DEPRESSION OF COLLATERAL BLOOD FLOW FOLLOWING ARTERIAL THROMBOSIS. R.G. Schnitzler and E.M. Hayworth.

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Permanent ligation of the feline aorta at the iliac bifurcation is followed by rapid opening of pre-existing collateral blood vessels. However, if ligation is combined with formation of atherosclerotic plaques, the collateral vessels do not function. This study was undertaken to determine if prostaglandin (PGF2α) treatment can improve collateral blood flow after arteriolar thrombosis. Permanent ligations were placed at the iliac bifurcation, circumflex iliac and sixth lumbar arteries in all cats. Control cats (8) were acutely ligated. In all other cats a clot was produced in the aorta by injection of 0.1 ml of thromboplastin. Clotted cats were untreated (8); had blood 5-HT depleted using a single dose of serotonin (1 mg/kg i.v.) followed by para-chlorophenylalanine (p-CBA) (100 mg/kg orally) every 3 days (9); or were treated prior to surgery with a 5-HT antagonist, cinanserin HCl (6 mg/kg i.v.) (6). Collateral circulation was determined by blood flow measurements and arterograms 3 days after occlusion of the aorta. The hindlimb blood flow of untreated clotted animals was 20% of the acutely ligated control animals 3 days following surgical occlusion. However, hindlimb blood flow was 90% of control in reserpine and p-CBA treated cats and 80% of control in cinanserin HCl treated cats. Blood flow measurements were not correlated with arterograms. These results suggest: (1) The clinical consequences of arterial thrombosis cannot be entirely attributed to mechanical occlusion of an artery, but may be due to depression of protective collateral blood flow induced by thrombosis; (2) Serotonin is an important factor in this depression of collateral blood flow, and (3) Isolation of the factors responsible for collateral inactivation could permit the development of therapeutic intervention.


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The influence of cross-linking upon the kinetics of fibrinolysis has been studied in an in vitro system by monitoring the release of radioactive label, peptide materials, fragment X and D-dimer. Cross-linked (XL) and non-cross-linked (NXL) fibrin clots were prepared by clotting citrated plasma containing 25-i labelled fibrinogen with human thrombin. In the presence of the protease kinetically irreversible 25000M CaCl2 or 2M EDTA, and incubating for 2 hours at 37°C. After washing, clots were placed in buffer containing human plasminogen (glu- or lys-) in concentrations ranging from 0 to 200000 units per ml. Clots were transferred after 30 minutes to a solution of streptokinase (100000 units per ml) and the supernatants subsampled serially for 4 hours. NXL fibrin lysed progressively and sometimes completely. Maximal lysis rates were achieved with intermediate concentrations of plasminogen. XL fibrin lysed slowly and rapidly in a manner only after exposure to the higher concentrations of lys-plasminogen. XL-fibrin lysed more readily after exposure to glu-plasminogen than to lys-plasminogen. Analysis of the residues in XL fibrin clots by SDS-polyacrylamide electrophoresis revealed the presence of a small residual of NXL fibrin and incomplete cross-linkage of e chains. The NXL component lysed preferentially in streptokinase and the terminal clots contained only XL fibrin. Parallel effects may operate in vivo. The data support the contention that fibrinolytic mechanisms readily deal with NXL fibrin, and that only fibrin which has been XL occurs in thrombi and is of pathologic significance.


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In patients with pulmonary emboli, resolution has been shown to be more rapid in those receiving urinary urokinase than in those receiving heparin alone. A different source of urokinase has been shown to be more rapid in its effect on pulmonary embolism, namely human kidney cells grown in tissue culture. In a randomized, multicenter trial, two groups of 15 patients with pulmonary embolism received either the urinary or tissue culture urokinase. Blood samples prior to, during and after treatment were compared with regard to biochemical changes in the plasma fibrinolytic system. Both agents caused strikingly similar rates, degrees and durations of response as reflected in the whole blood euglobulin lysis time, urinary fibrin plate lysis zones, 125-I tagged clot lysis, plasma plasminogen, plasma clotting protein and serum fibrinogen degradation products. Bleeding occurred in about 50% of both groups of patients, primarily from cutaneous sites. The results indicate that the pharmacologic effect of tissue culture urokinase is the same as that of urinary urokinase, and it is reasonable to expect that both materials will be equally effective in the hemodynamic and clinical aspects of patients with pulmonary embolism.