795 PLATELET FUNCTION IN CHILDHOOD IDIOPATHIC THROMBOCYTOPENIC PURPURA (ITP). George R.Buchanan, Christine A. Holtkamp, The University of Texas Health Science Center at Dallas, Department of Pediatrics, Dallas, TX.

The risk of hemorrhage in ITP is related not only to the platelet count but also to the functional integrity of the platelets and microvasculature. Platelet function in adults with ITP has been reported by different investigators to either be enhanced (bleeding time (BT) shorter than expected for the degree of thrombocytopenia) or impaired (defective aggregation due to effects of anti-platelet antibody). These discrepant results are unexplained and data in pediatric patients are lacking.Therefore, we investigated platelet function in 46 children with acute ITP by modified template BT and in 22 children with chronic ITP by BT, platelet aggregation in response to epinephrine, collagen and ADP, and/or generation of malondialdehyde (MDA) following exposure of platelets to N-ethylmaleimide. BT, performed on 185 occasions in the 68 patients, was nearly always prolonged (> 7 1/2 minutes) when the platelet count was under 100,000/μl and markedly prolonged (> 25 minutes) in 52% of children whose platelet counts were < 20,000/μl. BT values in the patients with ITP were not different from those in 20 children with thrombocytopenia due to decreased platelet production. BT was not affected by corticosteroid therapy independent of platelet count. Platelet aggregation and MDA measurements performed on 18 occasions in 12 patients with chronic ITP were usually normal. We conclude that platelet reactivity is neither enhanced nor significantly impaired in childhood ITP.

796 TRANSIENT LUPUS-LIKE ANTICOAGULANT IN 3 FAMILY MEMBERS SHARING THE $A_{11}Bw_{35}$ HAPLOTYPE. James B. Bussel, Scott T. Miller, Margaret W. Hilgartner, Sanford Kempin, and Richard O'Reilly. New York Hospital-Cornell Univ. Med. College Division of Pediatric Hematology/Oncology, New York, N.Y.

The lupus-like anticoagulant is being seen more frequently in the pediatric population, particularly as a transient occurrence after a presumed viral URI. We herewith report the transient occurrence of lupus-like anticoagulant in a patient, his sister and his mother, all of whom shared the same HLA haplotype. The patient is a 6-year-old white male diagnosed as having AML in 9/80 who went into remission with CCSG-251 (combination adriamycin + ARA-C). The patient was randomized to the transplant arm of CCSG-251 and upon routine screening a PTT of 75 was discovered. Work-up revealed a circulating anticoagulant of the lupus-type (Rapaport, AIM 2/80) with decreased factors IX, and XII and a clear cut prolongation of the mixed PTT. The thrombin time, PT, and fibrinogen were normal. The patient's entire family was evaluated. The mother and the HLA-identical sister (donor) had the same abnormalities as the patient; while the two other siblings and the father did not. Follow-up studies within two months on the 3 affected family members reverted entirely to normal. The family has no history of autoimmune disease, bleeding, or thromboembolic problems. Family testing for VDRL, C2 or C4 deficiency, immune complexes and ANA was negative. In summary we report 3 members of a family sharing the $A_{11}Bw_{35}$ haplotype all of whom had the transient simultaneous occurrence of a weak lupus-like anticoagulant.

797 CYCLASES IN NORMAL AND LEUKEMIC LYMPHOCYTES. Ugo Carpentieri, Jose' J. Minguell, Frank H. Gardner. Univ. Texas Medical Branch, Depts. of Pediatrics and Internal Medicine, Galveston, TX. Spon. by F.C. Schmalstieg.

Persistent low level of c-AMP and persistent high level of cGMP in leukemic lymphocytes suggest a modified activity of the cyclases which synthetize them. Soluble and particulate guanylate cyclase (GC) and adenylate cyclase (AC) activities were studied in normal B-enriched and T-enriched lymphocytes, in lymphocytes of children with acute lymphocytic leukemia (ALL) and adults with chronic lymphocytic leukemia (CLL). GC activity was greater in normal T than B cells (10.2 vs 5.3 pmol/min/mg protein), increased little with isoproterenol and prostaglandins stimulation, and much more with sodium azide (NaN_3) and dehydroascorbic acid (DHA) stimulation (19 and 23 pmol for T cells and 9.1 and 17.2 pmol for B cells). GC activity was greater in both types of leukemic lymphocytes (23 pmol for ALL cells and 18 pmol for CLL cells) and was insensitive to stimulation with DHA and NaN_3. Particulate AC activity was greater in normal B than T cells (215 vs 80 pmol) and increased in both after stimulation with isoproterenol (300 pmol) and prostaglandins (400 pmol). In leukemic lymphocytes AC showed depressed activity (20 pmol in ALL cells and 55 pmol in CLL cells) and was insensitive to stimulation. These findings suggest that circulating T cells are more actively cycling or functioning than circulating B cells. They also suggest a derangement of the activity of both cyclases and/or their receptors in leukemic cells: this derangement may be a cause of leukemic cell escape from their microenvironment control.

● **798** ACTIN UNDERGOES RAPID AND REVERSIBLE POLYMERIZATION ASSOCIATED WITH PLATELET SHAPE CHANGE. James F. Casella and Shin Lin. (Sponsored by William H. Zinkham). The Johns Hopkins Univ., Dept. of Biophysics, and The Johns Hopkins Hospital, Dept. of Pediatrics, Baltimore.

Platelets undergo dramatic cytoskeletal changes following activation. Previous studies have suggested that these changes are related to the conversion of actin from monomeric (G) to the filamentous (F) form. The present study was designed to determine the polymerization state of actin under conditions associated with platelet shape change without aggregation, in the presence and absence of inhibitors of shape change. Cytochalasin D (CD) is an agent which inhibits platelet shape change as well as actin polymerization in vitro. EDTA-treated, gel-filtered platelets were exposed to the experimental conditions described below prior to Triton lysis. G-actin was measured by the DNAse assay of Blikstad et al. Total cellular actin was determined by assay of lysates exposed to guanidine HCl. Results were expressed as % of total actin measurable as G-actin ± SEM as follows: (1)unstimulated 67.5±1.4, n=32, (2)thrombin-stimulated 36.8±1.2, n=25, (3)CD-treated (before thrombin) 62.4±2.1, n=21, (4)CD-treated (after thrombin) 69.4±2.0, n=8, (5)ADP-stimulated 44.0±1.0, n=4, (6)Adenosine-treated (prior to ADP) 63.0±3.1, n=4, (7)CD-treated (prior to ADP) 66.8±5.7, n=4. These findings indicate that platelet actin is reversibly transformed from G-actin to F-actin during shape change. This transformation is blocked both by a drug which competitively inhibits stimulation and shape change (adenosine), and a drug which inhibits actin polymerization and shape change (CD).

799 "SPHEROCYTOSIS" IN SICKLE CELL ANEMIA Robert Chilcote, Dianne Gallagher, (Spon. Lawrence Gartner); Pritzker School of Medicine The Univ. of Chicago Hospitals, Wyler Children's Hosp., Dept. of Pediatrics, Chicago

The hematologic hallmark of sickle cell disease is the irreversibly sickled cell (ISC) a shrunken, dehydrated cell which resists hypotonic lysis. Less well recognized in sickle cell disease is another population of cells geometrically "spherocytic" with decreased surface area to volume ratio and increased osmotic fragility. In 59 stable patients with HbSS, we determined hematologic values, ISC counts, the proportion of red cells identified by Nomarski optics as containing "pits", and the proportion of osmotically labile cells. 80% of HbSS patients had an abnormal osmotic fragility curve characterized by a "tail" of hypotonically labile cells whereas none of the normal controls lysed in solutions less hypotonic than 0.5% saline. In patients with abnormal curves, 0.55% buffered saline hemolyzed 3.0 ± 2.7% of cells. HbSS patients with osmotically fragile cells had more ISC's (22 vs. 11%), lower Hgb's (7.7 vs. 8.5gm%), more reticulocytosis (20 vs. 15%) and lower Hb F values (7 vs. 12%) ($p < 0.05$ for all). Scanning electron microsopy of peripheral blood revealed ISC's and irregularly contoured spherocytic cells. In the group with abnormal fragility, the proportion of osmotically labile cells correlated inversely with Hgb, positively with reticulocyte count, positively with MCHC, and surgical splenectomy status ($p < 0.05$ for all); those with splenectomy had more spherocytic cells. This proportion did not correlate with "pit count", age (after 2 years), the patient's sex, or MCV. These results indicate that in addition to ISC's, a second population of damaged erythrocytes characterized by increased osmotic lability circulate in patients with sickle cell disease and may be important in the pathogenesis of anemia.

800 A THERAPEUTIC TRIAL OF 10 DRUGS VS. 4 DRUGS IN NON-HODGKIN'S LYMPHOMA (NHL). Robert Chilcote, Derek Jenkin, James Anderson, Peter Coccia, Phillip Exelby, Anna Meadows, Joseph Kushner, John Kersey, Stuart Siegal, John Wilson, Sanford Leikin, and Denman Hammond for the Childrens Cancer Study Group (CCSG), Los Angeles, California

NHL's of children are a heterogeneous group of malignancies which when disseminated respond poorly to therapy. In CCSG 551, a stratified prospective trial for children with NHL, we randomized 314 patients to receive 4 drugs (COMP) or 10 drugs (modified LSA_2L_2). All patients received radiation to bulk disease and prophylactic IT methotrexate. Patients were grouped by extent of disease (regional vs. disseminated), and histologic type (lymphoblastic vs. non-lymphoblastic). Of the 60 patients with regional disease, 85% remained free of disease at 24 mos, regardless of histology or treatment arm. Of the 254 patients with disseminated disease, 76% of those with lymphoblastic histology remained disease free at 18 months using 10 drugs while only 36% were still in 1st remission on the 4 drug protocol ($p < 0.05$). In contrast, 61% of those patients with non-lymphoblastic morphology remained in 1st remission at 18 mos on 4 drugs, but only 29% were still in 1st remission using 10 drugs (p 0.05). As the overall toxicity of the 10 drug protocol exceeded that of the 4 drug protocol, we now treat all patients with regional disease with local irradiation and the 4 drug protocol. For patients with disseminated disease the 10 drug protocol is superior for lymphoblastic disease while the 4 drug is advantageous for other histologies.