613 TIME AND CAUSE OF DEATH FROM HISTIOCYTOSIS X. Diane Komp, Kenneth Starling, Theresa Vietti, Thomas Miale and Jay Herson for the Southwest Oncology Group, Kansas City, Kansas.

The records of 52 children who died with histiocytosis X were reviewed to determine the cause of death and temporal relationship to diagnosis. 15% died less than 4 wks. from diagnosis;52% were dead within 8 wks. The highest early mortality rates were seen in children less than 1 yr. of age at diagnosis and those receiving combination chemotherapy as the first therapy. 44% of early death in children less than 1 yr. were attributed to infection compared to 17% in children over 1 yr. 8 of 10 early deaths in children receiving combination chemotherapy were attributed to complicating infection but no infectious cause was incriminated in 12 children receiving single agent therapy who died before 8 wks.

Primary and secondary immunodeficiency disorders have been reported in association with histiocytosis X in young infants. In contrast to Hodgkin's disease and acute leukemia, combination chemotherapy has not been demonstrated to improve response rates above those achieved by component single agents in patients with poor prognostic indicators such as age or organ dysfunction. The present study would again suggest caution with the use of highly immunosuppressive regimens in young infants with histiocytosis X.

TIME TO DEATH	<1 YR	1-2 YRS	>2 YRS	SINGLE AGENT	COMBO.
≤8 wks	18(64%)	7(50%)	2(20%)	12(36%)	10(67%)
>8 wks	10(36%)	7(50%)	8(80%)	24(64%)	5(33%)
TOTAL	28	14	10	36	15

614 IMMUNODEFICIENCY IN LYMPHOHISTIOCYTOSIS: DEFECTIVE CELLULAR IMMUNITY IN ASSOCIATION WITH HYPERLIPIDEMIA. Stephan Ladisch, David G. Poplack, Betty J. Holiman, and R.Michael Blaese. National Cancer Institute, Bethesda, Md.

Lymphohistiocytosis (LH) is a familial syndrome characterized by abnormal accumulation of non-malignant histiocytes in lymph nodes, liver, and spleen, erythrophagocytosis, hepatosplenomegaly, recurrent fever, wasting, coagulopathy, and early death.

We evaluated four patients and all had evidence of defective cellular immunity. Those patients tested were anergic to recall skin test antigens. In vitro evidence of abnormal cellular immune function included depressed lymphocyte proliferative responses to specific antigens (performed in normal plasma) and impaired monocyte-mediated cytotoxic function. Plasma from LH patients suppressed the responses of normal lymphocytes. Investigation of the suppressive plasma revealed hyperlipidemia, with triglyceride levels between 180-960 mg% (nl range = 25-150 mg%). Moreover, the degree of in vitro immuno-suppression by these plasmas correlated with the degree of hyperlipidemia.

An association between hyperlipidemia and suppression of in vitro lymphocyte responsiveness has recently been reported (Waddell,J.C.I.) and may be in part responsible for the immune defect in our patients. However, the depressed lymphocyte and monocyte function seen in LH cells tested in normal plasma suggests that the immunodeficiency in lymphohistiocytosis may be the result of both an intrinsic mononuclear cell defect and a circulating immunosuppressive factor.

615 REVERSIBILITY OF CELLULAR CHANGES IN IRON DEFICIENT POST-WEANING RATS. Philip Lanzkowsky, Gungor Karyalacin, Abdul Kazi. Sch. of Med., Health Sciences Ctr., State Univ. of N.Y. at Stony Brook and Long Island Jewish-Hillside Med. Ctr., Dept. of Pediatrics, New Hyde Park, New York.

The purpose of this study was to determine the extent and the reversibility of cellular change occurring in rats made iron deficient during the post-weaning period. Two groups of 23 Sprague-Dawley rats were studied. Group I was fed an iron deficient diet from 21 to 49 days and from 49 to 147 days received the same diet plus intramuscular iron whereas Group II were fed a control iron-sufficient diet from 21 to 147 days. At 21 days, 6 rats of each group were sacrificed and no significant difference was found in body weight, hemoglobin, serum iron, serum protein, organ weight, DNA, RNA, protein and organ iron in brain, liver, heart, spleen and kidney. At 49 days, 9 rats of each group were sacrificed and Group I had significantly lower body weight, hemoglobin, hematocrit, serum iron, brain weight, RNA, protein and iron; liver weight, DNA, RNA, protein and iron and kidney weight, DNA, RNA, protein and iron compared to Group II. At 147 days, 8 rats in each group were sacrificed and no significant differences were observed in any parameters. This work revealed that an iron deficient diet in rats from 21 to 49 days of age results in significant iron deficiency anemia and cellular changes in brain, liver and kidney and that by 147 days of age, these hematologic and cellular changes are corrected by iron administration and are not evidence of permanent cellular damage.

616 SECOND PRIMARY MALIGNANT DISEASE (SPMD) IN CHILDREN DURING REMISSION OF ACUTE LYMPHOCYTIC LEUKEMIA (ALL). Philip Lanzkowsky, Ashok Shende, Danuta Blicharski. Sch. of Med., Health Sciences Ctr., State Univ. of N.Y. at Stony Brook and Long Island Jewish-Hillside Med. Ctr., Dept. of Pediatrics, New Hyde Park, New York.

Of 104 children treated with ALL from August 1970 to December 1976, two developed second primary malignant disease. A four year old white child in complete remission of ALL for 3 years developed chronic myelogenous leukemia. (Hays, T., Hutter, J.J., Lanzkowsky, P., Shende, A. and Holton, C.P.: Abstract, Western Society for Pediatric Research, 1975). The other SPMD, malignant histiocytic lesions of bone, occurred during the early remission phase of ALL in a 4 year old child. Induction of remission of ALL was successfully attained and while in continuous remission 5 months after the initial diagnosis, he developed bone pain in the left leg and left eye and multiple lytic lesions of the orbit, femoral epiphyses, tibia, fibula and vertebral bodies. Biopsies of these lesions revealed them to be malignant histiocytic in nature. During a 10 month follow-up, he remains in remission of ALL. It appears that patients with one primary malignant disease are apt to develop a SPMD and treatment of malignant disease in such patients might actually percipitate the SPMD due to the disruption of balance between the immunologic surveillance system and the oncogenic agent and/or due to emergence of drug resistance.

617 COMPARATIVE EFFECTS OF CONTINUOUS FLOW CENTRIFUGATION (CFC) AND NYLON FILTRATION (NF) ON SERUM COMPLEMENT (C3) AND CARBON MONOXIDE DIFFUSING CAPACITIES (D_LCO) IN LEUKAPHERESIS DONORS. Myron I. Liebhaber, David A. Stempel, F. Ralph Berberich, Lawrence G. Fickenscher, Norman J. Lewiston, Jordon R. Wilbur. (Spon. by John J. Miller). Children's Hospital at Stanford, Dept. of Pediatrics, Palo Alto, California.

Fehr et. al., Clin. Res. 23:522A, 1975, reported a reduced D_LCO in NF leukapheresis donors, presumably on the basis of C3 activation and leukocyte plugging of pulmonary capillaries.Since hazard to donors was implied, we compared the effects on C3 and D_LCO of NF with another method of collection, CFC. Twenty-five NF and twelve CFC collections were studied. D_LCO and C3 were measured immediately before and after the four hour procedure. Hemoglobin (Hgb) was also measured to permit correction for dilutional effects and blood loss. Post procedure results are expressed as percentage change from initial values.

Method	D_LCO	C3	Hgb
Filtration	+4.8%	-17.8%	-11.7%
Centrifugation	-6.6%	-20.0%	-12.6%

The D_LCO values were not significantly altered by NF when post procedure values were corrected for the decrease in Hgb concentration. D_LCO for CFC ($p<.05$) and C3 values for both NF and CFC ($p<0.01$) were significantly reduced, although these changes are probably too small to be clinically important. No pulmonary symptoms were reported in either group. We conclude that neither NF nor CFC presents a clinical risk of complement activation with resulting pulmonary sequelae to the white cell donor.

618 IMPAIRED PRODUCTION OF T LYMPHOCYTE MITOGENIC LYMPHOKINES AND MONOKINES IN PEDIATRIC MALIGNANT DISEASE. Sanford Leikin, Elaine Esber, Joost Oppenheim, George Washington Univ. Sch. of Med., Children's Hosp., Washington, D.C. and NIDR, Nat. Inst. of Health, Bethesda, Md.

Cellular immune responses are crucial in tumor immunity. The capacity of children with neoplasia to produce factors involved in cellular immune activity was studied. We have found that normally supernatants from mitogen or antigen stimulated peripheral blood mononuclear cell (MNC) cultures contain two factors, lymphocyte derived thymic stimulating factor (TSF) and monocyte derived lymphocyte activation factor (LAF) which are detected by the in-vitro proliferation of mouse thymocytes. TSF production is stimulated by phytohemagglutinin (PHA) and streptolysin-O (SLO) whereas LAF is activated by lipopolysaccharide (LPS).

The production of TSF and LAF in response to PHA, SLO and LPS was, therefore, compared in normal subjects and children with untreated and treated leukemia and various solid tumors. The production of TSF in response to PHA and SLO was depressed in 11/15 and 6/12 patients, respectively. The production of TSF and LAF by patients with limited tumor load, off chemotherapy fell into the normal range. Patients in remission on chemotherapy and those with extensive disease had decreased TSF. Two patients with the most advanced tumors had both depressed TSF and LAF. These results indicate that TSF production decreases in patients with malignancy and that the suppression of LAF occurs with disease progression. The elaboration of these factors may play a role in modifying the malignant process, or may be modified by the malignancy or its treatment.