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INCREASED THROMBIN GENERATION DURING COLLECTION OF BLOOD FROM DONORS TAKING ORAL CONTRACEPTIVES (OC). O.H. Skjensberg (1), P. Kierulf (2), L.F. Engebretsen (2), G. Gjønnes (1), H.C. Godal (1). Haematological Research Laboratory (1) and Central Laboratory, Ullevål Hospital, University Clinic, Oslo, Norway.

450 ml blood was drawn into Fenwal PVC-bags from 26 OC-users and 28 non-users. The groups were comparable with regard to sex, age, smoking habits and blood collecting time. Thrombin generation was estimated as the fibrinopeptide A (FPA) concentrations in the bags immediately after ending the donations. The blood was also analyzed following storage at 4°C for 24 hours.

Subsequent to donation, the median FPA level in the control group was 4.2 (range 1.8-18.9) and in the OC-group 7.5 (range 2.2-113.7) ($p < 0.05$), reflecting a more pronounced thrombin generation during collection of blood from OC-users. The level of prekallikrein (PKK) was also higher in blood drawn from OC-users (97.0% (73-128) in the control group versus 121.5% (79-166) in the OC-group ($p < 0.001$)), as was the level of FVIII:C, the latter difference was, however, not significant ($p = 0.06$). The A1-III concentrations were similar in the two groups.

No cold promoted activation could be observed following storage of the bags at 4°C for 24 hours, neither was any change observed in the levels of FPA, PKK or A1-III. There was no difference between the groups with regard to decay of FVIII:C upon storage.

We conclude that thrombin generation is more pronounced during collection of blood from donors taking OC. Only some of the OC-users seem to generate appreciable amounts of FPA (19% above 30 ng/ml), and it is important to notice that all bags containing alarmingly high levels of FPA were drawn from women taking OC.

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PROSTACYCLIN PRODUCTION BY UMBILICAL ARTERIES FROM PREGNANCIES COMPLICATED BY SEVERE PREGNANCY INDUCED HYPERTENSION. M. McLaren, I.A. Greer and C.D. Forbes. University Department of Medicine, Glasgow Royal Infirmary, Glasgow, U.K.

Approximately ten per cent of all pregnancies are complicated by some degree of hypertensive disease. Since the level of blood pressure is closely related to foetal well-being, if the blood pressure is consistently elevated during pregnancy, there is an associated increase in perinatal mortality. Various workers have suggested involvement of prostaglandins in the pathogenesis of pregnancy induced hypertension (PIH). One of our previous studies showed unrecordable levels of plasma prostacyclin metabolites (PGI_2m) of $< 5\text{pg/ml}$ in all hypertensive patients during the third trimester, whereas none of the normal group developed unrecordable levels at any stage.

In this study we used an umbilical artery perfusion model to compare the ability of normal platelet poor plasma, which has been shown to contain a PGI_2 stimulating factor, to stimulate production of PGI_2 from arteries from normal pregnancies and pregnancies complicated by PIH. Arteries from two patients suffering from PIH with persistent diastolic pressure of $> 90\text{mm}$ mercury were exhausted of spontaneous PGI_2 production before perfusion with normal platelet poor plasma. In each case an artery from a normal pregnancy was used as a control. In each experiment levels of PGI_2 rose from a baseline level of $< 50\text{pg/ml}$ to $> 1000\text{pg/ml}$ in the normal arteries, whereas the arteries from PIH patients showed no significant rise. It would seem therefore that our finding of unrecordable levels of plasma PGI_2m in hypertensive pregnancies may be related to defective endothelial cell production.

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PRESENCE OF PEROXIDES IN PLASMA OF RATS TREATED BY ORAL CONTRACEPTIVE ENHANCING AGGREGATION OF NORMAL PLATELETS. M. CIAYATTI, D. BLACHE, S. RENAUD. INSERM Unité 63 - 22 Av. Doyen Lépine - 69500 BRON - FRANCE.

Platelets and plasma were prepared from normal and oral contraceptive (ethinylloestradiol + lynestrenol) treated female rats. Thrombin and ADP-induced aggregation of normal platelets resuspended in incomplete Tyrode's buffer were studied after being preincubated either in normal plasma (N.P) or in plasma from oral contraceptive (OC.P) treated animals. Aggregation was drastically enhanced in OC.P as compared to N.P (about 3 fold) after only 4 min preincubation at room temperature. If normal platelets were pretreated by butylated hydroxytoluene (BHT) and incubation and aggregation performed as above, the aggregation of N.P and OC.P treated platelets were identical. The dose of BHT was chosen so as not to affect normal platelet aggregation. Similarly, when OC.P was pretreated with an active preparation of peroxidase (3 U/ml plasma) and reduced glutathione (2mM), the enhancement of aggregation of normal platelets preincubated in OC.P was completely abolished compared to platelets incubated in N.P. When platelets were incubated with N.P or OC.P pretreated by catalase, platelet-induced aggregation was still found to be potentiated in OC.P comparatively to N.P although the absolute extent of aggregation was decreased in both cases as compared to no catalase pretreatment of the plasmas. The peroxidized fatty acid fraction was isolated from N.P and OC.P and tested on the aggregation of normal platelets. A far greater potentiating effect on platelet aggregation was found with the peroxidized fraction extracted from OC.P comparatively to that from N.P. Malonaldehyde was also found increased in plasma from OC.P compared to N.P if measured very quickly after the sampling. From these data we conclude that the potentiating effect of OC.P on platelet behavior might be mediated by lipid hydroperoxide, rather than by hydrogen peroxide probably through oxydative injury to platelets.

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SERUM BINDING ABILITY OF PGI_2 IS DECREASED IN NORMAL AND ABNORMAL STATES OF PREGNANCY. H.I. Saba (1), W.F. O'Brien and R.A. Knuppel (2). Division of Hematology, Departments of Internal Medicine (1) and Maternal-Fetal Medicine (2), University of South Florida and J.A. Haley Veterans Hospital, Tampa, FL, U.S.A.

Several abnormalities of hemostasis have been observed in pregnancy. We have recently reported the findings of circulating platelet aggregates, thrombocytopenia and platelet exhaustion in pregnant states indicated platelet hyper-reactivity (Am J Ob Gyn 155:486;1986). Currently, we have attempted to delineate the pathogenesis of this phenomenon. Sera from 36 normal pregnant subjects and nine pregnant subjects with pre-eclampsia were examined for their ability to bind PGI_2 . Thirteen age-matched non-pregnant subjects' sera was used as controls. 350 μl of sera from these subjects was incubated for three minutes with 35 μl of radiolabeled sodium salt of PGI_2 . The mixture was then eluted on a Sephadex G25 column. Thirty samples of 0.35 ml were collected. Two peaks of radioactivity were obtained. The first peak was protein-bound PGI_2 , and the second contained unbound PGI_2 and its hydrolytic product, 6keto $\text{PGF}_{1\alpha}$. Percent binding was determined by (count in first peak/total count eluted) $\times 100$. The albumin (ALB) and total protein (TP) was also measured to evaluate their relationship with the binding.

GROUP	#	% BINDING	P	ALB	TP
Control	13	37.6 \pm 3.6		4.5 \pm 0.2	6.0 \pm 0.6
Normal Pregnancy	36	24.2 \pm 5.2	<.001	3.6 \pm 0.3	5.8 \pm 1.0
Pre-eclampsia	9	12.8 \pm 6.8	<.0001	3.1 \pm 0.21	5.8 \pm 0.6

Results indicate that PGI_2 binding ability of sera from normal pregnant and pre-eclampsia subjects is markedly impaired. Pregnant groups when compared to controls exhibit statistically significant difference. The ALB and TP failed to suggest a relationship with binding abnormality. Studies being performed on platelet aggregation indicate that impairment of PGI_2 binding in the subject's sera accompanied the loss of antiaggregatory influence of this PGI_2 . These studies suggest that platelet hyper-reactivity in normal and abnormal pregnancy may be related to impairment of PGI_2 binding in their blood, and cause instability and rapid hydrolysis of this important platelet antiaggregatory agent available from the vascular wall.