Time

14.30 **0581** PHOSPHOLIPASE $A_2$-INDUCED PLATELET AGGREGATION, RELEASE AND LYSIS.

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Activation of washed platelets by exogenous phospholipase $A_2$ ($PlA_2$) purified from crotalus terrificus terrificus venom was studied. Platelets were labeled with $^{14}$C-serotonin and $^{51}$chromium and resuspended in Tyrode/albumin(TA). With 1-5 µg/ml(final conc.) of crotalus $PlA_2$ no direct platelet alterations were observed. These platelets, however, were refractory to collagen - but not to thrombin or HLA-specific antibodies.
1o-5o µg/ml crotalus $PlA_2$ rapidly induced platelet aggregation and release
1oo µg/ml crotalus $PlA_2$ induced platelet lysis.
$PlA_2$-induced platelet alterations were inhibited by EDTA, $PGE_1$, ASS and apyrase. Crotapotin, an acid peptid isolated from crotalus venom, forms complexes with crotalus $PlA_2$ and specifically inhibits $PlA_2$-induced platelet alterations.
Conclusion: $PlA_2$-induced platelet alterations are due to liberation of arachidonic acid from phospholipids of the platelet membrane inducing prostaglandin and thromboxane synthesis. With high concentrations of $PlA_2$ breakdown of membrane phospholipids will lead to platelet lysis.

14.45 **0582** PLATELETS RELEASE A NEW MEDIATOR, PLATELET-ACTIVATING FACTOR, WHICH ACCOUNTS FOR ADP AND THROMBOXANE-INDEPENDENT AGGREGATION.

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Platelet aggregation induced by low concentrations of ionophore A23187 (I) or thrombin (T) is due to ADP and to metabolites of arachidonic acid (AA), as shown by its inhibition by aspirin and by ADP scavangers. High concentrations of I or T surmount inhibition, thus involving other mediator(s). Platelet-activating factor (PAF) is a l-lysophospholipid released from macrophages among other cells, in the presence of I. We now show that PAF is released from rabbit platelets during aggregation by I, T and collagen, but not by AA nor by PAF itself. Formation and release of PAF by platelets is unaffected by cyclo-oxygenase blockers or by ADP scavengers, but is suppressed by inhibitors of phospholipase A2 activity (dibutyryl cyclic AMP and bromophenacyl bromide). Platelet PAF exhibits similar absorption characteristics on silicic acid thin layer and hight pressure chromatography, and sensitivity to N. naja phospholipase A2 as compared to PAF from leukocytes. PAF may be, like ADP and thromboxane A2, a final effector for platelet aggregation and be responsible for the aspirin-resistant third pathway of platelet aggregation.

15.00 **0583** THE PROSTAGLANDIN-3 FAMILY AND THE PREVENTION OF THROMBOSIS.

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In the search for the cause of the rare occurrence of ischemic heart disease in Eskimos the interest is focused on cis 5,8,11,14,17 eicosapentaenoic acid (C20:5). C20:5 is not a precursor for proaggregatory prostaglandins whereas vascular tissue can convert it to a potent antiaggregatory substance. Greenlanders in whom C20:5 occurs in high concentrations in the plasma lipids in stead of C20:4 should have a balance between platelet aggregatory and antiaggregatory ability dislocated towards the latter. In a expedition to North-West Greenland during the autumn of 1978 this hypothesis was veryfied.
The platelet aggregation after ADP and collagen stimulation and the bleeding time in Eskimos differed significantly from those of age and sex matched Danish controls. Investigations of haemostatic characteristics ruled out other explanations of the prolonged bleeding time and decreased platelet aggregability in Greenlanders.
The observations might have great inplications in the prevention of thrombosis, pointing at the possible role of the prostaglandin-3 family.