Hyponatraemia and seizure due to overdose of trazodone

Drs G BALESTRIERI, B CERUDELLI, S CIACCIO, and D RIZZONI (Clinica Medica University of Brescia, 25100 Brescia, Italy) write: We describe a case of trazodone overdose in which hyponatraemia and seizures occurred.

A 72 year old woman was admitted to hospital 10 hours after taking about 350 mg of trazodone. She had suffered from anxiety and depression for 10 years and had been prescribed trazodone 25 mg daily and oxazepam. She was also taking propranolol for hypertension. She denied alcohol misuse. Physical examination did not show any abnormality. She was fully oriented with a blood pressure of 180/100 mm Hg and a pulse rate of 86 beats/min.

Glucose and saline infusions were started at a rate of 1000 ml of 5% glucose and 500 ml of 0.9% saline a day. Twenty hours later she was sweaty and anxious. Her blood pressure was 210/110 mm Hg and her pulse rate 120 beats/min. She experienced two brief tonic-clonic seizures, which were treated with intravenous diazepam. At this stage her serum sodium concentration was 118 mmol/l, potassium 3.8 mmol/l, chloride 84 mmol/l, creatinine 62 µmol/l, urea 10.1 mmol/l, and uric acid 0.23 mmol/l. Her packed cell volume was 0.41, serum osmolality 246 mmol/l, and urine osmolality 538 mmol/l. She was treated with fluid restriction, and in the next three days hyponatraemia gradually resolved. An electroencephalogram was normal. Computed tomography of the brain showed a small ischaemic lesion of the subcortical white matter of the right hemisphere, which was not thought to be recent. She was discharged nine days after admission having had no further seizures.

Trazodone's pharmacological properties are poorly understood.¹ Its antidepressant effect is thought to result from its influence on serotonergic neurotransmission and α receptor blockade. Side effects are rare, and trazodone is considered to be fairly safe in overdose.^{2,3} The profound hyponatraemia in this case suggests inappropriate secretion of antidiuretic hormone. This has been associated with tricyclic antidepressants and other psychotropic drugs⁴ but not, to the best of our knowledge, with trazodone overdose.

1 Baldessarini RJ. Tricyclic antidepressants. In: Goodman A, Roll T, Nies A, Taylor P, eds. *Goodman and Gilman's the pharmacological basis of therapeutics*. 8th ed. New York: Pergamon Press, 1990:405-14.

2 Gamble DE, Perterson LG. Trazodone overdose: four years of experience from voluntary reports. *J Clin Psychiatry* 1986;**47**: 544-6.

3 Lansky MR, Selzer J. Priapism associated with trazodone therapy: case report. *J Clin Psychiatry* 1984;**45**:232-3.

4 Hayes PE, Kristoff CA. Adverse reaction

to five new antidepressants. *Clin Pharm* 1986;**5**:471-80.

5 Garson M. Syndrome of dilutional hyponatraemia secondary to tricyclic antidepressants. *Practitioner* 1979;**222**:411-2.

6 Ananth J, Lin KM. SIADH: a serious side effect of psychotropic drugs. *Int J Psychiatry Med* 1986;**16**:401-7.

Antibiotic sensitivity testing in enteric salmonella

Drs Y J DRABU, A K SHARMA, A YARDUMIAN, and Mrs P H BLAKE-MORE (North Middlesex Hospital, London N18 1QX) write: The role of antibiotics in bacterial diarrhoea has been under debate since the new quinolones were introduced.¹ Evidence indicates that ciprofloxacin can be used to treat bacterial diarrhoea^{2,3} as well as to eradicate carriage of salmonella.⁴ Reports are beginning to appear of resistance of salmonella to quinolones associated with resistance to other, unrelated antimicrobials.^{5,6} This leads to therapeutic problems. We report resistance of *Salmonella virchow* to quinolones in a patient with sickle cell disease which highlights problems in laboratory and clinical management.

A 24 year old West Indian with mild sickle cell disease required admission to hospital for his disease roughly every 12 months. He received oral phenoxymethylpenicillin prophylactically. In September 1988 *S virchow* was found in his stool. He was asymptomatic and did not give a history of gastroenteritis or travel abroad. He did not receive any treatment then but when admitted to hospital with an exacerbation of his sickle cell disease in February 1989 was treated empirically with a seven day course of ciprofloxacin 500 mg 12 hourly. He recovered rapidly and was discharged home after three days, whereupon he stopped taking his antibiotic treatment.

He first attended the North Middlesex Hospital in July 1989, where he was found still to be carrying *S virchow* in his stool. Again he was given no specific treatment for this, but in May 1990 he developed signs and symptoms of a urinary tract infection. Culture confirmed the presence of *Escherichia coli*. He was prescribed a seven day course of ciprofloxacin 500 mg 12 hourly. Details of his past drug treatment were unavailable. His symptoms resolved after three days, and again he stopped his course of antibiotic. *S virchow* was isolated from his stool after the second course of ciprofloxacin.

The table shows the sensitivities of the isolate to antibiotics over the period. The initial isolate, obtained in September 1988, was sensitive to nalidixic acid and ciprofloxacin. Resistance to nalidixic acid developed with a concomitant reduction in

susceptibility to ciprofloxacin after the initial course of ciprofloxacin. This had not been detected in July 1989 because antibiotic sensitivity tests had not been done.

Ciprofloxacin is not licensed for the treatment of bacterial diarrhoea, yet in our hospital, and many others, it has become the antibacterial of choice for severe bacterial diarrhoea and invasive salmonellosis. Resistance to quinolones is still rare in *Salmonella* sp, and splenic infarction in our patient in conjunction with the incomplete course of antibiotic may have contributed to the development of resistance in this case.⁸

We urge clinicians and microbiologists who are treating bacterial diarrhoea to use quinolones with restraint and suggest that tests of sensitivity to quinolones should be done routinely in cases of enteric salmonella infection. In the North East Thames region eight of 16 laboratories routinely test isolates obtained in cases of enteric salmonella infection against ciprofloxacin and none test them against nalidixic acid (an indicator of potential resistance to quinolones). Most hospitals in England and Wales send isolates of salmonella to the Division of Enteric Pathogens, Colindale, for epidemiological purposes, including sensitivity testing. Currently resistance to antibiotics is not reported by the reference laboratory. It would clearly be valuable for the referring laboratory if resistance to quinolones was reported.

1 Dupont HL, Corrado ML, Subbaj T. Use of norfloxacin in the treatment of acute diarrhoeal disease. *Am J Med* 1987;**82**: 79-83.

2 Pichler HET, Diridl G, Stickler K, Dietmar W. Clinical efficacy of ciprofloxacin compared with placebo in bacterial diarrhoea. *Am J Med* 1987;**82**:329-32.

3 Goodman LJ, Trenholme GM, Kaplan RL, Segreti J, Tunes D, Petrak R, et al. Empiric antimicrobial therapy of domestically acquired acute diarrhoea in urban adults. *Arch Intern Med* 1990;**150**:541-6.

4 Ericsson CD, Johnson PC, Dupont HL, Morgan DR, Bitsura JM, De La Cabada FJ. Ciprofloxacin or trimethoprim-sulfamethoxazole as initial therapy for travellers' diarrhoea. *Ann Intern Med* 1987;**106**:216-20.

5 Diridl G, Pichler H, Wolf D. Treatment of chronic salmonella carriers with ciprofloxacin. *Eur J Clin Microbiol* 1986;**5**:260-1.

6 Piddock LJV, Whale K, Wise R. Quinolone resistance in salmonella: clinical experience. *Lancet* 1990;**335**:1459.

7 Howard AJ, Joseph TD, Bloodworth LLO, Frost JA, Thurn H, Rowe B. The emergence of ciprofloxacin resistance in *Salmonella typhimurium*. *J Antimicrob Chemother* 1990;**26**:296-8.

8 Zumla A, Lewis D, Brown J. Ciprofloxacin treatment of recurrent *Salmonella typhimurium* septicaemia in the splenectomized and immunocompromised patient. *J Antimicrob Chemother* 1988;**21**:809-10.

Acute anaphylaxis due to topical chlorhexidine acetate

Dr R J EVANS (Royal Infirmary of Edinburgh, Edinburgh EH3 9YW) writes: I report a case of acute anaphylaxis associated with the topical application of a dressing containing chlorhexidine acetate 0.5%.

A 19 year old man attended the accident and emergency department with a partial thickness burn to his left arm. The burn was cleaned and dressed with a tulle gras dressing impregnated with soft white paraffin BP containing the antiseptic chlorhexidine acetate BP 0.5%. The patient then complained of pruritus and feeling lightheaded. Examination showed a widespread erythematous rash, periorbital oedema, and mild angio-oedema. He had a sinus tachycardia and a systolic blood pressure of 90 mm Hg. Auscultation showed only an expiratory wheeze. He was treated for acute anaphylaxis with oxygen, intravenous colloid, antihistamines, nebulised β agonists, and corticosteroids. He made a complete recovery. His burn was subsequently dressed with a semi-permeable adhesive film and healed with no further complications.

The patient's history included exposure to chlorhexidine for a burn sustained in 1987. He had also suffered from asthma as a child and was allergic to cats. The only other drugs given on this occasion were a mixture of 50% nitrous oxide and 50% oxygen for analgesia while the wound was being dressed. A scratch test with chlorhexidine acetate 0.05% gave a positive result. Re-exposure to nitrous oxide produced no reaction.

We have found one previous report of a severe allergic reaction with hypotension and generalised flushing after application of a chlorhexidine dressing.¹ In addition, in six patients who developed life threatening reactions allergy to topical chlorhexidine was confirmed by intradermal, scratch, and epicutaneous tests.² It has been suggested that the mechanism of action is mediated by IgE antibodies.³

1 Cheung J, O'Leary JJ. Allergic reaction to chlorhexidine in an anaesthetised patient. *Anaesth Intensive Care* 1985;**13**:429-30.

2 Okano M, Nomura M, Hata S, Okada N, Sato K, Kitano Y, et al. Anaphylactic symptoms due to chlorhexidine gluconate. *Arch Dermatol* 1989;**125**:50-2.

3 Ohtoshi T, Yamauchi N, Tadokoro K, Miyachi S, Suzuki S, Miyamoto T, et al. IgE antibody-mediated shock reaction caused by topical application of chlorhexidine. *Clinical Allergy* 1986;**16**:155-61.