PAPERS AND ORIGINALS

Growth Pattern and Dietary Intake of Children with Chronic Renal Insufficiency

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Summary

The growth pattern and dietary intake of 33 children with varying degrees of renal insufficiency has been investigated. The development of impaired renal function in infancy has a more deleterious effect on linear growth than has its onset in later years. A reduction in growth velocity may occur once the glomerular filtration rate falls below 25 ml/min/1·73m². There was a significant reduction of the energy, protein, and vitamin D intakes of children with renal insufficiency compared with those recommended for their age, and of energy intake compared with that of normal children of their own height. Reduced growth velocity occurred when energy intake fell below 80% of that recommended. The reduction in the intake of energy and nutrients in these children may in part be responsible for their growth retardation.

Introduction

Short stature is a well recognized consequence of chronic renal insufficiency in childhood (West and Smith, 1956; Chantler and Holliday, 1973). Little attention was paid to the problems of the growth of these children until the advent of treatment with intermittent haemodialysis and renal transplantation, since when attempts have been made to improve their growth and eventual adult height (Simmons *et al.*, 1971).

Though there are several contributory factors a reduced energy intake is probably the most important cause of this growth retardation in uraemic children (Chantler and Holliday, 1973. Simmons *et al.* (1971) observed an increased growth velocity in children receiving intermittent haemodialysis when their diet was supplemented with extra calories. Most attempts to improve growth, however, have been directed towards children in the terminal stage of the disease. We feel that it may be more profitable to study the growth pattern and investigate whether "catch-up growth" is possible in children at an earlier stage of the disease before they develop the severe metabolic disturbances of terminal renal failure.

We report here our observations on the growth pattern and dietary intake of 33 children who were attending this hospital with varying degrees of renal insufficiency.

Patients and Methods

The 33 children were attending the renal clinic at this hospital. All had a glomerular filtration rate (G.F.R.) below 70 ml/min/1·73m², as assessed by endogenous creatinine clearance in 28 and slope clearance of ^{51}Cr-labelled edetic acid in five children with reflux nephropathy. The children were divided into two groups (see tables I and II). In group 1 impaired renal function dated from infancy, and in group 2 the onset of renal disease and impaired renal function occurred in later childhood. Children with gross proteinuria or the nephrotic syndrome were not included in the study.

Height was measured with a wall stadiometer and weight with beam scales, the child wearing only light underclothing. Previous height and weight recordings were obtained from the hospital records. Centiles were plotted from the charts of Tanner *et al.* (1966). Bone age was assessed by the method of Greulich and Pyle (1959). Creatinine clearance was determined from duplicate three-hour urine collections during a water-induced diuresis (Glasgow *et al.*, 1970). Slope clearance of ^{51}Cr-labelled edetic acid was determined by the method of Chantler and Barratt (1972).

The dietary intakes of 29 children were assessed by one of us (G.M.). Two methods were used—a seven-day recall history, followed by a three-day weighed recording performed at home. For the latter the mothers were provided with scales, and instructions were carefully explained. All food, including sweets and snacks between meals, was weighed; where applicable this was done after cooking. The volume of all drinks was also recorded. Any food remaining at the end of a meal was weighed and recorded. The weighed recordings were performed on a

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TABLE I—*Details of Children with Renal Insufficiency dating from Infancy (Group 1)*

Height Centile*	Diagnosis	Age (Years)	Bone Age (Years)	G.F.R. (ml/min/1·73m²)
90	Haemolytic-uraemic syndrome	6·0	6·0	45
75	Haemolytic-uraemic syndrome	4·5	4·5	60
50	Dysplasia	13·4	12·5	11
25-50	Hydronephrosis	10·3	10·5	30
25-50	Reflux nephropathy	8·3	8·0	61
25	Haemolytic-uraemic syndrome	2·5	2·0	25
25	Dysplasia	9·4	7·0	21
10-25	Megacystis-mergaureter	9·5	9·5	17
10-25	Reflux nephropathy	7·0	4·5	45
10-25	Reflux nephropathy	3·6	3·0	58
3-10	Reflux nephropathy	5·0	2·5	41
3	Reflux nephropathy	1·9	1·0	53
3	Posterior urethral valve	4·1	3·0	44
3	Unknown	5·2	3·5	24
3	Hypoplasia	0·5	—	5
3	Hydronephrosis	1·0	—	22
1-2	Posterior urethral valve	4·1	2·0	25
<1	Reflux nephropathy	14·0	12·5	10
<1	Dysplasia	15·7	14·0	10
<1	Dysplasia	2·7	1·0	21
<1	Dysplasia	7·4	3·5	48
<1	Renal calculi and chronic pyelonephritis	16·3	12·0	25
<1	Dysplasia	11·3	8·0	10

*Centiles <1 = More than 2·3 S.D.s below mean.

TABLE II—*Details of Children with Renal Insufficiency beginning in Later Childhood (Group 2)*

Height Centile	Diagnosis	Age (Years)	Bone Age (Years)	G.F.R. (ml/min/1·73m²)	Age at Presentation (Years)
75	Chronic pyelonephritis	9·0	9·5	58	5·0
75	Nephronophthisis	4·1	3·5	5	3·7
50	Schönlein-Henoch nephritis	16·4	16·0	40	11·0
25-50	Nephronophthisis	8·1	6·0	30	8·0
25-50	Mesangiocapillary glomerulonephritis	10·6	10·0	2	7·0
25	Alport's syndrome	16·0	15·0	15	2·5
25	Schönlein-Henoch nephritis	14·8	14·5	25	6·5
10	Interstitial nephritis	4·6	3·5	60	4·0
3-10	Glomerulonephritis with crescents	9·1	7·5	20	8·6
1	Nephronophthisis	8·3	8·0	20	8·0

Thursday, Friday, and Saturday to include two weekdays and one day of the weekend. Three days was considered to be the longest period for which we would get maximum parental co-operation. These recordings are to be repeated at six-week intervals for 12 months as an extension of this study. All but one of the children were on a free diet with no protein restriction; the remaining child (in group 2) was on a reduced protein intake and had a G.F.R. of 2 ml/min/1·73m². The energy and nutrient values of the food consumed were calculated from the tables of McCance and Widdowson (1967).

The intakes of energy and nutrients observed in our patients were compared with those recommended by the Department of Health and Social Security (1969) for normal British children and with those observed in normal children in two British surveys (Department of Health and Social Security, 1968; Cook *et al.*, 1973), in which techniques similar to ours were used, except that recordings were made over seven days and not three days.

Results

LINEAR GROWTH

The height centiles and respective ages of all the children are shown in tables I and II. There were 25 boys and 8 girls. Their ages at the time of study ranged from 6 months to 16 years. In the children with renal insufficiency dating from infancy (group 1) there was no significant difference ($P=0·9$ by Student's t test) in ages between those above the third centile for height and those below this level. Of the 23 children in this group 12 (52%) were on or below the third centile for height at the time of study, while the 10 children whose onset was in later childhood (group 2) were more normally distributed around the 50th centile for height, only one child being below the third centile.

When growth was expressed as a percentage of the 50th centile for growth velocity the children in group 1 were shown to have a growth velocity within 90% of that normally expected until their G.F.R. fell below 25 ml/min/1·73m². Below this level 6 out of 11 children (55%) had a growth velocity of less than 75% of that normally expected for their age.

The most accurate index available of the size at birth of the children who developed renal insufficiency in infancy was their birth weight. At this stage of development there was no significant difference in their distribution by weight above and below the 50th centile ($P=0·8$). Children in the lower centiles for birth weight were not necessarily the shortest in stature in later years.

The growth pattern through childhood of 15 children who developed renal disease in infancy, for whom we have adequate data, is shown in fig. 1. From the age of 2 years all the children either increased in height or remained on their respective centiles until the G.F.R. fell below 25 ml/min/1·73m² and they developed renal rickets or showed delayed puberty.

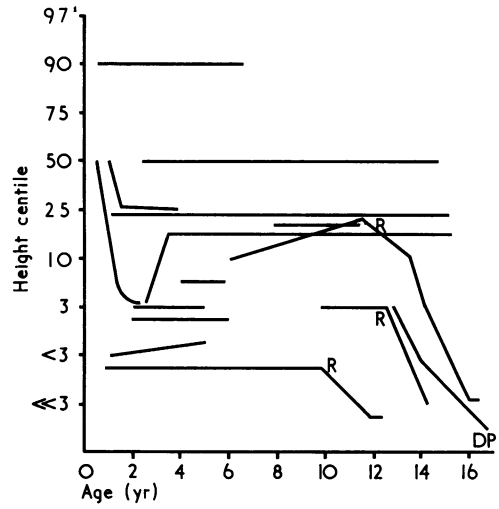

FIG. 1—Growth patterns of children with renal insufficiency dating from infancy. DP=Delayed puberty. R=Rickets.

BONE AGE

Skeletal maturity was assessed by bone age in 31 children. Of these, 15 had a delay greater than one year but in only three was the delay beyond three years. The degree of delay in bone age was not significantly different in the older children, suggesting that this occurred at an early age and was not necessarily progressive.

DIETARY INTAKE

The dietary intake of energy, protein, vitamin D, and calcium was assessed in 29 children. The findings showed a generalized reduction in intake of all constituents rather than a reduction in any one. The findings of the repeat three-day intakes were similar to the initial recordings. As the study progressed the three-day weighted record was found to be a more realistic estimate of the daily intake than the seven-day recall history.

Energy.—Analysis of the three-day weighed recordings (fig. 2) showed that 23 children (79%) had an energy intake of

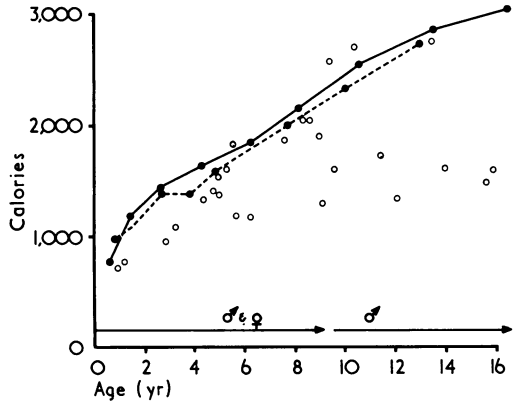

FIG. 2—Relation between observed energy intake and age of children with renal insufficiency. (Over age 9 only boys are shown.) Solid line indicates recommended daily energy intake (D.H.S.S., 1969). Broken line indicates average daily energy intake of normal children (D.H.S.S., 1968; Cook *et al.*, 1973).

less than the average recommended for children of the same age. The seven-day history also showed that 22 out of 27 (82%) had an intake below that recommended for children of a similar age. As many of the children were smaller than normal for their age they might not have required as great an energy intake. But when the observed energy intake of children with renal insufficiency was compared with that recommended for normal children of similar height 18 of the 27 children (67%) still had a reduced intake. A significant correlation ($r=0{\cdot}72$; $P<0{\cdot}001$) was found between growth velocity and energy intakes of those children with renal disease dating from infancy when these were expressed as a percentage of the 50th centile expected for normal children of the same age (fig. 3). From the regression line it can be calculated that normal growth would be expected with an energy intake above 80% of that recommended, whereas cessation of growth could be predicted with an energy intake of below 40%. There was no significant correlation ($r=0{\cdot}34$; $P>0{\cdot}1$) between energy intake, expressed in a similar manner, and G.F.R.

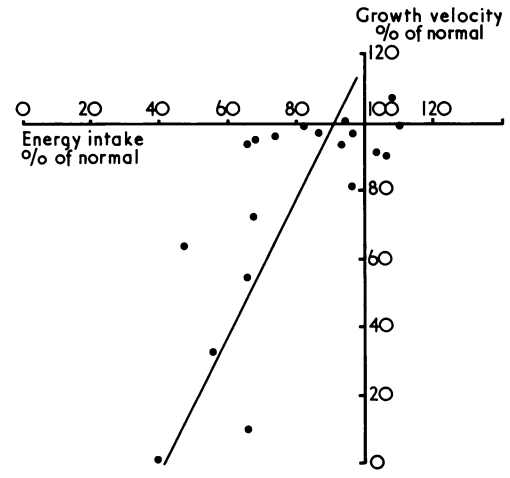

FIG. 3—Relation between growth velocity, expressed as percentage of expected 50th centile velocity, and energy intake, expressed as percentage of that recommended for same age. ($r=0{\cdot}72$; $P<0{\cdot}001$.)

Protein.—The observed protein intake of normal British children was in excess of that recommended (fig. 4). Assessment of protein intake by three-day weighed recordings of children with renal insufficiency showed that 20 out of 29 (69%) had an intake below the average recommended for children of similar age; five children (17%) had a protein intake below the stated minimal protein requirements for children of their age (Department of Health and Social Security, 1969).

Vitamin D and Calcium.—In analysing the intakes of vitamin D two children who were receiving milk fortified with vitamin D were excluded from the results. Vitamin D intake was severely reduced in all except one child (fig. 5). The average observed dietary intake in normal children was approximately 2·5 μg (100 IU) daily, which is the normal amount recommended for British schoolchildren. The calcium intake of children with renal insufficiency was little different from that of normal children, though six had an average calcium intake below that recommended for growing schoolchildren.

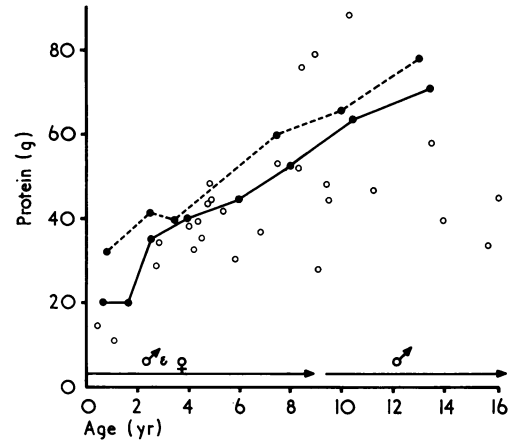

FIG. 4—Relation between observed protein intake and age of children with renal insufficiency. (Over age 9 only boys are shown.) Solid line indicates recommended daily protein intake (D.H.S.S., 1969). Broken line indicates average daily protein intake of normal children (D.H.S.S., 1968; Cook *et al* 1973).

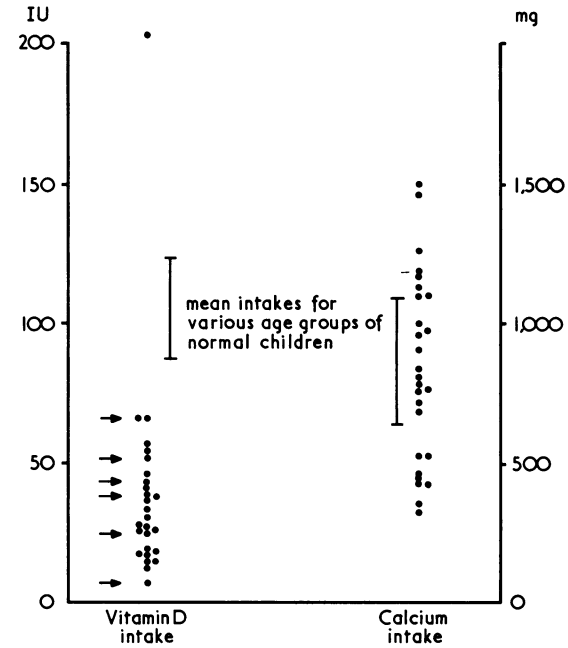

FIG. 5—Observed vitamin D and calcium intakes of children with renal insufficiency compared with mean intakes for various age groups of normal children (D.H.S.S., 1968; Cook *et al.*, 1973). Children with rickets are arrowed.

Discussion

This study showed that the onset of chronic renal insufficiency

in infancy is more likely to have an adverse effect on growth than its development in later childhood. More than half (52%) of the children who developed renal insufficiency in infancy were in later years on or below the third centile for height, whereas the stature of those whose renal insufficiency developed in later childhood was closer to normal. A reduction in growth velocity of six children occurred when the G.F.R. fell below 25 ml/min/1·73m², and some of these had developed renal rickets or had delayed puberty which may have accounted for this.

The pattern of growth of the children whose renal insufficiency dated from infancy is shown schematically in fig. 6. At birth they were of a normal size as judged by their weight. Most presented in infancy with an exacerbation of their renal failure and for a period they failed to thrive. This may have been due to a reduced energy intake with associated anorexia and vomiting. Many of the metabolic disturbances of renal failure may also result in failure to thrive (Chantler and Holliday, 1973). Despite, this initial delay in infancy, however, their growth progressed steadily through childhood but at a lower centile until they developed renal rickets or had delayed puberty.

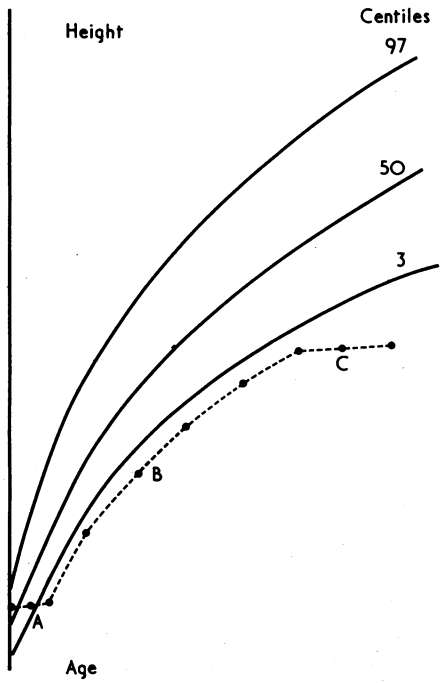

FIG. 6—Schematic representation of growth of children with renal insufficiency dating from infancy. A, B, and C represent periods of growth.

Experimental data have shown that failure to thrive soon after birth may lead to a permanent reduction in growth potential by a reduction in total cell number (Widdowson, 1970). Experience of children who suffered from malnutrition in infancy has shown that they may be smaller than a group of matched controls when examined in later years. Furthermore, any catch-up growth rarely occurs before puberty (Krueger, 1969). Children with renal insufficiency in infancy may fail to thrive at this critical period of their development and suffer a permanent reduction in their growth potential.

DIETARY INTAKE

Analysis of the protein and energy intake of children with renal insufficiency showed that most were eating less than the recommended and observed intakes for normal children of the same age or height. This occurred at all ages and there was no significant correlation with the G.F.R. There was, however, a highly significant relation between growth velocity and energy intake. Our observations showed (fig. 3) that normal growth would be expected with an energy intake of above 80% of that recommended, whereas cessation of growth would be predicted with an energy intake of below 40%. This accords with the data of Simmons *et al.* (1971) relating to children receiving intermittent haemodialysis.

Energy intake is balanced by expenditure for basal metabolic rate, activity, and growth. Previous workers have noted the similarities of some of the findings in chronic renal failure and protein-energy malnutrition (Coles, 1972; Chantler and Holliday, 1973). Ashworth (1968), studying children with long-term reduction in energy intake and malnutrition, showed only a slight reduction in basal metabolic rate and a predominant reduction in energy expenditure from activity and growth. Furthermore, the proportion of calories required for growth when recovering from malnutrition may be in excess of that utilized for normal growth (Ashworth *et al.*, 1968). Chantler *et al.* (1973) showed that the energy cost of growth in uraemic rats was higher than in matched controls. Catch-up growth can occur with energy supplementation to the diet of uraemic children, but this is when growth retardation has occurred in the terminal stages of renal failure (stage C, fig. 6) (Simmons *et al.*, 1971). Similar catch-up growth has also been shown in uraemic rats receiving extra calories by gavage (Chantler *et al.*, 1973).

CALCIUM AND VITAMIN D INTAKES

Though there was a normal distribution for the calcium intake of children with renal insufficiency six had an intake below that recommended for normal children. All children except one had a suboptimal intake of vitamin D. In addition there is impairment of vitamin D metabolism and reduced calcium absorption from the gastrointestinal tract in patients with renal insufficiency (Wills, 1971).

All the children with longstanding renal disease and a G.F.R. of less than 15 ml/min/1·73m² had evidence of renal osteodystrophy and rickets. In two of these the onset of clinically recognizable rickets was extremely rapid and led to permanent deformities before the diet could be adequately supplemented with vitamin D. We suggest that all children with renal insufficiency should receive an adequate calcium intake and dietary supplements of vitamin D at a dose appropriate to their clinical, biochemical, and radiological findings rather than await the development of overt rickets, with the possibility of permanent deformities occurring.

CATCH-UP GROWTH

The pattern of growth of children with renal insufficiency from infancy is shown in fig. 6. Catch-up growth has been reported after secondary growth retardation in uraemic children on receiving energy supplementation of the diet (Simmons *et al.*, 1971) or treatment of renal rickets (Dent *et al.*, 1961), and also in some children after renal transplantation (Reimold, 1973). It is not known whether these children have potential for catch-up growth during their earlier years (fig. 6 B). As explained above, they may have a reduced cell number and therefore a diminished growth potential. Alternatively many have a reduced intake of energy and vitamin D compared with normal children and impaired absorption of calcium, all of which could result in a reduced growth rate. Little information is available on the long-term effects of undernourishment during early childhood. A report on a group of 30 girls who were undernourished during this period showed that they had delay in skeletal growth, in bone age, and in the onset of the menarche (Dreizen *et al.*, 1967). Their eventual adult height, however, was the same as that of a group of matched controls; they continued to grow and reached their ultimate stature at an older age.

This delay in development occurs in children with renal

insufficiency, but adolescence, when a growth spurt should occur, coincides with the very time that the majority reach the stage of terminal renal failure. Furthermore, the corticosteroid therapy which renal transplantation necessitates may also retard optimum growth. The degree of catch-up growth that is possible in these children remains to be determined.

We suggest that careful attention should be given to the dietary intake of energy and nutrients of all infants with renal insufficiency in an attempt to prevent growth retardation during this vulnerable period. It therefore follows that if such a dietary programme is to be successful in achieving normal growth the detection of chronic renal insufficiency in infancy is of paramount importance. In older children, once failure to thrive and growth retardation have occurred the opportunity to promote catch-up growth may be lost.

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References

Ashworth, A. (1968). *British Journal of Nutrition*, 22, 341.
Ashworth, A., Bell, B., James, W. P. T., and Waterlow, T. C. (1968). *Lancet*, 2, 600.
Chantler, C., and Barratt, T. M. (1972). *Archives of Disease in Childhood*, 47, 613.
Chantler, C., Adelman, R. D., MacDonell, R. C., and Holliday, M. A. (1973). Paper read at the Paediatric Research Society, October.
Chantler, C., and Holliday, M. A. (1973). *Clinical Nephrology*, 1, 230.
Coles, G. A. (1972). *Quarterly Journal of Medicine*, 41, 25.
Cook, J., *et al.* (1973). *British Journal of Preventive and Social Medicine*, 27, 91.
Dent, C. E., Harper, C., and Philpot, O. R. (1961). *Quarterly Journal of Medicine*, 30, 1.
Department of Health and Social Security (1968). *Pilot Study of Nutrition of Young Children in* 1963. London, H.M.S.O.
Department of Health and Social Security (1969). *Recommended Intakes of Nutrients for the United Kingdom*. London, H.M.S.O.
Dreizen, S., Spirakis, C. N., and Stone, R. E. (1967). *Journal of Pediatrics*, 70, 256.
Glasgow, E. F., Moncrieff, M. W., and White, R. H. R. (1970). *British Medical Journal*, 2, 687.
Greulich, W. W., and Pyle, S. I. (1959). *Radiographic Atlas of Skeletal Development of the Hand and Wrist*, 2nd edn. California, Stanford University Press.
Krueger, R. H. (1969). *Lancet*, 2, 514.
McCance, R. A., and Widdowson, E. M. (1967). *Medical Research Council Special Report Series*, No. 297. London, H.M.S.O.
Reimold, E. W. (1973). *Pediatrics*, 52, 235.
Simmons, J. M., Wilson, C. J., Potter, D. E., and Holliday, M. A. (1971). *New England Journal of Medicine*, 285, 653.
Tanner, J. M., Whitehouse, R. H., and Takaishi, M. (1966). *Archives of Disease in Childhood*, 41, 454, 613.
West, C. D., and Smith, W. C. (1956). *American Journal of Diseases of Children*, 91, 460.
Widdowson, E. M. (1970). *Lancet*, 1, 901.
Wills, M. R. (1971). *Biochemical Consequences of Chronic Renal Failure*, p. 54. London, Harvey, Miller and Medcalf.

Deterioration in Renal Function after Beta-blockade in Patients with Chronic Renal Failure and Hypertension

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Summary

Treatment of hypertension with beta-blocking agents in three patients with moderately severe chronic renal failure was followed by rapid deterioration of renal function. In two of the patients the need for maintenance haemodialysis was accelerated but renal function in the third reverted to pretreatment levels after the drug was stopped. These findings suggest that until more is known about the effects of beta-blocking drugs they should not be given to patients with moderately severe renal failure.

Introduction

Beta-adrenergic receptor blocking agents (beta-blockers) have a proved place in the management of patients with hypertension. Their use in large numbers of patients has shown that they do not cause deterioration of renal function, even in patients with pre-existing mild renal failure (Pritchard and Gillam, 1969; Lydtin *et al.*, 1972). It has been suggested that a beta-blocker given together with a vasodilator might be the treatment of choice for hypertension complicating chronic renal failure (*British Medical Journal*, 1973). We report three patients with chronic renal failure and hypertension whose renal function greatly deteriorated after beta-blockade.

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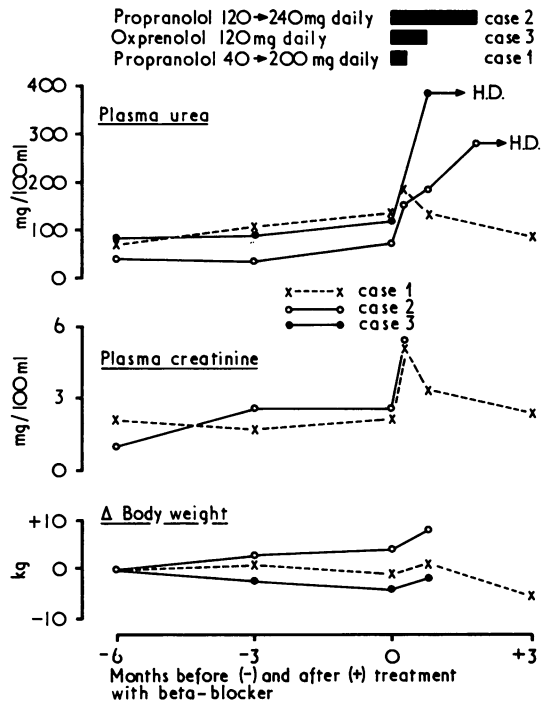
Case Reports

The patients in two of the cases (cases 2 and 3) were referred to the unit after renal function had deteriorated. The results of biochemical and blood pressure investigations were obtained from



Plasma urea and creatinine concentrations and body weight before and after initiation of antihypertensive therapy with beta-blockers. Rectangular bars indicate duration of beta-blocker treatment. H.D. = haemodialysis.