

ues. Peripheral blood responses were generally consistent with previous "macro" lymphocyte reports for similar leukemic patients. However, 12 of 30 patient marrows were nonresponsive to PHA on at least one occasion, and only 6 leukemic marrows were positive to the antigen battery—each only to a single antigen. Some immune and clinical correlates of these studies will be discussed.

Monocyte function in children with neutropenia. ROBERT L. BAEHNER, and RICHARD B. JOHNSTON, JR. *Children's Hosp. Med. Ctr., Harvard Med. Sch., Boston, Mass.*

It has been reported that normal monocytes kill *S. aureus* as effectively as do PMN but patients with congenital neutropenia (CN) have increased number of circulating monocytes in the presence of uncontrolled infection. Therefore, we have compared the metabolic and bactericidal responses of CN monocytes from 2 such patients, the monocytes from 2 patients with cyclic neutropenia, patients with chronic infection, to the PMN from normals and patients with acute infection. At a bacteria to phagocyte ratio of 2-3:1 in an *in vitro* system which measured the combined effect of uptake and intracellular killing of *S. aureus*, PMNs consistently killed about 95% of the inoculum during 2 hours. In contrast, monocytes from all patients failed to diminish the number of bacteria during the incubation. PMNs initiated ingestion sooner, took up *S. aureus* or zymosan particles faster, and ingested more bacteria or particles than did monocytes. Furthermore, despite a brisk respiratory burst, pentose shunt stimulation and hydrogen peroxide production by monocytes, there was less iodination of bacteria by monocytes than PMN. Granule myeloperoxidase was significantly less in monocytes (163 ± 47) from all patients compared to PMN (390 ± 10). Cell associated bactericidal activity by monocytes was markedly diminished compared to PMN. These studies show that monocytes from patients with neutropenic syndromes function similarly to monocytes from children with subacute infection. Such monocytes are less bactericidal than PMN because of the combination of decreased phagocytic capacity and lower activity of the intracellular mechanisms related to peroxidation of bacteria.

Successful treatment of inoperable embryonal rhabdomyosarcoma.

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Embryonal rhabdomyosarcoma, when inoperable or metastatic, has usually been a rapidly fatal cancer. Intensive combination chemotherapy (VAC) with Vincristine (VCR), Actinomycin-D (AMD) and Cyclophosphamide (CYT) in conjunction with radiotherapy is effective in the treatment of this tumor. Twenty-one children with inoperable or metastatic embryonal rhabdomyosarcoma, or undifferentiated sarcoma suggestive of embryonal rhabdomyosarcoma, were treated in the 3-year period 1967-1969. Sixteen of them (76%) are alive without evidence of disease 1-4 years after initiation of therapy. Therapy consisted of biopsy, Co⁶⁰ radiation 5000-6000 rads tumor dose, and VAC chemotherapy. Surgery was subsequently utilized when feasible. The chemotherapy consisted of VCR 2 mg./M² IV weekly x12, AMD 75 mg./Kg. divided into 5-8 daily doses every 3 months for 5 or 6 courses, and CYT given either as 2.5 mg./Kg./day for 2 years or 10 mg./Kg./day for 7 days every 6 weeks. The type of CYT therapy was dependent on tumor location and extent.

"Total therapy" of childhood acute lymphocytic leukemia.

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In 1962 studies were initiated to determine, first, whether a significant 5 year cure rate of childhood acute lymphocytic leukemia (ALL) was attainable with present therapeutic agents and secondly, how best this could be accomplished. The basic plan was (1) to induce complete remission promptly, (2) to administer multiple antileukemic drugs for 2-3 years with the purpose of eradicating all residual leukemia and (3) to prevent nervous system leukemia by "prophylactic" central nervous system (CNS) therapy early during remission. From early pilot studies with relatively few patients the program has evolved to more elaborate investigations involving large numbers of patients and comparisons of alternate treatment methods. Of 37 children who developed complete remission (CR) in studies I-III (1962-65) 7 survive in CR for 6 to 8 years and have been off all therapy for 3 to 5 years. Study IV (1965-67) demonstrated the superiority of full dosage over half dosage of combination chemotherapy. Of 31 patients entering CR in Study V (1967-68) 20 remain in continuous CR for 2½ to 3 years; therapy has been discontinued in the majority and will soon be terminated in the remainder. In Study VI (1968-70) 94 children in CR were randomized for craniospinal radiation (2400 R) or none. Of 45 who received craniospinal radiation only 2 developed initial relapse in the CNS and 35 remain in continuous CR for 8 months to 2½ years. Of 49 who did not receive radiation, 25 have developed CNS relapse. It is concluded that a significant 5 year cure rate is an attainable goal in ALL, that ALL can no longer be considered an incurable disease, that CNS therapy inhibits CNS relapse, and that palliation is no longer an acceptable approach to the management of this disease.

Diphenylhydantoin induced coagulation abnormalities. M. HILGARTNER, G. E. SOLOMON, and H. KUTT (Intr. by Carl H. Smith). *Cornell Med. Ctr. N. Y., N. Y.*

Bleeding within the first 24 hours of life has been reported in some infants whose mothers received anticonvulsants. This study was designed to evaluate the relationship between Diphenylhydantoin (DPH) and coagulation defects. Eight cats were given DPH intraperitoneally daily (two cats received 2.5mg./kilo, two cats 5mg./kilo, four 10mg./kilo). These animals were followed weekly for coagulation abnormalities, neurologic toxicity and DPH blood levels. Cats receiving 10mg./kilo, for 8 to 15 days showed a decrease in Factors I, II, V, VII and X plus ataxia. Cats receiving 2.5 and 5.0mg./kilo showed a decrease in the same factors to a lesser degree. After one week of treatment with DPH, Factors I, II, V, VII and X were decreased 50% in all animals. Vitamin K dependent Factors II, VII and X returned to normal in cats on low doses of DPH. These Factors continued to fall in cats receiving 10mg./kilo. Animals on low dosage of DPH appeared to adapt and no longer showed a coagulation abnormality. Factor V fell initially and then rose above base line values in all cats after one week suggesting transient liver dysfunction. Factor VIII remained normal in all the animals. To prove that the coagulation defect was dependent on Vit. K three cats were treated with 10mg./kilo DPH and 1mg. Vit. K daily. This combination prevented the clotting abnormalities without preventing neurologic signs of DPH toxicity. Cord blood levels of DPH have been found increased over mother's DPH blood levels suggesting a mechanism for infant toxicity. Since this study in