589 INCREASING SAFETY OF EXCHANGE TRANSFUSION. W.D. Cochran, Dept. of Ped., Harvard Med. Sch., Boston Hosp. for Women, Boston, MA. (Intro. by H.W. Taeusch)

In the period 1963-1976, 1006 exchange transfusions have been carried out with heparinized blood with only 4 deaths being directly related (0.39%). Of the "directly related" deaths none occurred during the procedure but, on review, no other primary cause could be identified. Three of these 4 deaths occurred in infants who had also had fetal transfusions. Of these three, two died of a graft vs. host (GVH) reaction and one of a sudden apparent anaphylactoid reaction not related to any obvious mismatch. The fourth infant had an intracranial hemorrhage. Since the occurrence of the two GVH infants, irradiated blood has been used for all infants needing intrauterine transfusions and subsequent exchange transfusions and no further GVH has been seen. Of the 951 surviving infants one had 3 intrauterine transfusions and 19 exchange transfusions and, though needing a period of respirator support, at 3 years of age is in excellent health. There were 51 deaths not attributable to the exchange transfusion procedure per se, ranging from hydrops, extreme prematurity, HMD, to chronic lung disease of prematurity, prior intracranial hemorrhage and congenital anomalies.

From 1950-1960 800 exchange transfusions were carried out using ACD blood and there were 12 deaths occurring during the exchange transfusion procedure (1.5%) mostly thought primarily due to the procedure. It is proposed that exchange transfusions, when carried out with present methods, are extremely safe procedures in terms of short range morbidity and mortality and should not be "avoided at all costs."

590 TRANSFUSION REQUIREMENTS AND SPLENECTOMY IN COOLEY'S ANEMIA. Alan R. Cohen, Alicejane Markenson, and Elias Schwartz, Univ. of Pa. Sch. of Med., The Children's Hosp. of Phila., Dept. of Peds. and New York Hosp.-Cornell Med. Center, Dept. of Peds., New York.

The identification of patients with thalassemia major who will clearly benefit from splenectomy is often difficult. Modell (Br Med Bull 32:270,1976) has evaluated transfusion requirements based upon weight, mean hemoglobin level and amount of administered whole blood. We have modified this index using the pre-transfusion Hb level and quantity of packed red cells. Transfusion requirements, expressed as the volume of transfused packed RBC's in one year divided by weight at mid-year, were studied in 48 patients with thalassemia major and intact spleens and 18 patients after splenectomy. The patients with spleens (3-24 years old) required 131-367 ml/kg/yr (mean 223) to maintain a pre-transfusion Hb level of 7.8-9.8 g/dl. The 18 patients (5-28 years old) who underwent splenectomy required 80-155 ml/kg/yr (mean 126) to maintain a pre-transfusion Hb level of 8.3-10.6 g/dl. In 8 patients studied before and at least six months after splenectomy, the amount of administered blood decreased 24-74% (mean 48%), despite an increase in the mean pre-transfusion Hb level from 8.5 to 9.6 g/dl. Post-splenectomy transfusion requirements in all eight patients were in the predicted range. As illustrated by these data, the transfusion index allows easy identification of those patients with Cooley's anemia who will benefit from splenectomy and permits prediction of the decrease in blood requirements following splenectomy.

591 BACTERIAL KILLING AND OXIDATIVE METABOLISM IN CHLORPROMAZINE (CPZ) TREATED POLYMORPHONUCLEAR LEUKOCYTES (PMN): A MODEL FOR CHRONIC GRANULOMATOUS DISEASE (CGD). Harvey J. Cohen, Margaret E. Chovaniec, Seth Ellis, and Genevieve Laforet (Spon. by David G. Nathan). Harvard Medical School, Children's Hospital Medical Center, Boston, MA.

PMN from patients with CGD ingest and degranulate normally but do not produce superoxide (O_2^-) or H_2O_2 in response to phagocytic stimuli. They kill streptococci but not staphylococci. CPZ mimics both the metabolic and bactericidal defects found in CGD PMN. Addition of 10-50 μM CPZ results in increasing inhibition of both O_2^- and H_2O_2 production by PMN treated with opsonized zymosan or digitonin (DIG). CPZ both prolongs the lag time for maximal O_2^- production and decreases the final linear rate. These effects cannot be reversed by washing the PMN in CPZ-free buffer. CPZ inhibits ZYM or DIG induced hexosemonophosphate shunt (HMP) activity but not resting on methylene blue induced HMP activity. Ingestion of opsonized particles and release of granular enzymes are unaffected by up to 100 μM CPZ. Incubation of PMN with DIG and CPZ results in undetectable NAD(P)H-dependent O_2^- production in membrane fragments. CPZ inhibits NAD(P)H-dependent O_2^- production in membrane fragments. 50 μM CPZ prevents the killing of staphylococci but not streptococci by human PMN. At 25 μM CPZ there is a delay in the killing of staphylococci. Thus, the metabolic, enzymatic, and bactericidal defects seen in PMN treated in vitro with CPZ are similar to those found in CGD PMN, and determination of site of CPZ attachment to PMN may aid in understanding the molecular basis of this disorder.

592 PARTIAL EXCHANGE TRANSFUSION IN THE TREATMENT OF NEONATAL HYPERVISCOSITY. William F. Coyer, Paul F. Twist, Jr., Harry L. Messmore, Loyola Univ. Stritch School of Medicine, Depts. of Peds. and Med., Maywood, IL (Sponsored by John D. Madden)

Polycythemia and hyperviscosity contribute to neonatal morbidity and mortality by decreasing blood flow and nutrient delivery. Partial exchange transfusion (PET) is being used to treat hyperviscosity, however, its effect on whole blood viscosity (WBV) has not been demonstrated using current rheologic methods. WBV was measured at 37°C before, during and after PET in 7 hyperviscous neonates using the Wells-Brookfield Coneplate Viscometer, model LVT. Heparinized whole blood specimens (2 ml) were collected on infants with a central hematocrit (HCT_c) > 64% and PET performed on those infants whose WBV was > 2 SD above the mean for sheer rates of 22.5, 45, 90 and 225 sec^{-1}. Central hematocrit and WBV were measured before, at the midpoint, immediately after, and 24 hours after the PET. The PET volume, using 5% albumin, was calculated to reduce the HCT_c to 50%.

PET reduced the pre-exchange HCT_c from 69± 3.1% to 51± 4.5% after the PET ($p=.001$), and it reduced WBV to near mean levels at all 4 sheer rates ($p=.001$). The reduction in HCT_c was significant during both the first and second half of the PET. Minimal rebound in HCT_c and WBV was observed at 24 hours. PET is an effective way of lowering HCT_c and WBV. Reducing the HCT_c to 60% returns WBV to within 2 SD of the mean.

593 POST-THYMIC T CELL LYMPHOMA: OCCURRENCE IN THREE SIBLINGS AND ASSOCIATION WITH GARDNER'S SYNDROME. Barbara Cushing, Chung Ho Chang, Jacqueline Roskamp, and Joseph Kaplan. Wayne State Univ. School of Medicine, Children's Hospital of Michigan, Department of Pediatrics, Detroit.

Three siblings developed a similar type of lymphoblastic lymphoma. Like their father, they all had multiple cafe au lait spots, and one was found at autopsy to have intestinal polyps typical of Gardner's syndrome, a condition with a known dominant inheritance of malignancies. HL-A type in 2/2 affected children tested was 9, 17/W28, W5. All three children presented with cervical and/or mediastinal lymphomas and died 1-8 months after diagnosis of central nervous system metastasis. Tumor cells from 2/2 tested were T lymphoblasts. They formed rosettes with sheep erythrocytes, lacked surface Ig and reacted with heterologous anti-T but not anti-B cell serum. In the one child so tested, lymphoblasts lacked the enzyme terminal transferase indicating a lymph node rather than thymic T cell origin. Moreover, unlike children with thymic lymphoblastic lymphoma who usually progress to or have at diagnosis an associated T cell leukemia, none of these three children developed bone marrow involvement. We conclude that these children had a tumor which appears to be a post-thymic T cell lymphoma, and that a genetic predisposition for this tumor occurs in Gardner's syndrome.

594 HIGH RISK ACUTE LYMPHOCYTIC LEUKEMIA (ALL): PROBLEM OF EARLY RELAPSE. Gary V. Dahl, Rhomes J.A. Aur, Stephen L. George, Gaston Rivera, Alvin M. Mauer. St. Jude Children's Research Hospital, Memphis. Tennessee 38101

Over the past two decades there has been an increase in the proportion of children with ALL achieving long-term disease-free survival. An exception is found in patients now being identified as having high risk features (HRF). To determine if a cause for their treatment failure could be recognized, all children with ALL entered on "Total Therapy" Studies I-IX were analyzed. The relationship of 5 initial features and outcome of therapy was determined in 802 untreated children with ALL treated here from 1962-1977. The initial features chosen for analysis were: Mediastinal mass, leukocyte count above 100,000/mm^3, age under 2 years, early CNS disease and black race. One or more HRF were present in 261 (33%) of the patients. Complete remission (CR) was achieved by 224 (86%) of patients with HRF and by 516 (95%) of patients without these features. The median duration of CR was 9 months in patients with HRF in contrast to 36+ months for all other patients.

Regardless of the therapeutic changes made in Studies I-IX, the proportion of HRF patients remaining in complete remission from each study is consistently 20% or less. We conclude that most patients with HRF achieve CR and that the most important reason for poor prognosis is the short duration of CR. At least 80% eventually relapse. This observation suggests that (1) the leukemic cells in these patients develop resistance to therapy rapidly; and (2) the emergence of resistant cells should be prevented by modifying maintenance chemotherapy.