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THE INFLUENCE OF SURGERY ON PLASMINOGEN ACTIVATOR INHIBITOR. H. Neerstrand (2), U. Hedner (2), O. Lützen (2), O. Hauch (1), L. Nannestad Jørgensen (1), H. Nerstrøm (1), T.R. Kølle (1), P. Wille-Jørgensen (1). Kommunehospitalet, Copenhagen, Denmark (1) and Novo Industri A/S, Bagsvaerd, Denmark (2).

In a previous study we have shown that plasminogen activator inhibitor (PAI) decreased in normal healthy volunteers during the day from 6.3±3.1 IU/ml (x̄±ISD) at 7.15 a.m. to 2.8±2.3 IU/ml at 3 p.m.
The aim of the present study was to investigate the effect of major elective abdominal surgery on PAI.
Eight patients received 2,500 XaI units of low molecular weight heparin (Logiparin™) (Gr.1) and 7 patients received 3,500 XaI units of Logiparin (Gr.2).
The PAI activity was measured amidolytically according to Chmielewska et al 1983.
The plasma level of PAI (IU/ml) was (x̄±1SD):

	Time	Gr. 1	Gr. 2
Day of surgery	8 am	5.4±2.3	6.9±2.6
Day of surgery	3 pm	6.9±2.0	7.6±3.1
1st postoperative day	8 am	8.4±1.3	9.5±0.9
5th postoperative day	8 am	5.6±2.4	6.0±2.3
5th postoperative day	12 am	4.7±1.9	6.9±2.2
5th postoperative day	3 pm	5.1±2.4	7.6±1.2
6th postoperative day	8 am	6.0±2.4	6.0±1.1

We found that PAI did not decrease during the day of surgery but the PAI level was significantly higher on the morning after surgery than the previous morning ($p < 0.05$). The 5th postoperative day the PAI level had returned to pre-operative values in the morning, but did not decrease during the day as seen in normal volunteers. The PAI levels were not influenced by the different doses of heparin.
Thus PAI was found to increase postoperatively and the normal decrease in PAI during the day seems to be abolished for at least five days after surgery.

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EFFECTS OF PENTOSAN POLYSULPHATE (ELMIRON) ON FIBRINOLYSIS. O. Haglund (1), L. Wibell (2) and T. Saldeen (1). Department of Medicine (2) and Department of Forensic Medicine (1), University of Uppsala, Uppsala, Sweden.

Decreased fibrinolytic capacity is thought to be an important component in the pathogenesis of different thrombotic states. There is a need for agents improving the fibrinolytic capacity, especially perorally (p.o.) active drugs. Since long the semi-synthetic heparinoid Pentosan Polysulphate (PPS) has been shown to have a stimulating effect on fibrinlysis when given parenterally. Also p.o. administered drug has been claimed to improve fibrinolysis. However, the degree of gastrointestinal resorption has not been thoroughly assessed and the mechanism behind the effect of PPS on fibrinolysis is not known.
8 healthy male volonteers and 14 patients with a history of venous thrombosis were studied. Before and after administration of PPS blood samples were taken and plasminogen activator activity (tPA-act), antigen (tPA-ag) and plasminogen activator inhibitor (PAI) were determined. The volonteers were given 50 mg PPS i.v. and blood was sampled before and after 30 minutes. In a second experiment they received 400 mg PPS p.o. follwed by blood sampling after 2 hours. They also received 400 mg of PPS daily p.o. for 25 days. The patient group were given 500 mg PPS p.o. 8 a.m. and blood was collected 6 hours later. To exclude influence of diurnal variation blood was also taken 2 p.m. the day before. The plasma level of PPS after p.o. administration was determined by a sensitive modified radioassay for heparin.
30 minutes after i.v. injection of PPS PAI was essentially unchanged, tPA-activity was slightly increased but tPA-ag showed a strongly significant decrease. 400 mg PPS p.o. resulted in an increase in tPA-ag after 2 hours. 400 mg PPS during 25 days resulted in a significant decrease of PAI with no changes in tPA-act and tPA-ag. 500 mg PPS given as a single dose in the morning did not cause greater changes of PAI than expected from the diurnal variation. The uptake of PPS following p.o. administration is low with a bioavailability of only 0,5 - 1 %.
The low bioavailability of p.o. administrered PPS suggest that some of the advantagous effects of PPS on fibrinolysis might be caused through local effects in the intestine. The strong decrease of tPA-ag without significant changes in the other parameters may reflect an accelerated elimination of tPA-PAI-complex. The mechanism of the improved fibrinlysis following administration of PPS is still unsettled but our resluts may indicate that PPS initially facilitates the elimination of the tPA-PAI complex with a secondary increase of the tPA-ag. The tPA-ag may bind to PAI with a secondary decrease of the active component of this inhibitor. However, a more direct effect of PPS on PAI cannot be excluded.

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PAF ANTAGONISM AND THE RESPONSE TO ALLERGEN. S. SANJAR, D. SMITH, J. MORLEY, L. MAZZONI, C. TAPPARELLI. Preclinical Research, Sandoz AG, **Basel CH-4002, Switzerland.**

Intravenous infusion of platelet activating factor (PAF) causes platelets to aggregate and accumulate within the lung. A similar effect is observed when allergen is injected into sensitised animals. Since PAF is released in allergic reactions, it might be considered to be a mediator of this phenomenon.
Intrathoracic accumulation of 111-Indium labelled platelets was detected by use of collimated sodium iodide crystal detectors as a part of an automated isotope monitoring system (AIMS 8000, Mumed ltd.). Intravenous infusion of PAF (600 ng/kg/h) caused progressive increase of the intrathoracic platelet content (TPC) (59%). Infusion of small doses of allergen (BGG, 300 ug/kg/h) produced comparable increase of TPC, whether animals were sensitised actively (1 mg/kg BGG+FCA i.p. and boosted two weeks later) (30%) or passively (i.v. injection of 0.25 ml anti-BGG serum) (53%) or received intravenous injections of preformed immune complexes. At a dose of 2 mg/kg/h, ginkgolide B (-5%) or kadsuranone (-1%) fully inhibited increased TPC in response to PAF. However, at higher doses (6 mg/kg/h) ginkgolide B did not diminish TPC in animals that were actively (33%) or passively (60%) sensitised, nor did kadsuranone (6 mg/kg/h) diminish the response in passively sensitised animals (42%) compared to vehicle animals (43%). These observations can be extended to acute bronchospasm and airway hyperreactivity which are secondary to platelet activation in these animals. It can be concluded that PAF formation appears to be a minor determinant of the acute response to allergen in the guinea-pig.

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COMPARISON OF THE EFFECT OF ASPIRIN (ASA) AND CHOLINE MAGNESIUM TRISALICYLATE (CMT) ON PLATELET AGGREGATION IN WHOLE BLOOD EX-VIVO B J Z Danesh (1), A R Saniabadi (2), R I Russell (1), G D O Lowe (2), C D Forbes (2). Gastroenterology Unit (1) and Department of Medicine (2), Royal Infirmary, 10 Alexandra Parade, Glasgow, G31 2ER, Scotland, UK.

Suppression of platelet aggregation by ASA limits the therapeutic use of this drug as an analgesic in patients with bleeding tendencies. CMT is a non-acetylated salicylate derivative with analgesic and anti-inflammatory effect similar to that of ASA. We compared platelet aggregation in human whole blood ex-vivo, three hours after ingestion of ASA and CMT. Using a whole blood platelet counter, platelet aggregation was quantified by measuring the fall in the number of single platelets at peak aggregation in response to collagen (1µg/ml) arachidonic acid (AA, 0.5 mM) as well as spontaneous aggregation. In double blind and random order, 12 healthy volunteers received a single oral dose of ASA and CMT containing 500 mg equivalent salicylate, on two separate occasions, 10 days apart. Despite a comparable absorption of salicylic acid from the two drugs, ingestion of ASA resulted in a marked inhibition of platelet aggregation induced by collagen, AA and spontaneous aggregation, whereas such effects were not observed after CMT ingestion.

	ASA		ASA	
	Pre	Post	Pre	Post
Collagen	82±5	18±6	81±4	87±3
	p<0.005		NS	
Arachidonic Acid	80±3	55±6	86±2	82±2
	p<0.01		NS	
Spontaneous Platelet Aggregation	41±7	21±2	36±5	33±3
	p<0.01		NS	

Values are mean±SEM

We suggest that CMT may have therapeutic potential as an alternative to aspirin when inhibition of platelet aggregation can induce bleeding complications.