

SIGNIFICANCE OF MEDIASTINAL MASS (MM) IN ACUTE LYMPHOBLASTIC LEUKEMIA (ALL), Yaddanapudi Ravindranath, Joseph Kaplan, W. W. Zuelzer,\* Wayne State Univ. Sch. of Med., Children's Hosp. of Mich., Child Res. Ctr., Dept. of Ped., Detroit.

Children with T cell lymphoblastic lymphoma (TLL) (J. Kaplan, et al, Cancer Res., 1974, in press) frequently present with MM and subsequently develop rapidly progressive leukemia. Four such children died between 3 and 14 months after onset of bone marrow involvement. Since childhood leukemia presenting with MM (ALL+MM) may actually be a generalized form of TLL, a retrospective study was conducted to compare the clinical course of 9 such patients and 74 children with typical ALL. Therapy of both groups was similar. The % of surviving patients and % in complete remission in both groups at 6, 12 and 18 months after diagnosis are shown in the following table:

	% ALIVE			% COMPLETE REMISSION		
	6 mo.	12 mo.	18 mo.	6 mo.	12 mo.	18 mo.
ALL+MM	89	44	22	33	33	11
	(p>0.8)	(p<0.05)	(p<0.05)	(p<0.05)	(p<0.05)	(p<0.1)
ALL	95	95	89	89	70	61

In comparison to other children with ALL, those presenting with MM had more frequent early relapses and shortened survival. These findings indicate that, with a representative mode of ALL therapy, children with ALL+MM do poorly when compared to children with typical ALL. This difference may be related to a T cell origin of tumor cells in ALL+MM. Therapeutic regimens different from those currently used for ALL may be indicated for children with ALL+MM.

TISSUE FACTOR PROCOAGULANT CAPACITY OF NEONATAL LEUKOCYTES. Rodney P. A. Rivers and William E. Hathaway. University of Colorado Medical Center, Dept. of Pediatrics, Denver, Colo.

Recent studies have demonstrated that leukocytes are an important source of a procoagulant which has been characterized as tissue factor (TF). Since DIC or intravascular thrombosis is often seen in newborn infants who have sepsis or severe hypoxia-acidosis, the procoagulant capacity of cord-derived leukocytes has been studied.

Leukocytes were separated from blood and suspended in adsorbed autologous serum to give a segmented neutrophil + band count of 20,000/cu mm. The suspensions were incubated at 37°C and TF activity was detected by a shortening of the unactivated partial thromboplastin time using normal plasma as substrate, pre-incubated with inosithin. Cord-derived cells from normal term infants and control adult cells were studied in parallel; the former release tissue factor less quickly than do adult cells when unstimulated, but on exposure to endotoxin, similar amounts of TF are released at comparable rates. PH reduction to 6.5 with lactic acid caused a very rapid increase in procoagulant activity, suggesting a different mechanism of release from the synthesis and release of TF induced by endotoxin; the cells remained responsive to endotoxin following this brief release of TF.

These mechanisms may be important factors in the pathogenesis of hypercoagulability and DIC in infants with perinatal asphyxia and septicemia.

THE POTENTIAL CURABILITY OF EWING'S SARCOMA IN CHILDREN. Gerald Rosen, Giulio J. D'Angio, Charlotte Tan, and M. Lois Murphy, Depts. of Ped. and Radiation Therapy, Memorial Sloan-Kettering Cancer Center, New York, N. Y.

Four drug adjuvant chemotherapy (dactinomycin, adriamycin, vincristine and cyclophosphamide) was added to local radiation therapy to treat patients with Ewing's sarcoma. The entire involved bone was treated with 6000-7000 rads (Co<sup>60</sup>). Cyclic chemotherapy was started concomitantly with radiation therapy, and was continued for 24 months. Of 14 patients, 10 had no evidence of metastatic disease, 2 had bone marrow invasion with extrinsic cells, and 2 others had pulmonary metastases at the time of diagnosis. The latter 2 received irradiation (2000 rads) to the lungs. 13/14 patients are free of disease for a median time of 24 months from the time of diagnosis. Seven of these patients having completed chemotherapy, remain free of disease for from 2-24 months after the cessation of chemotherapy. One patient developed metastatic disease at 32 months (6 months after stopping therapy). Meningeal disease has not been observed in any of the 14 patients. Major complications included reversible congestive heart failure in 2 patients (necessitating lowering the cumulative dose of adriamycin for subsequent patients) and the local effects of combined therapy on the primary tumor site attributable to the devitalization of bone and soft tissue.

These preliminary results indicate that Ewing's sarcoma may be a potentially curable disease with early referral to centers equipped to institute aggressive combined therapy.

IMPROVEMENT OF CEREBRAL VASCULAR DISEASE IN SICKLE CELL ANEMIA FOLLOWING TRANSFUSIONS. Marie O. Russell, Herbert I. Goldberg, Shlomo Friedman, Martin Reivich and Elias Schwartz. Univ. of Penna. Sch. of Med., Children's Hosp. of Philadelphia, and Stroke Research Ctr., Phila. Gen. Hosp., Phila., Pa.

Cerebrovascular accidents (CVA) are a major clinical problem in sickle cell disease. We have studied four affected children soon after CVA and one year later to evaluate the effect of chronic transfusion therapy on arterial abnormalities. Percutaneous femoral-cerebral angiography was performed after careful preparation of patients by partial exchange or repeated transfusions to achieve a normal hemoglobin concentration and reduction of Hb S to about 20%. There were no complications of angiography. When possible, the right and left carotid and basilar systems were visualized and cerebral blood flow was measured with <sup>133</sup>Xe. Major cerebral artery disease, often more extensive than was clinically evident, was found in all cases. Three of the four children were transfused for one year. Two showed complete resolution of occlusive disease. In a third child in whom transfusions were not started until after a second CVA, some affected vessels had improved after a year, but others showed no change or chronic narrowing. Cerebral blood flow (<sup>133</sup>Xe), initially decreased in this child, was normal on the second study. A fourth child not transfused between studies showed severe occlusive disease with progression. These data suggest cerebrovascular damage in sickle cell disease may be reversible with long-term transfusion therapy.

ENHANCED TRITIATED THYMIDINE (<sup>3</sup>HT) UPTAKE IN OSTEO-SARCOMA CELLS IN VITRO BY PATIENT'S OWN SERUM; SUPPRESSION OF <sup>3</sup>HT UPTAKE WITH 17B ESTRADIOL (E<sub>2</sub>). P.E. Scranton, J.H. McMaster, F.M. Kenny, F.H. Taylor, Depts. of Orthopaedics, Pediatrics, and Commun. Med. (Biostatistics), U. of Pittsburgh School of Medicine, Pgh., Pa.

The effects of hormone and hormone-sera combinations on <sup>3</sup>HT uptake by osteosarcoma tumor cells were evaluated. Multiple studies consistently showed a five-fold enhancement of <sup>3</sup>HT uptake by serum from an osteosarcoma patient, compared to control inactivated serum, and 2x enhancement compared to normal human serum. Thymidine uptake factor corresponds to somatomedin. As somatomedin regulates bone and cartilage growth, 17B Estradiol, a known inhibitor of somatomedin, was tested in physiologic ranges: 80 pg/ml and 200 pg/ml. Inhibition of <sup>3</sup>HT uptake was 14% and 22%, respectively. These data support our ongoing and previous clinical and biochemical evidence that osteosarcoma patients may have elevated somatomedin; i.e. high tumor incidence at adolescence when somatomedin is highest, abnormal glucose tolerance and insulin levels. Estrogen therapy could be beneficial in management of this disorder.

DEPLETION OF VITAMIN C IN PATIENTS WITH THALASSEMIA MAJOR.

EFFECT OF VITAMIN C REPLETION ON DESFERRIOXAMINE INDUCED URINARY IRON EXCRETION. Shah, N.R., Wolff, J.A., Sitarz, A.L., Lee, C.K., Massa, E. and Diaz, R. College of Phys. & Surg., Columbia U. and Babies Hosp., Dept. of Ped., New York, N.Y.

Patients with iron overload have vit. C deficiency in tissue stores as measured by vit. C content in the white blood cells. It has also been shown that repletion of vit. C tissue stores increases the efficacy of iron chelation in urine by Desferrioxamine (DF). Sixteen patients with thalassemia major all on a hypertransfusion program and some on chelation therapy as well were studied for vit. C content. Fourteen of the 16 had depletion of vit. C content (4.5-21.5 mcg x 10<sup>8</sup> WBC; normal range: 30.0-44.2 mcg x 10<sup>8</sup> WBC). Urine was collected for 24 hours after giving 500 mgm of DF, I.M. Iron excretion in urine varied from 0.2-2.3 mgm% of urine (mean 0.95). Patients were given vit. C 500 mgm d. to 500 mgm t.i.d., orally. At 6 weeks, urinary iron excretion, after 500 mgm of DF, I.M., was restudied. There was definite increase in iron excretion in all but one patient (mean 1.5 mgm% of urine). The mean increase for 12 children was 0.56 mgm% of urine. This difference was significant (P<.001). The amount of iron excreted was greater in older patients (i.e. those more overloaded with iron). It would be important to know the simultaneous excretion of iron in the stools and urine after vit. C repletion, as there may be significant change in excretion of iron both in stools and urine. Patients with thalassemia should receive vit. C as the majority are deficient in this vitamin.