

Whereas it may be difficult systematically to follow up cohorts of women who have had amniocentesis under specified conditions, this objective could be achieved if readily accessible information systems were in place covering amniocentesis use in the population, and congenital anomalies. The coexistence of these two information systems would also (and as their main objective) allow the evaluation of the impact of prenatal screening in the population. It is unfortunate that, in most areas of Europe, either one or both of these information systems is lacking.

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Sedative and hypnotic withdrawal states in inpatients

SIR,—We read with interest Dr Moss' letter (Aug 31, p 575) reporting on sedative-hypnotic drug withdrawal states in inpatients as a result of house staff being warned against the routine prescription of benzodiazepines for night-time sedation. We have done a prospective study of the part played by hospital admission on the introduction and withdrawal of hypnotics and tranquillisers, and would like to comment on Moss' letter.

119 consecutive patients admitted to an internal medicine department were studied. 31% of the patients were receiving a hypnotic or tranquilliser before admission. Although this figure slightly increased during the period in hospital (35%), 14 patients had hypnotics or tranquillisers withdrawn. 31 additional withdrawals occurred at discharge; among the 42 patients receiving these drugs while in hospital only 11 were prescribed such medication at discharge. It can be expected that some of those who had drugs withdrawn will subsequently resume this therapy. However, our study does show that drug withdrawal is especially common at discharge. House-staff need to be aware of the dangers of iatrogenic withdrawal arising not only during admission but also after discharge.

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Sexual disturbances during omeprazole therapy

SIR,—Omeprazole is the first of a new class of drugs that inhibit gastric secretion by altering the activity of $H^+/K^+-ATPase$.¹ Although it has a minor inhibitory effect on the synthesis of adrenal steroids, it has no important clinical effects on endocrine or sexual function.²

A 77-year-old man was treated with omeprazole 20 mg once daily for oesophagitis induced by tiaprofenic acid, diagnosed endoscopically. This patient also used transdermal glyceryl trinitrate for angina pectoris for many years. During omeprazole treatment painful nocturnal erections developed, without an increase

in libido; these erections disappeared when the drug was stopped 6 weeks later. Treatment was resumed intermittently by the patient because of recurrent and irregular epigastric pain. After each tablet, pain regressed for 36 h but painful erections recurred during this same period. Since abdominal pain had disappeared with this irregular treatment over 2 months, omeprazole was stopped and no more sexual disturbances appeared. He had no history of perineal injury or intracavernosal injections. There was no inflammation of penis or traces of injections. Blood counts were normal.

Glyceryl trinitrate, a potent vasodilator, was excluded as a possible cause because it was continued after sexual disorders disappeared. Although omeprazole does not seem to affect sex-hormone metabolism, gynaecomastia has been reported in one man.³ Since erections appeared in our patient during omeprazole treatment and recurred after each tablet, a causal relation is possible; furthermore, erections persisted for 36 h, the time during which omeprazole inhibits acid secretion.⁴

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Pharmacotoxic psychosis after memantine in Parkinson's disease

SIR,—Dopamine has proved in animals to be of less importance in the regulation of psychomotor functions than previously believed.¹ A clear behavioural activation can be produced in rodents after suppression of glutamatergic neurotransmission, even in the absence of brain dopamine. It has therefore been proposed that N-methyl-D-aspartate (NMDA) antagonists are potentially useful as antiparkinsonian drugs.² Antiglutamatergic drugs for the treatment of Parkinson's disease are the non-competitive NMDA receptor antagonists amantadine and memantine.^{3,4} The antiparkinsonian activity of memantine may be explained by its action at the NMDA receptor,⁴ since the K_1 value of memantine is below the brain concentration achieved in the treatment of Parkinson's disease.⁵ Reduced activity within glutamatergic pathways might be an important factor in the pathophysiology of schizophrenia.⁶ The therapeutic use of NMDA antagonists in Parkinson's disease may therefore have the potential to cause psychotic side-effects. We have examined the motor performance and the occurrence of pharmacotoxic psychosis after administration of memantine in patients with Parkinson's disease.

Four patients with Parkinson's disease received 10-30 mg memantine daily for up to six weeks, in addition to their usual medication, with a view to improving their motor performance (table). Improvement in motor symptoms was rated according to Webster (modified scale⁷). The degree of pharmacotoxic psychosis was rated according to Moskovitz.⁸ Only one patient showed a mild improvement in motor symptoms after memantine treatment for three weeks. In two of the other three, however, memantine produced pharmacotoxic psychosis.

These results suggest that memantine in doses producing little or no antiparkinsonian effects is likely to cause pharmacotoxic psychosis. Amantadine is known to have dose-dependent anti-kinetic effects in parkinsonian patients and psychosis is a frequent adverse reaction.⁹ Although these NMDA antagonists show some antiparkinsonian activity at sufficiently high doses, the risk of psychotic side-effects is considerable. In Parkinson's disease there are few data confirming a disturbance of glutamatergic function in limbic or cortical areas and supporting a glutamatergic hypothesis of

CLINICAL EFFECTS OF MEMANTINE IN PATIENTS WITH PARKINSON'S DISEASE

Patient	1	2	3	4
Age (yr), sex	84, F	64, M	66, M	87, F
Duration of disease (yr)	6	7	3	12
Hoehn & Yahr stage	IV-V	IV-V	IV-V	IV-V
Daily treatment (mg)	Levodopa (150), amantadine sulphate (200), terguride (1.5)	Levodopa (50), amantadine sulphate (300), terguride (0.75)	Procyclidine (7.5)	Amantadine sulphate (100), terguride (1.5)
Daily memantine dose (mg) (duration)	30 (3 wk)	20 (1 wk)	10 (6 wk)	10 (2 wk)
Clinical effect of memantine	Mild improvement of motor symptoms	No improvement in motor symptoms, pharmacotoxic psychosis	No improvement in motor symptoms	No improvement in motor symptoms, pharmacotoxic psychosis
Motor score ⁷ (before/after memantine)	80/60	70/70	80/80	85/85
Psychosis score ⁸ (before/after memantine)	0/0	0/2	0/0	0/1

pharmacotoxic psychosis. However, since memantine can induce pharmacotoxic psychosis at doses that are only slightly effective, glutamatergic activity in brain areas responsible for psychosis might be reduced and further inhibited by the NMDA receptor antagonist.

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to the sensation of nausea. The sequence of gastric arrhythmia → nausea → vasopressin secretion (or vasopressin secretion → nausea) needs further investigation. The results of such investigations may improve our understanding and treatment of this noxious and very common symptom called nausea.

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Nausea and vasopressin

STR,⁵—A *Lancet* editorial¹ has highlighted the intriguing relation between vasopressin and a very poorly understood symptom, nausea. Its summary of our work² indicated that nausea and increased vasopressin were not present in subjects with abnormal gastric myoelectrical activity (gastric tachyarrhythmias) induced during illusory self-motion. However, we did find gastric arrhythmia present in those with nausea and increased vasopressin, and our observations in fact support a potential gastric or vagal mechanism that results in nausea and vasopressin secretion. By altering vagal (or splanchnic) viscerceptive afferent nerve activity projecting through the tractus solitarius to the hypothalamus,^{3,4} the disruptive shift from normal gastric myoelectrical activity to arrhythmia may be related to the stimulation of hypothalamic vasopressinergic neurons and the release of vasopressin. Consistent with this notion, a study of ipecacuanha showed that the early gastric irritant phase of induced nausea was associated with increases in plasma vasopressin.⁵

An unresolved question in man remains whether or not nausea releases vasopressin or release of vasopressin somehow contributes

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Aspergillus antigen latex test for diagnosis of invasive aspergillosis

STR,⁵—Invasive aspergillosis is a frequent infectious cause of death in bone-marrow transplant recipients.¹ Although the detection of aspergillus antigen in serum, urine, or broncho-alveolar lavage fluid can allow the rapid diagnosis of such infection,^{2,3} the lack of simple commercial tests has restricted the routine application of this approach.

Over the past 15 months we have conducted a prospective evaluation of a new latex agglutination test ('Pastorex Aspergillus', Diagnostics Pasteur) for the detection of circulating aspergillus galactomannan. The latex used in this test is sensitised with a rat IgM monoclonal antibody and can detect galactomannan at concentrations as low as 15 ng/ml.

366 serum samples from 20 patients undergoing bone-marrow transplantation were tested. Samples were collected at least three times per week for 4 weeks or more after transplantation. 300 µl of serum was mixed with 100 µl of edetic acid, heated to 100°C for 3 min, then centrifuged at 10 000 g for 10 min. 20 µl of supernatant was mixed with 5 µl of sensitised latex on an agglutination card, agitated at room temperature for 5 min, and the result read. The control provided (*Aspergillus fumigatus* galactomannan antigen, 75 ng/ml) was included in all sets of tests and gave positive results throughout.

13 patients (199 samples) had negative results on all occasions; 11 had no clinical, radiological, or microbiological findings suggestive of aspergillus infection. In 1 patient a bronchoalveolar lavage (BAL) specimen taken 7 weeks after transplant yielded *A fumigatus*; 16 serum samples taken during the first 10 weeks after transplant were negative. In a second patient *A fumigatus* was recovered from sputum taken 28 weeks after transplant; 23 serum samples taken up to 34 weeks after transplant were negative.