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CHARACTERIZATION OF SYNOVIAL AND PLASMA FIBRIN DEGRADATION PRODUCTS IN RHEUMATOID ARTHRITIS. A.N.Whitaker, P. Masci, R.A. Hazelton, J.J. Morrison. Department of Medicine, University of Queensland, Princess Alexandra Hospital, Woolloongabba, Queensland, 4102, Australia.

The presence of fibrinogen/fibrin derivatives in vasculitic and synovial lesions of rheumatoid disease has long been recognized, although a pathogenetic role for them has not been clearly defined. In this study species of fibrin (ogen) derivatives have been characterized from joint aspirates from 32 patients (40 samples) with rheumatoid disease, and from 12 cases of seronegative arthridities, using immunoadsorption and SDS PAGE (reduced and unreduced gels); and quantitated by immunoassays utilizing the D dimer specific monoclonal antibody DD-3B6/22. The dominant fibrinogen derivatives in synovial aspirates were identifiable as derivatives of the degradation of crosslinked (XL) fibrin and included large quantities of XL high molecular weight degradation products. By enzymeimmunoassays (EIA) levels of XL fibrin derivatives ranged from 12 - 194 µg/ml. Elevated levels of XLFDP (0.5 - 11.4 µg/ml) were also found in the majority of plasmas studied (29/38). A significant correlation was demonstrated between synovial and plasma concentrations of XLFDP ($r = 0.455$, $p < 0.005$). A significant correlation also existed between erythrocyte sedimentation rate and plasma XLFDP ($r = 0.664$, $p < 0.001$) but not between ESR and synovial XLFDP. Autologous mixed lymphocyte reaction, measured in 26 patients, did not correlate with XLFDP levels. The synovial fluid data are consistent with the sequential alteration of fibrinogen by thrombin, $XIII_a$ and plasmin (and/or elastase). Although the activation of fibrinolysis in the joint may be protective, the capacity for XLFDP to mediate bone and joint damage or to initiate immune responses is as yet unknown, whether in inflammatory arthritis or in haemophilic arthropathy. The plasma XLFDP level may provide an index of disease activity in rheumatoid disease, although the extent to which this measures transfer from synovial accumulations to plasma remains to be determined.

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DEVELOPMENT OF A NEW ASSAY METHOD FOR THE DETECTION OF DD/E COMPLEX. K. KUROSO, S. IKEMATSU, M. HADA, M. FUJIMAKI and K. FUKUTAKE. Dept. of Clin. Pathol., Tokyo Medical College, Tokyo, Japan.

A new assay method for the detection of DD/E complex derived from crosslinked fibrin is developed. This assay is performed on a microtitre plate using capture/tag antibody technique, in which the monoclonal antibody against D dimer fragment (DD-3B6, MAbCO) is coated and anti-E fragment polyclonal F(ab)'2 conjugated with horse radish peroxidase is for a tag-antibody. Antigen dilution curve is drawn in the range of 0.01-1.0 µg/ml of purified DD/E complex. DD/E complex can be measured specifically and other high molecular weight derivatives from crosslinked fibrin show a little crossreaction, though fibrinogen and fibrinogen degradation products show no crossreactivities on this assay. D dimer fragment dissociated from DD/E complex after further plasmin digestion is less reactive in this assay, while this type of D dimer can be detected by DIMERTEST-EIA (MAbCO). These data suggest that an early stage of plasmin digestion of crosslinked fibrin can be detected by this method. A trace amount of DD/E complex curculating in plasma from a small thrombus is possibly detected, because this assay gives an excellent high sensitivity with the detection limit of 0.01 µg/ml. Normal value of plasma DD/E complex (n=50) indicates below 0.12 µg/ml as 90 percentile. Patients with DIC (n=24) show high levels of DD/E complex between 0.6 and 40 µg/ml. These elevated levels of DD/E complex may suggest consequently the existence of the plasmic digestion of crosslinked fibrin in the cases with DIC. In summary, it is concluded that the development of this assay will add one technique to discriminate between fibrinolysis and fibrinogenolysis and this assay is useful for the quantitative detection of DD/E complex produced in an early stage of fibrinolysis seen in various thrombotic disorders, and for the evaluation of the efficacy of thrombolytic therapy.

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CLINICAL RELEVANCE OF PLASMA FIBRIN DEGRADATION PRODUCTS DETERMINATION IN PATIENTS WITH DEEP VEIN THROMBOSIS (DVT). M.F. Aillaud(1), C. Roul(1), A. Elias(2), J.L. Bouvier(2), A. Serradimigni(2), I. Juhan-Vague(1).
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We have studied fibrin degradation products, D-dimer, in citrated plasma with an ELISA assay using monoclonal antibodies (Asserachrom D-Di Stago).

35 patients with DVT < 7 days were studied at day 0 (D0) that is upon admission before treatment with streptokinase (n=6), heparin (n=5) or LMWH CY222 Choay (n=24). Phlebographies were scored by Marder's index (MI).
At D0, MI = 24.28 ± 10.85 (m ± SD), the mean (± SD) of D-dimer was : 4056 ± 5545 ng/ml (range 950-19000) (normal values < 500 ng/ml). No correlation was found between D-dimer and MI and between D-dimer and clinical delay of DVT.

The evolution of D-dimer was studied during 7 days in patients treated with heparin or LMWH (n=29). Blood sampling was undertaken at D0 and at 8 h AM, 1 hour before injection at D1, D3, D5, D7. The evolution of thrombolysis was evaluated by comparing MI at D0 and D7. Among patients with MI at D0 > 10 (n=25) two groups were compared : - successful group : 8 patients with decrease of MI at D7 > 80% ; - failure group : 11 patients with decrease of MI at D7 < 20% :
D-dimer at D0 were higher in successful group ($p < 0.05$) ; these results could be explained by better endogenous thrombolysis in this group. The percentages of the decrease of D-dimer at D3 and at D7 compared to D0 were higher in the successful group : Successful group versus Failure group (m ± SD) = % decrease at D3 : 46.4 ± 29.2/ 13.4 ± 11 ($p < 0.05$) ; % decrease at D7 : 52.3 ± 31.5/ 24.2 ± 26.3 ($p < 0.05$) (in agreement with Soria and al, -IX th International Congress of Phlebology, September 1986, Kyoto) ; these results could be explained by a smaller clot mass to be lysed in successful group.

In conclusion the level of D-dimer at D0 and the intensity of the decrease of D-dimer during 7 days (as from D3) may have a predictive value for in vivo thrombolysis.

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NORMAL FIBRINOPEPTIDE A (FPA) AND ELEVATED FIBRINOGEN DEGRADATION PRODUCTS AFTER LONG DISTANCE RUNNING. P. Bärtsch, A. Haeberli and P.W. Straub. Department of Medicine, Inselspital, University of Bern, Switzerland.

Physical exercise leads to a shortening of activated partial thromboplastin time (PTT) and euglobulin lysis time (ELT). Whether this activation causes in-vivo thrombin and plasmin action remains controversial however. 19 well trained long distance runners were examined 25 min (range 5-53) after termination of a 100 km race (post-race values) run in 577 min (457-755) and 5 days later after at least one day without physical exercise (control values). FPA, platelet factors and fibrin(ogen) split products (fragment E and Bβ 15-42) were measured with radioimmunoassays. ELT was assessed before and after venous occlusion (VO). The table gives mean values ±SD:

	Post-race	Control	
PTT (sec)	30.2 ± 2.8	35.3 ± 3.0	$p < 0.001$
FPA (ng/ml)	0.7 ± 0.2	1.0 ± 2.0	ns
BTG (ng/ml)	40 ± 16	23 ± 7	$p < 0.001$
ELT before VO (min)	123 ± 95	196 ± 87	$p < 0.005$
ELT after VO (min)	66 ± 90	103 ± 72	$p < 0.005$
Fragment E (ng/ml)	57 ± 16	35 ± 7	$p < 0.001$
Bβ 15-42 (ng/ml)	8.5 ± 2.5	6.5 ± 2.5	$p < 0.001$
Fibrinogen (g/l)	2.3 ± 0.4	2.6 ± 0.3	$p < 0.025$
Plasmaprotein (g/l)	71.5 ± 4.7	69.2 ± 3.3	$p < 0.05$

Thrombin time, platelet count, platelet factor 4 and haematocrit did not change significantly. FPA was normal in all post-race samples and did not correlate significantly with the time lag between arrival and blood sampling, indicating that activation of blood coagulation in exhaustive physical exercise of long duration does not lead to in-vivo fibrin formation. Activation of fibrinolysis, however, results in circulating plasmin activity as demonstrated by the elevation of the fibrin(ogen) degradation products fragment E and Bβ 15-42. Since the polyclonal antibodies used in the latter assay crossreact with Bβ 1-42, these results alone do not allow to judge whether plasmin degrades fibrin or fibrinogen. However, lack of fibrin formation suggests fibrinogenolysis rather than fibrinolysis.