Editorial

Iatrogenic Illnesses

Physicians face the problem of : how to use the potent armamentarium of drugs available today without inadvertently causing harm. Clinical therapeutics has become an increasingly complex field, the same dose of a drug administered to different individuals or the same individual at different times may achieve a therapeutic, a toxic or an inadequate effect.

In U.S.A it has been estimated that 5% of hospital admissions are caused by drug reactions, and that once in the hospital 18 to 30% of hospitalized patients have adverse drug effects. The vast scope of this problem has led Cluff to suggest that:

"Whenever a sick person is seen, irrespective of the nature of the illness, the doctor should ask himself: could this be drug-related?.

In addition to the adverse effects of the drug itself, there are adverse effects which may come about from interactions with other drugs the patient is taking and from host factors (pharmacogenetic predispositions).

In this editorial, I shall limit my talk on the iatrogenic psychiatric effects of medication prescribed for non - psychiatric purposes and which are often extremely troublesome both to physician and patient.

A recent work conducted in U.S.A. has estimated the overall psychiatric adverse reaction frequency in approximately 9.000 patients to be 2.8% and concluded that : psychological disturbance, directly attributable to drugs commonly used in medical inpatient populations, can justifiably be regarded as an important and common problem.

Particularly for the psychiatrists practicing in general hospitals, the disorders designated as brain syndromes are among those for which consultation is most frequently requested. In one study, the diagnosis of the "psychotic brain syndrome" probably approximates 5 to 10% in the medical departments of general hospitals. Among those patients over 60 years old, 40 to 50% are reported to show evidence of delirium on admission to hospitals. In the young the highest incidence occurs in those subjected to surgical procedures associated with pain and / or emotional stress. As for those receiving anesthesia a large proportion of children exposed to a barbiturate basal anesthetic with later nitrous oxide as inhalant become delirious. In general, 8% of patients given anesthetics demonstrate some evidence of delirium.

Although clinicians have learned to expect certain toxic mental changes to occur as the result of overdosage, the realization that a patient's altered mental state may

result from therapeutic dose levels of a given drug is not always obvious. Alterations in mood or sensorium may be attributed to the underlying disease state, or it may be suggested that the patient is anxious or depressed because he knows he is ill. Obviously, these explanations are often true. However, difficulties may be encountered in the differential diagnosis between iatrogenic and symptomatic or reactional psychiatric manifestations. Thus, anxiety or depression manifested by a patient suffering from congestive heart failure could actually stem from digitalis toxicity and 3 to 4% of patients intoxicated with digitalis preparations may show delirium. The digitalis glycosides poison both the mind and the heart.

If the psychic symptoms due to digitalis overdosage are not widely appreciated and if this cause of disorientation goes unrecognized and the drug is continued, death may result.

Similarly patients with systemic lupus erythematosus (SLE) may develop mental symptoms. In the pre-cortisone, pre-ACTH era, SLE patients were noted to have such symptoms as stupor, delirium and toxic psychosis. With the introduction of steroids and ACTH into the treatment of SLE, considerable relief was brought to many of these patients.

However, the use of these therapeutic agents has added a dimension of diagnostic confusion. When are mental symptoms, if they develop, signs of SLE such that increasing dosages of cortisone are called for, and when are such symptoms the sign of steroid toxicity? This question proved to be very difficult to answer as psychosis may occur in association with one period of steroid use but may not reappear in the same patient in the future even at the same or higher dosages.

Three clinical pictures may occur as manifestations of iatrogenic hypercortisolism.

1. The patient may become depressed with suicidal tendency.
2. Excited and elated.
3. Unusual and frightening psychological experiences e.g perceptual abnormalities, derealization, hallucinations and incoherence.

In management of hypercortisolism, risk of suicide must be assessed and arrangements made for the patient's safety. Excited and irrational behaviour must be attended to and staff and relatives assisted in coping with the patient. Cortisol excess must be reduced. The steroid doses should be reduced to physiological levels over a period of several days.

Abrupt cessation, especially if the dose has been very large or prolonged, may result in rebound depression and increased anxiety. The risk of precipitating a crisis of adrenal insufficiency with abrupt cessation of treatment is, of course, the primary concern.

Moderate doses of phenothiazines may be useful if psychotic thought processes are present, if anxiety levels near panic, or if behaviour is too disruptive. Antidepressant medication may be delayed until cortisol metabolism returns to normal, since improvement is likely before the usual 2 to 3 week lag with antidepressants has elapsed. Some authors have recommended E.C.T. for severe depression in these patients, but they should be evaluated radiologically before E.C.T. for osteoporosis.

The pharmacotherapy of tuberculosis has been described as "Selective toxicity" Every chemotherapeutic agent useful in man against mycobacterium tuberculosis extracts its toll in a significant proportion of the patients using these agents. The therapeutic and toxic doses are often not greatly different. Hence streptomycin and viomycin induce damage to the eighth cranial nerve; para-amino-salicylic acid induces gastrointestinal disorders; pyrazinamide induces hepatic difficulties; and isoniazid, iproniazid, cycloserine and ethionamide induce nervous and mental disturbances. During the last several decades, the trends in treating tuberculosis have gravitated toward polypharmacy. Combinations of three to five different agents, having different mechanisms of action, are administered simultaneously in the maximally tolerated dosage. If an unfavourable reaction occurs, whether it be a mild gastrointestinal upset, hepatitis, convulsions, or a psychosis, it becomes very difficult to identify the culprit.

Numerous articles and various studies have reported on the mood and behavioural changes noted to occur concurrently with the administration of oral contraceptives for various obstetrical and gynecological conditions. From 1 to 6% of females using oral contraceptives feel worse and the drug has to be discontinued in these cases. Thus depression in association with oral contraceptives has been reported. Incidence has ranged from 2 to 30% depending on the population reported. There have been reports of psychoses occurring in close temporal association with oral contraceptive use. It is believed that psychoses occur more frequently in patients with a history of psychotic episodes.

In conclusion, I would like to recall the words of Weatherall who stated that: "All drugs are either ineffective or dangerous, just as all knives are either blunt or sharp. To use a potent drug without Knowing which organs it will go to and how long it will stay there is like using a knife blindfold. Medications are an ally to patients and their physicians but, like some allies, they have their dangerous side.

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