EVALUATION OF CYCO-OXYGENASE PATHWAY IN PLATELETS OF THE NEWBORN. E.G. Corby, W.G. Good, J. Barber and T.P. O'Barr. Clinical Investigation Service, Fitzhugh Army Medical Center, Denver, CO, USA

A possible deficiency of cyclo-oxygenase in platelets of the newborn infant has been considered as an explanation for their impaired aggregation to stimuli which function by promoting the release of ADP, (Corby and Zuck, Thromb. and Haemostas., USA 36:201-207, 1976). Cyclo-oxygenase activity was evaluated in washed platelets from paired mother and cord blood samples by measuring the incorporation of radioactivity into metabolites during incubation with (1-14C) arachidonic acid. Platelets from both the mothers and newborns showed normal aggregation to arachidonic acid. Thin layer radiochromatograms of methylated incubation products were essentially identical. Three major peaks of radioactivity, which did correspond to identified arachidonic acid metabolites, were noted (Halstensen et al. Proc. Natl. Acad. Sci., USA, 72:1466-1470, 1975). Platelets from mothers and newborns incorporated similar amounts of radioactivity into 5,6-epoxyeicosatrienoic acid (EET), 12,14-epoxyeicosatrienoic acid (EET), and 12,14-EET. Since these two compounds are derived from the endoperoxide prostaglandin F2, (PGF2), which is believed to initiate the release reaction, the pathway leading from arachidonic acid to PGF2, is probably fully developed in platelets of the newborn infant. It may be speculated that the lack of response by these platelets to external stimuli is related to either the availability or the formation of metabolically available arachidonic acid.

A NEW PATHWAY FOR ARACHIDONIC ACID METABOLISM IN HUMAN PLATELETS. S. Rittenhouse-Simmons, P.A. Russell, D. Drykin. Boston VA Hospital, Boston, Massachusetts.

We are reporting a novel pathway of arachidonic acid metabolism in the phosphatides of thrombin-activated platelets. For kinetic studies of arachidonic acid turnover, platelet phosphatides were isolated by incubation of platelet rich plasma with (9H)-arachidonic acid for 15 minutes at 37oC. The activated asters were removed during subsequent pelleting. Platelet phosphatides were resolved and quantitated following two-dimensional silica paper chromatography of chloroform/methanol extracts of incubated platelets. Planarlamin phosphatidylethanolamine (PE) was isolated by its known absorption to licoferin with MgCl2. In subsequent experiments, iso-flavonide platelets were incubated with (15H)-glycerol to monitor de novo phosphatide synthesis. (9H)-Arachidonic acid was released from phosphatidylcholine and phosphatidylethanolamine (PE) and labeled platelets exposed to thrombin and appeared in increasing amounts at 15 minutes at a glycerol-octane: (9H)-arachidonic acid was not found in FPE of resting cells. Maximum transfer occurred with 5 U/ml of thrombin and 15 min. of incubation, with a 50% drop in 30 min., and was completely inhibited by aspirin, indomethacin, or diclofenac.

The presence of this pathway, which did not appear to be the hematopoietic activation of (9H)-arachidonic acid to PGF2, was not accompanied by a stimulation of (15H)-glycerol uptake into this phosphatide. We suggest that perturbation of the platelet may activate a phospholipase A2 leading to turnover of arachidonic acid in FPE, which is rich in this fatty acid. Such turnover may provide substrate for conversion by cyclo-oxygenase and lipoxygenase of cyclo-oxygenase metabolites, and therefore, may alter a locus for regulation of prostaglandin synthesis in the human platelet.


Platelet (PGLA) metabolites of dideoxy-l-lysologaric acid (DGL) inhibit platelet aggregation (Kernoff et al, this meeting). In vivo, antithrombotic effects of DGLA might be limited by its rate of -deasumotase to arachidonic acid (AA), which enhances platelet aggregation when administered to man. In the rabbit and mouse deasumotase is particularly active but in the guinea-pig cat and rabbit it appears insignificant. We now report on the metabolism of single oral doses of DGLA in 3 human volunteers. Lipoic acid was extracted from blood fractions and separated into different lipid classes before estimation of fatty acid composition by gas-liquid chromatography. PGLA, generated from platelets by maximal stimulation with thrombin, was isolated by argentation chromatography and estimated by spectrometry. Maximal plasma DGLA/AA ratio (C3-C5) occurred at 3-4 hrs when the DGLA/AA ratio in triglycerides had increased 9-12 fold. Between 5-24 yrs DGLA accumulated in phosphatidyl充电. There were no consistent increases in the AA content of blood lipids and no increases in platelet production of its metabolite PGF2. Small increases in platelet PGF2 synthesis occurred, indicating that orally administered DGLA reaches a precursor pool in man. These results support our hypothesis that cholinically-administered DGLA may be of therapeutic value as a antithrombotic agent. (Willis, Stone, et al 1977).


Prostaglandin (PG) metabolites of dideoxy-l-lysologaric acid (DGL) inhibit platelet aggregation (Kernoff et al., this meeting). In vivo, antithrombotic effects of DGLA might be limited by its rate of deasumotase to arachidonic acid (AA), which enhances platelet aggregation when administered to man. In the rabbit and mouse deasumotase is particularly active but in the guinea-pig cat and rabbit it appears insignificant*. We now report on the metabolism of single oral doses of DGLA in 3 human volunteers. Lipoic acid was extracted from blood fractions and separated into different lipid classes before estimation of fatty acid composition by gas-liquid chromatography. PGLA, generated from platelets by maximal stimulation with thrombin, was isolated by argentation chromatography and estimated by spectrometry. Maximal plasma DGLA/AA ratio (C3-C5) occurred at 3-4 hrs when the DGLA/AA ratio in triglycerides had increased 9-12 fold. Between 5-24 yrs DGLA accumulated in phosphatidyl choline. There were no consistent increases in the AA content of blood lipids and no increases in platelet production of its metabolite PGF2. Small increases in platelet PGF2 synthesis occurred, indicating that orally administered DGLA reaches a precursor pool in man. These results support our hypothesis that chronically-administered DGLA may be of therapeutic value as an antithrombotic agent. (Willis, Stone, et al 1977).