Mania in Down's syndrome

SIR: In the last couple of years a number of articles appeared claiming that mania does not occur in Down's syndrome (*Journal*, March 1985, **146**, 319–320). However, quite the opposite can be postulated theoretically and is found in practice.

The biochemical basis for the induction of secondary mania is variable. In Down's syndrome a variety of endocrinological as well as neuropathological abnormalities are present which could precipitate secondary mania. One finds increased incidence of both head injury and epilepsy. A number of psychosocial factors also indicate that there should be an increased incidence of mania (e.g. higher parental age and higher social class). So, restricting one's line of argument to just reduced levels of catecholamines and indoles in Down's syndrome (Singh, 1988) is not particularly useful, even if these are considered as a final common pathway; also, drugs that bind to catecholamine or indole sites quickly do not lead to the altered mental state at the same speed.

The characteristic histology of dementia of Alzheimer's type is found in all people with Down's syndrome over the age of 30 years, and the hallmark neurotransmitter abnormality is a deficit in a cholinergic system of the brain. In Down's syndrome it manifests clinically as hypersensitivity to cholinomimetic agents (Sacks *et al*, 1989). Improvement following treatment of manic patients with cholinomimetic agent RS 86 in a double-blind study, has been shown to occur within days (Krieg *et al*, 1986), and thus one could suggest that a deficit in a cholinergic system is only one of the factors which predisposes people with Down's syndrome to develop mania at some stage.

The case notes of 27 Down's syndrome patients were examined and one case of recurrent mania was found.

Case report: The patient is a 46-year-old woman who, because she was an orphan with Down's syndrome, has spent her whole life in various institutions. Her personality was described as pleasant and friendly and she was conscientious at work. At the age of 32 years she had an episode of disturbed behaviour characterised by elevated mood ('smiling all the time'), decreased sleep ('up most of the night'), her speech becoming very loud and pressurised, and disinhibited behaviour (she took all her clothes off in front of the other patients and staff). She also became physically aggressive, lashing out at passers by and overturning tables and chairs in the dining room. The only abnormal belief that she had at that time was that she was pregnant. She was treated with neuroleptics and gradually over a period of two months returned to her previous level of functioning. There were three other almost identical episodes lasting several months which all responded to neuroleptics. There were no clear depressive episodes. Her general health was good apart from a couple of episodes of gastroenteritis. The following investigations were normal: full blood count, urea and electrolytes, chest X-ray, thyroid function tests and electroencephalogram (EEG). Although EEG was normal there were two reports from nursing staff that this patient had a *grand mal* seizure. As this seemed an isolated incident she was not treated with anti-epileptic medication. The attempts to reduce the maintenance medication of promazine: (100 mg b.d.) to a lower dose resulted in a relapse of disturbed behaviour as described above. At present she is well on promazine (100 mg b.d.) and orphenadrine (100 mg b.d.).

Kraepelin (1896) considered that "imbecility may form the bases for the development of other psychoses such as manic depressive insanity, the psychoses of involution and dementia praecox". This stance should be preserved and many cases of Down's syndrome could substantiate that this was hardly a simplistic view.

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Mania complicating ECT

SIR: There are several reports of euphoric and hyperactive states following electroconvulsive therapy (ECT). These range in duration from minutes (Sackeim *et al*, 1983) to at least several days (Lewis & Nasrallah, 1986), and vary in the degree of associated cognitive impairment (Devanand *et al*, 1988). Mitigating factors may include a personal history of mania (DeQuardo & Tandon, 1988), the locus of application used (Sackeim *et al*, 1983), and concomitant use of antimanic medication (DeQuardo & Tandon, 1988). Persistent symptoms have been treated medically (Devanand *et al*, 1988). Without providing details, Barrett (*Journal*, April 1989, **154**, 575) reports that his practice is to continue a course of ECT in spite of emerging manic symptoms, viewing such complications as representing affective disorder "modified rather than fully treated". The following is otherwise the first reported case in

which ECT has been used to treat a manic episode attributable to ECT.

Case report: A 65-year-old woman with a 40-year history of bipolar illness, refractory to several combinations of lithium, anticonvulsants, neuroleptics and verapamil, presented in a characteristic manic and psychotic state. She responded dramatically to a course of ECT (five treatments), and was discharged in complete remission on chlorpromazine and verapamil. Within two days after the first of her scheduled series of monthly maintenance ECT treatments, she began to deteriorate, and quickly became severely manic. She again responded dramatically to ECT (beginning 12 days after her maintenance treatment), with markedly reduced symptoms after the first of four additional treatments. All treatments were non-dominant unilateral, and there was no post-ictal agitation or delirium noted.

Although ECT is an effective treatment for mania (Small *et al*, 1988), there are no specific reports of its use in the management of the frankly manic state that rarely complicates ECT. In this case, the patient's historical resistance to medical antimanic measures overwhelmed the natural tendency to remove the presumed responsible factor. The fact that ECT did not induce a secondary mania, but rather altered the course of an idiopathic bipolar illness, distinguishes this case from those involving less clearly manic presentations and from manic syndromes occurring in persons without such a history. The utility of ECT in these other instances has yet to be tested.

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Alprazolam withdrawal symptoms

SIR: Alprazolam is extensively used as an anxiolytic, antipanic and antidepressant, but like other benzodiazepines, a major problem with it is withdrawal symptoms (Browne & Hauge, 1986). As a withdrawal symptom of benzodiazepines, psychosis is very rare (Owen & Tyrer, 1983). Here we report a case of visual hallucination and paranoid ideation without amnesia, following the tapering off of a low dosage of alprazolam.

Case report: A 69-year-old married woman, weighing 43 kg, visited our hospital with symptoms of depressive mood, loss of interest in her surroundings, concentration difficulties, insomnia, anorexia, and fatigue, and was diagnosed as having major depression (DSM–III). She had been taking alprazolam (1.2 mg/day) because of these symptoms for the previous four months, but had had no psychiatric problems before this episode. Mianserin (10 mg/day) was started while alprazolam was gradually tapered off. The alprazolam dose was 0.8 mg/day for the first two days, 0.4 mg/day for the next three days, and from the sixth day, it was completely discontinued. On the morning of the third day after alprazolam was withdrawn, she saw newspaper writing on the stool every time she went to the lavatory. In addition, she felt as if someone was standing in front of her house. These symptoms were also observed on the next day, but to a lesser degree. There were no other withdrawal symptoms. On the fifth day of alprazolam withdrawal, these symptoms disappeared. She could recall them clearly and no amnesia was observed. Three weeks after the start of mianserin treatment, the patient completely recovered from her depression.

In this case, visual hallucination and paranoid ideation, which had never been observed before, occurred about 60 hours after the last dose, and disappeared by the fifth day of alprazolam withdrawal. Therefore, it is considered that these symptoms were associated with alprazolam withdrawal. As a withdrawal symptom of alprazoram, paranoid ideation without consciousness disturbance is very rare (Noyes *et al*, 1985; Bleich *et al*, 1987), and regarding hallucination, this is the first case to our knowledge. In general, a high dosage and abrupt discontinuation have been considered as risk factors of benzodiazepine withdrawal symptoms (Owen & Tyrer, 1983). However, in this case, the dose was 1.2 mg/day, which is lower than in the reported cases with alprazolam withdrawal symptoms (Browne & Hauge, 1986; Noyes *et al*, 1985; Bleich *et al*, 1987). Furthermore, the drug was gradually tapered off. Zipursky *et al* (1985) also reported that a 68-year-old man became delirious after his low dosage (1.5 mg/day) of alprazolam was tapered off. In addition, Greenblatt *et al* (1982) suggested that elderly patients have a high incidence of drug side-effects, including those from benzodiazepines. Therefore, it is possible that in elderly patients, alprazolam withdrawal symptoms occur, even when the dosage is low and is gradually reduced. We suggest that alprazolam should be withdrawn from elderly patients at an