PART III

DIALYSIS 2

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ALUMINIUM STUDIES IN DIALYSIS ENCEPHALOPATHY

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Summary

The dialysis encephalopathy syndrome has a geographical distribution related to the aluminium content of the dialysis water supply. There is a close relationship between concentrations of water aluminium and serum aluminium, and patients with dialysis encephalopathy have serum aluminium concentrations greater than 400 μg/litre. High serum aluminium is also associated with osteomalacic bone disease, and worsening anaemia.

In dialysis encephalopathy, elevated concentrations of aluminium are found in CSF and in grey matter, and an aluminium burden of 2–8 g is calculated from whole body in vivo analysis.

There is sufficient evidence for an aluminium toxicity syndrome to warrant specific removal of aluminium by water purification systems.

Introduction

The cause of the dialysis encephalopathy syndrome has not been proven with absolute certainty, but there is accumulating evidence to implicate aluminium [1–5]. From a number of in vivo studies further evidence is presented to confirm that the syndrome is due to aluminium toxicity.

Water and Serum Aluminium

In the West of Scotland, the incidence of the dialysis encephalopathy syndrome (14 cases) has been confined to those regions with a high aluminium content in the water from which dialysis fluid is prepared. No case of encephalopathy (or of osteomalacic osteodystrophy) has occurred in patients (n = 60) who dialyse in Glasgow itself, where the water aluminium is less than 30 μg/litre. This compares with a mean water aluminium concentration of 420 μg/litre (SEM ± 36) from the homes of the 14 patients with dialysis encephalopathy.

Comparison of serum aluminium concentrations from different groups of
renal patients (including 9 with dialysis encephalopathy) is shown in Figure 1.

The individual values are also shown for four hospital dialysis patients who
do not take aluminium hydroxide.

Patients with dialysis encephalopathy have a mean serum aluminium con-
centration of 630 μg/litre (SEM ± 53 μg/litre) which is considerably higher
than any other group. In two cases the subsequent development of encephalo-
pathy was predicted from serum aluminium levels of over 700 μg/litre. Water
purification systems were instituted in each case, but both patients progressed
to develop neurological problems within a few months, despite falls in serum
aluminium (Figure 2). This may be relevant to those studies which failed to
show good correlation between serum aluminium concentrations and dialysis
encephalopathy.

Figure 2. Progress of patients with very high serum aluminium concentrations — including
effect of water purification
High levels of aluminium (over 350 μg/litre) are seen in four other patients who have shown no signs of encephalopathy, and the progress of these cases is as follows — one received a transplant; one died suddenly; and two, who suffered from osteomalacia and increased anaemia, remain on regular dialysis therapy with water purification (Figure 2).

This close relationship of serum aluminium to water aluminium is further illustrated by data from three patients followed through chronic renal failure, hospital dialysis training (water aluminium less than 30 μg/litre) and home dialysis. Prior to the installation of water purification systems, these patients were temporarily exposed to a significant aluminium content in the water supply to their homes and the effect on serum aluminium is shown in Figure 3.

![EFFECT OF DIALYSIS](image)

Figure 3. Progress of patients exposed to high water aluminium concentrations. (Water aluminium shown on right)

The mean aluminium concentration in the home dialysis water supply is shown in each case.

**Brain and CSF Aluminium**

Post-mortem analyses of brain samples have not shown the histopathological features described elsewhere [6], but aluminium concentrations are similar to those described [1,6], with varying concentrations in different parts of the brain — for example, 13.0 μg/g (dry weight) in the grey matter of the frontal cortex from a typical case who had a serum aluminium of 535 μg/litre.

CSF was obtained from three patients with dialysis encephalopathy and was found to contain higher aluminium concentrations than CSF from 'control' samples.

Three patients with dialysis encephalopathy had CSF aluminium concentrations of 50, 45 and 40 μg/litre compared with 18 and 15 μg/litre from two
dialysis patients who did not have encephalopathy. The control group, including three patients with senile dementia, had a mean CSF aluminium concentration of 7.5 μg/litre (n = 9; range 4–15 μg/litre).

Bone and Total Body Aluminium

There is evidence [3] that aluminium plays a part in the osteomalacic type of dialysis osteodystrophy. By means of total body in vivo neutron activation analysis, whole body measurements of calcium (Ca), phosphorus (P) and aluminium (Al) were undertaken in a number of dialysis patients, including three with dialysis encephalopathy complicated by osteomalacic osteodystrophy.

With this technique, Al and P are activated to the same isotope (28Al) and the aluminium content has to be derived by a subtraction calculation dependent on the P/Ca ratio. As there are no significant differences between home and hospital dialysis patients other than the aluminium content of the dialysis water supply, the observed difference in P/Ca has been assumed to be solely to aluminium. The P/Ca ratio and the calculated (additional) aluminium burden for home dialysis patients (where it exceeds 2g Al) are shown in Figure 4.

Anaemia due to Aluminium Toxicity

A fall in haemoglobin concentration has been observed in patients suffering from dialysis encephalopathy. A retrospective assessment showed that this fall was already occurring in the months prior to the development of neurological problems. A similar fall in haemoglobin was also seen in two further patients who have no evidence of encephalopathy, but who suffer from osteomalacic osteodystrophy and have elevated serum aluminium concentrations. This
worsening of dialysis anaemia is particularly noteworthy in patients MM, CS and AF, who have polycystic renal disease.

Figure 5 shows the haemoglobin levels in patients with encephalopathy and/or high serum aluminium concentrations detected during 1977.

Conclusion

Aluminium is the suspected cause of the dialysis encephalopathy syndrome. The water supply from which dialysis fluid is prepared is the major source of aluminium, and there is good evidence to suggest that osteomalacic osteodystrophy and worsening anaemia are further features of an aluminium toxicity syndrome.

Much of the evidence incriminating aluminium is based on post-mortem analyses, but this study provides in vivo data as further confirmatory evidence. There are good correlations between the dialysis encephalopathy syndrome and water, serum and CSF aluminium concentrations. Whole body analysis is also suggestive of an increased body burden of aluminium in affected patients.

There is sufficient evidence to warrant ‘protection’ of patients by specific removal of aluminium from the dialysis water supply, but this may not necessarily prevent aluminium toxicity in patients who have already accumulated a significant tissue burden of aluminium.

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References

Open Discussion

KERR (Newcastle) It is our impression that a very high tap water aluminium causes encephalopathy and an intermediate level, as we have in Newcastle, causes bone disease before encephalopathy. Did your two patients with bone disease who have not yet developed encephalopathy come from an intermediate water aluminium area?

ELLIOTT I agree with Professor Kerr. We would hypothesise that those patients exposed to very high levels of aluminium have a significant amount of free aluminium carried in the blood and it seems reasonable to assume that this free fraction is the one which crosses the blood-brain barrier and causes the encephalopathy.

BONE (Liverpool) What seasonal variations have you observed in the aluminium content of the water?

ELLIOTT The addition of aluminium sulphate is common practice in the West of Scotland but it seems to be so inappropriately done that there is no obvious seasonal variation.

KLINKMANN (Rostock) Do you routinely use aluminium bases as phosphate-binders in your patients?

ELLIOTT We use them routinely.

KLINKMANN In what dosage?

ELLIOTT A common preparation would be Alucap in a dosage of 8 capsules daily, that is four grams.

KLINKMANN This may add a little bit.

ELLIOTT Well, I showed four hospital dialysis patients who do not take Aludrox in any form and they had serum aluminium levels no different from anybody else. Some were higher than other patients who did take Aludrox.
PARSONS (London) We have been interested in the interaction between fluoride and aluminium because there are middle molecular weight complexes of fluoride and aluminium which can get through the dialyser. Has your prevalence of encephalopathy anything to do at all with fluoride concentration in the water?

ELLIOTT The answer is no, because in Western Scotland fluoride is not routinely added, and is not present in many of the water supplies. There are only one or two areas where there is fluoride in the water and these areas do not have encephalopathy, but there is insufficient experience in our area.

PARSONS Are you quite happy that your present type of water treatment, a deioniser, is removing all the substances? It should remove alum-containing substances but you do not seem to get your water completely free.

ELLIOTT We really were not happy with aluminium removal by deionisers and we have chosen to use reverse osmosis machines. Based on measurements before the machine and the water coming out of the machine, as far as we can detect, it removes virtually all aluminium.