577 4'-DEMETHYL-EPIPODOPHYLLOTOXIN-β-THENYLIDENE GLUCOSIDE (VM-26)(NSC-122819): A NEW DRUG FOR NEUROBLASTOMA. W. Archie Bleyer*†, William Krivit**, Ronald L. Chard† and Denman Hammond (for the Children's Cancer Study Group, Los Angeles) University of Washington*, Children's Orthopedic Hospital†, Seattle; University of Minnesota School of Medicine and Hospitals**, Minneapolis; Departments of Pediatrics.

Neuroblastoma remains a great challenge in pediatric oncology. The demonstration of an effective new drug for neuroblastoma would be a worthwhile addition to the present surgical, radiation and chemotherapeutic modalities.

VM-26 is a lipophilic podophyllotoxin with demonstrated activity in human tumors. CCSG studied its effect in 14 children with advanced stage IV neuroblastoma resistant to 3-6 chemotherapeutic agents. VM-26 was given as a 1 hour intravenous infusion on a weekly schedule of 130 mg/m^2 x 3, 150 mg/m^2 x 3, then 180 mg/m^2 until progression of disease. Of 12 evaluable patients, one had a complete response of 211 days duration, four had partial responses of 21+, 21+, 58 and 78 days duration, four had either static disease or transient subjective responses, and three had no response. Dose-limiting toxicity was hematologic, with severe leukopenia occurring in five patients and thrombocytopenia in four patients. The toxicity was temporary in that most patients were able to tolerate the scheduled dosage escalations.

A response rate of 42% is taken as evidence for further trials of this drug in neuroblastoma.

578 EARLY ANEMIA IN INFANTS WITH SICKLE CELL DISEASE - RELATIONSHIP TO A VULNERABLE POPULATION OF RED CELLS. Audrey K. Brown, A.N. Rao, Tito C.M. Sobrinho, Mae Hee Kim. SUNY-Downstate Medical Center, Department of Pediatrics, Brooklyn, New York.

Hematological parameters were studied in 33 infants with sickle cell disease from birth to 2 years of age. The hemoglobin was below normal for age as early as 6 weeks and remained low thereafter (average 8.7 gm%). Significant reticulocytosis was noticed as early as one month of age, and by three months, it averaged 7.6%. Hb F concentration in these infants declined more slowly than in normal infants and at 6 months of age averaged 25.6%; at 1 year the Hb F concentration was about 20%. The intracellular distribution of the Hb F (by the Betke-Kleihauer technique) was heterogeneous at all ages. Even in infants less than 3 weeks of age, "ghost"cells containing no Hb F (presumably therefore containing only Hb S) were seen. Our data indicate that in newborn infants with Hb S (as in those with Hb A) a population of cells containing little or no Hb F is present even when there is a high concentration of Hb F in the blood. In infants with Hb S, sickling and hemolysis of this vulnerable cell population would explain the uniform early development of hemolytic anemia by 6 weeks of age.

579 WHITE BLOOD CELL (WBC) COUNT AND ERYTHROCYTE SEDIMENTATION RATE (ESR) IN SICKLE HEMOGLOBINOPATHIES: COMPARATIVE VALUES DURING STEADY STATE, BACTERIAL INFECTION, AND VASO-OCCLUSIVE CRISIS. George R. Buchanan and Bertil E Glader, Harvard Medical School, Children's Hospital Medical Center, Department of Pediatrics, Boston.

Total and differential WBC counts were determined during the steady state (periods free of infections or crises) in 88 children with sickle hemoglobinopathies. In 22 children with SC disease and 8 with S-thalassemia these values were similar to normal children. In 58 children with SS disease the WBC count was elevated, just as in other children with asplenia and hemolysis.

	Total WBC	Segs	Bands
	(10^3 cells/μl blood)		
Steady state (58)*	12.3**	5.4	0.1
Vaso-occlusive crises (35)	16.4	10.4	0.3
Bacterial infection (16)	22.0	10.5	4.6

*number of SS patients **mean value

During vaso-occlusive crises the total WBC count and absolute level of segmented neutrophils were further elevated. In documented bacterial infections, however, the elevated total WBC counts were associated with increased levels of both segmented and band neutrophils. The mean uncorrected ESR in children with SS disease was 13 mm/hr during the steady state (33 pts), 12 mm/hr during vaso-occlusive crises (12 pts), and 39 mm/hr in documented bacterial infections (3 pts). Contrary to current concepts, these data suggest that simple tests such as the total and differential WBC count and ESR may be useful in distinguishing vaso-occlusive sickle cell crisis from bacterial infection.

580 A THROMBOCYTOPENIA (T) GIANT PLATELET SYNDROME WITH DEFECTIVE PLATELET AGGREGATION AND A VON WILLEBRAND (VW)-LIKE PLASMA DEFECT. George R. Buchanan and Robert I. Handin (Spon. by Samuel E. Lux), Harvard Medical School, Children's Hosp. Med. Center and Peter Bent Brigham Hosp., Dept. of Pediatrics and Medicine, Boston. A 17-year old girl with life-long T, unresponsive to splenectomy, was evaluated because of easy bruising, epistaxis, and recurrent hemarthroses. Platelets (P) were reduced in number (50,000-140,000/μl) and their size was greatly increased (3-5 μ in diameter) on peripheral blood smear. Bone marrow contained increased megakaryocytes, and ^{51}chromium-labeled autologous P survival was normal (7.8 days), suggesting ineffective thrombopoiesis as the cause of the T. Bleeding time (BT) was consistently greater than 25 min., and P did not aggregate normally when incubated with collagen or epinephrine but did respond to ristocetin. Although rate of uptake of ^{3}H-serotonin was reduced, P ATP/ADP ratio was normal, excluding a storage-pool defect. The patient's Factor VIII level measured by coagulation assay ($VIII_{AHF}$) or by ability of her plasma to support ristocetin-induced aggregation ($VIII_{VWF}$) varied from 35-150% and 27-160% respectively, while Factor VIII-related antigen was always normal (over 60%). Transfusions of both cryoprecipitate and P, but neither alone, transiently shortened BT (to 7-9 min.) and controlled bleeding symptoms. Post-transfusion increments in $VIII_{AHF}$ were consistent with VW disease. Family history and coagulation studies were unremarkable. This patient appears to have a unique combined defect in thrombopoiesis, intrinsic P function, and in $VIII_{VWF}$. Effective therapy has required both normal P and Factor VIII-containing products.

581 USE OF PROTHROMBIN COMPLEX CONCENTRATES (PCC) IN HEMOPHILIACS WITH INHIBITORS: LACK OF CORRELATION BETWEEN CLINICAL RESPONSE AND LABORATORY PARAMETERS. George R. Buchanan and Sherwin V. Kevy (Spon. by Bertil E. Glader), Harvard Medical School, Children's Hosp. Medical Center, Dept. of Pediatrics, Boston. Proplex (P), Konyne, and Auto-Factor IX (A) are PCC which can promote hemostasis in patients with hemophilia A with circulating inhibitors against Factor VIII. This is achieved by the variable amounts of procoagulant substances (presumably activated clotting proteins) present in the PCC. Six patients have received 337 infusions of PCC for 95 bleeding episodes, including iliopsoas hemorrhage, life-threatening upper airway bleeding, pseudotumor, and surgical procedures (laminectomy, laparatomy, dental extractions). No untoward thrombotic complications occurred, and circulating inhibitor levels fell in 4/6 patients while remaining constant in the 2 others. Many infusions were beneficial, but clinical responses were variable and unpredictable over a wide dosage range. To evaluate this inconsistency, we tested 15 different lots of P and A and found all of them to contain activated factors as evidenced by: (1) the ability of 1:100 to 1:5000 dilutions to shorten the unactivated partial thromboplastin time (PTT) of normal and hemophilic plasma in vitro, and (2) transient shortening of patients' prothrombin time and PTT after each dose. There was no correlation between these laboratory parameters of accelerated coagulation and cessation of bleeding. Therefore, efficacy of PCC must be judged primarily by clinical response rather than by laboratory tests demonstrating activation of coagulation.

582 THE ZETA SEDIMENTATION RATE (ZSR) IN CHILDREN. James J. Campbell, Marie J. Stuart and Douglas A. Nelson. Depts. of Peds. and Path., SUNY, Upstate Med. Ctr., Syracuse, N.Y.

The ZSR has certain technical advantages over the erythrocyte sedimentation rate (ESR), and is not influenced by the presence of anemia. A study was undertaken to establish normal values for the ZSR in infants and children, and to compare the diagnostic utility of the ZSR as opposed to the ESR in children believed to have active inflammatory processes. The normal values for the ZSR in infants and younger children (mean ±2SD) were significantly lower than in the older age group:

AGE	ZSR	(N)
<2 yrs.	41.9 ± 11.0	55
3-10 yrs.	45.4 ± 8.4	44
11-19 yrs.	47.3 ± 7.8	28

The ESR showed a similar, although not statistically significant trend. There were 6 children considered normal who, however, had increased ESRs but normal ZSRs. 4/6 were anemic, and may therefore have had falsely elevated ESR values. Among the 70 tests obtained on children believed to have clinically active inflammatory processes, 2/70 (3%) had normal ZSRs and ESRs. 6/70 (9%) had increased ESRs with concomitantly normal ZSRs, whereas 6/70 (9%) had normal ESRs with elevated ZSRs. These findings suggest that the ZSR is comparable to the ESR as an index of disease, and is recommended as a technically superior substitute for the ESR in infants and children.