872 DECREASED RED CELL DEFORMABILITY (RCD) IN BACTERIAL MENINGITIS. Richard H. Sills (Spon. by J.R. Humbert). State Univ. of NY, Children's Hospital, Department of Pediatrics, Buffalo, NY.

Haemophilus influenzae meningitis has been associated with anemia. Although the mechanism of this anemia has not been investigated, accelerated red cell destruction has been assumed because of the rapid decrease in hemoglobin in the absence of bleeding. To further define this pathophysiology, the RCD of patients with meningitis was studied by measuring the filtration time of washed red cells through polycarbonate filters. Eleven patients with Haemophilus influenzae meningitis, 3 with meningococcal meningitis, 9 with aseptic meningitis and 30 normal children were studied. The filtration time of the Haemophilus influenzae meningitis group (81.2 $\pm$ 96.1 secs) was significantly prolonged ($P < 0.01$) compared to the aseptic group (24.7 $\pm$ 6.4) and a group of normals (24.1 $\pm$ 5.3). The 3 children with meningococcal meningitis had filtration times of 73.5, 18.7 and 34.9 secs. Only 3 of 11 Haemophilus influenzae meningitis subjects fell within the normal range. Nine of 14 patients with bacterial meningitis were anemic versus 1/9 in the aseptic group.

This study demonstrates that RCD is significantly diminished in children with bacterial meningitis. This decreased deformability may result in a diminished red cell survival and account for the postulated hemolytic anemia associated with this illness. The mechanism by which the RCD is altered remains to be elucidated.

873 EFFECTS OF PHOSPHODIESTERASE INHIBITORS (PI) UPON THE DEFORMABILITY OF SICKLE CELLS. Richard H. Sills, Julian L. Ambrus, Clara M. Ambrus, Nefissa Meky, (Spon. by J.R. Humbert) Depts. of Peds. & Med., Children's Hospital of Buffalo & Roswell Park Memorial Institute, Buffalo.

We studied the in vitro effect of 3 PIs upon the deformability of red cells (RCD) from patients with homozygous sickle cell disease (SSD). The subjects were clinically stable and had not been transfused. The RCD was quantitated by measuring the filtration time (FT) of a red cell suspension through polycarbonate filters under aerobic conditions. Venous samples were incubated with one of 3 PIs (RA233 .12 mg/cc, pentoxifylline .18 mg/cc, aminophylline .1 and .02 mg/cc) and alone as a control. FTs were measured after 30 and 60 minutes of incubation. RA233 treated cells from 6 patients exhibited FTs of 190.6$\pm$86.3 secs at 30 min and 190$\pm$109.9 at 60 min versus control values of 274.6$\pm$131.3 and 323.5$\pm$119.5 respectively. These differences are significant ($P < 0.05$ & $P < 0.005$). The improvement at 30 versus 60 min with RA233 was not significantly different. Pentoxifylline and the 2 concentrations of aminophylline were each studied in 6 patients. All samples exhibited improved FTs but this did not attain statistical significance with these small groups. Six normal patients did not exhibit a significant change in FT with RA233.

RA233, a PI, improves the deformability of oxygenated sickle cells in vitro. The mechanism of this alteration is not known. Further in vitro studies of RA233 and the other PIs are indicated to justify clinical trials of these agents in the prevention of the vasoocclusive symptoms of SSD.

874 THYROID DYSFUNCTION AFTER BONE MARROW TRANSPLANTATION (BMT), Charles A. Sklar, Norma K. Ramsay, and BMT Team, University of Minnesota, University of Minnesota Hospitals, Dept. of Pediatrics, Mpls.

Thyroid function studies were followed prospectively in 24 patients (pts), all long-term (>1yr) survivors of BMT. There were 13 males, 11 females. Pts ranged in age from 1.6-22.5 yrs. (mean 12.5) yrs. 13 pts. had aplastic anemia, 8 leukemia, and 3 lymphoma. 21 pts received either 750 R total body (11) or total lymphoid (10) as a single dose plus cyclophosphamide as prep for BMT. The remaining 3 pts received chemotherapy alone. Thyroid function was normal pre-BMT in 11/11. Duration of follow-up ranged from 1-4.5 (mean 2) yrs.

10 of 24 (42%) pts. developed biochemical evidence of thyroid dysfunction, 6-20 (mean 12) mos after BMT; 8 had elevated TSH (>6μU/ml) with normal T_4I (5-10.5), 1 had elevated TSH (30μU/ml) and low T_4I (3.8), and 1 had both a low TSH and T_4I consistent with TSH deficiency. In addition, 2 pts developed transient elevations of T_4I (12.6 and 25.3) within one month of irradiation, unassociated with clinical hyperthyroidism. Females had a higher incidence of thyroid dysfunction compared to males ($p<0.05$). Thyroid function abnormalities did not correlate with pt. age, type of radiation, or previous chemotherapy. Thyroid studies have remained normal in the 3 pts not irradiated. We conclude that single dose radiation therapy given for BMT results in a high incidence of thyroidal damage.

875 PLASMA CYCLIC NUCLEOTIDES IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA (ALL). Josef P. Skala, Paul C.J. Rogers, and Ian A. MacLaren. Department of Paediatrics, University of British Columbia, Vancouver, Canada.

Guanosine 3':5' monophosphate (cGMP) and adenosine 3':5' monophosphate (cAMP) are known to participate in the regulation of cellular proliferation and differentiation, the processes intimately associated with neoplastic transformation. Plasma concentrations of both cGMP and cAMP were therefore examined in 32 patients with ALL at the time of diagnosis, during remission, and (in 4 cases) at relapse, and were compared to values determined on 65 controls matched for age. Blood was collected into EDTA tubes from supine and relatively calm children, plasma was quickly separated, frozen and kept at -60°C until assayed. The control group exhibited a significant decrease in plasma cGMP with increasing age whereas cAMP concentrations remained almost constant from the first through the tenth year. Plasma concentrations of cGMP in ALL patients at diagnosis were significantly higher than control values; the most pronounced difference was observed in the 7 - 10 year-old group which also showed elevated cAMP values. Both nucleotides decreased during the remission period and the recurrence of the disease coincided with another rise in cGMP values. Preliminary data indicate that plasma cGMP in ALL reflects the cGMP content of white cells but the significance of our results will have to emerge from further studies. However, if confirmed on a larger group of patients, the simple and inexpensive cGMP determinations may serve as another diagnostic test to help in early detection of subclinical recurrence of the disease. (Supported by B.C. Health Care Research Fdn.)

876 MULTIPLE ENDOCRINE NEOPLASIA (MEN) TYPE III AND UROLOGIC ABNORMALITIES, Gary Slepowitz, and Joseph Kochen, Cornell Univ. Med. College, North Shore Univ. Hosp., Dept. of Pediatrics, Manhasset, N.Y.

The association of thyroid medullary carcinoma, pheochromocytoma, mucosal neuromas and characteristic physical features has been designated MEN III. A case is documented with previously unreported urologic abnormalities and incidental G6PD deficiency. An 11 year old girl presented with growth retardation, chronic diarrhea, enuresis, recurrent urinary tract infections, neurogenic bladder, hydroureters and hydronephrosis. She had a Marfan-like appearance, thickened eyelids and lips, tongue nodules, prominent corneal nerves, joint laxity and muscle wasting. Cervical adenopathy was present, but no palpable thyroid nodules, abdominal organomegaly or masses. Studies showed a "cold" nodule on thyroid scan, a suprarenal mass by ultrasound, multiple lytic lesions on skeletal survey and an extradural mass on myelogram. There was a markedly increased urinary VMA and plasma epinephrine, norepinephrine, CEA (380 ng/ml, normal <2.5) and calcitonin (154,500 pg/ml, normal 30-135). Biopsy of rib lesion showed infiltration by small round tumor cells filled with numerous membrane delimited secretory granules, consistent with a neural crest origin. Since the neurogenic bladder may reflect a disorder of autonomic innervation, its association with tumors of neuroectodermal origin suggests a common underlying defect of embryonal migratory neuroblastic elements.

877 FETAL RED CELLS (FC) DIFFER IN ELASTICITY, VISCOSITY, AND ADHESION FROM ADULT RED CELLS (AC). Clark M. Smith II, David P. Tukey, William Krivit, and James G. White, University of Minnesota Health Sciences Center, Depts. of Pediatrics and Laboratory Medicine, Mpls., 55455

Blood hyperviscosity occurs in 3-5% of full-term infants, usually accompanies central venous hematocrit (HCT)>65%, but may occur at HCT 60-65%. Small differences in red cell deformability have major influence on blood viscosity at high HCT. We studied the whole cell deformability of washed FC and AC by counting the % cells aspirated more than 10μm into 2μm pore diameter nuclepore filters. FC were more deformable with 88±7% having aspiration length >10μm compared to 19±4% for AC ($p<.01$). More extensible membranes have lower membrane elasticity (μ in 10^{-3} dyne/cm); μ was calculated from small nipple extensions into 0.6μm pore diameter nuclepore filters. FC had lower μ than AC ($\mu FC=4.39$, $\mu AC=8.06$; $p<.05$). Subpopulations of FC separated by density gradient showed invariant μ with increasing MCHC and decreasing cell volume. Work from a collaborating laboratory (Blackshear et al, 1980 Gotenburg Filtration Symposium) has shown increased membrane viscosity (η) of FC ($\eta FC=6x10^{-4}$; $\eta AC=3x10^{-4}$ poise-cm). More FC were adherent to the filter than AC in the special, purged filter chamber (FC 9.0%, AC 0.3%). The altered whole cell deformability and membrane elasticity of FC would ameliorate the flow retardation influences of FC membrane viscosity and adhesion. Evaluation of these rheological properties in newborn hyperviscosity syndrome may determine who would benefit from phlebotomy.