# PROBLEMS IN THE TREATMENT OF ACUTE OLIGURIC RENAL FAILURE ENCOUNTERED IN 51 BANTU PATIENTS REFERRED TO A RENAL UNIT

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Until such time as the clinical picture of acute uraemia has a sound physiological basis, treatment will remain largely empirical. The excellent results obtained with the introduction of fluid restriction and non-protein diets, and the use of the artificial kidney, have obscured our lack of knowledge of the underlying processes producing most of the symptoms and signs that we associate with this syndrome. We know that hyperpotassaemia may cause cardiac arrest, that severe metabolic acidosis may be fatal, that we must avoid overhydration, and that a blood-urea level of over 350 - 400 mg. per 100 ml. implies that other retained metabolites are reaching high levels. Recently, the poor prognosis in septic and traumatic cases has been stressed. However, (*a*) no explanation has yet been found for the gastro-intestinal lesions, pericarditis, anaemia, bleeding tendency, or extensive neurological manifestations of uraemia; and (*b*) there is no correlation between the blood urea and these clinical manifestations, and there is no correlation between the clinical manifestations of uraemia, the degree of renal impairment, and the chemical abnormalities found.

If death is not attributed to sepsis, hyperpotassaemia, metabolic acidosis or congestive failure from overhydration, it is vaguely described as 'uraemic'. Alternatively, if the blood or serum levels of urea, potassium, or carbon-dioxide content did not reach those commonly considered dangerous, it might be tempting to think that the extreme metabolic upset did not cause the patient's death.

Uraemia has therefore become a useful term to cover our ignorance, and we have begun to use 3 biochemical estimations as a yardstick of the course of acute oliguric renal failure, despite the fact that they do not necessarily parallel the clinical state or one another.

As long as this position exists, there is little incentive to discover the true physiological basis of symptoms and signs, since we can dialyse earlier and earlier to avoid running into unexplained difficulties. However, haemodialysis is still an expensive and highly specialized procedure available in very few centres in South Africa, and it is essential that medical treatment be understood and practised as widely as possible. Further advances in medical treatment can come only when we know more of basic physiology.

This introduction is not aimed at belittling the value of the artificial kidney. There is no doubt that haemodialysis is often a life-saving procedure. We contend, though, that improvements are necessary in the machine itself, to enable it to clear the blood of retained metabolites more adequately. Further, we shall show how some complications such as hyperpotassaemia and acidosis can usually be medically controlled, whereas other problems, such as unexpected deaths, hepatorenal failure, and infection in uraemic patients, require emphasis and study.

## MATERIAL

We present here the records of the first 51 Bantu patients referred to our renal unit for opinion, during the 21 months up to February 1961. This number does not represent all hospital uraemic patients over this period, since

TABLE I. DIAGNOSIS IN 51 PATIENTS REFERRED FOR POSSIBLE DIALYSIS

| *Diagnosis* | *Patients* | *No. dialysed* | *Survival in dialysed patients* |
|---|---|---|---|
| Prerenal uraemia .. .. | 3 | 1 | 1 |
| Renal uraemia .. .. .. | 39 | 18 | 6 |
| Acute oliguric renal failure (uncomplicated) .. .. | 8 | 4 | 3 |
| Acute oliguric renal failure and severe sepsis or trauma | 4 | 4 | 2 |
| Acute oliguric renal failure and jaundice .. .. | 11 | 9 | 1 |
| Acute oliguric renal failure and chronic disease .. | 5 | 1 | 0 |
| Chronic renal disease .. | 11 | 0 | 0 |
| Postrenal uraemia .. .. | 7 | 2 | 1 |
| Miscellaneous .. .. .. | 2 | 2 | 0 |

each individual firm treats its own patients, and commonly refers only those who are failing to respond to conservative medical therapy or where a further opinion is required.

Table I is an overall record of the cases referred, the diagnoses made, the number dialysed, and the results obtained.

### ANALYSIS OF PATIENTS DIALYSED

*Acute Oliguric Renal Failure*

The 18 patients dialysed in this group included 9 patients with septic abortion; 2 patients with traumatic injuries (one following multiple fractures, the other a stab wound of the chest with severe shock); 3 patients with acute nephritis; 1 patient with heat stroke; 2 postpneumonic patients; and 1 post-hysterectomy patient.

*Prerenal Patients*

The patient dialysed (case 1) had the following history: hypertension with chronic nephritis, on hypertensive therapy; developed intestinal obstruction and an emergency operation was performed; severe vomiting and collapse occurred after operation, with no improvement after 5 days' conservative therapy; recovered.

*Postrenal Patients*

*Case 2:* Post-hysterectomy obstruction of ureters; dialysed before remedial surgery; recovered.

*Case 15:* Pelvic mass with ureteric obstruction; grossly uraemic and hyperpotassaemic; dialysed before surgery; died. At autopsy ovarian carcinoma with gross chronic renal damage was found.

*Miscellaneous Patients*

*Case 8:* Severe liver failure following cholecystectomy; ruptured duodenum, general peritonitis, severe shock, anuria which was either prerenal or renal; died, no autopsy.

*Case 22:* Poisoning of unknown type, admitted in coma; died of cerebellar haemorrhage just after completion of dialysis.

### INDICATIONS FOR DIALYSIS

In contrast to many authors[11,18,21] we have adopted a markedly conservative policy in accepting patients for dialysis. This has been partly due to the lack of trained personnel and the difficulties encountered in the framework of a general hospital. The main reason, however, is that except in extreme emergency all patients have had a trial of medical treatment first, when every effort has been made to correct and maintain electrolyte and fluid balance. As will be seen in Table I, practically all the patients dialysed were in acute renal failure, usually acute tubular necrosis. One patient had chronic renal disease with a severe superimposed acute condition. The other patients were dialysed to render them fit for diagnostic or therapeutic surgery, or as a last resort where it was felt that reversing the metabolic disturbance might enable the patient to recover from coma, acute infection or surgery. We have had no experience in dialysis in patients with known poisoning (e.g. barbiturates, bromides or salicylates), in children, or in cardiac patients failing to respond to ordinary treatment.[7]

The usual indications for dialysis in suitable cases have been considered by various authors to be:

1. Deterioration in the clinical condition of the patient, especially with regard to change in the level of consciousness and neurological symptoms and signs.[3,5,8,14,17]
2. Urea and electrolyte blood levels:
   (*a*) Blood urea over 350 - 400 mg. per 100 ml.[1,3,12,14,17]
   (*b*) Serum potassium over 7 mEq./l.[1,8,14,17]
   (*c*) Serum carbon-dioxide content under 13 mEq./l.[1,8,14,17]

There is a slight variation in the recommended blood-urea levels, but on the whole there is a very large measure of agreement.

Our decision concerning the time for dialysis has been almost entirely a clinical one, since we consider:

(*a*) The blood-urea level is not a reliable index of retention of other potentially fatal metabolites. This is especially so after one dialysis, because some substances — including urea — are much more readily dialysed than others and thus a low blood-urea level may be misleading.[6,10,17] On clinical grounds initial dialysis was considered necessary in our patients at blood-urea levels varying between 245 and 720 mg. per 100 ml. (Table V).

TABLE II. CONTROL OF SERUM-POTASSIUM LEVEL BY RECTAL ION EXCHANGE RESINS, CONTRASTED WITH BLOOD-UREA LEVELS TAKEN SIMULTANEOUSLY

| *Patient* | *Initial level* | | *Level 24-72 hours after resins begun* | |
|---|---|---|---|---|
| | *Potassium (mEq./l.)* | *Urea (mg. per 100 ml.)* | *Potassium (mEq./l.)* | *Urea (mg. per 100 ml.)* |
| A.J. .. | 6·8 | 150 | 5·8 | 192 |
| F.M. .. | 8·0 | 470 | 6·4 | 535 |
| G.M. .. | 6·7 | 310 | 4· | 385 |
| L.K. .. | 6·2 | 260 | 5·6 | 345 |
| | | | (4·4) | (370) |
| M.M. .. | 5·8 | 73 | 5·4 | 180 |
| P.M. .. | 8·0+ | 265 | 6·0 | 230 |
| P.L. .. | 6·5 | 425 | 4·5 | 480 |
| P. .. | 6·0 | 275 | 4·8 | 275 |
| R.M. .. | 7·7 | 345 | 7·0 | 375 |
| V.N. .. | 7·8 | 368 | 4·9 | 500 |
| | | | (3·4) | (625) |
| A.L. .. | 7·0+ | 410 | 6·5 | 350 |
| A.M. .. | 7·7+ | 560 | 7·0 | 720 |
| A.Z. .. | 7·0+ | 390 | 4·5 | 410 |
| H.D. .. | 7·0 | 390 | 3·5 | 360 |
| G.K. .. | 7·5 | 340 | 5·0 | 465 |

(*b*) As shown in Table II, the potassium level could be controlled by rectal administration of cation-exchange resins in most of our patients. The 15 cases shown in this table were unselected, and represent our experience with this treatment. Resins were not given at any predetermined level of potassium, but electrocardiographic and clinical evidence of hyperpotassaemia were considered more important in deciding that they should be used. However, a figure of 7 mEq./l., in a patient whose potassium was rising regularly on serial estimation, was usually taken to be an indication for resins. In many cases resins needed to be given only once or twice a day and could be stopped after 1 or 2 days. The more severe or less easily controlled patients were given 6-hourly dosage. Resins were used in the sodium cycle and were preceded by bowel washout; 15 - 20 G. were dispersed in 200 ml. of warm water and run in. In Table II the serum-potassium levels before and 24 - 72

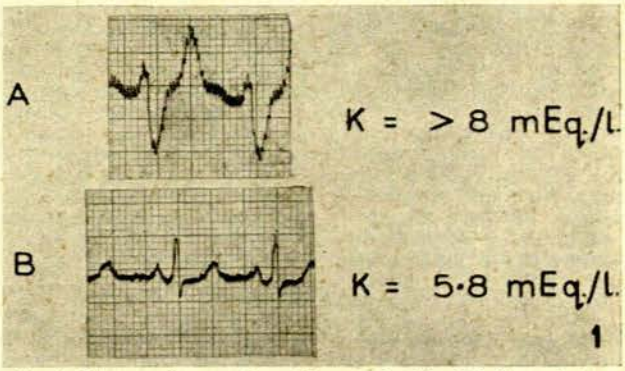


*Fig. 1.* Electrocardiograms (case 15) — standard lead 2. (A = before dialysis, B = 45 minutes after beginning of dialysis.)

hours after the start of therapy are contrasted, and blood-urea levels taken at the same time are also noted. Apart from the early diuretic phase of renal shutdown, the urea and potassium levels might be expected to rise together, and it will be seen that in most cases the treatment reversed this trend. Resins have been used by others for hyperpotassaemia either orally[6,9] or rectally,[1,13] but we feel their efficiency by the rectal route has not been sufficiently stressed. Since we have employed them we have had only one patient in whom dialysis was performed for hyperpotassaemia; that was a woman who arrived in hospital with the electrocardiograph shown in Fig. 1 (A), where we felt death might occur at any moment. The electrocardiograph after 45 minutes of dialysis — no potassium having been added to the first bath — is shown in Fig. 1 (B). The relevant potassium levels are indicated in the figure.

(*c*) The carbon-dioxide content of the blood can likewise, in our experience, usually be medically controlled,[1,9] at least as far as bringing it to a reasonably safe level is concerned.

TABLE III. CONTROL OF ACIDOSIS BY ORAL OR INTRAVENOUS ALKALIS, CONTRASTED WITH BLOOD-UREA LEVELS TAKEN SIMULTANEOUSLY

| *Patient* | *Initial level* | | *Level 24-96 hours after therapy begun* | |
|---|---|---|---|---|
| | *$CO_2$ content (mEq./l.)* | *Urea (mg. per 100 ml.)* | *$CO_2$ content (mEq./l.)* | *Urea (mg. per 100 ml.)* |
| J.P. .. | 6·6 | 350 | 28·7 | 445 |
| L.K. .. | 11·0 | 260 | 12·4 | 380 |
| M.M. .. | 9·4 | 215 | 22·2 | 385 |
| P. .. | 11·0 | 275 | 14·1 | 255 |
| G.M. .. | 8·1 | 405 | 16·2 | 435 |
| | (10·3) | (408) | (14·8) | (575) |
| J.S. .. | 11·3 | 380 | 11·0 | 470 |
| S.D. .. | 6·0 | 410 | 13·0 | 330 |
| H.D. .. | 11·3 | 390 | 18·6 | 360 |
| | (13·0) | (248) | (21·5) | (316) |
| G.K. .. | 10·9 | 408 | 15·8 | 465 |
| A.Z. .. | 7·9 | 385 | 12·1 | 410 |

This is shown in Table III. The patients in this table are also unselected cases and represent our experience to date. We have not dialysed any patient purely on the basis of metabolic acidosis, although some of our patients were severely acidotic when dialysis was performed. Acidosis in renal failure is produced either by sodium loss or by retention of acids. Although theoretically the use of sodium alkaline salts should be helpful only when sodium loss causes acidosis, in practice there has been little evidence of marked acidotic breathing, and patients have done well on alkalis and have not developed tetany or other complications.

In general, therefore, our decision concerning dialysis has been made when a patient showed increasing drowsiness, disorientation or confusion, and usually before twitching, tremors, convulsions or coma occurred.

Vomiting has not been a serious problem, nor has diarrhoea. Diagnostic difficulty has been met in some cases where hepatic damage, anaemia or severe infection were present, because it was not known to what extent these factors were contributing to the mental state. This was especially so when patients were admitted to hospital in a confused or drowsy condition. Usually though, where it was possible to see the patient daily from early on in the illness, a few simple observations of state of consciousness and orientation would be sufficient to decide for or against continued conservative therapy. Restlessness at night, and the rate of rise of blood urea each day[5,15,17] were also found valuable as indices of the probable need for dialysis. We have thought of using the electroencephalograph as a means of assessing cerebral changes and their reversal by dialysis, but so far have not been able to do so.

## MEDICAL THERAPY

Some years ago we aimed at giving patients a diet of 1,000 - 1,200 calories a day, and used a modified Bull's mixture for oral therapy. Later, when it was shown that if 100 - 200 grams of carbohydrate were provided in the diet, further protein sparing with higher calorie diets was minimal, we changed to 100 - 200 grams of carbohydrate a day. This was given by mouth — if at all possible — in the form of glucose or lactose solutions and glucose sweets. If intravenous therapy was thought advisable, polythene tubing was passed into the superior or inferior vena cava, and 40% dextrose was given by slow drip through a paediatric dropper. As a routine, 1,000 units of heparin were added to each vacolitre, and this was of immense help in preventing clotting even with a very slow drip rate. Fluid requirements were met with 400 - 500 ml. a day, added to the urinary volume of the previous day. Unfortunately, we were unable to weigh our patients daily.

Occasionally the Bantu would object strongly to the diet given, and would be found eating titbits brought in by anxious relatives and friends. We therefore kept in reserve a special diet (prepared by our senior dietician — Miss H.C. Pledger) — Table IV, which, though containing 10 G. of protein and a little potassium, approximated sufficiently closely to a Bantu diet to be much more acceptable. Our main concern with this diet was the water content, either in the food or as water of oxidation. For the complete diet this was estimated to be close to 1,000 ml. Usually, therefore, we did not use the diet before the early diuretic phase, if we could persuade the patient to continue 'starving'. Adequate vitamins were also given by mouth or injection.

TABLE IV. DIET RECOMMENDED FOR BANTU PATIENTS WHO REFUSE ORAL GLUCOSE OR LACTOSE SOLUTIONS—10 G. PROTEIN DIET *

| *Constituent of diet* | *Grams* |
|---|---|
| Raw mealie meal .. .. .. .. | 90 |
| Cooked polished rice .. .. .. | 90 |
| Plain boiled sweets .. .. .. | 60 |
| Tinned or stewed fruit: | |
| pineapple .. .. .. .. | 120 |
| *or* peaches .. .. .. .. | 45 |
| *or* pears .. .. .. .. | 75 |
| White sugar .. .. .. .. | 20 |
| Unsalted fresh butter .. .. .. | 30 |

* This furnishes 10 G. of protein, 1,000 calories, 0·29 G. of potassium, and approximately 1,000 ml. of water (including cooking water, water of oxidation, and water content of foodstuff). The mealie meal is weighed raw and cooked with a measured amount of water in a double boiler with the lid on. The rice is boiled, washed, and served as dry as possible. The fruit is weighed and served without juice.

TABLE IVA. GUIDE TO DAILY DIVISION OF 10 G. PROTEIN DIET FOR PATIENTS WITH RENAL SHUT-DOWN

| | |
|---|---|
| *Breakfast:* | Porridge and sugar and butter. No milk |
| *8 a.m.:* | Give fluid (10% glucose solution) according to doctor's instructions. Sweets (boilings) |
| *Lunch:* | Boiled rice and butter. Special fruit pudding |
| *2 p.m.* | Sweets (boilings) |
| *Supper:* | Porridge and sugar and butter. No milk |
| *Do not give:* | Milk, tea, fruit squash, fruit juice or any food or beverage other than on list |
| *Give:* | *Fluid only in amounts directed by doctor* |

Check patient's locker daily for any food being kept in it.

Early in our experience these patients were nursed in an open ward, but we have been so impressed by the danger of infection (see below) that all patients are now isolated — usually in a side ward — and strict nursing precautions are taken to lessen the risk of infection. Bladder catheterization and indwelling catheters have been avoided if at all possible. Completely exact estimation of fluid loss is in

any case impossible, particularly in the presence of infection or hyperventilation, and severe pyelitis or cystitis commonly follows the presence of indwelling catheters in these patients.

Antibiotics were not given as a routine,[5] but were often indicated by the nature of the case and various complications. Streptomycin was avoided, and either penicillin or a broad-spectrum antibiotic was used. The dosage of these has recently been calculated in accordance with the recommendations of Franklin and Merrill,[6] who, in 1960, discussed antibiotic metabolism in anuria. Anabolic drugs were given as advised for obstetric cases by various workers.[14,16,17] Blood transfusions of packed cells were given freely if the haemoglobin level fell below 8 G. per 100 ml.[2,9] Insulin therapy of hyperpotassaemia was discontinued after we started using rectal resin, mainly because of 3 episodes of hypoglycaemia in different patients, and because of the efficacy of the resin itself. If alkalis were necessary, sodium lactate or sodium bicarbonate were added to the intravenous infusion, or sodium bicarbonate was given orally. The dosage varied with the degree of acidosis and was approximately 40 mEq. per day.[1]

Renal biopsy has been considered in a few cases, but only carried out in 1 (case 21). On this occasion it provided a definite diagnosis of acute glomerular nephritis with subacute changes. Especially where the history is unreliable or incomplete — this is common in Bantu patients — and a firm diagnosis cannot be made clinically, we feel there is a definite indication for renal biopsy. Unless one is prepared to try a blind biopsy, the main difficulty is to outline the kidneys. Straight X-ray of the abdomen or tomography of the kidney region may do this. Retrograde pyelography exposes the patient to further trauma and, in our opinion, is not justified.

## METHOD OF DIALYSIS

The Travenol twin-coil (disposable) artificial kidney was used for all dialyses.

### *Technical Difficulties*

We encountered technical difficulties, when using the artificial kidney, in connection with a number of factors; these are listed below:

1. Maintenance of an adequate flow of blood. To ensure this flow, the careful surgical placement of suitable catheters cannot be overstressed. We have made our catheters from polythene tubing drawn out to a suitable size. Glass catheters have not been tried so far. Surgically speaking, cutting down on the saphenous vein and radial artery, which are the two vessels we have commonly used, may not appear a difficult or hazardous procedure, but the whole dialysis depends on its being done efficiently. We have wasted hours trying to get a satisfactory circulation through the machine, and have had 2 very serious haemorrhages from cut-downs (cases 16 and 23), 1 of which was ultimately fatal. Ideally, these cut-downs should be done in an operating theatre, and not in the dialysis room, and the patient should be sent down to this room with catheters *in situ*, clotting being prevented by filling the catheters with heparinized saline before clamping. The saphenous-vein catheter should be passed well up into the inferior vena cava, but we have found that the arterial catheter should be passed for a distance of less than 1 inch up the radial artery; otherwise it tends to vibrate and become partially obstructed, with resultant poor blood flow.

2. Clotting in the filtration system. This is often related to poor circulation or to inefficient heparinization (cases 14 and 20). We give a total of 6,000 units of heparin into the solutions and blood used for priming the machine, and 2,000 - 4,000 units to the patient about 30 minutes before the dialysis begins. The clotting time of the patient's blood is kept in the region of 15 - 20 minutes during the dialysis. Apart from cases 14 and 20, clotting occurred in one of the venous outlet tubes from the machine on one occasion, and this section was replaced without stopping the dialysis. Heparin dosage has not been based on the weight of the patient and is very small compared with other forms of extracorporeal circulation. Since we do not know the cause of uraemic bleeding, and there is no reason to expect that heparin will increase that bleeding, this small dosage seems illogical. It has been dictated by caution.

3. The machine is primed as a routine at a pressure of at least 200 mm.Hg to test the coil, and also because we often ultrafiltrate to remove fluid. Occasionally at the onset of dialysis, when this pressure suddenly drops, air in excess gets into the airlocks and some passes along the venous return to the patient. This can be avoided by ensuring that this sudden drop of pressure does not occur. The continual measurement of pressure in the machine is the most important factor in a successful dialysis, and is an index from moment to moment of whether the dialysis is proceeding smoothly or complications are arising. We measure this pressure by attaching a Y-tube from one of the airlocks to a sphygmomanometer. The free end of the Y-tube is clamped off and can be used for pushing in air, should the airlock become overfull with blood and threaten to overflow into the manometer.

4. Since we use ultrafiltration on overhydrated patients, we have sometimes found it useful to have a slow dextrose drip running in a free vein to be ready for sudden changes in the patient's condition from too rapid removal of fluid. Pierce,[19] in experiments in dogs, noted that fluid had to be carefully removed, and that a drop of 5 - 7% of body weight could lead to death. The volume of fluid removed by ultrafiltration can be estimated graphically from the dialysing pressure and the blood flow.[14]

5. Poor flow through one of the coils while the other one is working well. This may be due to clotting somewhere in the machine, but may also occur from inefficient pumping action of the sigmamotor, and can often be improved by moving the tubes passing through the motor, or changing their position in the motor. The sigmamotor is an inefficient pump because frequent adjustment is necessary to avoid malocclusion.

6. Rupture of the coil may occur either through a fault in the coil, or through neglecting to watch the pressure in the system. This has occurred in 3 of 27 dialyses.

7. One coil was wasted when the cover of the tank fell onto the venous return tubes and wrenched them out of the coil.

### *Procedure*

We have found that the machine is comparatively easy to use and control. We have maintained a flow rate of about 250 - 300 ml. per minute without difficulty, provided the catheters were properly placed and malocclusion was avoided. We dialyse for 6 hours, with 2 changes of bath solution, and modify the first solution to some extent, depending on the clinical and chemical state of the patient. If we want to remove a large quantity of fluid, we add 1 - 2 extra litres of 40% dextrose to one or more baths; if the potassium is high, we put little or no potassium chloride in the first bath initially, adding this later. If the patient's haemoglobin is very low, we transfuse blood through the machine early on in dialysis so that excess potassium in the transfused blood can be rapidly removed. At the end of dialysis we sometimes give blood to the patient by displacing the blood in the coil by normal saline.

The blood pressure and pulse rate are recorded at 5-minute intervals; an electrocardiogram is taken before dialysis, and at intervals during dialysis — the machine being connected throughout. An oscilloscope would be better. We found our best index of the condition of the patient and the machine to be the pressure recording shown on the sphygmomanometer. We have not yet used regional heparinization, though in retrospect we consider we might have used this method on at least 3 patients.

DIFFICULTIES ENCOUNTERED IN THE PATIENTS DURING DIALYSIS

*1. Blood-pressure Change*

(*a*) Fall in blood pressure occurred in cases 4, 5 and 8. This was, however, readily controlled by 'wyamine', noradrenaline, or blood transfusions in small amounts.

(*b*) Rise in blood pressure occurred in case 21. Intramuscular 'serpasil' given on 2 occasions controlled this.

*2. Severe Bleeding from Cut-downs*

This occurred either during placement of catheters (cases 16 and 23), or as an ooze throughout the 6 hours (cases 6,9,11,17 and 22).

*3. Bleeding Elsewhere*

(*a*) From mouth and gums. In case 18 this led to marked laryngospasm. It was controlled by suction, aminophylline and calcium gluconate.

(*b*) From stomach and bowel (case 10). A small haematemesis and melaena occurred.

(*c*) Per vaginam. Case 14 had a severe bleed towards the end of dialysis, but this was from retained products of conception.

*Comment:* It was difficult to decide to what extent these bleeding episodes were related to heparinization. In many cases abnormal bleeding had been present before dialysis. However, we had a good deal of difficulty in maintaining a steady clotting time of 15 - 20 minutes. There was considerable variation in sensitivity to protamine and heparin (cases 11, 19, 20 and 22). Further, oozing from cut-downs often continued for hours after dialysis, even though the clotting time was normal. Altogether it seems most unlikely that heparin played a significant part.

*4. Clotting in the Catheters or Coil*

This occurred in cases 14, 16, and 20 at the onset of dialysis.

*5. Sedation*

We used pethidine or 'pethilorfan' in most patients. In one patient having fits throughout (case 16), intramuscular phenobarbitone and phenytoin were also given at intervals. Case 13 became deeply anaesthetized after 100 mg. of pethidine, and required 'lethidrone' and coramine throughout dialysis. He regained consciousness about 12 hours later.

*6. Cardiac Irregularities*

In a few cases extrasystoles occurred. In case 22 an idioventricular rhythm developed, and was controlled. Then frequent ectopic beats were noted, followed by ventricular fibrillation and death. Autopsy showed cerebellar and subarachnoid haemorrhages. In case 20 sudden cardiac arrest occurred. No cause was found at necropsy.

*7. Sudden Collapse*

In case 1 sudden, shock-like collapse developed during dialysis with ultrafiltration. This was relieved rapidly by intravenous administration of 5% dextrose-water, and was considered to be the result of excessive fluid loss from ultrafiltration in a non-oedematous patient.

TABLE V. THE FINAL ANALYSIS OF THOSE WHO DIED DURING OR AFTER DIALYSIS

| *Patient no.* | *Name* | *Electrolyte levels at death* | | | *Jaundice* | *Immediate cause of death* | *Autopsy findings* |
|---|---|---|---|---|---|---|---|
| | | *Urea (mg. per 100 ml.)* | *Potassium (mEq./l.)* | *$CO_2$ (mEq./l.)* | | | |
| 5 | C.T. | 300 | 4·6 | 17·3 | + | *Unexpected*—was improving. Died some days after dialysis | Perforated uterus. Large pale liver. Acute tubular necrosis. Peritonitis. *B. welchii* infection of uterus |
| 4 | F.M. | 395 | 6·8 | 8·6 | — | Died following an unsuccessful second dialysis. Rectal resins not being used at that time. Possibly hyperpotassaemia was main factor | Ruptured uterus. Peritonitis. Acute tubular necrosis |
| 3 | M.M. | 283 | 6·6 | 22·3 | — | Severe pneumonia and coma | Multiple fractures. Cortical necrosis of kidneys. Cerebral fat embolism. Pneumonia |
| 8 | M.D. | 260 | 7·5 | 11·3 | + | Shock following ruptured duodenum and general peritonitis after cholecystectomy. Was moribund at time of dialysis | No autopsy |
| 9 | V.N. | 265 | 5·6 | 18·2 | + | *Unexpected*—was improving. Sudden onset of auricular fibrillation and congestive cardiac failure | Perforated uterus. Peritonitis. Acute tubular necrosis. Large pale liver. Cystitis. *B. welchii* infection |
| 10 | R.M. | 215 | 4·6 | 14·4 | — | *Unexpected*—died suddenly after onset of mental confusion, a fit, pyrexia and coma | Acute necrotizing glomerulonephritis |
| 13 | G.M. | 270 | 4·6 | 17·6 | + | Case of heatstroke. Improving, then developed acute pneumonia while in early diuretic phase | No autopsy |
| 15 | M.M. | 200 | 6·0 | 14·1 | — | *Unexpected*—apparently improving. Epileptic fits followed by coma | Carcinoma of ovary. Obstruction of ureters. Marked pyelonephritis with destruction of kidneys |
| 16 | J.P. | 115 | 4·2 | 10·6 | — | Died of irreversible shock following severe haemorrhage from cut-down wound | Hydronephrosis. Severe pyelonephritis |
| 18 | J.D. | 405 | 6·2 | 15·0 | + | *Unexpected*—clinical diagnosis at time of death was pulmonary embolism | Acute tubular necrosis. Large pale liver (no histology) |
| 19 | A.M. | 450 | 4·8 | 12·7 | + | Staphylococcal empyema following stab wound, with broncho-pleural fistula and probably septicaemia | Acute tubular necrosis. Staphylococcal empyema |
| 20 | A.L. | 350 | 6·5 | 14·4 | + | *Unexpected*—died of sudden cardiac arrest during dialysis. At that time potassium 6·5mEq./l. Cause unknown | Acute tubular necrosis. Centrilobular necrosis of liver. Pneumonia |
| 21 | A.Z. | 310 | 4·8 | 17·4 | — | Developed acute staphylococcal laryngitis the day after dialysis. This spread to his lungs, and caused a septicaemia as well | Pneumonia. Staphylococcal septicaemia. Acute or subacute nephritis |
| 22 | N.M. | 280 | 3·5 | 19·2 | + | Emergency dialysis in a patient admitted in coma from unknown poison. Died during dialysis from ventricular fibrillation | Cerebellar and subarachnoid haemorrhage (brain only examined) |
| 23 | G.K. | 380 | 5·8 | 7·1 | — | Severe pelvic sepsis. Died some weeks after dialysis, following operation for drainage of pelvic abscess; ? pulmonary embolus | Acute tubular necrosis. Pelvic sepsis with tubo-varian abscess. No pulmonary embolus |

\+ = present, — = absent.

*8. Mental State*

The mental state of patients did not vary appreciably during dialysis. There was usually obvious improvement by the next day.

ASSESSMENT OF RESULTS IN DIALYSED CASES

We have dialysed 23 patients in this group of 51 — 4 on 2 occasions — with 8 recoveries (Table I). In acute renal failure without jaundice our recovery rate approximates to that of much larger series.[6,21] Our experience with jaundiced patients — 1 recovery in 9 dialysed patients — is sufficient, we think, to warrant further discussion of this group.

*Cause of Death in Patients Dialysed*

During, or within some weeks of, dialysis 15 patients died, and we were able to conduct autopsies on 13 (Table V). In 9 of the 13, severe infection was found at autopsy, and in many of these it was the decisive factor in causing death. In 2 of these proved *Staphylococcus aureus* infection, and in 2 others proved *B. welchii* infection, was present. General peritonitis was present in 3, and pneumonia in 4. In only 2 cases could it be said at autopsy that the renal condition was the major pathology, and in both these the renal condition was irreversible. However, although at autopsy there was more than sufficient pathology to account for death, in 6 cases death was sudden and unexpected (Table V). These patients were apparently improving and the urea and electrolyte levels were not considered dangerous, when there was a sudden change for the worse. Two had epileptic fits, went into coma and died, and a third developed a clinical picture confidently diagnosed as pulmonary embolism. A fourth developed auricular fibrillation and acute cardiac failure, the fifth died suddenly, possibly again from a cardiac cause, and the sixth from a cardiac arrest during an uneventful dialysis. Apart from the sixth case, death occurred 2 days or longer after dialysis.

At first we did not consider these 6 deaths to be due to uraemia, until we began to realize from our own observations and proof supplied in the literature[6,10,17] that serum or blood levels of urea, potassium, carbon-dioxide content and other readily estimated metabolites, are not a true index of the levels of other potentially dangerous substances, especially after a dialysis has removed those most easily dialysable. Our records of urea, various electrolytes and other products of protein metabolism, before and after dialysis, are very incomplete, especially in those patients dialysed early in our series. Table VI gives these records, and it is obvious that there is no consistent pattern, but that some substances are much more readily dialysable than others. Even after our most successful dialyses, the levels of creatinine, uric acid and inorganic phosphate were usually still very high indeed.

Shackman *et al.*,[20] in discussing 42 fatal cases in a series developing acute renal failure after surgery or surgical conditions, stated that in 28 of these death occurred with blood-urea levels of less than 450 mg. per 100 ml., serum-potassium levels of less than 6·5 mEq./l., and serum-$CO_2$-content values greater than 14 mEq./l. They did not therefore consider that these 28 patients died of renal failure, though they accepted that the renal state adversely affected the prognosis.

The same might be said of our unexpected deaths as far as biochemistry is concerned. We believe, however, that these 6 patients did in fact die of uraemia from poisoning by one, or more than one, constituent of uraemic plasma not estimated as a routine, probably accumulating at different rates in anuric patients, and not cleared adequately by dialysis. In support of this we can point to the great variability in blood levels of urea, potassium and carbon-dioxide content at which dialysis was clinically considered essential in this series (Table VI). In a number of our patients blood levels of urea, potassium and carbon-dioxide content had not reached values usually considered dangerous, and in others had far exceeded those values.

This problem will ultimately be solved when we know more about the sum-total of various uraemic poisons, but at present there seem to be 3 reasonable therapeutic approaches. One is to dialyse more frequently and try to maintain the blood chemistry close to a normal level. The second is to develop the efficiency of the dialysing machine, and we have recently noted with considerable interest new modifications of the twin-coil machine which obviously improve its performance greatly.[2] The third possibility is so to improve our clinical understanding and appreciation of these cases and our knowledge of the basic physiology, that we will dialyse entirely on clinical indications. Because of a shortage of trained personnel we could not dialyse very frequently and therefore relied almost entirely on the clinical indications previously discussed. With 6 unexpected deaths in our small series of dialysed patients we cannot pretend to have been very successful.

It is of interest, also, that we can fully substantiate the changing pattern of mortality in acute renal failure. Hyperpotassaemia, pulmonary oedema and acidotic coma probably accounted for only 1 death in our dialysed patients (case 4). Other workers[6,12,16] have stressed sepsis and especially staphylococcal infection. Unexplained deaths from auricular fibrillation, supraventricular tachycardia, or a picture suggesting pulmonary embolism, are also recorded.[6] Infection was certainly the predominant serious complication in our patients.

*Follow-up of Patients — Dialysed and not Dialysed*

In the early diuretic phase, with urine output over 400 ml. a day, and often considerably more than this, our experience substantiates that of others, which is that this can be a most dangerous time. The blood urea may continue to rise, or remain stationary at a high level for days or weeks, while electrolytes become normal or subnormal. The clinical condition remains stationary or deteriorates. Especially when infection is present, the handling of this phase is most difficult, and the tendency is to wait too long before dialysing.

In the late diuretic phase with falling blood urea we occasionally had to give intravenous fluids, since the weak, toxic patient became rapidly dehydrated, and was often unable to take sufficient fluid by mouth. We did not experience much difficulty in replacing lost electrolytes. This was also the time when persistent infection, especially of the urinary and genital tracts, had to be overcome, and often delayed recovery considerably.

We have not followed-up our recovered patients with attempts to assess residual renal damage.

TABLE VI. RECORD OF BLOOD CHEMISTRY: (A) IMMEDIATELY BEFORE, AND (B) SHORTLY AFTER, DIALYSIS

| Dialysed patient no. | | Urea (mg. per 100 ml.) | Chloride (mEq./l.) | $CO_2$ content (mEq./l.) | Sodium (mEq./l.) | Potassium (mEq./l.) | Creatinine (mg. per 100 ml.) | Uric acid (mg. per 100 ml.) | Calcium (mEq./l.) | Inorganic phosphate (mg. per 100 ml.) | Bilirubin (mg. per 100 ml.) | Outcome |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | A | 430 | 86 | 15·5 | 132 | 3·6 | 9·5 | — | — | — | — | |
| | B | 210 | 93 | 20·8 | 135 | 2·7 | — | — | — | — | — | Recovery |
| 2 | A | 340 | 79 | 11·3 | <110 | 5·2 | — | — | — | — | — | |
| | B | 140 | 88 | 19·0 | 126 | 4·7 | — | — | — | — | — | Recovery |
| 3 | A | 385 | 89 | 22·6 | 110 | 5·4 | — | — | — | — | — | |
| | B | 283 | 93 | 22·3 | 145 | 6·6 | — | 11·2 | 4·8 | 3·8 | — | Death |
| 4 | A | 500 | 90 | 9·4 | 130 | 5·4 | 11·0 | 13·8 | 4·9 | 8·6 | — | |
| | B | 395 | 94 | 19·4 | 140 | 5·4 | — | — | — | — | — | |
| 4a | A | — | — | 8·6 | — | 6·8 | — | — | — | — | — | |
| | B | — | — | — | — | — | — | — | — | — | — | Death |
| 5 | A | 255 | 100 | 13·4 | 125 | 6·0 | — | 8·2 | — | — | 14·8 | |
| | B | 166 | 105 | 15·5 | 137 | 5·0 | — | 4·6 | — | — | 27·6 | Death |
| 6 | A | 280 | 79 | 11·4 | 113 | 7·2 | — | — | — | — | — | |
| | B | 230 | 87 | 16·8 | 134 | 6·8 | — | 10·2 | 4·3 | 11·5 | — | |
| 6a | A | 245 | 88 | 13·0 | 120 | 6·8 | — | 11·4 | 4·3 | 11·5 | — | |
| | B | 115 | 90 | 22·2 | 125 | 3·2 | 7·8 | — | 6·5 | 8·6 | — | Recovery |
| 7 | A | 300 | 82 | 10·4 | 118 | 6·6 | 16·2 | 15·9 | 3·8 | 12·0 | — | |
| | B | 230 | 94 | 14·8 | 120 | 4·4 | — | 10·7 | 5·2 | 9·4 | — | Recovery |
| 8 | A | 260 | 98 | 11·3 | 120 | 7·5 | — | — | — | — | — | |
| | B | — | — | — | — | — | — | — | — | — | — | Death |
| 9 | A | 610 | 67 | 16·0 | 127 | 3·2 | 21·0 | 21·6 | 4·3 | 9·9 | 5·1 | |
| | B | 210 | 98 | 21·0 | 135 | 3·6 | 14·0 | 10·3 | 4·0 | 4·2 | 5·3 | Death |
| 10 | A | 375 | 97 | 7·9 | 130 | 7·0 | — | — | — | — | — | |
| | B | 123 | 102 | 17·9 | 132 | 4·2 | — | — | — | — | — | Death |
| 11 | A | 580 | 90 | 17·6 | 137 | 4·5 | — | — | — | — | — | |
| | B | 255 | 102 | 21·0 | 140 | 4·0 | — | 6·9 | — | 5·7 | — | Recovery |
| 12 | A | 575 | 77 | 14·8 | 130 | 6·0 | 8·0 | 12·5 | 2·8 | 16·0 | — | |
| | B | 170 | 99 | 18·6 | 131 | 5·0 | 6·4 | 5·0 | 6·0 | 5·9 | — | Recovery |
| 13 | A | 495 | 81 | 13·4 | 115 | 4·2 | 9·3 | 14·2 | 2·5 | 10·0 | 3·1 | |
| | B | 270 | 96 | 17·6 | 133 | 4·6 | — | 13·5 | 3·0 | 6·0 | 3·3 | Death |
| 14 | A | 370 | 72 | 12·4 | 117 | 4·2 | 10·0 | 14·1 | 3·8 | 15·8 | — | |
| | B | 200 | 99 | 20·0 | 140 | 5·6 | 5·3 | 8·6 | 5·5 | 9·3 | — | Recovery |
| 15 | A | 310 | 120 | <5·0 | 145 | >8·0 | — | 11·3 | 4·7 | 6·6 | — | |
| | B | 73 | 104 | 18·6 | 145 | 5·8 | 9·9 | 3·4 | 7·8 | 3·5 | — | Death |

| Dialysed patient no. | | Urea (mg. per 100 ml.) | Chloride (mEq./l.) | $CO_2$ content (mEq./l.) | Sodium (mEq./l.) | Potassium (mEq./l.) | Creatinine (mg. per 100 ml.) | Uric acid (mg. per 100 ml.) | Calcium (mEq./l.) | Inorganic phosphate (mg. per 100 ml.) | Bilirubin (mg. per 100 ml.) | Outcome |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 16 | A | 445 | 129 | 28·7 | 160 | 3·6 | 6·8 | 10·9 | 3·8 | — | — | |
| | B | 335 | 94 | 17·9 | 135 | 3·2 | — | — | — | — | — | |
| 16a | A | 335 | 94 | 17·9 | 135 | 3·2 | — | — | — | — | — | |
| | B | 115 | 90 | 10·6 | 125 | 4·2 | 3·6 | 4·5 | 5·7 | 5·4 | — | Death |
| 17 | A | 370 | 67 | 13·8 | <110 | 4·0 | — | 12·8 | 2·7 | 15·6 | — | |
| | B | 180 | 97 | 20·0 | 128 | 5·4 | — | 7·5 | 4·8 | 8·6 | — | |
| 17a | A | 340 | 82 | 18·2 | 125 | 4·2 | — | 13·3 | 2·5 | 12·4 | — | |
| | B | 60 | 104 | 20·4 | 140 | 5·4 | — | 3·2 | 8·4 | 5·5 | — | Recovery |
| 18 | A | 470 | 70 | 11·0 | 110 | 4·4 | 11·2 | 21·5 | 2·5 | 15·2 | — | |
| | B | 205 | 97 | 19·0 | 135 | 4·6 | 9·5 | 10·3 | 5·5 | 8·8 | — | Death |
| 19 | A | 720 | 89 | 15·8 | 125 | 7·0 | — | 16·3 | 3·3 | 10·8 | — | |
| | B | 235 | 102 | 20·0 | 130 | 4·8 | — | 6·8 | 6·6 | 7·4 | — | Death |
| 20 | A | 350 | 70 | 14·4 | 120 | 6·5 | — | 10·2 | 3·6 | — | — | |
| | B | 205 | 102 | — | 130 | — | — | 6·7 | 5·6 | — | — | Death |
| 21 | A | 480 | 93 | 7·9 | 120 | 4·2 | 14·0 | 10·3 | 2·5 | 14·3 | — | |
| | B | 230 | 99 | 23·5 | 135 | 3·3 | 12·0 | 5·8 | 5·5 | 7·3 | — | Death |
| 22 | A | 280 | 92 | 19·2 | 128 | 3·5 | — | 16·7 | 4·0 | 4·0 | 6·2 | |
| | B | — | — | — | — | — | — | — | — | — | — | Death |
| 23 | A | 465 | 82 | 15·8 | 120 | 5·0 | 18·0 | — | — | 14·4 | <1·0 | |
| | B | 174 | 95 | 16·4 | 140 | 5·5 | 13·0 | 14·0 | 5·2 | 4·4 | — | Death |

*The Jaundiced Patient with Anuria*

Eleven such patients were referred to us. Two were not dialysed and died, while 9 were dialysed and of these only 1 (with mild toxic hepatitis following pneumonia) lived. Of the 11 patients 7 were women, and 6 of them had had abortions. In 2 of these oral abortefacients had been taken, and in 4 there had been vaginal interference; 2 of these 4 had *B. welchii* infections. The 7th woman developed acute tubular necrosis, pneumonia, and toxic hepatitis after hysterectomy. Of the 4 men, 1 lived; the 3 who died developed the condition following heatstroke, staphylococcal septicaemia, and cholaemia resulting from gallbladder surgery, respectively (Table V).

The jaundice was usually hepatic in type. Occasionally a haemolytic element was also present. Death occurred unexpectedly in 4 patients when their general and biochemical condition seemed to be improving. It was noted that:

1. Despite severe liver damage the blood-urea level was markedly raised.

2. Blood-sugar values did not fall very low, presumably because of the glucose given orally or intravenously in routine therapy.

3. Serum-potassium levels tended to remain low, or were easily controlled

4. Marked acidosis was common. It was most difficult, in these patients, to decide whether the clinical state was uraemic or cholaemic, and at what stage to dialyse. Autopsy revealed hepatic necrosis in those cases that were histologically examined, and large, yellow livers in those that were not so examined. The impression arose that dialysis sometimes hastened death. Indeed, 2 patients seen recently by one of us (K.J.K.), and rejected on the grounds that they were moribund, recovered on conservative therapy. They have not been included in this series.

The comparatively low serum-potassium levels in these jaundiced patients are of interest. A *British Medical Journal* editorial annotation[4] mentioned work by Read *et al.* They stated that patients with severe liver disease were sensitive to low serum potassium, and developed

coma after diuresis. In these patients, however, there was a rise in the alkali reserve. Possibly, though we have no evidence to support this, dialysis with removal of serum potassium to a normal level had some part to play in the deaths of our jaundiced patients.

### PATIENTS WITH NO KNOWN ANURIC PHASE, GOOD URINE VOLUME, BUT CLINICAL FAILURE TO IMPROVE

We have had 3 patients recently, not included in this group of acute oliguric renal failure, with acute pyelonephritis and very poor renal function. Despite the administration of fluids and antibiotics and the maintenance of a urine output of 2,000 ml. or more a day, the condition remained stationary with high blood-urea levels and deranged electrolytes. Clinically, they have shown drowsiness, disorientation and twitching. They resemble patients with acute tubular necrosis in the early diuretic phase with superadded infection, and are examples of severe acute renal failure without anuria or hypotension.[5] One patient recovered, while 2 died from their infection. Had they been clinically oliguric, we should have probably dialysed all 3.

The essence of the problem seems to us to be the control of the infection, and we feel that it is more than possible that dialysis of these patients would have enabled the infection to be overcome. This, though not entirely comparable, is supported by recent work,[18] discussing earlier dialysis in septic and traumatic cases of acute renal failure, with marked improvement in recovery rates. Also there is general evidence[12] that patients with sepsis have rapid electrolyte change and require earlier dialysis.

### DISCUSSION

This article discusses some unresolved problems of uraemia, and stresses the poverty of our knowledge of basic physiological mechanisms in the causation of signs and symptoms. It describes acute oliguric renal failure in the Bantu adult, the type of patient presenting for treatment, and the problem of jaundice and acute renal failure — 'hepatorenal' failure.

Further, though medical control of acidosis and hyperpotassaemia has been well described previously, we feel that the results we have obtained with alkalis and rectal administration of ion-exchange resins are most impressive. Medical therapy is of first importance, more especially for practitioners in parts of South Africa where artificial kidneys are not available, and therefore any advances in conservative therapy should be widely known.

We have stressed in this article that the blood-urea level is not a good index of uraemia; that hyperpotassaemia and acidosis can usually be controlled medically; and that the only important factor in deciding the need for dialysis is the clinical condition of the patient. This is especially so after 1 dialysis. We feel strongly that every effort must be made to improve the efficiency of the artificial kidney in the ways suggested,[2] and probably in other ways, so that the present discrepancy in dialysance of different substances is overcome. This will largely avoid the necessity for frequent dialyses, which are practically impossible to organize in the framework of an average general hospital. It may also lessen considerably the number of unexpected deaths.

Finally, we have stressed the importance of infection, both in oliguric patients and in others with good urine volume, in producing poor results. Every effort should be made to prevent infection, to diagnose it early, and to treat it as something of great significance.

### SUMMARY

1. Of 51 Bantu patients referred for dialysis, 23 were dialysed, 4 on 2 occasions.

2. The indications for dialysis, the method of conservative treatment, the method and complications of dialysis, and the assessment of results, are discussed.

3. A special study has been made of the control of serum-potassium levels with rectal resins, and the control of acidosis with alkalis.

4. A series of 9 jaundiced patients with acute renal failure is described, and our results are so poor that we question the value of dialysis in this group.

5. The changing pattern of mortality in acute renal failure, and the importance of infection in the outcome, are stressed.

6. The need for improvement in the efficiency of the artificial kidney is commented on.

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