625 CONTINUOUS IV AND SC DESFERRIOXAMINE THERAPY IN β-THALASSEMIA. Alicejane L. Markenson, Joseph H. Graziano, Henry Chang, Marc Bestak, Paul Meyers, Patricia Pisciotto and Denis R. Miller, New York Hospital-Cornell Medical Center, Department of Pediatrics, New York.

Desferrioxamine (DF) has recently proven to be extremely efficacious in inducing iron excretion when administered as an IV or SC infusion. To determine appropriate IV drug doses for thalassemic children of different ages, we performed 17 dose-response studies on patients from 5 to 26 years old. Each child received 4 one-week courses of IV DF at doses of 20, 40, 60 and 80 mg/kg. Three patients received SC DF by portable infusion pump at 20 mg/kg over 8 hours for one week and 16 hours another week. At 20 mg/kg, drug efficiency (urinary iron excretion/theoretical maximum excretion) was 55% in the youngest group but fell rapidly as the dose was increased. In contrast, drug efficiency was 86% in patients over 11 years and dropped off slowly to 62% at 80 mg/kg. At the same dose, SC DF given over 8 hours was shown to be almost as effective as 16 hours SC and 24 hours IV DF, permitting over-night SC administration. Thus, drug dose and route of administration should be adjusted according to age and requirements.

Urinary Iron Excretion (mg Fe/24 hours)

Age and Dose-related Response						IV vs SC DF at 20 mg/kg/day			
Age	No.Pts.	20	40	60	80mg/kg	Age	24hrs IV	16hrs SC	8hrs SC
5-10	6	14	23	26	29	11	34	-	33
11-15	6	34	57	83	100	20	40	28	29
16-26	5	40	62	100	115	26	58	53	44

626 PLASMA INHIBITOR OF PLATELET FUNCTION IN β-THALASSEMIA. Alicejane L. Markenson and Margaret W. Hilgartner, (Spon. by Denis R. Miller), New York Hospital-Cornell Medical Center, Department of Pediatrics, New York.

Patients with homozygous β-thalassemia often have moderate to severe epistaxis and/or a petechial rash with normal platelet count, PT and PTT. For this reason we have studied platelet function(PlF). Pre-transfusion evaluation included: Duke bleeding time (BT), PF_3 release (Stypven), aggregation (epinephrine, ADP, collagen), PT, PTT and platelet count. PlF was abnormal in 13/30 patients (43%) studied: 10/13 had recurrent epistaxis and/or petechial rashes, 3 had minimal symptoms; 13/13 had abnormal aggregation with epinephrine, 10/13 with ADP, and 10/13 with collagen; only 1 also had slightly low PF_3 release; BT was abnormal in 3/13. At time of study platelet count was normal in all, PT and PTT in most; none were receiving anti-aggregating drugs. Patients' platelets were isolated, washed by Ardlie buffer method, lysed and analyzed spectophotometrically for iron. No iron deposition in platelets was detected by this method. In other experiments, donor platelets were washed or gel-filtered to render them free of donor plasma; test plasma was then added to platelets and platelet aggregation assays were performed. Normal donor platelets were abnormal when tested in plasma from patients with abnormal PlF; platelets from 3 patients with abnormal PlF functioned normally in normal plasma but abnormally in "abnormal" plasma. Abnormalities of platelet aggregation are detectable in 1/2 symptomatic patients. Our data suggest that the PlF abnormalities detected in β-thalassemia may be due to a plasma inhibitor, rather than an intrinsic platelet defect.

627 *STIFFENED ERYTHROCYTES IN POLYCYTHEMIA OF CYANOTIC CONGENITAL HEART DISEASE (CCHD).* *Harold M. Maurer, Carolyn M. McCue, Nancy B. McWilliams, Charles Johnston, and Joyce Haggins. Medical College of Virginia, Depts of Pediatrics and Pathology, Richmond, Virginia.*

As the hct rises above 60% in CCHD, there is an increased threat of thrombotic and hemorrhagic complications due to blood hyperviscosity. Hyperviscosity has been attributed to increased RBC mass. Since RBC deformability is a determinant of viscosity and flow at high hcts, we studied RBC deformability in 22 children with polycythemic CCHD and in 10 controls, using a filtration system. Filterability is a function of cell deformability. Washed RBC's resuspended in Ringer's lactate-albumin solution were passed through a 3u polycarbonate filter using hydrostatic pressure (at 25°C), and flow velocity was calculated (ul/sec).

Controls had a mean hct of 41%± 2, mean MCV of 87fl± 2, and mean RBC flow velocity of 5.0 ul/sec±.7. Children with CCHD were divided into 2 groups: 10 patients with hcts between 50-60% (mean 57%±1), and 12 patients with hcts >60% (range 63-74%, mean 67%±1). Mean flow velocity (3.4ul/sec±.2) in the group with hcts >60% was significantly (p=.05) reduced as compared to controls and the <60% hct group. The latter had a mean flow velocity of 4.8ul/sec±.7, which was comparable to controls. All groups were similar in age (mean 9.5 yrs), sex ratio and MCV.

We conclude that RBC's become stiffened when the hct exceeds 60% in CCHD. Stiffened RBC's may contribute to the thrombotic complications observed in these patients.

628 INTRACRANIAL CALCIFICATIONS AND SYSTEMIC METHOTREXATE (MTX). Linda S. McIntosh, Diana B. Fischer, Stephen G. Rothman, Nancy Rosenfield, Richard T. O'Brien (Spon. by Howard A. Pearson) Yale-New Haven Medical Center, Dept. of Pediatrics, New Haven.

Children with acute lymphocytic leukemia were examined for intracranial calcifications with computerized tomography and skull x-rays. Of 39 patients in continuous complete remission for 6 months to 6 years, 10 had 1 or more subcortical calcifications. All patients had received similar induction chemotherapy (prednisone and vincristine + adriamycin) and CNS prophylaxis (whole-brain irradiation, 2400r., and 5 injections of intrathecal MTX). Maintenance chemotherapy varied. Significant association between presence of intracranial calcification and total cumulative dose of systemically administered MTX was found. Among age-matched children treated for 21 to 32 months, 1/5 receiving ≤ 4.5 gm. MTX had calcification, whereas 6/7 receiving > 4.5 gm. MTX (most intravenous)developed calcification (p=0.03). Among those treated for 11 to 20 months, 0/5 receiving ≤ 4.5 gm. MTX developed intracranial mineralization, as did 3/7 receiving > 4.5 gm. (p=0.16). Statistical analysis also suggests that ara-C may contribute to risk of brain injury. Of the 10 affected patients, 8 had signs of chronic MTX encephalopathy--limp, seizures or perceptual-motor handicap. Controlled prospective studies are needed to broaden these observations and to define the roles of brain irradiation and systemic chemotherapeutic drugs in the development of chronic nonleukemic encephalopathy.

629 CONTROLLED CLINICAL TRIAL OF PREDNISONE IN CHILDHOOD IDIOPATHIC THROMBOCYTOPENIA PURPURA (I.T.P.). Nancy B. McWilliams and Harold M. Maurer. Medical College of Virginia, Department of Pediatrics, Richmond, Virginia.

Twenty-seven children, 13 girls and 14 boys, from 1 - 17 years of age (mean 6.0 years) with acute I.T.P. were randomized to receive prednisone 2 mg/Kg/day for 3 weeks or no therapy. A history of preceding infection was obtained in 84.6% of the treated group and 92.8% of the controls. Initial mean platelet count for all patients (± SEM) was 21,000/cu mm ± 4,000 and did not differ significantly in the 2 groups (p >.05). Median follow-up time for the entire group was 17 months.

The median time to attain a platelet count of ≥150,000 was 21 days in the treated group vs. 60 days in the controls (p = .03). There was no relationship between initial platelet count, age and time to response. Of the 24 patients evaluable for long term outcome 5/11 (45.4%) of controls failed to achieve a normal platelet count and required treatment, including splenectomy in 1. In the treated group 2/13 (15.4%) relapsed and 1 required splenectomy.

We conclude that early steroid treatment in acute I.T.P. in children restores normal platelet counts significantly sooner than in those not treated and should be instituted at the time of diagnosis to prevent early complications.

630 PRELIMINARY INVESTIGATIONS OF ENDOTHELIAL CELL PARTICIPATION IN NEONATAL PLATELET DYSFUNCTION - T. D. Miale, A. M. Nelson and S. Ryan, Spon. by G. L. Schiebler, University of Florida, Gainesville, FL. 32610.

Neonatal platelet dysfunction is common and correlates with certain neonatal and maternal factors:

Degree of Platelet Dysfunction	Perinatal Drug Administration	Complications of Labor Delivery	Neonatal Sepsis +/or Respiratory Distress
None/Mild 6/24	5/6	0/6	0/6
Moderate 13/24	12/13	1/13	1/13
Severe 5/24	5/5	2/5	3/5

In addition, a thermo-labile inhibitor of platelet aggregation was demonstrated in 9/28 umbilical vein endothelial cells (UVECs) extracted by collagenase-IV treatment followed either by freeze-thawing or sonication. The addition of spermine or spermidine enhanced this inhibition. Perfusion experiments were conducted in which platelet-rich plasma was pumped at various rates in a pulsatile manner either through plastic tubing or with a portion of the tubing replaced by 10-15 cm. sections of fresh umbilical veins. An 8.7-fold overall reduction in platelet aggregation was observed with the insertion of this venous segment. This was most pronounced with ADP-induced aggregation but was also seen with ristocetin and epinephrine. Scanning and transmission electron micrographs demonstrated less interaction between platelets and endothelial cells following perfusion with UVEC extracts.