2012

IMPORTANCE OF SOME MOLECULAR MARKERS OF HEMOSTATIC ACTIVATION FOR THE DIAGNOSIS, THE CHOICE AND THE CONTROL OF PREVENTIVE AND CURATIVE THERAPY OF D.V.T. AND P.P.S.

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The measurement, before and after treatment, of some molecular markers of hemostatic activation (βTG, PF_4, TXB_2, FPA, 6 keto $PGF_{1\alpha}$) and the determination of their increased coefficient ratio ($\Delta^+ \beta TG/\Delta^+$ FPA, $\Delta^+ \beta TG/\Delta^+ PF_4$, Δ^+ 6 keto $PGF_{1\alpha}/\Delta^+ TXB_2$) combined with the estimation of other parameters (FVIII:C/FVIIIR:AG), AT III, PROT. C, ELT with and without ischemia) permited us to subdivide the deep venous thromboses in two groups.
The first one or "simple D.V.T." was observed in normal subjects with or without varicoses, and without other main pathology and was consecutive to a simple plasma factors activation, the second one or "complicated D.V.T." appeared in patients with other pathology (infections, neoplasms, trauma, metabolic disorders) and was consecutive to a combined activation of plasma factors and platelets.

D.V.T.	Nb	$\Delta^+ \beta TG / \Delta^+$ FPA	Δ^+ 6kétoPGF$_{1\alpha}$ / $\Delta^+ TXB_2$	$\Delta^+ \beta TG / \Delta^+ PF_4$	F.VIII:C / FVIIIR:AG	ELT
simple	100					
A	100	0.25-0.49*	0.98-1.28*	3 - 5	$\simeq$ 1	for N
B	100	0.84-1.20*	0.84-1.10*	3 - 5	$\simeq$ 1	for N
complicated	200					
A	200	1.48-2.90*	0.51-0.89*	3 - 5	< 1	for N
B	50	1.24-2.10*	0.54-0.82*	3 - 5	$\simeq$ 1	for N
C	150	1.05-1.31*	0.86-1.06*	3 - 5	$\simeq$ 1	for N

A:before treat.,B:after anticoagul.,C:after anticoagul. + platelet inhibitors / * extreme values (MV ± 2σ)

If anticoagulants (Heparine and/or VKA) alone were effective and sufficient for the treatment of "simple DVT" they were little or non active in the "complicated" forms and must be combined with platelet inhibitors to give the same result. The prevention of DVT in venous insuffisancy, consecutive or not to DVT, must be performed in the same way. A comparative study with various types of platelet inhibitors permited us to establish a scale of activity and to observe a benefic synergism with some combinations.

2013

CHANGES IN PGE_2 AND TXB_2 FORMATION BY PLATELETS OF ATHEROSCLEROTIC RABBITS.

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The synthesis of thromboxane B_2 (TXB_2) and prostaglandin E_2 (PGE_2) were studied in groups of 9 rabbits fed a normal diet or a diet containing 0.3 % of cholesterol. After 16 weeks, a platelet rich suspension containing 300.000 platelets/mm^3 was prepared. Portions were incubated at 37°C with arachidonic acid (AA). Biosynthesis of PGE_2, TXA_2 and TXB_2 was evaluated by the bioassay cascade system (rabbit coeliac and mesenteric artery and rat fundus strip) and by radioimmunoassay (RIA) :

Table I : Amounts of PGE_2 and TXB_2 biosynthetized by rabbit platelets

AA	INCUBATION TIME	GROUP	PGE_2 ng/ml ± SEM
100 µg/ml	1 min	Normal	216.01 ± 23.86
		Atherosclerotic	162.83 ± 0.89*
	10 min	Normal	287.39 ± 29.02
		Atherosclerotic	232.90 ± 29.44
30 µg/ml	1 min	Normal	77.23 ± 1.62
		Atherosclerotic	37.43 ± 0.56*
	10 min	Normal	128.55 ± 1.62
		Atherosclerotic	60.64 ± 0.48**

* $P < 0.05$; ** $P < 0.005$ ($n > 6$).
No significant differences were recorded for TXB_2 after 1 or 10 minutes incubation.

A small portion of blood without EDTA was allowed to clot at 37°C during 1 hour. TXB_2 was measured in the serum by RIA. The mean ± SEM obtained for the atherosclerotic rabbits (82.70 ± 9.28 ng/ml) was significantly higher than the one for the normal group (42.66 ± 11.45 ng/ml) ($P < 0.02$, $n = 9$ for both groups. From these results it can be concluded that platelets of atherosclerotic rabbits apparently synthetize less PGE_2 when incubated with AA, and more TXB_2 during a standardized clotting process.

2014

SULPHINPYRAZONE (SP) AS A CAUSE OF ACUTE RENAL FAILURE (ARF) : A REVIEW.

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A total of 41 patients (all but one since 1980, 10 from our own group) have been reported with ARF due to SP. Their mean age was 58 years. 84 % of them received SP for coronary or cerebrovascular disease. Signs of pre-existing renal disease were absent in 91% of cases. Daily dosage of SP was < 400 mg in 21 %, 600 mg in 21 % and 800 mg in 58 % of the cases. ARF appeared within the first day of R/ with SP in 31 % of cases (median delay of 4 days). Oliguria was present in 41 % and lumbar or abdominal pain in 26 %. Urinalysis showed uric acid crystals in 13 %. Serum creatinine peaked at a mean of 7.2 mg%. Extrarenal signs (fever, rash) were rare (10 %). 3 patients (8 %) died; renal function recovered in the others, acute dialysis being needed in 6 cases (15 %). Renal histology (11 cases) showed either no lesions (2), minimal tubulo-interstitial lesions (3), discrete interstitial infiltration (2), acute interstitial nephritis (3) or acute tubular necrosis (1).
SP can cause ARF by 3 mechanisms which are not mutually exclusive : acute urate nephropathy, acute (immunological) interstitial nephritis or acute ischaemia due to inhibition of the renal synthesis of kallikrein-kinin and/or vasodilatory prostaglandins. We suggest that the latter mechanism is the most prevalent. The effect of SP on the renal prostaglandin synthesis is not settled; the urinary excretion of kallikrein is significantly depressed by SP.
In conclusion : since 1980, R/ with SP is a frequent cause of ARF.
Practically :

1) the indications for SP should be taken with care;
2) a progressive increase in the dosage of SP may decrease the incidence of ARF.

2015

INFLUENCE OF β-LACTAM ANTIBIOTICS ON THE PLATELETS --
IN VITRO EFFECTS OF SOME β-LACTAM ANTIBIOTICS ON THE BIOCHEMICAL RESPONSES OF RAT PLATELETS --

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The inhibitory mechanism of β-lactam antibiotics on rat platelets were studied using carbenicillin (CBPC) as a representative of the antibiotics. CBPC suppressed all the thrombin-induced cellular responses including shape change, secretion, and aggregation, however, it only suppressed aggregation of ADP-induced responses. This suggests that ADP binding to its own receptor was not affected by the drug while that of thrombin was inhibited. Inhibition of thrombin binding was confirmed using ^{125}I-thrombin. In the case of ADP-stimulated platelets, fibrinogen binding, which has an essential role for ADP-induced primary aggregation, was significantly suppressed by CBPC. Increase of a net negative charge of the membrane surface was observed after treatment of the platelets with antibiotics, and good correlation was obtained between suppression of the platelet responses and degree of net negative charge of the antibiotics especially on the penicillin analogues. These findings strongly suggest that the inhibition of ligand binding to their own receptors is due to the increase of the negative charge of the platelet membrane, which is probably caused by the antibiotic bound to the platelet membrane.