naturally or as the result of therapy supports this view. In evaluating the usefulness of one or other type of therapy to promote thrombolysis, a significant percentage of failures is to be expected.

REFERENCES

Dalal, P. M., Shah, P. M., Sharp, A. A., and Allington, M. J. (1969). To be published.

RECENT PROGRESS IN THROMBOLYTIC THERAPY

A. AMERY, J. VERMYLEN, AND M. VERSTRAETE (*Leuven University, Belgium*) This study compares the effect on fibrinogen and plasminogen levels of the infusion of a high (1,200,000 units) and medium (250,000 units) standardized initial dose of streptokinase. In both groups the administration of the initial dose was followed by a continuous infusion of 100,000 units of streptokinase per hour.

Immediately after the initial dose of 1,200,000 units of streptokinase, the plasma plasminogen was already below 1% of the normal value in half the patients. No significant further change in the distribution was found in samples withdrawn after 24 hours of maintenance therapy; at that time the plasma plasminogen concentration was below 1% of the normal value in 48% of the patients and below 5% of the normal value in 93% of the patients.

Immediately after the initial dose of 250,000 units of streptokinase the plasma plasminogen level was below 1% of the normal value in only 13% of the patients. Nevertheless, after 24 hours of maintenance therapy, the plasminogen level had reached values which were practically identical to those observed following the high initial dose; in 55% of the patients the plasma plasminogen level was less than 1% and in 86% of the patients less than 5% of the normal value.

The changes of the fibrinogen levels, as observed with the fibrin polymerization time test, also showed some interesting differences. When 1,200,000 units of streptokinase were given as the initial dose, there was a very marked drop of the fibrinogen level but after 24 hours' maintenance therapy there was a significant increase. When 200,000 units of streptokinase were infused there was a smaller immediate fall of the fibrinogen level but after 24 hours' maintenance therapy it had decreased still further. It should be emphasized that the biological fibrinogen assay used in this study is influenced not only by the actual fibrinogen level but also by the presence of those fibrinogen degradation products which interfere with polymerization.

PLASMIN, PLASMIN INHIBITORS, AND DEGRADATION PRODUCTS OF FIBRINOGEN IN HUMAN SERUM DURING AND AFTER INTRAVENOUS INFUSION OF STREPTOKINASE

INGA MARIE NILSSON (*Coagulation Laboratory, University of Lund, Malmö, Sweden*) The variation of plasminogen, plasmin, plasmin inhibitors, fibrinogen, and its split

products has been studied in sera from patients before, during, and after a 24-hour intravenous infusion of streptokinase. The amounts of α_1 -macroglobulin, α_2 -antitrypsin, and degradation products of fibrinogen in the serum have been estimated by immunological techniques. To separate plasminogen from an assumed complex between inhibitors and plasmin, sera were fractionated by gel-filtration in Sephadex G 200 and the eluted fractions were examined immunologically with specific antisera for the presence of plasminogen, plasmin, α_2 -macroglobulin, or α_1 -antitrypsin. The thrombin inhibiting capacity of the fractions was also estimated.

It has been found that practically all plasminogen activated to plasmin within the first hours of the infusion. The plasmin was recovered mainly as a complex with the 'immediate inhibitor', *ie*, α_2 -macroglobulin. This complex was almost completely eliminated within 24 hours, during which time the α_2 -macroglobulin in serum decreased by about 50%. Alpha₂-macroglobulin did not recover its initial level until three to four weeks after the infusion. The plasminogen recovered its original concentration within about 48 hours. No complex formation could be demonstrated between plasmin and the slow inhibitor, *ie*, α_1 -antitrypsin. Alpha₁-antitrypsin increased markedly after the infusion of streptokinase. The thrombin-inhibiting capacity of the macroglobulin fractions after gel filtration varied mainly with the concentration of α_2 -macroglobulin, while the inhibiting capacity of the fractions containing albumin was almost unchanged during the infusion of streptokinase. The concentration of the degradation products was highest four hours after the beginning of the infusion. Only trace amounts were demonstrable 24 hours after the end of the infusion.

In our earlier investigations we questioned whether the 'intrinsic clot lysis' theory alone can explain the dissolution mechanism of thrombi *in vivo* (Hedner, Nilsson, and Robertson, 1966). We found no difference between the plasminogen content of plasma and that of serum, and our experiments argue against plasminogen being adsorbed to the fibrin during clot formation. Also in thrombi, we found the plasminogen values to be very low. Most workers administer large doses of streptokinase in order to suppress the plasminogen to a very low level and thereby prevent plasmin formation but we wonder whether it is not possible to get active plasmin. Plasminogen is synthesized very rapidly, and even if it is suppressed to almost nil, plasminogen will continuously be produced and there will be at least some plasminogen present during therapy. The most important antiplasmin, α_2 -macroglobulin, decreased rapidly in the beginning of the streptokinase infusion and unlike most other proteins it is synthesized very slowly, in the course of three to four weeks. This means that even if the plasminogen level is low during therapy, the plasmin formed on activation is not inactivated by α_2 -macroglobulin and may help to cause thrombolysis by its adsorption to fibrin.

REFERENCE

Hedner, U., Nilsson, I. M., and Robertson, B. (1966). *Thromb. Diath. haemorrh.* 16, 38.