region and to swap ideas on this rather ill-defined yet important problem.

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The Pathogenesis of Depersonalisation: A Hypothesis

SIR: Depersonalisation/derealisation are common symptoms of anxiety and of affective disorder, and are not uncommon features of other psychiatric syndromes. They are also common in various organic states (e.g. hypoglycaemia) and are frequently likened by patients to dreaming, which occurs at a time of demonstrable alteration in cerebral activity. Furthermore, these phenomena are disorders of perception, which suggests some organic basis. Is it possible that depersonalisation/derealisation are *always* manifestations of demonstrable organic abnormality in the brain?

Hyperventilation, too, is a common symptom of anxiety, and depersonalisation is common in hyperventilation. Anxiety is frequent in most psychiatric syndromes, and it might be reasonable to suppose that whatever the primary psychiatric diagnosis, it is only the patient who is anxious and hyperventilating who develops depersonalisation. In such patients the depersonalisation would be the result of the changes in metabolism and cerebral blood flow produced by the hyperventilation. The hypothesis would be that only those patients who were over-breathing would be depersonalised, whilst those patients who were not over-breathing would not suffer depersonalisation. At the same time the proviso has to be made that not all patients who are over-breathing would necessarily experience depersonalisation, as there might be some individual variation in the propensity to develop this symptom.

Having made this hypothesis, I set out to test it. As a first step I began to look for patients with depersonalisation who were not over-breathing, with a view to comparing various measures in them with patients who were over-breathing. It has, however, proved to be increasingly difficult, if not impossible, to find such patients who were not over-breathing. I think this may be because, since I have become aware of the hypothesis, I am not overlooking hyperventilation in such patients, whereas previously I might have been. Thus the investigation might not turn out to be as easy as it seemed at first, not an unfamiliar situation. In the meantime, however, the idea appears to have spread in this hospital and I have found over the past few months or more that it has been quoted to me as 'received knowledge' in teaching sessions with undergraduates and with junior doctors. For this reason I seek the hospitality of your columns to go on record as its originator.

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'Neuroleptic Malignant Syndrome' Without Neuroleptics

SIR: In support of the suggestion by Singh & Maguire (*Journal*, December 1987, **151**, 863) that the term neuroleptic malignant syndrome (NMS) should be revised, we report a fulminating case, exhibiting all of the diagnostic criteria proposed by Levenson (1985) but which occurred when lithium and phenelzine were employed in therapeutic doses. The patient had never taken neuroleptic drugs.

Case report: A 42-year-old woman presented to casualty with a rapid onset of restlessness, sweating, and confusion. She had a history of depression with intermittent agitation and some phobic symptoms of several years duration. Her medication comprised the following: phenelzine (15 mg three times daily), lithium carbonate (800 mg daily), L-tryptophan (1 g daily), diazepam (2 mg three times daily), and triazolam (0.25 mg daily). Phenelzine had been commenced six weeks previously, replacing clomipramine which had proved ineffective over four months. Relatives believed that the patient took her medications only as prescribed.

Within three hours she was comatose. Pupillary and corneal reflexes were lost. Trunk and limbs were hypertonic and held in rigid hyperextension. Tendon reflexes were brisk, but plantar responses were flexor. Temperature rose from 38.5°C on admission to 42.5°C four hours later. She had a tachycardia and became hypotensive.

A diagnosis of NMS was made and she was treated with intravenous dantrolene (60 mg three times daily), commenced within four hours. Body temperature returned to normal within 14 h; blood pressure and heart rate were controlled with dopamine and practolol.

Investigation showed mild leucocytosis and initially normal biochemical parameters of hepatic, renal, and muscle function. Serum creatine phosphokinase became elevated, reaching a peak of 41 355 U/l (normal values 24–175) on the third day. Cerebrospinal fluid was normal. Blood and urine cultures were negative. Intravenous benzylpenicillin and gentamicin were commenced before results of these became available.

Severe disseminated intravascular coagulation occurred after 12 h. Acute renal failure and continuing infusion of blood products necessitated treatment by peritoneal dialysis. Mechanical ventilation was instituted. By day five, elevated transaminases and alkaline phosphatase indicated severe hepatocellular damage. Profound hypoglycaemia

occurred suddenly and was treated promptly. The patient succumbed to repeated asystole on the sixth day.

Serum taken on admission contained: lithium, 0.38 mmol/l (therapeutic range 0.5–1.0); diazepam, 0.33 mg/l; and nordiazepam, 0.5 mg/l. No tricyclic antidepressant was detected. Unfortunately, assay for monoamine oxidase could not be performed.

Autopsy showed massive centrilobular hepatocellular necrosis and some fibrin thrombi within glomeruli. Muscle histology and histochemistry were normal.

This appears to be the first case of NMS associated with therapeutic doses of lithium and MAOI. Perhaps the particular sequence of drugs employed, with phenelzine replacing clomipramine, was an important factor in this instance. The current nomenclature might easily have hampered early diagnosis and appropriate treatment, although in this case intravenous dantrolene was not successful.

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Reference

LEVENSON, J. (1985) Neuroleptic malignant syndrome. *American Journal of Psychiatry*, **142**, 1137–1145.

Clastogenic Factors and Abnormal Plasma Fractions in a Female Patient with Severe Aggressiveness

SIR: A patient with a very long history of severe and therapy-resistant aggressive-destructive features has been examined.

Case report: The patient is a 32-year-old woman. Psychiatric problems have been present since early age, and the parents consulted a child psychiatrist when the patient was 4 years old. She has been in hospital from the age of 10, for 22 years. Several modes of different long-term intensive psychotherapy as well as numerous types of psychopharmacological agents have been tried. During the past five years she has been committed to an isolated ward as a single patient with a total of 15 mental health assistants. She is presently being treated mainly with long-term psychotherapy. Over the years there have been no signs of improvement.

The symptoms leading to this tragic situation are aggressiveness, destructiveness, feeding problems of anorexic-bulimic type, smearing with faecal matter, strange rituals, overactivity, paranoid features, and communication problems. She has a normal intelligence level and has been able to learn to speak, read, and write, and communicates intensively by letter.

An extensive investigation of the patient was started, and during chromosomal examination according to Gustavson *et al* (1983), a hyperdiploidy of her lymphocytes cultured in plasma was noted. This finding, indicating mitotic instability, led to the search for clastogenic factors in the plasma of the patient. Elaborate biochemical studies revealed two abnormal plasma fractions: one polypeptide with a molecular weight of $3–12 \times 10^3$ and one protein with a molecular weight of more than 10^5. When blood plasma was dialysed against an excess of phosphate-buffered saline (pH 7.4), most of the clastogenic activity was retained in fractions larger than 12×10^3. Similar abnormal plasma fractions were also found in her mother and one of her younger brothers.

Several other examinations have been performed, and detailed results will be presented elsewhere. Hypothetically, the clastogenic factors and the abnormal protein fractions in the plasma may be related to the psychopathology of the patient. We ask readers to contact us if they have observed a similar case or may provide us with a clue to this severe psychiatric disturbance.

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Atypical Koro

SIR: Koro is a relatively rare symptom complex that has been reported to occur throughout the world. The typical episode was described among the Chinese by Yap (1965) as an "unfamiliar state of acute anxiety with partial depersonalisation leading to the conviction of penile shrinkage and to fears of dissolution". Koro has also been reported in a variety of non-Chinese subjects (Edwards, 1984). Atypical cases of koro are generally of a chronic nature and are secondary to a variety of other psychiatric conditions (Yap, 1965). Generally, cases described among South-east Asians are related to an