

Table 1 Drugs used in serotonin syndrome

Chlorpromazine	25 mg intramuscular <sup>7</sup>
Cyproheptadine	4 mg every 2–4 hours (0.5 mg/kg/day) <sup>8,9</sup>
Propranolol	20 mg three times a day by mouth <sup>10</sup>
Methysergide	2–6 mg/24 hours <sup>11</sup>
Benadryl	50 mg intramuscular <sup>12</sup>
Clonazepam	0.5 mg intravenous <sup>13</sup>

(D) The presence of at least three of altered mental status, agitation, tremor, shivering, diarrhoea, hyperreflexia, myoclonus, ataxia, or fever.

Differential diagnoses include sepsis, neuroleptic malignant syndrome, sympathomimetic overdose, heat stroke, anticholinergic toxicity, delirium tremens, baseline psychiatric symptoms, and lethal catatonia. There is considerable overlap with neuroleptic malignant syndrome, and many patients may be taking both antidepressants and neuroleptic drugs. Patients with neuroleptic malignant syndrome tend to be more toxic, with a higher fever and myoclonus is uncommon, the muscle rigidity tending to be leadpipe.

Severity ranges from mild, self limiting symptoms that spontaneously resolve to severe cases with rhabdomyolysis and renal failure. In one study, 70% of cases resolved within 24 hours, although 40% required intensive care unit admission.<sup>7</sup> Mortality is estimated at 11%.

The basic principles of management are the prompt discontinuation of serotonergic medications and provision of adequate supportive care. With this management most cases resolve within 24 hours. Supportive care includes fluid resuscitation for dehydration, rhabdomyolysis and hypotension, and active cooling in high fever.

If symptoms are severe or persistent a number of drugs may be used, most of which block postsynaptic serotonin receptors (table 1<sup>6</sup>). Hyperthermia (temperature >40.5° C) indicates severe disease with significant complications and mortality. Drugs may be used to limit excessive muscle contraction, which contributes to fever, rhabdomyolysis, and musculoskeletal respiratory failure. The most widely used are benzodiazepines, particularly clonazepam, which will control myoclonus and prevent seizures. Theo-

retical arguments exist for the use of  $\beta$  blockers, which act at 5-HT<sub>1A</sub> receptors, in addition to their negative chronotropic effect.

Several authors report successful treatment with chlorpromazine,<sup>7</sup> a relatively potent 5HT<sub>2</sub> antagonist, although it may lower the seizure threshold, as occurred in this case. Cyproheptadine is also reported to be effective.<sup>8,9</sup> Management of complications such as seizures, ventricular tachycardia, or respiratory compromise involve standard techniques.

### Summary

Serotonin syndrome is a potentially life threatening condition which may be seen in the emergency department in patients taking antidepressants, the early recognition and treatment of which is vital if morbidity and mortality are to be avoided. The diagnosis should be considered in patients presenting with altered mental state, fever, or neuromuscular changes. The increasing use of venlafaxine and other potent serotonergic drugs in potentially suicidal patients may result in increasing numbers of such patients presenting to emergency departments with symptoms of serotonin syndrome following deliberate overdose.

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## Puffer fish poisoning

Jonathan Field

### Abstract

**Regarded by many as a delicacy, puffer fish (*Lagocephalus scleratus*) is a lethal source of food poisoning with a high mortality. It contains tetrodotoxin which can cause death by muscular paralysis, respiratory depression, and circulatory failure. A case of mild intoxication is reported and the literature reviewed.**

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### Case report

A 36 year old Korean seaman presented to the accident and emergency (A&E) department at 0300 hours. He was accompanied by a shipmate who indicated, in broken English, that he had been poisoned by an unusual type of seafood that he'd caught and prepared himself about 4–5 hours previously. He identified the puffer (toad) fish photographed in Straun Sutherland's book of *Australian Animal Toxins*.<sup>1</sup>

On examination he was having some difficulty breathing and articulating. His pulse rate

was 96/minute, blood pressure 160/100 mm Hg, and respiratory rate 20/minute. His limbs were symmetrically flaccid with a grade 2/5 weakness and absent deep tendon reflexes. He obeyed commands and his pupils were constricted. His oxygen saturation, breathing 100% oxygen, was 100%, arterial oxygen tension 13.3 kPa, carbon dioxide tension 4.9 kPa, and pH 7.37. Routine biochemistry and coagulation profile were normal. He did not require intubation or ventilation, was given intravenous fluids, nil by mouth, and nursed on his side.

Six hours later he had much improved. He indicated that he had tingling around his mouth and in his fingers, he now had no trouble breathing, and could speak normally. His power was now 4/5, his reflexes had returned, and his pupils normally reacting to light and accommodation.

He complained of nausea and continued to vomit throughout the day. He was able to mobilise by the next day but had a wide based, high stepping gait and positive Romberg's sign. This gradually resolved and by day 3 he had made a full recovery.

### Discussion

"... and whatsoever hath no fins and scales ye may not eat; it is unclean unto you" (Deuteronomy 14:9–10). The puffer fish is illustrated on an Egyptian tomb of the fifth dynasty dated 2500 BC.<sup>2</sup> Captain Cook was poisoned by it in 1774<sup>3</sup> and the voodoo poisons of Haitian folklore responsible for "zombification" reportedly contains tetrodotoxin.<sup>4</sup>

Puffer fish, or Fugu, is a delicacy in Japan where specially trained chefs prepare it, and in 1989 a Fugu restaurant opened in New York City.<sup>5</sup> The small amount of toxin present in correctly prepared fish produces a mild tingling around the mouth, which, together with the thought of sharing a potentially fatal dish with your friends, supposedly adds to the gastronomic experience.<sup>1</sup>

Tetrodotoxin is also found in the venom on the blue ringed octopus found around Australia and involved in human fatalities through bites.<sup>6</sup>

### PHARMACOLOGY

Tetrodotoxin blocks sodium channels through which sodium ions flow during the rising phase of the action potential. It binds to receptors close to the extracellular surface, quite different to local anaesthetics which bind to receptors near the inner end of the channel.<sup>7</sup> It acts on peripheral nerves, motor, sensory, and autonomic.<sup>8</sup>

It has a direct central effect on the chemoreceptor trigger zone causing nausea and vomiting, on the respiratory centre depressing respiration,<sup>9</sup> and may cause a drop in blood pressure by relaxing vascular smooth muscle and blocking peripheral autonomic nerves.<sup>8</sup> Response to cholinesterase inhibitors also suggests a reversible competitive blockade at the motor end plate.<sup>10 11</sup>

Tetrodotoxin is one of the most toxic substances known; it is 275 times more lethal

than cyanide and 50 times more potent than strychnine or curare.<sup>12</sup>

### CLINICAL PRESENTATION

In any case of suspected food poisoning accompanied by neurological signs, the history should focus on the consumption of seafood. Symptoms typically begin within 30 minutes of ingestion and range from mild paraesthesia and nausea to full paralysis, hypotension, and death from respiratory failure.<sup>13</sup> Death has been recorded within 17 minutes of ingestion<sup>14</sup> and overall mortality may reach 60%,<sup>15</sup> but epidemiological evidence suggests that those who survive 24 hours fully recover.<sup>5</sup>

Considerable caution must be taken when pronouncing death due to puffer fish poisoning. The toxin may produce a deceptive state of apparent suspended animation,<sup>10</sup> similar to the phenomena of awareness under anaesthesia, which is the reason why it holds such favour with the Voodoo priests in Haiti.<sup>4</sup>

### TREATMENT

There is currently no effective antidote to tetrodotoxin poisoning. Treatment is entirely supportive and may involve mechanical ventilation or inotropic support.<sup>16</sup>

Gastric emptying procedures have been advocated as essential<sup>1 5 9 10 16</sup> but are now losing favour with the emergency medicine community in the treatment of acute poisoning.<sup>17</sup> Activated charcoal is said to effectively bind the toxin.<sup>15</sup> Advocated treatments yet to be of proved benefit include cholinesterase inhibitors, naloxone, cysteine, gastric lavage with sodium bicarbonate,<sup>15</sup> antihistamines, and steroids.<sup>16</sup>

Future effective treatment is a possibility. When monoclonal neutralising antibody was injected into mice poisoned with oral tetrodotoxin it resulted in 100% survival compared with 0% survival in the control group.<sup>18</sup> No reports have yet appeared of its use in man.

### Conclusion

Our case provides a clear illustration of the variety of neurological signs and symptoms produced by tetrodotoxin, and reinforces the need for vigilance in the A&E departments of our multicultural society.

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## EMERGENCY CASEBOOK

### Delayed spinal cord compression in ankylosing spondylitis

A 45 year old man with long standing ankylosing spondylitis tripped and fell backwards against a concrete pillar when walking to catch a bus. He did not lose consciousness and presented to the casualty department 20 minutes later complaining of pain in his neck and left shoulder. On examination he was tender over his vertebra prominens and had paraesthesiae over the left C8 dermatome. No other focal neurology was found. Spinal x rays showed fusion of most of the cervical and thoracic vertebral bodies but no fractures were seen. A diagnosis of C8 root compression was made and he was referred to the orthopaedic team for further assessment.

Four hours later he complained of numbness up to his umbilicus. On examination he now had a flaccid paralysis of his lower limbs and reduced left upper limb power. A magnetic resonance imaging scan of his spine revealed an epidural haematoma extending from C5 to T5 on the dorsal aspect of the spinal cord (fig 1). The neurosurgical team performed an emergency cervical laminectomy to decompress the spinal cord, during which the C4 spinous process was found to be fractured.

Minor trauma in patients with ankylosing spondylitis can result in vertebral fractures, which bleed into the spinal canal and form haematomas causing delayed spinal cord compression.<sup>1</sup> Because of the distorted anatomy in ankylosing spondylitis, spinal fractures may be difficult to identify on plain x rays.<sup>2</sup> In the case described, the vertebral fracture found during surgery could not be seen on the cervical films. The fact that the patient had sustained a serious injury only became apparent when his neurological status rapidly deteriorated. Thus, when patients with ankylosing spondylitis present to the A&E department following an episode of trauma, a period of neuro-observation is useful and should signs of spinal cord compression develop, urgent neurosurgical consultation is indicated.



*T-1 weighted MRI scan of cervical spine showing epidural haematoma (arrow) on dorsal aspect of spinal cord.*

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