restaurant, 9 at another and 1 each at two other restaurants, while 2 had eaten mussels at home.

Because of the possible protective effect of alcohol the amount of wine or spirits consumed with the mussels was recorded. Nine patients had not imbibed at all. Two had drunk between 250 and 374 ml of wine (one also having a tot of spirits), 2 drank 375 - 479 ml, 3 had taken over 500 ml and 1 had had over 750 ml. The effect of this is discussed below.

Onset of symptoms was rapid, being less than 30 minutes in 10 cases, 30 minutes - 2 hours in 5, and over 2 hours in 2 cases.

Clinical Features

While circumoral numbness and tingling was the most usual presenting feature it was present in only 82% of cases, whereas 88% of patients had paraesthesia of the fingers and hands at some stage of their illness.

Clinical features are detailed in Table I. There is little to suggest that case 13 was in fact a case of PSP.

Overall, 6 patients were ambulatory, 6 bedridden and 5 hospitalized.

Identification of the Dinoflagellates and Mussels Involved

Poisonous mussels seized from the restaurants involved as well as those collected along the coast were identified by the Sea Fisheries Branch as C. meridionalis.

In situ mussel and water samples were collected from Lambert's Bay to Gordon's Bay (Fig. 1). At Bloubergstrand, where unconcentrated water samples revealed the presence of a few red water organisms (G. catenella), an N50V net was consequently towed behind a boat to sample a larger body of water. These samples contained numerous G. catenella cysts. As they far outnumbered the living cells it was clear that the tail-end of the outbreak had been sampled.

In the vicinity of Bloubergstrand hundreds of thousands of black mussels littered the beaches. At Yzerfontein adult white mussels were washed up in immense quantities. Mussel mortalities on a smaller scale were reported from further north (Fig. 1), but except for a few crabs, no other marine life was affected and, as previously reported, no evidence of toxicity in the Cape rock lobster Jasus lalandii (which feeds on these mussels) has been found to date. Many dead sea birds (oystercatchers, Southern black-back gulls and Hartlaub's gulls) were seen on the beaches.

Mussel collecting was carried out between Lambert's Bay in the north and Walker Bay to the south-east. As the results from the bio-assays became available, the following picture began to emerge. Maximum toxicity occurred in the Jutten Bay area (7 283 µg/100 g), decreasing
### TABLE I. CLINICAL AND EPIDEMIOLOGICAL FEATURES OF THE PATIENTS DIAGNOSED AS HAVING PSP

<table>
<thead>
<tr>
<th>Case</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
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<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>12</th>
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<th>14</th>
<th>15</th>
<th>16</th>
<th>17</th>
<th>Totals/means</th>
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<tr>
<td>Sex</td>
<td>M</td>
<td>M</td>
<td>M</td>
<td>M</td>
<td>M</td>
<td>M</td>
<td>M</td>
<td>F</td>
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<td>F</td>
<td>F</td>
<td>M</td>
<td>F</td>
<td>M</td>
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<td>Estimated dose of toxin (MU × 10^6)</td>
<td>21,9</td>
<td>38,3</td>
<td>38,3</td>
<td>5,5</td>
<td>36</td>
<td>5,4</td>
<td>31,5</td>
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<td>18</td>
<td>9</td>
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<td>&lt;30</td>
<td>60</td>
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<td>&gt;120</td>
<td>&gt;120</td>
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<tr>
<td>Vertigo</td>
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<td>9 (53%)</td>
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<tr>
<td>Weakness of upper limbs</td>
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<td>+</td>
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<td>6 (35%)</td>
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<tr>
<td>Dysarthria</td>
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<td>6 (35%)</td>
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<tr>
<td>Headache</td>
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<td>6 (35%)</td>
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<td>Weakness of lower limbs</td>
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<td>5 (29%)</td>
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<td>Vomiting</td>
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<td>Nystagmus</td>
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<td>4 (24%)</td>
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<td>Nausea</td>
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<td>1 (6%)</td>
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<td>Loose stools</td>
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<td>1 (6%)</td>
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<td>2</td>
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</table>
in concentration to the north and south (Fig. 1). The values are given in $\mu g$ toxin per 100 g mussel flesh.

A monthly monitoring programme was launched and mussels were collected at strategic locations. The results are shown in Fig. 2. After 1 month a marked reduction in toxicity levels was evident and within 3 months the levels dropped to below 80 $\mu g/100$ g.

Relationship between Amount of Toxin and Alcohol Ingested and Severity of Reaction

Fig. 3 illustrates a lack of correlation between the estimated dose of saxitoxin ingested and the severity of the illness, which cannot be explained by the amount of alcohol ingested. Calculation of Spearman's correlation coefficient showed that no statistically significant correlation was present ($D^2 = 255.5; \rho = +0.62$).

Treatment and Clinical Response

No specific therapy is available and supportive measures were all that could be offered. All patients recovered within a few days, although some reported continued debility and malaise for some weeks afterwards.

Immunogenicity of Saxitoxin

Sera from 2 patients (Table II) did not provide protection to mice in this test. All mice died and no significant extension of death time was observed in either case. It appears that neither of these patients produced protective antibody in response to paralytic shellfish poisoning.

DISCUSSION

Red Water

Blooms of toxic and non-toxic dinoflagellates and ciliates in Cape waters usually result under calm conditions after upwelling (i.e. when dispersal is minimal) and when temperature, light and nutrient factors are optimal for an accelerated growth rate (some species can reproduce asexually at a rate of two doublings per day).
Unfortunately, owing to the sparsely populated nature of the west coast of South Africa, scientific observations of discoloured water are usually only noted when the bloom is in its final stages. Initiation and maintenance stages of the bloom have not been scientifically documented and the mechanisms of bloom formation are not well understood.

Gonyaulax catenella

This dinoflagellate is chain-forming and armoured. It is bio-luminescent at night and renders sea water an orange-brown colour. Its extreme toxicity has been known for 40 years and it has recently been shown that roughly 1 MU of toxin is produced per 40,000 cells. The organisms occur in maximum numbers when the temperature is between 14°C and 15°C, although they occur over a range of 9.5°C - 16°C.

Saxitoxin

The structural formula of saxitoxin is known. According to Narahashi, this neurotoxin blocks impulse conduction of giant axons in squid at very low concentrations, i.e. it inhibits the sodium/potassium pump that controls the electrical conduction in the nerve. The prevention of nerve impulses to the diaphragm may cause death by respiratory paralysis within 24 hours after ingestion by humans.

From the limited study reported it would appear that the immunological response to saxitoxin does not confer protection; thus prospects of developing an antiserum are probably poor.

Toxic Effects on Marine Life

Three toxic outbreaks along the Cape west coast have occurred during the past 20 years. Those occurring in 1966 - 1967 and in 1967 - 1968 have been well documented and by 1973 (i.e. 6 years later) there was still no sign of any recovery in the white mussel populations of the affected areas. It is likely that the current episode will also have similar long-lasting effects.

## Table 11. Death of Mice After Injection of Serum/Toxin Mixture

<table>
<thead>
<tr>
<th>Sample</th>
<th>Mean to death</th>
<th>Serum saxitoxin mixture (MU/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum 1</td>
<td>9 min 0 sec</td>
<td>1,17</td>
</tr>
<tr>
<td>Serum 2</td>
<td>7 min 40 sec</td>
<td>1,30</td>
</tr>
<tr>
<td>Patient B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum 1</td>
<td>5 min 40 sec</td>
<td>1,70</td>
</tr>
<tr>
<td>Serum 2</td>
<td>4 min 22 sec</td>
<td>2,22</td>
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<tr>
<td>Pooled normal human serum</td>
<td>8 min 25 sec</td>
<td>1,21</td>
</tr>
<tr>
<td>Saxitoxin control</td>
<td>8 min 15 sec</td>
<td>1,23</td>
</tr>
</tbody>
</table>

Clinical Features and Treatment

Although the severity of illness is usually regarded as being related to ingested dose, this was not obvious in the cases reviewed, although the clinical features were quite typical. It was fortunate that no deaths occurred, although several of the patients were estimated to have ingested more than 30,000 MU of toxin. Previous suggestions that alcohol may have a protective effect could not be substantiated, and the general picture seemed to indicate a wide range of individual susceptibility to the effects of the toxin.

A major difficulty with clinical diagnosis is that the symptoms are often interpreted as those associated with drunkenness.

There is at present no antidote to paralytic shellfish poisoning, but it has been shown that saxitoxin may behave as a hapten when conjugated to a suitable protein carrier. Antiserum prepared against bovine serum albumin/saxitoxin conjugates protected mice from the lethal effects of a challenge dose containing 0.35 μg saxitoxin.

As mortality has been ascribed to respiratory paralysis, it is presumed that with modern life support systems even such patients could be kept alive until all the toxin has been excreted.

It is regrettable that urinary excretion of saxitoxin and serum creatinine kinase levels were not determined in these cases, as the former could have given a better picture of the ingested dose and the latter is thought to indicate the severity of the intoxication.

Epidemiological Control

Control of the outbreak was greatly facilitated by the mass media, as has been the experience elsewhere, and by the inspection of restaurant premises and seizure of mussel stocks by City Health and Sea Fisheries inspectors. That both approaches were needed was proved in the case of at least one restaurateur who was unimpressed by the publicity and claimed that he knew all about mussel poisoning and had an antidote to give anyone poisoned in his restaurant. Rather than put this to the test, inspectors confiscated and destroyed his mussels.

Public awareness of the hazard will doubtless wane with time and practitioners are likely to face repeated episodes of such illness in brave or foolhardy gourmet patients.

For public health protection, officials are faced with two choices: to monitor shellfish toxicities or to close the coast to shellfishing altogether. The former course, with suitable warnings to the public, is recommended.

Acknowledgements are made to the many members of staff of our organizations who assisted in this project. The Medical Officer of Health, City of Cape Town, the Director, Sea Fisheries Branch, and the Chief, Health Laboratory Services, Cape, are thanked for permission to publish.

REFERENCES

The Respiratory Depressive Effects of Intravenous Buprenorphine in Patients in an Intensive Care Unit

J. W. DOWNING, N. M. GOODWIN, J. HICKS

SUMMARY

Buprenorphine hydrochloride, a new, potent, long-acting synthetic opiate analgesic, with partial agonist-antagonist activity, was administered intravenously to two groups of patients in an intensive care unit. Arterial blood was drawn for blood gas analysis before (control) and at regular intervals after drug administration, to determine the effects of intravenous buprenorphine on respiration in critically ill patients, each acting as his or her own control.

Intravenous buprenorphine 0.4 mg (group I — 10 patients) caused a significant reduction in mean respiration rate and an increase in mean PaCO₂ but did not alter heart rate, PaO₂ or base excess values.

Intravenous buprenorphine 0.2 mg (group II — 10 patients) was associated with a less significant reduction in the rate of breathing and elevation of PaCO₂.

Both 0.4 mg and 0.2 mg buprenorphine produced effective relief of pain, sedation, and reduction in restlessness, and allayed anxiety. Our results suggest that intravenous buprenorphine 0.2 mg can be safely recommended for the prolonged relief of postoperative pain in adults.


Buprenorphine hydrochloride, a new, potent long-acting analgesic, is a synthetic opiate with partial agonist-antagonist activity. It is 40 - 50 times more potent than morphine and has twice its duration of action. Buprenorphine produces a similar degree of respiratory depression as does morphine, but causes appreciably more drowsiness.\(^{1,4}\)

In this article our observations on the changes induced in blood gas status and respiration rate by intravenous buprenorphine 0.4 mg and 0.2 mg administered to patients treated in the intensive care unit (ICU) at Addington Hospital, Durban, are presented. The degrees of anxiety abatement, decrease in restlessness, sedation or drowsiness, and pain relief afforded by this new analgesic are also documented.

PATIENTS AND METHODS

A total of 20 patients was admitted to the study, and all gave their informed consent for the investigation. In most cases their body mass was unknown, as most were admitted as emergencies to the ICU, where no means of weighing bedridden patients exist at present.

No patient with clinical evidence of raised intracranial pressure or with a recent history of myocardial infarction was admitted to the study. Pregnant women, patients sensitive to opiates and those unable to communicate meaningful information about their pain were also excluded. Those who received concomitant interfering or potentially interacting medication (sedatives, analgesics, general anaesthesia) were studied at least 6 hours after such drug administration.

The first 10 patients (group I) were admitted as emergency cases to the ICU. Clinical data referring to group I patients appear in Table I.

Experience in 1 patient in this group, in whom the respiration rate was markedly depressed after intravenous buprenorphine 0.4 mg, together with the observation that respiratory depression was possibly submaximal at 3 hours, necessitated modification of our study programme. The dose of buprenorphine was reduced by half to 0.2 mg, and further blood sampling was started 4 hours after