812 PLATELET ACTIVATION IN SICKLE CELL DISEASE. Jay Greenberg and Elias Schwartz. University of Pennsylvania School of Medicine and The Children's Hospital of Philadelphia, Department of Pediatrics, Philadelphia, Pa.

Abnormalities in platelet number and function have been described in patients with homozygous sickle cell disease (SS), suggesting that platelets play a role in this disorder. We studied platelet shape and circulating platelet aggregates (AGG) in SS patients as a guide to in vivo activation. One drop of freely flowing blood was collected by venipuncture into a siliconized vial containing 1% glutaraldehyde in 0.38% citrate. Using phase microscopy, 200 platelets were examined to see whether they were deformed (DEF) (spherical shape with $\geq$ 1 spinous process), AGG ($\geq$ 2 adherent DEF platelets), or in their natural discoid shape. Results were expressed as % activated, computed as 100 x (DEF + AGG)/total. Thirty pediatric patients (ages 1-18 years) with a diagnosis of SS or SC disease were evaluated and found to have a mean activation of 65.3 $\pm$ 26.9% (1SD). A normal population of 15 adults had a mean of 22 $\pm$ 8.8% ($P \leq 0.001$). Age, recent vasoocclusive crisis, pneumonia, aspirin, and chronic transfusion therapy were separately analyzed and found not to have a significant effect. A 4-year-old with SS was studied before, during, and after transfusion therapy for debilitating recurrent crises. Activation corrected from a baseline of 88% prior to therapy to 25% following 6 mos. of transfusions, but gradually returned to 65% at the time of the first crisis following the cessation of transfusions. These observations further indicate that platelets are involved in the pathophysiology of sickle cell disease.

813 CONTROLLED STUDY OF TREATMENT FOR DISSEMINATED INTRAVASCULAR COAGULATION (DIC) IN THE NEWBORN. Steven J. Gross, Judith Andersen, and Howard Filston (Spon by G.W. Brumley) Duke Univ. Med. Ctr., Depts. of Ped, Med., and Surg., Durham.

DIC was diagnosed in 31 newborns by the following laboratory criteria: platelet count <100,000/mm^3, PTT >90 sec (nl <36 sec), PT ratio >1.5 (nl=1.0), and fibrinogen <150 mg/dl. Primary underlying diseases were identified and treated. Infants were assigned randomly to one of 3 treatment regimens: I. Exchange transfusion with CPD whole blood q 12 hr until coagulation improvement. II. Fresh frozen plasma (15 ml/kg) and platelets (1 unit) q 12 hr until coagulation improvement. III. No coagulation therapy. The 3 groups were similar for birthweight, gestational age, Apgar scores, underlying disease processes, and degree of abnormality of initial coagulation studies. Data indicate mean $\pm$ SD.

	I (n=10)	II (n=10)	III (n=11)
Birthweight (gm)	1362 $\pm$ 752	1359 $\pm$ 614	1406 $\pm$ 450
Gestational age (wk)	29.8 $\pm$ 4.8	31.0 $\pm$ 5.0	31.0 $\pm$ 2.4
Apgar at 5 minutes	6.8 $\pm$ 1.6	7.0 $\pm$ 2.2	5.6 $\pm$ 2.3
Underlying Disease			
Sepsis	2		2
NEC/Sepsis	3	5	4
Asphyxia	4	4	5
Maternal coagulopathy	1	1	
Survival	6 (60%)	5 (50%)	8 (73%)

There were no differences in rates of improvement in coagulation studies or survival in the 3 groups. Outcome was more dependent on success of treatment of underlying pathologic processes than on treatment specifically directed at the coagulopathy.

● **814** ALTERED PATTERN OF SPECTRIN PHOSPHORYLATION IN SENESCENT HUMAN RED CELLS. William Harris Jr, Neil Levin, and Samuel Lux. Division of Hematology, Harvard Medical School, Children's Hospital Medical Center, Boston, MA.

The membrane protein spectrin is important in the maintenance of red blood cell (RBC) membrane shape and stability. We have previously shown that it is phosphorylated at 4 sites clustered near the C-terminus of its smaller subunit. These phosphates may control spectrin's interaction with other membrane proteins. To test whether spectrin phosphorylation changed with RBC age, intact RBCs were labeled with $^{33}PO_4$, fractionated by density, and assayed for age (using marker enzymes) and for the position and number of $^{33}PO_4$'s in spectrin dimer. ^{33}P-spectrin prepared from old (average=90 d of age) and control RBCs had identical numbers of ^{33}P phosphates; however the distribution of ^{33}P was altered in old RBCs. ^{33}P-label in the most distal phosphorylation site was reduced from 0.95±0.05 moles/mole spectrin dimer to 0.25±0.05(n=4) and was proportionally increased in a more proximal site(s). Similar changes occurred in RBCs incubated in the absence of substrate for 20 hrs (but not for 12 hrs). Phosphorylation of purified ^{33}P-spectrin from old RBCs with spectrin kinase and γ-^{32}P-ATP produced the same number and distribution of phosphates as control. We conclude that the location of spectrin phosphates in senescent or metabolically-depleted RBCs is altered. This may be caused by enzymatic redistribution of isotopic label or by a structural alteration of the distal phosphorylation site. This change may contribute to the membrane instability and eventual demise of the aged RBC.

815 ABNORMAL IMMUNE RESPONSES TO EPSTEIN-BARR VIRUS (EBV) ASSOCIATED WITH AN ILLNESS MIMICKING JUVENILE CHRONIC MYELOGENOUS LEUKEMIA (JCML) IN TWO CHILDREN. Henry G. Herrod, Lois W. Dow and John L. Sullivan. (Spon. by Fred Barrett). University of Tennessee Center for the Health Sciences, St. Jude Children's Research Hospital and University of Massachusetts Medical Center, Memphis, TN 38101 and Worcester, MA 01605

EBV infection has been associated with diseases ranging from infectious mononucleosis to X-linked lymphoproliferative syndrome. We have evaluated a 21-month-old white boy and a 15-month-old black girl with suspected JCML whose presenting features included lymphadenopathy, hepatosplenomegaly, decreased platelets and leukocytosis. Evaluation was negative for a malignant process. Representative immunologic studies of the patient blood cells included:

Pt.	% E-rosette	%sIg (+)	PHA Response (SI)	T-Lymphocyte Colony Formation
1	31.3	8.8	11	172
2	18.2	51.2	10	79
Control	62.4±7.3	4-15.4%	>30	1359±522

Antibodies to EBV viral capsid antigen and EBV early antigen persistently were elevated. Natural killer cell activity was diminished in both patients and showed little augmentation with fibroblast interferon. No EBV specific cytotoxicity was detected. The patients have been followed for 30 and 20 months on no therapy with clinical improvement. These patients have alterations in cell mediated immune responses and abnormal immunoregulation of antibody production to EBV. Because of their clinical presentation such patients need to be distinguished from those with true malignancies.

816 NEUTROPHIL FUNCTION IN TRANSFUSION-INDUCED IRON OVERLOAD. James R. Humbert, Ganesh N. Deshpande, Maria V. Gauto, State University of New York and Children's Hospital of Buffalo, Department of Pediatrics, Buffalo.

Iron overload damages a wide variety of organ systems, and is accompanied by an increased susceptibility towards infections in some patients. The contribution of neutrophil (PMN) dysfunction to such infections has not been explored. We investigated PMN functions in seven chronically transfused children with documented iron overload (3 each with thalassemia major and sickle cell disease, and 1 with pure red cell aplasia). All patients had received monthly transfusions for over 6 years and had ferritin levels above 3000 ng/ml. A modification of Tan's technique was used to assay PMN bactericidal activity and phagocytosis towards Staphylococcus aureus 502 A. Results are reported in percent viable intracellular (IB) or extracellular (EB) bacteria after 30 or 120 minutes of incubation. PMN oxygen consumption (expressed as mM $O_2/10^9$ PMNs) was measured by polarigraphy after stimulation with phorbol myristate acetate. All results ($\bar{x}$ $\pm$ SE) are indicated in the table below.

	IB_{30}	IB_{60}	EB_{30}	EB_{60}	O_2
Patients(8)	4.0±1.4	4.1±0.8	21.0±2.4	7.5±1.8	27.1±4.1
Controls(12)	3.9±0.5	4.3±0.8	20.5±2.2	7.8±2.3	25.0±3.6

PMN functions of iron overloaded patients appear to be normal. The abnormal propensity toward infections of such patients does not seem to be caused by a deterioration of their PMN phagocytic or bactericidal mechanisms.

817 SUBCUTANEOUS DEFEROXAMINE (ScDF) PLUS HYPERTRANSFUSION (HiTx) IN THALASSEMIA MAJOR (TM): A THREE YEAR FOLLOW-UP. Adlette Inati, Richard Propper, and David Nathan. Harvard Medical School, Children's Hospital Medical Center, and the Sidney Farber Cancer Institute, Boston, MA.

12 TM patients (pts.) aged 5-25 yrs. on moderate Tx protocol were begun on HiTx and ScDF with yearly monitoring of serum ferritin (SF), height age (HA), bone age (BA), cardiac function (CF [eccho, EKG, treadmill, Holter]), and GTT. Net negative iron balance was maintained. Results are tabulated.

Comparison of Initial and 3 Yr. Follow-Up Study by Presenting Age Groups

				# of Pts. with Normal Measurements							
Pt.	Age	Mean SF (µg%)		HA		BA		CF		GTT	
#	(Yrs.)	0*	3*	0*	3*	0*	3*	0*	3*	0*	3*
3	5-8	4325	1100	3	3	3	3	3	2	3	3
6	10-15	6750	3950	5	3	2	2	3	2	4	4
3	20-25	7330	4500	0	0	0	0	1	1	1	1

*Yr. of study at which measurement was made

The above data suggests that young pts. with TM may be protected from iron overload sequelae by the early administration of HiTx and ScDF. Similar therapy in older patients does not seem to prevent the development of or improve existing overt pathology.