GENERAL INDICATIONS FOR THE USE OF THE ARTIFICIAL KIDNEY*

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This paper reviews the indications for the use of the artificial kidney and reports our experience at Groote Schuur Hospital over the past 2 years. A full analysis appears in a separate communication.[1]

THE RÔLE OF THE ARTIFICIAL KIDNEY

Dialysis with the artificial kidney serves a twofold purpose. Firstly, the clinical condition in acute renal failure is much improved and morbidity is diminished by preventing or modifying the development of complications. The main factors contributing to mortality, such as infections, cardiopulmonary complications, bleeding and coma, may be favourably influenced. Secondly, the biochemical disturbance of uraemia is modified in that the abnormal electrolyte status and the acidosis are corrected, azotaemia is reduced, and hypothetical, as yet unidentified, toxic substances may be eliminated. In addition, overhydration can be countered by ultrafiltration. Dialysis in no way affects the kidneys except by altering the abnormal internal environment. Technical and physiological details concerning the operation of artificial kidneys are well reviewed elsewhere[2-5] and will not be considered.

INDICATIONS FOR THE USE OF THE ARTIFICIAL KIDNEY

The main groups of conditions which may require treatment with the artificial kidney include the following: acute renal failure, chronic renal failure, and systemic intoxications. In addition, both hepatic failure and intractable oedema have been treated by haemodialysis.

A. Acute Renal Failure

We have used the term 'acute renal failure' to designate a functional and not a pathological state.

Although the difficulty in differentiating acute renal circulatory insufficiency from acute tubular necrosis may be considerable, we believe that postrenal obstructive lesions, except peri-ureteric fibrosis, usually do not present difficulty in diagnosis. In our series, cases with acute circulatory insufficiency (prerenal uraemia) have not been dialysed. Acute tubular necrosis is by far the most common cause of acute renal failure. Among the less common causes are bilateral renal cortical necrosis and possibly the 'failed reflow' kidney.[6]

1. *Acute Tubular Necrosis*

This includes ischaemic and/or toxic varieties and is conveniently divided into:

Group I

(*a*) 'Medical'—nephrotoxic; haemolytic; and miscellaneous, e.g. 'hepatorenal failure', infections, and shock.

(*b*) 'Obstetric'—concealed accidental haemorrhage; postabortal; and miscellaneous, e.g. postpartum, and posteclamptic.

Group II

'Surgical'—postoperative; and post-traumatic, including 'crush syndrome' (ischaemic muscle necrosis).

The separation into two broad groups is of value, since the prognosis is much worse in group II, where there is 'accelerated' uraemia with early hyperkalaemia and rapid evolution of azotaemia. It is in this group, too, where, despite early dialysis, results are disappointing. These cases may be associated with a medical complication, e.g. transfusion reaction. The dominant feature of the illness is often the primary condition and this commonly overshadows the renal failure as a cause of death.

2. *Bilateral Renal Cortical Necrosis*

This condition has been described particularly in association with concealed accidental haemorrhage, but may also occur in the same clinical settings as acute tubular necrosis. Furthermore, the differentiation of the two conditions may be difficult. For these reasons it must be included in any analysis of acute renal failure caused by acute tubular necrosis. Where the cortical involvement is subtotal, recovery is possible. Examination of a renal biopsy specimen does not necessarily provide an accurate assessment of the extent of the damage and, therefore, energetic treatment should not be lightly abandoned. The necrosis in some of these cases is partial and dialysis may then be life-saving.

Table I reflects the incidence of the main sub-groups in which the abovementioned conditions are encountered.

TABLE I. THE MAIN CLINICAL SETTINGS OF ACUTE RENAL FAILURE—PERCENTAGE INCIDENCE FROM 5 RENAL CENTRES

	Group I				*Group II*			
	Obstetric		*Medical*		*Post-operative*		*Post-traumatic*	
	%	*No.*	%	*No.*	%	*No.*	%	*No.*
Philadelphia[7]	**16**	16	**46**	46*	**32**	32	**6**	6
Albany[8]	**13**	10	**16**	13	**50**	40	**21**	17
Hammersmith[9,10]	**18**	20	**15**	16	**41**	45**	**26**	29
Leeds[5]	**40**	25	**21**	13	**29**	18	**11**	7
Cape Town	**45**	25	**18**	10	**24**	13	**13**	7

Bold-face figures indicate percentage incidence.

* No less than 24 of these 46 medical cases were attributable to intravascular haemolysis.

** Five cases associated with a surgical condition, but in which no operation was performed, are excluded from group II here.

The experience at Groote Schuur Hospital is compared with that of 4 other centres.[5,7-10]

3. *Vascular Accidents*

These are rare causes of acute renal failure, but cases have been reported. They include: (1) bilateral renal emboli,[11] and (2) bilateral thrombosis of renal artery and/or vein.[12]

4. *Acute Glomerulonephritis (and other Hypersensitivity States)*

The indication for dialysis is still uncertain. Because of the occurrence of spontaneous resolution in most cases of

* The disposable twin-coil artificial kidney.

glomerulonephritis, the artificial kidney should be used only when biochemical disturbance threatens life. Merrill[13] has observed that some patients fail to do well despite an excellent biochemical response.

5. *Acute Pyelonephritis*

Acute pyelonephritis rarely causes acute renal failure. If associated with diabetes it may produce severe renal medullary necrosis (necrotizing papillitis). When pyelonephritis occurs as a complication of polycystic kidneys, it may result in oliguric renal failure which may require dialysis.

6. *Postrenal Obstruction*

Apart from the postrenal obstructive conditions arising extrarenally (including calculous obstruction with so-called reflex anuria) there is an uncommon group which for convenience may be termed intrarenal obstruction. Renal tubular obstruction may accompany the ureteric obstruction attributable to sulphonamide[14] and uric-acid crystals (treatment for leukaemia with TEM,[15] irradiation[16] and nitrogen mustard[17]).

B. **Chronic Renal Failure**

In this group cases must be carefully selected. Complicating factors may precipitate acute renal failure, and there is always a possibility of recovery from such an acute episode (illustrated in Fig. 1).

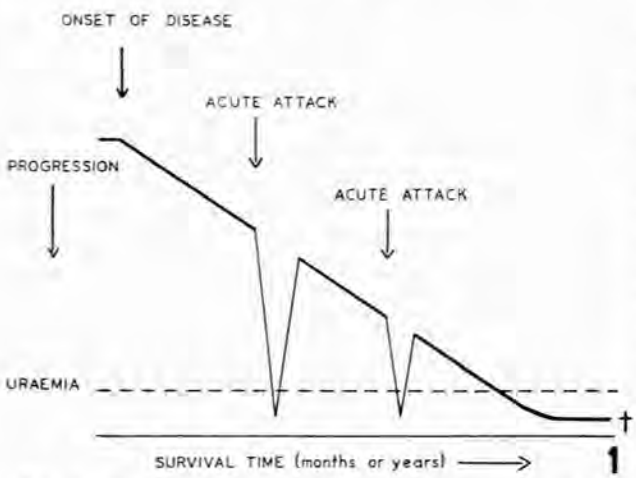

Fig. 1. Illustrating the effects of 2 acute episodes in the course of chronic renal disease. For simplicity, recovery is shown as a return to the original line of progress.

Dialysis during an acute episode may be followed by a remission allowing the patient months or even years of happy productive life. The course of polycystic kidneys, in particular, is a prolonged one, except when complicated by some acute illness, commonly pyelonephritis.

It is very difficult to estimate the degree of progression in any individual patient. Useful aids are a careful history (including details of drugs), any previous assessment of renal function, including glomerular filtration rate, microscopic examination of the urine for evidence of an acute nephritic process or of urinary infection, and radiological evaluation of the size of the kidneys. This X-ray investigation is particularly helpful and is too frequently omitted. Small kidneys suggest chronic disease. Renal biopsy, too, may be of value and patients have been prepared for this procedure by dialysis.

In this chronic group there is always the danger of post-dialytic oliguria. This has been attributed to a decreased total serum osmolarity, resulting mainly from reduction in the blood-urea concentration. The oliguria has been prevented by dialysing against a bath fluid with a high urea concentration.[18]

Some cases of chronic renal failure may be partially reversible, and these include the following:

(*i*) *Metabolic*—hypokalaemic syndrome,[19] and hypercalcaemia (hyperparathyroidism, sarcoidosis, hypervitaminosis D, myeloma).

(*ii*) *Unilateral renal disease*—uraemia in this group usually means advanced disease of *both* kidneys. It is doubtful whether it is ever reversible.

(*iii*) *Drugs*—e.g. phenacetin, sodium bicarbonate (milk-alkali syndrome).

These cases can usually be managed conservatively by treating the cause. When the patient is already dangerously ill and the diagnosis is in doubt, dialysis is essential. Furthermore, it may enable a necessary operation to be performed.

However, there are ethical considerations. Where the patient has reached the terminal stage of the disease it is open to question whether dialysis is justifiable. This can be a very difficult decision and each case must be treated on its merits, especially in view of the promising advances in the field of renal homotransplantation.[20]

C. **Systemic Intoxications**

The incidence varies from centre to centre. We had no cases in our series. In this group the danger is not failure of renal excretion, although some of the drugs may also be nephrotoxic. The artificial kidney removes dialysable toxic substances (e.g. salicylates, barbiturates and bromides) more rapidly than the normal kidney. It is the treatment of choice where the severity of the intoxication threatens life. This is especially so in aged infirm patients with severe associated disease; the hazards of protracted immobilization include respiratory infections and feeding difficulties and may be avoided by early dialysis.[21]

D. **Hepatic Failure**

Ammonia intoxication is believed to play a part in terminal hepatic failure and in the recurrent acute hepatic failure of chronic hepatic disease. Two special precipitating causes are of importance: (1) Ammonia intoxication from ingestion of protein in the diet, or administration of ammonium chloride, and (2) gastro-intestinal haemorrhage. Ammonia is dialysable[22] and, with regional heparinization,[23] dialysis may be feasible in the cases where sudden accumulation of large amounts of blood in the gut may be responsible for severe ammonia intoxication. Dialysis is of limited value in hepatic failure, but associated uraemia would be an added factor in favour of the procedure.

E. **Intractable Oedema**[24]

While treatment of overhydration in acute renal failure

is successful, the removal of fluid by ultrafiltration in cases with severe intractable oedema has been only partially successful, the fluid often re-accumulating.

THE OPTIMUM TIME FOR DIALYSIS

The artificial kidney has its main use in treating acute renal failure caused by acute tubular necrosis. Many of these patients do not require dialysis with an artificial kidney, but in the early phase of oliguric renal failure it is not always possible to predict in which cases dialysis will be necessary — hence prompt transfer to a renal centre is essential.

Clinical and biochemical criteria vary in different centres, but there is general agreement that clinical assessment is more important except when severe hyperkalaemia is present. Usually, however, in severe hyperkalaemia clinical deterioration has occurred. Severe overhydration from previous mismanagement is an indication for urgent dialysis. Early evidence of deterioration (clouding of consciousness) should be heeded and dialysis should not be delayed until nausea, vomiting, stupor, and convulsions have developed. Biochemical indices are of assistance in deciding the optimum time for dialysis: (1) blood urea $>$ 300 mg. per 100 ml., (2) serum potassium $>$ 7 mEq./l., and (3) serum carbon dioxide $<$ 12 mEq./l.

There is general agreement concerning the serum-potassium and CO_2 levels, but the blood-urea levels cited by others as indications have been higher — in the region of 400 mg. per 100 ml.[5,9,25]

While the abovementioned biochemical findings suggest the advisability of dialysis, it must be remembered that none of these figures is an absolute indication in itself, and must be considered in conjunction with the clinical state of the patient.

Daily investigation of the blood-urea level is a valuable guide to the management. However, the absolute blood-urea level is less important than the daily rate of increase, and may enable the probable day of dialysis to be fixed in advance. Any acceleration in the relatively constant daily increase in blood-urea concentration should be noted.

CONTRAINDICATIONS

Apart from free gastro-intestinal bleeding, there are virtually no contraindications to dialysis. However, unnecessarily early or frequent dialyses in cases of mild to moderate severity, and ill-considered and misguided effort in hopeless chronic cases should be avoided. Even the possibility of profuse bleeding need not be a contraindication to dialysis, since regional heparinization is an established technique[23] in some clinics. Bleeding is not generally a major hazard to successful dialysis. It should be noted that, despite the fears of many, heparinization does not seem to result in further bleeding.

RESULTS

In the course of management of 55 patients with acute renal failure, 30 have been treated with the artificial kidney. A further 5 patients with chronic renal failure have undergone dialysis. The results are shown in Table II.

We think it is important to divide cases of acute tubular necrosis into two groups, since the course and prognosis are vastly different in these groups. Many reports do not make this differentiation and erroneous conclusions have been reached.

TABLE II. RESULTS OF TREATMENT IN 60 PATIENTS WITH RENAL FAILURE

	Patients	*Dialysed*	*Died*	*% Mortality*
Acute renal failure:				
Group I:				
Obstetric ..	25	16	5	20
Nephrotoxic ..	2	1	0	0
Miscellaneous ..	8	4	3	37
Total ..	35	21	8	23
Group II:				
Postoperative ..	13	5	7	54
Post-traumatic	7	4	6	86
Total ..	20	9	13	65
Chronic renal failure	5	5	5	100

Note: (1) In 4 of the acute cases the renal lesion was irreversible—3 patients with bilateral cortical necrosis and 1 with 'failed reflow' kidney.
(2) Six of the acute, and 1 of the chronic, cases were dialysed twice.

Most important is the time of transfer of potential cases for dialysis to centres with artificial-kidney units.

TABLE III. RESULTS OF TREATMENT OF VARIOUS TYPES OF ACUTE RENAL FAILURE FROM 5 CENTRES *

	Total	*Dialysed*	*Died*	*% Mortality*
Group I:				
Obstetric:				
Philadelphia ..	16	7	4	25
Albany ..	10	5	0	0
Hammersmith	20	11	4	20
Leeds	25	17	2	8
Cape Town ..	25	16	5	20
Nephrotoxic:				
Philadelphia ..	9	2	5	55
Albany ..	9	7	2	22
Hammersmith	6	2	1	17
Leeds	1	1	0	0
Cape Town ..	2	1	0	0
Intravascular haemolysis				
Philadelphia	24	16	7	29
Albany ..	4	2	0	0
Hammersmith	—	—	—	—
Leeds ..	3	0	0	0
Cape Town	—	—	—	—
Miscellaneous:				
Philadelphia ..	13	4	6	46
Albany ..	—	—	—	—
Hammersmith	10	4	3	30
Leeds	9	8	4	44
Cape Town ..	8	4	3	37
Group II:				
Postoperative:				
Philadelphia ..	32	18	23	72
Albany ..	40	23	28	70
Hammersmith	45	23	37	82
Leeds	18	14	14	77
Cape Town ..	13	5	7	54
Post-traumatic:				
Philadelphia ..	6	4	5	83
Albany ..	17	12	9	53
Hammersmith	29	16	22	76
Leeds	7	5	4	57
Cape Town ..	7	4	6	86

* Centres are the same as in Table I.

The best results are obtained with early dialysis in a comparatively well patient; the transfer of a desperately ill patient well into the oliguric phase (although sometimes unavoidable) is too often encountered. In such circumstances poor results can be expected. With regard to acute tubular necrosis in the uncomplicated group I case, the course can be predicted from the daily rise in blood urea (usually < 30 mg. per 100 ml.) and with the knowledge that the average duration of the oliguric phase is 12 days.[1,9,26] In the group II case with accelerated uraemia (> 50 mg. per 100 ml. per day) the course and prognosis is quite different, and hyperkalaemia and uraemia are often marked before the end of the first week; here dialysis is often required before the fifth day.

Selection of cases in artificial-kidney centres is inevitable; a hospital becomes known for its artificial-kidney unit and patients are referred there for special management. Control series are therefore not adequate. Although there is considerable difficulty in assessing results, comparison of the results from several centres shows a surprising uniformity (Table III).

As a generalization, it can be said that the mortality of the 'medical' group I case has been considerably reduced since the introduction of the conservative régime with the intelligent use of the artificial kidney. This is especially seen in the obstetric group, except where infected abortion has made peritonitis and septicaemia (often with *Cl. welchii* infection) additional hazards. Despite the frequency of these factors in our series, the mortality rate of 20% compares favourably with that of other centres. The mortality remains high in the 'surgical' group II case of acute tubular necrosis, but better results have been achieved by Parsons *et al.*[27] by using a machine with a larger dialysing surface and instituting dialysis when the blood-urea nitrogen was 120 - 150 mg. per 100 ml. Previously, a level of 180 - 200 mg. per 100 ml. (blood urea 385 - 428 mg. per 100 ml.) was used as an indication. It is in this group, with a daily rise of blood urea exceeding 50 mg. per 100 ml., that the advantages of prophylactic haemodialysis[26] need to be established.

SUMMARY AND CONCLUSIONS

In general, indications for dialysis with an artificial kidney include acute, and some cases of chronic, renal failure, certain systemic intoxications, and possibly hepatic failure and intractable oedema. In deciding the optimum time for dialysis, biochemical criteria are important, but must be considered in conjunction with the clinical status.

The commonest cause of acute renal failure is acute tubular necrosis. These cases may be divided into groups I and II according to the course and prognosis, the group II cases having accelerated uraemia with a poorer prognosis despite early dialysis. The experience at Groote Schuur Hospital over a 2-year period is presented.

The importance of recognizing and treating a precipitating cause in chronic renal failure, and the rôle of dialysis in some of these patients is stressed.

Acknowledgement is made to Dr. J. G. Burger, Medical Superintendent, Groote Schuur Hospital, for the excellent facilities; to our colleagues Drs. S. J. Saunders, I. Bouchier, S. Bank, L. Isaacson, and J. Foster for their help in operating the artificial kidney; and to the Departments of Anaesthesia and Surgery for assistance.

This report represents part of the programme of the CSIR/UCT Renal-metabolic Group.

REFERENCES

1. Eales, L. and Simenhoff, M. L.: In the press.
2. Merrill, J. P. (1952): New Engl. J. Med., **246**, 17.
3. Aoyama, S. and Kolff, W. J. (1957): Amer. J. Med., **23**, 565.
4. Keleman, W. A. and Kolff, W. J. (1958): A.M.A. Arch. Intern. Med., **102**, 871.
5. Parsons, F. M. and McCracken, B. H. (1959): Brit. Med. J., **1**, 740.
6. Sheehan, H. L. and Davis, J. C. (1959): J. Path. Bact., **78**, 105.
7. Kiley, J., Powers, S. R. and Beebe, R. T. (1959): New Engl. J. Med., **259**, 1156.
8. Bluemle, L. W., Webster, G. D. jnr. and Elkinton, J. R. (1959): A.M.A. Arch. Intern. Med., **104**, 180.
9. Loughridge, L. W., Milne, M. D., Shackman, R. and Wootton, I. D. P. (1960): Lancet, **1**, 35.
10. Shackman, R., Milne, M. D. and Struthers, N. W. (1960): Brit. Med. J., **2**, 1473.
11. Case Records of Mass. Gen. Hosp. Case 36081 (1950): New Engl. J. Med., **242**, 291.
12. Harrison, C. V., Milne, M. D. and Steiner, R. E. (1956): Quart. J. Med., **25**, 285.
13. Merrill, J. P. (1957): J. Chron. Dis., **5**, 138.
14. Andersen, A. H. and Andersen, I. B. (1948): Acta med. scand., **80**, 259.
15. Kravitz, S. C., Diamond, H. D. and Craver, L. F. (1951): J. Amer. Med. Assoc., **146**, 1595.
16. Lear, H. and Oppenheimer, G. D. (1950): *Ibid.*, **143**, 806.
17. Richmond, G. H. and Beardsley, G. D. (1953): Ann. Intern. Med., **39**, 1327.
18. Merrill, J. P., Legrain, M. and Hoigne, R. (1953): Amer. J. Med., **13**, 519.
19. Relman, A. S. and Schwartz, W. B. (1956): New Engl. J. Med., **255**, 195.
20. Merrill, J. P., Murray, J. E., Harrison, J. H., Friedman, E. A., Dealy, J. B. and Dammin, G. J. (1960): *Ibid.*, **262**, 1251.
21. Schreiner, G. E. (1958): A.M.A. Arch. Intern. Med., **102**, 896.
22. Kiley, J. E., Welch, H. F., Pender, J. C. and Welch, C. S. (1956): Proc. Soc. Exp. Biol. (N.Y.), **91**, 489.
23. Gordon, L. A., Simon, E. R., Rukes, J. M., Richards, V. and Perkins, H. A. (1956): New Engl. J. Med., **255**, 1063.
24. Kolff, W. J. and Leonards, J. R. (1954): Cleveland Clin. Quart., **21**, 61.
25. Anthonisen, P., Crone, C., Munck, O., Brun, C., Lassen, N. A. and Thomsen, A. C. (1956): Lancet, **2**, 1277.
26. Bull, G. M., Joekes, A. M. and Lowe, K. G. (1950): Clin. Sci., **9**, 379.
27. Parsons, F. M., Hobson, S., Blagg, C. R. and McCracken, B. H. (1961): Lancet, **1**, 129.