Obstetric interventions included hysterectomy (1), balloon occlusion (2) ERPC (1), hysterotomy (1), cervical tear repair (2) and vaginal pack (2). Obstetric cause of haemorrhage was identified to be uterine atony (4), retained products (2), uterine injury (2) and no identifiable cause (2). All women recovered fully.

Results: The profound coagulopathy in these women was characterised by a reduction in fibrinogen that was out of proportion to the anomalies in other clotting parameters and platelet counts. Treatment with cryoprecipitate reversed this reduction and controlled the haemorrhage although 5/8 patients required significant surgical intervention.

Conclusions: 1.The coagulation anomalies in these women are indicative of a defibrination syndrome that differs from DIC in the disproportionate reduction in fibrinogen level and the relatively rapid and complete resolution with blood product replacement and treating uterine pathology.

2. Two stage TOPs in late second trimester is associated with significant morbidity.

Disclosure: No relevant conflicts of interest to declare.

Abstract# 4045

Rituximab Use in Four Patients with Acquired von Willebrand's Syndrome. Priya C. Singh*, Jamie E. Siegel*, Jaime Caro*, Emmanuel C. Besa. *Department of Hematology, Thomas Jefferson University Hospital, Philadelphia, PA, USA.*

Treating Acquired von Willebrand's Syndrome (AVWS) is a challenge requiring multiple therapeutic modalities to achieve success in controlling and preventing bleeding episodes. From review of the literature, clinical use of rituximab, an anti-CD20 monoclonal antibody, in AVWS has not been reported. We present our experience with four patients treated with rituximab for steroid or intravenous immunoglobulin (IVIG) refractory and/or dependent AVWS associated with IgG monoclonal gammopathy of undetermined significance. Rituximab at a dose of 375mg/m^2 was administered intravenously weekly for 4 consecutive weeks in the first patient. After 3 cycles of rituximab, we observed a correction of her bleeding time to normal, improvement of her prolonged aPTT, a decrease in her monoclonal IgG and cessation of her bleeding episodes for 29 months. She relapsed and was retreated with rituximab at the same dose for 3 cycles with no improvement in aPTT and bleeding time. She has had no further bleeding episodes after compliance with epsilon aminocaproic acid for one year. The second patient received rituximab intravenously at a dose of 375 mg/m^2 weekly for 4 weeks. Prolonged aPTT was unchanged after treatment. He was asymptomatic for 8 months and then received prophylactic IVIG and von Willebrand Factor concentrate (Humate-P) for elective hand surgery. The third patient had a concomitant worsening idiopathic neuropathy and received rituximab 375mg/m^2 intravenously daily for 2 consecutive days two weeks apart for his neuropathy. His neuropathy and prolonged aPTT did not improve and he developed gastrointestinal bleeding 1.5 months later. The fourth patient received rituximab 150mg/m^2 intravenously weekly for 4 consecutive weeks. Prolonged aPTT was unchanged after treatment. He experienced no bleeding symptoms for 38 months. Factor VIII, Ristocetin Cofactor, von Willebrand Antigen and IgG levels were not significantly affected by rituximab use in cases 2-4. Rituximab seemed to be most effective in the first and fourth cases. The dosing and number of cycles is unclear. Success in the first case with multiple cycles of therapy may be needed for response and warrants further evaluation. Additionally, it appears therapy needs to be reinforced with other agents to prevent or stop bleeding. It was well tolerated with no infectious complications in our patients. Only one patient had an infusion related reaction, which did not require stopping therapy. Further prospective studies are needed to evaluate the efficacy of rituximab and establish the dosing and treatment duration in AVWS.

Disclosure: We present our experience with rituximab use for Acquired von Willebrand's Syndrome since it has not been reported in the literature.

Abstract# 4046

The Impact of Rebleeds in Cost Modelling of Treatment Strategies in Patients with Hemophilia A and Inhibitors. Angela Huth-Kuehne*,[1] Peter Lages*,[1] Rainer Zimmermann*.[1] (Intr. by Guenter K.H. Auerswald) *[1]Haemophilia Center, SRH Kurpfalzkrankenhaus, Heidelberg, Germany; [2]Haemophilia Center, Prof. Hess Kinderklinik, Bremen, Germany.*

Introduction: To investigate the cost-effectinvess of the treatment in patients with hemophilia and inhibitor, the expected number of rebleeds in home treatment is an important factor if one compares different treatment options e.g. APCC or rFVIIa . To evaluate the economic impact in mild to moderate bleeds in home treatment we used a robust established model to compare 1st, 2nd and 3rdline treatment either with rFVIIa or APCC. For the rate of rebleeds we refer to published data on a broad basis.

Methods: To compare the economic impact of different treatment regimes, this model refers to an on-demand home treatment of bleeding episodes in adult hemophiliacs (mean body weight 75 kg) and is based on a previously published flow-diagram and calculation formula (Knight 2003). Dosage per bolus: rFVIIa 90µg/kg, aPCC 60 U/kg. Costs for German market were fixed at 1.21 €/IU for APCC, 0.73 €/µg for rFVIIa and 308.98 € /day in hospital. 3 treatment strategies (TS) were calculated:

TS 1:
APCC at home, followed by in hospital APCC (2nd-line) and rFVIIa (3rd-line)
TS 2:
APCC at home, followed by in hospital rFVIIa (2nd-line) and rFVIIa (3rd-line)
TS 3:
rFVIIa at home, followed by in hospital rFVIIa (2nd-line) and rFVIIa (3rd-line)

The model was based on published data on dosing and outcome of therapy in each treatment phase. Probability of failure to control bleeding or rebleeding after first-line home treatment was set at 23.5% with APCC and 9.1% with rFVIIa.

Results: Median costs for TS 1 are 23,521 Euro per bleeding episode as compared to 21,963 Euro for TS 2 and 14,328 Euro for TS 3. The difference is caused by costs for first attempt to control bleeding at home (APCC 16,335 Euro as compared to rFVIIa 11,333 Euro) and costs at later stages of treatment. Further analyses show, that favorable result for TS 3 is robust to changes of different parameters such as patients' weight.

Conclusions: First line treatment with rFVIIa in case of on demand treatment seems to be the most cost effective option in inhibitor treatment in a home treatment setting or in- hospital treatment. Local prices have to be taken into consideration.

Reference: 1. Knight C, Haemophilia 2003.

Disclosure: No relevant conflicts of interest to declare.

Abstract# 4047

Successful Treatment of Intra-Cranial Hemorrhage with Repeated Doses of Activated Recombinant FVII in a Newborn with Severe Factor VII Deficiency. Roula Farah*,[1] Dany Hamod*,[1] Elie Bechara*,[1] Nancy Melick*,[1] Paul Hage*,[1] Muriel Giansily-Blaizot*,[2] Ahmed S. Sallah.[3] *[1]Pediatrics, Balamand University, Beirut, Lebanon; [2]Pediatrics, CHU, Montrellier, France; [3]International Operations, Novo Nordisk A/S, Athens, Vouliagmeni, Greece.*

Factor VII deficiency is a rare inherited bleeding disorder. Intracranial hemorrhage can occur in approximately 1 to 10% of the cases. We report the case of a one month old girl from Lebanon who presented with vomiting, abnormal cry, lethargy and partial seizures. She was diagnosed prenatally with severe factor VII deficiency after detection of a splice-site mutation in exon 2 of the FVII gene (IVS2+1 G→C) that was described previously in her sister who died at the age of 4 months from severe intracranial hemorrhage. The parents are first degree cousins and are both heterozygous. She has a healthy heterozygous two year old sister.

An emergency head CT Scan showed intra ventricular and right hemispheric intra parenchymal hemorrhage, peri-hemorrhage edema and minimal midline shift. The patient was placed immediately on mechanical ventilation and anti-epileptics and activated recombinant factor VII (rFVIIa, NovoSeven) was administered intra-venously at 60 ug/kg for the first dose then 30 ug/kg/dose every 4 to 6 hours for 10 days then once a day for 5 days. She was treated conservatively with no surgery. Stabilization of the hematoma was observed with gradual improvement of her neurological condition. Communicating hydrocephalus developed later and a ventriculo-peritoneal shunt was placed on day 16 post-hemorrhage. Subsequently, she received weekly infusions of rFVIIa at 30 ug/kg/dose for 4 weeks after this episode and showed no bleeding symptoms. Follow-up two months later showed axial hypotonia and a mild left sided spasticity. Auditory evoked potentials were normal. However, afte prophylactic rFVIIa was dicontinued, the patient developed sub-arachnoid hemorrhage and was placed again on weekly prophylactic infusions of rFVIIa at 30 ug/kg/dose. The patient tolerated the infusions very well. No side-effects were observed. Conclusion: rFVIIa is safe and effective in Factor VII deficient newborns with intracranial hemorrhage. Rapid treatment at the onset of hemorrhage is critical to reduce mortality and improve the outcome. Prophylactic factor VII infusions can be proposed in this setting to minimize the risk of subsequent bleeding episodes. The ideal dosing and schedule for treatment and/or prophylaxis will have to be defined. Despite the short half-life of rFVIIa, weekly infusions in our experience seemed safe and effective in reducing the incidence of further bleeding episodes.

Disclosure: The sponsoring author: Ahmed S Sallah is employed by Novo Nordisk A/S.

Abstract# 4048

Using Recombinant Activated Factor VII (rFVIIa) in Refractory Bleeding: A Community Hospital Experience. Alaa Muslimani*,[1] Hamed Daw.[2] *[1]Internal Medicin, Cleveland Clinic Health System, Fairview Hospital, Cleveland, OH, USA; [2]Oncology/Hematology, Cleveland Clinic Cancer Center (Moll Pavilion), Cleveland Clinic Health System, Fairview Hospital, Cleveland, OH, USA.*

Introduction: Recently, there has been an increase in using rFVIIa for uncontrolled bleeding in non hemophilic patients. While evidence-based guidelines exist for using rFVIIa in hemophilia, none are available for its off-label use. We report four cases who were treated with rFVIIa for massive uncontrolled hemorrhage.Method: Four [3 female (F) and one male (M)] critically ill patients with a median age of 59.25 years (range 49-78) exhibiting massive, life-threatening bleeding were treated with rFVIIa after conventional therapy [transfusion of fresh frozen plasma (FFP), red blood cell (RBC), platelet (Plt) and cryopreciptate (cryo)] had failed to control the blood loss. The starting dose was 90 µg/kg. If there was no response within 20 minutes, a second dose of 90 µg/kg was given. The median rFVIIa number of treatments were 4 (range 1-8). Treatment efficacy was evaluated after each dose and was based on : the amount of hemorrhage judged visually, and the number of red blood cell units required to maintain a stable hemoglobin level of > 8g/dl. Clinical response was rated as complete (no transfusion requirement, or change from severe to minor type of bleeding), partial (decrease of hemorrhage from severe to moderate), or failure (no change of hemorrhage and/or no change in transfusion requirement). rFVIIa was given in conjunction with transfusion of packed RBC in order to avoid further loss of clotting factors. If there was no response after a total of >200 µg/kg, the indications for rFVIIa administration were re-checked.

Results: After administration of rFVIIa, three patients had a complete response with cessation of bleeding. There was a decrease in the transfusion requirements in the single non-responder case who later died of massive myocardial ischemia.

Most studies have shown that use of rFVIIa yields better results when given earlier rather than later. Nevertheless, our first patient encounter showed good result despite initiation of the therapy 3 weeks after the onset of bleeding. Finally, patient number 3 showed the first successful reported use of rFVIIa for bleeding associated with multiple myeloma. Conclusion:

1. **Anchor Name: (/p1/col2/para1)** *[NHSM (Neha Sharma)]*