

**930** NUTRITION IN SICKLE CELL ANEMIA (HB SS). Elliott Vichinsky, Mel Heyman, Deborah Hurst, Danny Chiu, Barbara Gaffield, Karen Thompson, Klara Kleman, Bertram Lubin. Children's Hospital Medical Center of Northern California, Oakland; Department of Pediatrics, UCSF.

To evaluate the role of nutrition in Hb SS we performed anthropometric and laboratory measurements on 95 Hb SS patients and determined the effects of caloric supplementation on these parameters and on clinical course. Height and weight were both below the 5th percentile in 17% of patients. Laboratory studies included vitamin C (ng/10<sup>8</sup> cells), vitamin E (mg/dl), zinc (µg/ml), selenium (ng/ml), and lipids (mg/dl).

	Vitamins		Minerals		Lipids		
	C	E	Zinc	Selenium	Cholesterol	HDL	LDL
Patients	18	.79	.60	90	106	31	64
Control	30	1.31	.83	110	186	50	132

Immune status was measured as a reflection of nutritional adequacy. Total T cell (patient/control, 44%/78%), helper T cell (23%/55%), and suppressor T cells (17%/32%) as well as skin test reactivity were depressed. Two patients with marked growth retardation, multiple laboratory abnormalities and frequent sickle cell complications received dietary supplementation with nasal gastric hyperalimentation for 4-10 months. Improvements in growth, weight, skin test reactivity, T cell numbers, and clinical status were noted. We conclude that nutritional assessment and intervention may minimize complications associated with sickle cell disease.

**931** LIPOXYGENASE PRODUCTS OF ARACHIDONIC ACID (AA) METABOLISM INHIBIT PROLIFERATION OF HUMAN NEUROBLASTOMA CELLS IN VITRO. E.J.Werner\*, R.W. Walenga\*, R.L.Dubowy\*, M.J.Stuart, Dept. of Peds. SUNY, Syracuse, New York.

In vivo studies have suggested a role for cyclooxygenase inhibitors in the control of tumor metastases. As cyclooxygenase inhibition may increase the production of lipoxigenase products of AA metabolism we investigated the effect of the lipoxigenase derivatives 12-Hydroxyeicosatetraenoic acid (12-HETE) and 15-Hydroxyeicosatetraenoic acid (15-HETE) on tumor cell proliferation in vitro. To prepare 12-HETE, human platelets were incubated with AA in the presence of indomethacin. 15-HETE was prepared from soybean lipoxigenase. The material was purified by column chromatography and reverse phase HPLC. Identity and purity were confirmed by GC-MS. Neuroblastoma cells in tissue culture (SK-N-SH) were incubated in serum free RPMI-1640 or this media with 12-HETE, 15-HETE or AA. 12-HETE at concentrations at 20 µM, 30 µM and 50 µM induced respectively 16.3 ± 3.8% (ISE), 32.0 ± 4.4% and 63.6 ± 4.2% inhibition of <sup>3</sup>H-thymidine incorporation compared to control (p < .01). 15-HETE at the same concentrations produced inhibitions of 14.5 ± 7.7%, 20.9 ± 2.8% and 46.1 ± 12.1% respectively (p < .01). AA had no effect. At higher concentrations (30 and 50 µM) 12HETE produced a greater effect than 15HETE. When evaluated in the presence of serum, 12-HETE (120 µM) produced a 20.6 ± 2.8% inhibition of the increase in total DNA content over 48 hours, while 15-HETE (120 µM) produced a 16.5 ± 5.3% inhibition. We conclude that 12-HETE, the product of platelet lipoxigenase, and 15-HETE, a product of neutrophil and monocyte lipoxigenase inhibit human neuroblastoma cell growth in vitro and may play a role in modulating tumor proliferation in vivo.

**932** PNEUMATOSIS INTESTINALIS (PI) IN BONE MARROW TRANSPLANT (BMT) PATIENTS. Andrew M. Yeager, Marjorie E. Kanof, Rein Saral, Alan M. Lake, and George W. Santos (Spon. by William H. Zinkham). The Johns Hopkins Univ. School of Medicine, Oncology Center and Dept. of Pediatrics, Baltimore, MD.

Pneumatosis intestinalis (PI) is characterized by accumulations of intramural gas along the gastrointestinal tract. Three patients developed PI after allogeneic BMT. A 6 yr old boy with acute non-lymphocytic leukemia received busulfan (BU) and cyclophosphamide (CY) prior to BMT from his HLA-identical sister. He developed acute graft-versus-host disease (AGVHD) and was on prednisone. On day 63 post BMT he developed melena, and PI was noted on abdominal x-ray (AXR). Blood culture was positive for *Hafnia alveoli* and stool culture grew *Candida krusei* and *Escherichia coli*. An 8 yr old boy with acute lymphocytic leukemia received BMT from his sister after CY and total body irradiation. He was treated for severe AGVHD with prednisone and cyclosporine. Abdominal tenderness and PI were noted 52 days post BMT; stools were positive for *E. coli*, rotavirus and adenovirus. A 4 yr old girl with severe aplastic anemia was treated with androgens, antilymphocyte globulin, and haploidentical parental marrow infusion. Eighteen mos post BMT she had abdominal pain and tenderness; AXR showed colonic PI. Blood and stool cultures were negative. All patients received systemic antibiotics and "nothing by mouth" for 10-14 days. PI resolved within 5-13 days after onset. PI may occur in the profoundly immunocompromised state after BMT; AGVHD and/or viral or bacterial pathogens may be contributory or complicating factors. With conservative therapy, PI has had a good outcome in these patients.

**933** ERYTHROCYTE CREATINE LEVELS (EC) AND THE DIAGNOSIS OF HEMOLYTIC DISEASE IN NEWBORN INFANTS (HDN) - Alvin Zipursky, Elizabeth J. Brown,

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In the diagnosis of HDN the reticulocyte count is insensitive, inaccurate and assesses red cell production only in the few days prior to testing. In adults it has been reported that EC is elevated in young erythrocytes and as an index of mean cell age is a valuable test for the diagnosis of hemolytic disease. Young cord erythrocytes, isolated by density centrifugation, had EC levels greater than older cells. EC (mg/dl ± SD) was 8.7 ± 1.33 in 7 women, 5.7 ± .64 in 6 men, 10.1 ± 2.97 in 12 fullterm newborns and 10.4 ± 2.57 in 26 premature newborns. In ABO-HDN cord blood EC was elevated (28.9 ± 18) in 9 infants in whom spherocyte counts (glutaraldehyde-fixed cells) were abnormally high and who developed jaundice in the first 24 hours of life. EC was also elevated in Rh disease and in other forms of HDN. These data suggest that in HDN, EC is a valuable diagnostic test. In 19 successive infants with idiopathic hyperbilirubinemia requiring phototherapy, EC in cord blood was 3.9-10 mg/dl and quantitative assessment of erythrocyte morphology (Am. J. Ped. Hem./Onc. 4, p.45, 1983) was normal in all cases. Thus using accurate assessment of red cell morphology and mean cell age, no evidence of HDN was found in these cases, suggesting that an occult hemolytic process, evident at birth, is an unlikely contributing cause to the pathogenesis of idiopathic hyperbilirubinemia in newborn infants.

## IMMUNOLOGY

**934** CHEMOTACTIC ACTIVITY IN HUMAN COLOSTRAL MILK - CORRELATION WITH PHAGOCYTTIC CELL CONCENTRATION. M. Aker, C. Audera, R.A. Polin, and S.D. Douglas, U. Pa. Sch. Med., Child. Hosp. Phila., Dept. Pediatrics, Phila., PA.

Colostrum was obtained about 3 hours after breast feeding from 27 healthy mothers, 1-3 days after delivery. The phagocytic cell concentration of colostrum varied considerably amongst different donors. Ten samples were hypercellular (>5x10<sup>6</sup>/ml); 6 were cellular (1-5x10<sup>6</sup>/ml) and 11 were hypocellular (<1x10<sup>6</sup>/ml). The chemotactic activity of colostrum was measured in serial dilutions on day of collection using microchemotaxis chambers (neuroprobe) on mononuclear phagocytes (MNP) from peripheral blood of normal donors. In all assays, FMLP was included as the reference standard. In order to minimize the error introduced by variability in chemotactic responsiveness of different MNP preparations, the results are expressed relative to chemotaxis elicited by optimal concentration of the reference standard (10<sup>-8</sup>M, migration 20-35%). The relative chemotactic potency (RCP) of hypercellular colostrum was highest (142±25%, dil.1:100) and differed significantly from the RCP of cellular or hypocellular samples (p<0.01). Similarly, RCP of cellular colostrum was greater than than of hypocellular samples (102±13 and 38±10% respectively, p<0.01). The overall RCP of colostrum correlated with the total phagocyte concentration (y=64.9+45.6log x; r<sup>2</sup>=0.897), as well as, with the absolute polymorphonuclear and MNP concentrations. Thus, phagocytic cell content of colostrum is proportionate to the potency of its chemotactic activity and the generation of chemotactic activity is likely to provide the immunologic bases for influx of phagocytes into colostrum.

**935** ABNORMAL FMN FUNCTIONS ASSOCIATED WITH A HERITABLE DEFICIENCY OF A HIGH M.W. GLYCOPROTEIN (GP138). D. Anderson, E. Schmalstieg, S. Kuhl, L. Boxer, J. Abramson, M. Tosi, B. Rudloff, B. Hughes, & C. W. Smith. Baylor College of Medicine, Houston, Texas, et al.

A 4 y/o female with delayed umbilical cord severance, granulocytosis, periodontitis & recurrent soft tissue infections demonstrated severely diminished leukocyte mobilization (Rebuck window). SDS-PAGE of patient PMN homogenates revealed deficient (<5% normal) GP138, a major surface glycoprotein complex of normal PMNs. As shown with a NaB<sup>3</sup>H<sub>4</sub> labelling technique, GP138 was undetectable on the surface of patient PMNs & was diminished (20% normal) on maternal PMNs. Adhesion-dependent functions of patient PMNs including directed migration, attachment & spreading (plastic or glass), aggregation (C5a, fMLP or PMA), orientation in chemotactic gradients, antibody-dependent cellular cytotoxicity (due to diminished target cell binding), & phagocytic ingestion of particles selectively opsonized by C3b (O1-Red-0, <sup>14</sup>C Staph. & zymosan) were profoundly diminished (p < .001 in each assay). Fc receptor "facilitated" phagocytosis & spreading & EA rosette formation by patient PMNs were normal. Adhesion independent patient PMN functions including specific binding of f-Met-Leu-<sup>3</sup>H-Phe & fMLP, C5a &/or PMA mediated shape change, O<sub>2</sub> generation, degranulation (MPO & lactoferrin), microtubule assembly (tubulin IF) & alterations of membrane fluidity (ESR) or surface charge (cell electrophoresis) were normal. Thus, GP138 represents a critical surface glycoprotein(s) which is functionally related to the C3b receptor & is required for adhesion-dependent functions facilitating the inflammatory response in host defense.