ISSN 0720-9355 E 6807 F

Diagnostik, Therapie und Grundlagenforschung

# HÄMOSTASEOLOGIE

Hämorrhagien und Thromboembolien

Für weitere Kongress-Angebote besuchen Sie uns am Stand Foyer Saal 3 Stand Nr. 2

Schriftleitung:
H. D. Bruhn, Kiel
S. Eichinger, Wien
J. Harenberg, Mannheim
H. G. Lasch, Gießen
B. Lämmle, Bern
Ch. Mannhalter, Wien
R. Schneppenheim, Hamburg
W. Schramm, München
E. Seifried, Frankfurt/M.

## Kongressausgabe

48. GTH-Jahrestagung

Von-Willebrand-Faktor

www.schattauer.de

1/2004

Februar 2004
Hämostaseologie 2004; 24: 1–83

Schattauer

## P79

### Activation of coagulation parameters during a simulated long-distance flight in high risk populations

Fußhoeller G. (2,3), Zichner L. (2), Böhmer D. (3), Stüben U. (4), Scharrer I. (5), Bauersachs R. (1)
(1) Med. Klinik IV, Klinikum Darmstadt, (2) Orthopädische Universitätsklinik Frankfurt am Main Friedrichsheim, (3) Zentrum für Sauerstoffüberdrucktherapie, Tauch- und Höhenmedizin an der Orthopädischen Universitätsklinik Frankfurt/Main, (4) Deutsche Akademie für Flugmedizin, Frankfurt am Main, (5) Johann Wolfgang Goethe Universitätsklinik Frankfurt am Main

**Objectives:** To date, no causal link between the manifestation of venous thromboembolism (VTE) and long-distance flights has been identified. Recent studies have shown various effects on the coagulation system. For clarifying these effects and for documenting coagulation alterations in a thrombophilia population, we have examined 72 subjects exposed to a 12 hour simulated long-distance flight.
**Methods:** Three age and sex matched groups with differring risk for VTE were examined after providing informed consent (n=3x24): Group I comprised subjects without F-V-Leiden mutation and no prior VTE; II, subjects with F-V Leiden and no prior VTE, and group III, with F-V-Leiden and a personal history of VTE. Other forms of thrombophilia or homozygousity were excluded in all subjects. Samples were taken at 0, 2, 6, 9, 12 hours of the simulated flight and 48 hours afterwards. Parameters included D-Dimere Prothrombin-time, APTT, fibrinogen, F1+ F2, PAI and VWF. Complete compression ultrasound (CCUS) were carried out before and directly after the testing. In cases of conspicuous labratory results there was an additional CCUS was scheduled one week later.
**Results:** 24 hours after beeing exposed to low-pressure a 62 year old patient with FV-Leiden and prior DVT developed a pulmonary embolism. D-Dimer had been negative during the simulated flight, and increased at 48 hours. Overall, the three groups exhibited an increase of D-Dimer levels after 12 hours, and a decrease of PAI, reaching its maximum after 6 hours. VWF antigen increased until 6 hours and subsequently returned to baseline.
**Conclusions:** In connection to a long-term exposition to low-pressure during immobile conditions a complex activation of the coagulation system occurs. The results of this study suggests that thromboprophylaxis is warrented for high risk patients during long-distance flight.

## P80

### Thrombosis in pediatric patients of Costa Rica – first report

Salazar-Sanchez L. (1), Navarette M. (2), Cartin M. (1), Carrillo J.M.I. (2), Jimenez-Arce G. (1), Herrmann F.H. (3)
(1) CIHATA, University of Costa Rica, (2 )Hematology Department, Children Hospital of Costa Rica, (3) Human Genetics, University of Greifswald, Greifswald, Germany

Thrombosis in children are a rare event. Several factors likely contribute to the low incidence of thrombosis in children. The vascular endothelium of children has not accumulated damage from diseases such as hypertension, diabetes, or hiypercholesterolemia, and it has not been exposed to acquired thrombotic risk factors.
**Objective:** To characterize the clinical and laboratory findings in our pediatric patient with thrombosis.
**Patients and methods:** Patients of the Costa Rica Children Hospital with documented venous or arterial thrombosis, from January 2000 to January 2003 were studied. The diagnostic panel included measurement of protein C (PC), protein S (PS) antithrombin III (ATIII), lupus anticoagulant (AL), anticardiolipin antibodies (ACA), fibrinogen (Fgo). Genetic studies of the factor V Leiden (FVL), G20210A prothrombin (PT20210) and C677T methylenetetrahidrofolate reductase (MTHFR) polymorphisms were performed by PCR analysis. Statistical analisis were perfomed using computer database and Epi. Info. 6 program.
**Results:** Forty five patients with thrombosis (M/F: 28/17) were involved. Mean age of 6.13 years with standard deviation of 4.83 years. Twenty eight patients had stroke (62.2%), seven patients had venous thromboembolism (VTE) (15.5%), and eleven had other thrombosis (mesenteric, renal, etc)(22.3%). The mean value of: ATIII : 106.6%, 3 patients had <60%; PC: 84.6%, 3 patients had less 50%; PS: 90.4%; Fgo: 329.9 mg/dl, four patients had more of 500mg/dl. Six patients had ACA (14.6%). Sixteen patients had family history (42.1%). We identified 3 heterozygotes of FVL (8.1%), 1 heterozygotes of PT20210 (3.0%) and 22 heterozygotes (61.1%) and 8 homozygotes (22.2%) of MTHFR. Eleven patients were anticoagulated: 3 with heparin (9.1%), 5 with warfarin (12.5%) and 3 with both (9.1%). All children anticoagulated with warfarin were monitored with INR of 2-3 for 3 or 6 months.
**Conclusion:** The key finding in the present study deals with the identification of risk factors related with thrombosis in the CR pediatric patients and the association of these risk factors. That is a first report and more patients are necessary to final conclusions

## P81

### High sensitivity CRP in deep venous thrombosis: positive correlation with clinical probability (Wells) score

Korte W. (1), Wuillemin W. (2), Caliezi C. (3), Riesen W. (1)
(1) Institute for Clinical Chemistry and Haematology, Kantonsspital St. Gallen, Switzerland, (2) Division of Haematology, Kantonsspital Luzern, Switzerland, (3) Div. of Angiology, Inselspital/University Hospital Bern, Switzerland

**Objectives:** High sensitivity CRP has been shown to have some predictive value in atherothrombotic disease. In suspected venous thrombotic disease however, CRP has been claimed not to be of value for evaluation of patients. We postulated that the extent of low level inflammation, which makes part of the disease process in deep venous thrombosis (DVT), might be more precisely determined with a high sensitivity CRP assay; and that the extent of inflammation might correlate with the extent of the clinical disease and thus a clinical probability (Wells) score.
**Patients and methods:** Patients with suspected DVT were evaluated by medical history, physical exam, DVT pretest probability (Wells score), compression ultrasound or venography and D-dimer testing. High sensitivity CRP was measured from samples stored at -70° C using the Dade Behring assay on a Dade Behring nephelometer, D-dimer was quantified using the Timaquant D-dimer (Roche Diagnostics).
**Results:** DVT was found in 40 of 87 patients evaluated. HsCRP was significantly increased in patients with DVT (median 11.75 mg/l vs. 3.4 mg/l, p = 0.0003). HsCRP concentrations were correlated to crude Wells scores (r = 0.363, p = 0.002). HsCRP values > 4 mg/l were related to high probability Wells' scores (Odds Ratio 2.62, 95% CI 1.01 - 6.82) and DVT (Odds Ratio 3.41, 95% CI 1.36 - 8.53). There was a gradual increase in hsCRP concentrations with crude Wells Score numbers.
**Conclusions:** We show here that low degree inflammation as quantified with a hsCRP assay correlates with clinical probability (Wells score) for DVT as well as the actual presence of DVT. This is a novel finding and it seems worthwhile to evaluate the use of hsCRP in the work-up of patients with suspected DVT in combination with a D-dimer assay.

## P82

### Antibodies and HIT II – therapeutically relevant diagnostics

Zimmermann I. (1,2), Pachmann U. (1), Seybold D. (2), Moessmer G. (3), Neumeier D. (3)
(1) TZB Transfusionsmedizinisches Zentrum Bayreuth, (2) Medizinische Klinik, Krankenhaus Hohe Warte Bayreuth, (3) Institut für Klinische Chemie und Pathobiochemie, Klinikum rechts der Isar, Technische Universität München

**Objectives:** As soon as the diagnosis HIT II is posed, heparin has to be substituted by an alternative anticoagulation. HIT II is suspected if, during heparin therapy, a vessel is clotted and/or platelets decrease by more than 50%. The diagnosis of HIT II, however, is confirmed by laboratory testing only in 10-15% of the suspected cases. In the remnant 85-90% of cases the treating physician is confronted with the differential diagnoses of thrombocytopenia. Additional therapeutic consequences can only be taken if a differentiation can be made into antibody-related and non-antibody-related thrombocytopenias.
**Material and methods:** In a sample of 867 consecutive cases of suspected HIT II it was immediately tested, whether the serum of the patients was able to induce heparin-dependent aggregation of donor platelets (HIPA-test), and whether the platelets of the patient were covered with platelet-associated IgG and/or IgM antibodies in the absence and in the presence of therapeutic heparin concentrations (PSIFT). If the HIPA test was positive this was defined as HIT II. If heparin-independent antibodies were detected this was defined as AIT (autoimmune thrombocytopenia) and if heparin-dependent antibodies were detected in absence or presence of AIT this was defined as HEP-ITP (heparin-dependent immune thrombocytopenia).
**Results:** According to these definitions, the following numbers of cases were found for HIT II positives(negatives) and AIT pos/HEP-ITP pos 41(182), AIT pos/HEP-ITP neg 73(328), AIT neg/HEP-ITP pos 2(10), AIT neg/HEP-ITP neg 35(196).Thus, 151 patients were found to be HIT II positive and 716 patients HIT II negative. 235 patients were HEP-ITP positive and this was true for 43 patients with HIT II. Heparin-independent antibodies to platelets were detectable in 624 patients consistent with autoimmune thrombocytopenia.
**Conclusions:** The methodological proceeding developed by us according to clinical requirements results not only in 10-15% but in as much as about 80% of HIT II- suspected cases in a prompt and therapeutically relevant diagnosis. If HIT II or a heparin-induced immune thrombocytopenia is confirmed heparin should be substituted by alternative anticoagulation. If platelet-associated antibodies are detected, however, AIT- therapy is a promising option. The groups partly overlap. Thus, only a small number of non-immunologic cases of thrombocytopenia remains needing further clarification.