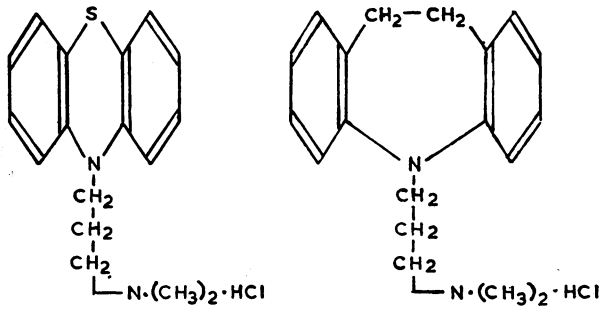
Medical Memoranda

Hypothermia Induced in a Myxoedematous Patient by Imipramine Hydrochloride

The "cooling" effect of the phenothiazines, particularly chlorpromazine, is well known (Courvoisier *et al.*, 1953). Mitchell *et al.* (1959) have shown that chlorpromazine can precipitate a hypothermic myxoedema coma in a hypothyroid patient. A similar pharmacological action would not be surprising from chlorpromazine and imipramine hydrochloride ("tofranil") owing to the close structural similarity of these two agents:



CHLORPROMAZINE IMIPRAMINE HYDROCHLORIDE

Sigg (1959) showed, however, that the cooling effect of imipramine on experimental animals was much less than that of chlorpromazine.

Case Report

A widow aged 57, with suspected myxoedema since childhood, was admitted to the psychiatric unit because she had been expressing paranoid ideas against her neighbours, and was in a state of extreme neglect. Since childhood she had received only sporadic thyroid replacement therapy, and in fact no thyroid or equivalent had been taken for the last 10 years.

Physical examination revealed a thin, anaemic woman 4 ft. 5 in. (134.5 cm.) tall, weighing 82 lb. (37.2 kg.). The scalp hair was coarse and was falling out on the occipital region, but her eyebrows were bushy. The skin was dry and rough. Her voice had the typical fruity, croaking quality of myxoedema. Temperature on admission was 97.4° F. (36.3° C.), pulse 76, and B.P. 150/90.

Associated with the signs of myxoedema were definite traits of mongolism such as short fingers, the fifth turning markedly inwards, and prominent transverse palmar creases. The epicanthic folds were not pronounced, but the bridge of the nose showed marked flattening. No abnormal signs were detected in the other systems.

Her paranoid ideas disappeared without specific treatment, and she entered into the activities of the ward. Her intelligence was that of a high-grade mental defective. During this period of improvement she fell on the ward floor, sustaining a haematoma of the occipital region. She was confined to bed and became drowsy, though capable of being roused and of eating. No new abnormal signs were detected in the nervous system, and *x*-ray examination of the skull showed no fracture. She remained apathetic, depressed, and was easily moved to tears; consequently a course of imipramine was given. After two days' treatment a consistently low temperature was recorded. The patient was in a pre-comatose state, and could be roused only with difficulty; feeding was impossible.

Investigations.—Hb, 52.5%; W.B.C., 5,600/c.mm., with normal differential count; blood cholesterol, 190 mg./100 ml.; fasting blood sugar, 107 mg./100 ml.; blood urea, 104 mg./100 ml. Electrolytes (mEq/l.): Na 125, Cl 107, K 4.1. CO_2 combining power, 20.4. Plasma proteins, 6.5 g./100 ml. E.C.G.: sinus tachycardia, low-voltage complexes, and flat T waves. The Wassermann reaction was negative.

The temperature, recorded by a full-scale thermometer, was 93° F. (33.9° C.) after a total dosage of 200 mg. of imipramine. The drug was stopped immediately and her

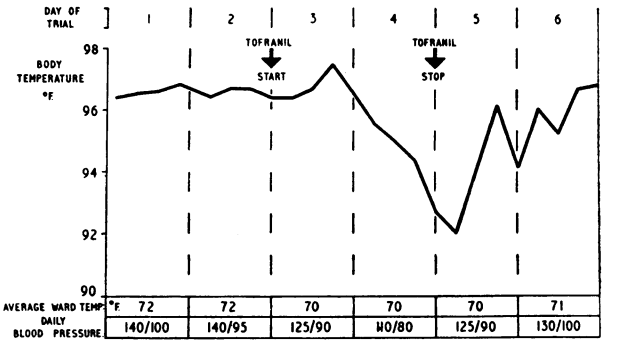


Chart showing temperature during trial.

temperature rose to 98° F. (36.7° C.) in 24 hours. The hypothermic episode was thought to be due to the imipramine, but other factors such as ward temperature had not been recorded during the episode. A further course of imipramine was therefore given, and the patient's rectal temperature was recorded four-hourly with the ward temperature. The Chart shows the temperature curve 24 hours before imipramine was given and while the drug was administered, hypothermia being observed 48 hours after starting the second administration. At no stage did we observe the excessive sweating sometimes attributable to this drug.

The onset of hypothermia was similar in both attempts to use imipramine; the rise in temperature after the second attempt, however, was protracted and erratic. L-Thyroxine was given immediately; since then her progress has been uneventful.

Comment

As chlorpromazine is capable of inducing a hypothermic coma in myxoedematous patients, it was possible that a similar drug, such as imiprazine hydrochloride, could also induce hypothermic coma. No such experience has yet been recorded. The patient reported here would undoubtedly have sunk into deep coma if she had not been observed carefully and the drug withdrawn promptly. Furthermore, the dose of the drug had not been excessive (100 mg. daily). The speed with which the temperature was lowered is alarming when one considers that the patient was in bed continuously in a warm ward (70° F.; 21.1° C.).

Drugs of the phenothiazine group and related substances are often prescribed for patients who are not under continual observation, and it is felt that caution is needed, particularly in the presence of hypothyroidism, if serious and often fatal calamities due to hypothermic coma are to be avoided.

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