THROMBIN B-LOOP PEPTIDE (B-LP) HAS SPECIFIC RECEPTORS ON MACROPHAGES. Sherin Devaskar, Lynn Karycki, George Wilner and Arnold Kahn. St. Louis and Washington Universities, Pediatric Research Institute, Cardinal Glennon Children's & Jewish Hosps. Dept. of Pediatrics & Pathology, St. Louis, MO.

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α-Thrombin, a serine protease with potent procoagulant activity, has the capacity to stimulate the proliferation of fibroblasts, vascular endothelial cells and macrophages. However, for the latter cell type, esterolytically intact enzyme is not required and, in fact, the mitogenic potency of the molecule appears to reside in a limited unique region of thrombin termed the B-loop peptide (B-LP). In an attempt to determine the mechanism by which B-LP mediates mitogenesis, B-LP sensitive J774.1 macrophage cells were fixed in paraformaldehyde and incubated for 1 hr with ^{125}I B-LP in the presence and absence of exogenous unlabeled ligand (10^{-10}-10^{-7})(n=5). The data show that the J744.1 cells possess a specific, saturable B-LP receptor that exhibits a Kd of ~1.12 nM; a value that coincides with the concentration of peptide necessary to optimally elicit a mitogenic response in these cells. Native α-thrombin, inactivated DIP-thrombin and unlabeled B-LP displace bound ^{125}-labeled B-LP from J774 cells at equimolar concentrations suggesting that all the 3 peptides interact with a common receptor site on macrophages. Scatchard analysis indicates that ~ 4000 such receptors are present per cell. We suggest that ligand activation of these receptors is responsible for triggering the biological response associated with thrombin-stimulated macrophages, and therefore, is likely pivotal in promoting the accumulation of these cells during the processes of inflammation and wound healing.

LOSS OF HEPATITIS B ANTIBODY IN HTLV-III POSITIVE HEMOPHILIA PATIENTS John H. Drake, Richard T. Parmley, Howard A. Britton, Department of Pediatrics, The University of Texas Health Science Center at San Antonio, San Antonio, Texas

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Patients with hemophilia were evaluated for the presence of HTLV-III virus exposure. The presence of this antibody was then correlated with the loss of existing antibody to hepatitis B surface antigen (HBsAb) or the inability to develop HBsAb after receiving commercially available hepatitis B vaccine. Of the 115 patients studied, 54 were HTLV-III positive whereas 61 were HTLV-III negative (see Table). Evidence of HBsAb (n=37) or exposure to hepatitis vaccine (n=10) was found in 87% of HTLV-III positive patients at some time during their care in our clinic. However, 17% demonstrated subsequent antibody loss and/or did not respond to hepatitis vaccine. This unusual HBsAb response was restricted to patients ≤ 17 years of age (63% of all patients). This result contrasted to only a 2% loss of HBsAb or vaccine non-response in the HTLV-III negative patients who had previously been positive for HBsAb (n=24) or were given the hepatitis vaccine (n=16). This result suggests that loss or alteration of hepatitis B immunity in children occurs as a result of HTLV-III infection or exposure.

		HBsAB +		HBsAB -		Unusual HBsAB[1]	
	N	N	%	N	%	N	%
HTLV-III +	54	38	70	7	13	9	17
HTLV-III -	61	40	65	20	33	1	2

[1]Loss of HBsAb or failure to respond to vaccine ($p < 0.005$, Fisher absolute probability test).

ACUTE MIXED LINEAGE LEUKEMIA: UNIQUE KARYOTYPIC, GENOTYPIC, AND PHENOTYPIC FEATURES. Jonathan Ducore, Richard Wasserman, and Nancy Schneider (Spon. by George Buchanan). Univ. of Tex. Health Science Center, Dept. of Pediatr. and Path. Dallas, TX.

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A 9 yo black male with acute leukemia showed a unique chromosome abnormality and unusual phenotypic and genotypic features. He presented with fever, lethargy, weight loss, and cervical adenitis without organomegaly or enlarged thymus. The Hgb was 4.6 gm/dl, platelets 50,000/dl, and WBC 25,000/dl, 96% blasts of moderate size with scanty-cytoplasm and indistinct nucleoli. Some were larger with more cytoplasm and had nucleoli. The marrow blasts were larger, had large nuclei, prominent nucleoli, a moderate amount of basophilic cytoplasm and no auer rods. They were 42% Sudan black and 20% peroxidase positive, FAB-M1. Immunophenotyping showed T-cell markers (Leu 1,9)-88%, B-cell markers (Leu 12)-44%, myeloid markers (My 9)-5%, Dr (Ia)-0%, and TdT-29%. The cells were negative for surface and cytoplasmic immunoglobulin (Ig). Karyotyping showed 46,XY,t(1; 10) (p32; p13), in all cells analyzed. Southern blots showed Ig heavy chain and T-cell receptor ß-chain gene rearrangement. In summary, the patient had acute leukemia with L1 or L2-M1 peripheral blasts. The marrow cells were FAB L2-M1 and histochemically were M1. Immunophenotyping showed features of B-cells (leu12) and T-cells (leu1,leu9). The Ig heavy chain and T-receptor ß-chain genes were rearranged. All cells had a new translocation, t(1:10) (p32:p13).

HEMATOLOGIC MANIFESTATIONS OF PEDIATRIC AIDS. Maadhava Ellaurie; Kiran Shah; Larry Bernstein; Arye Rubinstein. Albert Einstein College of Medicine, Department of Pediatrics, Bronx,New York.

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The hematologic manifestations of 100 pediatric patients with AIDS/ARC were reviewed. Acute or chronic anemia was present in 94% of all patients. Two patients had autoimmune hemolytic anemia and 1 patient had an aplastic anemia. A positive Coombs test was detected in 40% of all patients. Leukopenia and neutropenia occurred in 50% and 40% of patients respectively. Antineutrophil antibodies were detected in 2 patients. Ten of 13 children developed neutropenia on Bactrim. Forty percent of all children were lymphopenic. Monocytosis and eosinophilia occurred in 66% and 40% of patients respectively. Thrombocytopenia was seen in 33% and of these 25% developed a persistent thrombocytopenia. Platelet antibodies were detected in 10 of 11 patients. Pancytopenia occurred in 20% of children with opportunistic infection (O.I.). Acquired Von Willebrands disease and autoantibodies to Factors X, XI and XII were seen in 2 individuals. Peripheral smears revealed ovalocytes, microcytosis, hypochromia and atypical lymphocytes. Bone marrow examination showed hypercellularity, myeloid hyperplasia and increased plasma cells and lymphocytes. Decreased erythropoeisis, dysmyelopoeisis, dyserythropoeisis and megaloblastic changes were occasionally seen. Bone marrow cultures were positive for mycobacterium avium intra cellulare (4), candida (2) and CMV (1) in a total of 7 patients.

GENETIC MANIPULATION OF HUMAN HEMATOPOIETIC CELLS WITH RETROVIRUS VECTORS. Zeev Estrov, Melvin H. Freedman, John H. Dick. University of Toronto, Hospital for Sick Children, Division of Hematology and Department of Genetics. Toronto, Canada.

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We transferred new genetic information into human cell lines and hematopoietic stem cells using retrovirus vectors. These vectors, containing the dominant selectable gene (neo) for resistance to the antibiotic G418, were introduced into amphotropic helper viruses to achieve a high frequency transduction into human cells. Human cell lines or freshly obtained human marrow cells were co-cultivated with irradiated vector producing cells, and cultured in clonogenic assays with and without G418. Survival curves of non-transfected cells with increasing concentrations of G418 resulted in a dose-dependent inhibition of colony growth with a final dose of 500 to 800 µg/ml. Transfected promyelocytic leukemia (HL-60), erythroleukemia (OCI-M2) and different lymphoid cell lines with N2 and SV(X) vectors, revealed G418 resistant colonies in frequencies ranging from 3.2 to 44%. Similar frequencies were found with human marrow cells. Transfection with either N2 or NEOμ vectors produced G418 resistant hematopoietic progenitor colonies of the erythroid (BFU-E) granulocyte-macrophage (CFU-GM), and mixed (GFU-GEMM) lineages in frequencies ranging from 8 to 40% after 14 days in culture. We conclude that selected retrovirus vectors can be successfully used to insert new genetic information into pluripotent and committed human hematopoietic progenitor cells.

EVALUATION OF HEMOGLOBIN SATURATION DURING SLEEP IN CHILDREN WITH SICKLE CELL DISEASE. Beatrice A. Files, Beatrice C. Lampkin, Karen A. Kalinyak, Jeffrey S. Lobel, Debbie Brocker, Timothy D. Guilfoile, Children's Hospital Medical Center, Cincinnati.

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Vaso-occlusive sickle cell crises have been described with onset during sleep. Nineteen sleep studies were performed on 14 children with sickle cell disease to evaluate oxygen saturation during sleep. The patients, age 4 to 17 years, were selected based upon the number and frequency of crises, and history of nocturnal crises. Total sleep time (TST) and percent TST as rapid eye movement (REM) were comparable to normals for age. Changes in respiratory dynamics (apnea and hypopnea) and oxygen saturation were monitored during sleep. Four individuals experienced 1 to 2 episodes of apnea per night. Six children in 8 studies demonstrated 1 to 48 hypopneic events. Oxygen desaturation was defined as a ≥ 4% drop from baseline or ≤ 90% actual saturation. The duration of desaturation was quantitated in 14 of 19 studies. Desaturation associated with apnea or hypopnea was appreciated in only four studies. The total accumulative duration of desaturation was 1 to 9 minutes per study. Oxygen desaturation not associated with changes in respiratory dynamics occurred in all but one patient. The average duration of desaturation was 20 minutes (range 3 to 100 min.) These data reveal marked oxygen desaturation during sleep in a subset of patients with sickle cell disease, and suggest a relationship between desaturation and increased frequency of vaso-occlusive crises.