Hypercoagulability and Thrombotic Episodes in Uraemia

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Platelet function and blood coagulation tests were performed on 67 uraemic patients in six German haemodialysis centres. It was the purpose of the present investigation to define coagulation parameters in hypercoagulable patients with repeated thrombotic episodes.

METHODS
Recalcification time, fibrinmonomer test, determination of factor I, II, V, VII, VIII and X, thrombingeneration (v. Kaula) and platelet rotation test (Wright) were performed as described before (Andrassy et al, 1971).

RESULTS AND DISCUSSION
Studies of the plasma coagulation system have so far failed to show clear cut correlations between changes of the activity of plasma coagulation factors and the occurrence of a hypercoagulable state with thrombotic shunt complications (Quinton et al, 1962; Erickson et al, 1966).

In a study of 67 uraemic patients we found 11 patients (16.5%) with a history of fistula complications. Six of these patients (9% of all patients) had cloting at time of the study. Eight fistulae thrombosed within ten days of the operation, three fistulae thereafter. Confirming earlier reports, we found no definite pattern of plasma coagulation factors in uraemic patients with thrombosis of fistulae (with the exception of elevation of factor VIII). However, we found consistently higher platelet adhesiveness and pathologically increased thrombin generation tests compared with a non clotting uraemic control group. This finding is the more surprising since various parameters of platelet function are usually impaired in chronic renal insufficiency (Salzmann & Neri, 1966; Altschuler et al, 1960) — Tables I and II.

It is well known from the studies of Breddin that a group of individuals in the normal population show increased platelet adhesiveness. This group which is presumably composed of individuals with vascular disease seems
<table>
<thead>
<tr>
<th>Recalcification time</th>
<th>Fibrinogen (mg/100 ml)</th>
<th>Factor II (80-120%)</th>
<th>Factor VII (80-120%)</th>
<th>Factor V (80-120%)</th>
<th>Factor VIII (60-180%)</th>
<th>Factor X (60-120%)</th>
<th>Control patients</th>
<th>Uraemic patients without thrombotic episodes (n=56)</th>
<th>Uraemic patients with thrombotic episodes (n=11)</th>
<th>Difference of uraemic patients with and without thrombotic episodes (P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(70-120 sec)</td>
<td>81±147 sec*</td>
<td>93±237 sec</td>
<td>39±194 mg/100 ml</td>
<td>117±137 sec</td>
<td>105±29%</td>
<td>310±34%</td>
<td>210±34%</td>
<td>310±34%</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>(70-120 sec)</td>
<td>39±194 mg/100 ml</td>
<td>102±33%</td>
<td>102±33%</td>
<td>210±34%</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
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</tbody>
</table>

* given as ± SEM
Table II. Platelet function in uraemic patients with and without thrombosis of AV fistula (Cimino)

<table>
<thead>
<tr>
<th>Thrombin generation test</th>
<th>Platelet rotation test</th>
</tr>
</thead>
<tbody>
<tr>
<td>-</td>
<td>(25 - 50%)*</td>
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<tr>
<td>12.8 ± 4.3 sec**</td>
<td>21.7 ± 2.1%</td>
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<tr>
<td>8.9 ± 1.92 sec</td>
<td>65 ± 22%</td>
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<tr>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Control patients
Uraemic patients without thrombotic episodes (n=56)
Uraemic patients with thrombotic episodes (n=11)
Difference of uraemic patients with and without thrombotic episodes (p)

* percent platelets adhering to the glass surface
** given as X ± C

to have a high risk of thrombotic complications (e.g. coronary occlusion). Possibly the hypercoagulable group is composed of individuals from the above group who happened to have uraemia. Other mechanisms such as disturbance of the proactivator-activator system etc (Breddin et al, 1970) cannot be excluded. The changes observed seemed to play a causal role in the mechanism of thrombotic occlusion since clotting episodes in patients with Scribner shunts were constantly preceded by an episode of increased platelet adhesiveness and accelerated thrombin generation. Local factors in the anastomosis (especially turbulence) may also be involved, since in several patients platelet adhesiveness was shown to be higher in the venous part of the Cimino fistula.

Acetylsalicylic acid is known to diminish platelet adhesiveness. Therefore it seemed worthwhile to carry out a clinical trial on platelet adhesiveness in uraemia and its influence on fistula clotting. So far ten patients with increased platelet adhesiveness who had up to three unsuccessful fistula operations before acetylsalicylic treatment have now good fistula function after prophylactic therapy with acetylsalicylic acid (3 x 0.5 g/day). During haemodialysis serum levels were not in the toxic range (300 µg/ml). Significant clinical complications (particularly gastrointestinal bleeding) were not encountered with this dosage and with rigorous antacid therapy. A prospective study on the prevention of clotting episodes in hypercoagulable patients with increased platelet adhesiveness is currently under way.
REFERENCES