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ADRIAMYCIN AS A MAINTENANCE AGENT IN ACUTE LYMPHOBLASTIC LEUKEMIA. Eva V. Hvizdala, Diane M. Komp, Abdel H. Ragab, William M. Crist. Pediatric Division, Southwest Oncology Group, Kansas City, Kansas, 66103.

Adriamycin (ADM) in a low weekly dose (10mg/M^2) was used as a single agent for maintenance of remission (RMS) in 24 previously treated children with acute lymphoblastic leukemia (ALL). The dose was escalated by 2mg/M^2 weekly until WBC count remained between 3,000-3,500/mm^3. The therapy was discontinued when cummulative dose of ADM reached 500mg/M^2, or changes compatible with ADM toxicity were demonstrated on echocardiogram. Results of therapy are shown in table:

Stage of Disease	No. of Patients	Duration of RMS (Weeks) Median	Range	No. of Patients in Cont'd. RMS
2nd RMS	16	25.06	7 - 64+	6
3rd RMS	8	15	3 - 52	0

In 2 patients ADM was discontinued when cummulative dose of 500 mg/M^2 was reached and they have remained in continuous RMS for 64+ and 152+ weeks respectively. The toxicity was minimal: myelosuppression 8/24; changes on echocardiogram 2/24.

Although no strictly comparable historical groups are available, 8 weeks has been an average median duration of RMS in previously reported studies of unmaintained early RMS or later RMS, maintained by single agent. Our results demonstrate that weekly ADM can be effective in maintaining RMS in children with ALL.

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THE FATE OF CHILDREN WITH ACUTE LYMPHOCYTIC LEUKEMIA (ALL) WHO DEVELOP CENTRAL NERVOUS SYSTEM (CNS) LEUKEMIA DURING THEIR INITIAL HEMATOLOGIC REMISSION. B. Jones and O. Glidewell for Cancer and Leukemia Group B. W.Va. Univ., Morgantown, W.Va. 26506

From 1971 to 1974 children with previously untreated ALL were entered on protocol 7111. Ninety-six of the 646 evaluable patients developed CNS leukemia: 6 during their initial therapy, 18 prior to receiving "prophylactic" treatment to the CNS and 72 subsequent to such therapy but before (64) or simultaneously with (8) a bone marrow relapse.

Twenty-two (23%) of these patients are still in their initial marrow remission for a median duration of 53 months (24-73 months). Only 4 of these 22 had initial white counts over 30,000 and none of them were under 2 years of age at the time of diagnosis. Of the 74 who have had marrow relapses concomitant with or following a CNS relapses 27 had initial white counts over 30,000 and 11 of them were under 2 years of age at diagnosis.

The survival subsequent to the first relapse when the first relapse occurs in the CNS was superior (median 15.5 months) to that seen with initial marrow relapse (7.3 months) or simultaneous marrow and CNS relapse (4.2 months).

While it is certainly preferable that children with ALL do not relapse, these data suggests that our present ability effectively to treat overt CNS leukemia exceeds our ability to maintain long second hematologic remissions.

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HIGH HOMOGLOBIN A_2 LEVELS IN HOMOZYGOUS SICKLE CELL ANEMIA. Peri Kamalakar, James R. Humbert, Philip P. Dembure, Michael D. Garrick, and Raymond A.R. Hadley, State University of New York at Buffalo, The Children's Hospital of Buffalo, Department of Pediatrics, and Department of Biochemistry, Buffalo.

Elevated hemoglobin (Hb) A_2 levels are seen in heterozygous β thalassemia and rarely in pernicious anemia, Hb Zurich, and Hb Tacoma but have not been reported in homozygous sickle cell anemia (HSCA) in the English literature. We measured Hb A_2 by cellulose acetate Hb electrophoresis and densitometry in 34 children with HSCA. Nine of them (26%) displayed Hb A_2 levels of 3.2 to 4.7% (normal values for our laboratory: 0.7 - 3.0%). Their Hb values (7.4 to 9.2 g/dl) and reticulocyte counts (468 to 700 x 10^9/l) did not differ from those of the other 25 patients. Eight of these nine children showed normal to high MCVs ranging from 77 to 100 fl; one had an MCV of 63 fl. Globin chain separation by carboxymethylcellulose chromatography following the method of Cleggs and Weatherall was performed in five of the nine high HB A_2 children including the one with the low MCV, and all showed a normal α/β chain ratio ranging from 0.91 to 1.05. The fetal Hb in these five subjects ranged from 1.2 to 6.6% and was not different from the values of the other 29 HSCA patients. An elevated Hb A_2 level may be found in a significant proportion of HSCA patients. In addition to careful analysis of the MCV, globin chain synthesis studies may be necessary to differentiate these patients from subjects with sickle-β thalassemia.

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ZINC DEFICIENCY IN CHILDREN WITH SICKLE CELL DISEASE (SCD). Karayalcin, Gungor and Lanzkowsky, Philip, SUNY at Stony Brook, Health Sciences Ctr and Long Island Jewish-Hillside Medical Ctr., Department of Pediatrics, New Hyde Park, New York.

Zinc deficiency in adults with SCD has been previously reported (Prasad, A.S., et al: JAMA 235:2396, 1976). The present study was carried out to investigate zinc status in children with SCD. Forty-seven children with SCD and matched controls aged 1 to 19 years were studied for hair, red blood cells (RBC), plasma and urine zinc content. The results were analyzed in two age groups; one consisting of 34 patients and their matched controls, aged 1 to 13 years and the other 12 patients and their matched controls aged 14 to 19 years. Results are shown in the Table:

Age	1-13 years			14-19 years		
	SCD	Control	p Value	SCD	Control	p Value
Hair ug/ml	106.7	132.1	< 0.01	105.4	133.2	< 0.01
Plasma ug/ml	115.4	132.3	< 0.01	113.3	137.5	< 0.005
RBC ug/gm Hb	43.9	40.0	N.S.	41.9	42.2	N.S.
Urine ug/gm creatinine	531.9	565.3	N.S.	654.1	473.2	< 0.02

In both age groups, hair and plasma zinc levels are significantly lower in SCD compared to controls. Urine zinc was higher in SCD compared to controls in the older age group. These results indicate that zinc deficiency occurs in children with SCD. The hyperzincuria in the older group of children with SCD may be due to defective tubular reabsorption of zinc and be another manifestation of the SCD nephropathy, the severity of which increases with age.

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FACTOR XI AND XII IN CRITICALLY ILL NEONATES. M. Karpatkin, (Spon. by S. Piomelli), NY Univ. Med. Ctr.

It has been reported that factors XI and XII are low in neonates and rise slowly in the post-natal period, lowest levels are reported in the premature. This study demonstrates that in very sick newborns, levels of these factors are extremely low, irrespective of gestational age and do not rise in the immediate postnatal period. Of 25 consecutive babies in the ICU with severe RDS or sepsis and no evidence of bleeding, PTT was > 80 secs in 23 on at least one occasion (mean 116, range 84-200, mean control 43). All corrected with contact product; (mean 41 secs, range 31-50; mean control 30), indicating low factor XI and/or XII. In 14 babies these factors were measured. Factor XI was 4-47% (mean 17%) and factor XII 9-38% (mean 20%). These levels are lower than those previously reported in newborns; also in 5 infants of comparable age not in the ICU, PTT was 47-77 secs. Mean age at time of study was 2.8 days, range 1-8, mean birth weight 1628g (range 700-3250). There was no correlation between birth weight or age and factor levels. In 5 babies studied 1-4 days later, levels declined in 4 and were unchanged in 1. In vitro inhibition could not be demonstrated. There was no evidence of DIC or gross hepatic disfunction (PT mean 14.3 secs, range 11-17, fibrinogen > 150mg%, FSP < 3.38µg/ml, factor VIII > 70%). Thus in very sick newborns factors XI and XII are extremely low. This is unrelated to birth weight but may relate to poor clinical status. Other factors were in normal range for age, suggesting specific impairment of a particular liver enzyme or increased catabolism of XI and XII.

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HEMATOLOGIC FINDINGS IN ISOVALERIC ACIDEMIA. J. Kelleher, M. Yudkoff, R. Cohn, R. Hutchinson and S. Segal. Divisions of Metabolism and Hematology, Dept. Pediatrics, Univ. of Pennsylvania, and Children's Hospital of Philadelphia, Philadelphia, PA. 19104

Hematologic abnormalities have been associated with some inborn errors of metabolism, including maple syrup urine disease and methylmalonic acidemia. We have evaluated two neonates with isovaleric acidemia. Both patients had pancytopenia during the first week of life when serum isovaleric acid levels were in excess of 50 mg/dl. Hemoglobin, granulocyte and platelet counts decreased further, reaching nadirs by the 2nd week of life of 7.8 and 8.0 g/dl, 26 and 150 cells/mm^3, and 8,000 and 50,000 platelets/mm^3, respectively, even as serum isovaleric acid levels were decreasing in response to therapy. Recovery was gradual, requiring 2 weeks for restoration of normal values. The granulocytes were the last to return to normal. A striking monocytosis (40% and 60%) was noted during the recovery phase in both infants. One infant also had an eosinophilia of 19%. Bone marrow examination in one patient revealed large numbers of immature mononuclear cells, with small numbers of early erythroid and myeloid precursors. Bone marrow culture showed an increased number of granulocytic colony forming units. Survival of random donor platelets was normal. These findings suggest that the hematologic abnormalities of isovaleric acidemia probably are referable to an inhibition of normal cell maturation rather than a depletion of marrow precursors or increased destruction of mature cells.