818 SIGNIFICANCE OF ELEVATED B_2 MICROGLOBULIN (B_2m) IN THE CEREBROSPINAL FLUID (CSF) OF CHILDREN WITH ACUTE LEUKEMIA (AL). Indira A. Warrier, Yaddanapudi Ravindranath, Antranik Bedros, Jan Cejka; (spon. by S. Inoue), Children's Hospital of Michigan (CHM), Detroit, Michigan 48201.

Recent reports have indicated that elevated CSF levels of B_2m in AL patients may precede the cytologic diagnosis of central nervous system (CNS) involvement. This prompted us to reevaluate the CSF B_2m levels obtained on 42 AL patients at CHM during the years 1974-1975. All but 3 had acute lymphoblastic leukemia (ALL) 36 ALL children were receiving CNS prophylaxis consisting of intrathecal (IT) Methotrexate (MTX) and fractional radiation to the CNS (IMFRA) given at 10 wks. intervals. CSF was obtained at the time of administration of IT MTX either for prophylaxis or for overt CNS relapse. The level of B_2m in the CNS prophylaxis group (36) varied from 0.4 to 3.65 mg/l ($\bar{x}$ 1.55 mg $\pm$ .79). 4 had elevated levels of B_2m (>3 mg/l, $\bar{x}$ +2SD) at a time when CSF was free of leukemic cells. Three eventually developed CNS leukemia 2 mos., 8 mos., and 4 yrs. later. The CSF B_2m level at the time of overt CNS relapse in 6 AL children varied from 0.93 - 5 mg/l ($\bar{x}$ 3.18 $\pm$ 1.78). This differed significantly ($p < .001$) from the CNS prophylaxis group. B_2m level was > 3 mg/l in 5/6. These data confirm the prior observations of others that CSF B_2m levels are elevated during CNS relapse. Thus elevated levels may indicate impending relapse. Prophylactic IT MTX in itself does not appear to significantly alter the normal CSF B_2m levels.

821 MAGNESIUM SULPHATE ($MgSO_4$): FURTHER CONFUSION IN THE INTERPRETATION OF THE NEWBORN CBC. Sudha Kashyap, Joan A. Regan and L. Stanley James, Div. of Perin. Med., Dept. of Ped., Coll. of P&S, Columbia Univ., NY.

$MGSO_4$ is frequently used as a tocolytic agent and in the treatment of toxemia of pregnancy. Thus, $MgSO_4$ is a common antenatal drug administered to the very low birth weight infant (VLBW i.e. < 1500 gms).

In a prospective study of non septic VLBW infants during the past 12 months mean corrected total white blood cell counts (WBC) during the first 24 hours of life were significantly depressed among infants exposed to $MgSO_4$ in utero (N=42, mean gestational age=29 weeks, mean wt.=1082, mean 5'Apgar Score=7.0) in comparison to those whose mothers did not receive the drug. (N=45, mean gestational age=29.1 weeks, mean wt.=1070 gms, mean 5' Apgar Score=7.0). The mean corrected WBC were $9.3x10^3$ vs $12.0x10^3$ ($p < .037$). Total neutrophil (TNC) were found to be depressed in $MgSO_4$ group in comparison to the non $MgSO_4$ group with mean TNC 4166 vs 6008.

More importantly, the incidence of leukopenia (WBC < 6000) was significantly higher in the $MgSO_4$ treated group, 38% vs 13.3% ($p < .05$) but did not differ from that seen in a matched group of VLBW infants with blood culture proven sepsis, 38% vs 33%.

These data lead us to conclude that $MgSO_4$ administered to the mother may result in depression of the WBC and TNC in her infant. In the presence of $MgSO_4$, leukopenia and neutropenia cannot be validly interpreted as evidence of infection in the newborn.

● **819** LEUKEMOID REACTION IN DOWN'S SYNDROME: IN VITRO MATURATION OF CIRCULATING STEM CELLS. Susumu Inoue, Mark J. Ottenbreit, Y. Ravindranath, and Jeanne M. Lusher. Wayne State Univ., School of Medicine, Detroit.

A marked increase in WBC count with blast cell predominance in blood is a well known hematological abnormality seen in neonates with Down's syndrome. Differentiation of true leukemia from a transient leukemoid reaction is often difficult. Examination of in vitro colony formation and maturation by circulating stem cells may be helpful in separating the two entities. We studied a newborn infant with trisomy 21 Down's syndrome who had juandice, 5 cm palpable liver and 1 cm palpable spleen. The Hb, WBC and platelet count at day 3 of life were 12.5 gm %, 62,300 with 58% blasts and $90.5x10^3/mm^3$, respectively. Blood group incompatibility and intrauterine infections were excluded. The marrow showed 17% blasts. Prominent large basophilic granules were present in late myeloid precursors. The patient was simply observed. During the next 6 weeks the hematological picture returned to normal. Cultures of blood stem cells using the methylcellulose system were done on two occasions at day 9 of age (WBC $38.5x10^3$, 47% blasts), and at day 26 of age (WBC $17.7x10^3$, 6% blasts). The first blood formed 1,525 myeloid and 213 erythroid, and the second blood 256 myeloid and 17 erythroid colonies/ml of blood, respectively. No maturational difficiency was observed by cytological study of representative colonies. This normal maturation pattern is consistent with the spontaneous resolution of the clinical picture. The technique may be a useful tool in predicting the outcome.

822 DECREASED NUMBERS OF T CELLS AND SUBPOPULATIONS, INCREASED MITOGEN REACTIVITY AND DEFECTIVE IMMUNOGLOBULIN SYNTHESIS IN ACUTE LYMPHOBLASTIC LEUKEMIA IN LONG TERM REMISSION. Jacob Katz, Barbara N. Walter, Rosalie A. Kwock, Dana Larson, Gent A. Bennetts, Jerry Z. Finkelstein. University of California, Irvine Medical Center, Department of Pediatrics, Orange, California

Fifteen patients with acute lymphoblastic leukemia in long term remission were studied. Nine patients were in remission for 6 months to 4 years following 5 years of chemotherapy and 6 patients were 3 years into remission and receiving maintenance chemotherapy. T cells were enumerated by the E-sheep-red-cell rosette method, subpopulations of T cells ($T\gamma$ and $T\mu$) by ox-red cell IgM and IgG rosette formation, B cells by membrane immunoglobulin fluorescence. Mitogen stimulated cultures used phytohemagglutinin, concanavalin A and pokeweed mitogen. Immunoglobulin synthesis was estimated by a radioimmunoassay of the supernatant of pokeweed mitogen stimulated cultures. The total leukocyte count was significantly decreased ($p<0.01$), the absolute lymphocyte count was comparable ($p>0.1$). T cells were significantly decreased ($p<0.005$). Subpopulations of T cells, $T\gamma$ and $T\mu$ cells showed significantly lowered numbers, more so in the patients who were receiving chemotherapy, ($p<0.05$). Mitogen stimulated cultures in 3 patients showed normal to increased H^3 thymidine incorporation in fetal calf serum, allogenic serum and autologous serum. Preliminary studies detected low immunoglobulin levels in pokeweed mitogen stimulated supernates of 2 patients tested.

820 NEUROPSYCHOLOGICAL AND NEUROPHYSIOLOGICAL TESTING IN CHILDREN WITH LEUKEMIA. Thomas A. Kaleita, W. Donald Shields, Melanie Dreisbach, Mark Nuwer. (Spon. by Stephen A. Feig), UCLA School of Medicine, Departments of Pediatrics and Neurology, Los Angeles, California.

The neurological consequences of childhood leukemia and its treatment have become increasingly important with the improvement in long-term survival. The WISC-R and Frostig Test of Visual Perception were performed on a series of patients admitted to UCLA Medical Center for Bone Marrow Transplantation (BMT). In addition, Visual Evoked Potentials (VEP), Brainstem Auditory Evoked Potentials (BAEP), and Somatosensory Evoked Potentials (SEP) were administered prior to BMT. Thus, the observed abnormalities reflect previous disease and/or treatment.

There were consistent findings of visual-motor deficits in 8 of 11 leukemia patients. This was evidenced in 5 patients by a profile of comparatively high scores on Picture Completion and Picture Arrangement subtests (WISC-R) and low scores on Block Design (WISC-R) and Form Constancy (Frostig) subtests. Three of 5 patients were found to have lesions of the optic nerve on VEP while 2 of 3 patients produced slow nerve conduction studies on BAEP. Two of 4 patients had abnormal SEP. The three children with optic nerve lesions on VEP showed impairment of visual-motor skills.

These neuropsychological and electrophysiological tests are valuable in the evaluation of the long-term nervous system sequelae of childhood leukemia and its treatment.

823 PHARMACOKINETICS OF VINCRISTINE IN CHILDREN WITH CANCER. Jim C. Kimball and V. Sagar Sethi (Spon. by William B. Lorentz), Bowman Gray School of Medicine, Departments of Pediatrics and Medicine, Winston-Salem, North Carolina.

The pharmacokinetics of vincristine sulfate (VCR) have not been studied in children. Using a radioimmunoassay, VCR concentrations of serum and urine were measured in 4 children with malignancies (ages 5 to 16). Serum samples were obtained from 1 min. to 48 hrs. following intravenous bolus injections of VCR (2mg./M^2, maximum dose 2.0mg.). Urine samples were obtained up to 90 hrs. following the injection of VCR. The pharmacokinetic data were analyzed by a non-linear regression program, NONLIN. A three compartmental open model fits the raw data better than a two compartmental model. The half-lives of the triphasic decay curves α, β, and γ were 2.4, 27.3, and 1620.0 min., respectively. The mean volume of distribution was 251.85 liters. First order rate constants (min^{-1}) for distribution and/or elimination of VCR were K_{10}=0.038, K_{12}=0.133, K_{21}=0.044, K_{13}=0.119, K_{31}=0.003. The total body clearance was 140.43 ml/min/1.73M^2 while the ACU was 28,588 (nM·min). Urinary excretion demonstrated a concentration of $> 1.0 \times 10^{-7}$M in the urine up to 78 hrs. following the injection. Up to 37% of the administered drug could be recovered in the urine by 90 hrs. The low elimination constant (K_{31}) from poorly perfused tissues to plasma and a long biological half-life (27 hrs.) indicate a slow release of VCR from the body and may account for the neurotoxicity associated with this drug. (Supported in part by NIH grant CA 12197).