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POST-OPERATIVE CHANGES IN FACTOR XIII and FIBRONECTIN. M.Reitz (1), H. Sauer (2), G. Witzke (3), M. Neher (2). Institute for Phisiological Chemistry (1), Surgical Clinic (2), University of Mainz, D-6500 Mainz, Behringwerke AG (3), D-3550 Marburg, BRD

Wound healing processes after surgery are not restricted to certain areas but affect the whole body; the coagulation system in particular is involved. We studied Factor XIII and fibronectin in the blood plasma of 16 patients before surgery, after surgery and on the 1st, 3rd and 7th days after surgery; fibronectin was determined using LC-Partigen^{R} immunodiffusion plates and Factor XIII by Behringwerke rapid test. In 11 patients normal wound healing was observed (group A), while in 5 patients complications occured (group B). Factor XIII: normal group (A): fall in concentration compared with the preoperative value up to the 7th day after surgery; group with complications (B): fall in concentration more pronounced than in the normal group up o the 7th day after surgery.

Factor XIII activity $\bar{x} \pm SD$	Pre-operative	Post-operative	1st day	3rd day	7th day
Group A n = 11	125.0 % ± 48.7	93.2 % ± 11.7	86.4 % ± 20.5	70.0 % ± 25.8	54.6 % ± 21.9
Group B n = 5	90.0 % ± 13.7	85.0 % ± 13.7	60.0 % ± 28.5	25.0 % ± 0	35.0 % ± 13.7

Fibronectin : Normal group (A): Fall in concentration compared with the preoperative value up to the 1st day after surgery, followed by a rise in concentration; group with complications (B): fall in concentration more marked than in the normal group, less marked rise in concentration than in the normal group. Complications in wound healing were characterized by an increased fall in Factor XIII and fibronectin.

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COAGULATION FINDINGS IN ULCERATIVE COLITIS AND THE BENEFICIAL EFFECT OF FACTOR XIII CONCENTRATE SUBSTITUTION. R. Suzuki and Y. Takamura. 3rd Department of Internal Medicine, Yokohama City University, School of Medicine, Japan.

Reports suggest that there is a tendency towards hypercoagulability in ulcerative colitis (UC). However, few reports deal with factor XIII which plays an important role in the wound healing process. In the present study, 8 coagulation parameters including factor XIII activity were determined in 5 patients with UC at the active stage and in 15 patients at remission. A comparison of the two groups shows that, in the active-stage patients, the levels of factor XIII activity were significantly lower, platelets and fibrinogen higher, and the PT prolonged.

	Active stage	Remission stage	
F XIII Activity (%)	51.1 ± 12.9	115.4 ± 3.2	p<0.01
Platelet (x10^{4}/ul)	40.9 ± 7.4	27.9 ± 1.4	p<0.01
Fibrinogen (mg/dl)	366.2 ± 52.8	268.0 ± 26.3	
PT (Sec)	13.0 ± 0.4	11.9 ± 0.1	p<0.01
APTT (Sec)	39.4 ± 3.2	37.6 ± 1.3	
Plasminogen (%)	95.2 ± 11.6	110.1 ± 5.4	
α2-Plasmin Inhibitor (%)	146.2 ± 10.5	130.0 ± 3.5	
FDP (ug/dl)	8.3 ± 5.8	4.0 ± 0.7	

Furthermore, Factor XIII concentrate (Fibrogammin P^{R}) was administered to 4 patients with active-stage UC and abdominal symptoms. Here, the symptoms (i.e. abdominal pain, melaena, diarrhea, etc.) disappeared in accordance with the increase in factor XIII activity. Endoscopy revealed that treatment with factor XIII concentrate (Fibrogammin P^{R}) had a beneficial effect on mucosal edema, redness and hemorrhage as well as on healing of erosions and ulcers. The results suggest that the level of factor XIII activity is a remarkably good measure of the severity of UC and that administration of factor XIII concentrate may be useful for treatment.

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QUANTIFICATION OF FACTOR XIIIa-MEDIATED FIBRIN CROSSLINKING USING HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY-BASED IDENTIFICATION OF CROSSLINKED γ-CHAINS AND γ-CHAIN COMPONENTS. U. Kiso, H. Kaudewitz and A. Henschen. Max-Planck-Institute for Biochemistry, Martinsried/Munich, FRG.

Factor XIIIa catalysis the formation of isopeptide bonds in fibrin whereby first and quickly the C-termini of two γ-chains in adjacent molecules are crosslinked and then much more slowly several α-chains. The crosslinking sites of the γ-chain are well-known, but those of the α-chain still only tentatively and partially identified. The crosslinking reaction has previously usually been monitored by sodium dodecylsulfat-polyacrylamide gelelectrophoresis (SDS-PAGE) of the mercaptolysed fibrin or fibrin degradation products. More recently, specific antibodies against the crosslinked γ-chain region have been produced which allow immunological assays for crosslinking products, i.e. for D-dimer.

The present study deals with novel, high-performance liquid chromatography (HPLC)-based procedures for the identification and quantification of crosslinked γ-chains or γ-chain products. The degree of crosslinking was determined by quantifying the dimer either of the total γ-chain or of its C-terminal cyanogen bromide fragment. For this propose factor XIIIa-containing fibrinogen was incubated with thrombin in the presence of calcium ions and cysteine. The reaction was interrupted by the addition of a urea-mercaptoethanol solution after various periods of time and the samples analysed in parallel by reversed-phase HPLC and SDS-PAGE. In both systems the steady decrease first in γ- and then in α-chain and simultaneous increase in γ-chain dimer was observed. The dimeric γ-chain appeared as a well separated and defined peak on HPLC. In the alternative approach crosslinked fibrin, fibrin degradation products or γ-chain were first cleaved by cyanogen bromide and then the resulting fragments were analysed by reversed-phase HPLC. Also here a characteristic component appeared which was identified by sequence analysis as the dimeric C-terminal fragment of the γ-chain and which only was present in crosslinked material.

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POLYMERIZATION OF FIBRINOGEN AND FIBRONECTIN CATALYZED BY FACTOR XIII. R.Procyk (1), M. Block (1) and B. Blomback (1)(2). Plasma Proteins - Coagulation Laboratory, New York Blood Center, N.Y., U.S.A. (1) and Karolinska Institutet, Stockholm, Sweden (2).

Factor XIII catalyzed the formation of gels in solutions containing physiological concentrations of fibrinogen and fibronectin. Oligomeric intermediates were isolated from reaction mixtures at early times prior to gel formation by chromatography on gelatin-Sepharose and by FPLC using Superose 6 columns. The products of two simultaneous polymerization reactions were characterized: fibrinogen oligomers (fibrinogenin) from the polymerization of fibrinogen, and conjugates of fibrinogen-fibronectin (heteronectin) from heteropolymer formation involving the two proteins.

At a constant concentration of fibrinogen (2.5 mg/mL) and factor XIII (0.4 U/mL), the appearance of different sizes of fibrinogen polymers depended on the concentration of fibronectin added to the reaction mixture. At fibronectin concentrations in the range of the normal plasma level of 0.3 mg/mL, fibrinogen formed oligomers of various sizes up to heptamer before incorporating a molecule of fibronectin. At a high fibronectin concentration (3.2 mg/mL) most of the fibrinogen reacted with the fibronectin at the monomer stage, although small amounts of fibrinogen dimers and trimers were also formed.

Heteronectin formation coincided with the appearance of filamentous and particulate matter. This material became incorporated into a gel structure if sufficient fibrinogen was present in the reaction mixture (about 0.5 mg/mL). If these factor XIII catalyzed polymerization reactions occur in the microvasculature under conditions where the fibrinogen concentration might be significantly lowered, the production of fibrinogen-fibronectin polymeric material without gel formation would be favored.