776 DIAGNOSTIC IMPLICATIONS OF N-MYC ONCOGENE EXPRESSION AND AMPLIFICATION IN PEDIATRIC RENAL TUMORS. Perry D. Nisen, Mark Rich, Elizabeth Gloster, Elsa Valderrama, Olga Saric, and Ashok Shende. Spon. by Phillip Lanzkowsky. SUNY Stony Brook, Schneider Children's Hospital, Divisions of Hematol. -Oncology, Pathology, and Urology, Long Island Jewish Med. Center, New Hyde Park, NY

Molecular and tissue culture techniques were used to characterize unusual bilateral renal tumors from a young boy. The left kidney demonstrated histopathologic and electron microscopic features of both neuroblastoma and Wilms' tumor. The contralateral kidney exhibited multiloculated cystic nephroma (MLCN). In vitro tissue culture of tumor cells induced neurite outgrowth. Hybridization experiments with an N-myc oncogene DNA probe revealed that the left renal neoplasm exhibited greater than ten-fold N-myc gene amplification in chromosomal DNA; N-myc was not expressed or amplified in the MLCN or in normal kidney tissue, however. While N-myc expression in RNA and histopathologic features could not clearly distinguish between Wilms' tumor and neuroblastoma, neurite outgrowth and gene amplification strongly suggested that this neoplasm would behave as an aggressive neuroblastoma. The diagnostic, prognostic and therapeutic implications of these findings will be discussed.

777 GROWTH HORMONE RESPONSE TO GROWTH HORMONE RELEASING FACTOR (GRF) IN SICKLE CELL DISEASE. Sharon E. Oberfield, Doris L. Wethers, John Kirkland, Lenore S. Levine. College of Physicians and Surgeons, Columbia University, St. Luke's/Roosevelt Hospital Ctr. Dept. of Pediatrics, New York and Baylor College of Medicine, Dept. of Pediatrics, Houston, Texas.

Many children with Sickle Cell Disease (SSD) have patterns of growth during childhood and adolescence consistent with constitutional delay in growth and pubertal development (CDGD). We evaluated the growth hormone (GH) response to a rapid intravenous infusion of growth hormone releasing factor (GRF 1-44,1 ug/kg) in 6 children with Sickle Cell Disease whose growth patterns and bone ages were consistent with CDGD. The control population included children with (n=3) and without (n=4) CDGD. Since the peak responses of the control children with and without CDGD were not different (32.3 +/- 8.9, M +/- SD vs 26.5 +/- 2.5, M +/- SD, p>.05), these responses were combined for statistical analysis. All patients demonstrated normal GH responses to GRF stimulation. All patients had a peak GH response within 2 S.D. of the control mean peak GH response. The mean peak GH response of the patient population to GRF (29.2 +/- 14.3 ng/ml, M +/- SD), was not significantly different from the mean peak GH response of the combined control group (29.0 +/- 6.3, M +/- SD, p=.976). Further, when the peak GH responses of the patients with SSD (n=6) and the controls with delayed bone age (n=3) were combined, the mean peak GH response of the group with delayed bone ages was not different from that of the control children without retarded bone ages (30.2 +/- 12.2, M +/- SD, n=9 vs 26.5 +/- 2.5, M +/- SD, n=4, p=.567). SM-C levels were low for chronological age in 2 patients, in one of whom it was normal for bone age. These findings suggest that pituicyte GH response to GRF is intact and is not the cause of the observed impaired growth in patients with SSD.

†778 AN INITIATION CODON MUTATION IN THE α1 GLOBIN GENE OF A BLACK FAMILY WITH HbH DISEASE Nancy F. Olivieri, Annette O. Poon, Lebe S. Chang, Alan M. Michelson, Stuart H. Orkin, and The Hospital for Sick Children, Division of Hematology/Oncology, Department of Pediatrics; University of Toronto, Toronto, Ontario, Canada.

In α thalassemia, molecular analysis has revealed deletion and non-deletion defects, of which deletion mutations are the most common. To date the non-deletion defects described have involved the α2 globin gene. Analysis of the molecular basis of HbH disease in a black family revealed the non-functional gene to be entirely α1 like, with a single nucleotide change in the initiation codon (A→G). This represents the first assignment of a non-deletion mutation in this racial group and the first mutation identified in the α1 globin gene. Since this mutation, which abolishes the NCOI site in the initiation codon, is detectable in genomic DNA by NCOI digestion, Southern blot analysis should provide a rapid screening method for the occurrence of this lesion in blacks with α thalassemia.

779 EVALUATION OF MEGAKARYOCYTES IN CHILDHOOD IDIOPATHIC THROMBOCYTOPENIC PURPURA (ITP). Thomas A. Olson, Richard F. Levine, and Pamela K. Shoff (Spon. by Gerald W. Fischer), Walter Reed, Peds, VA Med Center, Wash DC, USUHS, Bethesda, MD.

The clinical course of ITP in children usually differs from that in adults, yet distinctions by marrow characteristics have not been established. Megakaryocytes (megas) were examined for size, ploidy, maturation and morphology in 8 children and 8 adults with ITP, and 8 normal marrows. Either buffy coat wedge or cover slip squash smears were prepared. (Control values differed for each.) Feulgen-stained megas (100-300) were examined as previously described. Wright-stained material was also examined. There were no differences in the megas of normal children and adults. In all children with acute ITP, megas were increased in size (mean volume 4X normal), ploidy (medians 2 doublings higher, to 64N) and maturation stage (86% mature vs control 43%). In contrast, in adults with acute or chronic ITP the megas showed no differences in size, ploidy, or maturation compared to controls. Some dissociation of mega ploidy and maturation was seen in adults, but not enough to alter the profile of any one parameter. In conclusion, the megas of acute childhood ITP were different than adults'. Similar enlargement and maturation is seen in animals whose megas are stimulated by injection of anti-platelet serum. The absence of these large, mature megas in adult ITP may reflect the chronicity of this disease in adults. Studying children with chronic ITP with regard to marrow mega characteristics may provide information to help identify those children with acute ITP with a propensity to develop chronic ITP.

780 MICROMEGAKARYOCYTOSIS AND HEREDITARY THROMBOCYTOPENIA, Thomas A. Olson, Richard F. Levine, Pamela K. Shoff, John Kelleher (Spon.by Gerald W. Fischer), Walter Reed, Peds, VA Med Center, Wash DC, Bay State Med Ctr, Springfield, MA, USUHS, Bethesda, MD

Two sibs (BS and RS) and a first cousin (BT) have been followed for several years for easy bruising, epistaxis, and low platelet counts (BS and RS 12-30,000, BT 30-60,000). BT has an unaffected sibling. Chronic Idiopathic Thrombocytopenic Purpura (ITP) was suspected but the number of megakaryocytes (megas) seemed decreased. Splenectomy in BT led to a transient rise in platelets (max 90,000) before falling to, and remaining at, pre-operative levels. Pre-existing (BS, RS, and 4 normal children) and fresh (BT) marrow samples were Feulgen stained and examined for number, size, ploidy, and maturation (N=300 cells). With Feulgen staining, mega numbers were increased (2x) compared to controls. The mean mega diameter in all three patients was decreased (19 μm vs 26 μm control). Also, the patients' megas were lower in ploidy.

	4N-8N	32N	64N
Patients	64%	6%	0
Controls	36%	25%	9%

Maturation appeared retarded (Feulgen) but seemed to have an approximate normal distribution with Wright stain. Since mega size is related to levels of ploidy and maturation, the defect in these patients may be due to inadequate ploidization. Actual mega numbers may be increased though micromegakaryocytes may be missed on routine bone marrow smear. This family represents a form of thrombocytopenia that could be confused with chronic ITP and which will probably not respond to splenectomy.

781 ADRIAMYCIN CONTINUOUS I.V. INFUSION-HYPERFRACTIONATED RADIATION THERAPY FOR THE TREATMENT OF RECURRENT PEDIATRIC SOLID TUMORS. Jorge A. Ortega, Daljit Soni, Barton R. Wald, Nomie A. Shore, (Spon. by Stuart E. Siegel), USC Sch. of Med./Childrens Hosp. of Los Angeles, Dept. of Peds and Rad. Ther., Los Angeles,CA

The prognosis of most pediatric solid tumors is poor upon development of recurrent disease. The study was designed to test the efficacy of Adriamycin (ADR) I.V. continuous infusion (CI) given simultaneously with hyperfractionated (HFT) radiation therapy (XRT) to such patients. The rationale for the study was: 1. ADR enhances XRT lethality of human cancer cells in vitro by inhibiting XRT repair process. 2. Small doses of XRT when given more than once daily may prevent tumor repopulation to a greater extent than higher doses given once daily. The study consists of ADR I.V. CI 12mg/m^2/day x5 days and XRT tumor dose 100 rads twice a day at 6 hours intervals x5 days. Courses were repeated at 3-4 weeks intervals. Three children have been treated; 1 Ewing's sarcoma (ES), 1 fibrosarcoma and 1 hemangiopericytoma, all have previously received ADR 480, 60 and 460mg/m^2 respectively. The patient with ES has also received 5400 rads to the primary tumor. All 3 patients achieved partial remission after 2 courses of ADR I.V. CI-HFT-XRT and complete surgical excision of primary tumor was performed in the patient with ES after the 3rd course. Two patients developed progressive disease outside the XRT field 3 and 6 months post-therapy. The 3rd patient's tumor is still under control while receiving the 3rd dose of therapy. This preliminary data suggests that the simultaneous administration of ADR I.V. CI-HFT-XRT can be an effective therapy for recurrent pediatric malignancies and should be tested in a larger number of patients.