

## TRACE ELEMENT BINDING TO PLASMA PROTEINS IN HAEMODIALYSIS

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### Summary

The protein distribution of cadmium, copper and lead and their plasma values in haemodialysis have been studied. The plasma protein distribution has been measured by means of chromatographic fractionation of serum with a Sephadex G-150 column. The plasma values of cadmium, copper and lead were measured by atomic absorption with a graphite chamber. There is a significant increase ( $p < 0.01$ ) in plasma concentrations of cadmium, copper and lead. Cadmium is distributed in 60 per cent with small molecular weight proteins. Copper shows four peaks, with 70 per cent corresponding to ceruloplasmin. Lead has a peak corresponding to plasma components with small molecular weight.

### Introduction

The plasma values of trace elements in haemodialysis have been previously studied [1-3], but not their distribution in plasma proteins. Studies have shown the existence of nitrogenous compounds of middle molecule size [4,5] which are reputed to be associated with uraemic toxicity [6-8]. We have studied the distribution of cadmium, copper and lead in plasma fractions.

### Materials and methods

Twenty patients on haemodialysis, average age  $42 \pm 18$  years, treated for  $36 \pm 11$  weeks by haemodialysis, have been dialysed for four hours, three times weekly, with a cuprophan dialyser,  $1.2 \text{ m}^2$ . Ten healthy people  $40 \pm 13$  years of age served as a control group. The cadmium, copper and lead measurements were performed by atomic absorption spectrophotometry with a graphite chamber. The plasma protein distribution was studied by chromatographic fractionation of serum in Sephadex G-150, treated with sodium borohydride and followed by analysis of trace elements in the fractions obtained.

## Results

The plasma values of cadmium, copper and lead are shown in Table I. The dialysis patients have significant increases ( $p < 0.01$ ) when compared with the normal subjects. Variations before and after haemodialysis are only significant for copper ( $p < 0.01$ ) with an increase.

TABLE I. Values of cadmium, copper and lead in haemodialysis

	Controls	p	Haemodialysis		
			before	p	after
Cadmium $\mu\text{g}/\text{dl}$	$0.5 \pm 0.1$	$< 0.01$	$0.8 \pm 0.2$	NS	$1.0 \pm 0.3$
Copper $\mu\text{g}/\text{dl}$	$103 \pm 29$	$< 0.01$	$131 \pm 22$	$< 0.001$	$184 \pm 47$
Lead $\mu\text{g}/\text{dl}$	$23 \pm 3$	$< 0.001$	$114 \pm 17$	NS	$116 \pm 14$

NS=not significant

Chromatography with Sephadex G-150 and trace elements in each of the peaks are shown for controls in Figure 1, for cadmium in Figure 2, for copper in Figure 3 and lead in Figure 4.

The plasma distribution of cadmium is in three peaks (a, b, c) of the fractionation with 60 per cent in the small molecular weight plasma components; there is no variation in distribution after haemodialysis.

The copper appears distributed in four peaks (a, b, c, d), the most important of which corresponds 70 per cent to ceruloplasmin and 10 per cent, 20 per cent and 10 per cent to the other types; after haemodialysis the one corresponding to ceruloplasmin increases.

The lead appears in a peak corresponding to small molecular weight plasma components.

## Discussion

We have been able to determine an increase in cadmium concentrations in the tissues of patients with haemodialysis [2,9]. Some of the increase in cadmium in some tissues could be as a consequence of its redistribution. In Figure 2 the cadmium appears in the peak belonging to middle molecules, which leads us to think that the toxic effects of these molecules could be due to cadmium. It seems that cadmium may inhibit  $1,25(\text{OH})_2\text{D}_3$  cholecalciferol production [10]. It is well known that cadmium may remove zinc from a number of metallo-enzymes, so that a total charge increase of cadmium causes a zinc deficiency. The administration of zinc may reduce some of the symptoms produced by experimental intoxication with cadmium.

An increase of plasma copper in haemodialysis has been found by the redistribution of copper (Figure 3), 70 per cent of which is associated with ceruloplasmin which increases after haemodialysis. Another peak belongs to middle

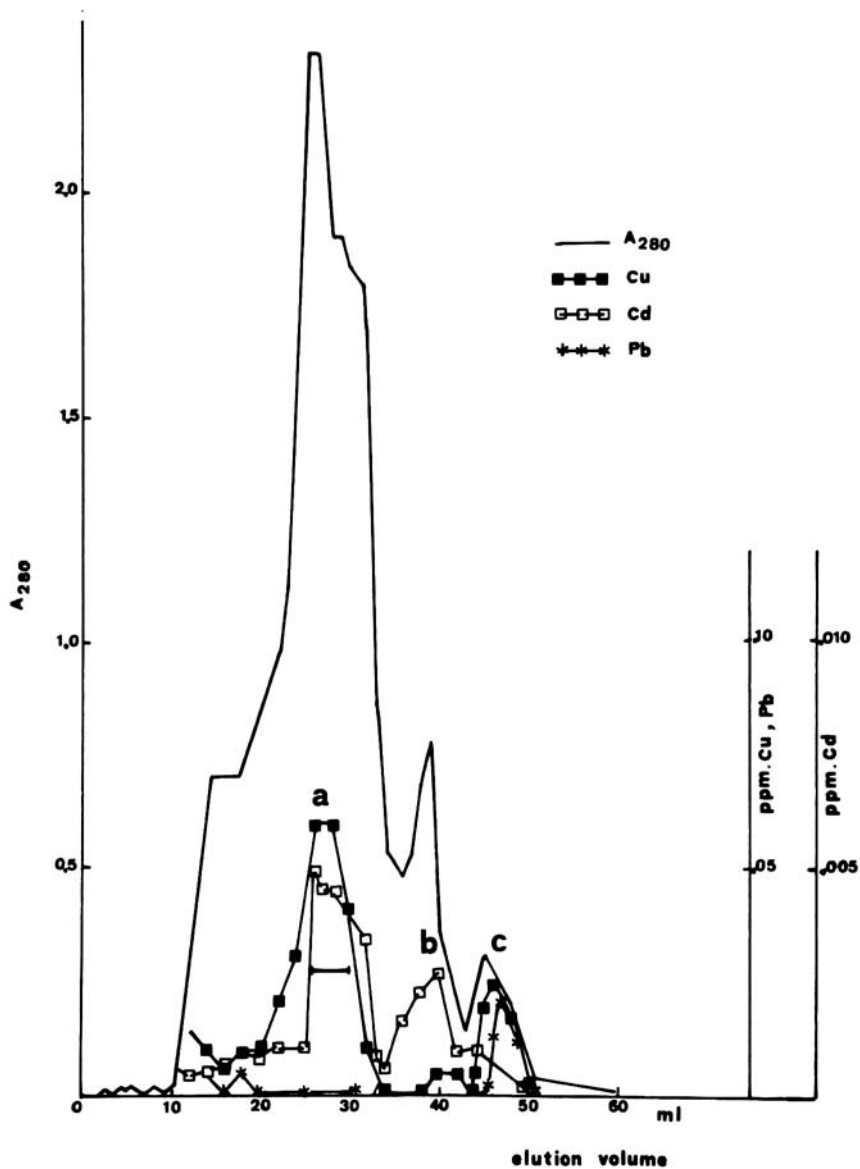


Figure 1. Sephadex G-150 chromatograms of normal plasma

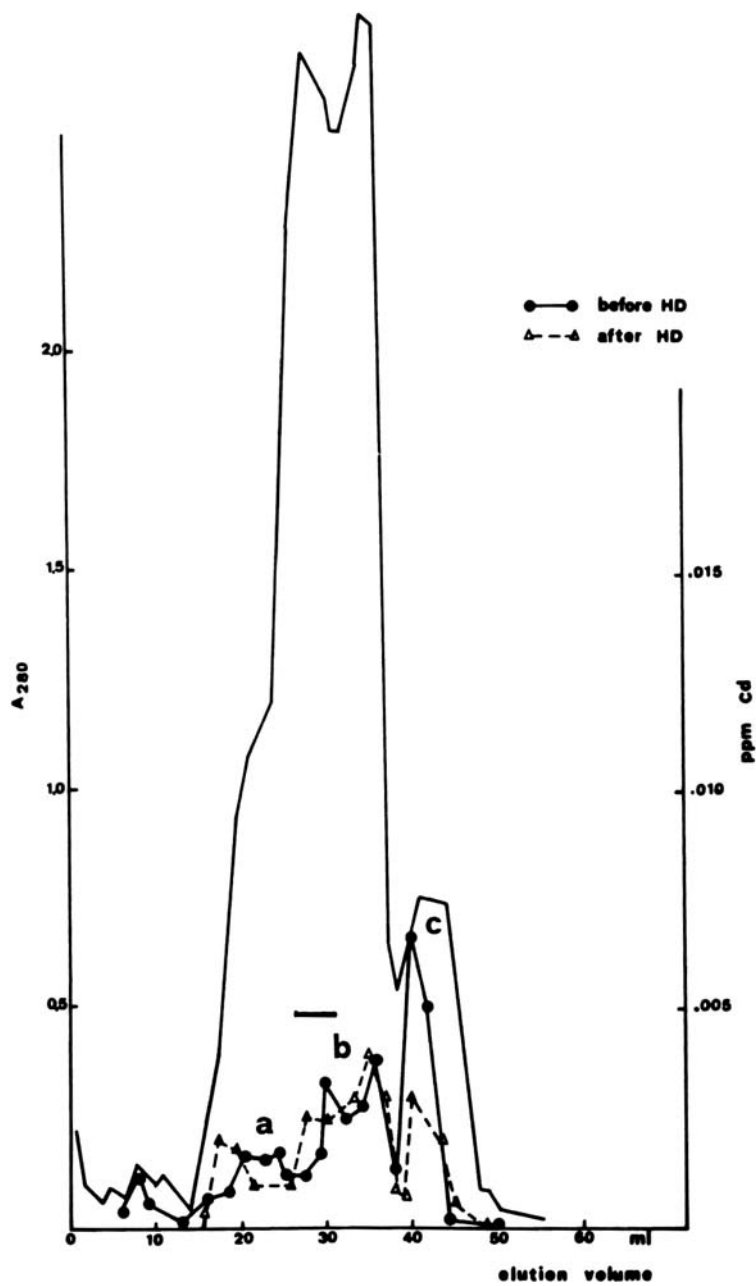


Figure 2. Sephadex G-150 chromatograms of plasma cadmium in haemodialysis patients

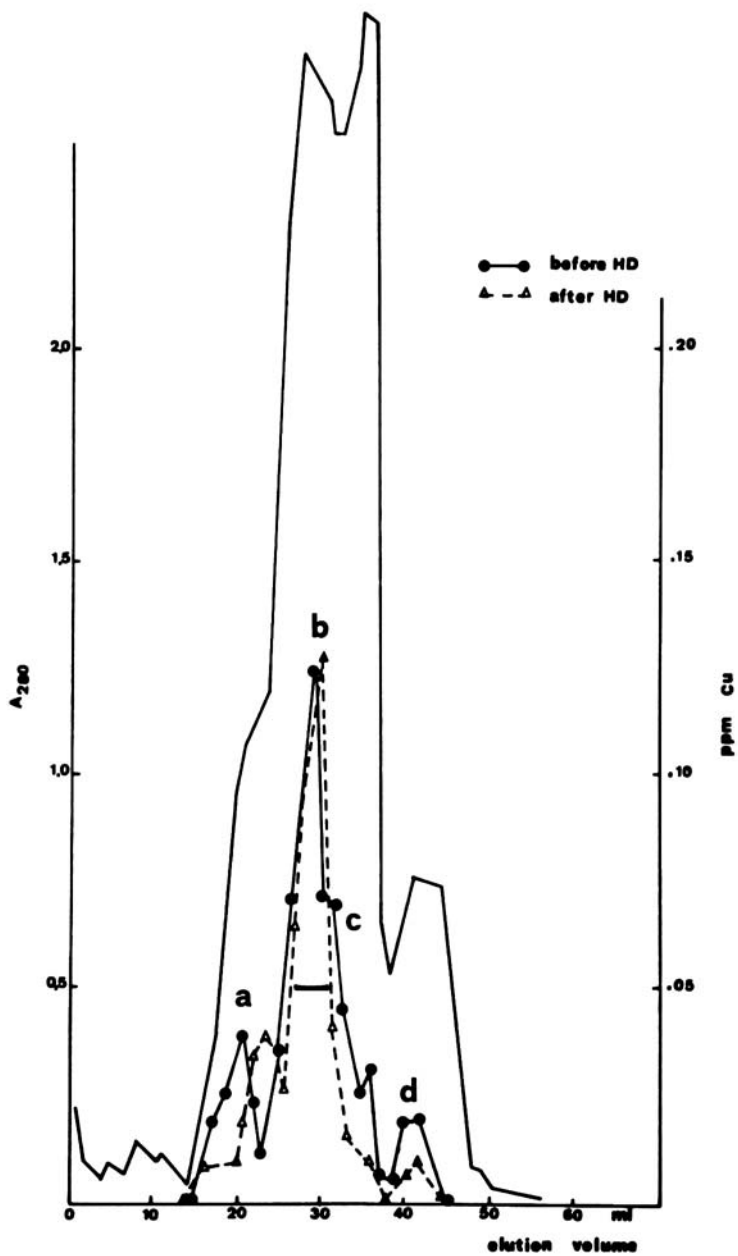


Figure 3. Sephadex G-150 chromatograms of plasma copper in haemodialysis patients

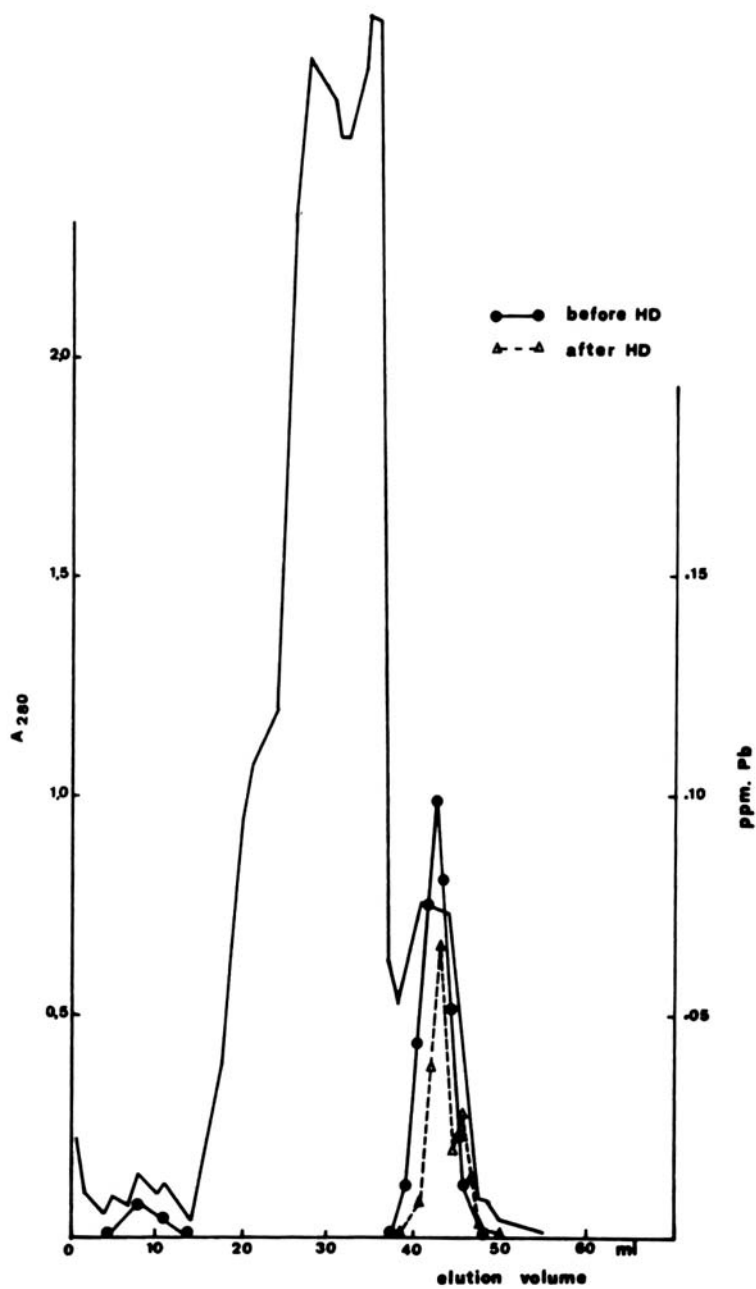


Figure 4. Sephadex G-150 chromatograms of plasma lead in haemodialysis patients

molecules. Although normal concentrations of lead have been found in blood of haemodialysis patients, we have found it to be high, being linked to a plasma fraction of small molecular weight (Figure 3).

It is well known that lead excess has an effect on red cell metabolism, neutralizing the enzymes which participate in haem biosynthesis. The increase of lead in haemodialysis patients and the plasma fraction of small molecular weight, may have a bearing on the haematological disorders of these patients.

## References

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