adenosine, so that its use is restricted to the short term. Despite this a preparation of adenosine is now available commercially, and several hospitals are producing their own preparation.[8]

Adenosine is best given as a fast bolus into a large peripheral vein and followed by a saline flush. Its very short action allows several doses to be given one after the other without risk of a cumulative effect. A low dose should be given initially and then increased if atrioventricular nodal blockade is not achieved. This is preferable to giving a single large dose because of the transient side effects of flushing and dyspnoea. The datasheet in the United Kingdom recommends an initial dose of 3 mg for adults, and occasionally arrhythmias will be terminated by this low dose. Further doses of 6 mg and then 12 mg may be given if necessary at one to two minute intervals. The upper limit for any single dose of adenosine is 12 mg—based on the finding that just over 90% of paroxysmal supraventricular tachycardias are terminated by that dose.[9] Adenosine has, however, been used safely at higher doses, and a further increment to 18 mg may increase the likelihood of termination of a supraventricular arrhythmia, although this high dose is usually associated with an increase in the severity of side effects. The dose for children is calculated on a basis of 0·05 mg/kg, increasing by 0·05 mg/kg increments to a maximum bolus dose of 0·25 mg/kg.[10] The most important drug interactions are with aminophylline, which antagonises the effects of adenosine, and with dipyridamole, which accentuates and prolongs its effects. Adenosine should be used cautiously in patients with asthma, in whom bronchospasm may be exacerbated.[11]

Adenosine is the drug of first choice for terminating paroxysmal supraventricular tachycardia in the presence of left ventricular dysfunction, concomitant β blockade or severe hypotension because of its very short half life and proved safety in these circumstances. Intravenous verapamil may be preferred in patients with asthma. In terms of the treatment of uncomplicated paroxysmal supraventricular tachycardia there seems little to choose between adenosine and verapamil. The claim that termination with adenosine is faster than with verapamil (promotional literature for Adenocor, Sanofi Winthrop, 1992) has little relevance to clinical practice. The difference between 20 seconds to termination with adenosine and 60 seconds with verapamil (after injection over 15 seconds) is not important for a patient with a stable arrhythmia—and the total time to termination is likely to be longer for adenosine if several injections are required. Nevertheless the fact that adenosine may be used without precipitating haemodynamic deterioration in patients with broad complex tachycardia[2 5 13] means that both accident and emergency departments and cardiac care units would be safer places for patients with arrhythmias if the first instinct of the doctor on the spot was to reach for adenosine rather than verapamil.

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1 Faulds D, Chrisp P, Buckley MM-T. Adenosine: an evaluation of its use in cardiac diagnostic procedures, and in the treatment of paroxysmal supraventricular tachycardia. *Drugs* 1991;41:596-624.
2 Griffith MJ, Linker NJ, Ward DE, Camm AJ. Adenosine in the diagnosis of broad complex tachycardia. *Lancet* 1988;i:672-5.
3 DiMarco JP, Sellers TD, Lerman BB. Greenberg ML, Belardinelli L. Diagnostic and therapeutic use of adenosine in patients with supraventricular tachyarrhythmias. *J Am Coll Cardiol* 1985;6:417-25.
4 Moser GH, Schrader J, Deussen A. Turnover of adenosine in plasma of human and dog blood. *Am J Physiol* 1989;256:C799-806.
5 Rankin AC, Oldroyd KG, Chong E, Rae AP, Cobbe SM. Value and limitations of adenosine in the diagnosis and treatment of narrow and broad complex tachycardias. *Br Heart J* 1989;62:195-203.
6 Drury AN, Szent-Györgyi A. The physiological activity of adenine compounds with especial reference to their action upon the mammalian heart. *J Physiol* 1929;68:213-37.
7 Honey RM, Ritchie WT, Thomson WAR. The action of adenosine upon the human heart. *Q J Med* 1930;23:485-9.
8 Clarke C, Cairns CJ, Coutrouzas H, Terry D. The preparation and use of adenosine injection. *Pharmaceutical Journal* 1990;244:595-7.
9 DiMarco JP, Miles W, Akhtar M, Milstein S, Sharma AD, Platia E, *et al*. Adenosine for paroxysmal supraventricular tachycardia: dose ranging and comparison with verapamil. *Ann Intern Med* 1990;113:104-10.
10 Till J, Shinebourne EA, Rigby ML, Clarke B, Ward DE, Rowland E. Efficacy and safety of adenosine in the treatment of supraventricular tachycardia in infants and children. *Br Heart J* 1989;62:204-11.
11 Cushley MJ, Tattersfield AE, Holgate ST. Inhaled adenosine and guanosine on airway resistance in normal and asthmatic subject. *Br J Clin Pharmacol* 1983;15:161-5.
12 Adenocor®. Promotional literature. Sanofi Winthrop Ltd, 1992.
13 Garratt CJ, Griffith MJ, O'Nunain S, Ward DE, Camm AJ. The effects of intravenous adenosine on antegrade refractoriness of accessory AV connections. *Circulation* 1991;84:1962-8.

Juvenile myoclonic epilepsy

Underdiagnosed and treatment may have to be life long

Juvenile myoclonic epilepsy, formally recognised as a syndrome by the International League Against Epilepsy in 1985, accounts for about one in 10 cases of epilepsy.[1] Clinical awareness of the syndrome among non-neurologists, however, is low, resulting in delays of several years between the onset of symptoms and correct diagnosis.[1 2] Additionally, the best treatment, prognosis, and possible need to continue treatment long term are not widely appreciated.[2]

Typically the age at onset of juvenile myoclonic epilepsy ranges from 8 to 18 years. Patients experience single or repeated bilateral irregular jerks without loss of consciousness. The jerks occur more commonly on waking or in the mornings and are often but not always associated with generalised tonic-clonic seizures or absence seizures. Results of neurological examination are usually normal, but in 60-90% of cases the electroencephalogram shows the typical 4-6 Hz bilaterally symmetrical polyspike and wave pattern with normal background. Flickering light results in an epileptiform discharge in the electroencephalogram in up to 40% of patients.[3]

A typical history and electroencephalogram make the diagnosis straightforward, but some patients who experience only myoclonic seizures do not present to medical attention until they experience a generalised tonic-clonic seizure, having previously interpreted the myoclonic episodes as morning jitters or clumsiness.[1 4 5] Misinterpreted symptoms[2 4] or the mistaken reassurance provided by a normal electroencephalogram may lead to a delayed or incorrect diagnosis. Specifically seeking a history of myoclonic episodes significantly improves diagnostic accuracy.

Juvenile myoclonic epilepsy has a familial component. Two studies have suggested that a genetic component is located on

the short arm of chromosome 6.[6] Autosomal recessive inheritance has been proposed as its mode of transmission,[6,7] but further confirmation is awaited. At present it seems likely that other factors, possibly other genes, modify the expression of a juvenile myoclonic epilepsy gene on chromosome 6.

The recognition that non-pharmacological factors, such as emotional stress, sleep deprivation, alcohol use, and menses, seem to precipitate seizures[1,3] allows patients to gain some control of their seizures; most patients, however, will require treatment with drugs. Unfortunately, no prospective, controlled studies of drug treatment for juvenile myoclonic epilepsy have been performed and current information on use of anticonvulsant drugs has been derived exclusively from retrospective studies and anecdotal reports.[8] Currently the drug of choice is sodium valproate,[9] which completely suppresses seizures in 80-90% of patients.[7] Treatment of those patients who respond poorly to valproate is difficult and often requires more than one antiepileptic drug. No other single drug stands out as the ideal second line agent. Though anecdotal reports suggest that most other anticonvulsant drugs may be helpful, overall results are disappointing. In many patients carbamazepine exacerbates myoclonus and juvenile myoclonic epilepsy.[10-13]

Juvenile myoclonic epilepsy usually persists throughout life, and patients in their seventh decade have been reported. Attempted drug withdrawal, even after complete suppression of seizures for two or more years, leads to relapses in 80-90% of patients.[1,2,8] It is therefore important that a correct diagnosis is made so that patients with juvenile myoclonic epilepsy may be advised that treatment is usually required life long.

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1 Janz D. Epilepsy with impulsive petit mal. *Acta Neurol Scand* 1985;72:449-59.
2 Penry JK, Dean JC, Riela AR. Juvenile myoclonic epilepsy: long-term response to therapy. *Epilepsia* 1989;30(suppl 4):19-23.
3 Dreifuss FE. Juvenile myoclonic epilepsy: characteristics of a primary generalised epilepsy. *Epilepsia* 1989;30(suppl 4):1-7.
4 Obeid T, Panayiotopoulos CP. Juvenile myoclonic epilepsy: a study in Saudi Arabia. *Epilepsia* 1988;29:280-2.
5 Delgado-Escueta AV, Bascal FE. Juvenile myoclonic epilepsy of Janz. *Neurology* 1984;34:285-94.
6 Delgado-Escueta AV, Greenberg DA, Treiman L, Liu A, Sparkes RS, Barbetti A, *et al*. Mapping the gene for juvenile myoclonic epilepsy. *Epilepsia* 1989;30(suppl 4):8-18.
7 Panayiotopoulos CP, Obeid T. Juvenile myoclonic epilepsy: an autosomal recessive disease. *Ann Neurol* 1989;25:440-3.
8 Resor SR Jr, Resor LD. The neuropharmacology of juvenile myoclonic epilepsy. *Clin Neuropharmacol* 1990;13:465-91.
9 Sodium valproate [editorial]. *Lancet* 1988;ii:1229-31.
10 Clement MJ, Wallace SJ. Juvenile myoclonic epilepsy. *Arch Dis Child* 1988;63:1049-53.
11 McKee PJW, McGinn G, Larkin JG, Brodie MJ. Myoclonic epilepsy—pitfalls in diagnosis and management. *Scott Med J* 1991;36:18-9.
12 Snead OC, Hosey LC. Exacerbation of seizures in children by carbamazepine. *N Engl J Med* 1985;313:916-21.
13 Shields WD, Saslow E. Myoclonic, atonic and absence seizures following institution of carbamazepine therapy in children. *Neurology* 1983;33:1487-9.

Ecstasy and the dance of death

Severe reactions are unpredictable

Ecstasy is the popular name for 3,4-methylenedioxymethamphetamine, a synthetic amphetamine derivative. Patented in 1914 by the E Merck Company as an appetite suppressant, it lay virtually forgotten until the 1970s. Apart from a mild amphetamine-like stimulant effect it induces a feeling of euphoria and benevolence and, although it tends to enhance perception, its hallucinogenic potential is low. Because of these properties its psychotherapeutic potential began to be explored in fields as divergent as marriage guidance, alcoholism, and enhancement of perception in elderly people—all without benefit.

While its therapeutic possibilities were being discarded its potential for misuse was being discovered, and its use in the United States as a recreational drug became widespread. As a result it was banned there in 1985. In Britain it is banned under the Misuse of Drugs Act 1971 as a class A drug. It is also a schedule 1 drug, indicating that it has no medicinal uses and requires a Home Office licence to give it.

Retrospective questioning of 100 users of 3,4-methylenedioxymethamphetamine showed that 90 experienced a feeling of closeness to others.[1] It has, however, many adverse effects. In one study 75-150 mg of pure 3,4-methylenedioxymethamphetamine was given orally to 29 volunteers by psychotherapists.[2] All 29 experienced undesirable physical symptoms: 28 lost their appetite, 22 had trismus or bruxism (grinding of the teeth), nine had nausea, eight had muscle aches or stiffness, and three had ataxia. Sweating was common, and tachycardia and hypertension were recorded. Afterwards, 23 noted fatigue for hours or days, and 11 had insomnia.

In Britain the drug is taken orally as tablets or capsules with a 3,4-methylenedioxymethamphetamine content of about 50-150 mg; the street price is around £15 for a single dose. Tolerance occurs; some users increase the dose over weeks or months of use to as many as 10 or more tablets during the course of an evening. The most important difference between the American and British experience of the drug is that while it tends to be taken alone or at parties in the United States, it is used in Britain almost exclusively as a "dance drug."

At the currently popular "rave" parties the dancing is hard and fast so that the pharmacological effects of the drug may be compounded by physical exertion. Animal studies show that the drug may cause excessive heat production due to serotoninergic mechanisms, which is greater at high ambient temperatures.[3] Very few cases of severe or fatal reactions have been recorded in the United States despite extremely widespread use.[4] In Britain at least seven deaths and several severe adverse reactions have followed its use as a dance drug.[5] Previous experience of the drug is no guarantee of safety.

The case report on page 29 is typical of the acute severe complications which may occur.[6] Convulsions, collapse, hyperpyrexia, disseminated intravascular coagulation, rhabdomyolysis, and acute renal failure may all follow ingestion of 3,4-methylenedioxymethamphetamine as a dance drug; complications may escalate in number and severity if the patient does not receive treatment soon enough. Fortunately, the patient described in the case report recovered following intensive supportive treatment.

Drug agencies are aware of the risk of hyperthermia and advise those who use the drug to wear loose clothing, to drink liquid to facilitate thermoregulation, and to stop dancing when feeling exhausted. Some club owners have provided