43. STUDIES OF PLATELET AGGREGATION IN DIABETIC COMA

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Previous studies have shown that diabetics may have enhanced platelet aggregation in response to adenosine diphosphate (ADP) (Colwell, 1973, Excerpta Medica I.C.S. 175, 383; Chambers, 1975, Federation Proceedings, 34, 481) and also enhanced platelet adhesiveness to foreign surfaces. It has been suggested that both long-term complications, e.g. glomerulosclerosis and retinopathy, and short-term complications, e.g. cerebral and vascular complications of diabetic coma, can arise secondary to this phenomenon (Rathbone, 1970, Pathology, 2, 307; Szirtes, 1970, Advanced Cardiology, 4, 179; Kwaan, 1971, Journal of Clinical Investigation, 50, 57a; Heath, 1971, Diabetologia, 7, 308; Kwaan, 1972, Diabetes, 21, 108; Timberley, 1974, Lancet, i, 952).

Platelet aggregation in response to 5-hydroxytryptamine (5HT) and ADP was studied in diabetic patients: (a) presenting in coma, (b) in those well controlled by diet alone, oral agents or insulin. Aggregation was measured as a change in optical density in platelet rich plasma (PRP) and results expressed as rate velocity (uv/min) to 5HT, % rate aggregation 5HT/ADP and % area 5HT/ADP response.

Non-diabetic controls have a 10% incidence of abnormal platelet function as determined by enhanced aggregation rate and irreversibility of response. All twelve diabetic coma subjects exhibited abnormal responses during the period studied. Most were investigated on at least four occasions—usually before treatment of the coma and then on alternate days. Such a group have never previously been studied, especially in response to 5HT.

In one patient a minor subclinical episode of disseminated intravascular coagulation (DIC) was observed which spontaneously subsided after 3 days. Of the twenty-three well-controlled diabetics, seventeen (i.e. 74%) exhibited abnormal responses—the majority being treated by oral agents or insulin. There was no correlation with length of diabetic history but the majority of those with complications (nine patients) gave abnormal responses.

44. THE URIC ACID PROFILE OF REMISSION IN ACUTE MYELOID LEUKAEMIA

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Hyperuricaemia has been frequently associated with acute leukaemia. A recent study (Mir & Delamore, 1974, British Medical Journal, iii, 775) has shown that this relationship does not apply to acute myeloid leukaemia (AML) and that hypouricaemia, due to incomplete tubular reabsorption of urate, may be a frequent complication in this disease. It is not clear if this variable reabsorption of urate by the renal tubule is a mechanism invoked by the kidney to eliminate excess acid released from leukaemic cells. This study was undertaken to investigate this component of urinary urate excretion, and to examine the renal mechanism for urate homeostasis in various stages of acute myeloid leukaemia.

Eleven unselected patients with AML and variants admitted to the sixth M.R.C. trial on AML, and seven normal subjects were studied. Complete renal clearance studies, before and after pyrazinamide to estimate separately the tubular secretion and reabsorption of urate, were carried out on admission in all patients, at remission in five patients, and in two of these in relapse.

The mean urinary excretion in leukaemic patients was 0.774 ± 0.057 mg/min (SEM) at a mean serum urate level of 4.16 ± 0.54 mg/100 ml. This was significantly higher (P<0.005) than the mean uric acid excretion rate of 0.595 ± 0.035 mg/min obtained from forty-three normal studies, including some after RNA feeding, at a mean serum urate level of 0.63 ± 0.27 mg/100 ml. The fractional urate excretion (FUR urate), the percentage of urate excreted during maximal suppression of tubular secretion of urate (Cure/Cur after pyrazinamide), was 2 ± 0.2% in seven normal subjects as compared with 12.68 ± 2.16% after chemotherapy in leukaemic patients (P<0.001). FUR urate tended to increase variably during leukaemic activity, lowering the serum urate level, but tubular secretion of uric acid (TSs,) showed a more predictable relationship to the urate load, which itself appeared to be related to the tumour cell mass in the body. Thus the level of serum urate was determined by both TSs, and FUR urate. This altered the normally direct dependance of serum urate on TSs, to an inverse relationship, creating a broadly distinguishable urate profile of leukaemic relapse and remission. Based on this, a tolerance ellipse was constructed representing the remission 'zone', with its major axis showing the direction of remission, and a leftward shift along the minor axis indicating relapse.

45. SERUM URIC ACID CHANGES FOLLOWING ACUTE MYOCARDIAL INFARCTION

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University of Cambridge, and Addenbrooke's Hospital, Cambridge

Although hyperuricaemia has frequently been reported in patients with coronary heart disease, no report is as yet available of the serial changes in serum uric acid concentration following an acute myocardial infarction. This study was undertaken to investigate these changes in successive patients admitted to a coronary care unit at Addenbrooke's Hospital, Cambridge, England, over a period of 6 months. There were seventy patients with definite evidence of myocardial infarction (W.H.O. Criteria, 1959) and twenty-three patients with evidence of ischaemic changes only. Serum uric acid, creatinine, and aspartate transaminase concentrations were measured on the first, fourth, seventh and fourteenth days after admission.

The mean serum uric acid concentration of the infarct group was significantly higher than that in the ischaemic group on all the days tested (Table 1). There was also a significant rise in the serum uric acid level between the first and seventh day in the former group, but no significant change in the latter. The highest serum uric acid
### Table 1. Serum uric acid concentration (mg/100 ml)

<table>
<thead>
<tr>
<th></th>
<th>First day</th>
<th>Fourth day</th>
<th>Seventh day</th>
<th>Fourteenth day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infarct group (n = 70)</td>
<td>5.83*</td>
<td>6.27**</td>
<td>6.39**</td>
<td>6.31**</td>
</tr>
<tr>
<td></td>
<td>±0.17</td>
<td>±0.24</td>
<td>±0.21</td>
<td>±0.20</td>
</tr>
<tr>
<td>Ischaemic group (n = 23)</td>
<td>4.79*</td>
<td>4.60**</td>
<td>4.63**</td>
<td>4.65**</td>
</tr>
<tr>
<td></td>
<td>±0.25</td>
<td>±0.24</td>
<td>±0.20</td>
<td>±0.30</td>
</tr>
</tbody>
</table>

Results expressed in mean± SEM.
* P<0.005; ** P<0.001.

### Table 2. Serum uric acid concentration (mg/100 ml) in acute myocardial infarction

<table>
<thead>
<tr>
<th></th>
<th>First day</th>
<th>Fourth day</th>
<th>Seventh day</th>
<th>Fourteenth day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diuretics group (n = 38)</td>
<td>5.95</td>
<td>6.87*</td>
<td>6.58</td>
<td>6.42</td>
</tr>
<tr>
<td></td>
<td>±0.25</td>
<td>±0.36</td>
<td>±0.31</td>
<td>±0.27</td>
</tr>
<tr>
<td>Non-diuretics group (n = 32)</td>
<td>5.72</td>
<td>5.50*</td>
<td>6.19</td>
<td>6.19</td>
</tr>
<tr>
<td></td>
<td>±0.21</td>
<td>±0.26</td>
<td>±0.30</td>
<td>±0.31</td>
</tr>
</tbody>
</table>

Results expressed in mean± SEM.
* P<0.01.

concentration correlated with the Norris index -- severity of infarction (r = 0.302, \( P<0.01 \)) but not with the highest aspartate transaminase level (r = 0.108, \( P>0.05 \)).

The raised serum uric acid concentration could be due either to increased production or decreased excretion. The former seems unlikely as there was no correlation with aspartate transaminase (indicating myocardial necrosis). The significant rise in serum creatinine and its correlation with uric acid suggests that decreased excretion may be responsible. In the infarct group the serum uric acid concentration was higher in those receiving diuretics (thirty-eight patients) indicating that these drugs cause some increase in uric acid (Table 2). However, in both groups the serum uric acid concentration was higher than that in the ischaemic group, suggesting other mechanisms, possibly lactic acidemia, increased acetoacetate and/or β-hydroxybutrate concentration, may play a part by altering the renal handling of uric acid. These organic acids are thought to share a common secretory mechanism with uric acid and may produce hyperuricaemia by competing with uric acid for this secretory site. The possible significance of this data will be discussed.

### 46. DIABETES OF ACUTE MYOCARDIAL INFARCTION

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Edelmann (1934, *Weiner Klinische Wochenschrift, 47*, 165) and others have described disturbance of carbohydrate metabolism following myocardial infarction, but there have been few reported metabolic-clinical correlations. However, Wahlberg (1966, *Acta Medica Scandinavica*, Supplement 453, 1) found an association between survival after varying periods and carbohydrate intolerance assessed by an intravenous glucose tolerance test (IVGTT) performed from 3 weeks to 5 months after infarction.

In the present study, circulating concentrations of insulin and intermediaries of carbohydrate and lipid metabolism were measured on admission, and during the first few days following acute myocardial infarction. An IVGTT was performed on post-infarction days 7, 8 or 9. Acute infarction was verified by pre-set criteria and the course of illness followed clinically, enzymatically and electrocardiographically. All known diabetics were excluded.

A substantial number of patients had ‘diabetic type’ metabolic impairment, sometimes to a severe degree. Of the thirty patients analysed, eighteen had IVGTT \( K_g \) values below 1.25 (i.e. diabetic-like) and twelve above, while morning blood sugars on day 2 ranged from 65 to 145 mg/100 ml in both groups. Clinical features assessed included (1) evidence of left ventricular ‘failure’ and (2) significant dysrhythmias, e.g. multifocal, coupled or R-on-T ventricular ectopics, ventricular or supraventricular tachycardias, atrial or ventricular fibrillation, and heart and bundle branch blocks. These clinical features occurred more frequently in association with carbohydrate intolerance. Thus of the twelve patients with higher \( K_g \) values only two had these features, while of the other eighteen patients, sixteen had clinical disturbances (including one death and two resuscitations).

These observations re-open the possibility of benefit from insulin treatment in that proportion of patients with