of closed sterile drainage. Disposable sterile plastic bags are convenient, but many that have appeared on the market are unsatisfactory, since though they are sterile initially they become contaminated during use (Roberts, Linton, Pollard, Mitchell, and Gillespie, 1965). The bag should remain closed during use and should be designed to prevent reflux of urine into the drainage tube. This is important, since small numbers of bacteria may pass from the urethra to the bladder and thence to the bag, where they may multiply and, if reflux is allowed, re-enter the bladder in large numbers. The longer the period of drainage the greater the chance of infection arising in this way. It would be dangerous to place a disinfectant in a non-rigid receptacle, since compression might force it back into the bladder. Kunin and McCormack (1966) described the use of a reservoir drainage bag without a valve. However, it is difficult to compare their results with ours, because few of their patients were gynaecological. Moreover, most of their patients received antimicrobial drugs, whereas none of ours did. Several drainage bags with valves have appeared on the market. We have found the valve of the Meredith bag to be the most efficient of those we have seen. In laboratory tests in which the bag was filled with contaminated urine it was impossible to force bacteria back through the valve by compressing the bag. However, when a partly filled bag was laid gently on the floor, and not compressed, a slow reverse flow could sometimes be detected. In practice, such slow leakage would be opposed by the flow of urine, which also would oppose the movement of motile bacteria.

Perhaps the greatest risk of infection during closed drainage is by bacteria that gain access to the catheter when the receptacle is detached because it is full. It follows that if reflux can be avoided it should be safer (and more economical) to use the bag as a reservoir and empty it periodically without detaching it from the drainage tube and catheter. The infections that occurred in our patients during drainage into reservoir bags were attributable, for the most part, to invasion of the bladder by bacteria, especially *Pr. mirabilis*, which passed along the outside of the catheter, probably because they were rather insen-

sitive to the chlorhexidine that was used to exclude bacteria from this route.

Patients and nurses preferred the plastic bags to the glass drainage bottles, which ambulant patients found cumbersome. It remains to be seen how efficient the bags will be during longer periods of drainage and after prostatectomy, when it is sometimes necessary to irrigate the bladder.

Summary

Sterile disposable plastic bags with non-return valves were used for closed drainage of urine after gynaecological operations. It was found best to use the bag as a reservoir, joining it to the catheter before the patient left the theatre and not detaching it until the indwelling catheter was removed four days later. The bag was emptied periodically through an opening distal to the valve. Of 74 patients who were treated in this way, 17 (23%) became infected. This was a slightly greater rate of infection than that observed during a previous period when bottles containing formaldehyde were used as receptacles. The infections probably were not attributable to faults in the drainage bag or valve, but to bacteria which passed from the urethra into the bladder outside the catheter, despite the precautions taken to exclude them.

We thank Eschmann Bros. and Walsh Ltd. for a supply of Meredith drainage bags.

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Medical Memoranda

Methaqualone Addiction and Delirium Tremens

Brit. med. J., 1967, **3**, 92-93

Four cases of addiction to the non-barbiturate hypnotic methaqualone have been reported (Madden, 1966). The probability that these patients were physically dependent on methaqualone has been disputed (Martin, 1966) because of failure to show an abstinence syndrome. We now document another case, which was associated on withdrawal with the clinical syndrome of delirium tremens characteristic of the barbiturate-alcohol type of dependence.

CASE REPORT

A 47-year-old married man had suffered from rheumatoid arthritis since 1947. In turn he took increasing quantities of barbiturates (developing macrocytic anaemia), of an analgesic mixture containing phenacetin (developing nephrocalcinosis and renal tubular acidosis), of thalidomide (developing peripheral neuropathy), and later chloral hydrate.

For four years before admission he had been taking increasing doses of methaqualone, and for at least some months before admis-

sion had taken neither alcohol nor any other drug. In the weeks prior to being admitted (January 1966) he was taking 60 150-mg. tablets of methaqualone daily.

He was found unconscious one evening (two days before admission) and his stocks of methaqualone were destroyed. Next evening he was restless and confused, and complained of seeing strangers in dark corners of the room.

On admission he was in delirium with obvious tremor. He was anxious and restless, and had visual hallucinations of which he was afraid. His temperature was 100° F. (37.8° C.), with brisk reflexes, and blood pressure 130/70. The liver was palpable 2 cm. below the costal margin. A combination of promazine 600 mg. daily, phenobarbitone 1 g. daily, and paraldehyde 10 ml. intramuscularly as required for states of agitation was only partially successful in controlling his restlessness and led to intoxication (with slurred speech, ataxia, and nystagmus). However, the administration of thioridazine (Melleril) in doses up to 800 mg. daily, starting on the fourth day, resulted in dramatic improvement and rapid recovery.

DISCUSSION

Delirium tremens has not only been produced experimentally by withdrawal of addicting doses of barbiturates (Isbell *et al.*, 1950) and alcohol (Isbell *et al.*, 1955), but has now been recorded also with chloral hydrate, paraldehyde, glutethimide

(Doriden), methypylone (Noludar), ethchlorvynol (Arvynol), and meprobamate (Miltown, Equanil) (*Brit. med. J.*, 1964; Wood and Flippin, 1965). The clinical features described in these studies correspond very closely with those found in our patient.

Methaqualone has been shown to be a potent hypnotic (Parsons and Thomson, 1961; Duchastel, 1962). It is marketed in the United Kingdom as Melsedin, and in combination with diphenhydramine as Mandrax. It is sold in the U.S.A. as Quaalude. Melsedin was described as a non-barbiturate hypnotic that "produces natural sleep" and to which neither tolerance nor addiction had been attributed. The makers have told us that they now know of four cases of addiction, in addition to the one reported here, three of the patients concerned having a history of addiction also to barbiturates or alcohol (J. W. Buckler, personal communication, 1966).

Mandrax is claimed to have an action that is "quite different from that of the barbiturates and almost all other hypnotics." No addiction had been reported to the makers, who pointed out (February 1966) that their product had been generally available for only four months (A. L. Macnair, personal communication, 1966).

Though recent neurophysiological methods of investigation of the action of drugs on sleep (Oswald and Thacore, 1963; Oswald and Priest, 1965) may eventually clarify the relevance of withdrawal syndromes, at present the clinical picture of

delirium tremens is one means of categorizing the pharmacological action of psychotropic drugs. Apart from the remarkable experiments of Isbell and his colleagues it seems that at present we must rely on those patients who abuse their drugs to assist us in this classification.

We are grateful to Professor J. A. Strong for permission to report this case, and to the manufacturers for the information mentioned above.

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Thrombocytopenic Purpura in Patient with Autoimmune Haemolytic Anaemia, Successfully Treated with Mercaptopurine

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Before the introduction of corticosteroids in 1949 splenectomy and blood transfusions were the only well-established treatments for autoimmune haemolytic anaemia (Dacie, 1954; Schwartz and Dameshek, 1962). Corticosteroids rapidly became the treatment of choice, splenectomy being reserved for refractory cases. Dameshek and Schwartz (1960) reported the use of purine antagonists in the management of autoimmune haemolytic anaemia, and this has now been accepted as an additional treatment. It has been suggested that primary thrombocytopenic purpura and acquired haemolytic anaemia might have a common aetiology (Evans *et al.*, 1951), since thrombocytopenia may be a feature of autoimmune haemolytic anaemia, and in a proportion of cases platelet antibodies can be demonstrated.

In the following case a relapse of thrombocytopenic purpura occurred in a patient with autoimmune haemolytic anaemia who had previously been treated by corticosteroids and splenectomy. High doses of corticotrophin temporarily controlled the thrombocytopenia, which later was successfully treated with mercaptopurine.

CASE REPORT

A 17-year-old youth was admitted to hospital in January 1962 with a three-months history of increasing weakness and lassitude. Immediately before admission he developed high fever, became jaundiced, and started passing dark urine. There was no relevant past or family history, and no history of blood transfusion or exposure to drugs or poisons.

Physical examination showed a febrile, pale, jaundiced youth with slight hepatosplenomegaly. Investigations showed haemoglobin 3.5 g./100 ml.; reticulocytes 31%; W.B.C. 22,800/cu. mm., normal differential; platelets 48,000/cu. mm.; serum bilirubin 5.2 mg./

100 ml. (1.5 mg. direct). A direct Coombs test was positive. Autoimmune haemolytic anaemia was diagnosed and treatment with prednisone was started, and within four weeks the peripheral blood picture had returned to normal. On a maintenance dose of prednisone 10 mg./day he remained well, with a normal haemoglobin and platelet count, until early in 1964, when he developed a diffuse petechial rash. Platelets numbered 24,000/cu. mm., and after increased doses of prednisone (20 mg./day) had failed to control the thrombocytopenia splenectomy was performed in March 1964. The platelet count did not rise greatly after operation, and prednisone 10 mg./day was restarted with considerable improvement. On this dose of prednisone for the next year the platelet count remained between 100,000 and 200,000/cu. mm.

In July 1965 he was readmitted to hospital with a recurrence of purpura and a platelet count of 20,000/cu. mm. A corticotrophin infusion produced a satisfactory rise in platelet count to 200,000/cu. mm., and this was maintained as long as the dosage of corticotrophin was not dropped below 80 i.u./day. During a two-months course of corticotrophin administration the patient gained 35 lb. (15.9 kg.) and developed many features of Cushing's syndrome.

In October he was admitted to hospital for a trial of mercaptopurine. On examination he presented the appearance of Cushing's syndrome, with moonface, buffalo hump, high colour, and abdominal striae. Blood pressure was 160/120. The initial peripheral blood picture was: Hb 14.9 g./100 ml.; W.B.C. 11,800/cu. mm., normal differential; platelet count 230,000/cu. mm.; E.S.R. 3 mm. in first hour; blood was also examined for lupus erythematosus cells with negative results. A direct Coombs test was positive in a dilution of 1/16, but serological study failed to reveal platelet or leucocyte agglutinins or incomplete platelet antibodies, and the red cell antibody showed no specificity. Apart from a serum potassium of 2.7 mEq/l. on admission, later corrected by oral potassium supplements, other electrolytes were all normal. The urine contained a trace of sugar. Blood-volume studies showed a normal red cell mass and plasma volume, and $T_{\frac{1}{2}}^{51}\text{Cr}$ red cell survival was 27.5 days.

At the time of admission on 4 October he was receiving corticotrophin 40 i.u. b.d. On the following day treatment with mercaptopurine 150 mg. o.d. was started, and during the next three weeks the corticotrophin was gradually reduced, finally being stopped on 24 October. Meanwhile the patient noticed transient symptoms of dizziness and lassitude. At the same time the urine became free of sugar, the blood pressure settled to normal, and he lost 14 lb. (6.4 kg.) in weight. During a 23-days course of treatment with