the patient is conscious he must be taught to play an active part in his own re-education, and his activities must be carefully supervised.

Bed exercises in the early stages are followed by exercises while learning to stand, and, later, by practice in walking with a stick and a little assistance, and, finally, by walking with a stick unaided on the flat and then on the stairs.

During the treatment of all these conditions suitable occupational therapy should be provided, and general interest be stimulated by encouraging visiting, reading, conversation with other patients, and by wireless programmes (via headphones and *not* loudspeakers, unless a room can be set aside for such purpose).

If these principles are adhered to then success in treatment will depend upon early and full treatment, attention to detail in an atmosphere of optimism, strength of the team-work, confidence of the patient in the team, and the experience and activity of the physician.

Summary

The results of inactivity both to the individual and to the community are outlined, and an argument is put forward for the maintenance of full activity and independence among the elderly and for their rehabilitation.

Inactivity may be brought about by psychological, physical, or social conditions; preventive measures against these are described.

Medical conditions which particularly predispose to inactivity are enumerated, and principles underlying their management and treatment are discussed. Warning is given that long periods of rest necessitated by illness must be regarded as "danger periods."

Points stressed are: that good results depend on a high standard of medicine, on really good team-work, and on an atmosphere of optimism and activity; combined with the patient's confidence and co-operation in his treatment.

Some suggestions are made with regard to the treatment of arthritics and hemiplegics.

USE OF INTRAVENOUS AMPHETAMINE SULPHATE IN ACUTE BARBITURATE POISONING

BY

J. D. N. NABARRO, M.D., M.R.C.P.

First Assistant, Medical Unit, University College Hospital

The possible use of intravenous amphetamine sulphate in conjunction with other remedies in cases of acute barbiturate poisoning is seldom considered in this country. When Alles (1933) was investigating the pharmacological properties of this drug in dogs under barbiturate anaesthesia he found that the animals often awoke after its injection. Myerson (1940), in a review of the rationale of amphetamine sulphate treatment, mentioned its possible value in counteracting the effects of barbiturate poisoning. Freireich and Landsberg (1946) reported 14 cases of this condition in which the drug was used; but few of these were severe, and the maximum dose employed was 400 mg. Newman and Feldman (1948) have reported a series of cases of poisoning in which massive doses of picrotoxin were used, supplemented in four by amphetamine sulphate. In the treatment of one of their patients who was 135 hours in coma, 14,190 mg. of picrotoxin and 1,950 mg. of amphetamine sulphate were given.

Pharmacological Aspects

Barbiturate poisoning may cause the death of the patient either by depression of the respiratory centre or through the development of bronchopneumonia. The former is more likely to occur with very large doses and with the short-acting derivatives, whereas the latter is associated with prolonged coma. Specific treatment is therefore directed at stimulation of the respiratory centre and hastening the recovery of consciousness. Picrotoxin has an established place in the management of these cases, principally as a stimulant of the respiratory centre. It has much less action on the cerebral cortex, but on account of its convulsant properties must be used with care.

Amphetamine is widely known as a cerebral stimulant, and its power of awakening both men and animals under the influence of various narcotics has often been reported (Reifenstein and Davidoff, 1938; Myerson *et al.*, 1939), although it has been found to increase the death rate in mice after LD50 doses of barbiturate (Chakravarti, 1939). The action of amphetamine on the respiratory centre has been the subject of conflicting reports, and no consistent stimulant action can be demonstrated. In addition to its effect on the central nervous system amphetamine is a powerful sympathomimetic agent. It produces a rise of blood pressure and should therefore be used with care in older patients and hypertensive subjects. Disturbances of cardiac rhythm following its administration have also been reported (Anderson and Scott, 1936; Waud, 1938).

The very large amounts of amphetamine used in Newman and Feldman's case and in that reported below raise the question of the fate of the drug in the body. When given by mouth in normal doses, part is excreted in the urine, in which it may be detected for some days (Beyer and Skinner, 1940; Monroe and Drell, 1947), and the remainder is probably metabolized (Beyer, 1942). There are a few reports in the literature of the results of large doses being taken by patients not under the influence of narcotics. Transient hypertension, excitement, or confusional states have followed the ingestion of amounts up to 450 mg. (Ehrich *et al.*, 1939; Monroe and Drell, 1947). A few deaths have been attributed to the drug, usually after much smaller quantities, and presumably due either to idiosyncrasy (Smith, 1939) or, as in one case, to subarachnoid haemorrhage (Gericke, 1945). The administration of large doses to monkeys has been found to produce toxic degeneration of the nerve cells and perivenous haemorrhages in the meninges (Ehrich *et al.*, 1939).

Case Reports

Over a period of 18 months intravenous amphetamine sulphate has been used, usually in conjunction with other remedies, in the treatment of seven cases of acute barbiturate poisoning. Four were mild cases with coma lasting a few hours, and in three of these picrotoxin seemed more effective in awakening the patient, although the amount of amphetamine used was probably inadequate in the light of subsequent experience. In the fourth, recovery was little accelerated by either drug. The other three cases had points of particular interest and are recorded in more detail.

Case 1

A woman aged 29 was admitted two and a half hours after taking 80 gr. (5.3 g.) of sodium amytal. The stomach was washed out and picrotoxin (100.5 mg. intramuscularly and 115.5 mg. intravenously) was administered over the next 17

hours. In spite of this the patient remained comatose, and tendon reflexes were obtainable for only a few minutes after each injection. During the next 75 minutes 70 mg. of amphetamine sulphate was given intravenously, and after this the patient woke up and spoke. After an hour without treatment she relapsed into coma and 6 mg. of picrotoxin failed to rouse her. Thirty minutes later a further intravenous injection of 10 mg. of amphetamine again woke the patient, and when this was repeated one hour later she became fully conscious and required no more treatment. (This patient was treated in collaboration with Dr. A. G. Spencer.)

This case demonstrates the superiority of amphetamine over picrotoxin as an awakening agent in the later stages of the treatment of a case of severe barbiturate poisoning. Its action in shortening the period of unconsciousness should reduce the risk of bronchopneumonia.

Case 2

An asthmatic patient, aged 54, 24 hours before admission took 2 gr. (0.13 g.) of phenobarbitone and $1\frac{1}{2}$ gr. (0.1 g.) of pentobarbitone sodium, followed while in a drowsy state by a further 9 gr. (0.58 g.) of pentobarbitone sodium. He was unconscious and cyanosed on arrival at hospital, with widespread rhonchi all over his chest and a respiration rate of 25. He was given 20 mg. of amphetamine intravenously, after which he opened his eyes, and a further 10 mg. 45 minutes later restored him to full consciousness.

This was a mild case of barbiturate intoxication, but in view of the patient's pulmonary condition it was essential to terminate the coma as quickly as possible. Amphetamine sulphate in quite small doses proved effective.

Case 3

A man aged 38 took 96 gr. (6.3 g.) of phenobarbitone and was admitted to hospital 31 hours later deeply comatose, with stertorous respirations at a rate of 16 a minute and a blood pressure of 100/68. The pupils were small with poor reaction to light; the corneal and tendon reflexes were sluggish and plantar responses flexor. The stomach was washed out, but only traces of barbiturate were present in the fluid. In the first three hours 180 mg. of amphetamine was given intravenously; the pupils became dilated and fixed, and the coma and blood pressure were unchanged. During the next three hours 69 mg. of picrotoxin was given intravenously and the blood pressure rose to 120/80. For the next 32 hours picrotoxin, 12 mg., and amphetamine, 20 mg., were given every half-hour, the injections being made into a glucose-saline drip every 15 minutes. Muscular twitching appeared and the dose of picrotoxin was reduced to 6 mg.; after a further 13 hours the twitching became more marked and picrotoxin was discontinued.

Over the next five hours amphetamine only was given; the patient's condition deteriorated, his coma became more profound, and respiration was shallower. Picrotoxin was then restarted, and eight hours later the condition had improved and the amphetamine was discontinued to see if this led to any change in the patient's condition; there was no deterioration of either blood pressure or respiration. However, after another four hours vigorous muscle-twitching occurred and the picrotoxin was permanently stopped and amphetamine in 20-mg. doses recommenced. Seventeen hours later, when 116 hours had elapsed since the drug had been taken, the urine for the first time was free from barbiturates. The patient, however, remained deeply comatose; lumbar puncture was performed and a normal cerebrospinal fluid was obtained which did not contain any barbiturate. Twelve hours later the coma lightened, and after another eight hours the patient regained consciousness—137 hours after taking the tablets. Amphetamine was continued in decreasing amount and at lengthening intervals for a further 15 hours.

Over a period of 121 hours the patient received 4,230 mg. of amphetamine sulphate, 1,086 mg. of picrotoxin, and by intravenous drip 8 pints (4.5 litres) of 5% glucose in

normal saline, 12 pints (6.8 litres) of 5% glucose in half-normal saline, 14 pints (8 litres) of 5% glucose, and 1 pint (570 ml.) of plasma. He was also given penicillin, vitamins of the B complex, two-hourly inhalations of 5% CO₂ in oxygen, and was frequently turned from side to side. During this prolonged coma the lungs remained completely clear, and great credit must go to the house-physician (Dr. D. A. Hodgson) and the nursing staff for their conscientious care of the patient. He was subsequently transferred to a mental hospital in which he had previously received treatment. His physician noted no change in his mental condition; the only sequelae to the poisoning and its treatment were thromboses in the leg veins into which the drip had been given. Lamson *et al.* (1949) have shown that in some animals the intravenous infusion of glucose potentiates the action of barbiturates; however, no such effect has been reported in humans, though the relationship has not apparently been specifically investigated.

Comment on the Cases

Many of the properties of amphetamine already referred to make it questionable whether the use of this drug in barbiturate poisoning is ever justified. In mice it increases the death rate from large doses of barbiturate. In man it raises the blood pressure and may produce cardiac arrhythmias; some patients show idiosyncrasy to the drug, which may be fatal. It disappears from the body very slowly, partly by an uncertain metabolic process and partly in the urine; hence with these large doses the amount accumulated must be considerable. In monkeys it produces histological changes in the brain cells.

Kempf (1946) has discussed its possible value, and points out that in mild cases there is little to be gained in the ordinary way by awakening the patient rather than letting him "sleep it off." Case 2 represents an exception to this: the patient was an asthmatic, and if his coma had persisted much longer he would probably have developed bronchopneumonia. Amphetamine in quite small doses proved effective, and there is little reason to suppose that such an amount would be dangerous. The use of larger doses in the severer cases requires more justification.

The outcome in Case 3 is unusual. The patient had taken a fatal dose of phenobarbitone, nearly all of which was probably absorbed, and he did not come under treatment until 31 hours after the drug had been ingested. He received large doses of picrotoxin and amphetamine in the course of treatment, and it is important to try to assess what part, if any, they played in his recovery. During the first three hours, when amphetamine was being administered, his condition remained poor, whereas picrotoxin at once stimulated the medullary centres and removed much of the immediate anxiety. Forty-eight hours later, when muscular twitching necessitated a break in picrotoxin therapy, there was definite deterioration despite the continued administration of amphetamine. Newman and Feldman (1948) recommend that picrotoxin should be used until preconvulsive muscular twitchings appear and amphetamine treatment then be started. It seems, however, that picrotoxin may have to be recommenced if the patient's condition is not maintained. In the early stages of this patient's treatment amphetamine had no demonstrable beneficial effect, but it is possible that subsequently it accelerated the recovery of consciousness. The progress of the first case showed this very clearly. No undesirable results seem to have followed the very large amounts of amphetamine administered.

Management of Cases of Acute Barbiturate Poisoning

These cases are not very common, and frequently first come under treatment during the night. The remedies used are often employed in a half-hearted and haphazard fashion. The following programme is outlined for the management of severe cases in deep coma.

1. If there is marked respiratory depression restorative measures should be applied at once. Intravenous picrotoxin, 6 mg., should be given, and if there is no response 12 mg. every 30 minutes. Oxygen administration may be useful, and in extreme cases the use of a mechanical respirator should be considered.

2. When respiration is restored, or in less severe cases immediately on admission, the stomach should be washed out with 16 pints (9 litres) of saline. (The stomach contents should be retained for examination.) Twenty grammes of magnesium sulphate should be left in the stomach.

3. The intravenous administration of picrotoxin, 12 mg. every 30 minutes, should be continued. A careful watch must be kept for twitching of the facial muscles; picrotoxin must be stopped if this occurs, and amphetamine, 20 mg. at similar intervals, should be given. If the coma then deepens, picrotoxin, 6 mg., every 30 minutes should be restarted; otherwise amphetamine should be continued until the patient regains consciousness and for some hours after, in decreasing doses and at lengthening intervals.

4. If the patient shows no response after the first few hours it is desirable to cut down on a leg vein and set up a drip infusion. A plaster cast should be applied to the leg, otherwise as the patient becomes restless serious damage may occur. The analeptic drugs are given into the tubing of the drip. The fluid given should be glucose (5%) in varying concentrations of saline according to the urinary chloride content. The rate of flow must be regulated to maintain a good urinary output without causing any pulmonary oedema.

5. Rectal wash-outs should be done daily in order to remove any barbiturate in the lower bowel.

6. Milk by gastric tube should be given, and probably vitamin-B complex by intramuscular injection as long as a glucose drip is running.

7. To prevent pulmonary infection prophylactic penicillin should be given, also CO₂ and oxygen inhalations every two hours, and the patient should be nursed on his side and turned frequently.

In mild cases in which the patient exhibits spontaneous movements, a stomach wash-out is in many cases all that is needed; but if for any reason rapid awakening is desirable, one or two intravenous injections of 20 mg. of amphetamine at 30-minute intervals may be given. Some patients admitted shortly after the ingestion of the drug may present a deceptive appearance and should be watched carefully, since they may sink deeper into coma.

Summary

Intravenous amphetamine sulphate is a useful ancillary drug in the treatment of acute barbiturate poisoning. In mild cases in which rapid awakening is desirable it is effective and safe. In severe cases it is of little value in the early stages, but it may shorten the duration of coma if given later, particularly when picrotoxin is producing preconvulsive muscular twitchings.

A case is described in which the patient took 96 gr. (6.3 g.) of phenobarbitone 31 hours before admission to hospital. He recovered after 137 hours in coma. Treatment included 4,230 mg. of amphetamine sulphate and 1,086 mg. of picrotoxin.

A programme for the management of cases of acute barbiturate poisoning is outlined.

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PREGNANCY IN A RUDIMENTARY HORN OF A BICORNUATE UTERUS

BY

DOUGLAS LATTO, M.B., Ch.B., M.R.C.O.G.

AND

RICHARD NORMAN, M.R.C.S., L.R.C.P.

D.Obst.R.C.O.G.

(From the Nuffield Department of Obstetrics and Gynaecology, Radcliffe Infirmary, Oxford)

This case of pregnancy in a rudimentary horn is discussed at some length because of the great danger there may be to the patient. Unlike tubal gestation, in which less than 50% rupture and present the classical picture, 90% of the cases of pregnancy in a rudimentary horn rupture, and as this occurs about the sixteenth week the bleeding is profuse. Very little has been written on this subject recently, and the relatively high incidence of the condition is not generally realized.

Pregnancy in a rudimentary horn was first described by Mauriceau and Vassal in 1669. Kehrer in 1900 collected 84 cases from the literature, and Beckmann in 1911 found 146 cases. DeLee and Greenhill (1947) state: "Perhaps 100 cases have been described. Mulsow found reports of only nine cases since 1911." Mulsow (1945) himself, however, said: "With the aid of the librarian of the Iowa State Medical Library at Des Moines, I have been able to review the records of nine cases which have been reported since Beckmann's review in 1911." In the *Index Medicus* for the past 25 years we have found over 40 reported cases: in all probability, therefore, well over 200 cases have now been described.

Case Report

The patient was admitted to the Radcliffe Infirmary on January 15, 1950, complaining of severe abdominal pain of four hours' duration. She had had vague pain in the right iliac fossa for the past week, and had felt sick but had not vomited. Menstruation had been regular until September 16, 1949, since when there had been amenorrhoea. There was very little else of significance in her history except that she had a normal full-term pregnancy in 1946, a spontaneous breech delivery; also she had rather severe hyperemesis in the first three months of this pregnancy.

The patient looked distressed and was obviously very ill, with restlessness and air-hunger. The skin was cold and clammy,