895 CLINICAL IMPACT OF NEONATAL THROMBOCYTOPENIA--A PROSPECTIVE ONE YEAR STUDY. Valerie Castle, Maureen Andrew, John Kelton, Cedric Carter, (Spon. by Ronald G. Davidson), McMaster University Medical Centre, Chedoke-McMaster Hospitals, Department of Pediatrics and Medicine, Hamilton, Canada.

Thrombocytopenia is frequently (22%) observed in a neonatal intensive care unit but the relative hemostatic risk imposed by the thrombocytopenia has not been extensively studied. We have conducted a prospective, comparative study of 97 consecutive neonates in the intensive care unit with platelet counts $< 100x10^9$/L and 80 age and disease matched neonates with normal platelet counts ($> 150x10^9$/L). The clinical impact was assessed by: 1. a modified template bleeding time; 2. investigation for the presence of intraventricular hemorrhage (IVH) in infants < 1500 gm and 3. evaluation of each infant for bleeding using a hemorrhage score (0-10). This study demonstrated that thrombocytopenia is not only a laboratory abnormality but has a significant impact on the hemostatic integrity of the neonate. The bleeding time was inversely related to the platelet count and became progressively more prolonged when the platelet count fell below $100x10^9$/L. The frequency of IVH in the thrombocytopenic infants was 82% compared to 50% in the controls ($x^2, p < 0.001$). Clinical hemorrhage occurred in 86% of the thrombocytopenic infants compared to 35% of the controls ($x^2, p < 0.001$) with the hemorrhage score being highest in infants with the most severe thrombocytopenia. Possible etiologic factors such as umbilical catheters, phototherapy, polycythemia, maternal or infant drugs and suspected or proven sepsis were equally distributed between both groups. This study demonstrates that thrombocytopenia in the neonate positively correlates with an increased risk of hemorrhage.

● **896** IMAGING NEUROBLASTOMA IN PATIENTS WITH RADIOLABELED MONOCLONAL ANTIBODY AS A BASIS FOR TARGETING THERAPY Nai-Kong V.Cheung, Sarah E.Strandjord, Peter F.Coccia, Floro Miraldi. Case Western Reserve University, Rainbow Babies and Childrens Hospital and University Hospitals of Cleveland, Departments of Pediatrics and Radiology, Cleveland.

We have shown in previous studies that iodine 131-labeled monoclonal antibody (Mab) 3F8 could image human neuroblastoma (NB) xenografts in mice with excellent tumor to tissue ratios and could ablate such tumors with minimal toxicities. We now report our human imaging studies as the basis for targeting radiotherapy. Patients with NB were injected iv with 1.5 to 5 mCi iodine 131 labeled Mab 3F8. Serial gamma scannings were done. Tumor localization was apparent by 15 hours. Tissue radioactivity (uCi/cc) was calculated based on orthogonal gamma images. There was no focal uptake in the normal brain, liver, spleen or the adrenal gland. Tumor to nontumor ratios were 10-20:1 between 15 to 140 hours after injection. Sites of uptake were confirmed as tumors at surgery in selected patients. Tumor to tissue ratio was 4-14: 1 for blood, 16-58:1 for liver, 5-19:1 for kidney, 10-36:1 for red marrow, and 540-1940:1 for CSF. In all patients sites of iodine uptake were consistent with tumor by conventional radiological studies. Deiodination with stomach excretion was significant. From tissue decay curves, relative radiation to normal organs were 4-12% (to blood 37%) of the tumor dose. Toxicities included pain and shortness of breath, both being reversible. No hematological side effects were noted. The radiolabeled Mab 3F8 might have clinical potentials for the imaging and therapy of human neuroblastomas.

897 A "BILAYER-COUPLE" MECHANISM MEDIATES RBC SHAPE ABNORMALITIES IN PATIENTS WITH CERTAIN CONGENITAL DISORDERS OF GLYCOLYSIS OR LIPID METABOLISM. Robert Chilcote, (Spon. Marc O. Beem), Univ Chicago, Wyler Children's Hosp, Chgo.

Characteristic echinocytic (E) RBC occur in hemolytic anemias caused by deficiency of the glycolytic enzymes TPI, PK, or GPI, while acanthocytosis (A) occurs in Hallervolden-Spatz disease and hypolipoproteinemia, but the basis for these shape abnormalities is unknown. To determine whether the defect was intrinsic or induced by patient's plasma, combinations of RBC and plasma taken from patients and controls were incubated 90' at 37°. Patient RBC were also incubated for 15' at 0°C with chlorpromazine (CPZ), a membrane active amphipath known to reverse E produced in vitro. E and A were quantitated by microscopy. In all 5 disorders patient plasma failed to induce E/A in normal RBC and the E/A of patient cells persisted in normal plasma. However, CPZ reversed both E and A of patient RBC (15-50% 1%). Shape correction was instantaneous at 0°C, suggesting that CPZ acted by diffusion and did not influence cell metabolism. According to the bilayer-couple hypothesis, the results also imply that these disorders alter the effective surface area of the membrane's interior leaflet relative to the exterior and provide a new model for investigation of these apparently diverse disorders.

● **898** REGULATION OF NEUTROPHIL PRODUCTION AT BOTH THE CFUc AND MYELOCYTE LEVELS. RD Christensen and G Rothstein, (Spon. by Michael A. Simmons) U of Utah, SLC UT.

The mechanisms for increasing neutrophil (neut) production in neonates are not clear, but we postulate that regulation exist not only at the CFUc, but also at the myelocyte level. We previously observed regulation at the CFUc level in non-infected neonatal rats, which had very rapid CFUc proliferation (thymidine suicide >2 x adult). However, during infection, in contrast to adults, their CFUc proliferative rate did not increase further. In the present study we devised an assay, requiring only .05 ml blood, for neut myeloperoxidase (MPO), an enzyme synthesized by promyelocytes and halved between daughter cells with each myelocyte division. Thus, MPO/mature neut can be a marker for the number of myelocyte divisions. In premature and term rats, MPO/neut was low ($1.5\pm0.1x10^{-7}$units/neut in premature; $1.5\pm0.7x10^{-7}$ u/neut at term) but increased to $3.0\pm0.4x10^{-7}$ at 3 wks and $5.8\pm0.7x10^{-7}$ at 6 wks, consistent with extra myelocyte divisions in neonates, amplifying their production of mature neut. During the first 24h of a sublethal group B streptococcal infection, MPO/neut increased to $4.0\pm0.6x10^{-7}$u/neut in neonates ($p < 0.001$), and from $3.9\pm0.5x10^{-7}$ to $6.5\pm0.8x10^{-7}$ in 4 wk-olds ($p<0.005$), likely from deleting one myelocyte division, thus shortening the time required to produce mature neut. Therefore, in non-infected growing neonates, neut production appears to be accelerated by increasing the CFUc proliferative rate and amplified by increasing the number of myelocyte divisions. In infected neonates, CFUc proliferation is not further accelerated, but production time is shortened by deleting one myelocyte division.

899 EXTRAGONADAL ENDODERMAL SINUS TUMOR IN EARLY CHILDHOOD: TREATMENT RESPONSE AND LONGTERM EFFECT. Barbara A. Cushing, Arvin I. Philippart, A. Joseph Brough, Lakshmi Das. (Spon. by Jeanne M. Lusher.) Wayne State University School of Medicine, Dept. of Pediatrics, Detroit.

Endodermal sinus tumor is the most common form of germ cell malignancy found in the infantile testis. Histologically identical tumor may originate in extragonadal sites in young children, predominately in sacrococcygeal teratomas or presacral space. Extragonadal endodermal sinus tumors in young children appear to respond to cisplatinum (DDP) combinations, unlike the poor response reported in extragonadal, mainly mediastinal and retroperitoneal, germ cell tumors in the adolescent or adult. Treatment methods and results in six children with endodermal sinus tumor occurring in sacral sites are the subject of this report. All presented to Children's Hospital of Michigan (1975-82) between ages 12-31 months (median 20 mo) with unresectable or disseminated disease. Two of six underwent resection of a benign sacrococcygeal teratoma within the first month of life and returned with metastatic disease to lungs and retroperitoneal node or liver. Three children presented with previously undetected sacral mass, one with bone and lung metastases. Approach to the two without metastatic disease included vincristine-cyclophosphamide-dactinomycin; one survives disease free at nine years. The sixth child, the only male, presented with urinary retention secondary to presacral primary and multiple lung nodules; he is disease free at 32 months following four courses of DDP-velban-bleomycin. The remaining living child has had a 36 mo course of recurring disease responsive to four different DDP combinations.

900 EFFECT OF EXOGENOUS GROWTH HORMONE IN PATIENTS WITH THALASSEMIA MAJOR J DiMartino, E Stoner, PJ Giardina, MW Hilgartner, MI New, Dept Pediatrics, The New York- Hosp-Cornell Med Ctr, New York 10021

Exogenous growth hormone (GH) (0.1 U/kg/IM TIW) was administered to 4 female patients with Thalassemia Major (TM) and severe short stature to determine if their growth rate would improve. At the start of the study, all were < 1%ile in height, had a growth rate < 3 cm/yr, bone age < 12 yrs, nl TSH and T4 levels, nl GH response to L-Dopa/glucagon, and had no previous therapy with hormonal agents. After 6 months of GH treatment, Pt.1 had an increase in growth rate from 3 to 4.8 cm/yr. Pt. 2 also had an increase in growth rate (5.1 cm/yr); however there was a concurrent advancement in puberty. Pts. 3 and 4 had no improvement in growth velocity. However, pt. 3 was found to have a mildly elevated TSH 3 months after GH was started. The data suggests that treatment with exogenous GH may be associated with an improvement in growth rate in some TM patients.

Pt	Age	Bone age (Pre Rx)	Somatomedin generation test (U/ml) (Pre/post 4 d)	Growth rate (cm/yr) (Pre Rx/on Rx)
1	14.2	11.5	1.1/1.6	3.0/4.8
2	16.5	11	0.5/0.72	3.0/5.1
3	15.7	10-11	0.77/1.0	2.4/1.2
4	19.6	11	0.15/0.08	1.0/1.6