

625

TRANSIENT LACTASE DEFICIENCY IN IRON DEFICIENCY ANEMIA. Lanzkowsky, Philip; Karayalcin, Gungor; Kazi, Abdul and Miller, Fredrick, SUNY at Stony Brook

N.Y., Health Sciences Ctr. and Long Island Jewish-Hillside Medical Ctr., Departments of Peds & Pathology, New Hyde Park, NY. Histochemical studies of intestinal biopsies in 8 patients with severe iron deficiency anemia revealed that 7 had absent lactase and 1 absent sucrase, whereas maltase was normal in all biopsies. The lactose absorption test was abnormal in 3 of 4 patients in which this test was done. This observation led us to study intestinal disaccharidase activity in iron deficient rats in the post-weaning period. Twenty-two Sprague-Dawley rats were divided into two groups. Group I was fed an iron deficient diet from weaning (21 days) to 56 days and thereafter was given intramuscular iron. Group II was fed a control iron sufficient diet. At 21 days of age, 3 rats from each group were sacrificed and showed no significant difference in their hematologic values and in the disaccharidase activity. At 56 days, 4 rats of each group were sacrificed and Group I had a significantly lower hemoglobin level and lactase activity (7.0 ± 1.2 gm/dl and 0.0003 ± 0.0004 IU/mg protein) compared to Group II animals (13.8 ± 0.6 gm/dl and 0.135 ± 0.042 IU/mg protein, respectively). There was no significant difference in intestinal sucrase and maltase in the two groups. At 63 days, 4 rats in each group were sacrificed and no significant differences were observed in these parameters. This reveals that in some iron deficient children and in rats made iron deficient from 21 to 56 days of age lactase deficiency develops which is reversible by iron therapy.

628

THE EFFECT OF CYTOMEGALOVIRUS ON IN VITRO GRANULOPOIESIS, Victor K. Lui, Abdelsalam H. Ragab, John A. Stewart, Harry Findley and M. Susan Kennedy, Emory University School of Medicine, Department of Pediatrics and Division of Virology, Center for Disease Control, Atlanta.

Viral infections are known to cause neutropenia. Our studies were performed to investigate how cytomegalovirus (CMV) produces granulocytopenia. The double layer agar technique was used in all the studies. Bone marrow cells from children with acute leukemia were infected with varying concentrations of CMV and then plated on normal underlayers in agar. A dose related suppression was observed of the colony forming cells (CFC). The myeloid cells in the colonies showed vacuolations and toxic changes. Normal peripheral blood cells were also infected with CMV and underlayers were prepared. A dose related suppression was also observed of the colony stimulating activity (CSA) producing cells. When the same cultures were repeated with CMV inactivated by U-V light, the CFC suppression was substantially less. It may be concluded that CMV induces granulocytopenia by suppression of CFC and CSA-producing cells.

626

THE MEASUREMENT OF PLATELET-ASSOCIATED IMMUNOGLOBULIN G (PAIgG) IN EVALUATING CHILDHOOD IDIOPATHIC THROMBOCYTOPENIC PURPURA (ITP). A.L. Lightsey, H.M. Koenig, R. McMillan, J.R. Stone. Naval Regional Medical Center, and Scripps Clinic, San Diego. (Sponsored by J.D. Connor).

ITP in children is an acquired hemorrhagic disorder due to excessive destruction of circulating platelets. Most children have acute self-limited illness, however, 10-20% develop a chronic disease. A method previously described (Blood 50:137, 1977) was used to measure PAIgG in our childhood ITP cases. Serial PAIgG values were obtained during the clinical course in some cases. Platelets from controls and ITP subjects were resuspended in 0.05 M citrate buffer and gel filtered through a sepharose 2B column. A known quantity of washed platelets was assayed for PAIgG using the Fab anti-Fab immunoassay. Results were expressed as nanograms IgG per 10^9 platelets (ngIgG/ 10^9 plts). Mean PAIgG value in 7 acute ITP children was $12,552 \pm 8874$ ngIgG/ 10^9 plts; 13 chronic ITP children had PAIgG value of 3956 ± 1090 . Both values were significantly greater than age-matched normals and thrombocytopenic controls of 1446 ± 580 ($p < .001$). The chronic ITP values were significantly lower than acute ITP ($p < .003$). Elevated values in acute ITP became normal with clinical recovery. Three children with chronic ITP post splenectomy had values return to normal. One child with chronic ITP refractory to splenectomy responded to cyclophosphamide with a fall in PAIgG values. We conclude the following: 1) the measurement of PAIgG is useful in the diagnosis and follow-up of childhood ITP cases, and 2) PAIgG values may assist in differentiating acute and chronic disease in children.

629

SEVERE FACTOR VIII AND FACTOR IX DEFICIENCY IN FEMALES

Jeanne M. Lusher and Campbell W. McMillan, for the Cooperative Study Group for Spontaneously Occurring Inhibitors Developing in Hemophiliacs.

A survey of eleven hemophilia centers participating in the NHLBI-sponsored "cooperative study of Factor VIII inhibitors developing in hemophiliacs", produced data concerning 27 females with extremely low levels of factor VIII or IX. Ten of the 27 have hemophilia A, 5 hemophilia B, and 12 have severe von Willebrand's disease (vWD). The 15 females who have severe F. VIII or F. IX deficiency as an isolated defect exemplify several of the possible genetic explanations for the occurrence of hemophilia in females (dominant inheritance, mosaic Turner's syndrome, abnormality involving X-chromosome, and extreme Lyonization). All 15 bruise excessively and several have had recurrent hemarthroses. Two of these girls, ages 5 and 10 years, have evidence of chronic hemophilic arthropathy and one has twice undergone synovectomy. All twelve females with severe vWD have mucous membrane bleeding. In addition, 5 of the 12 have recurrent hemarthroses and 3 have evidence of chronic joint disease. However, the major problem in the post pubertal females with vWD has been extreme menorrhagia. While one underwent hysterectomy because of this problem the others have been managed with anovulatory drugs or plasma infusions and EACA. Despite menorrhagia, 4 pregnancies and deliveries have been uneventful in two of these women. No unusual bleeding occurred at the time of childbirth; however, when menses began again bleeding was again extreme. This interesting phenomenon may reflect increased levels of F. VIII activity, antigen and ristocetin cofactor activity during pregnancy.

627

A NEW SYNDROME OF REFRACTORY SIDEROBLASTIC ANEMIA WITH VACUOLIZATION OF MARROW PRECURSORS, ASSOCIATED WITH EXOCRINE PANCREATIC INSUFFICIENCY. Jeffrey S. Lobel, Samuel A. Kocoshis, Nancy L. Krejmas, Joan Windmiller, Ahti T. Lammi, and Howard A. Pearson, Yale U Sch Med, Dept Ped, New Haven, and Royal Alexandra Hosp for Children, Sydney, Australia.

Four children were studied with a severe, transfusion dependent, macrocytic anemia with onset in infancy, characterized by striking cytoplasmic vacuolization of erythroid and myeloid precursors. Marrow aspirates were normocellular to slightly hypercellular with a marked increase in iron; 3 had ringed sideroblasts. Neutropenia and thrombocytopenia developed shortly after the anemia in each. Electron microscopy suggested the vacuolization represented degenerative change in dying cells. In vitro cell culture showed a decrease in CFU-C and CFU-E, with abnormal colony morphology. Therapy with multiple hematinics was without effect. There was no evidence of nutritional deficiency, toxin or drug ingestion, or of a primary disease previously associated with similar hematologic changes. All children had lab evidence of exocrine pancreatic dysfunction, while only 1 was symptomatic. In 2 children pancytopenia began spontaneous resolution by 2 years of age. The other 2 children died at 2 years of age, having severe pancreatic fibrosis and extreme splenic hypoplasia at autopsy. This differs from the Bodian-Schwachman syndrome in the predominance of anemia, precursor vacuolization, sideroblastic changes, and the degree of pancreatic fibrosis. We postulate an undefined congenital metabolic abnormality affecting a pathway common to at least hematopoietic stem cells and the exocrine pancreas.

630

UNSTICKLING OF "IRREVERSIBLY" SICKLED GHOSTS BY CONDITIONS WHICH INTERFERE WITH SPECTRIN-ACTIN POLYMERIZATION. Samuel E. Lux and Kathryn M. John. Harvard Med. School, Children's Hosp. Med. Center, Dept. of Medicine, Boston.

Red cell (RBC) membrane shape depends, in part, on the RBC membrane skeleton; a protein meshwork of spectrin and actin which laminates the inner membrane surface. We have shown (JCI 58:955, 1976) that irreversibly sickled cells (ISCs) form ISC shaped ghosts and skeletons, which suggests the ISC shape is caused by an acquired skeletal defect. In this study we sought conditions that would alter or reverse this abnormal shape. Ghosts of ISC-rich RBCs were loaded with various agents, incubated at 37°C for 35 min and examined by phase microscopy. In isotonic media ISC ghosts retained an ISC shape. Addition of ATP, ADP, Mg^{++} , Ca^{++} , EDTA (all 1mM), DTT (5mM) and various combinations of these agents did not alter this shape. However ISC shaped ghosts became round and indistinguishable from normal in hypertonic NaCl (>400mM), hypotonic NaCl (10-50mM) or isotonic NaCl containing small amounts of Zn^{++} (0.1-0.5mM). ISC shape reversal was time and temperature dependent, and did not correlate with elution or proteolysis of any protein detectable on SDS gels, but did correlate with the formation, in vitro, of a high molecular weight complex of spectrin and actin. Conditions which promoted ISC ghost reversal inhibited formation of this complex. These observations indicate that the ISC shape is not maintained by covalent bonds and suggest that ISCs may be stabilized by abnormal interactions between the spectrin and/or actin components of the membrane skeleton and that disruption of these bonds may allow the skeleton to resume a normal shape.