637

TWO CLASSES OF HUMAN ERYTHROID BURST FORMING UNITS WITH DIFFERENT RESPONSES TO ERYTHROPOIETIN (EPO): BFU-E_A AND BFU-E_F. D. Nathan, D. Hillman, B. Alter, R. Gorer, B. Clarke, B. Forget and D. Housman. Harvard Medical School, Children's Hospital Medical Center and Sidney Farber Cancer Institute, Boston, MA; MIT Center for Cancer Research, Cambridge, MA, and Yale Medical School, Yale-New Haven Hospital, New Haven, CT.

To examine the control of the production of Hb F containing RBC (F cells), marrow (BM) and blood (PB) mononuclear cells of three healthy males were grown in plasma clots at various Epo concentrations. The number and size of BM CFU-E colonies (at 7 days) and BM and PB BFU-E colonies (at 14 days) were determined. The clots were also incubated with ^{3}H-leucine and the newly synthesized globin chains quantified by carboxymethylcellulose chromatography. The results show that marrow CFU-E and BFU-E are very sensitive to Epo. Half maximal growth is at 0.1-0.25 I.U. Both BM precursors produce Hb A, while Hb F synthesis is below the limits of detection. In contrast, PB BFU-E are less sensitive to Epo. Half maximal growth is at least 0.5 I.U. In addition, they produce 15-20% Hb F. Thus in normal erythropoiesis, BM contains mainly BFU-E_A which respond to physiologic Epo concentrations, becoming CFU-E_A and finally adult RBC. BFU-E_F differentiate minimally in BM at normal Epo concentrations. Instead, they circulate in PB. In anemia, high Epo concentrations stimulate BFU-E_F proliferation. F cell production is therefore due to Epo dependent expansion of the BFU-E_F pool.

638

NEUTROPHIL CHEMOTAXIS, PHAGOCYTOSIS, AND BACTERICIDAL ACTIVITY IN NORMAL VOLUNTEERS RECEIVING PREDNISONE. Uri Z. Nordan, James R. Humbert, Gary A. Rich, and Byung H. Park, State University of New York at Buffalo, The Children's Hospital of Buffalo, Department of Pediatrics, Buffalo.

To evaluate the in vivo effect of prednisone on neutrophil (PMN) functions, prednisone (40 mg./day) was given orally for 3 days to 8 normal volunteers. PMN chemotaxis toward activated serum and PMN random migration were measured in modified Boyden chambers. NBT reduction after stimulation by phorbol myristate acetate was measured by use of flow-cytophotometry. Phagocytosis and bactericidal activity of Staphylococcus aureus were determined by the method of Tan et al. Twenty-four hours and 72 hours after the first prednisone dose the average absolute number of PMNs increased by 64% and 41% respectively from the initial $3.31 \pm 1.0 \times 10^9/1$ (mean $\pm$ 1 SD). Chemotaxis was significantly decreased after 24 hours ($P < 0.005$) while the 72-hour chemotaxis returned to normal values in 2 subjects and remained low in the remaining 4. The increased random migration of PMNs which was found in 2 volunteers was also suppressed during the study period. Although phagocytosis of Staphylococcus aureus remained unaffected, bactericidal activity 72 hours after the first prednisone dose was significantly diminished as compared to initial values or to the values of untreated paired controls ($P < 0.02$). This decrease in bactericidal activity was observed following 30 minutes but not 120 minutes of PMN-bacteria interaction. NBT reduction by PMNs was not impaired. Short-term treatment with prednisone interferes with PMN chemotaxis and bactericidal activity and may therefore compromise host-defense mechanisms.

639

UNILATERAL OPTIC NERVE DISEASE, A COMPLICATION OF CHEMOTHERAPY OF ACUTE LYMPHATIC LEUKEMIA (ALL). Sylvia Norton and James A. Stockman III. Depts. of Ophthal. and Peds., SUNY, Upstate Med. Ctr., Syracuse, N.Y.

Ocular complications are not uncommon with the use of vincristine (VCR) but usually consist of ophthalmoplegias. A single case of optic neuropathy, presumably caused by VCR, has been previously reported in a patient with Hodgkin's disease (Am. J. Ophthal. 81:146, 1976). We have observed this complication in two subjects with ALL. In each case, severe unilateral retrobulbar pain occurred 5-7 days following the administration of VCR (2.0 mg/m^2) during maintenance therapy. In the first subject, an 8 yr. old, eye exam several months after the onset of ocular symptoms revealed a visual acuity of 20/80 in the affected eye which failed to improve with refraction. A positive Marcus Gunn pupil, defective color vision and a central scotoma were noted. Fundoscopy was normal. Eye exam prior to the onset of symptoms had been unremarkable. In the second case, a 6 yr. old, acuity was 20/40 in the affected eye unimproved by refraction. Pupillary constriction in response to light was followed by rapid dilatation. Color vision was normal but a paracentral scotoma was present. A vitritis localized over the optic disc caused the disc to appear pale and indistinct. In each subject the contralateral eye exam was normal. In both cases repeated spinal fluid cytologies have been negative. Optic nerve disease in these cases is presumably related to the use of VCR. Retrobulbar or eye pain following the administration of VCR calls for careful ophthalmologic examination.

640

VIRAL INDUCED HISTIOCYTIC MEDULLARY RETICULOSIS. Maura C. O'Leary, Norma K.C. Ramsay, William Krivit, John H. Kersey, and Mark E. Nesbit. University of Minnesota, Department of Pediatrics, Minneapolis, 55455.

Histiocytic Medullary Reticulosis (HMR) is characterized by fever, hepatosplenomegaly, pancytopenia and bone marrow histiocytic infiltration with erythrophagocytosis. The etiology is uncertain and the outcome is usually fatal despite treatment with chemotherapy. We have studied two patients with apparent viral induced HMR with extensive bone marrow involvement, erythrophagocytosis, granulocytic arrest and pancytopenia. An 18 month old boy with HMR had an adenovirus titer of 1:1024 and a 17 year old male had elevated Epstein-Barr virus titers (IgG= 1:320; IgM=1:2560). These patients had severe coagulopathies with thrombocytopenia (<50,000 cmm), prolonged hypofibrinogemia (<0.10 gm/DL) and elevated fibrin split products. Both patients had liver abnormalities with hyperbilirubinemia and elevations in hepatocellular [SGOT=1764 and 125 IU/L (N<27)] and hepatocanalicular [γ GT=333 and 203 IU/L (N<25)] enzymes. Lymphocyte response as tested by phytohemagglutinin and poke weed mitogen was depressed. T and B cells and serum immunoglobulins were normal except for an IgE level of 4790 IU/ml (N<444) in the first patient. Both patients had repeated episodes of lessening severity over several months. Improvement in clinical status was accompanied by a return to normal of all laboratory studies. These patients emphasize that severe viral infection can cause HMR and that a viral etiology must be excluded in patients with HMR prior to consideration of cytotoxic chemotherapy.

641

AIRWAY OBSTRUCTION AND SUPERIOR VENA CAVA SYNDROME SECONDARY TO NON-HODGKINS AND HODGKINS LYMPHOMA. Jorge A. Ortega, Hossein Mahour, Hart Isaacs, Gussie R. Higgins (Sponsored by Harry T. Wright), University of Southern California, Childrens Hospital of Los Angeles, Department of Pediatrics.

Mediastinal compression causing airway obstruction (AWO) and superior vena cava (SVC) syndrome may be a presenting manifestation of childhood lymphoma. From 1967 through December 1977, 75 children with Non-Hodgkins Lymphoma (NHL) and 49 with Hodgkins Lymphoma (HL) were seen at our institution. Eighteen patients with NHL had primary mediastinal involvement, and of these 8 presented with moderate to severe AWO and/or signs of SVC syndrome. In 6 of these patients diagnosis was established in 3 by thoracotomy, 2 by cervical lymph node biopsy and 1 by thoracentesis. Two patients presented with severe AWO requiring corticosteroids for 2 days prior to the diagnostic surgical procedure. In 7 patients signs of AWO and/or SVC syndrome improved rapidly following initiation of corticosteroid and cyclophosphamide. Of the 49 patients with HL, 13 presented with mediastinal disease and of these only 4 had evidence of mediastinal compression, none severe. These 4 had diagnostic biopsy and staging laparotomy prior to treatment. In summary, severe AWO and/or SVC syndrome was more likely to occur in patients with NHL with mediastinal primary. General anesthesia may be hazardous in some patients, requiring a short course of corticosteroid therapy to alleviate the mediastinal compression prior to the diagnostic operative procedure.

642

DEMONSTRATION THAT HISTIOCYTOSIS-X MAY BE AN AUTOIMMUNE DISORDER AND SUCCESSFUL TREATMENT WITH THYMIC HUMORAL FACTOR. Michael Osband and Robertson Parkman. (Spon. by David G. Nathan). Children's Hospital Medical Center, Departments of Hematology-Oncology and Immunology and Sidney Farber Cancer Institute, Department of Pediatric Oncology, Boston, MA 02115

To test the hypothesis that histiocytosis-X may be a primary autoimmune disorder and not a true cytoproliferative malignancy, we assayed the reactivity to autologous antigens of Ficoll-Hypaque separated peripheral blood mononuclear cells (PBM) from controls and patients with histiocytosis-X. The PBM of 4/4 patients demonstrated reactivity to autologous antigens in one or more assays. None of 10 controls demonstrated any autoreactivity in the assays. The assays used were: cytotoxicity of ^{14}C labelled cultured autologous fibroblasts, cytotoxicity of ^{51}Cr labelled autologous lymphocytes, and stimulation of PBM protein synthesis by actinomycin-D treated autologous lymphocytes. Pre-incubation of patients' PBM with thymic humoral factor (THF) eliminated the abnormal autoreactivity in all three assays. Because THF abolished in vitro reactivity, one patient, a chemotherapy failure, was treated with THF. He is now in complete remission, requires no additional THF therapy, and his PBM no longer demonstrates autoreactivity. Histiocytosis-X may be caused by inadequate regulation of autoreactive lymphocytes, whose response to autologous antigens produces the manifestations of the disease. The lack of regulation may be due to a thymic deficiency that can be corrected with THF replacement therapy.