

# DIALYSIS ENCEPHALOPATHY IN KUALA LUMPUR\*

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## SUMMARY

*The clinical syndrome of dialysis encephalopathy which has been observed all over the world has also been seen here. The clinical syndrome and clinical course are reported; it has been associated with high levels of aluminium in untreated water used for haemodialysis. Since the introduction of water treatment, this disease has not been observed.*

## INTRODUCTION

The clinical syndrome of dialysis encephalopathy was initially reported from Denver in 1972,<sup>1</sup> and has since been observed all over the world.<sup>2-5</sup> One of our patients on chronic haemodialysis developed this disorder in 1976, and several more were subsequently diagnosed over

the years. This report summarises the clinical findings of a review of all patients diagnosed to have dialysis encephalopathy in our department since 1974.

## MATERIALS AND METHODS

All patients with end stage renal disease on chronic haemodialysis in the Nephrology Department were included in this review, including patients who were subsequently transplanted. Patients suspected of developing encephalopathy had a neurological assessment, and investigations including lumbar puncture, brain scan, skull X-rays, EEG and where considered appropriate, carotid angiography and computerised axial tomography scan (CT) of the brain were performed to exclude other possible causes.

## Dialysis Technique

All patients were dialysed four to six hours, three times every week with the Kiil dialyser or disposable dialysis with surface area of about 1.0M.<sup>2</sup> After 1978, only disposable dialysers were used. The haemodialysis concentrate was made by the hospital pharmacy using distilled water. The calcium in the dialysate was 3.5 meq/l. All patients were given oral vitamins and aluminium hydroxide. Skeletal X-rays were performed once or twice every year.

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The tap water was treated at source with aluminium sulphate and hydrated lime, filtered and then disinfected with chlorine. This tap water used in the dialysis unit was not treated until 1980, when a reverse osmosis system became functional. Water treatment for patients on home haemodialysis has been by reverse osmosis or by deioniser.

Serum samples of patients developing dialysis encephalopathy in 1979 were stored for analysis for aluminium content.

Water samples and serum samples were analysed for aluminium content by atomic absorption spectrophotometry.

## RESULTS

18 patients developed dialysis encephalopathy out of 210 patients treated up to September 1981.

The early features of dialysis encephalopathy included restlessness, malaise and weakness, depression, euphoria, poor memory and concentration, difficulties coping at work or at home and altered behaviour. Altered behaviour included episodes of a lady (usually prim and proper) walking stark naked in the house; locking himself

inside a bathroom at home and refusing to come out, until the door was broken down – the patient is known to be normally normal and responsible.

Another patient who was a policeman pulled out the needles out of his arm and walked out in the middle of dialysis on two occasions, and had previously been normal. All this occurred in patients who were previously normal, and who could not recollect these incidents later. All this occurred weeks to months before dialysis encephalopathy was diagnosed. Speech difficulties including slurring, stuttering, hesitancy in speech and complete aphasia were commonly observed. Generalised and focal seizures (fits) and myoclonic jerks were also common features. The disease was relentlessly progressive and most patients became bedridden and stuporous before death. Treatment with anticonvulsants appeared to control seizures, but did not affect progress of the disease.

Generalised and focal seizures (fits) were the initial presenting feature in 11 patients and was observed in 16 patients. Speech disorders occurred in 15, two of whom had mild manifestations such as hesitancy and stuttering speech, while 13 had severe dysphasia and became totally aphasic. Speech disorder was the initial presenting feature in four patients.

Marked behaviour disorders such as depression, euphoria, paranoia and hallucinations were observed in 13 patients, mostly after the diagnosis of encephalopathy was obvious. In three patients, this was observed up to three months before other features were manifested.

**TABLE I**  
TOTAL NUMBER OF PATIENTS ADMITTED  
TO CHRONIC HAEMODIALYSIS PROGRAMME,  
1974 TO SEPTEMBER 1981

Year	Patients
1974	12
1975	9
1976	10
1977	16
1978	17
1979	41
1980	54
1981 (September)	51
<b>Total</b>	<b>210</b>

**TABLE II**  
CLINICAL FEATURES OF DIALYSIS  
ENCEPHALOPATHY

Speech Disorder	15 (4)
Seizures : Generalised	16 (11)
Myoclonus	15 (-)
Behaviour Disorder	13 (3)
Myopathy	5

Note: Presenting clinical features in brackets ( ).

The period on dialysis before the onset of encephalopathy varied between 4.5 to 54.75 months with a mean of 22.9 months. Survival after diagnosis varied between 2.75 months to 18 months with a mean of 6.9 months. All 18 patients died. No post mortem studies were performed.

Skull X-rays were all normal.

Lumbar puncture studies in 11 patients were all normal.

Brain scan performed in 13 patients were normal in 12 and revealed abnormal uptake in one hemisphere in one patient. Further examination of this patient by CT scan and carotid angiography were normal.

Multiple fractures involving the ribs, necks of femur, humerus, and the scapula were noted in eight patients, four of whom had severe proximal myopathy. One other patient had marked myopathy without obvious bone changes on X-ray.

Routine biochemical investigations were not remarkable showing no differences from patients who were not affected.

The aluminium concentration in the tap water was 870  $\mu\text{g/l}$  and after treatment by reverse osmosis was below 20  $\mu\text{g/l}$ . The level after treatment by deioniser was 50  $\mu\text{g/l}$ .

The serum aluminium levels of six patients with encephalopathy varied between 190–400  $\mu\text{g/l}$  with a mean of 267  $\mu\text{g/l}$ , while that of 10 patients who did not develop encephalopathy varied

between 150–840  $\mu\text{mol/l}$  with a mean of 399  $\mu\text{g/l}$ . The levels of five patients with end stage renal disease (s. creatinine exceeding 1000  $\mu\text{mol/l}$ ) who were not on haemodialysis were between 60 and 250  $\mu\text{g/l}$  with a mean of 124  $\mu\text{g/l}$ .

Following the introduction of the reverse osmosis system for water treatment in January 1980, only one patient developed encephalopathy, which occurred during a period of one month (June 1981) when this system broke down, and dialysis had to be performed with untreated water. He developed typical clinical features and EEG changes were characteristic. Haemodialysis was stopped for a week until he could be dialysed again with treated water, and over a period of three months, his clinical features and EEG reverted to normal.

### Electroencephalogram (EEG)

Electroencephalograms of the patients with symptoms of dialysis dementia were invariably abnormal. Most have the characteristics described in dialysis dementia such as spike and slow wave complexes bilaterally synchronous and generalised; or bursts of synchronous rhythmic high voltage slow waves at 3 – 4 Hz (Fig. 1): or minimal non specific theta. One of the patients, the sole survivor, in this series, had interesting EEG features. At the beginning of the recording he had only bursts of high voltage rhythmic slow waves at 3 – 4 Hz. These became accentuated and lateralised to the (L) hemisphere and continuous during hyperventilation and subsequently was manifested by PLEDS (periodic lateralised seizure discharges) in the left temporal region; (Figs. 2, 3).

TABLE III  
DURATION OF HAEMODIALYSIS BEFORE  
ONSET OF ENCEPHALOPATHY

Period on dialysis before onset of encephalopathy	Under 6/12 mths	6-12/12mths	1-2 yrs	2 yrs
Number of Patients	2	3	4	9

At the time of recording he manifested symptoms of dysphasia, abnormal behaviour amongst others. In this patient too, a repeat EEG was normal (Fig. 4) a few weeks later when the symptoms subsided. It is worthwhile to note that his dysphasia and abnormal behaviour are correlatable with the abnormal EEG pattern recorded.

## DISCUSSION

Dialysis encephalopathy is a distinct clinical entity and our observations were similar to that described elsewhere.<sup>1-6</sup> Other possible causes of encephalopathy were excluded from the history and from clinical investigations. The diagnosis of dialysis encephalopathy was made from the clinical features and observing the clinical course of the illness for a period varying from 4.5 months to 54.75 months, supported by the characteristic EEG findings.

The clinical features of dialysis encephalopathy were characteristic, though individually

not specific. The most common features were speech disorder, generalised seizures and myoclonus. Generalised seizures were the most common presenting feature, while myoclonus which was a commonly observed sign occurred later in the course of the illness. The onset of the illness were generally insidious and the occurrence of seizures dramatically attracted attention, leading to the diagnosis being made. However invariably the family and haemodialysis staff had noticed mono-speech and behavioural changes before the onset of the seizures. The altered behaviour were sometimes dramatic and occurred before there were other obvious signs of encephalopathy, and were reminiscent of temporal lobe seizures.

The EEG is invariably abnormal and characteristic, although the features are not specific. The aetiology of this disorder is unknown although many possibilities have been postulated,<sup>7</sup> and reports from many centres implicate high aluminium concentration in the dialysate.<sup>6,8-10</sup> It has also been shown that the brain grey matter

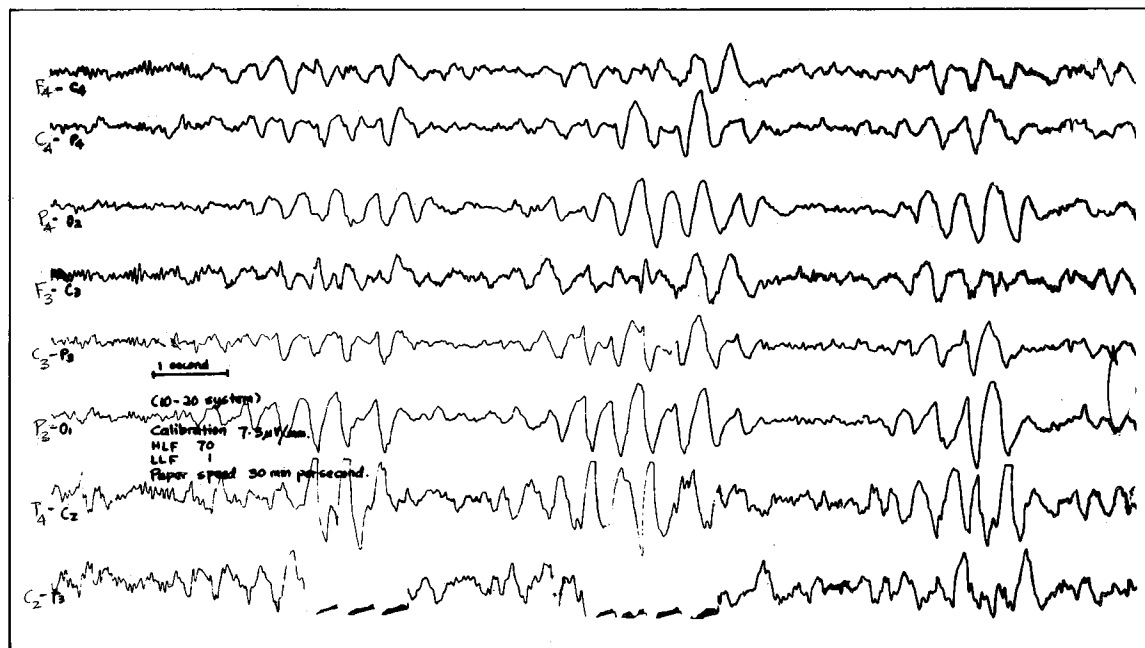


Fig. 1 EEG of a 47-year old male with dialysis dementia. Note the burst of rhythmic high voltage slow waves which are bilaterally synchronous in the resting EEG

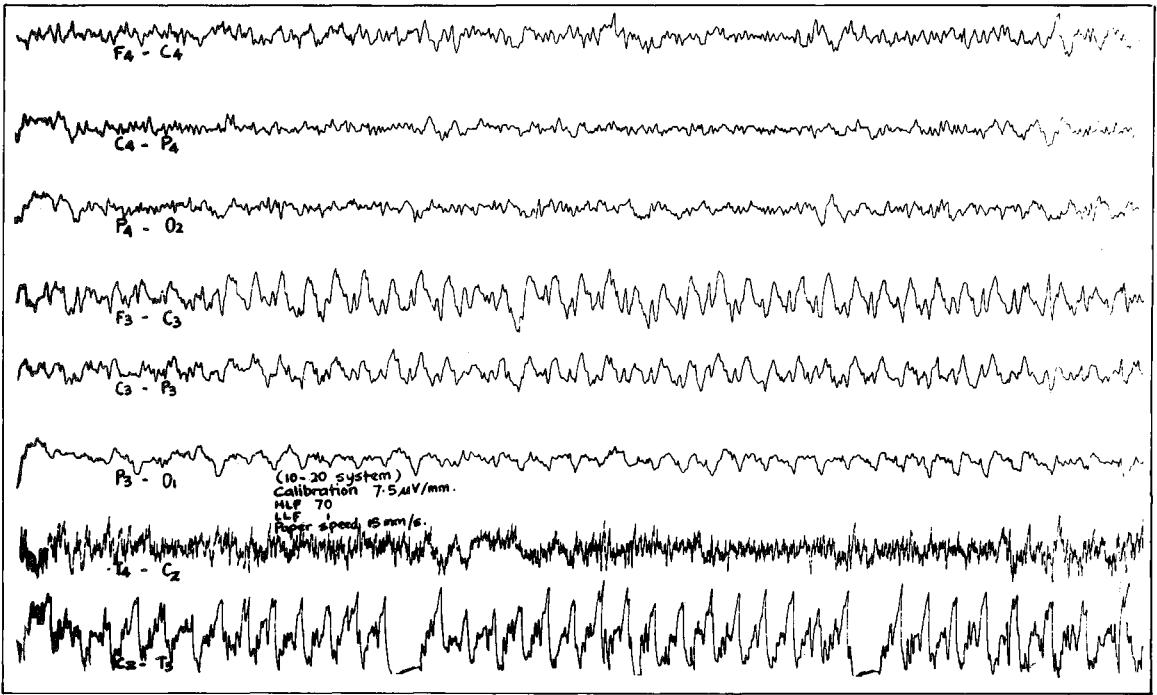


Fig. 2 A 43-year old male with EEG carried out on 4 May 1981. Patient had symptoms of dialysis dementia. Note epileptiform activity in the (L) hemisphere during hyperventilation (at 2 min.).

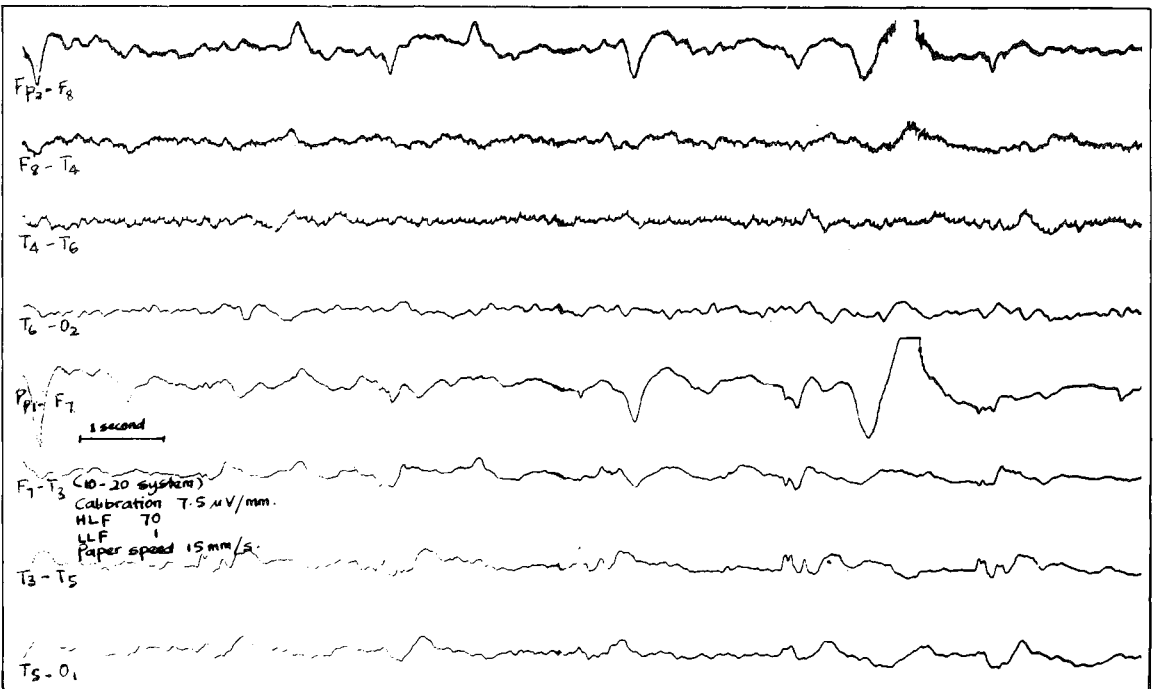


Fig. 3 A 43-year old male's EEG done on 4 May 1981, when he had symptoms of dialysis dementia. Resting EEG 140 min. post HB. Note LH PLEDS

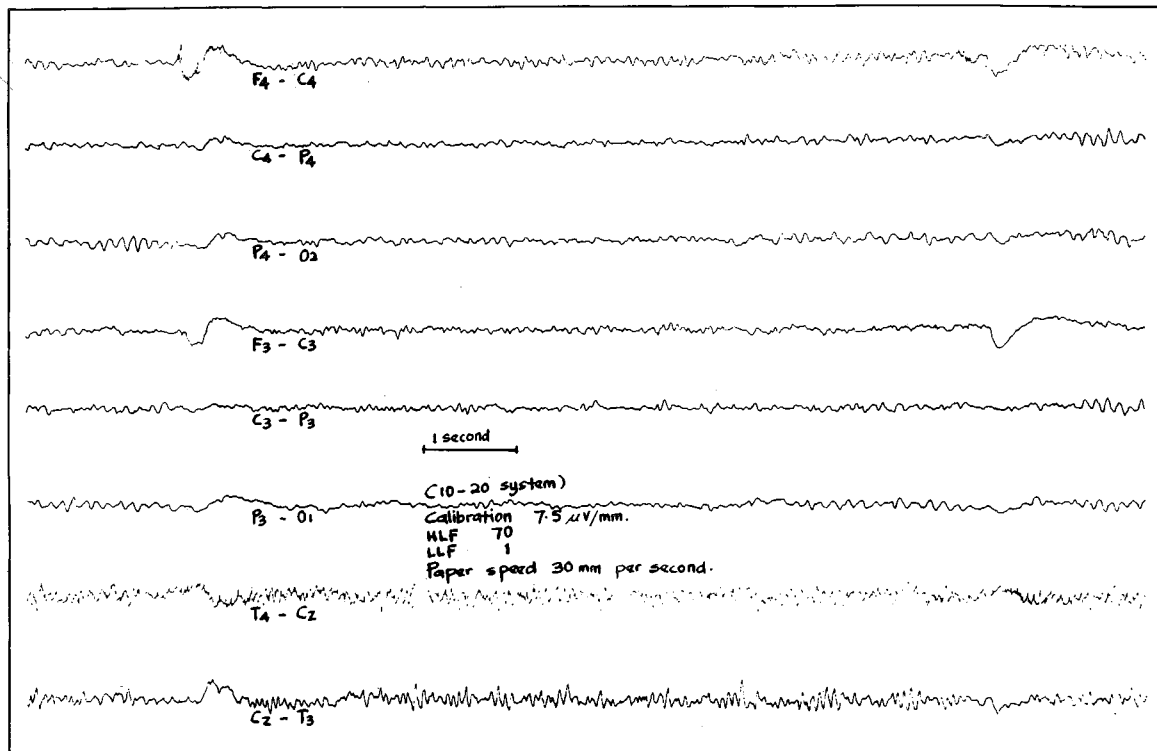


Fig. 4 EEG of the 43-year old male (as previously seen in Fig. 2) who had symptoms of dialysis dementia. This EEG is normal and was done on 4 June 1981.

aluminium was higher in dialysis encephalopathy patients than other patients on haemodialysis,<sup>11</sup> whose levels were also elevated, and it was postulated that phosphate binding aluminium gels might be incriminated in the aetiology. However patients who have never taken aluminium hydroxide have also developed this disorder.<sup>8</sup> Disordered cerebrospinal fluid dynamics have also been described in these patients,<sup>12</sup> but its relationship with the serum aluminium concentration remains unclear.

High serum aluminium concentrations has been observed in patients with encephalopathy in areas where the water contained high concentrations of aluminium.<sup>7-9</sup> However it was also observed that aluminium retention occurred in patients with impaired renal function,<sup>9</sup> although it was greatest among patients with dialysis encephalopathy. Among our patients with chronic renal failure, all had elevated serum aluminium concentrations, but were lowest among patients

not on haemodialysis. Among patients on haemodialysis the mean serum aluminium levels were higher among patients without encephalopathy. This differs from the observations of Elliot,<sup>9</sup> but is consistent with the observations of Ward *et al.*,<sup>13</sup> who observed no difference in serum aluminium levels of patients on haemodialysis, whether they developed encephalopathy or not. It was suggested that the elevated serum aluminium levels reflected recent exposure to high aluminium levels in the dialysate.<sup>9,13</sup> The strong association between bone disease and encephalopathy has been observed at several centres<sup>7,8,13,14</sup> has also been seen here. Five of the patients who had the most clinically severe osteomalacia were those who were dialysed the longest. The osteomalacia were resistant to treatment with calciferol, dihydrotachysterol and 1 alphahydroxycholecalciferol.

Following the introduction of the reverse osmosis water treatment system, the incidence

of encephalopathy was dramatically reduced. Only one patient developed encephalopathy over a period of 50 months, and this occurred during a period when there was a breakdown in the water treatment system. Figs. 2 and 3 show the EEG of this patient who had symptoms of dialysis encephalopathy while dialysed using untreated water, and Fig. 4 show the EEG returning to normal one month later after being dialysed with treated water,, dramatically emphasising the importance of adequate water treatment for haemodialysis. This is our only patient who has survived this disease. Although the aetiology by strong circumstantial evidence, whatever that causes it, is effectively removed by water treatment by the reverse osmosis system and by deioniser.

Ward *et. al.*,<sup>13</sup> has shown that effective water treatment has also reduced the incidence of osteomalacia among their haemodialysis patients. This has not been looked into among our haemodialysis patients yet, and we do not know whether the incidence of bone disease has been reduced following the introduction of water treatment to our unit. However the devastatingly progressive and crippling effects of encephalopathy and osteomalacia makes it extremely important that patients dialysed in areas where the aluminium levels in the water are high must have their water effectively treated.

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