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LOW-TOXICITY OUTPATIENT ADOPTIVE IMMUNOTHERAPY OF METASTATIC CANCER WITH AUTOLOGOUS LYMPHOCYTES GENERATED BY IN VITRO IMMUNIZATION (IVI), M.E. Osband and G.A. Carpinito, Boston U Sch Med and Boston City Hosp, Dept of Pediatrics and Urology, Boston.

We have previously described results with a novel form of adoptive immunotherapy using in vitro immunized (IVI) autologous lymphocytes. We now report results from an on-going study using an improved version of that method. Patient lymphocytes are depleted of suppressor T-cells and in vitro immunized for 60 hours in medium containing autologous serum, mixed lymphocyte culture supernatant and a 3M KCl autologous tumor extract. The resultant IVI cells are washed, depleted again of suppressor cells and infused into the patient. All patients also receive cimetidine to block in vivo suppressor cells. Patients will be treated monthly for 6 months. To date, 30 patients have received a total of 113 cell infusions, all delivered on an outpatient basis, (average of 10^9 IVI cells/infusion). Toxicity has been minimal, consisting only of mild, transient fever and chills accompanying 42 of the infusions (37%). Twenty-one patients have reached the first evaluation timepoint at 3 months.

	Progression	Stable	MR	PR	CR	Total
Renal	12	3		1		16
Pancreas	1		1			2
Colo-Rectal	1					1
Melanoma				1	1	2

(MR=minor response;PR=partial response;CR=complete response)

This approach to immunotherapy is safe and appears to be biologically active, in that 7 of 21 evaluable patients (33%) have evidence of stable disease or objective response after only 3 months of treatment.

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TREATMENT OF HISTIOCYTOSIS-X WITH SUPPRESSIN A: RESULTS FROM A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY. Michael Osband, Chandrakant Panse and Philip Lavin, Boston University School of Medicine and Boston City Hospital, Dept of Pediatrics, and Harvard Medical School, Dept of Surgery, Boston.

We have previously described that thymic hormones might be useful in the treatment of histiocytosis-X. Based on those data, the Office of Orphan Products Development at the FDA is sponsoring a randomized, double-blind, placebo-controlled clinical study to determine if Suppressin A, a mixture of thymic hormones that specifically induce the differentiation of suppressor T-lymphocytes, is biologically active in histiocytosis-X. Patients are randomized to receive either Suppressin A or placebo for 42 days, after which they are re-evaluated and the code broken. To help in the evaluation of biological activity, four distinct clinical scoring systems were created: 1)organ specific; 2)whole body; 3)vital systems (respiratory, hepatic and hematopoetic function); and 4)overall performance status. The results to date from the initial 13 patients who have completed the six-week treatment course in this on-going study are:

Scoring System	Suppressin A (N=8)			Placebo (N=5)		
	Resp	Stable	Prog	Resp	Stable	Prog
Organ Specific	4	1	3	0	4	1
Whole Body	4	4	0	0	5	0
Vital Systems	3	5	0	0	5	0
Performance Status	4	1	3	0	5	0

(Resp = Responder; Prog = Progressor)

These data indicate biological activity of Suppressin A in the treatment of histiocytosis-X. These early trends of significance need to be confirmed through further patient recruitment and study.

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CHARACTERIZATION OF EPSTEIN-BARR VIRUS GENOMES IN TRANSPLANT LYMPHOMA/LYMPHOPROLIFERATIVE DISEASE. Donna F. Patton, Kenneth L. McClain. The University of Minnesota Hospital, Department of Pediatrics, Minneapolis, MN. and Baylor College of Medicine, Texas Children's Hospital, Houston, TX.

Epstein-Barr Virus (EBV)-related lymphomas (L) and B cell lymphoproliferative diseases (LPD) are recognized with increasing frequency in pts after organ and mismatched allogeneic bone marrow transplantation (BMT). The high incidence may be due to the profound immune suppression, multiple copies or unique characteristics of the viral DNA. We investigated tumor DNA from 8 pts with L or LPD post-BMT and 1 post-renal transplantation for EBV clonality and rearrangement of viral EBV DNA. Tumor tissue from all pts contained multiple (8-50) copies of EBV DNA as detected by probing Southern blots with radioactive EBV probes. To determine whether the EBV DNA was in a circular or linear configuration, we probed the blots of BamHI-digested pt DNAs with a Bam NJ het fragment. The NJ het region is highly variable, thus a single band suggests a clonal proliferation of the virus. The samples with 2 or more bands represent either oligoclonal virus or linear EBV in tumor tissue. 6/9 pt DNAs had a single band suggesting presence of circular EBV DNA. 2/9 had 2 bands of different sizes that may represent linear DNA or different virus strains. One pt had evidence of circular and linear DNA, or possible multiple strains of EBV since 3 bands of viral DNA were seen with the NJ het probe. Since 7/9 pts had single bands (suggesting circular, clonal EBV DNA when probed with NJ Het) this may indicate that the circular DNA is transcribing viral genes important in initiating or maintaining the LPD and L.

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THROMBOCYTOPENIA AND PLATELET ASSOCIATED IMMUNOGLOBULIN (PAIg) IN PATIENTS RECEIVING ACTINOMYCIN D. (AMD). SR Paul, DR Ambruso, NA Cusack, K James, J Ater, LF Odom, and J Roloff. Dept. of Peds, Univ. of Colo. Sch. Med., Children's Hospital and Bonfils Memorial Blood Center, Denver, Co 80262.

Association of severe thrombocytopenia related to increased destruction of platelets and administration of AMD has recently been reported (J Pediatr 104:611, 1985). To investigate the etiology of this phenomenon, we reviewed the clinical and laboratory status of 40 pediatric patients with solid tumors. Twenty-eitht of the 40 patients received AMD as part of their treatment. The presence of PAIg was determined by a previously described ELISA technique (Transfusion 24:348, 1984). Eight of the 28 patients receiveing AMD demonstrated thrombocytopenia associated with increased destruction and not myelosuppression by these criteria: a) documentation of thrombocytopenia less than 7 days after administration of AMD without the concomitant depression of other cell lines and b) no evidence of disseminated intravascular coagulation or other non-specific consumption. The median platelet count for thrombocytopenic patients was 80,000/ul (range 13,000-149,000). Thrombocytopenia associated with peripheral destruction did not develop in any of 12 patients not receiving AMD. Six of 8 thrombocytopenic patients on AMD had evidence of PAIg, while 9 of 19 non-thrombocytopenic AMD patients demonstrated PAIg. Also, 5 of 10 patients not receiving AMD had evidence of PAIg. Although thrombocytopenia associated with increased destruction was seen in nearly a third of patients receiving AMD, this phenomenon could not be associated with an increase in PAIg.

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PREVALENCE OF HEMOGLOBINS S AND C IN HISPANIC AND HAITIAN CHILDREN. Charles H. Pegelow, Astrid K. Mack. (Sponsored by Eduardo Bancalari) University of Miami, Jackson Memorial Hospital, Department of Pediatrics, Miami, Fl.

Hemoglobin (Hb) S and C prevalence was determined for several ethnic groups that comprised the population born at our hospital in 1985 by review of data obtained by cord blood screening. The infant's race and nationality were designated as that listed for the mother and prevalence calculated using data available for all births.

Race	Nationality	FAS	FAC	FS	FSC	Total
		Number (percent)				
Black	American	297(6.5)	114(2.5)	10(.22)	6(.13)	4564
	Haitian	119(8.0)	70(4.7)	8(.54)	5(.44)	1488
	Other	20(6.5)	13(4.1)	1(.32)	0	315
White	American	38(2.1)	6(.33)	0	1(.05)	1811
	Cuban	15(1.4)	7(.76)	0	0	1052
	Puerto Rican	12(4.3)	0	0	0	280
	Other Hispanic	40(2.4)	12(.72)	0	1(.06)	1677

The rates of FAS and FAC in all White children were higher than previous reports possibly because of the considerable proportion of Hispanics comprising this population. FAS and FAC were more frequently found in H than in BA ($p<.01$) as was FA ($p<.05$) although FAS prevalence in BA was less than some previous reports. These data provide further definition of Hb S and C prevalence in H and various white Hispanic populations and may be useful in determining what groups must be included when establishing screening programs.

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ELEVATION OF δ-AMINOLEVULINIC ACID DEHYDRATASE (ALAD) AND ERYTHROCYTE PORPHYRINS (EP) IN SICKLE CELL SYNDROMES. Sergio Piomelli, Carol Seaman, Damaris Carriero and Janice Mathis. *College of Physicians & Surgeons of Columbia University, Division of Pediatric Hematology-Oncology, New York, N.Y.*

In patients with sickle cell syndromes, EP levels may be markedly elevated. In 249 patients with sickle cell syndromes, we measured EP, ALAD, and ALAD after reactivation with dithiothreitol (*ALADSH*), in parallel with reticulocytes and pyruvate kinase (*PK*), two age-dependent parameters. EP, ALAD, ALADSH, reticulocytes and PK were much higher than normal in all patients, with the most marked elevation in patients with homozygous sickle cell disease. In many cases, the elevation of EP resulted from free protoporphyrin base, rather then Zn-protoporphyrin. The logarithm of EP was correlated both with reticulocytes and with the logarithm of PK; the regression lines intersected the normal ranges for EP and reticulocytes and for EP and PK respectively. For ALAD and ALADSH, there were similar correlations; however, the regression lines remained well above the normal ranges without intersecting them. The *in vivo* $t_{1/2}$ in the erythrocytes of both ALAD and ALADSH were estimated on discontinuous gradients of arabino-galactane at 43 days, indicating an age-dependent loss of enzyme activity, and not just oxidation of SH-groups with time. The *in vivo* $t_{1/2}$ of EP is 60 days (JCI 56: 1519, 1975). These data indicate that both EP and ALAD are increased in sickle cell syndromes as a result of young red cell age. However, the higher ALAD values and the unusual protoporphyrin species suggest additional factors, probably some degree of dyserythropoiesis or the presence of large numbers of normoblasts in these asplenic individuals.