There are other intriguing features of the present case. At no time was the patient hypertensive, in contrast to the usual situation in Conn's syndrome or bilateral adrenal hyperplasia. As Conn (1964) pointed out, however, the rise in pressure is variable and in the early stages may be minimal. The observations on blood pressure harmonize also with the measurements of plasma renin activity. In Conn's syndrome or bilateral hyperplasia renin activity is usually depressed, but in this patient the activity of the renal enzyme was normal. Again it must be postulated that the duration and degree of hyperaldosteronism were insufficient to depress plasma renin activity, offsetting the aldosterone effect. (Brunner *et al.*, 1970).

However the biochemical changes are explained, the possibility that a malignant adrenal lesion may be producing changes similar to those produced by a benign adenoma or bilateral hyperplasia makes it reasonable to advocate that detailed steroid studies should be done in all such patients; that the tumour, if present, should be located; and that if necessary one or both adrenal glands should be removed. Spironolactone has a place in the diagnosis and investigation

of primary aldosteronism but should not be used as a definitive treatment.

We thank Professor W. I. Cranston, under whose care the patient was at St. Thomas's Hospital; Mr. J. M. Pullan, who performed the adrenalectomy; Dr. Roger Hall, recently house physician to the medical unit; and the staff of the department of surgical pathology for the histological report. Dr. Lee acknowledges the generous help of the Lawson Tait Trust and the British Heart Foundation.

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Side Effects of Parenteral Long-acting Phenothiazines

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A patient on parenteral long-acting phenothiazines may present in the general hospital with unusual side effects causing considerable difficulties in diagnosis. In the present case the patient presented with a hypothalamic syndrome, the first to be reported, which adds weight to the hypothesis that this is one of the sites of action of these drugs in man.

Case History

A 24-year-old man had an eight-year history of intermittent addiction to drug, though he had not taken any for four months before the present illness. He was admitted to a psychiatric hospital in March 1971 with auditory hallucinations and delusions. These symptoms failed to respond to sedation or electric convulsion therapy and treatment was started with fluphenazine decanoate (Modecate) intramuscularly. He received 50 mg of this drug initially and 100 mg a week later. The following day he discharged himself from hospital.

Two days later his limbs became increasingly stiff and difficult to use, his speech was slurred, he was unable to swallow, and he became increasingly drowsy. A week later he was readmitted to the general hospital in a stuporous state.

On examination he was found to be obese (weight 117 kg), febrile (37.6°C), and mute. After repeated stimuli he could be roused and would follow an observer with his eyes. When left alone he rapidly lapsed into sleep. He had pronounced tremor of the lips, tongue, and hands, with extrapyramidal rigidity in all limbs. There were no other abnormal physical signs. A provisional diagnosis of encephalitis was made. The diagnosis of catatonic stupor was considered but rejected because the clinical features were atypical. Intravenous amylobarbitone sodium failed to render him more accessible.

Routine investigations showed nothing abnormal apart from a

neutrophil leucocytosis and the presence of large amounts of fluphenazine breakdown products in the urine.

Over the next seven days his temperature and white cell count remained high, though no site of infection was found. He did not respond to antibiotic therapy. The hypothalamic syndrome characterized by disturbance of temperature regulation and drowsiness from which he could be roused only by repeated stimuli persisted for a week. His temperature then returned to normal. This improvement coincided with a fall in the concentration of fluphenazine breakdown products in the urine to negligible levels. The extrapyramidal signs responded to intramuscular procyclidine hydrochloride (Kemadrin).

Comment

The long-acting phenothiazine fluphenazine enanthate has been valuable in reducing the incidence of relapse in schizophrenic patients. Fluphenazine decanoate is a similar depot injectable neuroleptic with a longer duration of action.

This is the first clinical report of a hypothalamic syndrome induced inadvertently by long-acting phenothiazines. The patient also developed extrapyramidal features which are sometimes associated with long-acting phenothiazine treatment. These side effects are related to age, sex, and dose but in addition there is an individual sensitivity factor (Simpson, 1967), though in the present case the dose given was considerably greater than that usually recommended (Capstick, 1968). In some patients the normal dose has been greatly exceeded without ill effect (Kline, 1970).

This case report illustrates the diagnostic difficulties that may be encountered in patients receiving long-acting phenothiazines, particularly if on admission the past medical history is not known. Because these drugs are rarely prescribed in the general hospital setting their side effects are less well known and may escape recognition.

The diagnosis of long-acting phenothiazine-induced side effects should be considered in patients who present with stupor, disturbance of temperature regulation with no evidence of underlying infection, and extrapyramidal signs.

We wish to thank Dr. P. W. Dykes for permission to report details of this case.

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