619 INHIBITORS OF HEME PRODUCTION IN TRANSIENT ERYTHROBLASTOPENIA OF CHILDHOOD. H.M. Koenig, A.L. Lightsey, D.A. Seaward, W. Wang, and L.K. Diamond. Departments of Pediatrics, Naval Regional Medical Center, San Diego, and University of California Medical Center, San Francisco.

Transient erythroblastopenia of childhood (TEC), congenital hypoplastic anemia (CHA), and iron deficiency anemia (IDA) are characterized by anemia, reticulocytopenia, and decreased erythropoiesis. Differences in erythrocyte size, enzyme activities, membrane antigens, hemoglobin F, and protoporphyrin content; serum iron, iron-binding capacity, and ferritin levels; and spontaneous recovery from TEC are significantly diagnostic to differentiate these conditions. Inhibitors of heme production have not been found in CHA serum. To determine if inhibitors of heme production occur in TEC or IDA 1 ml human bone marrow cultures were incubated under controlled conditions in pairs with and without erythropoietin (EPO) added. Fe⁵⁹ was added to the cultures for the last 4 hours of incubation and EPO stimulated Fe⁵⁹ heme production measured. To check for inhibitor activity, 1 µl of test serum was added to culture pairs. Serum from 8 untransfused TEC patients produced a 23±22% inhibition of Fe⁵⁹ heme production. In contrast, serum from 2 untransfused CHA and 7 IDA children produced a 43±34% stimulation of Fe⁵⁹ heme production. As recovery occurred, serial serum specimens from 2 TEC patients demonstrated gradual disappearance of inhibitor activity. We conclude that a transient inhibitor of heme production occurs in TEC but not in CHA or IDA. This inhibitor may be an immune response and be the mechanism for anemia in TEC.

620 A PROSPECTIVE ANALYSIS OF INFECTIONS OCCURRING IN CHILDREN WITH ACUTE LEUKEMIA. Helen V. Kosmidis, Thomas Shope, Adnan Dajani, Y. Ravindranath and Jeanne Lusher. Wayne State University School of Medicine, Dept. of Pediatrics, Children's Hospital of Michigan, Detroit.

A 20-month prospective study was undertaken to determine the role of bacterial and viral infections as a cause of fever in children with acute leukemia (AL) and to determine if respiratory and gastrointestinal colonization could predict subsequent bacterial infection. 47 children with newly diagnosed AL had viral and bacterial cultures and serum obtained at the time of diagnosis, during febrile episodes and at the time of periodic clinic visits while asymptomatic and afebrile. 72 febrile episodes were documented. (27 during the initial induction phase and 45 subsequently.) A cause for the fever was found on 31 occasions and among those 15 bacterial and 9 viral agents were isolated. In 7 others with pneumonia or otitis media no etiologic agent was found. Of the 31 episodes of documented infections, 20 occurred during induction or relapse, and 11 while in remission.

Colonization of the upper respiratory or gastrointestinal tract with the infectious agents was documented prior to the infection in only 4 of the 15 bacterial infections.

It is concluded that (1) viruses as well as bacteria are significant infectious agents in children with AL and (2) the bacterial infections were predictable in 4 of the 15 cases by periodic determinations of the flora during afebrile periods. In this series no deaths occurred as the result of viral infection alone, while 6 of the 11 children with bacterial sepsis expired.

621 GROWTH AND DEVELOPMENT IN CHILDREN WITH SICKLE CELL TRAIT: A MATCHED-PAIR PROSPECTIVE STUDY. Michael S. Kramer, Yolanda Rooks, and Howard A. Pearson, Yale U. Sch. of Med., Yale-New Haven Hosp., Dept. of Ped., New Haven, Ct.

To remove the methodologic flaws of studies claiming that sickle cell trait (Hb AS) impairs physical growth and cognitive development, we prospectively investigated 25 matched pairs (50 subjects) of Black children chosen from a cord blood electrophoresis screening program. For each child with Hb AS, an Hb AA child was matched at birth for sex, birth date, birth weight, gestational age, 5' Apgar score, and socioeconomic status. At ages 3-5 years, each child was evaluated, within one month of his match, by persons "blind" to the hemoglobin genotype. The results are shown below, together with P_q (probability of no difference) and P_g (probability of missing a true AA-AS difference as large as Δ):

Variable	Mean Diff. (AA-AS)	P _q	P _g	Δ
Height	+0.132 cm	>.50	.05	+2.3 cm
Weight	+0.336 kg	.48	.05	+1.1 kg
Head Circumference	-0.600 cm	.17	.05	+0.1 cm
Skinfold (Triceps+Subscap.)	-0.348 mm	>.50	.05	+1.1 mm
Upper Arm Muscle Area	+0.595 cm ²	.29	.05	+1.5 cm ²
Bone Age	-0.224 years	.37	.05	+0.2 yrs.
McCarthy Cognitive Index	-6.261 points	.05	.01	+1.3 pts.
Peabody Picture Vocab. IQ	-3.250 points	>.50	.05	+5.4 pts.

These results, which demonstrate that 3-5 year-old children with sickle cell trait have no deficits in standard measures of growth and development, emphasize the importance of rigorous methodology when clinical groups are assembled and compared.

622 ERYTHROGENESIS IMPERFECTA IN SEVEN INDIVIDUALS IN THREE GENERATIONS: William Krivit, Edward Nelson, Dorothy Sundberg. Univ. of Minnesota, Dept. of Pediatrics and Laboratory Medicine and Pathology. Minneapolis 55455

Erythrogenesis imperfecta usually begins in infancy and responds to steroid therapy. Because recent observations indicate a widening spectrum, attention to significant variants is important. The K family presents several unusual findings of erythroid hypoplasia syndrome. Well documented episodes of severe anemia due to marrow erythroid hypoplasia (ErHy) has occurred in three generations in 3 females and 4 males and is transmitted as an autosomal dominant. In each the anemia presents in the neonatal period. The affected females have had recurrence of severe anemia in each of 6 pregnancies which have spontaneously remitted at parturition. Transfusions are required to maintain hemoglobin above 5 Gm%. The anemia has been normocytic normochromic with M.C.V. in normal range. The innumerable bone marrow examinations have been typical ErHy while in exacerbation but normal during remission. An important difference from other reports is that during the 20 years this family has been followed, therapy with steroids has not been successful. A most remarkable observation has been a reticulocyte response to diathermy treatment noted on several occasions. The female infants remit by 2 years of age whereas the males do not fully respond until 5 years of age. No evidence of thymoma has been seen in this family. All affected individuals have normal growth and development. The pathogenesis of this distinctly different ErHy is currently under investigation. This family provides an important addition to our knowledge of pure red cell anemia.

623 INFLUENZA IMMUNIZATION IN CHILDREN WITH LEUKEMIA. Beverly J. Lange, Steven A. Shapiro, Allan M. Arbeter (Sponsored by Stanley A. Plotkin). University of Pennsylvania School of Medicine, Children's Hospital of Philadelphia, Philadelphia, PA.

To determine if children with acute lymphoblastic leukemia (ALL) can mount a primary response to immunization with a new antigen and a secondary response to a known antigen, 39 children with ALL and 51 sibling controls received 2 doses of bivalent split-product influenza vaccine, A Victoria/75, A New Jersey/76 (A/Vic, A/NJ). Before immunization 90% of patients and controls had hemagglutination inhibiting antibody (HAI) to A/Vic of ≥1:8; none showed HAI antibodies to A/NJ. Four weeks after the first dose 74% of patients and controls showed at least a 4-fold rise in HAI titer to A/Vic. Only 48% of patients on chemotherapy responded to the first A/NJ immunization compared to 68% of controls and 89% of patients off therapy. Following the second dose, 86% of patients on therapy demonstrated at least a 4-fold rise in titers to both viruses with geometric mean titers of 1:68 to A/Vic and 1:43 to A/NJ. Patients who were off therapy developed higher HAI titers than controls. The results demonstrate that patients receiving chemotherapy can produce anti-influenza antibody in response to immunization with either an old antigen or a new antigen. Responses to the new antigen in patients on chemotherapy are more sluggish than those of controls but adequate antibody levels are achieved with booster immunization.

624 CELLULAR CHANGES IN RATS MADE IRON DEFICIENT IN UTERO AND DURING WEANING PERIODS. Lanzowsky, Philip; Karayalcin, Gungor and Kazi, Abdul, SUNY at Stony Brook, N.Y., Health Sciences Ctr. and Long Island Jewish-Hillside Medical Ctr., Department of Pediatrics, New Hyde Park, N.Y.

A total of 120 Sprague-Dawley rats were divided into 3 groups. Group A was born to normal mothers (NM) and suckled on iron deficient anemic mothers (AM) until 21 days of age. This group was subdivided into Group A₁ fed an iron deficient diet until 49 days of age and then given IM iron plus an iron sufficient diet (ISD) and Group A₂ given IM iron plus ISD from 21 days. Group B was born to AM and suckled on NM and thereafter fed an ISD and Group C, born to and suckled on NM and thereafter fed on ISD. At birth pups of AM (Group B) had significantly lower body weight, hemoglobin (Hb); brain DNA; spleen weight, DNA, protein and iron compared to pups of NM (Group C). At 21 days, Group A₂ had significantly lower body weight, Hb, serum iron, brain weight and iron; liver weight, DNA, RNA, protein and iron; spleen weight, DNA, RNA, protein and iron; kidney weight, RNA and iron compared to Group C. There was no significant difference between Group B and C. At 49 days, Group A₁ had significantly lower body weight, Hb, serum iron; brain weight, DNA and iron; liver weight, DNA, RNA, protein and iron; spleen RNA and iron; kidney weight, DNA, RNA, protein and iron compared to Group C. At 102 days, no significant differences were observed in any parameters in all groups. Iron deficiency in rats in utero and during weaning periods results in significant cellular changes in brain, liver, spleen and kidney which are corrected by iron administration.