morning suit and was constantly pacing the floor, his mood elevated, he was overbearing and slightly aggressive in manner. There was marked pressure of speech and flight of ideas. This state persisted for six weeks and was followed by a period of depression. There is no evidence that he was hypomanic prior to his mother's death. There had been a hypomanic episode some two months beforehand but this lasted less than a month and there is well documented evidence that his mood remained stable up to the time he had leave from work after his mother's death.

Almost two years later his father died and five days afterwards he was again admitted in a similar state. Again there was no evidence to suggest that his mood was elevated before the event.

This patient had an established manic-depressive disorder and had been subject to mood swings with no apparent precipitant. On these two occasions and on a possible third occasion when a hypomanic episode followed his wife leaving him, there was a clear precipitating event.

(2) A 24 year old single woman was admitted from the police station in a manic state. She had been found wandering naked and was grossly overactive, her mood alternated between elation and aggression, her speech was constant, with flight of ideas, punning and clang associations. Three weeks previously her adoptive father had committed suicide. She had felt pressure from the family as there had been a suggestion that she had been responsible for her father's depressive illness. During the three weeks after his death she had become progressively more disinhibited, over-active and promiscuous. Again, there is no suggestion that her mood was different before the death.

She had no previous history of affective disorder. However, a year before this episode she had been diagnosed as having a personality disorder. It is possible that her behaviour at this time indicated a mild hypomanic episode. Since the reported incident she has had one depressive swing starting three days after she gave birth. This depressive swing was followed by a period of mild hypomania.

I am grateful to Dr F G Spear, Consultant Psychiatrist, for permission to report these cases.

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Lithium Carbonate and Piroxicam

SIR: The report by Walbridge and Bazire (*Journal*, August 1985, **147**, 206–207) of an interaction between lithium carbonate and piroxicam prompts us to report details of a patient who also experienced lithium toxicity, probably attributable to this combination.

Case report: A 62 year old female with a 20 year history of manic depressive illness was started on lithium in March 1984 during her twelfth admission to hospital. Initially her renal function was checked and showed a plasma creatinine of 80 μmol/L. Her plasma lithium was stabilised at 0.6–0.75 mmol/L (checked monthly) with a dose of 800 mg of lithium carbonate at night. Ten months later, on 24.1.85, piroxicam 20 mg daily was prescribed for osteoarthritis of her right knee. Concurrent medication was as follows: amitriptyline 150 mg at night from 16.1.85 (previously on dothiepin 75 mg at night started before 1984), chlorpromazine 175 mg daily (from before 1984), procyclidine 5 mg tds from 14.1.85, and temazepam 20 mg at night from 11.1.85. Her January lithium level (taken on 8.1.85) was slightly raised at 0.85 mmol/L, possibly due to a recent loss of weight. At the end of January, she became noticeably agitated and tremulous: and during the next few days developed ataxia. During this period she was eating and drinking very little. A lithium level, done on 7.2.85 was 2.85 mmol/L with a raised plasma urea of 12 mmol/L and plasma creatinine of 142 μmol/L. All drugs were stopped and i/v fluid replacement started. Plasma lithium fell in four days to 0.35 mmol/L and plasma creatinine was inside the normal range (60–120 μmol/L) within 48 hours. Renal function tests continue to show mid-range values at the present time. She was also treated for an E. coli urinary tract infection with Amoxycillin starting 8.2.85. The lithium toxicity in this patient was probably exacerbated by dehydration and a urinary tract infection, but we consider that a piroxicam/lithium interaction could have contributed significantly.

Although the lithium/non-steroidal anti-inflammatory drug (NSAID) interaction has been well established, the mechanism is not completely understood. One mechanism, that of suppression of renal prostaglandin synthesis by NSAIDs leading to a fall in GFR and thus a reduced clearance of lithium has been clearly implicated in some cases (Nadarajah & Stein, 1985). This is reversible but the risk may be greater with NSAIDs with a long half-life (Adams *et al*, 1986). Walbridge and Bazire suggest using an NSAID with a short half-life, e.g., ibuprofen, to reduce the extent of the interaction; however reports have shown marked increases in plasma lithium concentration within a short time of initiation of ibuprofen therapy (Ayd, 1985; Leftwich *et al*, 1978).

In the light of this, it has been of concern to us that ibuprofen is now a non-prescription drug in the UK and can be bought freely over the counter. With this in mind, we now counsel our lithium patients on various aspects of their therapy with the use of information cards which specifically refer to the possibility of an interaction with ibuprofen. We ask our patients to show their card to any chemist they buy medicines from.

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Seasons of Birth and Sub-Types of Schizophrenia

SIR: Many studies show disproportionately higher rates of schizophrenic patients born during the winter months (Hare *et al,* 1974; Torrey *et al,* 1977). We undertook a study to find out if there is an excess of winter births among schizophrenic patients, and in particular if seasonal variations are related to the gender and sub-types of schizophrenic patients. We examined the seasons of birth of 472 patients with the diagnosis of schizophrenia admitted consecutively to a teaching hospital over a period of 5 years. We also studied the gender and paranoid vs non-paranoid sub-types of this subject group.

The total group did not show an excess of winter births, neither did the total male ($n=193$) and total female ($n=279$) schizophrenic patients. However, the male paranoid schizophrenic group ($n=102$) showed a significant ($P=0.05$) increase of births during the first quarter of the year. The different sub-group of female patients showed a homogeneous distribution of seasons of birth. We found a fairly stable distribution of seasons of birth among both the male and the female non-paranoid sub-groups (those with a greater genetic loading). According to Huxley's "genetic morphism" hypothesis (Huxley *et al,* 1964), the genes endow these sub-groups of patients with better capabilities of resisting various environmental factors. The homogeneous distribution of birth among the female paranoid sub-group could be explained on the basis of certain "built-in" protective factors for the female population (Seeman, 1981). Nature has provided the female with protective factors which may be responsible for their later onset of illness, better response to neuroleptics, fewer relapses, better work record, greater social adjustment, and significantly fewer peri-natal problems as compared to their male counterparts. Although there have been several explanations, the significantly greater number of births of males in the paranoid sub-group during the winter months has been explained on the basis of the two hypotheses, viz. pre- or perinatal birth trauma or the viral infection hypothesis (Torrey & Peterson, 1976). They contend that because of the higher prevalence of viral infection during colder months, the schizophrenic patient is infected with slow or latent viruses, which alter the function of nerve cells in critical areas of the brain without altering the histological structure. Since the direct evidence of viral infection is lacking, we proceeded to test the first hypothesis, i.e., that subtle birth trauma later predisposes to the development of schizophrenia in susceptible individuals. For this purpose we examined the birth dates of 44 (38 males and 6 females) patients with the diagnosis of minimal brain dysfunction admitted consecutively during the same period as those of our schizophrenic sample. This group of patients is known to have high incidence of subtle brain insults. However, we failed to find any seasonality of birth in this sample. Therefore, we may infer that in our sample the significant increase of births among male paranoid schizophrenics during the winter months could not be explained by factors related to peri-natal trauma. This finding tends indirectly to give more weight to the viral hypothesis of schizophrenia, especially among male paranoid schizophrenics.

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