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Letters to the Editor

Infection and infectious diseases

Sir,

Dr Critchley's criticism[1] of my 'condensed review'[2] contains errors when he states that it contained statements that could be misconstrued and do not reflect experience gained from three recent outbreaks. He quotes three references. The first[3] refers to his analysis of 27 patients with one type of botulism seen by a number of physicians in a small area of one small country. The second and third references[4,5] each refer to outbreaks in one patient. The world is larger than one country and writing for a journal that has an international readership demands a more than parochial view. My review started by mentioning 'his' outbreak but it is obvious that I thereafter took a broader look at botulism.

In individual outbreaks symptoms differ. I said 'symptoms of gastroenteritis are usually notable by their absence.' Christie[6] states 'unlike other forms of food poisoning, botulism produces almost no signs of gastrointestinal irritation' and this world view is held by others 'there may be little in the earliest symptoms that suggests foodborne disease.'[7]

Critchley objects to my comment that patients might be found dead. Whilst all patients survived and no unexplained deaths occurred in the outbreak described by Critchley, in areas of the world other than Britain the mortality rate may be higher. Schaffner[7] gives a figure of 25% given antitoxin, and intensive respiratory support – all of which may not be available in developing countries where the incidence and mortality of botulism would be higher. Whole families of Eskimos have been found dead[6] and in infant botulism *Cl. botulinum* or its toxin were found in 10/280 of unexpected sudden infant deaths in one study[8] and in 9/70 in another.[9]

Critchley states correctly that the presence of fever or drowsiness does not exclude botulism. However, the presence of *anything* does not exclude *any* diagnosis. Schaffner states 'patients are *afebrile*' (his italics) and 'development of fever signifies complicating nosocomial infection.'[7] Critchley states 'antibiotics are best reserved for secondary complications except in the presence of infantile or other toxico- infective forms of botulism' – so his recommendation is that antibiotics are *not* to be given. However, I said that 'some physicians give penicillin to eliminate gut carriage.' Opinions do differ – no one knows – so that the proper question that should be asked is, in our current state of uncertainty, 'Would prescribing antibiotics be likely to do more good than harm?'

I said that treatment includes urgent administration of antitoxin. Critchley states, correctly, that antitoxin treatment is only of *proven* (my italics) value in type E intoxication. Reading the literature it is apparent that antitoxin might be beneficial in other types – but how does a clinician know which type he is dealing with unless there is, at the time when individual patients present, an obvious outbreak with rapid accurate clinical and botulinum type diagnosis? Indeed, in the one well described and recent outbreak, botulism caused by type B toxin, all new patients and those whose condition had yet to stabilize received toxin.[3] If I had botulism, on balance, I would want antitoxin without waiting for type identification.

P.D. Welsby
Department of Infectious Diseases,
City Hospital,
51 Greenbank Drive,
Edinburgh EH10 5SB, UK.

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Intraocular pressure

Sir,

With tons of journals received weekly, I usually read the table of contents of each to decide which articles I should read in depth. I was immediately attracted to the paper by Al-Sereit *et al.*[1] when I read the title 'Intraocular pressure and papillary responses in patients with diabetes mellitus' in the Contents of the March issue of the *Journal*. I was curious to know if the papillary responses referred to the optic papilla or the renal papillae.

I, of course, was very surprised to find that it was the pupillary responses, not papillary responses, the article was about. Thanks to this printing error, I was glad that I learned something about the autonomic neuropathy in patients with diabetes mellitus.

Tsung O. Cheng, M.D.
Division of Cardiology,
The George Washington University,
2150 Pennsylvania Avenue, N.W.,
Washington, DC 20037, USA.

Reference

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It is a pleasure to have contributed, albeit inadvertently, to Professor Cheng's continuing medical education.

Editor
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Ketanserin overdose: a case report

Sir,

Ketanserin (3-{2-[4-<4-fluorobenzoyl>-1-piperidinyl]-ethyl}-2,4-[1H,3H]-quinazolinedione) is a serotonin antagonist available in Great Britain on a named patient basis for the treatment of Raynaud's disease, peripheral vascular disease and hypertension. The recommended daily dose is 20–40 mg twice daily. Known side effects include sedation, dizziness, headache, dry mouth and nausea[1] as well as prolongation of the QTc time and ventricular arrhythmias.[2,3] There are no published data on its effects in overdose in man. We report a case of self-poisoning with ketanserin and discuss its clinical manifestations.

A 16 year old schoolgirl with a history of Raynaud's disease presented 90 minutes after taking 160 20 mg tablets of ketanserin. She was somnolent and uncooperative but easily rousable and fully orientated. Her blood pressure was 100/60 mmHg, pulse 60/min and regular, temperature and respiration were normal. She was flushed and well perfused; hands, feet and ears, usually cold and cyanosed, were pink and warm. Her fingers were slightly swollen, there was conjunctival injection and the pupils were constricted but briskly reactive. No other abnormalities were found on physical examination. Potassium was low at 3.3 mmol/l, sodium, urea, creatinine and full blood count were normal. The electrocardiogram showed a prolongation of the QTc time to 0.53 ms. Gastric lavage was performed within 2 hours of ingestion. Treatment was supportive with elevation of legs and intravenous normal saline. Nausea, headaches or blurred vision were not observed or reported. Her blood pressure remained low at 90/50 mmHg during the first 12 hours. There was a relative bradycardia of 70/min and she felt faint on rising. By the next morning, 18 hours after admission, her blood pressure was 120/80 mmHg with normal postural response and a heart rate of 90/min. She remained well after discontinuation of intravenous fluids. Twenty-four hours after ingestion of the tablets she was still flushed, but her hands and feet were cool as usual.

Ketanserin levels were 2873 ng/ml 3 hours and 151 ng/ml 18 hours after ingestion. Ketanserinol concentration was 1155 ng/ml at 3 hours and 1117 ng/ml at 18 hours. Liver functions and repeat urea, electrolytes and creatinine were normal.

Ketanserin is well absorbed, achieving peak levels 30–120 min after oral administration but bioavailability is poor (50%) because of extensive first pass hepatic metabolism.[4] The mean terminal half life following single oral doses is 10–18 hours but increases to 29 hours after multiple doses because of reoxidation of its metabolite ketanserinol to ketanserin.[1] Steady state plasma levels during chronic oral treatment with 40 mg twice daily are 100–140 ng/ml.[5] The patient reported here took 3200 mg (59 mg/kg) ketanserin. Her levels fell from 2873 ng/ml at 2 hours to 151 ng/ml 18 hours after ingestion. This decline is much faster than expected from the elimination half-life. It is notable that the level of ketanserinol remained high. A failure of the reoxidation mechanism in the presence of very high ketanserin levels would explain the observed rapid clearance of ketanserin.

In conclusion, on the basis of this experience, ketanserin appears to be relatively safe in overdose in humans. The main problems were hypotension and relative bradycardia. We did not observe ventricular arrhythmias but the prolonged QTc time clearly put her at risk of developing torsades de pointe. Hypothermia might also be predicted, unless ambient temperatures are warm. However, more serious effects are clearly possible in elderly or hypertensive patients, and more experience is required to exclude significant toxicity.

Christine Roffe
Mark Tidmarsh
Trevor A. Howlett
Leicester Royal Infirmary, Leicester LE1 5WW, UK.

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Hepatitis B virus (HBV) and human immunodeficiency virus (HIV) infection in Spanish leprosy patients

Sir,

In 1967, Blumberg first reported an association between leprosy and the so-called Australian antigen. Moreover, he later reported that the prevalence of chronic HBV infection differed between lepromatous and tuberculoid forms of leprosy.[1] Some authors have confirmed a high prevalence of chronic HBV infection in leprosy patients,[2,3] while others have denied such an association.[4] Likewise, more recently, a possible link between leprosy and HIV infection has also been reported, namely, a high prevalence of HIV infection among leprosy patients[5] as well as a worse course of leprosy when HIV infection is associated.[6] Since most of these studies have been per-

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Tsung O. Cheng

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Notes