

DISTINGUISHING SICKLE TRAIT FROM SICKLE- β -THALASSEMIA IN THE ABORTED FETUS, Haig H. Kazazian, Jr. and Andrea P. Woodhead, Johns Hopkins Univ., Dept. of Ped., Baltimore.

Continuing studies of hemoglobin synthesis by reticulocytes of abortuses have provided further information necessary for prenatal diagnosis of sickle cell anemia and β -thalassemia.

Fetuses		Fetal Synthesis of Hb A and Hb S*			
No.	Size	%A (range)	%S (range)	A/S	Diagnosis
13	13-20 cm	9.3 (6.5-13.0)	--	--	AA
5	13-17 cm	4.6 (4.0-5.3)	1.8 (1.4-2.3)	2.5 (1.7-2.9)	AS
1	20 cm	1.9	3.0	0.6	Sickle- Thal

*The remainder of Hb synthesized was Hb F.

These data indicate that sickle trait and sickle- β -thalassemia can be distinguished in the fetus. Moreover, since the AS fetus with one β^A gene makes 50% as much Hb A as the normal fetus with two β^A genes, the percent of Hb A synthesis in fetuses with β -thalassemia trait who have one normal β^A gene should be similar to that observed in the AS fetus (4.6) and, therefore, different from that of the normal fetus (9.3). Thus, in all probability β -thalassemia trait can be distinguished from normal during fetal life.

ACUTE LYMPHOBLASTIC LEUKEMIAS AND LYMPHOMAS OF CHILDHOOD WITH T CELL ORIGIN: CLINICAL FEATURES AND PROGNOSIS. John H. Kersey, Kazimiera J. Gajl-Peczalska, John R. Luckasen, and Mark E. Nesbit. Dept. of Lab. Med. & Pathology, Dept. of Ped., Univ. of Minn., Minneapolis 55455.

Lymphoblasts from peripheral blood, bone marrow, or tumors of children with acute lymphoblastic leukemia (ALL) and lymphoma were studied using surface markers of thymus-dependent (T) and thymus-independent (B) lymphocytes. Ten of 15 children with ALL had significant numbers of lymphoblasts with markers of T lymphocytes, i.e., receptors for sheep erythrocytes and/or Human T Lymphocyte Antigen (HTLA). Lymphoblasts carried HTLA more frequently than sheep erythrocyte receptors, suggesting that childhood lymphoblastic leukemias represent T cells in varying stages of differentiation. Lymphoblasts from one of the ten also carried a B surface marker, i.e., receptors for a modified complement component. None of the patients had lymphoblasts with B cell markers alone (i.e., surface immunoglobulin or receptors for substituted complement components). A lymphoma with apparent subcutaneous origin and subsequent peripheralization was also studied and found to involve T cells. Thymic enlargement was seen in two cases in which ALL and lymphomas involved T cells and in no cases not involving T cells. Patients with ALL involving T cells generally had higher initial peripheral leukocyte counts and a shorter initial remission after therapy than did those where ALL did not involve T cells.

IMMUNOGLOBULINS IN ACUTE LEUKEMIA IN CHILDREN. A. Samy Khalifa, Hiroichi Take, Jan Cejka, W. W. Zuelzer.* Wayne State Univ. Sch. of Med., Child Res. Ctr., Children's Hosp. of Mich., Dept. of Ped., Detroit.

Levels of immunoglobulins G, A and M were studied in 120 cases of acute leukemia between 7 months and 16 years of age. Eighty-three cases had acute stem cell leukemia (ALL) and 37 had acute myelogenous, monocytic or atypical leukemia. (Estimations during radial immunodiffusion were done at diagnosis, after induction of remission and after 6 weeks of maintenance therapy.)

In ALL the initial levels of all 3 immunoglobulins at diagnosis and before starting therapy, tended to be low in spite of the prevalence of infection. Further decreases occurred after induction, but thereafter the levels increased to reach pre-therapy levels despite maintenance therapy. Levels of IgG below the 350-380 mg% had a bad prognostic significance. In patients receiving periodic central nervous system (CNS) irradiation, the IgA levels were significantly lower than in patients not so treated, but the incidence of intercurrent infections was not significantly altered.

In the group of myelogenous or atypical leukemia, high or normal initial levels of immunoglobulins were found in all but two at diagnosis. The trend during induction and maintenance followed the same pattern as in ALL.

HISTAMINE AND CORTISOL LEVELS IN SOME HEMATOLOGICAL DISORDERS. A. Samy Khalifa, W. W. Zuelzer,* Jeanne Lusher, Abner Robinson, John Singley. Wayne State Univ. Sch. of Med., Child Res. Ctr., Children's Hosp. of Mich., Dept. of Ped., Detroit.

Whole blood (WB) and plasma (Pl) histamine and Pl cortisol were determined in 20 cases of acute leukemia at diagnosis, after induction therapy and during maintenance. Twelve cases of I.T.P., 7 cases of Henoch-Schönlein purpura and 8 cases of aplastic anemia were also studied and results compared to 50 normal controls.

-A significant reduction of WB and Pl histamine was found at diagnosis in acute leukemia and aplastic anemia. The depletion level, particularly in WB, was more marked in aplastic anemia cases. After onset of remission in acute leukemia, the histamine levels of WB and Pl became abnormally high; at maintenance Pl histamine returned to normal levels, while WB histamine remained high.

-In I.T.P. no significant change in histamine levels was found.

-In Henoch-Schönlein purpura the histamine levels were significantly elevated.

-The Pl cortisol levels were significantly higher than normal in acute leukemia cases, decreased but still elevated in remission and during maintenance. They were significantly higher than normal in I.T.P., Henoch-Schönlein purpura and aplastic anemia.

COAGULATION STUDIES ON PATIENTS WITH SICKLE CELL DISEASES Charles T. Kisker, Helen I. Glueck, Marilyn H. Gaston, Judy A. Bean; University of Iowa College of Medicine, Dept. of Pediatrics & Preventive Medicine; University of Cincinnati College of Medicine, Dept. of Pediatrics & Internal Medicine

Repeated measurements of coagulation factor activities were done on blood from 16 patients with Sickle Cell Disease over a one year period. Sixty-two coagulation profiles were available for analysis during well periods and 12 profiles on 6 patients were obtained during painful crisis. The profiles included measurements of the prothrombin time, partial thromboplastin time, thrombin time, platelet count, quantitation of F₂ factors I, II, V, VII, VIII, IX, X, XI, XII, measurement of fibrin split products, fibrin monomer, and platelet aggregation with collagen ADP and epinephrine. Factor II was significantly lower than normal, platelet counts were significantly increased, and platelet aggregation with collagen epinephrine and ADP were impaired in approximately one-third of patients in the absence of known ingestion of platelet active drugs. Fibrin monomer as measured by radioactive amine incorporation (JCI 50:2235, 1971) was increased once in each of 4 patients but there were no increased levels of fibrin split products in the serum and no significant differences in results during well and painful crisis periods. Therefore, no evidence of chronic intravascular coagulation was found. The decreased concentration of prothrombin may be a result of liver impairment. The increased platelets and abnormal aggregation are unexplained.

SELECTIVE MICROVASCULAR TRAPPING OF SICKLED CELLS. Joseph Kochem*, Silvio Baez*, Eva Radel*, Albert Einstein Col. of Med., Montefiore Hosp. & Med.Ctr., Depts. Pediatrics, Anesthesiology, Bronx, New York. (Introduced by Laurence Finberg)

A decrease in sickled cells is seen during painful crisis in some patients with sickle cell anemia. This may be due to a selective trapping of sickled cells at the sites of vaso-occlusion. To explore this possibility further, an animal model was utilized. Rats with jugular vein catheters were transfused with sickle blood (SB) saturated with carbon monoxide (CO) to yield an in vivo CO saturation of 20 to 25%. The rats were exposed to 100% O₂ to eliminate the CO, and then to 7% O₂. The mean survival of SB rats in 7% O₂ (39±21 min. [20]) was significantly shorter than that of rats transfused with normal human blood (128±55 min. [20]). Survival of SB rats subjected to hypoxia without prior exposure to 100% O₂ was 81±32 min. [16]. This improved survival (p<.001) was presumably due to inhibition of sickling due to CO retention. Examination of post mortem tissues showed localized obstruction of microvessels by dense aggregates of sickled cells. The relatively low proportion of sickled cells in larger vessels was consistent with the small number of sickle cells in post mortem blood specimens. These studies indicate that selective local trapping of circulating sickled cells occurs in the rat model. In man, unlike the rat, this is followed by stasis and further sickling, making it impossible to distinguish between the originally trapped sickled cells and cells that subsequently sickled. These findings suggest that trapping of circulating sickled cells may initiate the vaso-occlusive crisis. (Supported by USPHS Grant HL-14808)