ADDICTION TO CHLORODYNE

BY

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A 10-min. (0.6-ml.) dose of chlorodyne or tincture of chloroform and morphine contains morphine hydrochloride 1/48 gr. (1.35 mg.), chloroform 1½ min. (0.075 ml.), alcohol 1½ min. (0.075 ml.), ether 5/16 min. (0.02 ml.), as well as peppermint, treacle, and syrup.

Chlorodyne is readily available from pharmacists throughout the country without prescription. It is commonly used for the treatment of gastro-intestinal upsets, especially diarrhoea, for coughs and colds, and often for insomnia. Inquiry from local chemists confirmed that many regard it as a homely remedy for the treatment of such afflictions. A common similar preparation is Dr. Collis Browne's chlorodyne, which is widely advertised.

In the past two years three patients have been admitted to All Saints' Hospital with symptoms of chlorodyne addiction. They showed marked physical and mental deterioration and all had symptoms and signs suggesting neuropathy.

A review of their histories showed that they fulfilled the criteria for drug addiction laid down by the World Health Organization (1950). This is defined as "a state of periodic or chronic intoxication, detrimental to the individual and to society, produced by the repeated consumption of a drug (natural or synthetic). Its characteristics include: (1) an overpowering desire or need (compulsion) to continue taking the drug and to obtain it by any means; (2) a tendency to increase the dose; (3) a psychic (psychological) and sometimes a physical dependence on the effects of the drug."

Case 1

An unmarried labourer aged 43 had been admitted to hospital four times in two years. He started taking chlorodyne for diarrhoea in 1946. Before his last admission he had been taking 6 to 8 oz. (170–227 ml.) of the preparation daily. He was found in a semicomatose state on several occasions, and twice prior to admission was acutely psychotic. He complained of noises in the head, expressed paranoid delusional ideas, and described visual hallucinations of a religious nature. He threatened to commit suicide. Recently he had developed progressive unsteadiness in walking over a four-weeks period, with severe burning and pins-and-needles in all limbs.

He was emaciated, and showed marked generalized pigmentation of the skin. His blood-pressure was 100/65. Heart, lungs, and abdomen were normal. He was dysarthric with a gross tremor of the hands. There was a flaccid paralysis of the lower limbs with absent tendon reflexes. Power and reflexes were markedly diminished in the arms. All forms of sensation were impaired, particularly in the lower limbs, and the calves were tender. The plantar responses were flexor.

Investigations.—Blood count, blood urea, electrolytes, and liver-function tests: normal. W.R. negative. C.S.F. normal apart from protein 79 mg./100 ml. X-ray pictures of chest, spine, and pelvis normal. Pyruvate tolerance and serum vitamin B₁₂ normal. Urinary ketosteroids less than 1 mg./24 hours. Liver biopsy: severe cell damage with evidence of portal fibrosis.

Progress.—Within the protected environment of hospital the patient showed considerable improvement, but quickly relapsed each time he was discharged. The psychotic symptoms always cleared soon after admission to hospital. However, after his last admission he remained seriously ill physically for three months. He continued to complain of pins-and-needles and a burning sensation in all limbs, and after four weeks the right

plantar response became extensor. At the end of six months he was just able to hobble around the ward with the aid of crutches.

Case 2

An unmarried State-registered nurse aged 53 had been admitted to hospital five times since 1959. At the age of 30 she took chlorodyne for what she describes as gastric 'flu, and over the years took small amounts of the preparation for colds and stomach upsets. At the age of 49 she began taking it in excessive amounts, and for a period of six months prior to admission was consuming as much as 6 oz. (170 ml.) daily. She was often found in her home in a semicomatose state with empty bottles of chlorodyne lying around. In spite of this she maintained herself in employment as an industrial nurse, but for many years had been a burden to her employers, who were well aware of her addiction.

Before her first admission she was acutely psychotic, describing visual and auditory hallucinations, and expressing paranoid delusional ideas. She described flames emerging from the floor of her room, and in terror believed she was being enveloped. She complained of noises in her head which she attributed to faulty electrical wiring in her room. She believed her aged mother was trying to harm her, and on one occasion bit her severely on the leg. She complained of pins-and-needles all over her body.

She was emaciated, and weighed only 5 st. 9 lb. (35.8 kg.), her normal weight having been 9 st. (57.2 kg.). Her skin was sallow and pigmented, but there was no buccal pigmentation. The blood-pressure was 105/65. The other abnormalities were confined to the nervous system. She was dysarthric, and her pupils were contracted but not pin-point. She was ataxic, with gross tremor of both hands. Power and tone were diminished in all limbs and all the tendon reflexes were diminished or absent. The plantar responses were flexor. All forms of sensation were similarly impaired, especially in the lower limbs. There was oedema of both ankles and over the sacrum. No albumin or sugar was found in the urine.

Investigations.—The blood count, blood urea, electrolytes, liver-function tests, chest x-ray examination, E.C.G., E.E.G., and lumbar puncture were all normal. W.R. negative. Urinary 17-ketosteroids 1 mg./24 hours.

Progress.—She improved with intravenous "parentrovite" (vitamin-B complex and ascorbic acid), modified insulin, and chlorpromazine, and had no serious withdrawal symptoms. The neuropathy cleared completely over a period of three months. Over two years every effort was made to rehabilitate her, but she relapsed repeatedly. She used every opportunity to obtain supplies of chlorodyne and was found heavily under the influence of the preparation on several occasions within the hospital.

Case 3

An unmarried general labourer aged 41 had been admitted to hospital on three occasions over a period of 18 months. He began taking chlorodyne six years ago for stomach upsets, having seen it advertised in a national newspaper. He had been admitted on 10 occasions in two years to local general hospitals in a comatose or semicomatose state, and each time a diagnosis of chlorodyne-poisoning was made. On his last admission he was extremely ill and was heavily intoxicated by chlorodyne, the smell of which from the breath was unmistakable. On this occasion seven empty 1-oz (28-ml.) bottles of chlorodyne were removed from his pockets.

He was emaciated and weighed only 7½ stone (47.6 kg.), his normal weight having been over 10 stone (63.5 kg.). He showed a generalized pigmentation of the skin and his blood-pressure was 115/70. He was mildly confused and suicidal, and com-

plained of buzzing in the ears, and pins-and-needles and weakness in the legs. He was dysarthric and ataxic, with considerable loss of power in the legs, absent tendon reflexes, and impaired superficial sensation.

Investigations.—Blood count, blood urea, electrolytes, liver function tests, and chest x-ray picture: normal. W.R. negative. C.S.F. protein 80 mg./100 ml. Urinary 17-ketosteroids less than 2 mg./24 hours. Pyruvate tolerance and liver biopsy normal.

Progress.—After each admission he quickly responded to intravenous parentrovote, modified insulin, and chlorpromazine. His neurological symptoms and signs cleared after two weeks. After discharge or when on leave from the hospital he soon reverted to his old habits.

Discussion

In the patients described the average daily consumption of chlorodyne was at least 6 oz. (170 ml.). They were therefore taking 6 gr. (0.4 g.) of morphine and 360 min. (21 ml.) of chloroform daily. There existed an overpowering desire to continue taking the preparation, increasing the dosage from day to day. In the end they were totally dependent on it. Their progressive social and physical deterioration was no deterrent. All had been in an unconscious state several times, and one had been admitted to a general hospital in coma on no fewer than eight occasions. All were psychotic at one time or other, necessitating admission to a mental hospital. Visual hallucinations were present in two.

The similarity of presentation with severe physical debility, marked weight loss, sallow grey complexion, tremor, and dysarthria was striking. All had symptoms and signs of peripheral neuropathy, one of which, so far, seems irreversible.

Two patients had a low blood-pressure. This is a well-known effect of morphine and chloroform, but, together with the curious pigmentation of the skin and the low urinary 17-ketosteroids, suggested the presence of adrenal insufficiency. Two patients consented to liver biopsy. The extent of liver damage on biopsy in the first was remarkable. The hepatotoxic effects of chloroform and alcohol, however, are well known, and it is arguable that prolonged malnutrition may also have contributed. Unfortunately it is not possible to say with certainty whether the deleterious effects on the liver were due to morphine, alcohol, or chloroform.

All three patients showed behaviour disturbance. The degree of personality maladjustment prior to addiction was

difficult to determine, but they were emotionally immature, shy, sensitive people with a very low stress tolerance. Two were subject to marked mood changes from an early age, and the second patient was treated for depression by her family doctor at the age of 32. They were all unmarried and complained bitterly of the loneliness of their lives.

Over the past two years three other patients who were taking excessive amounts of chlorodyne have been admitted to this hospital, but the picture was complicated by addiction to barbiturates, amphetamines, or alcohol in addition.

A number of references have been made from time to time in the *Pharmaceutical Journal* to coroners' inquests on deaths due to chlorodyne-poisoning. In all cases there was a history of chronic addiction for many years. Coroners have commented on the ready availability of chlorodyne and the lack of legislation regarding its sale.

Seager and Foster (1958) described the cases of two patients who were addicted to the preparation, one of whom was acutely psychotic with visual and auditory hallucinations.

Personal inquiries from chemists in the area have established that there is no difficulty in obtaining at reasonable cost large quantities of this preparation, for which there is considerable demand. Its ready availability is to be deplored, and there is a strong case for amending existing legislation, so that chlorodyne becomes available on prescription only by inclusion in Schedule 4 of the Poisons Act.

Summary

The cases of three patients who were addicted to chlorodyne are described. There was evidence of serious mental and physical deterioration, including peripheral neuropathy.

The ready availability and the large quantities of morphine and chloroform consumed make chlorodyne a potentially dangerous drug. It is suggested that it would be better scheduled as a poison available only on prescription.

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Medical Memoranda

Hydatidiform Mole and Pregnancy Diagnosed By Sonar

[WITH SPECIAL PLATE]

The onset of pre-eclamptic toxæmia prior to the twentieth week of pregnancy is very suggestive of the presence of a hydatidiform mole. The definite diagnosis of hydatidiform mole can be very difficult, since biological tests for chorionadotrophin are often inaccurate; but recently the use of sonar has enabled the diagnosis to be made with certainty and immediately on examination (Donald and Brown, 1961; MacVicar, 1962; MacVicar and Donald, 1963).

CASE REPORT

A primigravida aged 26 who had had amenorrhœa for 16 weeks was admitted to hospital because of recent swelling of the ankles, feet, and hands. On admission she was found to have generalized oedema. Her blood-pressure was 190/100 mm. Hg, and the urine contained albumin (2.5 g./litre).

On examination the uterus, which felt cystic, appeared to be only slightly larger than the dates would suggest. On vaginal examination the cervix was long and not "taken up." No internal ballotement of foetal parts could be elicited. There was neither vaginal bleeding nor discharge. A "prepuerin" (Burroughs Wellcome Ltd.) pregnancy test was weakly positive only and a straight radiograph of the abdomen showed no foetal parts.

During the ensuing week the patient was treated with sedation and complete bed rest, but her blood-pressure remained raised, the highest reading being 220/125 mm. Hg. The urine, though microscopically clear, constantly contained albumin, the maximum amount being 4 g./litre. The oedema persisted. She