As has been stated earlier [5], the blood pressure response to fluid withdrawal by haemofiltration depends on the blood pressure at the start of the treatment procedure; in patients with severe hypertension a relatively small amount of ultrafiltrate removal is sufficient to induce a substantial decrease of blood pressure, whereas in patients with normo- or hypotension relatively large fluid removal is tolerated without further depression. This behaviour may be a strong point against the assumption that normalisation of blood pressure by haemofiltration is simply a function of dehydration. Other factors influencing the vascular tone have to be taken into consideration. One of these may be a more physiological adaptation of the circulatory system to intravascular fluid removal. We ourselves and other authors, could demonstrate that the peripheral resistance increases or at least remains stable in haemofiltration but decreases in haemodialysis [6–8].

Whereas plasma catecholamine levels showed a physiological response to body fluid removal in haemofiltration, no reaction or alternatively a decrease, was observed in haemodialysis [7,8]. Besides this, rapid 'refilling' of the extracellular space during and after haemofiltration, demonstrated here, may be an important factor in the prevention of vascular instability. Obviously the maintenance of a higher extracellular osmotic pressure, perhaps as a consequence of a higher extracellular Na⁺ concentration, may enhance this 'refilling' phenomenon [9].

The antagonistic effects of haemofiltration, normalisation of hypertension as well as prevention of hypotensive reactions, lead to a concept based on the present information about its effects on the determinants of blood pressure regulation (Figure 5). Contrary to haemodialysis, haemofiltration allows removal of sodium

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**Figure 5.** Schematic concept of blood pressure regulation in haemofiltration. BP = blood pressure; ECS = extracellular space; IC = intracellular space
by convective transport, i.e. without influencing the extracellular sodium concentration. The maintenance of a relatively high extracellular Na⁺ concentration results in stabilisation of extracellular osmotic pressure in spite of the removal of small molecular substances accumulated in uraemia (e.g. urea). Thus, fluid removed from the extracellular compartment by haemofiltration is rapidly substituted by a flux from the intracellular space due to osmotic gradients. The more pronounced expansion of the extracellular space — compared with haemodialysis — may prevent collapse reactions and thus stimulation of the renin-angiotensin system. Less collapse reactions mean less saline infusions, consequently facilitating the normalisation of high blood pressure.

Acknowledgments

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ROLE OF SMALL MOLECULE REMOVAL IN THE CONTROL OF TREATMENT MORBIDITY WITH HAEMODIALYSIS AND HAEMOFILTRATION

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In 1976, it was suggested that the critical factor in maintaining the blood pressure during isolated ultrafiltration (UF) was the stability of the serum osmolality, and that by inference the high incidence of symptomatic hypotension (SH) seen with efficient dialysis was due primarily to large drops in the serum osmolality [1]. A consequence of this ingenious study, limited to one series of acute experiments in only six selected patients, was the birth of the 'shifters' school. The 'shifters' believe that dialysis hypotension is due to hypovolaemia during ultrafiltration. The hypovolaemia is exaggerated by the passage of extracellular fluid into the cells at the same time as it is removed from the body. Their conclusions are based
upon precise space measurements and their results are often dubious [2,3]. I have never believed in the 'shifter' school, and felt that Bergström's conclusions [1] could not apply in a chronic situation. To study this matter in more detail we selected six patients [4] with a high incidence of symptomatic hypotension (drop in mean arterial pressure of more than 20% together with a requirement for nursing attention ± fluid replacement) during conventional haemodialysis lasting four hours and employing a 1m² cuprophane dialyser. The study was divided into three parts. Each part lasted for one month. During part 1 the dialysate flow rate (single pass) was 500ml/min; in part 2 the dialysate flow rate was 300ml/min and in part 3 the dialysate flow rate was 100ml/min. All other parameters were kept as near constant during all parts of the study. Thus, the Gambro Lundia 1m² 13.5μ cuprophan dialyser was used throughout the study for four hours three times per week. The dialysate electrolyte composition was kept constant at sodium 140mEq/L, potassium 2.0mEq/L, calcium 3.5mEq/L and acetate 40mEq/L without glucose. Blood flow was kept as constant as possible at about 200ml/min. Weight loss was kept linear by the use of an ABG Semca balancing device which kept the input and output dialysate flow to and from the dialyser

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- ∆ = mean pre to post change ± 1SD.

Figure 6. Reduction in serum urea during dialysis at three different dialysate flow rates.

(Reprinted from reference 4, with permission of the editor of the American Society of Artificial Internal Organs)
constant, whilst permitting ultrafiltrate (excess weight loss) to be removed by a separate pump and measured directly. Weight loss was also checked by a Datex metabolic bed scale and continuously recorded on a Kontron WW 1200 chart recorder. Blood pressure and pulse were recorded manually at 30min intervals. Serum sodium, osmolality, urea and haematocrit were measured before and after each dialysis in the last week of each part of the study.

The results were expressed as mean ± SD of all parameters measured during the last week of each part of the study. There was a progressive rise in the mean pre treatment level of serum urea from $35.0 ± 3.35$ mmol/L during the last week of part 1 to $43.8 ± 6.79$ mmol/L in the last week of part 3. The drop in serum urea ($Δ$urea) was similar in all three parts (Figure 6). Serum sodium concentrations did not alter from pre to post dialysis or between any of the parts of the study.

![Figure 7. Reduction in serum osmolality during dialysis at three different dialysate flow rates. $Δ$ as in Figure 6. (Reprinted from reference 4, with permission of the editor of the American Society of Artificial Internal Organs)](image)

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Serum osmolality changes paralleled those of serum urea, rising progressively from part 1 to part 3, but with a similar drop during dialysis in each part (Figure 7).

The pre dialysis body weight was similar for each part of the study and the mean weight loss in each part averaged 2.0kg. The percentage increase in haematocrit in each part was similar — about 10%. However, there was a significant reduction in the incidence of symptomatic hypotension in part 3 compared with parts 1 and 2 (Figure 8).

![Graph showing incidence of symptomatic hypotension during dialysis at three different dialysate flow rates.](image)

Figure 8. Incidence of symptomatic hypotension during dialysis at three different dialysate flow rates. (Reprinted from reference 4, with permission of the editor of the American Society of Artificial Internal Organs)

These results suggested that the critical factor in the aetiology of symptomatic hypotension was not hypovolaemia or changes in serum osmolality.

Thus the fact that the use of a high dialysate sodium concentration has been associated with less hypotension and acutely with a smaller reduction in serum osmolality [5] does not necessarily mean that in a chronic study a smaller reduction of serum osmolality would be obtained. Furthermore, the mechanism by which sodium prevents hypotension is still not clear. Other osmotically active agents such as mannitol also help to reduce SH [6], however, the cure of a condition does not mean that the absence of the therapeutic agent was the cause of the condition.

A similar observation was also first reported in 1976 [7], when Quellhorst
described his initial clinical results with post dilution haemofiltration (HF). The similarity between the clinical response seen with UF and HF was intriguing. Subsequently haemodynamic studies have shown that the peripheral resistance increases to the same extent in both treatments [8], and even when HF is associated with a very high urea clearance (> 200ml/min) and the reduction in serum osmolality is identical to that seen with high efficiency haemodialysis the phenomenon still occurs [9]. In the latter study the changes in peripheral resistance during acetate or bicarbonate haemodialysis were compared to HF with acetate or bicarbonate replacement fluid. The urea clearances were the same in HD and HF, but the dialysate sodium was 145mmol/L whilst the replacement fluid for HF contained only 139mmol/L. In spite of this sodium difference the increase of peripheral resistance during HF was far more appropriate than that seen during HD (Figure 9). In addition this effect was independent of the use of acetate or bicarbonate. These results have been confirmed and associated with increases in circulating catecholamines during HF or UF but not during HD be it with acetate or bicarbonate (Figure 10) [8]. More recently, the peripheral resistance response seen with simultaneous HD and HF (haemodiafiltration) has been shown to be less appropriate than with HF alone [10]. In addition it has recently been shown that the Polycrylonitrile RP6 device produces more vascular instability when it is used as a dialyser, even with a high dialysate sodium, than when it is used as a haemofilter [11].

The explanation of the phenomenon of improved vascular stability during HF is still unknown. It cannot be due to the removal of a large molecular weight
Figure 10. Correlation of volume removal induced mean intratreatment change of total peripheral resistance (TPR) and plasma noradrenaline (PNA) during isolated ultrafiltration (UF), post dilution haemofiltration (HF) and acetate haemodialysis (HDA) and bicarbonate haemodialysis (HDB). (Derived from Baldamus et al, 1980, reference 8)
substance alone, as the convective solute removal during UF is no greater than when HD is performed with conventional UF rates. Furthermore, it has recently been suggested that large molecular clearances during clinical HF are exaggerated if the clearance in vitro using an aqueous solution is compared with that using a protein-containing solution [12]. This suggests that the phenomenon may be related to factors other than solute removal. The possibility of the protein caking causing selective sodium retention due to an increased Donnan effect is an attractive hypothesis that has recently been suggested [13]; however, the phenomenon also occurs in predilution HF [14] where this effect would be less evident. An alternative explanation might be that the protein cake seen with HF alters the biocompatibility of the membrane and prevents activation of enzymes which liberate vasodilator substances such as prostaglandins when blood normally comes in contact with cellulosic membranes in HD [15]. Thus although SH is clearly multifactorial in origin, biocompatibility may be a key factor which up till recently has received little attention.

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THE ROLE OF SODIUM IN THE PREVENTION OF VASCULAR INSTABILITY DURING HAEMODIALYSIS

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Introduction

Haemodialysis with increased sodium dialysate concentration is effective in reducing intradialytic morbidity [1—3]. Hypotensive episodes during haemodialysis are due primarily to excessive decrease in plasma volume [4,5]. This