

**SUPPRESSIVE EFFECT OF NEONATAL THYMECTOMY ON OCCLUSIVE ARTERIAL THROMBOSIS IN SENSITIZED RATS.**  
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It has been found that lymphokines can induce thrombocyte aggregation and blood coagulation.

The present study investigated the development of occlusive arterial thrombosis (OAT) in both male and female Wistar rats with altered immunologic background in order to elucidate the immunologic mechanisms in the pathogenesis of OAT.

At the age of 10 weeks neonatally thymectomized rats and sham operated litter mate controls were sensitized with 500 µg of bovine serum albumin (BSA), injected with complete Freund's adjuvant in a single hind footpad and a second control sham operated rats were injected only with saline. All animals were skin-tested with 30 µg of BSA in saline at 7 and 14 days. Arthus reactions were read 3 to 4 hr. Both the average diameter in millimeters and thickness were recorded. Only reactions equal and greater than 7 mm in diameter were regarded as positive.

Experimental OAT was induced when rats reached 3 months of age using a polyethylene loop inserted in the abdominal aorta. The mortality rate (MR), dry thrombus weight (TW) and loop obstruction time (OT) served as criteria for assessment of thrombosis. According to all the criteria used there was a statistically significant suppression of the development of occlusive arterial thrombosis in the neonatally thymectomized rats of either sex. The previously observed sex difference in OAT was more pronounced.

The data presented suggested an involvement of immunologic mechanisms in the thrombogenesis in the arteries and that suitable inhibitors of the immune responses could prove to be of therapeutic value.

## 0772

**THROMBOCYTOSIS AND PLATELET ACTIVATION IN ALCOHOLICS DURING ALCOHOL WITHDRAWAL.** R.A.Hutton, R.Fink, D.T.Wilson and D.H. Marjot. Departments of Haematology and Chemical Pathology, Royal Free Hospital, London and Regional Addiction Unit, St. Bernard's Hospital, Ealing, UK.

In order to further investigate the basis of the increased thrombotic risk reported in association with acute alcohol withdrawal, we have carried out platelet studies in a group of alcoholics admitted to a formal alcohol detoxification programme.

All patients were alcoholaeic on admission but had taken no other platelet inhibiting medications for at least two weeks. Platelet counts, platelet aggregability, plasma betathromboglobulin (BTG) assays, platelet nucleotide levels and circulating platelet aggregates were measured sequentially over a 4-6 week period.

On admission, platelet aggregability was impaired, compared to normal controls, particularly using ADP or adrenaline as agonists, but all other platelet studies were within normal limits.

Following alcohol withdrawal, there was a progressive increase in platelet responsiveness which reached a peak after 2-3 weeks and had returned to normal by 5-6 weeks.

Compared to normal subjects, the treated group showed a statistically significant mean increase in platelet count, the level of circulating platelet aggregates, the plasma BTG level and in the aggregation response to ADP and adrenaline. There was also a small increase in the aggregation observed with collagen and Ristocetin and in the platelet nucleotide levels but these did not reach conventional statistical significance.

The changes were not associated with any clinically overt thrombotic complications during the period of study, but may contribute to the increased incidence of thrombosis reported by others.

## 0771

**AN IMBALANCE IN PLATELET-VASCULAR PROSTAGLANDIN SYNTHESIS INDUCED BY HOMOCYSTEINE AND HOMOCYSTEIC ACID.** Janet E. Graeber, Marie J. Stuart, Jeffrey Slott, Rodney E. Ulane, and Joseph D. Schulman, NICHD, NIH, Bethesda and SUNY, Dept. of Peds. Syracuse, New York, U.S.A.

Homocystinuria is a metabolic disorder characterized by serious vascular thromboses and elevated plasma levels of Homocysteine and Homocysteic Acid. The etiology of the thromboses is unknown. Platelets produce proaggregatory and prothrombotic Thromboxane A<sub>2</sub> (TXA<sub>2</sub>) while vascular endothelium produces antiaggregatory and antithrombotic PGI<sub>2</sub>. An imbalance in production of TXA<sub>2</sub> and/or PGI<sub>2</sub> can lead to bleeding or thrombosis. We investigated production of platelet TXB<sub>2</sub> (the stable end product of TXA<sub>2</sub>) and vascular 6-Keto-PGF<sub>1α</sub> (the end product of PGI<sub>2</sub>) in platelets and vascular endothelium exposed in vitro to Homocysteine and Homocysteic Acid, 0.4 to 2.0 mM. Conversion of <sup>14</sup>C arachidonic acid (AA) to platelet TXB<sub>2</sub> was increased in the presence of Homocysteine or Homocysteic Acid. In 8 paired experiments, mean platelet TXB<sub>2</sub> increased to 19.4±3.5% (1SE) in the presence of Homocysteic Acid, compared to control values of 14.6±3.6% (p<0.01). Similarly, in 4 paired experiments platelet TXB<sub>2</sub> was increased (18.7±2.3%) in the presence of Homocysteine, when compared to a mean value of 7.8±1.1% (p<0.05) in the control platelets. No differences in vascular 6-Keto-PGF<sub>1α</sub> production were observed in 6 paired experiments when vessels were incubated with either buffer, Homocysteine or Homocysteic Acid (0.73±0.07; 0.7±0.05; 0.76±0.07%). These studies demonstrate that Homocysteine and Homocysteic Acid alter platelet and vascular AA metabolism by increasing production of prothrombotic platelet TXA<sub>2</sub> without a compensatory increase in antithrombotic vascular PGI<sub>2</sub>. Such an imbalance may explain the marked thrombotic tendency seen in patients with homocystinuria. It also provides evidence for the use of thromboxane synthetase inhibitors in this disorder.

## 0773

**COAGULATION AND HEMORHEOLOGY IN CEREBROVASCULAR DISEASE. DIFFERENCES RELATED TO ANGIOGRAPHIC FINDINGS AND SEX.**

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A series of 102 cerebrovascular patients (CVP) investigated with aortic arch angiography, carotidography and CAT scan, were classified clinically in STROKE (55) and TIA (47) and pathologically as having IAL (51) or having no (NIAL, 51) identifiable arterial lesions. Coagulation and hemorheologic tests were performed at least 3 months after STROKE or 1 month after a TIA episode. All CVP as compared to controls (84) had significantly higher fibrinogen (Fg), F VIII AHF and RAG, blood (BV) and plasma (PV) viscosity, and poorer erythrocyte deformability (ED, as filtered erythrocyte volume, FEV), but no differences in euglobulin lysis time (ELT) even after venostasis (ELTV) and in circulating platelet aggregates (CPA, as 1/PAR). IAL vs NIAL CVP had higher Fg (mg% 285±74 vs 241±64; p<0.005); a trend to higher BV (cp 4.64±0.5 vs 4.53±0.6) and PV (cp 1.63±0.15 vs 1.58±0.15), but no differences in other parameters. In the subgroup IAL-STROKE more CPA (1/PAR 121±18) were found vs IAL-TIA (1/PAR 104±13; p<0.05). When compared to sex-matched controls CV males had more Fg (269±36 vs 220±38; p<0.01), higher BV (p<0.05) and PV (1.61±0.16 vs 1.45±0.13; p<0.001), and poorer ED (FEV ml/min 7.41±2.8 vs 10.6±3.2; p<0.005). CPA were higher in CV males than in CV females (1/PAR 122±31 vs 96±36, p<0.05). Conversely, CV females differed from their controls only for a higher PV (p<0.05). This study points out that most of the parameters considered, are especially altered in CV males rather than in CV females, thus suggesting sex-related differences in response to drugs acting on haemostasis and rheology in CV diseases.