and varying signs of precocious puberty and virilization. After puberty defeminization merging into virilization occurs and the clitoris rarely exceeds 1 cm. in diameter.

Virilizing ovarian tumours—the arrhenoblastoma, hilar-cell tumour, or adrenal rest tumour—all secrete androgens of some kind, although the 17-ketosteroids may not always be elevated. The general picture is usually seen in adult life, and is one of defeminization and virilization (Foss and Leverton, 1959).

Two other conditions deserve mention—constitutional virilism (Ferriman, Thomas, and Purdie, 1957), which is a common condition and may be familial or racial, and, finally, the Stein–Leventhal syndrome of hirsuties, obesity, amenorrhoea or oligomenorrhoea, and polycystic ovaries and infertility, which again probably occurs more often than is realized (Bailey, 1959).

The pseudofemale was a normal male in every respect before his conversion into an apparent female by means of massive and continued endocrine therapy and plastic surgery.

Similarly, the pseudomale is a hirsute well-muscled person who has been treated for years with androgens and usually had bilateral mastectomy and possibly plastic surgery to the external genitalia. It is not so easy for these patients to arrange for an oophorectomy or hysterectomy, and there is always the possibility that some gynaecological condition may arise. I know one such person who menstruates from time to time through her penile tube graft if she omits continuous androgen therapy.

Now, as Cawadias (1959) has reminded us, sex is a matter of total personality, dependent on the psychological personality as well as the genes, gonads, genital organs, and endocrines. Thus the management of these cases may involve considerable care and responsibility.

In Canada, Moore (1959) has determined the nuclear sex in 3,700 newborn infants, about equally male and female anatomically. Five anatomical males showed the presence of female nuclear chromatin. By the use of this simple screening test as a routine, it would be possible then to investigate the true chromosomal sex of babies in a doubtful category, and this would facilitate their correct upbringing, and treatment if necessary.

REFERENCES

- Arneaud, J. D., Annamunthodo, H., Pinkerton, J. H. M., and Cole, W. R. (1956). *Brit. med. J.*, **2**, 792.
 Bailey, K. V. (1959). *J. Obstet. Gynaec. Brit. Emp.*, **66**, 556.
 Barr, M. L. (1955). *Anat. Rec.*, **121**, 387.
 Broster, L. R., Patterson, J., and Camber, B. (1953). *Brit. med. J.*, **2**, 1288.
 Cawadias, A. P. (1959). *Lancet*, **1**, 369.
 Ferguson-Smith, M. A., Lennox, B., Mack, W. S., and Stewart, J. S. S. (1957). *Ibid.*, **2**, 167.
 Ferriman, D., Thomas, P. K., and Purdie, A. W. (1957). *Brit. med. J.*, **2**, 1410.
 Foss, G. L., and Leverton, J. S. (1959). *J. Obstet. Gynaec. Brit. Emp.*, **66**, 632.
 Goldberg, M. B., and Maxwell, A. F. (1948). *J. clin. Endocr.*, **8**, 367.
 Grumbach, M. M., Blanc, W. A., and Engle, E. T. (1957). *Ibid.*, **17**, 703.
 Harnden, D. G., and Armstrong, C. N. (1959). *Brit. med. J.*, **2**, 1287.
 — and Stewart, J. S. S. (1959). *Ibid.*, **2**, 1285.
 Hayles, A. B., and Nolan, R. B. (1958). *Proc. Mayo Clin.*, **33**, 200.
 Heller, C. G., and Nelson, W. O. (1945). *J. clin. Endocr.*, **5**, 1.
 — (1948). *Ibid.*, **8**, 345.
 Hinman, F. (1935). *Principles and Practice of Urology*. Saunders, Philadelphia and London.
 Jacobs, P. A., Baikie, A. G., Court Brown, W. M., Forrest, H., Roy, J. R., Stewart, J. S. S., and Lennox, B. (1959a). *Lancet*, **2**, 591.
 — MacGregor, T. N., Maclean, N., and Harnden, D. G. (1959b). *Ibid.*, **2**, 423.

- Jailer, J. W. (1953). *Bull. N.Y. Acad. Med.*, **29**, 377.
 Jost, A. (1953). *Recent Progr. Hormone Res.*, **8**, 379.
 Klinefelter, H. F., jun., Reifenstein, E. C., jun., and Albright, F. (1942). *J. clin. Endocr.*, **2**, 615.
 Moncrieff, A. (1958). *Lancet*, **2**, 267.
 Moore, K. L. (1959). *Ibid.*, **1**, 217.
 Nellhaus, G. (1958). *New Engl. J. Med.*, **258**, 935.
 Stern, C. (1959). *Lancet*, **2**, 1088.
 Stewart, J. S. S. (1959a). *Ibid.*, **1**, 1176.
 — (1959b). *Proc. roy. Soc. Med.*, **52**, 817.
 — Ferguson-Smith, M. A., Lennox, B., and Mack, W. S. (1958). *Lancet*, **2**, 117.
 Wilkins, L. (1957). *Diagnosis and Treatment of Endocrine Disorders in Childhood and Adolescence*, 2nd ed. Blackwell, Oxford.
 — Jones, H. W., jun., Holman, G. H., and Stempfel, R. S., jun. (1958). *J. clin. Endocr.*, **18**, 559.

TREATMENT OF RENAL FAILURE IN A UNIT WITH FACILITIES FOR HAEMODIALYSIS (TWIN-COIL ARTIFICIAL KIDNEY)

RESULTS WITH 80 PATIENTS

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Owing to the many and varied causes of acute renal failure, clinicians in practically every branch of medicine and surgery are faced from time to time with the problems of treatment of this condition. Conservative management of acute renal failure in the last 10 years has greatly improved results. It is now clear that haemodialysis with an artificial kidney is an important adjunct to treatment.

Since June, 1957, we have employed an artificial kidney (Kolff twin coil) at this unit. We give a brief survey of the treatment of patients admitted to the unit during the first two years since haemodialysis was available. No previous results with this type of artificial kidney have been published in this country apart from a short summary (Jackson, 1958). During the two-year period 78 patients have been admitted and 88 dialyses performed on 57 of them. A further two patients were dialysed once each in their own hospitals. The patients, 75% of whom were civilians, have been referred from over a wide area, mainly from the Midlands, South of England, and Wales.

In any unit admitting patients primarily for the treatment of renal failure, a considerable number will be found eventually to be in the terminal phase of a chronic renal disease, or to have an acute irrecoverable renal lesion, such as bilateral cortical necrosis or a rapidly progressive glomerulonephritis. The results of treatment of patients with an acute recoverable lesion

are simply stated. Either the patient survives or dies. In an evaluation of the overall results in the unit this simple assessment becomes meaningless. Subdivision of the patients into groups is essential if any proper analysis of treatment is to be made. Those who have died have been placed into one of three groups based on post-mortem pathological criteria: (1) recoverable acute lesions, (2) irrecoverable acute lesions, and (3) advanced chronic lesions.

Results of Treatment

Acute Recoverable Renal Failure

Details of the 45 patients in this group are set out in Tables I and II. In those patients with renal failure associated with jaundice due to a hepatic lesion (Table II) the prognosis is primarily dependent on the hepatic lesion, and in the great majority of them it is extremely poor. The separation of this group within that of acute recoverable renal failure is intended to emphasize this point and to avoid presenting an unnecessarily poor prognosis in the general group.

Of the 36 patients with acute recoverable renal failure without an associated hepatic lesion, 27 recovered from the renal failure. Ten suffered severe trauma with multiple injuries and one had severe extensive burns. Five of those with multiple injuries survived despite extreme degrees of trauma and periods of oliguria of 6, 20, 20, 16, and 71 days; dialysis was not performed in one, and 3, 2, 2, and 5 dialyses were performed in the other four. The extent of the trauma in the surviving patients (Cases 8/58, 11/58, 21/58, 18/59, and 23/59) is briefly set out in the case summaries, and Fig. 1 shows details of Case 11/58. Of the six patients

during an episode of peripheral vascular failure not apparently related to any metabolic disturbance. The extent of trauma in those dying was not necessarily greater than in those surviving, although severe cerebral damage militated against recovery.

Of the six patients with acute renal failure related to pregnancy, five survived. The one patient (Case 5/58) who died during the early diuretic phase had had a post-partum haemorrhage. After an oliguric period of 12 days her urine volume had risen to 2.5 litres at the time of death, which was due to pulmonary embolism from infected thrombi in the large veins at the site of intravenous catheters.

In the third group of patients with miscellaneous causes for the renal failure, 17 out of 19 recovered from the renal failure. Two of these subsequently died from unrelated causes. Of the two patients dying before recovery of renal function occurred, one (Case 5/59) developed a further cerebral haemorrhage from an angioma, probably associated with the heparinization for dialysis, and the other (Case 36/59) died with severe post-operative abdominal sepsis.

Nine patients were admitted with renal failure associated with jaundice due to a hepatic lesion (Table II). Only two of these nine survived; of the seven who died, six came to necropsy, and all showed pathological changes in the kidneys consistent with a diagnosis of acute tubular necrosis. The hepatic lesions included hepatitis, either virus or leptospiral, suppurative cholangitis, and obstructive jaundice after operation on the bile passages. The prognosis in hepatic jaundice complicated by renal failure is extremely poor. The precise relationship of the jaundice or hepatic dysfunction to the onset of renal failure is obscure, although both in the terminal stages of hepatic failure and after operations on the bile passages in jaundiced patients hypotension with renal ischaemia may play an important part (Hecker and Sherlock, 1956; Lassen and Thomsen, 1958). It is possible that a high concentration of bile pigments in the serum potentiates the renal damage (Wartman *et al.*, 1950), and it may be that only those patients survive in whom the jaundice is rapidly lessening during the early stages of renal failure. This was, in fact, the case in two patients who survived (Cases 40/59 and 44/59), and fits in with previous personal experience and scattered reports in the literature.

In the only fatal case in which the jaundice was diminishing (Case 42/59) an early return of renal function had occurred when the patient died of a cerebral haemorrhage. In this case dialysis was performed on five occasions, and the patient had shown considerable improvement after an initial critically ill condition. Although the build-up of nitrogen retention was rapid, the main reason for the short intervals between dialyses was the belief that in the presence of combined hepatic and renal failure there is a rapid accumulation of toxic metabolites, in particular ammonia, other than those found with isolated renal failure (Webster and Gabuzda, 1959). Although it is impossible to deny that the cerebral haemorrhage in this exceedingly ill patient may have been related to the heparinization during dialysis, his striking improvement, with an early return of renal function, would seem convincing evidence that frequent dialyses are the right policy in combined hepatic and renal failure.

It is surprising and disappointing that dialysis removes relatively small quantities of bile pigment; the biggest

FIG. 1.—Case 11/58, man age 45. Typical chart of a patient with multiple injuries and acute renal failure. Note the necessity for early transfer and dialysis. (See case history.)

who died after severe trauma or burns, one (Case 32/58) with severe cerebral contusion and another (Case 22/59) with a fractured skull and cerebral damage died within a few hours of admission. Another patient (Case 35/59), with abdominal injuries and a fractured pelvis, died shortly after the commencement of dialysis, 16 hours after admission. The first patient (Case 1/57) to be treated with haemodialysis in the unit died the day after dialysis. The small girl (Case 1/59) with 65% burns died soon after the completion of a short dialysis on the day after admission. Patient 28/59 had sustained cerebral contusion and extensive trauma necessitating leg amputation; she died in the early diuretic phase

TABLE I.—Patients with Acute Recoverable Renal Failure (36 patients—27 recovered from their renal failure)

Case No.	Sex	Age	Renal Lesion	Associated Conditions	Maximum Blood Urea (mg. 100 ml.)	Period of Oliguria (Days)	No. of Dialyses	Days in Renal Unit	Result
1/57	M	43	Acute tubular necrosis	Severe trauma; multiple fractures	400	7	1	3	Died
3/57	F	21	" " "	Ante-partum haemorrhage	300	10	0	21	Recovered
4/57	F	27	" " "	Septic abortion	570	21	3	75	"
1/58	F	37	Ureteric obstruction	Hysterectomy (carcinoma of cervix). Cerebral angioma	280	8	0	3	Died (recovered from renal failure)
3/58	F	57	Acute tubular necrosis (single kidney)	Right staghorn calculus. Right nephrectomy	360	19	1	43	Recovered
4/58	M	15	Acute tubular necrosis	Acute dilatation of stomach. Gastrostomy. Hypotension	540	8	1	17	"
5/58	F	20	" " "	Post-partum haemorrhage. Terminal septicaemia with pulmonary embolus	480	12	1	10	Died
8/58	M	33	" " "	Trauma. Multiple fractures. Diffuse pulmonary haemorrhage	430	6	0	49	Recovered
11/58	M	45	" " "	Trauma. Multiple fractures	580	20	3	55	"
19/58	M	23	" " "	Carcinoma of stomach. Gastrectomy. Prolonged vomiting. Bowel perforation	540	13	1	37	Died (recovered from renal failure)
21/58	F	46	" " "	Trauma. Multiple fractures	590	20	2	39	Recovered
22/58	M	26	" " "	Acute alcoholism. Epilepsy. Right infantile hemiplegia	580	15	1	33	"
23/58	M	35	" " "	Peptic ulcer. 1951 gastrectomy. 1952 gastro-enterostomy. Prolonged vomiting	450	14	1	24	"
25/58	F	35	" " "	CO poisoning. Muscle necrosis. Neurological sequelae	540	20	2	82	"
31/58	M	23	" " "	Resection coarctation of aorta	380	14	1	30	"
32/58	M	23	" " "	Trauma. Cerebral contusion. Therapeutic hypothermia	360	8	0	Hours	Died
1/59	F	7	" " "	Severe burns (65%)	360	Maintained urine volume	1	2	"
3/59	F	23	Pyelonephritis	Complicating pregnancy—onset at 34 weeks of pregnancy with premature labour and stillborn infant 35 weeks. Staphylococcal enteritis	500	21	2	36	Recovered
5/59	M	16	Acute tubular necrosis	Cerebral angioma. Intracerebral bleeding	550	9	1	2	Died
8/59	M	19	Acute glomerulonephritis	Bronchopneumonia	320	9	0	64	Recovered
9/59	M	19	Renal vein thrombosis	—	160	10	0	75	"
13/59	F	60	Acute tubular necrosis	Mitral stenosis. Pulmonary infarction	470	15	1	21	"
15/59	F	23	" " "	Concealed ante-partum haemorrhage after toxæmia of pregnancy. Foetal death <i>in utero</i>	410	20	1	32	"
18/59	M	17	" " "	Trauma. Multiple fractures	700	16	2	25	"
20/59	M	27	" " "	Dental abscess immediately preceding onset of renal symptoms	580	23	2	41	"
21/59	M	21	Glomerulonephritis	—	256	10+	0	14	"
22/59	M	35	Acute tubular necrosis	Trauma. Fractured skull	590	9	0	Hours	Died
23/59	M	54	Acute tubular necrosis and ? mild cortical necrosis	Trauma. Ruptured ileum. Amputation left leg, after thrombosis of femoral artery	600	71	5	134	Recovered
26/59	M	41	Acute tubular necrosis	Acute pancreatitis	380	12	0	18	"
27/59	M	39	" " "	Infected olecranon bursitis. Right nephrectomy. Secondary haemorrhage	520	52	4	76	"
28/59	F	68	" " "	Trauma. Subarachnoid haemorrhage. Multiple fractures. Right leg amputation	420	8	0	17	Died
30/59	M	68	" " "	Salicylate poisoning. Bladder-neck obstruction. Prostatectomy	394	12	1	96	Recovered
31/59	F	20	" " "	Septic abortion	550	24	1	31	"
35/59	M	50	" " "	Trauma. Pelvis fracture. Abdominal haematoma	400	5	1 (uncompleted)	2	Died
36/59	M	47	" " "	Haematemesis and melaena. Gastro-enterostomy. Wound abscess. Further laparotomy	490	14	1	4	"
41/59	F	44	" " "	Pyloric stenosis. Mitral stenosis Gastro-enterostomy (carcinoma stomach)	470	12+	1	16	Recovered

TABLE II.—Renal Failure in Patients with Jaundice (9 patients—2 recovered)

Case No.	Sex	Age	Renal Lesion	Associated Conditions	Maximum Blood Urea (mg. 100 ml.)	Period of Oliguria (Days)	No. of Dialyses	Days in Renal Unit	Result
29/58	M	73	Acute tubular necrosis	Obstructive jaundice. Cholecystectomy. Suppurative cholangitis	370	9	1	1	Died
30/58	M	51	" " "	Resection gangrenous gut. Hepatitis	465	6	0	2	"
7/59	M	40	" " "	Hepatitis	390	8	1	6	"
24/59	F	24	No post-mortem	Obstructive jaundice. Cholecystectomy. Intra-peritoneal haematoma. Secondary removal of gall-stones in common bile-duct	450	13	1	6	"
29/59	F	66	Acute tubular necrosis	Hepatitis. Cholecystectomy	470	24	4	16	"
38/59	M	52	" " "	Cholecystectomy. Obstructive jaundice. 2 exploratory laparotomies	450	15	2	13	"
40/59	M	43	" " "	Leptospirosis (Weil's)	560	6	1	19	Recovered
42/59	M	26	" " "	" Cerebral haemorrhage	540	22	5	18	Died
44/59	M	49	" " "	Cholangitis. Septicaemia (<i>E. coli</i>)	480	10	1	35	Recovered

fall in the serum bilirubin with a six-hour dialysis was from 51 to 38 mg./100 ml., when the blood urea fell from 500 to 190 mg./100 ml. (Case 42/59). That this is not due to release of bile pigment from the tissues maintaining the serum level is apparent from the very low concentration of bile pigment in the dialysing fluid. Nevertheless, repeated dialyses will also help to reduce the serum bilirubin level and possibly allow renal function to recover more rapidly.

Acute Renal Failure with Irrecoverable Renal Lesions

Of the 12 patients in this group, one had extensive symmetrical bilateral cortical necrosis; this was a woman of 25 (Case 16/59) who developed renal failure after concealed accidental haemorrhage at full term in her fifth pregnancy. A live child was delivered after rupture of the membranes, but it died in 24 hours. The patient was admitted to the unit on the eighth day of renal failure and was dialysed on one occasion (tenth day). She was subsequently managed conservatively, with the addition of norethandrolone ("nilevar"), but the urine volume never exceeded 300 ml. in 24 hours, and she died on the forty-sixth day of renal failure.

At necropsy 11 patients, all men, aged from 18 to 52 years, showed the pathological changes compatible with the diagnosis of "subacute glomerulonephritis." One man of 23 came to necropsy with very unusual arterial lesions in the kidneys resembling those seen in scleroderma. Full details of this patient and those with "subacute glomerulonephritis" will be published elsewhere.

A boy of 11 (Case 5/57) was admitted in acute renal failure associated with gross purpuric eruptions and abdominal pain. He was dialysed on one occasion, but died, still in severe renal failure, as a direct result of the rupture of the bowel. Necropsy showed widespread lesions typical of periarteritis nodosa. A woman of 59 was admitted with severe purpura and a blood urea of 700 mg./100 ml.; she died before dialysis was started. At necropsy the kidney showed diffuse necrotic lesions in the glomeruli. The adrenal glands were largely destroyed by haemorrhage. Thirteen dialyses were performed on 11 of these patients.

Renal Failure with Advanced Chronic Renal Lesions

Seventeen patients were admitted in renal failure and proved eventually to have chronic renal lesions. Of the 17, 13 died of renal failure, either while in the renal unit or shortly after transfer to their parent hospital. Nine of these 17 patients had chronic glomerular nephritis, five had long-standing post-renal obstruction; and of the other three, one had polycystic kidneys, one chronic pyelonephritis without obstruction, and one renal amyloidosis complicating chronic osteomyelitis (present for 35 years).

Of the four patients who survived, three had post-renal obstruction (severe hydronephrosis with one kidney, chronic prostatic obstruction, and colonic transplantation of both ureters), and all three greatly improved while in the unit, two of them each being dialysed once. The other was one of the patients with a chronic lesion and ankylosing spondylitis.

Of the 17 patients, 11 were dialysed on 15 occasions.

Poisonings

We have seen four patients (one in renal failure) with drug poisoning, three due to barbiturates and one due to

glutethimide (α -phenyl- α -ethylglutarimide; "doriden"). One patient with barbiturate poisoning was not dialysed as his level of consciousness was rising and the day after admission he regained consciousness. The patient with the glutethimide poisoning came to us too late; he died within three hours of admission and before we were able to start dialysis, which would have been expected to remove a considerable amount of the drug.

The other two with barbiturate poisoning were dialysed in their own hospitals. Case 24/58 has been described (Honey and Jackson, 1959). The second patient, a woman of 54 (Case 39/59), had taken a large dose of phenobarbitone and later developed a short period of renal failure. She was dialysed for eight hours in her own hospital with a successful outcome (Fig. 2).

FIG. 2.—Case 39/59, woman age 54. Phenobarbitone poisoning. Barbiturate removed:—Bath: dialysis—8 hours=2,560 g.; Urine: 17.4 litres in 8½ days=0.663 g. (Patient under the care of Dr. Clifford Parsons. Barbiturate estimations made by the biochemistry staff, General Hospital, Birmingham, where dialysis was performed.)

The artificial kidney may come to play a more active part in the treatment of severe barbiturate poisoning with or without the presence of renal failure, particularly in the large cities, where many cases of such poisoning occur.

The removal of barbiturate from a patient by an artificial kidney will depend on the degree of binding of the drug with the protein molecule. The longer-acting the barbiturate the better is the result of haemodialysis (Table III). Even mild renal failure may be an imperative indication for dialysis if intoxication is due to a dialysable compound.

TABLE III.—Barbiturate Poisoning. Expected Results from Haemodialysis

Barbiturate	Proprietary Name	Action	Blood Level to Produce Unconsciousness*	Expected Results from Haemodialysis
Barbitone	Medinal	Long	5-9	Very good
Phenobarbitone	Luminal	"	5-9	"
Butobarbitone	Soneryl	Intermediate	2-4	Moderate
Amylobarbitone	Amytal	"	2-4	"
Pentobarbitone	Nembutal	Short	1-2	Poor
Quinalbarbitone	Seconal	"	1-2	"

* mg./100 ml. expressed as the acid form of the barbiturate. (From *Micro-analysis in Medical Biochemistry*, 3rd ed., 1956, King, E. J., and Wootton, I. D. P. Churchill, London.)

Miscellaneous

Two patients are not included in the above groups. One had hypokalaemic alkalosis and was not dialysed but recovered. The other, aged 72, had myocardial ischaemia, a hypernephroma of one kidney, with obstruction to the other by glands causing prolonged anuria: he was dialysed twice but died.

Management of Patients**Conservative Treatment**

The successful management of acute renal failure depends largely on early diagnosis. The sooner proper metabolic care of the patient is begun the more likely is the course of the illness to be undramatic and conservative management, without recourse to dialysis, allow the recovery of renal function. Although acute renal failure may occur without oliguria (Sevitt, 1959), the metabolic disturbances are usually less and the failure to recognize the presence of the renal functional damage is not so dangerous to the patient as when oliguria occurs. The term "anuria" is often used to describe these cases, with the implication that they are only in renal failure when anuric. In fact, the majority have oliguria, but if anuria is present the most likely cause is a post-renal obstruction. An arbitrary 24-hour urine volume of 760 ml. as a definition of oliguria has been suggested (Joekes *et al.*, 1957), as at this rate of urine flow (0.5 ml./min.) well-marked urine concentrations should be expected, with a specific gravity of 1020 or more or an osmolality in excess of 1,000 ml. osm./l. in the presence of normal renal function. If with such a urine volume the specific gravity is below 1016, renal functional impairment must be assumed. If doubt exists about the presence of renal damage despite a good urine volume, the urinary urea concentration should exceed 2 g./100 ml., irrespective of the urine volume if the blood urea is over 100 mg./100 ml. (Taylor, 1957).

It cannot be too strongly emphasized that observations on the urine will facilitate an early diagnosis of acute renal failure, whilst isolated observations on the blood chemistry cannot differentiate between primary metabolic disturbances and renal failure.

Once the presence of acute renal failure is established simple metabolic control should be started immediately. Total fluid intake must be strictly controlled, and it is now fully established that the patient should be rationed to an electrolyte-free carbohydrate solution with no fat, whenever possible by mouth without intubation. While the optimal total calorie intake is still uncertain it should not fall below 400–600 calories for prolonged periods. Management varies, depending on the phase of acute tubular necrosis.

This aspect has been adequately discussed by many authorities, including Parsons and McCracken (1959). It is essential that the intake of fluid is restricted to not more than 600 ml. daily to cover insensible loss. The aim should be to maintain a daily loss of weight of about 300 g. during the oliguric phase. Lactose by mouth has been found to be tolerated better than glucose. Apart from patients with severe trauma the vast majority tolerate oral feeding, thus avoiding unnecessary intravenous therapy. Antibiotics are not now prescribed as a routine but only when indicated.

When the oral route is not possible (45 g. daily) large doses of rectal "resonium-A" up to 200 g. a day* have helped significantly to reduce the rate of rise of serum potassium.

With the onset of the diuretic, or recovery, phase (usually 1 litre or more urine output in 24 hours) great care is required in estimating electrolyte losses in the urine, particularly potassium and sodium, because supplements may be required.

Haemodialysis

Indications.—(1) Overhydration, particularly in the presence of pulmonary oedema, because of the constant risk of sudden collapse, with hypotension. (2) Hyperkalaemia of 7 mEq/l. or more, with electrocardiographic changes. (3) Acidosis of 12 mEq/l. or less which cannot be corrected. (4) Clinical deterioration is the single most important indication for dialysis. Patients should not be allowed to develop a state of established persistent vomiting, drowsiness, or twitching, whatever their biochemistry, because their subsequent management becomes more difficult. In patients with trauma our experience has shown it is essential to dialyse early owing to increased katabolism. (5) Poisoning by drugs, such as barbiturates and salicylates, associated with renal failure.

If surgery is essential in treating the primary condition causing the renal failure, then often a planned dialysis 24 hours before the operation is indicated, recognizing that a further dialysis perhaps 24 to 48 hours after operation may be necessary. There are no contra-indications to dialysis with this apparatus.

Technique.—The Kolff twin-coil artificial kidney (Travenol Lab. Inc.) has a fixed capacity of about 1,000 ml. Immediately before dialysis begins the circuit is tensed by the addition of small amounts of blood to a pressure of 200 mm. Hg. The flow-rate can be varied, but is usually maintained at about 350 to 450 ml./min. The pressure in the circuit can also be varied considerably; if ultrafiltration is not required to any extent the pressure is reduced accordingly. Artery-to-vein connexion with the "kidney" is used in most patients. Tapered polyvinyl chloride catheters (Portex) with a side-arm for sampling are used. They are presterilized and kept in separate nylon envelopes. The whole procedure of catheter insertion and dialysis is now performed by one medical officer and one sister. Modifications have been made to the "kidney" and are described elsewhere (Brennand and Bunker, 1960). In the case of cerebral injuries and patients with jaundice, regional heparinization as recommended by Anderson and Kolff (1959) may reduce haemorrhagic complications due to dialysis.

Dialysing Fluid.—The bathwater or dialysing fluid is that commonly in use containing potassium, sodium, chloride, and bicarbonate in concentrations equal to those found in normal plasma with 0.4% glucose. A high serum potassium is reduced to a normal level by omitting potassium from the bath for the first one or two hours. The bath is changed every two hours.

Results of Dialysis

Table IV shows an analysis of the range of the biochemical results and fall in blood urea for 62 dialyses of six hours' duration. Hyperkalaemia is corrected

*Preparation of resonium-A for rectal administration (100 g. dose).—Resonium-A, 100 g.; aqua dist., 150 ml.; "promulsin gel" (5% solution), 50 ml. Dilute the promulsin gel with the water and incorporate resonium-A in a mortar. Transfer to an M.R.C. 500-ml. intravenous-drip bottle.

Promulsin gel.—Promulsin powder, 50 g., aqua chlorof., ad 1,000 ml.

Note: 50 ml. of mucilage of tragacanth may be substituted for promulsin gel.

easily, also sodium and chloride concentrations in most patients. In seven dialyses (six patients) the serum sodium at the end was over 148 mEq/l.; however, four of these recovered. (The other two eventually died with hepatic failure and septicaemia.) Acidosis was corrected satisfactorily in most patients. At the end of dialysis a serum bicarbonate of 22 mEq/l. or less was present on five occasions, in three patients with chronic renal lesions and in two with colonic transplantation of the ureters. In the latter, serum bicarbonate of 6 and 8 mEq/l. were corrected to 21 and 22 mEq/l. respectively.

TABLE IV.—*Biochemical Results of Dialysis (Six Hours)*

No. of Dialyses:	62	60	60	60	62
	Blood Urea (mg. 100 ml.)	Serum Sodium (mEq l.)	Serum Chloride (mEq l.)	Serum Bicarbonate (mEq l.)	Serum Potassium (mEq l.)
Beginning of dialysis	700-116	161-112	124-70	32-6	9.2-2.1
Mean	467	134	92	17.4	5.9
Standard deviation	±95.5	±9.8	±9.4	±4.6	±1.4
End of dialysis	264-71	162-120	112-88	31-19	6.2-2.8
Mean	144	140	101	25.7	4.2
Standard deviation	±45.9	±8	±5.8	±2.8	±0.7

With regard to the fall of blood urea throughout dialysis, it is recognized that the urea clearance in the Kolff twin-coil is not as great as that in the Skeggs-Leonards or rotating-drum machines (Anthonisen *et al.*, 1956; Parsons and McCracken, 1958). However, this fact has not necessitated, in this unit, more frequent dialyses in any individual patient or prejudiced recovery. Of our 57 patients dialysed, 73% had one or two dialyses only.

The clinical state of the majority of patients has improved during or 24 hours after dialysis. Only a few patients have shown clinical deterioration during dialysis, associated with a hypotension which has been usually corrected with a small blood transfusion (200-300 ml.) into the extracorporeal circulation. Hypertension has not been a feature of dialysis, apart from two patients with malignant hypertension. Pulmonary oedema has been improved considerably. This change can be demonstrated radiologically. Where accurate weights before and after dialysis have been obtained, all patients showed a fall in weight, with a range of 0.6 to 4.5 kg., with fluid replacement in some patients. The loss of weight reflects removal of water due to ultrafiltration.

Cases of Extensive Trauma which Recovered

Case 8/58.—Late on April 16, 1958, a man aged 33 sustained the following injuries in a car accident: five fractured ribs, haemothorax with generalized alveolar haemorrhages, extensive bruising to the abdominal contents with a ruptured spleen, fractured pelvis, right femur, right and left tibiae and fibulae, and left elbow. The next morning he underwent a laparotomy and splenectomy, and 450 ml. of blood was withdrawn from the left chest. Later the same day a tracheostomy was performed. Within 24 hours of the accident he was given 19 pints (10.8 litres) of blood. Immediately after the accident he was oliguric, with a rapidly increasing uraemia. On the third day he was transferred to this unit, at which time the blood urea was 259 mg./100 ml. and the 24-hour-urine volume 248 ml. He was placed in an oxygen tent for three days. On the fifth day of renal failure he produced 1,500 ml. of urine in 24 hours and subsequently made a full recovery without dialysis because of the short oliguric phase.

Case 11/58.—A man aged 45 fell 80 ft. (24.4 m.) while cleaning windows on April 25, 1958. During his fall he

ricocheted on his back off some telephone wires. His injuries were: concussion, considerable bruising of the back with extensive comminuted fractures of right scapula, pelvis, and right acetabulum with displacement, and fractures of four ribs and of both femoral necks. He was transferred to this unit on the fifth day; details are shown in Fig. 1. He made a good recovery, returning to work but cleaning ground-floor windows only.

Case 21/58.—A woman aged 46 was injured in a car accident on August 3, 1958. She was concussed and sustained a fractured pelvis, right ankle, and humerus; the left diaphragm was perforated, and the stomach and spleen had herniated into the thorax. The same day she was operated on to repair the diaphragm. Over the next eight days the volume of urine ranged between 60 and 450 ml./24 hours and the blood urea rose to 400 mg./100 ml. On the ninth day she was transferred to this unit. During the next six days she was dialysed twice; on the 21st day after the accident she produced 1,500 ml. of urine and proceeded to an uneventful recovery.

Case 18/59.—On May 25, 1959, a youth of 17 was involved in a motor-cycle accident. He sustained the following injuries: severe concussion, numerous contusions, a fractured vertebra, fractured pelvis with right protrusion acetabuli and subluxation of the right sacro-iliac joint, compound comminuted fracture of the right femur, and a fracture of the right tibia. There was absent circulation to the right foot. The same day he underwent an operation to decompress a haematoma of the right calf and insert a Steinmann pin. By May 27 a definite line of demarcation had appeared across the right foot, with incipient gangrene distally. He had remained oliguric since the accident (0-350 ml./24 hours). On June 1, when admitted to Halton, he was disorientated, had produced only 200 ml. of urine in 24 hours, the blood urea was 550 mg./100 ml., and the serum potassium 6 mEq/l. During the next five days he was dialysed twice; on the 17th day after the accident he began a diuresis. The right foot improved throughout the oliguric phase, and eventually complete circulation was restored. During most of his illness his management was complicated by severe mental disorientation resulting from his post-concussional state. He made an uneventful recovery; by the 28th day the blood urea was 38 mg./100 ml.

Case 23/59.—At 11 a.m. on June 16, 1959, a man aged 54 was kicked in the left groin by a horse. By midnight a large haematoma had developed in the left lower abdominal wall and the left leg was numb, painful, and pulseless. A block at the left ilio-femoral arterial junction was demonstrated by aortogram. Laparotomy revealed gross peritonitis and a ruptured ileum from a necrotic left inguinal hernial sac. Resection of the bowel and artery was performed, the operation lasting nine hours. The immediate post-operative progress was favourable, but it was doubtful if full circulation had returned to the leg. During the eight days after the accident the volume of urine rose gradually from nil to 950 ml./24 hours, the blood urea to 510 mg./100 ml., and the serum potassium to 6.6 mEq/l. At this stage he was transferred to Halton; on arrival it was apparent that the left lower leg was not viable. Haemodialysis was performed on the 10th day and a left mid-thigh amputation on the day after. Post-operatively an extremely rapid rise in uraemia occurred, necessitating a further dialysis on the 12th day. He proceeded to a prolonged oliguric phase lasting 71 days from the day of injury; during this period he required five dialyses. On the 134th day he was referred back to his parent hospital with a urine volume of 4 litres and blood urea of 190 mg./100 ml. At the time of writing he had returned home and was in the early stages of rehabilitation with an artificial limb.

Discussion

Any analysis of the results of treatment of acute recoverable renal failure on a comparative basis is difficult, if not impossible, as underlying or complicating conditions, rather than the renal failure, may determine

the outcome. Some assessment of the results is, however, essential, as the main justification for specialized units treating renal failure must be a higher rate of success than in non-specialized centres. As stated in the introduction, all patients admitted to the unit have been placed into one of three categories of renal disease: (1) recoverable acute lesions, (2) irrecoverable acute lesions, and (3) advanced chronic lesions. It is primarily the results in the first group that must be considered.

A total of 45 patients with acute recoverable renal lesions are included in the present series. Nine of these cases occurred in association with hepatic lesions and have been separately presented, as it is argued that the prognosis depends entirely on the hepatic lesion. Only the two patients with diminishing jaundice recovered, the seven other patients dying with severe hepatic insufficiency. Of the other 36 patients with acute recoverable renal failure, 27 recovered from the renal failure. The background to the renal failure in these cases had a very wide spectrum, including extensive trauma. Of 10 patients with severe trauma, five survived; the severity and extent of the trauma was not necessarily less in the surviving patients, although cerebral damage was of grave prognostic importance, in keeping with the results reported by Taylor (1957), only 5 out of 31 patients surviving where acute renal failure complicated head injuries.

Lucké (1946) reviewed some 600 published cases of acute renal failure, and estimated the overall mortality as in excess of 90%. It was not until after 1946 that treatment based on simple metabolic lines during the period of renal failure profoundly altered the desperate prognosis of this condition.

Clinical application of haemodialysis has been effected by Kolff and Berk (1943), but not until the fundamental principles of metabolic care were applied in the management of the patients and further advances in dialysing technique had occurred could haemodialysis convincingly be accepted as altering the overall prognosis.

Hamburger (1957) reported 203 cases of acute renal failure treated routinely by haemodialysis; the mortality figure was only 9%, but many mild episodes of renal failure were included among the cases. The earliest report in this country of the use of haemodialysis (Bywaters and Joekes, 1948) described 12 cases, of which only four had reversible lesions, two of these patients surviving. Shackman and Milne (1957) reported 30 cases with renal failure, 14 of which were treated with dialysis. None of the latter patients survived, but in 10 of them conditions other than renal failure accounted for death or an irreversible renal lesion was present. Of the 16 patients treated conservatively, 12 survived. Brief mention is made of subsequent results (Shackman, 1959), in which 26 patients with recoverable renal lesions were dialysed on one or more occasions, of these 15 died. Parsons and McCracken (1959) reported 63 cases of acute reversible renal failure; 7 of 18 (39%) patients treated conservatively died, but six of these died shortly after admission before dialysis could be attempted, and 17 (38%) of 45 patients who were dialysed died. Four of the latter group had renal failure complicating hepatic lesions, and three of them died. In the present series, patients with acute reversible renal lesions, excluding those with primary hepatic disease, had a survival rate of 75%, there being little difference whether conservative management alone or dialysis was used (Table V). Patients with the more prolonged renal failure or other

complications were dialysed in the present series, and the very similar survival rate in those who were dialysed as in those who were not must be accepted as evidence for an improved rate of survival due to dialysis.

TABLE V.—Results of Treatment of Patients in the Different Groups

Group	Not Dialysed	Dialysed	Recovered from Renal Failure
1 Acute recoverable renal failure	10	—	6
1 Renal failure with jaundice	1	—	21
2 Acute irrecoverable renal lesions	—	8	0
2 Acute irrecoverable renal lesions	1	—	2
3 Chronic renal lesions	—	11	0
	6	—	Improved
	—	11	2
			2

Taylor (1957) reported 31 cases of renal failure complicating head injury. Conservative management only was used, and of the 31 patients only five survived. Whether haemodialysis could improve these results in such a group can be answered only on the basis of experience. With the technique of regional heparinization, where there should be no prolongation of the clotting-time in the patient's body, haemodialysis would then not entail the added danger of cerebral bleeding. The experience in Korea in 1950, with renal failure complicating severe trauma (Smith *et al.*, 1955), leaves little doubt that haemodialysis greatly improves the survival rate. In the present series the survival of five patients with extensive trauma, the case histories of which are recorded above, is striking, and it must be very doubtful whether in those with longer-lasting oliguria survival would have been possible without haemodialysis.

If it is accepted that some form of dialysis must be available for any patient with acute renal failure should the necessity occur, a further question arises of the type of dialysis that should be employed. Peritoneal dialysis has the advantage that only very simple equipment is required, but 36 hours' dialysis effects the same metabolic exchanges that occur with six hours' haemodialysis or less with an artificial kidney. As constant supervision of the patient is required throughout the peritoneal dialysis and considerable discomfort to the patient is at times caused, it is doubtful whether peritoneal dialysis could be accepted as the method of choice in patients in whom repeated dialysis at relatively short intervals may be required. Exchange transfusion is fundamentally obtaining the same effect as haemodialysis, but the large quantities of blood make this impracticable, quite apart from the possible disadvantages of introducing the necessary amount of blood from other individuals. Gastro-intestinal dialysis has a relatively poor effect on the biochemical abnormalities except in removing potassium; and this, together with the marked discomfort to the patient, suggests that the method is unsuitable.

The large number of reports of haemodialysis using different types of apparatus can leave no doubt that, used by an expert team, this is a safe and often essential procedure. The type of apparatus used is certainly less important than the experience of the team. It is possible to place the different types of artificial kidney into two main groups: (1) those with a large potential capacity in the dialysing membranes, which is, however, only partly filled (the Kolff rotating drum); and (2) those in

which the potential capacity in the dialysing membrane is fully filled (Alwall kidney, Kolff twin-coil kidney, Skeggs-Leonards kidney, and others). With both the Skeggs-Leonards and the Kolff twin-coil kidney there is reasonable certainty that the full capacity of the dialysing membrane can be filled before connecting the patient; this is possibly less easy in the Alwall kidney, where the prevention of distension of the dialysing membrane tube beyond the original filling is less certain.

Only in kidneys in the second group, with a restricted capacity in the dialysing membrane, can a positive pressure be built up with the gradient from blood to dialysing fluid, thus enabling water to be lost by ultrafiltration. Although this may not be of great importance in many cases that are dialysed, there is little doubt that it is extremely important to be able, with certainty, to prevent take-up of water from the dialysing fluid. Shackman and Milne (1957), using the rotating-drum type of artificial kidney, found that there was a take-up of water by the patient which they assessed at approximately 500 to 600 ml., and in several of their patients the occurrence of pulmonary oedema after dialysis apparently contributed to the fatal outcome. Parsons and McCracken (1959), while appreciating the inability of a rotating-drum type of kidney such as they used in their unit to remove water from the patient, suggested that the total clearance obtained with this type outweighed the disadvantages. We have no doubt that some form of artificial kidney of limited capacity is the apparatus of choice and is essential in treating overhydrated patients.

In some countries the number of units with facilities for haemodialysis has far exceeded that in this country, where in the last few years only three units specifically handling acute renal failure have been in existence. More recently a considerable number of artificial kidneys have been bought or constructed, and some of these are intended for use in units accepting any patients in renal failure. The figures of survival rates in specialized units such as have been presented in the present paper, taken in conjunction with the impossibility of predicting the length of the oliguric renal failure, would seem to lead to two conclusions: (1) all patients with more than a transient acute renal failure should be transferred to specialized units; and (2) the establishment of specialized units with facilities for haemodialysis should be on a planned regional basis, taking into consideration population densities.

Summary

A survey is made of the results of treatment of 80 patients in a unit with haemodialysis facilities during a two-year period. 78 patients were admitted and 88 dialyses performed on 57 of them. A further two patients were dialysed successfully once each in their own hospitals.

Acute recoverable renal failure occurred in 36 patients and 27 recovered from their renal failure. Nine further patients in this group, but with associated hepatic lesions, two of whom recovered, are discussed separately as the prognosis is thought to depend on the hepatic lesion. 29 cases of acute irrecoverable renal failure and chronic renal lesions are described and only four improved in these two categories. The use of the artificial kidney for barbiturate poisoning is discussed.

Emphasis is placed on early diagnosis of renal failure by observations on the urine rather than isolated

estimation of the blood chemistry, and treatment is discussed.

The clinical state of the patient is the single most important indication for dialysis; other factors are marked hyperkalaemia of 7 mEq/l. or more, a severe acidosis of 12 mEq/l. or less, and gross overhydration. A description is given of the technique and results of dialysis.

The results of the present and other series are discussed and two conclusions are drawn: (1) all patients with more than a transient acute renal failure should be transferred to specialized units; and (2) the establishment of specialized units with haemodialysis facilities should be on a planned basis, taking into consideration population densities.

Case histories are given of five patients who recovered from extensive trauma.

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REFERENCES

- Anderson, A., and Kolff, W. J. (1959). *Ann. intern. Med.*, **51**, 476.
 Anthonisen, P., Brun, C., Crone, C., Lassen, N. A., Munck, O., and Thomsen, Aa. C. (1956). *Lancet*, **2**, 1277.
 Brennand, R., and Bunker, N. V. D. (1960). *Ibid.*, **1**, 578.
 Bywaters, E. G. L., and Joekes, A. M. (1948). *Proc. roy. Soc. Med.*, **41**, 420.
 Hamburger, J. (1957). Third International Medical and Surgical Meeting, Turin.
 Hecker, R., and Sherlock, S. (1956). *Lancet*, **2**, 1121.
 Honey, G. E., and Jackson, R. C. (1959). *Brit. med. J.*, **2**, 1134.
 Jackson, R. C. (1958). *Proc. roy. Soc. Med.*, **51**, 1071.
 Joekes, A. M., Mowbray, J. F., and Dormandy, K. (1957). *Lancet*, **2**, 864.
 Kolff, W. J., and Berk, H. Th. J. (1943). *Ned. T. Geneesk.*, **87**, 1684.
 Lassen, N. A., and Thomsen, Aa. C. (1958). *Acta med. scand.*, **160**, 165.
 Lucké, B. (1946). *Milit. Surg.*, **99**, 371.
 McCracken, B. H., and Parsons, F. M. (1958). *Lancet*, **2**, 885.
 Parsons, F. M., and McCracken, B. H. (1958). *Brit. J. Urol.*, **30**, 463.
 — (1959). *Brit. med. J.*, **1**, 740.
 Seviitt, S. (1959). *Lancet*, **2**, 135.
 Shackman, R. (1959). In *Recent Advances in Surgery*, edited by S. Taylor. Churchill, London.
 — and Milne, M. D. (1957). *Brit. J. Urol.*, **29**, 434.
 Smith, L. H., et al. (1955). *Amer. J. Med.*, **18**, 187.
 Taylor, W. H. (1957). *Lancet*, **2**, 703.
 Wartman, W. B., Rusterholz, A. P., and Tucker, J. M. (1950). *Amer. J. Path.*, **26**, 235.
 Webster, L. T., jun., and Gabuzda, G. J. (1959). *A.M.A. Arch. intern. Med.*, **103**, 15.

At a recent meeting of the Institute of Actuaries, Mr. J. S. THOMPSON, Secretary Treasurer of the Hospital Service Plan of New Jersey, U.S.A., presented a memoir on "Insurance against Costs of Hospital and Medical Services in the United States ('Blue Cross' and 'Blue Shield')." The memoir outlined the present organization and scope of the two services, and their very rapid growth since the war. The author envisaged a continuing growth, with greater refinements of underwriting techniques, unless costs increased so far and fast that "the insuring public find the rates intolerable and demand that the whole health service enterprise be taken over by the Government."