EVIDENCE FOR ACTIVATED FACTOR VIII IN HYPERCOAGULABLE STATES. W. E. Hathaway, H. S. Hathaway, T. Downing and S. Clarke. Univ. of Colo. Med. Ctr., Dept. of Pediatrics, Denver, Colo.

Elevation of plasma factor VIII procoagulant activity can be seen in many hypercoagulable states including stress, acute phase reaction and chronic intravascular coagulation (IVC). In this study procoagulant factor VIII was measured by both the PTT-VIII assay and the thromboplastin generation time assay (TGT-VIII) and compared to an immunologic assay for VIII antigen. An in vitro study of thrombin and thromboplastin treated normal plasma showed PTT-VIII values of 168-568% of normal, TGT-VIII, 60-125%, and VIII-antigen, 84-100%. Similar in vivo findings were noted in patients with laboratory and clinical evidence of chronic IVC:

	% PTT-VIII	% TGT-VIII	% VIII-antigen
Sickle cell crisis	600	300	290
Sickle cell crisis	376	150	190
Venae cava thrombosis	336	140	200
Metastatic neuroblastoma	240	135	145
Ulcerative colitis	300	150	60

Another group (pregnancy, post-exercise, untreated tumor patients) showed elevated VIII levels which were the same by all three assays.

In conclusion, in hypercoagulability associated with IVC, measurements of factor VIII are like that seen in thrombin treated plasma (activated VIII) while in hypercoagulability seen with acute phase reaction the elevation of factor VIII is not related to activation.

EFFECT OF INTRAVENOUS UREA IN CONTROL OF PAIN FROM VASO-OCCLUSIVE CRISES IN SICKLE CELL ANEMIA

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The safety and efficacy of the use of urea for the clinical remission of painful crisis in Sickle Cell Anemia has been the subject of extensive investigations and controversy.

Twenty-eight crises, 7 occurring in children and 21 in adults, all homozygous for hemoglobin S, were evaluated in a double blind study to determine the clinical responses observed following administration of either 15% urea in 10% invert sugar (14 crises) or 10% invert sugar (14 crises.) There was no statistically significant difference in the duration of pain in those receiving urea in invert sugar compared with those receiving invert sugar alone. Among those receiving urea, there was no significant difference in the peak BUN level or the time at which the peak level was reached in those responding compared with those who obtained no response. The fluid balance in the urea treated group was variable and a trend towards negative fluid balance was noted in both the success and failure groups. Patients who were receiving invert sugar alone were generally kept in positive fluid balance.

The response to therapy was observed to be unrelated to (1) the severity and duration of pain or (2) to other modes of therapy received prior to the study and (3) to treatment with urea or invert sugar alone.

AMINO ACIDURIA IN CHILDREN WITH CANCER. Lawrence Helson, and Judith Clendenin. Memorial Sloan-Kettering Cancer Center, Department of Pediatrics, New York, N.Y.

The association of amino aciduria and cancer has been previously observed, however systematic study of excretion in specific tumors has not been investigated. The mean values of 17 amino acids excreted in 24 hour specimens were established in 28 healthy children. The mean values of the following amino acids expressed as mg/substance/gram creatinine were significantly elevated, i.e. a 4 fold increase or more, when compared with control values ( ) in 28 children with disseminated neuroblastoma: hydroxyproline 31.0 (1.0), glutamic acid 26.8 (4.6), aspartic acid 16.2 (3.9), citrulline 3.4 (0.2), allo-delta-hydroxylysine 11.2 (1.8), ornithine 5.2 (1.2), 3-methyl-histidine 104.0 (24.4). Normal or less than 4 fold increases in mean excretion values for proline (3.7), glutamine (62.4), ethanolamine (11.1), phosphoethanolamine (10.2), methionine sulfoxide (18.1), asparagine (28.7), glucosamine (0.7), carnosine (9.1), arginine (1.9), 1-methylhistidine (15.3) were found. Values from 12 other children with successfully treated neuroblastoma were similar to controls. Seven children with hepatic cancer had significantly increased excretion of all amino acids studied except phosphoethanolamine, methionine sulfoxide and asparagine. The source of the increased excretion appears to be extra renal in children with neuroblastoma and may in addition be due to abnormal liver function in children with hepatic cancer.

Supported by NCI Grant No. CA 05826.

INDIUM-BLEOMYCIN SCANNING IN PEDIATRIC MALIGNANT SOLID TUMORS. Helen Johnson, James J. Corrigan, Jr., Robert E. O'Mara, David Lilien. Department of Pediatrics and Radiology, University of Arizona Medical Center, Tucson, Arizona.

^{111}Indium labelled Bleomycin (IB) is a new radio-pharmaceutical which localizes in a wide variety of animal and human tumors. In this study of 13 children with malignant solid tumors 20 total body scans were performed. The scans were obtained 48 hours after intravenous administration of less than 2 millicuries of IB (Bleomycin less than 0.4 mg/dose). In 3 patients with lymphoma, 5 with neuroblastoma, 2 with rhabdomyosarcoma, 1 with leiomyosarcoma, and 2 with malignant teratoma an excellent correlation was observed between abnormal accumulations of IB and known sites of tumor involvement. The most precise imaging of tumor was for lymph node and soft tissue sites of disease, both above and below the diaphragm. At 48 hours IB was normally observed in liver, kidneys, and bone marrow. Hepatic and osseous involvement was difficult to assess, necessitating other specific scans for evaluation. The data suggest that tumor scanning with ^{111}Indium-Bleomycin is an extremely valuable technique for staging and serial evaluation of children with solid tumors.

HIGH DOSE METHOTREXATE (HDM) WITH CITROVORUM (CF) RESCUE IN THE MANAGEMENT OF BONE TUMORS. N. Jaffe, D. Traggis, S. Sallan, S. Andronian, D. Chan and E. Frei, III. (Intr. by D.G. Nathan). Child. Hosp. Med. Ctr., Child. Cancer Res. Fndn.,and Harvard Med. Sch., Boston, Mass.

Prognosis in osteogenic sarcoma (OS) and hemangioendotheliosarcoma (HES) is particularly poor once metastases appear. These tumors are generally resistant to chemotherapy. During the past 2 1/2 years 14 patients with metastatic OS and 2 with metastatic HE were treated with incremental HDM (50 to 800 mg/kg) over 6 hours at 2 to 3 weekly intervals followed by CF 2 hours later. Among 14 patients with OS, complete regression of pulmonary metastases occurred in 2 and partial regression in 2 others (duration of response 2-30+ months). Treatment was given for 2 years or until tumor recurred. One of 3 patients who relapsed on the 6-hour infusion responded again to 24-hour infusions. One patient with HE partially responded (duration 2 months) while the other remains free of disease 8+ months following initiation of HDM and eradication of metastases with radiotherapy. Of 150 courses of methotrexate, 20% were associated with side effects: nausea, vomiting, abdominal pain, stomatitis, skin lesions, renal impairment and myelosuppression. Side effects responded to additional CF. HDM with CF is now being used as adjuvant treatment in newly diagnosed patients. Of 12 such patients followed for 2-18 months, only 1 has developed a metastasis, a striking reduction in incidence. HDM appears to be of great value in bone tumor therapy in childhood. Supported by USPHS grant C6516.

HUMAN T CELLS BIND AUTOLOGOUS AND HOMOLOGOUS HUMAN RED CELLS. Joseph Kaplan (Intr. by C. S. Stulberg), Wayne State Univ. Sch. of Med., Children's Hosp. of Mich., Child Res. Ctr., Dept. of Ped., Detroit.

While binding of sheep erythrocytes is an established property of human T cells, T cell binding of human erythrocytes has not been well documented. We now report that, in a manner similar to binding of sheep erythrocytes, under appropriate temperature conditions, human T cells bind human autologous and homologous erythrocytes. When human lymphocytes or thymocytes were incubated with human red cells in ice for 30-90 min., resuspended, and examined at 4°, the percentages of rosettes formed were as follows: adult peripheral blood lymphocytes 9±4%; cord blood lymphocytes 9±6%; malignant T-lymphoblast cell lines 5%; thymocytes 22±10%. Only viable lymphocytes formed rosettes. Binding of human erythrocytes did not occur after lymphocyte suspensions were depleted of T cells, nor after treatment with non-cytotoxic concentrations of anti-thymocyte serum, trypsin or sodium azide. At 22°, or when vigorously agitated, rosettes rapidly fell apart. Similar numbers of rosettes formed with either autologous or homologous human erythrocytes.

The binding of autologous and homologous, as well as heterologous erythrocytes, in addition to being a convenient T cell marker, supports the concept that T cells have a general affinity for surface components of other cells.