Platelet adhesiveness, coagulation, and fibrinolytic activity in obesity

C. P. WARLOW, A. McNEILL, D. OGSTON, AND A. S. DOUGLAS

From the Department of Medicine, University of Aberdeen

SYNOPSIS In a study of 41 fasting subjects it was confirmed that fibrinolytic activity was reduced in obese persons: an increase in fibrinogen was also associated with obesity. There was no correlation between obesity and the platelet count, platelet adhesiveness to glass, the level of serum fibrin degradation products, or the whole blood clotting time in plastic tubes.

Obesity has been incriminated in the pathogenesis of occlusive coronary artery disease (Dawber, Moore, and Mann; 1957; Stamler, Lindberg, Berkson, Shaffer, Miller, Poindexter, Colwell, and Hall, 1960) and venous thromboembolic disease (Vessey and Doll, 1969; Kakkar, Howe, Nicolaides, Renney, and Clarke, 1970). In this study a number of haemostatic parameters, including platelet adhesiveness, fibrinolytic activity, and the clotting time in plastic tubes, have been measured in subjects of varying obesity.

Methods and Subjects

PLASMINOGEN ACTIVATOR
This was assayed by performing euglobulin clot lysis times by the method of Nilsson and Olow (1962). The results are expressed by plotting the times logarithmically against units of fibrinolytic activity (Sherry, Lindemeyer, Fletcher, and Alkjaersig, 1959), 10 units being arbitrarily equated with a lysis time of 50 minutes. Times of over 500 minutes were assigned a value of 1 unit for the purpose of calculation.

Plasminogen activator was also measured by placing 30 μl of resuspended euglobulin precipitation on fibrin plates prepared from 0.2% human fibrinogen (grade L, AB Kabi, Stockholm). After incubation at 35°C for 24 hours the area of lysis was estimated from the product of two diameters at right angles to each other.

A partially purified preparation of urokinase (Leo Pharmaceutical Products, Ballerup, Denmark) was used as a reference standard. The areas of lysis produced by the urokinase standard dilutions were plotted on a log-log scale and the fibrinolytic activity of the euglobulin precipitate obtained by extrapolation and expressed as Ploug units of urokinase (Ploug and Kjeldgaard, 1957).

PLASMA FIBRINOGEN
Plasma fibrinogen was measured by a modification (Ogston and Ogston, 1966) of the method of Ratnoff and Menzie (1951).

DEGRADATION PRODUCTS
Serum fibrin degradation products were assayed by the method of Merskey, Kleiner, and Johnson (1966) with minor modifications outlined by Bonnar, Davidson, Pidgeon, McNicol, and Douglas (1969).

PLATELET ADHESIVENESS
This was measured by a modification of the method of Payling Wright (1941). Blood was withdrawn with a polypropylene syringe and mixed with 1 vol of 3.8% sodium citrate in a polypropylene tube. After standing for 60 minutes rotation at 3 1/2 rpm in a glass bulb was started. A platelet count was made before and after rotation for 20 minutes. Platelet adhesiveness was taken as the difference in the platelet count expressed as a percentage of the pre-rotation count.

Subjects
Forty-one healthy volunteers and patients attending an obesity clinic comprised the subjects of this study. There were eight men and 33 women. Apart from obesity all were in good health. None had fluctuated markedly in weight in the weeks before testing. All subjects had fasted for 12 hours and none were taking any drugs known to influence haemostatic...
Platelet adhesiveness, coagulation, and fibrinolytic activity in obesity

The percentage of platelets lost after rotation of the samples of citrated blood was higher in the obese subjects, but the differences did not reach statistical significance. In addition, the correlation between observed/standard weight ratio and platelet adhesiveness was not significant ($r = 0.061; p > 0.1$).

The mean platelet count did not differ significantly between the obese and non-obese groups.

**Discussion**

The association of decreased plasma fibrinolytic activity with obesity has been noted by several investigators (Goldrick, 1961; Shaw and McNaughton, 1963; Ogston and McAndrew, 1964; Grace and Goldrick, 1968). The reduction in plasminogen activator levels, as assessed on fibrin plates, indicates that low fibrinolytic activity in obese subjects is not due to substrate differences in the euglobulin precipitate. The finding of increased fibrinogen levels in obese persons confirms previous observations (Ogston and McAndrew, 1964; Bennett, Ogston, McAndrew, and Ogston, 1966; Grace and Goldrick, 1968).

The mechanism of the low plasma fibrinolytic activity in obese persons has not been elucidated. It is not due to alteration in the level of inhibitors of the fibrinolytic enzyme system (Bennett et al, 1966), and the release of plasminogen activator response to venous stasis has been found to be normal (Grace, 1968). In spite of the low fibrinolytic activity the obese subjects had a normal level of fibrin degradation products, suggesting a normal mechanism for the removal of fibrin deposits. Relevant to this finding are the observations of Grace and Goldrick (1969) that tissue activation levels are normal in obese persons.

The effect of obesity on platelet adhesiveness has not, to our knowledge, been studied previously. Although the rotating bulb technique used in this study has a number of inherent disadvantages, it has demonstrated increased platelet adhesiveness in situations associated with an increased incidence of venous or arterial thrombosis. Examples include the postoperative period (Wright, 1942; Bennett, 1967; Ham and Slack, 1967; Negus, Pinto, and Brown, 1969), ischaemic heart disease (McDonald, Bray, and Edgill, 1958), and homocystinuria (McDonald, Bray, Field, Love, and Davies, 1964). We have, however, been unable to demonstrate an alteration in platelet adhesiveness in obese persons. In addition, in agreement with Grace, Sinnett, and Whyte (1970)

**ASSESSMENT OF OBESITY**

The ratio of the observed to standard weight was calculated from the weight-for-height standard of Kemsley, Billewicz, and Thomson (1962). No age adjustments were made.

**Results**

**FIBRINOLYTIC ACTIVITY**

Circulating plasminogen activator levels were assayed by two techniques. The measurement of activator by the euglobulin clot lysis time method may be influenced by variations in the concentration of other components of the euglobulin precipitate, in particular, fibrinogen and plasminogen. The fibrin plate technique avoids this possible source of error by the use of an exogenous substrate. The Table shows that the mean plasminogen activator levels, assayed by both techniques, were significantly reduced in the obese persons, and it is concluded that the increased fibrinogen concentration is not the explanation for the decreased activator levels. It may be noted that, in spite of the reduced activator levels in the obese groups, the level of serum fibrin degradation products did not differ significantly between the groups.

<table>
<thead>
<tr>
<th>Observations/Standard Weight Ratio</th>
<th>91-120 (n = 12)</th>
<th>121-150 (n = 17)</th>
<th>151-190 (n = 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (yr)</td>
<td>33.8</td>
<td>38.8</td>
<td>38.2</td>
</tr>
<tr>
<td>Plasminogen activator</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Euglobulin lysis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>time (units)</td>
<td>4.3 ± 1.6</td>
<td>2.7 ± 1.5</td>
<td>1.9 ± 1.2</td>
</tr>
<tr>
<td>Fibrin plate (units)</td>
<td>1.08 ± 0.53</td>
<td>0.66 ± 0.42</td>
<td>0.27 ± 0.14</td>
</tr>
<tr>
<td>Fibrinogen (mg/100 ml)</td>
<td>326 ± 39</td>
<td>356 ± 61</td>
<td>363 ± 39</td>
</tr>
<tr>
<td>Fibrin degradation products</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(µg/ml)</td>
<td>2.4 ± 3.0</td>
<td>2.9 ± 2.4</td>
<td>1.4 ± 1.9</td>
</tr>
<tr>
<td>Platelet adhesiveness (%)</td>
<td>31 ± 8.5</td>
<td>38 ± 8.4</td>
<td>37 ± 10.7</td>
</tr>
<tr>
<td>Platelet count (x 1000 mm²)</td>
<td>231 ± 44</td>
<td>223 ± 50</td>
<td>209 ± 34</td>
</tr>
</tbody>
</table>

Table: Mean changes with SD in fibrinolytic activity, fibrinogen, fibrin degradation products, platelet adhesiveness, and platelet count in obese and non-obese groups

Significance of differences from means of O/S ratio 91-120 group: $^{1}p < 0.05$, $^{2}p < 0.01$, $^{3}p < 0.001$.

**PLATELET ADHESIVENESS**

But...
we have found no relationship between obesity and overall measurements of blood coagulability.

Measurements of platelet adhesiveness to glass and the whole blood clotting time in plastic tubes lack sensitivity and have limitations as indicators of a prethrombotic state. In consequence, definite conclusions on the role of platelet adhesiveness and coagulation in the mediation of the relationship between obesity and thrombosis cannot be made. Our results would suggest, however, that alteration in fibrinolytic activity may be a more important factor in this relationship.

These studies were made possible by the technical assistance of Mrs Helen Lee and Mrs Naomi Hoogstadt. We are indebted to those members of the Aberdeen Silhouette Slimming Club who volunteered to take part in this study.

References
Platelet adhesiveness, coagulation, and fibrinolytic activity in obesity
C. P. Warlow, A. McNeill, D. Ogston and A. S. Douglas

doi: 10.1136/jcp.25.6.484

Updated information and services can be found at:
http://jcp.bmj.com/content/25/6/484

**Email alerting service**
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

**Notes**

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/