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CHANGES IN t-PA ACTIVITY AND INHIBITION AS PART OF THE ACUTE PHASE REACTION IN ACUTE MYOCARDIAL INFARCTION. J. Gram (1), C. Kluft (2), J. Jespersen (1). Section of Coagulation and Fibrinolysis, Ribe County Hospital in Esbjerg, Denmark (1), and Gaubius Institute TNO, Leiden, The Netherlands (2).

Acute myocardial infarction (AMI) is accompanied by sequential fluctuations in several plasma proteins indicative of an acute phase reaction. Global screening tests (ECLT and WBCLT) have revealed temporary depression of systemic fibrinolysis. However, such tests do not allow definite conclusions regarding the specific variables involved.
In a prospective study of 34 patients with AMI we determined selected variables involved in fibrinolysis, and in addition we investigated whether any fluctuation was related to the development of leg vein thrombosis (isotope-technique) or due to AMI. Blood samples were collected on days 1,2,4,6,8 after admission and eight weeks (recovery) after discharge. Euglobulin fibrinolytic activity was determined on fibrin plates. The measured activity was lower in the initial acute period (≤ 48 h after AMI) than in the recovery period ($p<0.05$). The intrinsic fibrinolytic proactivators (representing more than 95% of the total activator potential of plasma) did not change during the period of study. Levels in the euglobulins of C1-inactivator (the main inhibitor of the intrinsic system) were constant during the first 48 hours. This suggests that the observed reduction represents t-PA activity and this was verified by specific assay of t-PA. The t-PA inhibition capacity in plasma was elevated in the initial acute period compared to the recovery period (week 8; $p<0.05$). C-reactive protein and fibrinogen followed another pattern with the highest plasma level at day 4 and day 6, respectively. Plasma levels of C1-inactivator increased slowly with a peak at day 8. There was no difference of the determined variables between the DVT negative and positive group, suggesting that the observed changes were due to myocardial injury. Our findings show that components of the fibrinolytic system take part in the acute phase reaction following AMI, and that this involves a brief, initial period of reduced fibrinolytic potential (<48h). The initial, high levels of t-PA inhibition deserve consideration in regard to the institution of thrombolytic therapy with t-PA. (Undertaken within the frame of ECAT).

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EARLY SPONTANEOUS FIBRINOLYSIS IS RELATED TO THE EXTENSION OF ACUTE MYOCARDIAL INFARCTION. M. Hanss (1), D. Rousson (1), P. Touboul (2) and M. Dechavanne (1). Laboratoire d'Hémobiologie, Institut Pasteur, Faculté A. Carrel (1) and Hôpital Cardiologique (2), Lyon, France.

The relative importance of spontaneous fibrinolysis was studied during the early stage of acute myocardial infarction (AMI). Ten consecutive male patients (52.1 ± 5.7 years old) with AMI and without haemodynamic or rythmic complications were selected. Blood samples were obtained less than 5 hours (3.4 ± 0.8 hours) after the onset of symptoms. Enzyme linked immunosorbent assay procedures were performed to quantify the D-dimer antigen (Dd-Ag) and tissue plasminogen activator antigen (tPA-Ag) plasma levels. The creatine phosphokinase (CPK) peak level was measured in serum as an index of the AMI extension. Mean ± S.D. (range) levels were respectively 368 ± 342 (118-1100) µg/l for Dd-Ag, 12.9 ± 9.4 (4.5 - 29.1) µg/l for tPA-Ag and 1117 ± 856 (256-2800) U/l for CPK. Coefficient correlation (r) between these parameters are given in the table.

	Dd-Ag versus tPA-Ag	Dd-Ag versus log CPK	tPA-Ag versus log CPK
r	0.76	- 0.77	- 0.69
p	< 0.02	< 0.02	< 0.05

A significant linear correlation was observed between tPA-Ag and Dd-Ag. Moreover, plasma levels of these two parameters were inversely correlated to the logarithm of the CPK peak level. Thus abnormaly high tPA-Ag levels are detected in plasma from peripheric venous blood when likely marked fibrin lysis occurs and if AMI size is limited.

These data suggest that impaired fibrinolysis is probably involved in the progression of coronary occlusion during the early stage of AMI.

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ACTIVATION OF FIBRINOLYSIS BY PHYSICAL EXERCISE IN HEALTHY INDIVIDUALS WITH DIFFERENT SPORTING ACTIVITIES AND IN PATIENTS AFTER MYOCARDIAL INFARCTION. W. Speiser (1), W. Langer (1), A. Pschaick (1), E. Selmayr (1), B. Ibe (2) and P.E. Nowacki (2). Clinical Research Unit for Blood Coagulation and Thrombosis of the Max-Planck-Gesellschaft, Giessen, FRG (1) and Department of Sports Medicine of the Justus-Liebig-Universität, D-6300 Giessen, FRG (2).

Regular vigorous sporting activities are known to stimulate blood fibrinolytic capacity estimated by the venous occlution test, and have been reported to have a prophylactic effect against the development of coronary artery disease and myocardial infarction. In the present study, the influence of regular physical exercise on fibrinolysis was studied in healthy individuals and in patients after myocardial infarction taking part in a rehabilitation sports program. The activation of fibrinolysis after bicycle ergometry was investigated in 4 groups of subjects. Group A: 18 healthy male competitive athlets (23 ± 3.5 years of age, mean ± S.D.), Group B: 18 healthy male volunteers (25.7 ± 2.7 years) not engaged in any sporting activities, Group C: 17 healthy male volunteers (50.5 ± 7.7 years) regularly practicing sports, and Group D: 18 male patients after myocardial infarction (54.2 ± 7.9 years). Group A (13.9 ± 2.6 AU/ml, mean ± S.D.) and Group C (15.2 ± 2.9 AU/ml) revealed lower ($p < 0.05$) plasma plasminogen activator inhibitor capacities (PAI-cap) than Group B (18.5 ± 5.5 AU/ml) and MI-patients (20.7 ± 5.5 AU/ml). All groups showed a significant increase in plasma tissue plasminogen activator (tPA) antigen levels during exercise (Group A: 8.4 ± 6.7 ng/ml; Group B: 7.1 ± 6.2 ng/ml; Group C: 4.9 ± 3.0 ng/ml; and Group D: 3.0 ± 2.9 nl). After exercise significantly higher tPA activities were measured in persons with low PAI-cap at rest (Group A: 5.5 ± 6.4 IU/ml; Group C: 2.9 ± 3.3 IU/ml), whereas Group B (1.1 ± 3.0 IU/ml) and Group D (0.2 ± 0.7 IU/ml) showed only weak activities. Fibrinogen and fibrin split products (D-dimer) levels did not change during exercise testing. The present study indicates that 1. regular vigorous physical exercise enhances blood fibrinolytic activity by reducing blood PAI-cap in healthy individuals, 2. rehabilitation sport is not capable of reducing blood PAI-cap in MI-patients, and 3. the increased fibrinolytic capacity after physical exercise does not induce systemic fibrinolytic effects.

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DECREASED FIBRINOLYTIC CAPACITY IN SURVIVORS OF ACUTE MYOCARDIAL INFARCTION. P.L.Schoenfeld, E.Therville, P.Bethume, P.Leautaud, D.Wachel and J.J.Rodzynek. Ixelles Hospital, Brussels, Belgium.

Disturbances of several markers of fibrinolytic capacity have been reported in patients with an history of thrombotic pathologies. In this work we assessed Euglobulin Lysis Time (ELT) before and after venous stasis, t-PA release (t-PAr) expressed as the ratio of t-PA antigen after versus before venous stasis, and presence of t-PA inhibitor (t-PAi) in 2 populations: group 1, normal controls (n=50) and group 2, survivors of acute myocardial infarction (AMI)(n=17). The results were as follows :
1) ELT shortening after venous stasis = 46/50 in group 1 compared to 3/17 in group 2 ($p < 0.01$, χ^2 test);
2) t-PAr insufficient in 1/50 patients of group 1 compared to 15/17 patients of group 2 ($p < 0.01$, χ^2 test);
3) presence of t-PAi 3/50 in group 1 compared to 9/17 in group 2.
The 3 normal controls with t-PAi were also characterized by absence of ELT shortening after venous stasis. In group 2, the relationship between absence of ELT shortening and other parameters of fibrinolysis appeared as follows :

	presence of ELT shortening (n=3)	absence of ELT shortening (n=14)
presence of t-PAi	0/3	9/14
abnormal t-PAr	1/3	14/14

In patients of group 2 without ELT shortening after venous stasis, insufficiency of t-PAr was consistently more pronounced in those without detectable t-PAi.
We conclude that :
1) our data confirm the marked abnormalities of fibrinolysis in post-AMI patients;
2) these abnormalities appear to be related to insufficency of t-PAr, either alone or in combination with the presence of t-PAi.