

Impaired cognition and schooling in adults with end stage renal disease since childhood

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Aims: To determine cognitive and educational attainment in adults with end stage renal disease (ESRD) since childhood.

Methods: All Dutch patients with onset of ESRD at age 0–14 years between 1972 and 1992, who were born before 1979, were asked to perform the Wechsler Adult Intelligence Scale (WAIS) test. Educational attainment was assessed by a questionnaire. Determinants of cognitive performance were measured by reviewing medical charts in 37 hospitals. Data on cognition were compared to those of age matched controls who cooperated in the revision of the Dutch WAIS. National Dutch Statistics data were used to compare educational attainment.

Results: Data on intelligence and schooling were acquired in 126 of 187 patients (67%) and data on determinants of outcome in all patients. Clinical characteristics of participants and non-participants were comparable. Educational attainment of patients was low compared to the Dutch standard. Patient mean full scale IQ, performatory IQ, and verbal IQ were 10.4, 9.2, and 9.7 points lower, respectively, compared to those of 36 controls. The lowest scores were observed in tasks which require concentration, memory, and general knowledge. Patients currently on dialysis and transplanted patients had similar IQ scores. Cumulative dialysis duration of more than four years was associated with a 3.4 times higher chance of having a full scale IQ of 1 SD below the mean.

Conclusion: ESRD of childhood is associated with an impaired cognitive and educational attainment in adulthood. Long duration of dialysis may enhance intellectual impairment, which may not be reversible after renal transplantation.

Since the survival of children with end stage renal disease has increased dramatically over the past 30 years, concern has arisen about the long term impact of this condition on adult life. Several studies mention the risk of impaired cognitive functioning, lack of educational attainment, and unemployment in these patients.^{1–7} Uraemic toxicity and chronic anaemia have been suggested as potential determining factors for poor cognitive functioning.^{2–8} Apart from this, some of the primary diseases leading to end stage renal disease, such as cystinosis and systemic lupus erythematosus (SLE), may themselves be complicated by cerebral involvement.^{9–10} However, at present the true impact of renal disease on cognitive development in children is uncertain. As most studies to date focus on the individual change in neuropsychological performance during change of renal replacement therapy, data on the overall deleterious effects on intellectual functioning in adulthood are lacking. We therefore conducted a national long term follow up study in order to evaluate late physical, social, and psychological effects of renal insufficiency in children (LERIC) in all Dutch children who had commenced renal replacement therapy between 1972 and 1992, and who were born before 1 January 1979. In this paper we report their cognitive functioning and school performance.

METHODS

Patients

The LERIC cohort comprised all Dutch patients who had started chronic renal replacement therapy at age 0–14 years between 1972 and 1992, and who were born before 1979. Patients in whom renal function recovered within four months after commencing dialysis were excluded. Pre-emptive transplanted patients were included. The recruiting of the cohort has been described in detail elsewhere.¹¹

Data collection

The Dutch version of the Wechsler Adult Intelligence Scale (WAIS) was performed according to the standard procedure and used as a standard measurement of general intelligence.¹² The same experienced psychologist, who was unaware of the details of the medical history, conducted the WAIS for each patient. Patients on chronic haemodialysis performed the test at least one day after a haemodialysis session. The WAIS consists of eleven subtests: six subtests of verbal intelligence (information, comprehension, arithmetic, similarities, digit span, and vocabulary), and five subtests of non-verbal, performatory intelligence (digit symbol, picture completion, block design, picture arrangement, and object assembly). The subject's performance on the 11 subtests is represented in terms of scaled scores from 0 to 10 points, with a mean of 5 and a standard deviation of 2. Scores derived from these subtests include the Full Scale Intelligence Quotient, the Verbal Intelligence Quotient, and the Performatory Intelligence Quotient. At the time of this study the Dutch version of the WAIS-III was not available.

Details concerning educational attainment were attained by means of a structured questionnaire. Data were collected about total duration of renal replacement therapy, haemodialysis, peritoneal dialysis, and living with a functioning graft, respectively, and about total duration of anaemia, primary disease, the use of aluminium containing phosphate binders, aluminium toxicity, date of onset of renal replacement therapy, and age at onset of renal replacement therapy by

Abbreviations: ESRD, end stage renal disease; LERIC, late physical, social, and psychological effects of renal insufficiency in children; SLE, systemic lupus erythematosus; WAIS, Wechsler Adult Intelligence Scale

reviewing all available medical charts of all patients. For this purpose all 37 hospitals, in which patients of the cohort had ever been under care, were visited between November 1998 and September 2000. The methods of this data collection have been described in detail elsewhere.¹¹

The Dutch school system is divided into three phases. During the first phase children attend elementary school or, in case of learning disabilities special schools with adjusted programmes (so called (Z) MLK or schools for sick children). The second “high school” phase consists of pre-educational programmes for low skilled professions and intermediate skilled professions (and is called Voorbereidend Middelbaar Beroeps Onderwijs = VMBO), higher skilled professions (Hoger Algemeen Voorbereidend Onderwijs = HAVO), or academic professions (Voorbereidend Wetenschappelijk Onderwijs = VWO). These diplomas give access to schools for low, intermediate, and high skilled professions (Lager Beroeps Onderwijs = LBO, Middelbaar Beroeps Onderwijs = MBO, and Hoger Beroeps Onderwijs = HBO), and to university. Dutch health statistics provide reliable data only on completed levels of schooling for several age groups. Therefore we categorised the educational attainment according to the highest successfully completed level of schooling: low vocational training (only phase 1 or VMBO or LBO), intermediate vocational training (HAVO or VWO or MBO), or high vocational training (HBO or university).

Control group

At the time of this investigation a new, revised Dutch version of the WAIS was under development. We obtained data from 53 healthy controls aged 16–53 years old who participated in the development programme of the revised WAIS III, and who performed both the original and the revised version of the WAIS. Of all these subjects the level of schooling was documented. Swets Test Publishers who distribute the WAIS in the Netherlands¹³ supplied these data. Of these 53 subjects, 36 were within the age group of our patients and matched with the mean Dutch level of educational attainment, based on data from the Dutch National Bureau of Statistics (Centraal Bureau voor de Statistiek, 1999: www.cbs.nl). The WAIS scores of these 36 subjects were used as the comparison for the scores in our patients.

Analysis

Data are presented as means and standard deviations. The WAIS scores were corrected for age. Student's *t* test was used to compare mean Full Scale Intelligence Quotient, Verbal Intelligence Quotient, and Performal Intelligence Quotient of patients and controls.

Based on literature data, eight determinants were considered important in relation to cognitive development. All eight determinants were dichotomised based on clinical relevance as follows: age of onset of renal replacement therapy <6 years versus ≥6 years, duration of renal replacement therapy <18 years versus ≥18 years, duration of dialysis <4 years versus ≥4 years, dialysis versus functioning renal graft as renal replacement therapy modality at time of investigation, duration of a haemoglobin level less than 5 mmol/l (80 g/l) for less than 1.5 years versus ≥1.5 years, use versus no use of aluminium containing phosphate binders, onset of renal replacement therapy between 1972 and 1982 versus onset between 1982 and 1992, and diseases with possible primary cerebral involvement as primary disease (for example, cystinosis and SLE) versus other causes of end stage renal disease. To analyse the relation between schooling and cognition, the level of schooling was dichotomised into a group with low vocational training and a group with intermediate or high vocational training.

Full Scale Intelligence Quotient, Verbal Intelligence Quotient, and Performal Intelligence Quotient were analysed as

continuous variables and subsequently divided in two categories, one comprising all patients with values less than –1 standard deviation of the mean Intelligence Quotient of the control group (referred to as “poor” IQ), and the second comprising all patients with values ≥–1 standard deviation (referred to as “normal” IQ). The χ^2 test was used to analyse the univariate association between the categorical Full Scale Intelligence, Performal Intelligence Quotient, and Verbal Intelligence Quotient, and dichotomous determinants. All significant determinants of the univariate analysis (set at $p < 0.4$) were then entered into logistic regression models to assess their independent impact on intellectual functioning. The independent explanatory values of the characteristics were expressed as adjusted odds ratios, with 95% confidence intervals. The odds ratio can be interpreted as an estimation of the relative risk of impaired intellectual functioning given the presence of the determinant compared to the absence of that determinant. Calibration of the regression models was assessed with the Hosmer–Lemeshow goodness of fit test.¹⁴ This test compares observed and expected frequencies of outcome in groups based on the values of estimated probabilities, using the logistic model. In this test, a high *p* value indicates that the model is performing well—that is, there is no large discrepancy between observed and expected outcome.¹⁴

RESULTS

The cohort

The LERIC cohort consisted of 249 patients. Of these, 62 had died at the time of the outcome data collection. None were lost to follow up, but 47 patients refused to participate in the cross-sectional study, leaving 140 patients. In 10 of these, intelligence scores were not obtained for the following reasons: “lack of time” ($n = 6$), familiarity with the test ($n = 1$, a psychology student), and inability to complete the test because of language problems ($n = 3$). In two patients only the Verbal Intelligence Quotient could be tested because of visual disabilities; and in two only the Performal Intelligence Quotient could be tested because of deafness (thus for both IQ_v and IQ_p, $n = 128$). Therefore the Full Scale Intelligence Quotient test was performed in 126 of the 140 participating patients, 70 males and 56 females. No significant differences were found in age, gender, age of onset of renal replacement therapy, and therapy characteristics between participants and non-participants of the cross sectional study (table 1).

Mean age of all patients at the time of outcome data collection was 29.4 years (range 20.7–41.8). Mean age at onset of renal replacement therapy was 10.8 (range 1.9–14.9) years. Mean duration of renal replacement therapy was 18.2 years (range 6.8–30.0), of dialysis 4.1 years (range 0–25.7), and of living with a renal transplant 14.0 years (range 0–28.4). At the time of the investigation 98 patients had a functioning renal graft, 16 were on haemodialysis, and 12 on peritoneal dialysis.

Schooling

There was a significantly lower level of education in our patient group, compared to our control group that reflects the level of education of the Dutch population. Among the patients, only 42.8% had completed an intermediate or high vocational training, compared to 72.2% in the general Dutch population (table 2). Among the patients, 19.7% had received a high vocational training; only 11.1% had successfully completed this training, compared to 25.9% in the general Dutch population. The remaining 8.6% had either dropped out or were still attending school at the time of investigation.

Cognitive functioning

Mean Full Scale Intelligence Quotient, Verbal Intelligence Quotient, and Performal Intelligence Quotient were 107.9 (SD 15.2, range 62–143), 105.2 (SD 14.1, range 68–138), and 110.2

Table 1 Characteristics of surviving patients of the LERIC cohort

	Participants (n=126)	Non-participants (n=61)
Gender: male/female	70/56	33/28
Primary disease:		
Glomerulonephritis†	45 (36%)	19 (31.1%)
Interstitial nephritis/obstructive uropathy‡	39 (31.2%)	16 (26.2%)
Congenital kidney diseases§	23 (17.6%)	18 (29.5%)
Haemolytic uraemic syndrome	10 (8.0%)	5 (8.2%)
Cystinosis, oxalosis, and SLE	4 (3.2%)	10 (16.1%)
Other	8 (6.4%)	3 (4.9%)
Unknown	1 (0.8%)	0
Mean age of start RRT* in years (SD)	10.8 (2.9)	11.0 (3.0)
Mean age at time of investigation in years (SD)	29.4 (5.2)	29.5 (5.3)
Mean duration of RRT* in years (SD)	18.2 (5.3)	18.3 (5.1)
Mean duration of dialysis in years (SD)	4.1 (4.6)	4.2 (4.4)
Mean duration of functioning renal graft in years (SD)	14.0 (6.4)	14.1 (5.6)
On dialysis at time of investigation (n)	28 (22.2%)	13 (21.3%)

*RRT, renal replacement therapy; †including focal segmental glomerulosclerosis, rapidly progressive glomerulonephritis, membranoproliferative glomerulonephritis; ‡including reflux uropathy, urethral valves, neurogenic bladder, Prune Belly syndrome; §including polycystic disease, nephronophtisis, dysplasia.

Table 2 Educational attainment of patients, compared to the general Dutch population and our control group

	Patients (%) n=126	Dutch population (%)* n=4789000	Controls§ (%) n=36†
Basic school and low vocational training‡	57.1	27.2	27.7
Intermediate vocational training‡	31.7	47.0	47.2
High vocational training‡	11.1	25.9	25.0

*Dutch population 20–40 years of age: data from the Dutch National Bureau of Statistics (Centraal Bureau voor de Statistiek: www.cbs.nl); †data from Uterwijk¹³; ‡see text for details on schooling system; §difference patients–controls Mann–Whitney test, p=0.001.

Table 3 Wechsler Adult Intelligence Scores for patients and controls

	Patients (n=126)	Controls (n=36)†	Difference	95% CI*	p
Verbal IQ	105.2 (14.1)	114.9 (12.2)	–9.7	–6.4 to –14.7	<0.0001
Performal IQ	110.2 (15.4)	119.9 (11.5)	–9.2	–5.0 to –13.4	<0.0001
Full Scale IQ	107.9 (15.2)	118.2 (11.7)	–10.4	–6.4 to –14.5	<0.0001

*95% CI, 95% confidence interval; †data from Uterwijk.¹³

(SD 15.4, range 62–143), respectively. All these intelligence scores were significantly lower compared to the control group ($p < 0.0001$; table 3). Of all 126 patients, 60 (47.6%) had a Full Scale Intelligence Quotient lower than –1 SD of the mean Full Scale Intelligence Quotient of the control group. Of these 60 patients, 52 (86.7%) had a low vocational training, compared to 20 (30.3%) of all 66 patients with a Full Scale Intelligence Quotient higher than –1 SD. As table 4 shows, most significantly lower scores were found for those tasks which require education, memory, and general knowledge—that is, the verbal tests “information”, “comprehension”, and “similarities”, and the performal test “picture completion”, and for those tasks which require concentration—that is, the verbal test “arithmetic” and the performal test “digit symbol”.

There was no correlation between intelligence scores on the one hand and total duration of renal replacement therapy, use of aluminium containing phosphate binders, total duration of anaemia, or age at onset of renal replacement therapy on the other hand. Also, there was no difference in intelligence scores between those who started renal replacement therapy between 1972 and 1982 and those who started between 1982 and 1992. Patients with cystinosis or SLE ($n = 4$) had lower IQs (mean 95.5) which were –0.82 SD lower than the mean of the whole group. This difference was not statistically

significant in this small group of patients. No differences in mean intelligence quotient levels were found between patients on dialysis at the time of the outcome data collection

Table 4 Subtests of the Wechsler Adult Intelligence Scale for patients and controls

	Mean score Patients (n=126)	Mean score Controls (n=36)*	Difference p value
Verbal Scale subtests:			
Information	5.47 (SD 1.55)	6.31 (SD 1.69)	0.006
Comprehension	5.47 (SD 1.99)	6.94 (SD 1.71)	<0.0001
Arithmetic	5.37 (SD 2.02)	6.61 (SD 1.66)	0.001
Similarities	7.02 (SD 1.91)	8.11 (SD 1.74)	0.002
Digit span	5.83 (SD 2.09)	6.36 (SD 1.91)	0.15
Vocabulary	5.97 (SD 1.88)	6.81 (SD 1.62)	0.01
Performance Scale subtests:			
Digit symbol	6.10 (SD 2.20)	7.31 (SD 1.64)	0.001
Picture completion	5.83 (SD 1.90)	7.75 (SD 1.65)	<0.0001
Block design	6.30 (SD 1.80)	7.25 (SD 1.56)	0.003
Picture arrangement	6.64 (SD 2.05)	7.28 (SD 1.81)	0.08
Object assembly	6.24 (SD 1.82)	6.39 (SD 1.63)	0.64

*Data from Uterwijk.¹³

Table 5 Association between determinants and poor Full Scale Intelligence Quotient (IQfs <-1 SD), poor Verbal Intelligence Quotient (IQv <-1 SD), and poor Performal Intelligence Quotient (IQp <-1 SD): univariate analysis

Category intelligence	IQfs <-1 SD (n=60)	IQfs ≥-1 SD (n=66)‡	p value*	IQv <-1 SD (n=55)	IQv ≥-1 SD (n=73)‡	p value*	IQp <-1 SD (n=60)	IQp ≥-1 SD (n=68)‡	p value*
Age at onset RRT¶:									
<6 years (n)†	2	3	1.0	2	3	1.0	2	3	1.0
≥6 years (n)†	58	63		53	70		58	65	
Duration of RRT¶:									
<18 years (n)†	30	31	0.85	25	36	0.72	33	30	0.29
≥18 years (n)†	30	35		30	37		27	38	
Duration of dialysis:									
<4 (n)†	34	51	0.02	32	53	0.09	36	50	0.13
≥4 (n)†	26	15		23	20		24	18	
Duration of anaemia§:									
<1.5 y (n)†	37	46	0.36	33	51	0.26	36	47	0.35
≥1.5 y (n)†	23	20		22	22		24	21	
Aluminium exposure:									
Yes	48	57	0.24	45	62	0.41	48	58	0.29
No	12	9		10	11		12	10	
RRT at investigation:									
Dialysis (n)†	15	13	0.54	10	19	0.39	14	15	0.52
Renal graft (n)†	45	53		45	54		46	53	
RRT onset:									
1972-1981 (n)†	32	38	0.38	31	41	0.56	29	41	0.12
1982-1992 (n)†	28	28		24	32		31	27	
Primary disease:									
SLE, cystinosis (n)†	4	0	0.05	4	0	0.03	4	0	0.05
Other disease (n)†	56	66		51	73		56	68	

*p value χ^2 test; †number of patients; ‡in 2 patients only verbal IQ could be tested due to visual disabilities, and in 2 patients only performal IQ could be tested due to deafness (IQv n=128, IQp n=128; IQfs=126); §anaemia = Hb <5 mmol/l (<80 g/l); ¶RRT, renal replacement therapy.

compared to transplanted patients. Tables 5 and 6 give univariate and multivariate analyses of the association between the determinants and low intelligence quotient scores. According to multiple logistic regression analysis, the odds ratio of a cumulative dialysis period of more than four years for a low Full Scale Intelligence Quotient was 3.0 (95% CI 1.3 to 6.6, p = 0.007).

DISCUSSION

There was a lower level of educational attainment and lower Verbal, Performal, and Full Scale Intelligence Quotients in these patients compared to Dutch standards. A low intelligence was associated with a longer total duration of dialysis, but not with the actual modality of renal replacement therapy at the time of investigation.

End stage renal disease in children is a rare disorder. In the Netherlands, the incidence of patients with end stage renal disease under the age of 15 stabilised after 1987, varying between 19 and 34 new patients per year on a population of 16 million people.¹⁵ On 1 January 2001, 4705 people were under

chronic dialysis treatment in the Netherlands, of whom 61 (1.5%) were under the age of 15. Of the 4765 patients who were followed after transplantation, only 106 (2.2%) were less than 15 years old. However, as we previously reported, compared to adults the mortality in children with end stage renal disease is low.¹¹ As a result of this, a gradually growing population is emerging of adults with end stage renal disease since childhood.

Cognitive functioning in children with end stage renal disease (that is, measured before adulthood) has been assessed in a number of previous studies. Although some authors found no evidence of deleterious effects of end stage renal disease on cognition,¹⁶⁻¹⁷ most studies have shown a cognitive deterioration in children on dialysis.^{1-4 6 7 18-21} However, none of these studies examined the impact of paediatric end stage renal disease on their cognitive functioning in adulthood.

There was no difference between cognitive functioning of patients who were on dialysis at the time of investigation and those with a functioning renal graft. Most longitudinal studies in children emphasise the beneficial effect of transplantation on cognitive performance. Improvement of mental

Table 6 Association between determinants and poor Full Scale Intelligence Quotient (IQfs <-1 SD), poor Verbal Intelligence Quotient (IQv <-1 SD), and poor Performal Intelligence Quotient (IQp <-1 SD): multivariate logistic regression model

Intelligence score	Low IQfs†# OR† (95% CI)¶	Low IQv† OR† (95% CI)¶	Low IQp† OR† (95% CI)¶
Duration of RRT§ ≥18 y v <18 y	1.2 (0.2 to 9.2)		1.0 (0.2 to 7.0)
Duration of dialysis ≥4.0 y v <4.0 y	3.0 (1.3 to 6.6)**	3.6 (1.4 to 9.1)**	2.1 (1.0 to 4.6)*
Duration of anaemia ≥1.5 y v <1.5 y	1.4 (0.6 to 3.2)	1.5 (0.7 to 3.4)	1.5 (0.7 to 3.2)
Aluminium exposure‡: yes v no	0.6 (0.2 to 1.8)		0.8 (0.3 to 2.3)
RRT§ at investigation: dialysis v renal graft		0.3 (0.1 to 0.8)*	
RRT onset 1972-1982 v 1982-1992			1.7 (0.2 to 11.7)
Primary disease: SLE/cystinosis v other	>10 (0 to ∞)	>10 (0 to ∞)	>10 (0 to ∞)

*p<0.05; **p<0.01; †low IQfs, low IQv, and low IQp = <-1 SD; ‡OR = adjusted odds ratio; ¶95% CI, 95% confidence interval; §use of aluminium containing phosphate binders; ¶RRT, renal replacement therapy; #Hosmer and Lemeshow Goodness of fit test IQfs: p=0.82, IQp: p=0.77, IQv: p=0.96. NOTE: only significant determinants of the univariate analysis were entered in the model and only significant determinants in the multivariate model are shown (all set at p<0.4).

processing speed and sustained attention, and a better performance on vigilance and memory tasks without change of other functions, have been described in children with end stage renal disease after transplantation.^{7,18} Some authors describe improvement of verbal intelligence after transplantation,²⁰ others exclusively of performat tasks.¹⁶ Our results are consistent with the recent study of Brouhard and colleagues,⁷ who studied 124 children with end stage renal disease, one of the largest study cohorts in this field. They concluded that a low intelligence quotient and low educational achievement were not related to the current dialysis or transplant status, but only to end stage renal disease itself. In our study, intelligence was not related to the total duration of renal replacement therapy, but only to the duration of dialysis. This would support the hypothesis that cognition is affected by uraemia in childhood, and that in the long run these abnormalities may be either not or only partially reversible after transplantation. In our patients a long duration of dialysis was associated with a lower intelligence quotient. These findings are consistent with the data of Fennell *et al* and of Brouhard *et al*, who both also found a correlation between duration of dialysis and verbal intelligence deterioration in children with end stage renal disease.^{2,21}

In our study most deficits were found in tasks requiring concentration, memory, and general knowledge. Fennell *et al* found that children on dialysis performed worse on tasks of verbal ability, visual perception, and memory and visual motor skills.⁵ They also described changes over time in end stage renal disease on cognition and found improvement of reaction time and vigilance, but far less on memory functions.⁶ This is consistent with our findings in young adults with paediatric end stage renal disease. The question remains: if, and to what extent a low academic achievement in our patients actually reflects a lack of school attendance caused by the state of their chronic illness and long hospitalisation, and not their intellectual potency per se. As expected there was a high correlation between the level of schooling and cognitive functioning in our patients. However, no conclusion can be drawn from our data as to what extent low educational attainment has impaired cognitive development in our patients, and to what extent the academic achievement is a result of their cognitive ability.

Patients who started renal replacement therapy before the age of 6 did not perform worse than others in our study. Although some studies in children show similar results,^{21,22} one other study has indicated a more severe and permanent reduction of cognitive performance in patients with early onset of end stage renal disease.¹⁹ Our results could be biased by patient selection, since we followed a historical group, in which survival of patients who started renal replacement therapy at a very young age was low, as we reported previously.¹¹ On the other hand, this potential "positive" selection of patients underlines the meaning of the average impairment in cognitive development that we found in our patient group.

Limitations of the study

At time of our outcome data collection the Revised Version of the WAIS (the WAIS-III) was not yet available in the Netherlands. The Dutch version of the Wechsler Adult Intelligence Scale dates back to 1970.¹² Flynn has shown that mean scores of this test in the population have changed upwards over time.²³ He found an increase in the mean intelligence in 14 countries, ranging from 3 to 8 points per decade, and counted 20 points over 30 years in the Netherlands.²³ This is consistent with the findings of Uterwijk, who provided a Revised Version of the WAIS, based on the American WAIS-III.¹³ Subjects with a mean IQs score of 100 according to the new WAIS-III showed a mean IQs of 118.5 (SD 11.7) according to the old WAIS. Therefore, we decided to compare our results with the mean scores in this index group.

Cognition and educational attainment was measured in only 126 out of 187 patients, and our cohort comprised only a few patients who had started renal replacement therapy under the age of 6 years. Nevertheless, since no differences in the distribution of disease parameters and therapy mode existed between participants and non-participants of the study we believe that this group is representative for the whole group, and no obvious selection of a special high risk group seems to have occurred.

We were not able to establish retrospectively the exact amount of aluminium exposure to our patients. However, we found no relation between intelligence and the prescription of aluminium containing phosphate binders. Also, patients who started renal replacement therapy before the early 1980s, when the chronic prescription of aluminium containing phosphate binders became obsolete, had equal intelligence scores to those who started renal replacement therapy between 1982 and 1992. Therefore, we do not think that the exposure of aluminium has played a substantial role in the unfavourable cognitive development in our patients.

Conclusion

End stage renal disease in childhood may lead to an impaired cognition and lower level of educational attainment in adulthood. Intellectual impairment in these patients is associated with a long duration of dialysis and may not be reversible after transplantation. Early transplantation, a more vigorous avoidance of uraemia during dialysis, and early educational intervention may be targets to improve outcome in future patients.

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Fetal and Neonatal Edition, July 2002

The following articles—being published in the November 2002 issue of the *Fetal and Neonatal* edition of the *Archives of Disease in Childhood*—may be of general interest to paediatricians.

Leading article

Hyponatraemia in the first few days: is the incidence rising? *I A Laing, C M Wong*

Original articles

A confidential enquiry into cases of neonatal encephalopathy. *E S Draper, J J Kurinczuk, C R Lammong, et al*

Association between breast feeding and growth: the Boyd-Orr cohort study. *R M Martin, G Davey Smith, P Mangtani, et al*