a lead in the further understanding of the amine hypothesis of affective illness, especially mania.

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Dopamine Hypothesis of Neuroleptic Drug Action

SIR: The October issue (*Journal*, **151**, 455–465) contained three articles discussing the merits of the dopamine hypothesis of neuroleptic drug action. Since it is but a small step from there to a dopamine hypothesis of schizophrenia, and since various theorists and textbook authors have made that step, it seems appropriate to ask whether a better understanding of neuroleptic action is likely to tell us more about the underlying cause or causes of schizophrenia. I think that there are three reasons for pessimism in this regard. Firstly, the positive psychotic symptoms that respond to neuroleptic treatment are non-specific even when they are of the 'first rank', occurring in affective and organic disorders as well as in schizophrenia. Secondly, acute psychotic symptoms seem to be the least heritable component of schizophrenia, suggesting that they are only loosely related to the underlying biological predisposition. Finally, the severity of acute psychotic symptoms is a poor predictor of progressive decline with accumulating negative symptoms – a feature that seems much more distinctive of schizophrenia than the acute psychotic episodes themselves.

In the light of these considerations, it seems possible that a better understanding of neuroleptic drug action may reveal little about the origins of schizophrenia, just as an understanding of the actions of aspirin reveals little about the origins of influenza. A dopamine (or calcium-activated potassium conductance) hypothesis may no more explain schizophrenia than a prostaglandin hypothesis explains influenza. Of course, the treatment of positive psychotic symptoms is extremely valuable, and a better understanding of drug action may lead to future improvements in symptomatic treatment. At the same time, however, we may need to recognise that the search for better neuroleptics is relatively unlikely to lead to a specific treatment for schizophrenia, just as the search for a better febrifuge is unlikely to lead to a specific treatment for influenza.

Given the need for effective treatments for schizophrenia's relatively distinctive negative symptoms, the most appropriate research strategy may be to concentrate primarily on the correlates and origins of those features that generally distinguish schizophrenia from other psychotic disorders. Positive symptoms are striking and easily recognised, but they may be as much of a distraction to researchers as they are to patients. How intact are the research community's filters in the face of such absorbing noise?

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Lithium, Psoriasis, Abnormal Glucose Tolerance, and Thyroid Dysfunction

SIR: We wish to report a patient exhibiting several unusual effects related to treatment with lithium.

Case report: A fifty-year-old man presented to this unit in February 1974 because of heavy drinking. He was noted to have had psoriasis since his early teenage years, characterised by minimal skin lesions but severe, disfiguring nail changes.

In 1975 he developed a depressive illness, and despite treatment with antidepressants continued to be subject to frequent severe fluctuations of mood. Lithium carbonate was commenced in November 1976. His mood swings became less marked, and he remained euthyroid for five years. In May 1982 he presented complaining of headache. There were no clinical signs, but his free thyroxine index was marginally raised. Three weeks later he was admitted as an emergency to a general hospital with chest pain thought to be cardiac in origin. He was noted to have lost a stone in weight over the preceding month, and complained of thirst. On examination he was flushed and sweating with a marked fine tremor and palpable goitre. His pulse was 136/min and blood pressure 160/80. Reflexes were bilaterally brisk. ECG showed sinus tachycardia but no ischaemia. Elevated serum thyroxine confirmed the clinical diagnosis of thyrotoxicosis.

Throughout the hospital stay, intermittent glycosuria occurred and an oral glucose tolerance test was abnormal. This was thought to be secondary to hyperthyroidism, and glibenclamide was commenced. He remained hyperthyroid

four months after discharge, despite radioiodine and carbimazole. Further ^{131}I treatment rendered him hypothyroid, and thyroxine replacement was started. He also remained diabetic. There was no family history of endocrine disorder. Since commencing lithium he had noticed a marked improvement in his psoriasis. The skin lesions had gone and his nails had lost any sign of involvement. He is currently well, remains euthyroid, and has suffered no major mood swings for ten years. He is maintained on lithium (1250 mg/day), doxepin (50 mg nocte) and insulin (twice daily). He is free of any signs of psoriasis.

Reversible hyopothyroidism with lithium is well known (Schou *et al*, 1968). Hyperthyroidism complicating lithium therapy is rare, and the relationship between the two is unclear (Rosser, 1976). Hullin (1980) reviewed thirteen cases, of which most had other contributory factors.

The action of lithium on carbohydrate metabolism is complicated and there is conflicting evidence, some reports indicating increased glucose tolerance and others suggesting the opposite. The mixed metabolic and hormonal effects of lithium on glucose utilisation and the unknown effect of manic depressive illness itself on glucose homeostasis may account for this. Diabetes in long-term lithium therapy is known, but has occurred mainly in those previously predisposed. Glycosuria and impaired glucose tolerance are recognised in relation to thyrotoxicosis, but their persistence is unusual.

Treatment with lithium compounds is known to predispose to the development or exacerbation of psoriasis (Carter, 1972: Skoven & Thormann, 1979). We know of no other reported case or remission of psoriasis during treatment with lithium, and although the relationship of skin diseases in general to emotional disturbance is vague and ill-defined, the resolution, particularly of severe nail changes, correlated very closely with the onset of treatment with lithium.

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Disulfiram reaction during sexual intercourse

SIR: A 44-year-old woman who had been taking disulfiram (200 mg daily) for 2 months reported vaginal stinging and soreness during intercourse. Her husband experienced similar discomfort to his penis. This occurred only when her husband had consumed large amounts of alcohol within the preceding 12 hours. The reaction was less noticeable when she took 100 mg disulfiram daily, and when her husband was less intoxicated. A disulfiram-alcohol interaction may occur locally in some patients. Have other clinicians heard reports of this effect?

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Prasad's Syndrome

SIR: Prasad (1985) was the first to describe the manic presentation of Hashimoto's thyroiditis in a lady who had repeatedly failed to respond to all forms of conventional antipsychotic therapy. Once her condition was diagnosed, after detection of an increased antithyroid antibody titre and RAI uptake and the thyroid replacement treatment commenced, her psychiatric symptoms resolved.

Although manic presentation of other thyroid abnormalities have been reported, this was the first report of its kind in Hashimoto's disease, which led the author to conclude that a thorough thyroid screen may be useful in the differential diagnosis of 'resistant mania'.

Case reports: (i) A 50-year-old housewife was brought to the psychiatric out-patient clinic in a hyperactive state. Her speech was markedly pressured and she was expressing flight of ideas. According to her husband, she had been functioning normally until about a week prior to her referral when she started staying awake the whole night. Her behaviour steadily worsened and became unmanageable. She had no past history of psychiatric consultation and no family history of psychiatric illness. She was admitted to the psychiatric ward and commenced on haloperidol in increasing doses of up to 60 mg/day, when she started showing mild extrapyramidal side-effects. She remained on this dose for 6 weeks without any change in her mental state. Addition of lithium carbonate in doses of 200 mg b.d., with serum level of 0.6 mEq/l, did not bring about any change. At this stage, a comprehensive physical work-up revealed antithyroid antibody titre. She was commenced on thyroid replacement therapy. Her mental state improved rapidly and she has remained symptom-free for the past 6 months.

(ii) A 36-year-old divorced office secretary was brought to the psychiatric out-patient clinic following a referral from