

therapeutic effect but better side-effect profiles than more traditional antipsychotics (Lader, 1999).

A 30-year-old patient with paranoid psychosis for 5 years and seizures for 12 years, described on average two generalised seizures a year, improving with valproate. His psychosis had been controlled with zuclopenthixol for 2 years. He had normal electroencephalograms (EEGs) in 1986 and 1998, including a sleep study while taking zuclopenthixol but not valproate. His psychosis relapsed secondary to non-compliance with medication and so zuclopenthixol 400 mg twice weekly was recommenced. He improved, but owing to concerns over potential side-effects was changed to olanzapine 10 mg daily. Over the next 3 months he suffered increasing seizures culminating in a generalised or tonic-clonic seizure resulting in bilateral humeral head fractures, one of which required internal fixation.

There was no metabolic or electrolyte disturbance. An EEG showed multifocal and generalised epileptiform discharges similar to those seen with clozapine, which are unusual for zuclopenthixol. They resolved on withdrawal of olanzapine and reinstitution of zuclopenthixol.

Conventional neuroleptics lower seizure threshold, yet this patient with a history of epilepsy had normal EEGs while on zuclopenthixol. Manufacturer's trials gave a seizure rate, similar to other antipsychotics, of 0.88% patients (product data sheet, Eli Lilly). However, other epileptogenic factors were present in these patients and also in two subsequent case reports involving olanzapine and seizures (Lee *et al*, 1999; Wyderski *et al*, 1999).

Our patient thus represents the strongest case to date implicating olanzapine alone in lowering seizure threshold, with objective EEG support.

Post-marketing surveillance and case reports are a useful early warning system for reporting side-effects, for example, sertindole with cardiotoxicity and more recently olanzapine with impaired glucose tolerance. This serves to remind all practitioners of the importance of considering a possibly underemphasised side-effect within the context of a newly introduced therapy. Olanzapine should be used cautiously in patients who have a history of seizures.

Lader, M. (1999) Some adverse effects of antipsychotics: prevention and treatment. *Journal of Clinical Psychiatry*, **60** (suppl. 12), 18–21.

Lee, J. W., Crismon, M. L. & Dorson, P. G. (1999) Seizure associated with olanzapine. *Annals of Pharmacotherapy*, **33**, 554–556.

Wyderski, R. J., Starrett, W. G. & Abou-Saif, A. (1999) Fatal status epilepticus associated with olanzapine therapy. *Annals of Pharmacotherapy*, **33**, 787–789.

J. Woolley, S. Smith Maudsley Hospital, Denmark Hill, London SE5 8AZ

Olanzapine: concordant response in monozygotic twins with schizophrenia

There is growing evidence that genetic variation in several neurotransmitter systems (e.g. serotonergic) may influence the clinical response to different psychopharmacological drugs (Arranz *et al*, 1998, 2000). A previous paper (Vojvoda *et al*, 1996) described the concordant clinical response of a pair of monozygotic twins with schizophrenia when treated with clozapine. Now we report on two monozygotic twins concordant for DSM-IV (American Psychiatric Association, 1994) schizophrenia whose clinical response to olanzapine was also concordant.

The twins are now 60 years old. Twin 1 developed her first psychotic symptoms at age 21. Since then, she has been repeatedly admitted to hospital because of worsening of her psychotic symptoms, never returning to her premorbid level of functioning. She was treated with a wide variety of conventional antipsychotics, always with a poor response. Prior to her first psychotic breakdown, she suffered a seizure, and was treated with phenobarbital and valproate. At age 58 years she was started on olanzapine building up to a high dose (20 mg daily) to control her symptoms. With this drug she had a good response (both in positive and negative psychotic symptoms) and an improvement in her level of functioning.

Twin 2 had her first psychotic episode and hospital admission at age 24. Subsequently, she was treated with different conventional antipsychotics as well as with clozapine, but never achieved a successful recovery. She needed several hospital treatments and suffered two seizures, with normal electroencephalogram while taking clozapine and levomepromazine, and agranulocytosis under clozapine treatment. Encouraged by her sister's response to olanzapine, she was treated with 20 mg olanzapine daily. She showed a good

response, soon improving in both positive and negative symptoms, and in her level of functioning. Each twin is now symptom-free, working and living unaided. Their response to olanzapine treatment has been similar both in intensity and in the pattern of symptoms that have improved. To our knowledge, this is the first report describing monozygotic twins with similar illness characteristics who showed a similar response to olanzapine treatment. Our finding supports the view that, as with clozapine, genetic factors may be important in predicting response to olanzapine and other antipsychotic drugs.

American Psychiatric Association (1994) *Diagnostic and Statistical Manual of Mental Disorders* (4th edn) (DSM-IV). Washington, DC: APA.

Arranz, M. J., Munro, J., Sham, P., et al (1998) Meta-analysis of studies on genetic variation in 5-HT_{2A} receptors and clozapine response. *Schizophrenia Research*, **32**, 93–99.

—, —, **Birkett, J., et al (2000)** Pharmacogenetic prediction of clozapine response. *Lancet*, **355**, 1615–1616.

Vojvoda, D., Grimmell, K., Sernyak, M., et al (1996) Monozygotic twins concordant for response to clozapine. *Lancet*, **347**, 61.

I. Mata, V. Madoz Fundacion Argibide, Instituto de Salud Mental de Navarra, Apartado de Correos 435, 31080 Pamplona, Spain

M. J. Arranz, P. Sham, R. M. Murray

Department of Psychiatry, Institute of Psychiatry, London

Penile self-mutilation

Self-injurious behaviour, self-mutilative behaviour or self-harming behaviour are defined as deliberate destruction of body tissue without conscious suicidal intent (Feldman, 1988). An alternative definition of self-injurious behaviour is repetitive, direct physical self-harm that is evidently not life-threatening (Herpertz, 1995). Some other terms such as autoaggression, purposive accidents and focal suicide are also used. The three most commonly reported types of self-injurious behaviour are self-cutting of the skin, ocular self-mutilation and genital self-mutilation (Feldman, 1988). In Greilheimer & Groves's (1979) study a majority of cases of male genital self-mutilation had psychosis. Cases of non-psychotic genital self-mutilation include men with character disorders and transsexuality. Many of the patients seemed influenced by religious factors, such as

beliefs involving sexual guilt. Meninger (1935) viewed circumcision among Jews as a 'practical substitution' of the foreskin for the entire genitalia. In India, we have not before come across any report of penile auto-amputation.

A 24-year-old male was referred from a surgical ward for psychiatric evaluation after he had severed his penis with a knife. He came from a rural farming background and had received four years of formal education (up to 8 years). From childhood, he was preoccupied with religious matters and was always ready to eschew material gains for the betterment of his fellow man. In adulthood, he decided to adopt a true religious life after deciding to forego married life and a family of his own. He became popular in his village and the people would come to him to seek his blessings and guidance. He wanted to fulfil all the

obligations to attain *Moksha* (salvation). His extreme step of penile self-mutilation was also a step in the same direction as he did not want any sexual impulses to disturb him on his way to salvation. There was no past or family history of any psychiatric illness, chronic medical illness or drug misuse. On examination of his mental state, the patient was a pleasant and polite individual. Rapport was easily established. There was no evidence of any thought disorder, depression or perceptual abnormality. His orientation, memory and other higher mental functions were also normal. His explanation for penile self-mutilation was that he did not want to succumb to any sexual temptation which could obstruct his way to salvation.

The case is rare as he did not have any underlying psychiatric illness. His over-valued idea that sexual or married life is

contradictory to religious life is also not compatible with Hinduism. The subject did not have any sexual preoccupations but in his apprehension to save himself from any forthcoming sexual temptations, he performed penile self-mutilation.

Feldman, M. D. (1988) The challenge of self-mutilation: a review. *Comprehensive Psychiatry*, **29**, 252–269.

Greilshheimer, H. & Groves, J. E. (1979) Male genital self-mutilation. *Archives of General Psychiatry*, **36**, 441–446.

Herpertz, S. (1995) Self-injurious behaviour. *Acta Psychiatrica Scandinavica*, **91**, 57–68.

Meninger, K. A. (1935) A psychoanalytic study of the significance of self-mutilations. *Psychoanalytic Review*, **4**, 408–466.

M. S. Bhatia, S. Arora Department of Psychiatry, University College of Medical Sciences, Dilshad Garden, Delhi–110095, India

One hundred years ago

General paralysis in the Navy

IN the November number of the *Edinburgh Medical Journal* Surgeon F. H. A. Clayton, R. N., assistant medical officer at the Royal Naval Hospital, Yarmouth, publishes an analysis of the statistics of general paralysis as observed in the Royal Naval Asylum for a series of years, and discusses the question of its etiology, with especial reference to sexual excess, syphilis, and alcoholism. An investigation of this disease as it occurs in the navy possesses the advantage that the inquiry is limited to a distinct class of men who are particularly subject to it, whose medical history since entry has been recorded, and whose physical condition, environment, and even mental characteristics are much alike. That seamen are more liable than officers to this disease appears

from the fact that of 274 officers admitted in the last 25 years only 48 were paralytic cases, 12 of whom were warrant officers coming originally from the seamen class, whereas of 839 men 188 were paralytic cases. At present among 27 commissioned officers in the asylum there is no case, but, on the other hand, four out of six warrant officers and 18 out of 97 men come under that head. With respect to etiology Surgeon Clayton summarises his conclusions as follows: "Altogether, one inclines to accept the view that although syphilis or its toxins in many cases, by interference with nutrition, render liable to general paralysis many persons otherwise free, there is no evidence of direct connexion. The influences which act remotely are usually conditions tending to interference with nutrition and to promoting the growth of less

highly organised tissues while the proximate influences probably act by lowering vitality. A 'specific' cause, as yet unknown, capable of developing the disease *per se*, though often aided by various factors, and which usually selects those apparently most healthy and vigorous both in mind and body, seems to be indicated by all the evidence." As is well known, general paralytics always become bed-ridden and in the concluding paragraphs of his article Surgeon Clayton gives some useful hints for the prevention of bed-sores.

REFERENCE

Lancet, 10 November 1900, 1362.

Researched by Henry Rollin, Emeritus Consultant Psychiatrist, Horton Hospital, Epsom, Surrey