# Section of Experimental Medicine and Therapeutics

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# Treatment of Chronic Renal Failure

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## Dietary Treatment of Chronic Renal Failure

*Definition of Categories of Chronic Renal Failure*
From the point of view of therapy, renal failure can be categorized as follows:

(1) *Glomerular filtration rate (GFR) below 1·5 ml/min/1·73 sq. m:* These patients need dialysis. No dietary treatment will keep them alive without the aid of dialysis.

(2) *GFR between 1·5 and 3 ml/min/1·73 sq. m:* These patients require a strict Giovannetti-type diet; their blood urea will not come down to normal values; blood urea figures will range from 50 to 200 mg/100 ml after a month on diet, and their anæmia may improve spontaneously so that transfusions may be needed less frequently or not at all. Clinical improvement includes loss of gastrointestinal symptoms of renal failure. There may be severe sodium and potassium imbalance. Acidosis may be a problem.

(3) *GFR between 3 and 5 ml/min/1·73 sq. m:* These patients require a strict Giovannetti-type diet and may have a spontaneous improvement in their anæmia; all clinical symptoms of uræmia disappear. The blood urea will fall to normal levels. Occasional salt imbalance problems may occur. Acidosis and hyperkalæmia are not often seen.

(4) *GFR between 5 and 10 ml/min/1·73 sq. m:* Relaxed Giordano-Giovannetti diet, i.e. up to 35–40 g protein. Patients are usually asymptomatic. Anæmia will improve.

(5) *GFR above 10 ml/min/1·73 sq. m:* No special diet needed. Blood urea will usually be below 200 mg/100 ml. Anæmia may be troublesome.

*Purpose of Low-protein Diet*
Low-protein diets are given in renal failure to reduce protein metabolism to a minimum. Folin (1905) had shown that a 400 g starch and 300 g cream diet was associated with a fall in the nitrogen excretion to 4 g/day, equivalent to 26 g of protein broken down. Gamble (1947) thought that 100 g of carbohydrate in a protein-free diet would reduce protein breakdown to 40 g a day. Borst (1948) found that a protein-free diet in renal failure could result in 19–20 g of protein being broken down daily. If a protein-free diet causes a negative nitrogen balance, it is clearly undesirable for prolonged use. Giordano (1961, 1963) has shown that a diet inadequate in non-essential amino acids but containing at least minimal daily requirements of the essential amino acids in synthetic form was associated with a fall in blood urea, due probably to urea re-utilization in the synthesis of non-essential amino acids. Giovannetti & Maggiore (1964) prescribed a very low nitrogen diet containing the daily requirements of the essential amino acids in adequate amounts, in a natural form: we have modified the latter diet to suit British tastes (Shaw *et al.* 1965). Our diet contains 3–3·5 g of nitrogen, about 18·5–20 g of protein. We use it only if there are symptoms from renal failure, or if the blood urea is above 200 mg/100 ml on a normal diet. From our experience of over 42 patients who have been established for at least one month on the diet, the entire syndrome of uræmia, including anæmia, can be expected to disappear if the GFR is above 3 ml/min/1·73 sq. m. With a GFR between 1·5 and 3 ml/min there is a good chance that all symptoms will clear, but the blood urea will remain raised. A successful outcome cannot be anticipated with a GFR below 1·5 ml/min.

*Survival*
So far 20 patients on the diet have survived for long periods – the longest being 1·5 years. The duration of survival depends on the underlying

*Table 1*
**Survival on Manchester diet**

| Disease | No. of cases Total | Alive | Duration of survival (months) Mean | Range |
|---|---|---|---|---|
| Polycystic | 5 | 4 | 10·8 | 3–18 |
| Chronic glomerulonephritis | 14 | 4 | 5·36 | 1–13 |
| Malignant hypertension | 5 | 0 | 3·7 | 2·5–5 |
| Mixed infection of urinary tract plus chronic glomerulonephritis | 11 | 4 | 7·7 | 1–18 |
| Undiagnosable | 7 | – | – | – |

disease, the rate of deterioration in renal function and the fact that survival on the diet cannot be expected with a mean GFR value below 1·3 ml/min.

Table 1 shows that our best results have been in patients with polycystic disease, whose mean survival has been 10·8 months.

If there is malignant hypertension – essential or secondary – then the prognosis is much worse. The disease progresses rapidly, all 5 of our patients being dead with a mean survival of 3·7 months. Non-hypertensive chronic glomerulonephritics tend to be a mixed group; some patients have a very short survival, suggesting that they had been started on diet late in the course of the disease. The outlook tends to be better where the GFR is 3 ml/min or above. Table 2 shows the rates of deterioration in the three groups. Again it is apparent that deterioration is most rapid for malignant hypertension and least for polycystic disease.

The prognosis of polycystic patients particularly is often better than at first appears, because they may have infections or salt depletion which can be treated.

In patients on the Giovannetti diet there are several biochemical problems (*see* Shaw *et al.* 1965, Berlyne *et al.* 1965):

(1) *Hyperkalæmia:* This occurs in patients in the last few weeks of life, when not enough potassium can be excreted by the urinary and intestinal tracts. It is exacerbated by the severe metabolic acidosis often present in these patients. At first we treated this hyperkalæmia with sodium polystyrene sulphonate, but found that 2 of our patients developed left ventricular failure, possibly due to sodium absorbed from the sodium-cycle resin (Berlyne, Janabi & Shaw 1966); consequently we thought that calcium-cycle resins (zeokarb 225 – calcium) would be safer, and we confirmed that a calcium resin was reasonably efficient as a potassium exchanger *in vivo* (Berlyne, Janabi, Shaw & Hocken 1966). We have also found that, contrary to the established form of treatment of hyperkalæmia advocated by such authorities as Merrill (Flynn *et al.* 1961) sorbitol is contraindicated in the resin treatment of hyperkalæmia. Cation exchange resins take up most of their potassium when they are in the large bowel, and since there is a very high K/Na ratio in fæcal water the longer the resins are in contact with the colon the better. In sorbitol-induced diarrhœa (as advocated by Merrill) the resins are hurried through the colon and do not exchange effectively. Figs 1 and 2 show the effects of sorbitol diarrhœa and various amounts of constipation on fæcal water content and on potassium uptake by sodium and calcium resins. In diarrhœa the fæcal water content rises to 96·5% of the total fæcal weight if sorbitol is taken according to the regimen of Flynn *et al.* (1961). In constipation fæcal water may be only 52·5% of total fæcal weight. The higher the fæcal water content, the less potassium the resin takes up, whether it is initially sodium polystyrene sulphonate or calcium zeokarb 225 (Berlyne, Shaw & Janabi, unpublished).

(2) *Acidosis:* The problem of acidosis is serious; about 50% of our patients developed acidosis (pH < 7·3) and 25% fell below pH 7·2. It may be due to a combination of a fall in titratable acid caused by reduced filtered load of phosphate due to dietary-induced fall in serum inorganic phosphate, and partly due to the frequent urinary tract infections complicating advanced chronic renal failure.

*Table 2*
**Rate of deterioration in three varieties of chronic renal failure, during treatment with the Manchester diet**

| Disease | No. of cases | Rate of rise in plasma creatinine (mg/ 100ml/month)● | Rate of fall in urea clearance (ml/min/month)● | Rate of fall in creatinine clearance (ml/min/month)● |
|---|---|---|---|---|
| Polycystic | 5 | 0·20 (−0·18) | 0·35 (0·46) | 0·59 (0·03) |
| Chronic glomerulonephritis | 14 | 0·32 (1·4) | 0·22 (0·47) | 0·48 (0·61) |
| Malignant hypertension | 5 | 0·34 (2·5) | 0·47 (0·64) | 2·0 (0·54) |

●Harmonic means (arithmetical means in parentheses)

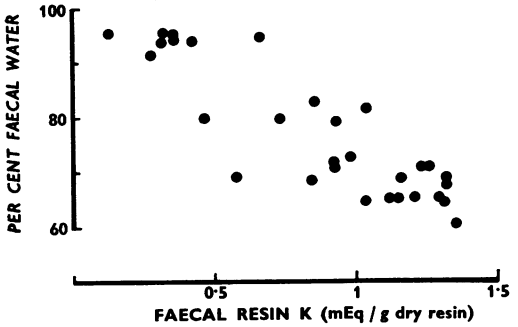


Fig 1 *The effect of bowel habit on potassium uptake by sodium cycle zeokarb 225*

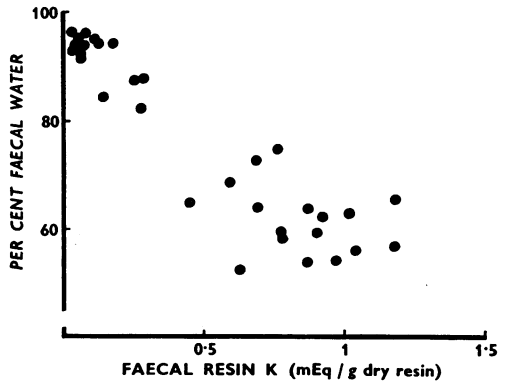


Fig 2 *The effect of bowel habit on potassium uptake by calcium cycle zeokarb 225*

(3) *Over- or under-salting:* Over-salting is often more of a problem than salt depletion. All our patients have some degree of salt leak, often 40–50 mEq/day, but there is often a sodium ceiling which may be less than 100 mEq/day. If more sodium is taken than can be excreted, œdema, exacerbation of hypertension, and heart failure may develop. The treatment is prevention, by titrating the salt leak in hospital, getting the patient to weigh himself regularly and cutting down the salt intake if the weight goes up.

(4) The modified syndrome of terminal renal failure: This has been described elsewhere (Berlyne & Shaw 1965). It is a change in the features of terminal uræmia. The patients on the modified Giordano-Giovannetti diet have no gastrointestinal symptoms (no nausea, vomiting, hiccup or diarrhœa), but they do have bleeding (into mucous membranes, skin and muscles) and severe agitation, with a blood urea below 250 mg/100 ml (and even as low as 130 mg/100 ml). Death occurs within five days unless dialysis is carried out.

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## Regular Hæmodialysis in the Treatment of Chronic Renal Failure

Regular hæmodialysis for chronic renal failure was instituted in Newcastle upon Tyne in December 1963. At this time experience in Seattle (Lindholm *et al.* 1963) and elsewhere had established that patients could be maintained in reasonable health and working capacity provided that the following minimum standards were maintained: (1) Dialysis for at least twenty-four hours per week, usually in two overnight sessions of twelve to fourteen hours each. (2) Use of a dialyser, such as the modified Kiil, which did not require priming with blood but had a surface area of about 1 sq. m. (3) Adequate blood flow through the dialyser (over 100 ml/min) from an efficient indwelling arteriovenous shunt. (4) Strict control of water and sodium intake, to prevent hypertension, with moderate restriction of dietary protein.

Less adequate dialysis schedules resulted in an 'underdialysis syndrome' of anorexia, weight loss, increasing pigmentation and pruritus, uncontrolled hypertension, gouty arthritis, metastatic calcification, pericarditis, peripheral neuropathy and mental change occasionally terminating in suicide.

Our first patient initially was seriously underdialysed. One month after starting regular dialysis for six hours every five days she developed a severe toxic psychosis with gross abnormality in the electroencephalogram, the mean frequency falling to 2 cycles per second. After two weeks on more intensive hæmodialysis her mental state returned to normal and the slow-wave activity