DEPRESSION OF COLLATERAL BLOOD FLOW FOLLOWING ARTERIAL THROMBOSIS. R.G.Schaub* and K.M.Meyers+ *Temple University Health Sciences Center, Philadelphia, PA and +Washington State University, Pullman, WA

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 a clot these protective collateral vessels do not function. This study was undertaken to determine if drugs which alter serotonin (5-HT) function can improve collateral blood flow after arterial 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 reserpine (0.1 mg/kg i.m.) followed by para-chlorophenylalanine (p-CPA) (100 mg/kg orally) every 3 days (9); or were treated prior to surgery with a 5-HT antagonist cinanserin HCl (4 mg/kg i.v.) (8). Collateral circulation was determined by blood flow measurements and aortograms 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 aortic occlusion. However, hindlimb blood flow was 90% of control in reserpine and p-CPA treated cats and 60% of control in cinanserin HCl treated cats. Blood flow measurements correlated with aortograms. 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 inhibition could permit the development of therapeutic interventions.

THE INFLUENCE OF CROSS-LINKING AND PLASMINOGEN ON KINETICS OF FIBRINOLYSIS. A.N. Whitaker and P.G. Gaffney. Department of Medicine, University of Queensland, Brisbane Australia and National Institute for Biological Standards and Control, Holly Hill, London, England.

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 125-I labelled fibrinogen with human thrombin, in the presence respectively of 40 mM Ca Cl2 or 2 mM 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 10 caseinolytic units per ml. Clots were transferred after 30 minutes to a solution of streptokinase (1000 units per ml) and the supernatants subsampled serially for 3 hours. NXL fibrin lysed progressively and sometimes completely. Maximal lysis rates were achieved with intermediate concentrations of plasminogen. XL fibrin lysed slowly and significant lysis was obtained 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 chains in XL fibrin clots by SDS-polyacrylamide electrophoresis revealed the presence of a small residuum of NXL fibrin and incomplete cross-linkage of α 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.

COMPARISON OF IN VIVO BIOCHEMICAL EFFECTS OF HUMAN UROKINASE PREPARED FROM URINARY AND TISSUE CULTURE SOURCES. Victor J. Marder, Joseph F. Donahoe, William R. Bell, John J. Cranley, Hau C. Kwaan, Arthur A. Sasahara, and Grant H. Barlow. Temple University Health Sciences Center, Philadelphia, PA, Abbott Laboratories, North Chicago, IL., Johns Hopkins Hospital, Baltimore, MD, Johns Hopkins Hospital, Baltimore, MD, Good Samaritan Hospital, Cincinnati, OH, VA Hospital, Chicago, IL, VA Hospital, W. Roxbury, MA, Abbott Laboratories, North Chicago, IL.

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 now been developed, 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, unheated fibrin plate lysis zones, 125-I tagged clot lysis, plasma plasminogen, plasma clottable protein and serum fibrin/fibrinogen degradation products. Bleeding occurred in about 50% of both groups of patients, primarily from cutdown sites. The results clearly indicate that the pharmacologic effect of tissue culture urokinase was 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.