●770 LYMPHOKINE-ACTIVATED KILLER (LAK) CELLS LYSIS OF NORMAL AND NEOPLASTIC CELLS EXPRESSING TRANSFERRIN RECEPTORS(TR). Gita V. Massey and Thalachallour Mohanakumar. (Spon. by Harold M. Maurer). Medical College of Virginia, Children's Medical Center, Richmond, VA 23298.

Use of LAK cells with interleukin-2 (IL2) in patients with metastatic cancers has shown some response with many side effects (i.e., extravascular fluid extravasation, anemia, fever, rash, diarrhea). To define the mechanism of target cell lysis and explain some of these side effects, we investigated the target structures of LAK cells. Cell lines were used as targets for LAK lysis in a 4 hr. chromium^{51} release assay. Cell surface antigens on targets (i.e., Ia2,Fc79,TR) were determined by immunofloures-cence with their respective monoclonal antibodies. Results show that TR, which is present on many transformed cells, and more significantly, on some normal cells, is a target of LAK cyto-toxicity. Tumor cell lines (K562,Daudi) used as targets for LAK lysis (both >60% lysed) express TR (>50%+). In contrast, blasts of 3 children with ALL did not express TR (<10%+) and were poorly lysed by LAK cells (<25%), while blasts of an adult ALL patient expressing TR (72.7%+) were 60.6% lysed. Normal bone marrow cells (36% TR+), endothelial cells (71.4%TR+) and fibroblasts (83.3%TR+) were all lysed (44.3%, 64.9%, and 31.7% respectively), and normal lymphocytes (<5% TR+ and 2% lysed) could be induced to express TR by Con A stimulation with concomittant increase in LAK lysis (34% TR+ and 31.4% lysis-day #3 in culture). Thus, results show that LAK cells can lyse not only tumor cells, but also normal cells expressing TR. This may explain the anemia and extravascular fluid leakage associated with LAK-IL2 immunotherapy.

771 EARLY RESPONSE TO INDUCTION THERAPY AND OCCULT TESTICULAR LEUKEMIA (OTL) AT END THERAPY PREDICT LATE RELAPSE (LR) IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) Denis R. Miller, Sanford Leikin, Vincent Albo, Peter Coccia, W. Archie Bleyer, John Lukens, Stuart Siegel, Harland Sather and Derman Hammond. Childrens Cancer Study Group (CCSG), Pasadena CA.

Determination of the optimal duration of therapy and identification of patients (pts) at risk of relapsing after therapy is discontinued are important strategies in ALL now that ≥50% of effectively-treated children are ≥3 year disease free sur vivors (DFS). Approximately 10-20% of pts sustain LR. Two CCSG studies, CCG 141 and CCG 160 series were designed to evaluate the significance of clinical and biologic prognostic factors in determining outcome. In CCG 141, the early response to induction therapy as determined by the percentage of blasts in the day 14 bone marrow (dl4BM) aspirate is a highly significant, independent predictor of DFS. In addition the overall relapse rate, isolated BM relapse rate and death rate were significantly higher in pts with OTL (N=23,9.7%) detected after 3 years DFS than in pts with negative biopsies (bx) (N=206,86.9%), p<0.001. DFS after testi-cular bx was significantly better in pts without OTL (p.0.005). BM relapse and death rates were significantly higher in pts with OTL than in boys (N=26,9.9%) who did not undergo bx. In a subsequent trial, CCG 160 series, of 1490 pts with complete data, dl4BM ranked 6th (p<0.001) by univariate analysis and 4th (p<0.001) by multivariate analysis as a predictor of DFS. CCG 160 pts were randomized after 2 yrs of DFS to receive 2 or 3 yrs of maintenance therapy. The dl4BM was the most significant pre-dictor of DFS after late randomization. The observed/expected (O/E) failure rate in pts with dl4 M1 (<5% blasts), M2(5-25%), or M3(>25%) BM ratings was 0.88,1.78 and 2.02 respectively, (p0.0002). Other significant predictors of LR were prognostic group (p0.0003) and initial WBC (p0.004). In conclusion, early response should be monitored closely and alternate induction reg-imens used for slow responders. At end therapy, the presence of OTL indicates significant, aggressive minimal residual dis-ease requiring intervention and intensification of therapy.

772 MANAGEMENT OF FEVER/NEUTROPENIA (F/N) IN CHILDREN WITH CANCER:A NATIONAL SURVEY Linda P. Miller, Denis R. Miller, Northwestern Univ Medical School,Children's Memorial Hospital, Dept. of Pediatrics, Chicago,

F/N is a frequent complication of treatment in a child with cancer; management is controversial and variable. We surveyed 70 pediatric oncology programs (POP) to determine the prevalent approach to this prob-lem. Of those surveyed, 80% responded representing an annual accrual of about 5000 new oncology patients (pts). Analysis of the data showed that criteria for antibiotics (Ab) are tem-perature between 38°C and 38.5°Ca and absolute neutrophil count (ANC) <500 (55%) with 34% using <1000 and 11% using <200. 91% of POP stop Ab after 3 days (d) if pts are afebrile with no documented infection (DI) and ANC now >500. However, if the ANC remains <500, 88% of POP continue Ab (for 7-14d or until ANC >500-1000 regardless of duration) even in the absence of fever or DI. Only 9% treat for 3 days. Duration of Ab for pts with DI averages 10d (range 7-14) depending on the site if ANC >500. Thus most POP treat pts with F/N as if infected whether inf is doc-umented or not. In neutropenic pts on Ab with persistent fever but no source 62% start amphotericin (ampho) 7d and 19% after >7d. 11% have no specific indications and 8% don't use ampho. After an afebrile period 55% do not treat recurrence of fever with ampho. Once started duration of treatment with ampho is extremely variable. There was good agreement among POP for F/N occurring during administration of blood product or chemotherapy known to cause fever. 65% culture and observe only; 16% treat with Ab until cultures are negative; 11% wait until ANC >500. On the use of trimethoprim/sulfamethoxazole (TM) or mycostatin (My) prophy-lactically during induction/consolidation: 30% do not use TM even for leukemia and 75% do not use My at all. In conclusion, although there are published guidelines and informal discussion of treatment of F/N, this study documents the acceptance of and adherence to these recommendations and defines the currently practiced standards of care. It defines fruitful areas for fur-ther clinical investigation.

773 HEPATITIS B (HB) IN CHRONICALLY TRANSFUSED CHILDREN: TO IMMUNIZE OR NOT? Scott T. Miller, Audrey K. Brown, Tzipporah Sklar, Laurene Olsen, David Tuchman, Sreedhar P. Rao, Department of Pediatrics, SUNY-Health Science Center at Brooklyn, New York.

It has been reported recently that the risk of con-tracting HB infection from chronic red cell transfusion is low if blood is obtained from volunteer donors and screened for HB sur-face antigen (SAg); immunization with HB vaccine is thus not recommended (J. Ped 1986;108:252). We have reviewed our ex-perience with HB in 24 patients, most with sickle cell disease and cerebrovascular accident. Transfusion duration ranged from 1-15 years (median 7) and donor exposure in 1985 14-49 units (mean 26)/ptn. Patients are transfused with frozen deglycerolized packed cells from volunteer donors screened for HBSAg. Three patients have shown evidence of HB infection. Two sero-con-verted after 2½ and 3 years of transfusion and were asymptomatic. A third patient began regular transfusions in 11/84 at 11 mos. of age due to recurrent acute splenic sequestration. HBSAg was first detected in 2/85 and has persisted through 5/86 despite sero-conversion by 4/85. Serum ALT reached a maximum of 1675 U/l in 4/85; the child was and remains clinically well. HB core AB and delta antigen were negative and HBeAg positive in 7/85. While HB infection was clinically mild, it has occurred in 3/24 patients; 1 child has become a chronic carrier of HB with significant social, if not medical, consequences. Additional concerns re-garding possible interactions between HB, hemochromatosis, and non-A-non-B hepatitis have led us to immunize all sero-negative patients receiving chronic red cell transfusions.

774 PREVALENCE OF α-THALASSEMIA (α-THAL) IN CHILDREN WITH SICKLE CELL DISEASE (SS) AND CEREBROVASCULAR ACCIDENT (CVA). Scott T. Miller, Ronald F. Rieder, Sreedhar P. Rao, Audrey K. Brown. SUNY-Health Science Center at Brooklyn, State University and Kings County Hospitals, Departments of Pediatrics & Medicine, Brooklyn, N.Y.

The presence of α-thal in patients with sickle cell disease may favorably alter clinical course and improve survival. The sugges-tion by Piomelli, et al (Ped Res 20:Abs 778,1986) that a decreased incidence of early, usually thrombotic, CVA may play a role in im-proving survival prompted us to ascertain the α-globin gene status of our SS population with CVA. Restriction endonuclease analysis using BamHI and BglII was performed on blood of 16 patients rang-ing in age from 2-10 years(mean 7yrs) at the time of CVA. Fourteen patients had the normal alpha-4 genotype and 2(12.5%) had a single gene "rightward" deletion. One α-thal SS patient developed a left hemiparesis and CAT scan evidence of bilateral infarction at age 27 mos., 2½ mos. after completing a year of regular transfusion for recurrent acute splenic sequestration; hemoglobin at the time of CVA was 7.2gm/dl. In spite of chronic transfusion therapy, she suffered a transient ischemic attack with right hemiparesis 6 years later related to acute anemia(hgb 6.6gm/dl), viral illness, and an enlarged spleen. The other patient with a single gene deletion and SS has done well on regular transfusion since pre-senting with right hemiparesis at age 7 yrs; hgb was 7.9 gm/dl and MCV 82 fl prior to CVA. The presence of α-thal does not preclude the possibility of CVA in young SS patients; large series with appropriate controls will be required to ascertain the degree to which the risk of CVA may be reduced.

†775 MOLECULAR AND CELLULAR BIOLOGY OF STAGE IV-S NEUROBLASTOMA Perry D. Nisen and James Garvin Jr., Schneider Children's Hosp., Div. Heme-Oncol., Long Island Jewish Med Center, New Hyde Park, NY and Columbia University Coll. Phys. and Surg., Dept. Ped. Heme-Oncol., New York, NY 10032
Spon. by Phillip Lanzkowsky

We determined levels of N-myc oncogene amplification and RNA expression in two infants with stage IV-S neuroblastoma, a rare subtype with limited metastatic potential and generally favorable outcome. Patient 1, age 5 mo, had a primary adrenal tumor with bone marrow metastasis and unfavorable histologic features. Patient 2, age 9 mo, had a primary adrenal tumor with skin and marrow metastases of favorable histology. Southern blots of chromosomal DNA from tumors of both patients showed no amplification of N-myc. RNA from the primary tumor of patient 1 exhibited approximately 10-fold enhanced expression of N-myc compared to a neuroblastoma cell line known to express a single copy of N-myc (defined as baseline). RNA from the primary tumor and involved lymph node of patient 2 revealed baseline levels of N-myc expression; a subcutaneous nodule exhibited 5-fold enhanced levels of expression, while normal adrenal tissue had no detectable levels of expression. A cell line was established from tumor cells of patient 2; these cells appeared to differentiate more readily than cell lines from stage IV tumors. Patient 1 manifested disease progression 1 month after diagnosis, while patient 2 remains disease free. Molecular and cellular characterization thus predicted the biological behavior of the tumors in each case.