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# Chronic renal failure and growth

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SUMMARY Growth was assessed in 38 prepubertal children with chronic renal failure for a mean (range) of 2·3 (1–4) years. At first clinic visit their mean (range) glomerular filtration rate was 17 (7–35) ml/min/1·73 $m^2$, their mean (range) age was 3·4 (0·2–9·1) years, and 23 (61%) were greater than two standard deviations below the mean for height. After intensive medical management of their chronic renal failure, half of the children who presented before 2 years of age showed appreciable catch up growth. Only a slow improvement in growth occurred in most children presenting over 2 years of age. At final assessment, the mean (range) glomerular filtration rate was 15 (6–42) ml/min/1·73$^2$ and 20 (53%) were greater than two standard deviations below the mean for height. There was no correlation between glomerular filtration rate and growth. There remained a group of children who continued to grow poorly. Many of these were of low birth weight, and had dysplastic kidneys.

Growth retardation is a major problem for children with chronic renal failure.[1–4] In 1983 we set up a clinic for children with severe chronic renal failure to enable optimal management of diet, electrolyte and acid-base balance, and bone disease.[5] We have analysed the effects of intensive medical management on the growth and renal function of prepubertal children attending the clinic.

## Patients and methods

All children aged less than 10 years who were prepubertal and who had attended Guy's Hospital chronic renal failure clinic for at least a year were included in the study (32 boys, six girls). The children attended the clinic at least once every three months, but most attended once every four weeks or more frequently. Most were taking energy supplements either as glucose polymers or as fat emulsions. Adequacy of diet was checked by prospective three day dietary assessments. If necessary, protein intake was adjusted so the plasma urea concentration was <20 mmol/l and serum albumin was normal. Acidosis was corrected with sodium bicarbonate. Sodium chloride supplements were gradually introduced until an improvement in growth was seen without producing oedema, hypertension, or hypernatraemia.[5] Since 1985 it has been our practice to maintain the plasma phosphate at the lower limit of the normal range for age using mild dietary phosphate restriction and calcium carbonate as a phosphate binder, and the plasma calcium at the upper limit of normal using 1,25 dihydroxycholecalciferol or 1α-hydroxycholecalciferol if necessary. We have shown this regimen to be successful in reversing and preventing secondary hyperparathyroidism.[6] Some children, however, had received aluminium hydroxide before 1985 or before attending the clinic. Infants with poor growth and energy intake were tube fed.[7] None were nephrotic or taking steroids. The children were measured using a Harpenden stadiometer by the same clinic nurse (<2 years of age, lying; >2 years, standing).

The following information was obtained from the notes:

(1) Chronological age at first clinic visit (years). The children were divided according to presentation before (group 1, n=16) or after (group 2, n=22) age 2 years. The mean (range) age of group 1 at presentation was 1·0 (0·2–1·8) and of group 2 was 5·2 (2·5–9·1) years.

(2) Height (cm) at first clinic visit and subsequently at yearly intervals. For each subject the height standard deviation score (Ht SDS) was calculated, according to the formula Ht SDS=$(x-\bar{x})/SD$, where $\bar{x}$ and SD are age matched population mean height and SD respectively and x is the subject's height. Normal population data was according to Tanner *et al.*[8]

(3) Bone age at yearly intervals.[9]

(4) Calculated glomerular filtration rate (ml/min/1·73 $m^2$) at yearly intervals.[10]

Clinical data have been given in more detail for group 1 (table 1) because the growth changes in this group were more dramatic and variable than in group 2. There was a high incidence of low birth weight, eight being below the 10th centile. This included seven of the 10 children with renal dysplasia with or without vesicoureteric reflux. Of the other six children, all of whom had obstructed urinary tracts, only one was below the 10th centile for birth weight. Ten infants were tube fed, and nine had received aluminium hydroxide. The overall mean (SE) concentrations of plasma sodium, bicarbonate, urea, albumin, calcium and phosphate, and haemoglobin were calculated from the values at each clinic visit. We achieved our aim of maintaining plasma sodium, bicarbonate, and albumin values within normal limits, and urea under 20 mmol/l, although the haemoglobin was low in some infants. In most children the plasma calcium concentration was at the upper limit and the phosphate at the lower limit of normal, and no infants had clinical evidence of osteodystrophy.

The causes of chronic renal failure in group 2 were as follows: renal dysplasia with or without vesicoureteric reflux (n=8), obstructive uropathy (n=3), infantile polycystic kidney disease (n=3), reflux nephropathy (n=2), cystinosis (n=2), and miscellaneous (n=4).

Statistical comparisons were by the Wilcoxon rank sum test.

## Results

The mean (range) Ht SDS, change from initial Ht SDS (Δ HtSDS), glomerular filtration rate, and bone age delay (bone age minus chronological age, years) at presentation and at yearly intervals are shown for groups 1 and 2 in table 2. Group 1 showed a continuing improvement in growth over the first three years despite an increasing bone age delay. Glomerular filtration rate improved continuously. In group 2, growth also improved over the first three years, again despite a progressive increase in bone age delay. Glomerular filtration rate declined slowly. There was no statistical difference in the change per year for any criteria in either group.

### GROUP 1

Fig 1 shows the individual longitudinal height data for the 16 children who presented to the clinic before the age of 2 years. Twelve children were greater than 2 SD below the mean at first clinic visit, and seven of these were greater than −3 SD. Table 3 shows the results in more detail. Over the first year, eight children improved their Ht SDS (mean Δ Ht SDS 1·0, range 0·2 to 1·6), while eight grew poorly

Table 1 *Details of patients in group 1*

| *Patient No* | *Birthweight centile* | *Diagnosis* | *Use of nasogastric tube* | *Use of aluminium hydroxide* | *Mean (SE) plasma concentration (mmol/l)* | | | | | *Mean (SE) plasma concentration (g/l)* | | *No of clinic visits/ year* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | *Sodium* | *Urea* | *Bicarbonate* | *Calcium* | *Phosphate* | *Albumin* | *Haemoglobin* | |
| 1 | 50 | Obstructive uropathy | − | + | 140 (0·8) | 16·8 (0·8) | 22·0 (0·7) | 2·45 (0·02) | 1·51 (0·08) | 43 (0·6) | 118 (2) | 5·0 |
| 2 | 75–97 | Obstructive uropathy | − | − | 139 (0·7) | 18·9 (0·9) | 22·0 (0·8) | 2·42 (0·02) | 1·52 (0·04) | 45 (0·5) | 113 (2) | 6·7 |
| 3 | 10–25 | Dysplasia (±reflux) | + | − | 138 (0·5) | 16·2 (0·7) | 27·6 (1·4) | 2·58 (0·02) | 1·39 (0·06) | 45 (0·7) | 101 (2) | 10·5 |
| 4 | 3–10 | Dysplasia (±reflux) | − | − | 138 (1·0) | 10·4 (0·8) | 21·1 (1·1) | 2·52 (0·03) | 1·58 (0·12) | 43 (0·8) | 124 (3) | 4·0 |
| 5 | 3–10 | Dysplasia (±reflux) | + | − | 137 (0·8) | 14·0 (0·7) | 20·5 (0·5) | 2·58 (0·03) | 1·31 (0·06) | 44 (0·7) | 91 (3) | 16·0 |
| 6 | 3–10 | Obstructive uropathy | + | + | 139 (0·8) | 16·8 (1·7) | 24·2 (1·5) | 2·55 (0·02) | 1·43 (0·09) | 44 (0·6) | 89 (2) | 11·5 |
| 7 | 3 | Dysplasia (±reflux) | − | − | 139 (0·8) | 18·2 (1·0) | 21·6 (1·5) | 2·56 (0·03) | 1·57 (0·11) | 44 (1·4) | 106 (2) | 4·0 |
| 8 | 10–25 | Dysplasia (±reflux) | − | + | 139 (0·4) | 7·0 (0·3) | 24·2 (0·5) | 2·52 (0·02) | 1·35 (0·03) | 41 (0·4) | 106 (2) | 8·6 |
| 9 | 75–97 | Obstructive uropathy | + | + | 135 (0·7) | 12·2 (1·0) | 24·6 (0·7) | 2·44 (0·03) | 0·99 (0·08) | 42 (0·6) | 78 (1) | 15·5 |
| 10 | 10–25 | Obstructive uropathy | + | + | 135 (0·6) | 5·1 (0·6) | 20·6 (0·9) | 2·57 (0·07) | 1·21 (0·06) | 44 (0·7) | 93 (3) | 15·0 |
| 11 | 10–25 | Dysplasia (±reflux) | + | + | 137 (0·5) | 17·3 (1·0) | 25·3 (0·9) | 2·53 (0·05) | 0·88 (0·05) | 45 (0·6) | 69 (1) | 13·0 |
| 12 | 3–10 | Dysplasia (±reflux) | + | + | 139 (0·5) | 11·9 (0·7) | 23·7 (0·9) | 2·58 (0·03) | 1·24 (0·05) | 43 (0·5) | 79 (1) | 14·5 |
| 13 | <3 | Dysplasia (±reflux) | + | − | 140 (0·6) | 8·2 (0·4) | 23·8 (0·9) | 2·53 (0·08) | 1·32 (0·08) | 44 (0·6) | 93 (4) | 14·5 |
| 14 | 3–10 | Dysplasia (±reflux) | + | − | 134 (2·6) | 6·1 (0·3) | 22·3 (0·6) | 2·62 (0·02) | 1·29 (0·06) | 45 (0·5) | 101 (4) | 17·5 |
| 15 | 25–50 | Obstructive uropathy | + | + | 142 (1·2) | 11·0 (1·0) | 22·0 (0·6) | 2·63 (0·04) | 0·91 (0·07) | 43 (1·7) | 93 (2) | 14·0 |
| 16 | 3–10 | Dysplasia (±reflux) | − | + | 138 (0·4) | 9·5 (0·6) | 21·7 (0·4) | 2·54 (0·02) | 1·14 (0·06) | 43 (0·5) | 115 (1) | 7·0 |

Table 2 *Height standard deviation score (Ht SDS), change from initial Ht SDS (△ Ht SDS), glomerular filtration rate (ml/min/1·73 m²), and bone age delay (years) at presentation to clinic and at yearly intervals thereafter. Results are mean (range)*

| | *Years after presentation* | | | | |
|---|---|---|---|---|---|
| | *0* | *1* | *2* | *3* | *4* |
| | | | *Group 1* | | |
| No of patients | 16 | 16 | 14 | 7 | 5 |
| Ht SDS | −2·9 (−4·1 to −1·5) | −2·6 (−4·3 to −0·3) | −2·4 (−4·0 to 0) | −2·0 (−3·5 to −0·1) | −2·2 (−3·3 to −0·2) |
| Δ Ht SDS | — | +0·3 (−1·4 to 1·6) | +0·6 (−0·8 to 2·1) | +0·9 (−0·8 to 1·8) | +0·9 (−0·6 to 1·6) |
| Glomerular filtration rate | 17 (7–37) | 18 (8–36) | 18 (8–33) | 21 (8–43) | 22 (7–40) |
| Bone age delay | −0·3 (−1·2 to 0·3) | −0·6 (−1·5 to 0·5) | −0·7 (−1·5 to 0·5) | −0·8 (−1·8 to 0·1) | −1·5 (−2·1 to −0·6) |
| | | | *Group 2* | | |
| No of patients | 22 | 22 | 12 | 8 | 5 |
| Ht SDS | −2·1 (−4·9 to 0·3) | −2·0 (−4·6 to 0·4) | −1·9 (−4·4 to 0·6) | −2·2 (−4·2 to 0·3) | −2·6 (−3·5 to −1·5) |
| Δ Ht SDS | — | +0·1 (−0·5 to 0·5) | +0·3 (−0·4 to 1·0) | +0·4 (−0·5 to 1·0) | +0·4 (−0·5 to 0·8) |
| Glomerular filtration rate | 18 (7–35) | 16 (6–29) | 19 (8–26) | 14 (6–21) | 15 (11–25) |
| Bone age delay | −0·9 (−2·4 to 0·6) | −1·0 (−3·2 to 0·3) | −1·2 (−2·8 to −0·4) | −1·3 (−3·3 to −0·3) | −1·6 (−2·3 to −1·0) |

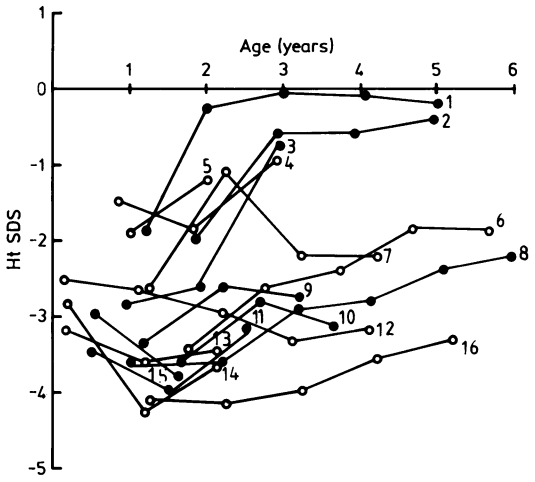


Fig 1 *Growth of 16 children (patient numbers 1–16) with chronic renal failure who presented to the clinic before 2 years of age (group 1). Birth weight <10th centile (○), birth weight >10th centile (●).*

Table 3 *Number of years studied, glomerular filtration rate (ml/min/1·73 m²) at start and finish of the study, and change in height standard deviation score (Δ Ht SDS) over the first year, the first two years, and overall, in the 16 infants who presented to clinic before 2 years of age (group 1)*

| *Patient No* | *No of years studied* | *Glomerular filtration rate* | | *Δ Ht SDS* | | |
|---|---|---|---|---|---|---|
| | | *Start* | *Finish* | *Overall* | *Over one year* | *Over two years* |
| 1 | 4 | 24 | 30 | +1·6 | +1·6 | +1·8 |
| 2 | 3 | 12 | 13 | +1·6 | +1·4 | +1·4 |
| 3 | 2 | 13 | 8 | +2·1 | +0·2 | +2·1 |
| 4 | 2 | 37 | 34 | +0·6 | −0·4 | +0·6 |
| 5 | 1 | 20 | 11 | +0·7 | +0·7 | — |
| 6 | 4 | 14 | 8 | +1·5 | +0·8 | +1·1 |
| 7 | 3 | 20 | 20 | +0·5 | +1·5 | +0·5 |
| 8 | 4 | 29 | 42 | +1·2 | 0 | +0·7 |
| 9 | 2 | 10 | 8 | +0·6 | +0·7 | +0·6 |
| 10 | 2 | 24 | 15 | +0·5 | +0·8 | +0·5 |
| 11 | 2 | 7 | 9 | +0·4 | −0·5 | +0·4 |
| 12 | 4 | 8 | 7 | −0·6 | −0·1 | −0·4 |
| 13 | 2 | 11 | 9 | −0·3 | −0·4 | −0·6 |
| 14 | 2 | 13 | 17 | −0·8 | −1·4 | −0·8 |
| 15 | 1 | 8 | 8 | −1·0 | −1·0 | — |
| 16 | 4 | 15 | 24 | +0·8 | −0·1 | +0·1 |

(−0·5, −1·4 to 0). By the end of the second year, 11 children had improved their rate of growth (0·9, 0·1 to 2·1), whereas only three had failed to do so (−0·6, −0·8 to −0·4). Continuing improvement in growth occurred in five of the seven children after three years, and three of the five children after four years. Growth over the first two years was better in the children of birth weight >10th centile (1·0, 0·1 to 1·6), than in those of birth weight <10th centile (0·2, −0·8 to 1·1), but this did not reach significance. All three of the children whose growth was declining after two years were of birth weight <10th centile, and had dysplasia with or without reflux.

Six of the 10 children who were tube fed showed an improvement in their rate of growth (patients 3, 5, 6, 9, 10, 11). In two (patients 3 and 5) a dramatic effect was seen (fig 2). Previous use of aluminium hydroxide did not affect growth, nor did the number of clinic visits per year. There was no relation between the concentrations of plasma

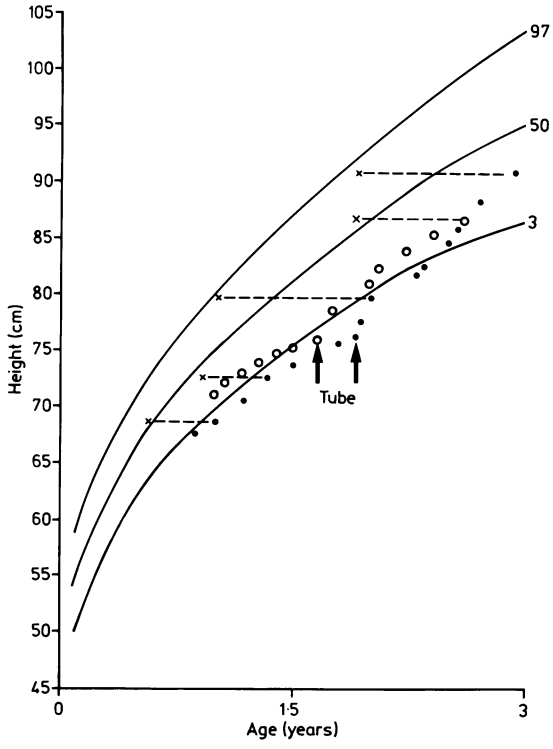


Fig 2 *Growth of two infants (patients 3 and 5, indicated by ○ and ●) with severe chronic renal failure before and after tube feeding.*

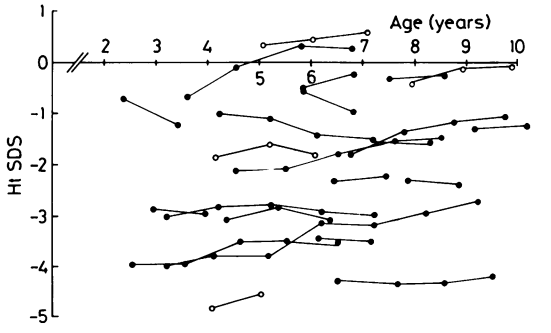


Fig 3 *Growth of 22 children with chronic renal failure who presented to the clinic after 2 years of age (group 2). Boys (●), girls (○).*

sodium, bicarbonate, urea, and albumin or the haemoglobin and growth.

GROUP 2

Fig 3 shows the individual longitudinal height data for the 22 children who presented to the clinic after the age of 2 years. Eleven were greater than 2 SD below the mean at first clinic visit, and seven of these were greater than −3 SD. Changes in rates of growth were less dramatic in this group. Thirteen children showed an improvement in Ht SDS over the first year (mean Δ Ht SDS 0·2, range, 0·1 to 1·0); in two Ht SDS remained unchanged; in seven it deteriorated (−0·2, −0·1 to −0·5). By the end of the second year, eight of the 12 children had improved their Ht SDS (0·4, 0·2 to 1·0), one remained unchanged, and two had shown a deterioration (−0·3, −0·1 to −0·4). Continuing slow improvement in growth occurred in five of the eight children after three years. Over the fourth year, Ht SDS of the five patients remained unchanged.

Four of the eight children with dysplasia with or without reflux were among the seven children greater than −3 SD below the mean for height at presentation.

There was no correlation between glomerular filtration rate and rate of growth in either group.

## Discussion

The beneficial effects of early transplantation on growth,[11 12] and the recent availability of growth hormone as a therapeutic possibility, make it particularly important that the growth patterns of children with chronic renal failure should be studied. Sixty percent of our children were already below the third centile for height when they were first seen in our clinic. Other centres have reported similar findings.[2 3] The rapid growth and high energy requirements during the first two years of life make this the time when most of the adverse effect on height occurs, and fall in Ht SDS has been reported to be as high as 0·6 SD per month.[2 3 13 14] Results of treatment to induce catch up growth in children with chronic renal failure who have suffered growth delay during this critical period have been disappointing.[2–4 14] In our experience, intervention during the first two years of life can result in dramatic catch up growth. There remains a group of infants, however, who do not respond to identical medical care. Many of these are of low birth weight and have dysplasia with or without reflux. It is recognised that some infants who are light for dates at birth because of an in utero environmental insult continue to grow poorly postnatally. This is thought to be a result of impaired growth potential at the cellular level.[15] It is interesting to speculate that the environmental insult that causes dysplasia with or without reflux may also affect growth potential.

After infancy less dramatic changes in rate of growth were seen, with most children showing a

slow improvement in Ht SDS. These findings are consistent with those reported from other centres.[2–4 14] The bone age delay indicates that there remains a potential for catch up growth, but it is still unknown why children with chronic renal failure do not catch up to their genetic potential. We were unable to find any correlation between the glomerular filtration rate and the rate of growth, in agreement with other reports.[2–4]

In conclusion, many children with chronic renal failure are short by the time they are seen by a paediatric nephrologist. Strict attention to diet, electrolyte and acid-base balance, and the prevention of osteodystrophy may result in dramatic catch up growth in some infants who are treated during the first two years of life. If treatment is delayed until after two years of age, a slow improvement in growth occurs in most children. There remains a group of children, however, whose growth is resistant to theoretically optimal management. Many of these are of low birth weight and have dysplasia with or without reflux. These children may benefit from an alternative approach such as transplantation before end stage renal failure is reached, or growth hormone treatment in supraphysiological doses.

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