LEUCOCYTE ELASTASE – A NEW MARKER OF BIOCOMPATIBILITY IN HAEMODIALYSIS
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Summary
Patients suffering from acute renal failure associated with septicaemia were compared to patients with chronic renal failure during haemodialysis. The fall of leucocytes during dialysis was markedly attenuated in septic patients with acute renal failure compared to patients with chronic renal failure. Plasma E-α₁ PI was dramatically enhanced in septic patients with acute renal failure prior to dialysis, whereas the intradialytic increase of E-α₁ PI was less in these patients compared to patients with chronic renal failure. Polysulfone membranes caused a lower degree of leucopenia and less release of leucocyte elastase than membranes made of cuprophan, both in patients with acute and chronic renal failure.

Introduction
During haemodialysis activation of leucocytes, either due to direct contact with the dialyser membrane or mediated by the complement system, may occur. Activated leucocytes display enhanced aggregability, resulting in marked neutropenia during haemodialysis [1]. Furthermore, activated leucocytes release large amounts of neutral proteinases, as was demonstrated for leucocytic elastase by Hörl et al [2]. This release of leucocyte elastase was found to depend strongly on the membrane material used for dialysis [3].

The present study evaluates neutropenia and the release of leucocyte elastase in patients suffering from acute and chronic renal failure during haemodialysis.

Methods
Twelve patients (9 males, 3 females) with acute renal failure aged 50.9±4.8 years (mean±SEM, range 18–74) entered the study. In all these patients acute renal failure was complicated by septicaemia. Dialysis was performed three to
four hours daily using hollow fibre dialysers made from cuprophan (Travenol 15–11, Deerfield, Illinois, USA) or polysulfone (F 60, Fresenius, Oberursel, FRG).

Nine chronically uraemic patients (1 female, 8 males), aged 48.8±1.4 years (mean±SEM, range 20–69), undergoing regular haemodialysis for 39.4±3.5 months acted as controls.

Whole blood samples were drawn from the patient’s arteriovenous fistula. Blood samples were obtained before and during haemodialysis. All samples were immediately anticoagulated with sodium citrate.

Plasma was separated within 30 minutes of collection, to prevent leakage of leucocyte constituents. The plasma specimens were stored at −30°C until assayed. Plasma elastase was measured as an elastase-α1 proteinase inhibitor complex (E-α1 PI) using a highly sensitive enzyme-linked immunoassay [4].

Blood cells were counted by an electronic counter (Coulter-Counter Model B).

Results

Routine laboratory findings in both groups of uraemic patients are shown in Table I. Patients suffering from acute renal failure with sepsis displayed higher haemoglobin, and higher leucocyte-, but lower thrombocyte-counts than patients with chronic renal failure.

Plasma creatinine was lower and BUN greater in patients with acute septic renal failure compared to patients with chronic renal failure.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Acute renal failure n = 12</th>
<th>Chronic renal failure n = 9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemoglobin (g/dl)</td>
<td>10.7±0.4</td>
<td>8.3±0.2†</td>
</tr>
<tr>
<td>Leucocytes (cells/mm³)</td>
<td>14,550±1,980</td>
<td>5,900±600†</td>
</tr>
<tr>
<td>Thrombocytes (cells/mm³)</td>
<td>78,500±10,800</td>
<td>183,000±18,000†</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>8.3±1.4</td>
<td>10.7±0.1*</td>
</tr>
<tr>
<td>BUN (mg/dl)</td>
<td>132±15</td>
<td>93±6*</td>
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</tbody>
</table>

Mean values±SEM
* p<0.05, † p<0.01 acute versus chronic renal failure

The effect of different membrane materials on the neutropenia in the early phase of haemodialysis in acute and chronic renal failure patients is shown in Figure 1.

As can be seen, there is profound neutropenia in chronic renal failure patients using cuprophan membranes (-68%). Whereas the initial neutropenia, seen with cuprophan membranes, is dramatically reduced (-23%) in patients on dialysis for acute renal failure. The polysulfone membrane caused less neutropenia both in patients with acute and chronic renal failure. Furthermore, the rebound
leucocytosis following the initial leucopenia of haemodialysis is more pronounced in patients with acute renal failure compared to patients suffering from chronic renal failure, notwithstanding the type of membrane used.

![Graph showing white cell count during haemodialysis](image)

**Figure 1.** White cell count during haemodialysis using cuprophan (○) and polysulfone (○) membranes in patients with acute (---) and chronic (----) renal failure

The different response of plasma E-α₁ PI during haemodialysis with cuprophan and polysulfone membranes in patients with acute and chronic renal failure can be seen in Figure 2. Patients with chronic renal failure have normal or slightly elevated plasma E-α₁ PI before dialysis. During dialysis with cuprophan, there is an enormous increase of E-α₁ PI up to 679±80ng/ml. This increase is markedly attenuated using polysulfone membranes for dialysing patients with chronic renal failure. On the other hand, patients suffering from acute renal failure display high values of E-α₁ PI in the range of 400ng/ml before dialysis treatment. With both membranes, the increase is less in patients, dialysing for acute renal failure. Again cuprophan membranes cause higher levels of E-α₁ PI than membranes made of polysulfone.

**Discussion**

In patients suffering from chronic renal failure, there is marked activation of leucocytes during haemodialysis with cuprophan membranes, resulting in
Figure 2. Plasma E-\( \alpha_1 \) PI during haemodialysis using cuprophan (●) and polysulfone (○) membranes in patients with acute (-----) and chronic (——) renal failure.

phenomena, such as neutropenia and release of leucocyte elastase. On the other hand, in patients with acute renal failure, complicated by sepsis, leucocytes are more numerous (Table I) and are already activated by the septic condition prior to haemodialysis. During haemodialysis, septic patients display less neutropenia in the early phase of the treatment compared to patients with chronic renal failure (Figure 1).

These data suggest that the aggregability of leucocytes in septic patients with acute renal failure is markedly attenuated. The use of polysulfone membranes for dialysis in these patients causes an even lower decrease of leucocytes (−9%). The rebound leucocytosis following haemodialysis-leucopenia is more pronounced in septic patients with acute renal failure compared to patients suffering from chronic renal failure.

As a second parameter of leucocyte activation, the release of leucocyte elastase was measured. Again leucocytes of septic patients with acute renal failure demonstrate striking differences compared to chronic renal failure patients before and during haemodialysis. Prior to dialysis septic patients with acute renal failure show a dramatic increase of E-\( \alpha_1 \) PI in the range of 400ng/ml, whereas patients suffering from chronic renal failure have only slightly elevated
E-α1 PI (normal range: 60–90ng/ml). However, the release of leucocyte elastase related to the dialysis procedure is markedly diminished in septic patients with acute renal failure compared to patients suffering from chronic renal failure. In general polysulfone membranes cause less liberation of leucocyte elastase than membranes made of cuprophan both in patients with acute and chronic renal failure.

References

1 Kaplow LS, Goffinet JA. *JAMA* 1968; 203: 1135