orrhagic events. *Conclusions*. Rituximab therapy is effective in the treatment of acquired hemophilia A with high titer inhibitor resistant to other immunesuppressive therapy lines.

1048

DYSKERATOSIS CONGENITA: UNUSUAL PRESENTATION WITH TROMBOCYTOPENIA IN EARLY AGE

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Backgrounds. Dyskeratosis congenita (DC) is rare, usually fatal inherited skin and bone marrow (BM) failure syndrome that displays considerable genetic and clinical heterogeneity. Classical DC is an inherited BM failure syndrome characterized by the mucocutaneus tried of abnormal skin pigmentation, nail dystrophy and mucosal leucoplakia A variety of the other somatic abnormalities have also been reported. At genetic level X-linked recessive, autosomal dominant (AD) and autosomal recessive (AR) forms of the disease exist where the genetic basis of the X-linked and AD forms have been determined. The X-linked form of DC is due to mutations in DKC1, the gene encodes dyscerin, a protein that is part of telomerase complex. Autosomal dominant DC is caused by mutations in TERC, which codes for the RNA component of telomerase. The DKC1 gene is expressed in all tissues of the body consistent with it having a *house keeping function* in the human cell. This correlates well with the multi system phenotype of DC. *Aims.* In this report we present unusual onset of DC with trombocytopenia as a first presentation at an early age. *Methods/Results.* A 4 years old male patient with DC, presented at the age of 18 months with isolated trombocytopenia presiding characteristic skin finding and nail dystrophy. The trombocytes count of 24. 000/mm^3 persisted without the presence of anemia or Neutrogena Trombocytopenia responded to kortikosteroides at a dose of 2.5 mg/kg per day. Six mounts late he was admitted in the hospital with sever anemia; trombocytopenia and neutrogena Severe aplastic anemia was later diagnosed. Clinical examination showed hyperpigmentation over the neck, and nails dystrophy. All the nails were dystrophic. To substantial the diagnosis the genes responsible for the X-linked and AD forms of DC (DCK1 and TERC) were screened for mutations. No abnormal patterns have been detected in patient in either gene. However, his mother appears to have a highly skewed pattern of X- chromosome inactivation that is characteristically observed in carriers of DKC1 mutations. *Conclusions.* This patient's clinical course is interesting because the thrombocytopenia developed as an isolated symptom at the age of 18 months and preceded the skin anomalies. The diagnosis of dyskeratosis congenita was made only after an evolution. The diagnosis of dyskeratosis congenita, should be considered in every child first seen with thrombocytopenia or aplastic anemia. In some patients the BM abnormalities may appear before the mucocutaneous manifestations and can lead to an initial diagnosis of 'idiopatic aplastic anemia'

1049

SUCCESFULL TREATMENT OF RECOMBINANT FACTOR VIIA OF THERAPY RESISTANT LIFETHREATENING BLEEDING IN TWO PATIENTS WITH THROMBOCYTOPENIA

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Thrombin formation has a crucial role in providing homeostasis. The hemostatic effect of activated recombinant FVIIa (rFVIIa) is mediated by an enhanced rate of thrombin generation. Recombinant FVIIa was developed initially for treatment of bleeding in Hemophilia A patients with inhibitors. Thereafter it was recognized that rFVIIa (NovoSeven) was a very valuable haemostatic agent also for different bleeding disorders such as nonhemophilic patients with acquired antibodies against rFVIII, congenital FVII deficiency, uncontrolled bleeding due to thrombocytopenia and functional platelet defects. Here we report the successful use of an activated recombinant factor VIIa in two patients with severe bleeding caused by therapy resistant thrombocytopenia. Patient 1; A 14 year old girl with Evans syndrome was unresponsive to the repeated therapy of immunoglobulin and corticosteroids for six years. She was recently presented with somnolence, severe headache, nausea and vomiting. The cranial computerized scan revealed left frontotemporal hemorrhage. Her initial platelet count of 2500/mm^3 was increased up to maximal 10-15,000/mm^3 despite vigorous platelet transfusions. Since we failed to achieve homeostasis we used rFVIIa at a dose of 100 microg/kg along with platelet suspensions which was followed by 50 microg/kg repeated doses at 2-h intervals for two times. The bleeding was taken to control and the symptoms of the patient improved gradually and she was discharged without any sequel. Patient 2 was an 18 year old girl with therapy resistant Fanconi's Anemia in whom platelet refractoriness was developed. She suffered from severe life-threatening menorrhagia. In this patient menorrhagia could not be controlled by repeated thrombocyte transfusions and oral contraceptive therapy. Recombinant FVIIa at initial dose of 90 microg/kg was given and it was repeated at the same doses at 2-h intervals for two times. Her hemorrhage decreased gradually and ceased completely after the third injection of rFVIIa. No side effects related to use of rFVIIa has been observed in these two patients. We concluded that recombinant factor VIIa should be considered as a therapy choice in life-threatening bleeding of the patients with therapy resistant immune thrombocytopenia and aplastic anemia in whom thrombocyte refractoriness is developed.

1050

BLOOD IN URBAN MULTIPLE CASUALTY INCIDENTS: THE EXPERIENCE OF A LEVEL 1 TRAUMA CENTER IN ISRAEL

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Background and Objectives: The issue of blood utilization and blood bank operating protocol in the setting of multiple casualty incidents (MCI) has not been elucidated. The objectives of the current study were to analyze the pattern of blood ordering and administration as weel as the timing and type of components, during MCIs, in order to determine the framework needed for the blood bank in a level I Trauma Center in the setting of such events. *Methods.* A retrospective study evaluating data collected in 18 consecutive terrorist attacks in the city of Tel-Aviv between January 1997 and February 2005. Data were retrieved from chart review and from the blood bank and emergency department (ED) computerized MCI registry programs and analysed by size of MCI, type and severity of victim injury, timing and type of blood and components. *Results.* Three hundred thirty two packed red blood cell (PRBC) units were transfused altogether, half of which were administered in the setting of massive transfusion (>10 PRBC units per 24 hours) to 4.7% of the patients. The ratios of transfused PRBC units per evacuated and admitted patients 'packed cell per patient index (PPI) - were 0.58±0.98 and 1.1±1.5, respectively. The PPI rose significantly when there were over 25 evacuated victims (p=0.039). The most frequent major blood group transfused was O (Rh positive and negative), 57% of all transfused PRBCs, about half of which were administered urgently, untested. Half of the blood units were supplied during the first two hours post admission. TASMC blood bank standard operating protocol (SOP) includes sending a blood bank liaison to the ED and OR to coordinate activity and supply urgent, untested, group O PRBC units. *Conclusions.* Roughly, one unit of blood per admitted victim in a small MCI and 2 units in a large MCI, half of which are group-O, may serve as a basic estimate of the transfusion needs in the first hours after urban MCIs. Blood bank operations must be coordinated with the other medical teams dealing with a MCI.

1051

INVESTIGATION OF PRIMARY HEMOSTASIS USING PFA-100 ANALYZER

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Backgrounds. LDL-apheresis is a method of extracorporeal elimination of serum LDL-cholesterol that is used for treatment of patients with severe hyperlipidemia resistant to diet and pharmacotherapy. Applicable markers that could be used to determine efficacy of this treatment to lower the activity of atherosclerosis are still to be found and remain unresolved. Activity of primary haemostasis plays an important role in the development of atherosclerotic complications. *Aims.* We hypothesize that investigation of primary haemostatic activity could be a quick and useful marker for monitoring LDL-apheresis efficacy. The aim of this work was to verify this hypothesis. *Methods.* Commercial analyser Dade Behring PFA-100, Germany (PFA, platelet function analyse) was used

for all investigations. This analyser enables quantitative measurement of platelet-mediated haemostasis in noncoagulable (citrated) blood. The method simulates platelet activation by mechanical stress - shear stress, and also simulates contact of platelets with collagen. There were 9 patients with familiar hypercholesterolemia in the study group (4 females and 5 males). Age ranges from 17 to 59 years (46,4 years average and 55 years median), 2 of them have homozygous hypercholesterolemia. Our aim was to investigate the changes before and after procedure two times in every patient. *Results.* 18 pairs of samples were examined using COL/EPI membrane (collagen/epinephrine) and 17 pairs of samples were examined using COL/ADP membrane (collagen/ADP), total number of samples was 70. Closure time (CT) values were prolonged after separation in all cases but CT prolongation was not statistically significant (p<0,14). No differences between homozygous and heterozygous patients were found. *Summary/Conclusions.* Investigation of primary haemostasis immediately after procedures using PFA-100 analyser is not a suitable marker and could not be used to determine the optimal intensity of particular LDL-apheresis procedures.

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1052

TWINING IS A SIGNIFICANT INDEPENDENT FACTOR IN THE DEVELOPMENT OF CHILDHOOD MALIGNANCIES

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In the past few years we have noticed a marked increase in the incidence of cancer among twins treated at the Pediatric Hematology-Oncology Unit (PHOU) of Soroka Medical Center (SMC) in Beer-Sheva, Israel. In this work, we reviewed the relationship between twinning and the risk of developing cancer during early childhood. Children born at SMC between Jan. 1991 and Sep. 2003, with any malignancy were included in the study if they were under 13-years-of-age at time of diagnosis. Three controls of the same sex were matched to each patient from the birth registries of the same day at SMC. A twin was not chosen as a control to its sibling. Data from patients, controls, and mothers were collected from medical records and included three areas of investigation: demographics and obstetric history of the mothers, delivery data, and gestational events and/or interventions (infertility including *in vitro* fertilization (IVF), ART, diabetes mellitus (DM), hypertension (HTN), urinary tract infections (UTI), iron deficiency anemia (IDA), and medications). A total of 143,087 deliveries, resulting in 145,503 children, were registered at the Soroka Medical Center (SMC) between January 1991and September 2003. Of those, 98.37% were singleton and 1.63% were multiple births (2,261 twins; 77 triplet and quadruplets), cumulating in 972,000 patient years of follow up. The crude incidence of cancer during childhood is 14:100,000 per year, while the incidence of cancer calculated for the children born during the study period was 10.5:100,000 per year. Of the 92 children with cancer, complete information was obtained for 65 patients (70.6%); eight (12.3%) were twins, four were born after ART (6.7%), two of whom were twins. Significantly more Bedouin children were found in the patients group. According to this data, the total expected number of cancer cases among twins born during the study period was 2.23, while the total observed number at the PHOU is 3.58 times higher (8 cancer cases), p<0.001. Twining *per se* was found to be an independent factor in the development of childhood cancer. Although seeming significant in a univariate analysis, this study cannot point to a significant multivariate correlation between ART and childhood cancer (p=0.07), most likely due to the small sample size. More children of Bedouin origin were found in the patients group possibly due to higher consanguinity rate and/or low socioeconomic status. However, to date, no studies have addressed this matter and more investigation is needed.

1053

SERUM AND SALIVARY IRON AND FERRITIN LEVELS IN PATIENTS WITH THALASSEMIA

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Backgrounds. The thalassemias are a group of autosomal recessive blood diseases of varying degrees of underlying genetic defects that include total or partial deletion of globin chains and nucleotide substitutions, deletions or insertions. Current therapy includes regular blood transfusions and iron chelation. Chronically increased iron load is due to excessive hemolysis, increased intestinal iron absorption and frequently blood transfusions that causes organ damage and dysfunction. Especially in childhood period, serum iron level measurement methods are tecnically invasive. Difficulty of the current methods used to evaluate the iron accumulation in organs suggests the importance of saliva usage for diagnosis. In this study, it has been supposed that salivary iron amount could be a marker of total body iron storage in patients with thalassemia. *Material and Methods.* 34 healthy children as control group were compared with 71 thalassemia major, 10 thalassemia intermedia and 15 thalassemia trait. Salivary and serum iron and ferritin levels were measured in all groups. *Results.* there was no statistically significant difference between the control group and other gorups by means of age and gender (p > 0.05). There was a correlation between serum and salivary iron and ferritin levels in thalassemia major, intermedia and trait groups (Table)

Table. Correlation between serum and salivary iron and ferritin levels in patients thalassemia.

	Salivary and Serum Iron	*Salivary and Serum Ferritin*
Control	r =0.885, p=0.000*	r =0.842, p=0.000*
T. Major	r =0.972, p=0.000*	r =0.364, p=0.034*
T. Intermedia	r =0.720, p=0.019**	r =0.891, p=0.001**
T. Trait	r =0.955, p=0.000**	r =0.831, p=0.000**

As a conclusion, salivary iron and ferritin levels increases as well as serum levels. This increasment in salivary iron amount may be an indicator of total iron accumulation. Therefore non invasive, salive samples for measurement of iron and ferritin may prefer instead of blood samples in patients with thalassemia. For this reason, we think that more extensive and controlled studies are needed to use the saliva as a routine diagnostic material.

1054

FERTILITY AND REPRODUCTION IN THALASSEMIA MAJOR

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Backgrounds. Therapeutic advances in thalassemia major have increased the average lifespan and improved the quality of life patients. Attainment of reproductive capacity and creation of a family has become a challenging task. Hypogonadotrophic hypogonadism due to hemosiderosis is still present and become a barrier in their desire for parenthood. Nowaday women with thalassemia can safely complete pregnancy, but the decision to conceive has to be carefully considered by a couple in consultation with their doctors. Patients with thalassemia who have a normal menstrual cycle may conceive spontaneously. Those suffering from primary or secondary amenorrhoea can be submitted with hormonal treatment in order to stimulate the production of ova and the induction of ovulation. *Aims.* Aim of our study is to exstimate the frequence of fertility (spontaneous or after induced ovulation) and pregnancy complications for mother and newborn, in patients admitted to the Paediatric Department- Thalassaemia Ward *G. Martino* Policlinico. *Patients and Methods.* We followed 36 women mean age 32 (18-46) years. All patients were treated according to the standard treatment protocol. 9/36 women with Thalassemia Major became pregnant and were the object of our study. At the beginning of pregnancy, average age was 26 years. Five pregnancies were spontaneous and four were induced after ovarian stimulation followed by natural insemination. Women who expressed the desire to become pregnant underwent a complete evaluation of psychological and clinical conditions. Glucose tolerance, tiroid, serum ferritin levels, hepatic and renal function tests, bidimensional echocardiography were performed before, during the pregnancy and after delivery. Also Bone Mineral Density (BMD) was measured, by the DEXA method, before pregnancy and after delivery. Once the patients were confirmed to be pregnant, iron chelator treatment was stopped. Mean pre-transfusional Hb and blood consumption have been monitored in order to keep pre-transfusional Hb at 10-10,5 g/dl levels. A complete obstetrical survey was performed every two weeks. *Results.* Our findings show that 8 babies were delivered by elective caesarean section at 37° weeks of gestational age (GA). The mean birthweight of the newborns was 2954 g. All babies were normal. Ferritin levels increased during pregnancy in all