

Studies on the fibrinolytic enzyme system in obesity

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SYNOPSIS Plasma fibrinolytic activity, inhibitors of fibrinolysis, and fibrinogen were estimated in 34 subjects of varying ratio of observed to standard weight. The inverse relationship between fibrinolytic activity and the ratio of observed to standard weight was confirmed. No significant correlation was found between anti-plasmin or anti-urokinase and the ratio of observed to standard weight. It was therefore concluded that the decreased plasma fibrinolytic activity in obese subjects is due to decreased production of plasminogen activator rather than to excessive inhibition.

Several investigators have shown that blood fibrinolytic activity is diminished in obesity (Goldrick, 1961; Shaw and MacNaughton, 1963; Fearnley, Chakrabarti, and Avis, 1963). We have previously reported a study confirming that fibrinolytic activity is reduced in obese subjects and showing that this reduction is not due to plasminogen deficiency (Ogston and McAndrew, 1964). We have examined a further group of subjects of varying observed/standard weight ratio to determine the role of inhibitors of fibrinolysis in this reduction.

METHODS AND MATERIALS

PLASMA FIBRINOLYTIC ACTIVITY Euglobulin clot lysis times were estimated by the method of Nilsson and Olow (1962) and expressed by plotting the values 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 taken as 1 unit. Such a technique has been shown to correlate well with specific assays of plasminogen activator (Fletcher, Biederman, Moore, Alkjaersig, and Sherry, 1964).

PLASMA FIBRINOGEN Fibrinogen was assayed by a modification of the method of Ratnoff and Menzie (1951).

ANTI-PLASMIN Anti-plasmin was estimated by the technique of Alkjaersig, Fletcher, and Sherry (1959) using activator-free plasmin prepared by auto-activation of plasminogen in 50% glycerol. The plasminogen used to prepare the plasmin was obtained from Kabi Pharmaceuticals Ltd.

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PLASMINOGEN-ACTIVATOR INHIBITOR This inhibitor was measured by determining the power of serum to inhibit lysis of a standard clot by the plasminogen-activator urokinase. The results are expressed as units of urokinase inhibited by the serum sample under the conditions of the assay. The urokinase was obtained from Leo Laboratories Ltd.

ASSESSMENT OF OBESITY The ratio of observed to standard weight was calculated from the weight-for-height standards of Kemsley, Billewicz, and Thomson (1962).

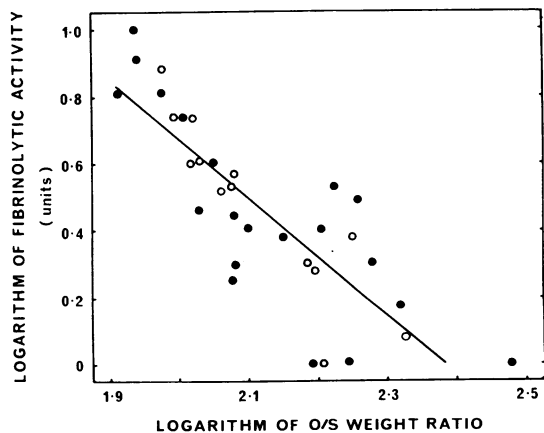


FIG. 1. Relationship between fibrinolytic activity and observed/standard weight ratio (regression $y = 4.17 - 1.75x$)

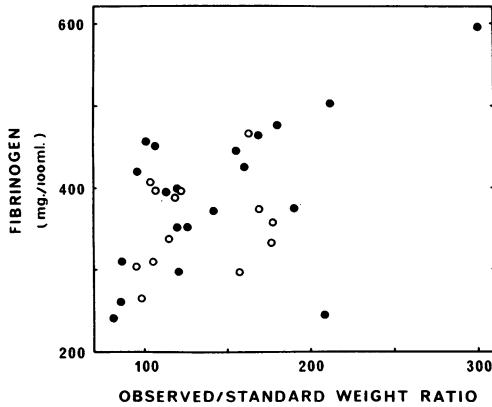


FIG. 2. Relationship between plasma fibrinogen and observed/standard weight ratio.

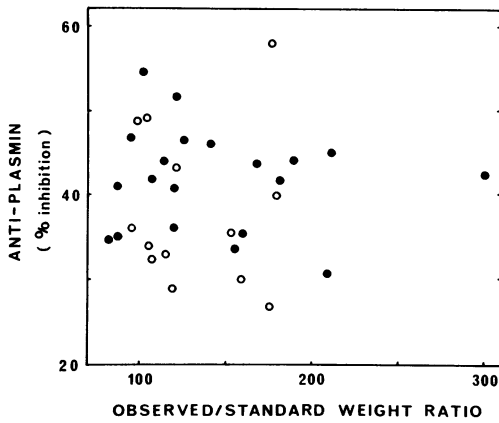


FIG. 3. Relationship between anti-plasmin and observed/standard weight ratio.

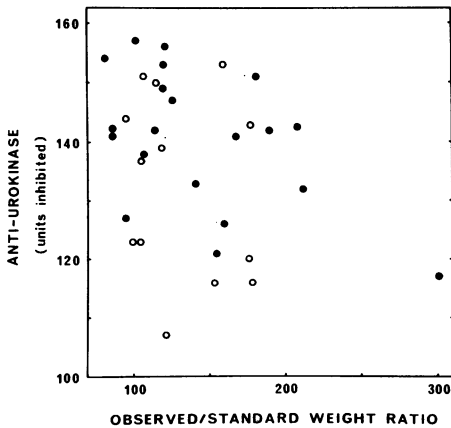


FIG. 4. Relationship between anti-urokinase and observed/standard weight ratio.

SUBJECTS The 34 subjects (14 males and 20 females) studied consisted of convalescent hospital patients with minor disorders and patients admitted to hospital for weight reduction. In two of these subjects all the estimations were not performed. The age range was 16-78 years (mean 46). All were confined to bed for at least 12 hours before venepuncture which was carried out between 8 and 9 a.m.

RESULTS

The relationship between fibrinolytic activity and the observed/standard weight ratio was curvilinear; the logarithmic transformation is shown in Fig. 1. This is a highly significant linear relationship ($r = -0.82$; $p < 0.001$). Figure 2 shows the correlation between plasma fibrinogen and the O/S weight ratio ($r = +0.51$; $p < 0.01$). The relationship between fibrinolytic activity and fibrinogen level was less marked ($r = -0.39$; $p < 0.05$).

Figures 3 and 4 present the anti-plasmin and anti-urokinase levels plotted against the O/S weight ratio. No relationship was present: for anti-plasmin $r = +0.02$ ($p < 0.1$); for anti-urokinase $r = -0.06$ ($p < 0.1$). It is concluded that obesity is not associated with increased blood levels of inhibitors of fibrinolysis.

CONCLUSION

In this study we have confirmed that blood fibrinolytic activity, measured by the euglobulin clot lysis time, is reduced in obesity (Ogston and McAndrew, 1964) and have again found some association between obesity and increased plasma fibrinogen levels. The euglobulin lysis time is primarily a measure of plasminogen activator since the inhibitors of fibrinolysis, anti-plasmin, and probably anti-activator (Bennett, 1965) are not included in the euglobulin fraction. We have found that there is no increase in anti-plasmin or anti-urokinase (used as a measure of anti-activator) in the blood of obese subjects.

Until more information about activator inhibitors is available, we conclude that the low blood fibrinolytic activity found in obesity is due to decreased production of plasminogen activator rather than to excessive inhibition.

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