

Friday, July 17, 1981

## Poster Presentations

### Prostaglandins – IV

11:00–12:30 h

Wentworth Room Boards 101–112

#### 0857

SELENIUM DEFICIENCY IMPAIRS THE BIOSYNTHESIS OF PROSTACYCLIN IN RAT AORTA. H. Bult, P. Van den Bosch, R. Van den Bossche, A. Van Hoydonck and A. G. Herman. Lab. of Experimental Pharmacology, University of Antwerp, 2610 Wilrijk, Belgium.

Prostacyclin (PGI<sub>2</sub>) synthase is inactivated by lipid hydroperoxides and it has been suggested that this occurs in atheromatous plaques (S. Moncada & J. R. Vane, New Engl. J. Med., 300, 1142, 1979). Glutathione peroxidase is a selenium (Se) containing enzyme which converts hydroperoxides to less toxic alcohols. Therefore, we investigated whether Se deficiency reduced the biosynthesis of PGI<sub>2</sub>. Rats were fed a diet with a reduced Se content (25 ppb) or a standard diet (142 ppb Se). After 7 months 4 rats from each group were killed. Urinary Se-excretion and Se content of the liver were significantly ( $P < 0.05$ , Student-t test) reduced. Aorta's were removed and rings (about 2 mg) were stirred in 1 ml Krebs' solution. After 5 and 15 min, the release of endogenous PGI<sub>2</sub> into the medium was assessed by its anti-aggregating capacity in rabbit platelet rich plasma and after 16 min the 6-oxo-PGF<sub>1α</sub> content of the medium was measured with RIA. Se deficient aorta's released less PGI<sub>2</sub> like activity (at 5 min, 46 % reduction,  $P < 0.05$ ; at 15 min, 25 % reduction) and less 6-oxo-PGF<sub>1α</sub> (43 % reduction,  $P < 0.05$ ). Similar experiments were performed with rings that were exhausted by 6 h preincubation in 100 ml 50 mM Tris, pH 7.5 in the absence of glucose. This procedure reduced the endogenous PGI<sub>2</sub> release in control aortic rings with respectively 81 % (bioassay) or 89 % (RIA of 6-oxo-PGF<sub>1α</sub>). In Se deficient, exhausted rings the endogenous biosynthesis of PGI<sub>2</sub> was strongly impaired as indicated by bioassay and measurements of 6-oxo-PGF<sub>1α</sub> (82 % reduction,  $P < 0.05$ ). Cyclo-oxygenase and PGI<sub>2</sub> synthase activities were measured by incubation of 20 mg aorta with respectively 10 μg 1-<sup>14</sup>C-arachidonic acid or 10 μg 1-<sup>14</sup>C-PGH<sub>2</sub>. After 20 min the reactions were stopped and the products formed were extracted, radiochromatographed and quantified by liquid scintillation counting. In Se deficient aortas, cyclo oxygenase activity was not affected whereas PGI<sub>2</sub>-synthase activity showed 37 % reduction ( $P < 0.05$ ). These results support the hypothesis that a low peroxide tone is a prerequisite for an optimum biosynthesis of PGI<sub>2</sub>.

#### 0858

THE RELEASE OF PROSTACYCLIN (PGI<sub>2</sub>) BY PENTOXIFYLLINE FROM HUMAN AND ANIMAL VASCULAR TISSUE AND ITS IMPLICATIONS FOR VASCULAR AND ANTIPLATELET ACTIVITIES. K. Schrör, R. Matzky, T. Kahlen, H. Darius. Pharmakologisches Institut der Universität Köln, Gleueler Str. 24, D-5000 Köln 41, West Germany.

The action of pentoxifylline (POF) on vascular tone and PGI<sub>2</sub>-release was studied *in-vitro* and compared to its antiplatelet activities. POF at concentrations of 10–40 μM dose-dependently increased the PGI<sub>2</sub>-formation of isolated bovine coronary arteries and veins *in-vitro*. Similar data were obtained with human umbilical arteries and veins. The maximum stimulation in all of the vascular tissues studied was about 2–3-fold above basal levels. Dose-dependent increase of PGI<sub>2</sub>-production was observed at concentrations of POF comparable to those which dose-dependently relaxed isolated artery strips, whereas the investigated venous tissue was relaxed by both POF and nitroglycerine but not by PGI<sub>2</sub>. In isolated guinea pig hearts the positive inotropic action of POF (100 μM) was blocked by propranolol (10 μM), whereas the coronary relaxation remained unchanged. POF did not influence the ADP- and collagen-induced platelet aggregation *in-vitro* in concentrations up to 100 μM. The data suggest that POF is able to increase significantly the vascular PGI<sub>2</sub>-formation at concentrations above 10 μM, whereas minimum concentrations for obtaining significant inhibition of platelet aggregation *in-vitro* are above 100 μM. This indicates that the reported clinical efficiency of POF in protecting blood cells and improvement of regional perfusion might in part be due to stimulation of the vascular PGI<sub>2</sub>-formation.