effect on ETP, ETP-APC, or TFPI levels. ETP-APC showed a negative correlation with TFPI antigen level and activity. Addition of TFPI blocking antibody caused dose dependent increases in ETP-APC and ETP. Treatment with LMWH restored TFPI antigen levels to normal with a concomitant decrease in ETP-APC. Our data suggest that TFPI deficiency associated with ETP dependent APC resistance could be a risk factor for pregnancy morbidity, and imply a potential role for heparin in the treatment of this condition.

**30** Differential effects of conventional and low dose oral hormone therapy (HT), tibolone and raloxifene on sensitivity to activated protein C system

A.L. Eilertsen[1,2], S. Liestøl[1], M. Mowinckel[1], H.C. Hemker[3], P.M. Sandset[1,2]. 1Department of Haematology, Ullevål University Hospital Trust, Oslo, Norway, 2Medical Clinic, Faculty Division, Ullevål University Hospital, Oslo, Norway, 3Synapse BV, Cardiovascular Research Institute, Maastricht, The Netherlands

**Introduction:** Recent studies have shown that Hormone Therapy (HT) is associated with an acquired resistance to activated protein C (APC).

**Objectives:** The aims of the present study were to evaluate a possible dose-response relationship and differential effects of different HT regimens on functionality of the APC system.

**Methods:** 202 healthy women were randomly assigned to receive once daily treatment for 12 weeks with tablets containing either low-dose HT containing 1 mg 17β-oestradiol + 0.5 mg norethisterone acetate (NETA)(n = 50), conventional-dose HT containing 2 mg 17β-oestradiol and 1 mg NETA (n=50), 2.5 mg tibolone (n = 51), or 60 mg raloxifene (n = 51). Normalized APC system sensitivity ratios (nAPCsr) were determined in plasma collected at baseline and after 12 weeks using a thrombin generation-based APC resistance test probed with either recombinant APC (rAPC) or thrombomodulin (TM).

**Results:** The conventional- and low-dose HT groups both increased nAPCsr consistent with reduced sensitivity to APC. The increase was more pronounced in the conventional-dose group and the difference between the two HT groups was statistically significant with rAPC and TM. Consequently, tibolone showed a different phenotype as compared with the low-dose HT group (p < 0.001). Raloxifene induced a small increase in nAPCsr with both rAPC and TM but the increase was less than in the low-dose HT group (p = 0.03 and p = 0.01, respectively).

**Conclusions:** Our findings suggest a dose-response relationship for oestrogen-progestin therapy on nAPCsr, whereas tibolone and raloxifene only marginally alter the sensitivity to APC.

**31** Thrombin activatable fibrinolysis inhibitor (TAFI) is not associated with fetal loss; a retrospective study

N. Folkeringa[1], F.J. Korteweg[2], N.J.G.M. Veeger[1], J.J.H.M. Erwich[2], A.L. Eilertsen[1,2], A. Trepat[2], F. Del Giudice[2], C. Oyenard[2], G. Hermann[2], G. Musso[2], C. Skutniksy[1]. 1Hematology Service, CEMIC University Hospital, 2Obstetricians, Buenos Aires, Argentina

**Objectives:** To evaluate: (1) the relationship between inherited thrombophilia (IT) and previous adverse pregnancy (pg) outcome (APgo) (2) treatment and outcome in a next pregnancy.

**Design:** retrospective, observational.

**Material and methods:** Patients (pts): Medical charts from 27 pts with IT referred to our hematological unit were evaluated. Diagnosis: Group 1: pregnancy loss 12 pts (10 weeks: 6, >10: 6); Group 2: 2 other pg complications: 8 pts (intrauterine growth restriction (IUGR), preeclampsia, oligoamnios and/or placental thrombosis). Group 3: family history of thrombosis and/or APgo: 7 pts. Laboratory tests: Deficiency of Protein C 1 pt, Protein S 7 pts, Antithrombin 2 pts, heterozygous for the factor V Leiden mutation: 11 pts and for prothrombin G20210A: 6pts; 5 have combined IT with a lupus anticoagulant.

**Evolution and treatment:** there were 21 new pg: 19/21 pg were treated with enoxaparin – Group 1: 9 pg; Group 2: 3 pg; Group 3: 7 pg. Outcome: Live birth rate 68% (13/19), stillbirth, 5 early abortions (3 from the same patient) and 3 IUGR. Enoxaparin doses range: 40–80 mg/d; anti-Xa activity: range 0.3–0.7 IU/dl.

**Conclusion and comments:** (1) Women with IT are at increased risk of adverse pregnancy outcome. (2) In our experience live birth rate in women treated with enoxaparin was 68%, we observed a wide heterogeneity in the evolution of different patients. (3) Additional effective tools to select and predict those patients with IH at higher risks of adverse outcome are required (doppler ultrasound, d-dimer, fibrin monomer etc.). (4) Fetal genotype contribution to adverse pregnancy outcome warrants further studies.