HEMATOLOGY AND ONCOLOGY

777 MANNOSIDOSIS: CATALYTICALLY ACTIVE EXTRACELLULAR ACIDIC α-MANNOSIDASE (α-man) DUE TO INCOMPLETE PROCESSING. Yoav Ben-Yoseph, Lisa C. Hahn, C.L. DeFranco and Henry L. Nadler. Northwestern U. Medical School, Children's Memorial Hospital, Department of Pediatrics, Chicago, Illinois.

Normal levels of acidic α-man activity have been found in the culture medium of a number of mannosidosis fibroblast lines. This observation is different from most other lysosomal storage diseases in which enzyme deficiency is evident both intra- and extracellularly. Studies were undertaken in order to determine if the extracellular α-man is in fact a product of the cells. Cells cultivated in medium containing fetal calf serum from which acidic α-man was removed by concanavalin A adsorption excreted normal amounts of α-man. The extracellular enzyme exhibited normal thermostability and normal kinetics. Incubation of mannosidosis extracellular enzyme with either normal or patient cell lysate resulted in a partial loss of acidic α-man activity whereas an additive value was observed when the normal extracellular enzyme was incubated with cell lysate of either type. Addition of medium from normal cell cultures to mucolipidosis II fibroblasts previously cultured in presence of [^{3}H] mannose resulted in reduction of the intracellular storage of mannose-containing macromolecules. In contrast, no correction could be demonstrated with medium from mannosidosis cell cultures. These findings suggest that the mutation in mannosidosis results in altered catalytic properties and thermostability only after complete intracellular processing. The final processing presumably takes place within the lysosomes and the extracellular enzyme which has escaped this step therefore does not express the defect.

778 9P TRISOMY CONFIRMED BY GENE DOSAGE EFFECT: REPORT OF 2 PATIENTS. Touran M. Zadeh, Steve J. Funderburk, Robert Carrel, and Kenneth W. Dumars. Division of Genetics, University of California, Irvine, California, and Division of Medical Genetics, University of California, Los Angeles, California.

Clinical features in patients with 9p duplication have been well delineated (de Grouchy 1977). This report is prompted by two patients seen in the Genetics Clinic at University of California Irvine Medical Center and University of California Los Angeles. Upon examination each patient demonstrated the following characteristics: brachycephaly, bulbous nose, worried facial expression, small deep-set eyes, short upper lip, down-turned mouth, large external ears, and varying degrees of mental retardation. The chromosomal karyotype in each patient revealed partial 9p duplication, one as a result of tandem duplication of 9p bands (p13→p24) and the second patient with an extra number 9 with deletion of the long arm distal to q13. Further study revealed both patients to have elevated galactose-1-phosphate-uridyl-transferase (GALT) levels.

These two patients demonstrate two significant observations: 1) the presence of minor dysmorphic features and varying mental retardation occurring with duplication of all or a segment of 9p; 2) the elevated levels of GALT certainly aided the interpretation of unusual chromosomal abnormalities.

779 TREATMENT OF FIBRODYSPLASIA OSSIFICANS PROGRESSIVA WITH THE SYNTHETIC RETINOID, Ro 10-9359 Michael A. Zasloff, (Spon. by J. Schulman), GBB:NIAMDD Bethesda, Maryland 20205

Fibrodysplasia ossificans progressiva (FOP) is a rare heritable disorder characterized by the progressive accumulation of heterotopic bone arising in the connective tissues of skeletal muscle, ligaments, and tendons. Although the mechanism underlying the formation of heterotopic bone in FOP is at present undefined, the formation of cartilage and bone in soft tissue is preceded by the appearance of proliferating fibroblastic-like cells, presumed to represent either chondroblast or osteoblast precursors. Since retinoic acid and several synthetic analogs have been shown to exert potent inhibition over the differentiation of cartilage precursor cells both in tissue culture and in the mammalian fetus, these drugs would appear to represent a rational therapeutic modality in FOP. We wish to report our initial findings of the effect of Ro 10-9359, a synthetic retinoic acid derivative, on heterotopic bone formation in two children with FOP treated over a period of 6 months. Although these patients have received Ro 10-9359 for too short a period to permit a conclusive assessment of efficacy the initial clinical response appears sufficiently favorable to warrant continued investigation in these and other patients.

780 MALNUTRITION IN CHILDREN HAVING SOLID TUMORS. Nancy Adkins, Samuel K. Morgan, Milton Westphal, Owen C. Grush. Medical University of S.C. Department of Pediatrics, Charleston, S.C.

Evidence of growth failure at diagnosis and of acute or chronic malnutrition during management was sought in 43 children who had solid tumors, 14 with Wilms' tumor, 17 with sarcoma and 12 with neuroblastoma. Growth failure at diagnosis was identified from height and weight percentiles, acute malnutrition from weight/height ratio, and chronic malnutrition was identified from the combination of height and weight/height percentiles. Each parameter was considered abnormal when it fell below the 10th percentile. Results were analyzed by the chi-square technique with $p \leq 0.05$ accepted as significant. Children with neuroblastoma had a higher incidence of growth failure at diagnosis, were more chronically malnourished and more often suffered acute malnutrition during therapy than children with Wilm's tumor or sarcoma. No statistically significant difference was found between patients with Wilms' tumor or sarcoma. Significant malnutrition as defined in this study was seen in all three groups of patients but was most marked in neuroblastoma. Thus, patients with neuroblastoma, particularly, should receive early nutritional assessment.

781 CHRONIC TRANSFUSION THERAPY IN SICKLE CELL ANEMIA (SSA) USING DONORS MATCHED FOR MINOR RBC ANTIGENS. D.R. Ambruso, J.H. Githens, R. Alcorn, W.M. Vaughn, T. Hays, S.F. Wallner, Univ. of Colo. Health Sciences Ctr., and the Colo. Sickle Cell Treatment and Res. Ctr., Denver, Colo.

Nine patients with SSA (ages 8-32) with stroke, corpulmonale, severe vaso-occlusive crises, and serious anemia have been transfused with leukocyte-poor red blood cells every 3-4 weeks for 6-to-30 months to keep the Hgb >10.5 gm %. Because the incidence of alloimmunization in previously transfused patients with SSA was high (24% in our population), black donors were matched closely with recipients for 17 minor blood group antigens, and a limited number of donors gave regularly to each patient. Before treatment, hematologic values included Hgb of 6.1-10.3 gm %, reticulocytes 6-34%. On chronic transfusion, the mean Hgb ranged from 10.0-14.2 gm % and reticulocytes from 0.7-11.5. All but one patient maintained a Hgb S of 5%-30%. These 9 patients had previously been intermittently transfused with 342 units of blood and had developed 10 antibodies. On the current program, 404 units of closely matched blood have been given with no new alloantibodies detected and no evidence of serum hepatitis. Subcutaneous deferoxamine has been instituted in 5 for iron overload. Clinical complications and symptoms were prevented in 8. Hospitalizations, clinic visits, and school absences were significantly decreased. Marked suppression of Hgb S was achieved in 8 of 9. The use of closely matched black donors appeared to greatly reduce the risk of isoimmunization to minor RBC antigens.

782 POOR CLINICAL STATUS IMPAIRS THE POSTNATAL RISE OF THE CONTACT FACTORS IN PREMATURE INFANTS. M. Andrew, M. Bhogal, M. Karpatkin, NYU Med. Ctr., Dept. of Pediatrics, NYC.

The postnatal development of the contact factors was studied with regard to gestational age (G.A.), postnatal age (P.A.), clinical status and protein synthesis. Sixty-four preterms (28-36 wks) were classified as healthy (IV fluids, antibiotics only) or sick (all other support). Infants with D.I.C. were excluded.

	Healthy		Sick		Term Cord
Day	1	7	1	7	
%X1	* 30±3(23)	48±7(19)	16±1(21)	30±4(10)	66±6(6)
%X11	29±4(23)	37±7(19)	16±2(21)	12±2(9)	64±5(6)
%PK	33±2(21)	52±14(8)	29±9(10)	32±16(5)	46±5(6)

* Mean ± S.E. (number of infants studied)

On day 1 all factors were low in all infants. They were higher in term cords than in healthy prematures ($p<0.05$): X1 and X11 were higher in healthy than sick prematures ($p<0.01$). By day 7 all factors in healthy prematures had risen (X1: $p<0.01$ PK: $p<0.001$). In sick infants X11 and PK did not rise and all factors were lower than in healthy infants ($p<0.05$). In sick infants who recovered, factors rose to the same levels as in healthy infants. The data do not reflect generally decreased protein synthesis as fibrinogen and AHF were the same in both groups. Factor X11 (day 1) by Laurell technique was greater than biologic activity. (N=12,25%± 3 vs 16%±3 $p<0.05$). We conclude that biologic activities of factors X1,X11&PK are modified by G.A.,P.A. and health status. This may in part be due to synthesis of factors with low biologic activity.