relapse occurs. The neurological lesions are in no way distinctive, and may affect any part of the nervous system. There is nothing to distinguish the toxic psychosis of carbon monoxide from that due to any other noxious process unless it be the history of exposure and the coincidental neurological damage.

Carbon monoxide has long enjoyed an evil reputation for causing irreparable mental and nervous syndromes. Yet of 43 survivors with severe neurological or psychiatric disorders all but 10 recovered (Shillito *et al.*, 1936). Recovery usually ceases within two years but may continue up to this time, so that there is no reason to give a gloomy outlook in the early acute case. The delayed case is a different matter. In two series "pseudorecovery," as this is sometimes called, has been followed by death in half the cases. Treatment of the neurological damage is confined to reassurance, rest, passive movement, and prevention of stretching the paretic muscles. Passive full-range movement of necrosed muscles is essential to prevent Volkmann's contracture and calcification. The treatment of psychiatric syndromes should be supportive psychotherapy.

Renal Failure

When acute renal failure has occurred with muscle necrosis the constant danger is the hyperkalaemia with a sudden rise to fatal levels. It can be seen from Fig. 3 that, in the case reported, large amounts of resonium-A only just controlled the hyperkalaemia temporarily. Dialysis in these cases should be carried out earlier than the clinical state would indicate and before the serum potassium has reached 7 mEq/l., or the serum bicarbonate 12 mEq/l. Serum-potassium levels were estimated twice daily together with the occasional E.C.G., though the latter we have found to be of less assistance in the assessment.

With this type of case we would go so far as to recommend transfer to a unit where the technique for haemodialysis is available, as soon as the possibility of muscle necrosis is suspected.

No myoglobinuria was found in this patient, as it was only on the third day that a search was made. The renal lesion was acute tubular necrosis, and it is anticipated that the patient will regain normal renal function within 12 months. The management of a difficult case of this nature is the same as with any acute renal failure with much tissue breakdown. Our experience has shown the necessity for the most careful and frequent assessment at the bedside, with all the facts assembled at least twice a day. Otherwise these patients can slip out of control rapidly. One should be prepared to dialyse early even though this may mean an extra dialysis. This is made evident by the reports of Fahlgren *et al.* (1957) and of Loughridge *et al.* (1958).

Summary

A case is described of carbon-monoxide poisoning with the following complications — skeletal-muscle necrosis, probable myocardial necrosis, acute renal failure, mental changes, and a radiculomyelitis of L 2-5.

The details of conservative management and haemodialysis (twice) by a Kolff twin-coil artificial kidney are given. The literature concerning muscle necrosis and renal failure, with the neurological sequelae, is reviewed.

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ARTIFICIAL RESPIRATION AND AN ARTIFICIAL KIDNEY FOR SEVERE BARBITURATE POISONING

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Most patients admitted to hospital suffering from barbiturate intoxication will recover provided that steps are taken to keep the airway clear, to maintain fluid balance, and to prevent hypostatic pneumonia (Nilsson, 1951; Locket and Angus, 1952). Some authors favour the use of analeptics such as picrotoxin and bemegride ("megimide") (Shulman *et al.*, 1955; Koppanyi and Richards, 1958), but there is little evidence that these drugs play any major part in the recovery of the patients (Eckenhoff and Dam, 1956). The essential of treatment, however, should be to maintain adequate respiration of the patient and an adequate circulation. The problem is similar to that of managing a deeply anaesthetized patient; the only difference is that the person with barbiturate intoxication usually remains in coma for a longer time. It may be possible to shorten the duration of coma substantially by dialysing

with an artificial kidney some of the ingested barbiturate out of the body (Alwall *et al.*, 1952; Walsh *et al.*, 1952).

A case, in which there was no renal failure, is described of recovery from an otherwise fatal dose of butobarbitone. Artificial respiration, using a mechanical pump, was employed to ventilate the lungs when spontaneous respiration had stopped; the blood-pressure being unrecordable, L-noradrenaline was used to maintain the circulation. An artificial kidney was brought to the patient and used to dialyse a substantial amount of barbiturate from the body.

Case Report

A 30-year-old man was admitted to the Radcliffe Infirmary as an emergency case on September 10, 1958. That day his wife had wakened at about 6.30 a.m. and had found it impossible to rouse him. At first she paid little attention to this, but became worried when, 20 minutes later, he still could not be awakened. She then noticed that he looked blue and was breathing noisily. On being sent for, the family doctor, thinking that the patient had suffered a cerebrovascular catastrophe, sent him to hospital, where he arrived at 10 a.m. He was deeply unconscious. Slight cyanosis was present, but this was relieved when a metal Waters airway was introduced into the mouth and mucus aspirated from the pharynx. He then looked quite peaceful and was breathing quietly; the body and limbs were warm. His axillary temperature was 96.4° F. (35.8° C.), pulse 112, and blood-pressure 90/60 mm. Hg. There was no neck stiffness, the pupils were moderately dilated and did not react to light. The tendon reflexes were absent, except for both biceps brachialis, from which a flicker could be obtained, and no plantar response could be elicited.

In view of the coma, in the absence of any localizing signs in the central nervous system, his good general condition, and the absence of evidence of other disease, a provisional diagnosis of barbiturate intoxication was made. After discussion with his wife she returned home and discovered that a box of butobarbitone ("soneryl") tablets which had been in the house for over two years was missing.

A stomach-tube was passed, its contents were aspirated, and he was catheterized. In the meantime blood analysis showed the presence of barbiturates in the plasma. This was done by a spectrophotometric method which is a modification by Broughton (1956) of the original method of Goldbaum (1952). The drug was identified as butobarbitone in a concentration in the plasma of 10.2 mg. per 100 ml. In spite of his fairly good general condition it was realized that he was in a dangerous state because, in this hospital, the previous highest recorded level of barbiturate in the blood, as butobarbitone, was 7.7 mg. per 100 ml. This was in the case of a young man who remained unconscious for 90 hours, in the first 72 hours of which he had been in deep coma. He passed no urine for 40 hours, his chest had given rise to some anxiety, and he had to be submitted to bronchoscopic aspiration. On regaining consciousness, his blood level of barbiturate was 2.5 mg. of butobarbitone per 100 ml. (Broughton *et al.*, 1956; Case 20).

The passage of the tube for gastric aspiration was followed by a fall of blood-pressure to 70/50 mm. Hg, but the pulse remained at 90. The blood-pressure then gradually rose again to about 88/55 mm. Hg. At 1.15 p.m. his breathing was slower and more shallow; this was accompanied by slight cyanosis and rise of pulse rate to 120 and blood-pressure to 140/100. By means of an Oxford inflator he was given oxygen through a face-mask for a couple of minutes, after which time the breathing was more natural and the blood-pressure fell to a steady level of 100/70 mm. Hg. At 2.30 p.m. a length of fine "polythene" tubing was passed through the nose into the stomach for feeding purposes. This was followed by a progressive worsening

of his condition. The blood-pressure fell and his breathing almost stopped. The lungs were intermittently inflated with oxygen for a few minutes, after which he was able to breathe spontaneously for a short period, the blood-pressure rising to about 70/50 mm. Hg. However, this state of affairs would last for only five minutes or so, then again respiration would become inadequate and the blood-pressure would fall.

At about 3.30 p.m. spontaneous respiration ceased and did not return; he was pulseless, with an unrecordable blood-pressure. Thereafter, oxygen was given at about 12 inflations a minute, using an Oxford inflator, and no attempt was made to discontinue this treatment. The pulse became just perceptible with a blood-pressure of 50/40 mm. Hg. A cuffed endotracheal tube was then passed through the mouth and the lungs were inflated. An intravenous infusion of L-noradrenaline in 5% glucose solution was given and the rate of infusion adjusted to maintain a systolic blood-pressure of between 110 and 140 mm. Hg. A tracheostomy was performed and a short cuffed endotracheal tube passed. This was connected to a Radcliffe positive-negative-pressure respiration pump, which was set to work at 14 inflations a minute and adjusted to give a volume of respired air of about 8 litres a minute.

Thus far, at 5 p.m., the man was still alive, with his respiration and circulation being artificially maintained. It was clear that this regime would probably be required for a long time, possibly six or seven days. An adequate unassisted circulation and respiration were unlikely to return until the blood level of barbiturate, which was now 12.4 mg. of butobarbitone per 100 ml., had fallen substantially. The only natural method of elimination of the drug would be by detoxication in the liver and excretion by the kidneys, and this was likely to be slow, as it was in the case previously mentioned. It was thought, therefore, that an attempt should be made to dialyse some of the barbiturate from the blood, for, if this was successful, it might be life-saving or at least would reduce substantially the period of coma, with its attendant risks. No appreciable effect, apart from transient convulsive twitching, had been attained with a total of 500 mg. of bemegride given intravenously at the rate of 100 mg. every five minutes.

Consequently, contact was made with the Renal Unit at Princess Mary's Royal Air Force Hospital, Halton, who agreed to the transfer of the patient for haemodialysis. However, it was thought to be a prohibitive risk to move the patient by road because of the precarious state of his circulation. At 9 p.m. the decision was made to transport the artificial kidney to the patient, a distance of some 30 miles (48 km.). This was possible as no immediate dialysis was contemplated on any of the patients already in the renal unit. At 10.30 p.m. a team of four with the Kolff twin-coil artificial kidney and equipment (see Fig. 1) left Halton, and two and three-quarter hours later, at

FIG. 1.—Kolff twin-coil artificial kidney with the equipment required for transport. Total weight 600 lb. (272 kg.). Team employed, four persons.

1.10 a.m. on September 11 dialysis was started. As the patient was not in renal failure it was decided to give intravenously 1.5 litres of fluid during dialysis, in order to maintain a reasonable urinary output. We were unable to weigh the patient, but from experience it was estimated that this amount of fluid would be lost owing to ultra-filtration.

During the seven hours of haemodialysis the patient's blood-pressure was maintained at about 130/100 mm. Hg. by varying the rate of infusion of L-noradrenaline.

At 4.45 a.m., after three and a half hours' dialysis, both pupils reacted to light, albeit sluggishly; painful stimulation by a strong pinch would evoke a slight movement of the limb and a temporary abortive attempt to fight against the rhythm of the mechanical respiratory pump.

At 5.30 a.m. he could breathe unaided for a short period, with a tidal air volume of between 350 and 400 ml.

At 8.10 a.m. dialysis was stopped because, during the preceding hour and a half, his peripheral circulation was not as good as it had been and a faster infusion rate of L-noradrenaline was being required to maintain the blood-pressure. At this time his temperature was 102.2° F. (39° C.), having been 96° F. (35.6° C.) at the beginning of dialysis. The state of the pupils and his response to painful stimuli were much as they had been halfway through the dialysis, though his responses varied. At the end of the period of haemodialysis the level of butobarbitone in the blood had fallen to 7 mg. per 100 ml. The dialysing bath fluid had been changed twice, at the second and fourth hours. In all, 1.51 g. of butobarbitone was recovered from the bath (Fig. 2). Dialysis was continued for seven hours, and by 10.30 a.m. the team with the kidney and equipment were back at Halton—12 hours after departure.

In the course of the next few hours the patient's condition steadily improved; the pupillary responses were brisker, he reacted to pain and made spontaneous swallowing movements. Unaided respiration was possible, though this was inadequate, and when mechanical breathing was started

again this provoked a cough. At 6.30 p.m. the pupils reacted consensually and a flexor plantar response could be obtained.

During that night he began a brisk diuresis. At 10 a.m. on September 12 both knee-jerks were present and he reacted to painful stimuli; voluntary respiration was possible, but it was thought to be still inadequate. That same evening he moved his arms and head from side to side, making vigorous swallowing movements during a trial period of spontaneous respiration, and he had a good cough reflex. Throughout that day the rate of infusion of L-noradrenaline had been reduced progressively without causing any fall in blood-pressure. It was discontinued eventually at 3.45 a.m. on September 13.

At 9.30 a.m. on September 13 the blood-pressure was 130/90 mm. Hg. No L-noradrenaline had been given for nearly six hours. He could breathe unaided at the rate of 36 breaths a minute, with a respiratory volume of 7.3 litres a minute. He moved all four limbs voluntarily and reacted quite briskly to painful stimuli. During the morning he responded to his name by opening his eyes. At 1 p.m. the mechanical respiratory pump was stopped finally and breathing thereafter was spontaneous. At 6 p.m. he could obey simple commands, and at midnight would utter a few syllables when spoken to.

The following morning, September 14, he was wide awake and talking and complaining of discomfort in the left arm where the arterial and venous catheters had been inserted. The tracheostomy tube was removed and also the indwelling urethral catheter. He took a light lunch unaided. Thereafter his progress was uneventful and he made a complete recovery apart from an anaemia—haemoglobin 70% (10.5 g./100 ml.). He was discharged from hospital on September 25, 15 days after admission. His progress is illustrated in Fig. 2, where it is shown that consciousness returned when the level of butobarbitone in the blood was 2.5 mg. per 100 ml. The amounts of barbiturate recovered from the urine and the dialysing bath are also recorded.

On recovery he had no recollection of having taken any sleeping tablets; he was cheerful and not in any way depressed. He remembered being disappointed that he had not slept very well for three or four nights before his admission to hospital and remembered where his wife had kept her box of butobarbitone tablets. Therefore we were forced to conclude that he had taken this massive dose of barbiturates accidentally; probably he took one or two tablets at first and later, in a drowsy state, took the remainder unknowingly.

Since discharge from hospital he has been seen in the out-patients department. He is back at his original occupation, well in health and in good spirits. He seems to be none the worse for his near-fatal adventure. Examination and testing by a clinical psychologist failed to demonstrate any recent intellectual deterioration such as might have occurred as the result of cerebral hypoxia or hypotension.

Discussion

This case illustrates the essential points in the management of severe barbiturate poisoning. If necessary, respiratory ventilation of the lungs can be carried out by a mechanical pump through a short cuffed endotracheal tube and an adequate blood-pressure maintained with L-noradrenaline. There is no doubt that haemodialysis by the artificial kidney substantially reduced the duration of coma with all its attendant dangers. The amount of butobarbitone removed from the body by dialysis, 1.51 g. in seven hours, was much greater than the amount eliminated in the urine, 0.63 g. in 7,795 ml. of urine passed in four and a half days. Not all barbiturates react to dialysis in the same way: phenobarbitone can be readily removed by dialysis, amylobarbitone is slightly dialysable, and so to a lesser extent is pentobarbitone, but secobarbitone is almost

FIG. 2.—Day-to-day progress showing blood-barbiturate levels measured as butobarbitone and also the amounts of butobarbitone recovered from the urine and dialysing bath of the artificial kidney.

undialysable (Sunshine and Leonards, 1954; Kolff, 1954). These differences are due to the variation in the binding of the barbiturate molecule to blood proteins. No reference could be found concerning the susceptibility of butobarbitone to dialysis, but from the experience in this case it would appear to behave in a similar fashion to amylobarbitone.

We consider that the artificial kidney will be required only in exceedingly severe cases of barbiturate poisoning not in renal failure. However, in the occasional case in which renal failure develops its employment will almost certainly be essential. It has been shown that the Kolff twin-coil artificial kidney is easily transportable, but only on rare occasions could this movement be contemplated. In general the majority of patients can be brought to the artificial kidney, which should not be moved from its parent hospital, apart from a second apparatus being available, unless (a) no patient in the unit requires dialysis, and (b) the distance involved is short—that is, not more than, say, 50 miles (80 km.).

This is the first time in this country that an artificial kidney has been moved to another hospital to treat a patient.

Summary

A case of severe but probably accidental poisoning by butobarbitone is described in which mechanical artificial respiration and an infusion of L-noradrenaline were employed when spontaneous respiration failed and the blood-pressure fell profoundly. The duration of coma was substantially reduced by using a Kolff twin-coil artificial kidney to dialyse butobarbitone from the blood, 1.51 g. being extracted in seven hours, compared with 0.63 g. from the urine in four and a half days. The artificial kidney was transported 30 miles (48 km.) by road to the patient, who made a complete recovery.

We thank Dr. A. M. Cooke, under whose care the patient was admitted, for his advice and encouragement to publish; the Director-General, Medical Services, Royal Air Force, for permission to publish the Service details; and Mr. G. Higgins, assistant biochemist to the United Oxford Hospitals, who carried out the numerous estimations of barbiturate and without whose help it would have been impossible to present this report. We gratefully acknowledge the help given by Mr. W. S. Lund, Mr. K. Cronin, Dr. A. Crampton Smith, and the members of the team from the R.A.F. Renal Unit—Squadron Officer M. Heyward, Flight Lieutenant N. V. D. Bunker, and Pilot Officer J. E. Scott.

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Pakistani citizens living in Glasgow have presented three mobile dispensaries to the Pakistan Government. This is in response to an appeal by Pakistan's Minister of Health, who visited Glasgow recently (*Pakistan News*, September 15).

C

GRISEOFULVIN IN TREATMENT OF INFECTIONS OF SCALP DUE TO MICROSPORUM CANIS

BY

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Griseofulvin is an antifungal antibiotic isolated originally from *Penicillium griseofulvum* by Oxford, Raistrick, and Simonart (1939). Investigations on its ability to control pathogenic fungi were initially in the field of plant pathology. Some success was obtained, and a product containing griseofulvin as the active principle has been marketed for the control of a disease of glasshouse crops. Its possible application in human and veterinary mycology was demonstrated by Gentles (1958), who studied its effect on ringworm infection in guinea-pigs. Subsequently, Lauder and O'Sullivan (1958) used it successfully in calves infected with *Trichophyton verrucosum*. The use of the drug in human infections was first reported by Williams, Marten, and Sarkany (1958). Since November, 1958, Messrs. Glaxo have generously made available supplies of the drug to various centres in the United Kingdom and elsewhere, and already the American workers Blank and Roth (1959) have recorded preliminary results in the treatment of 31 cases of various kinds of ringworm.

Present Series

In this paper the results of griseofulvin treatment of 19 cases of *Microsporum canis* infection and observations of side-effects (or rather their absence) in a total of 50 children with various kinds of ringworm are discussed.

Infections of the scalp hair by *M. canis* offer certain advantages over other fungus diseases in any trial of griseofulvin, since the effect of the drug can be readily observed by the behaviour of fluorescence of infected hairs under Wood's light. Most dermatologists agree that this type of infection does not require x-ray epilation, yet is hardly, if at all, influenced by topical treatment. Spontaneous cure takes place in most cases in about three months. Little is lost in practice by treating these children with a new, untried, but apparently safe oral fungicide. Cases of *M. audouini* infection have not been seen in Belfast for several years and consequently none was available for treatment.

Treatment.—The 19 patients with *M. canis* varied in age from 15 months to 12 years and all were given griseofulvin in a dosage of 0.25 g. three times daily. The duration of treatment varied from 3½ to 10 weeks (average 6 weeks), as we do not yet know the optimum duration of treatment. The results are summarized in Table I.

Clinical Appearance

There was nothing dramatic about the changes in the clinical appearances of the 19 cases, all but one of which had symptomless non-inflammatory patches. This contrasts with the striking improvement seen in cases of infection of the non-hairy skin by various dermatophytes, and also noted in our cases not included in this trial, and recorded by Williams *et al.* (1958) and