constant pressure. Flow velocity (μl/sec) was calculated. Cell suspensions were modified by adjusting temperature, pH and pO2 prior to filtration. Mean corpuscular volume (MCV), reticulocyte count and fibrinogen were measured. Viscosity of whole blood, 40% cells in autologous plasma and 80% washed cells was determined.

Filterability, as a measure of RBC deformation, was markedly decreased in newborn samples. Mean flow velocity was 2.2 μl/sec $\pm$ .6 (S.D.) for newborns and 4.5 μl/sec $\pm$ .8 for adults ($p < .001$). Lowered pH or pO2 in the prefiltrate resulted in significantly decreased filterability in newborn samples only. Filterability correlated poorly with MCV. Two infants with polycythemic hyperviscosity syndrome showed increased viscosity of whole blood, 80% cell suspension and markedly decreased filterability. An infant with pyknocytosis showed decreased filterability and elevated viscosity of an 80% suspension compared to normal newborns.

Decreased deformability of the fetal RBC may be related to shortened newborn RBC survival involving diminished ability to pass through the splenic microcirculation. The decreased fetal RBC deformability which can be aggravated by acidosis and hypoxia contributes to hyperviscosity in newborns with high hematocrits. The decrease in red cell survival and anemia in infantile pyknocytosis may also be related to altered RBC deformability.

Prediction of severity of disease in homozygous β thalassemia (β thal). YUET W. KAN and DAVID G. NATHAN. *Children's Hosp. Med. Ctr. and Harvard Med. Sch., Boston, Mass.*

The clinical consequences of homozygous β thal are variable. We have studied globin chain synthesis in the peripheral blood reticulocytes of the parents of patients with homozygous β thal to determine the likelihood of mild and severe β thal in families in which both parents have thal trait. Peripheral blood was incubated with U ^{14}C leucine. The ratio of the specific activities of β and α chain separated by urea CMC chromatography (β/α ratio) was determined. The β/α ratios of 14 parents of patients with severe disease was compared to those of 10 parents of patients with mild disease. The mean β/α ratio in the former group of parents was 0.49 with a narrow standard deviation of 0.06. The mean ratio in the group of parents of patients with mild disease was 0.68 with a wider standard deviation of 0.21. Two patterns were observed in the milder group: (1) the ratio in one parent was close to 0.50, while the other parent had a significantly higher ratio (0.71 to 1.09), and (2) both parents had moderately elevated ratios (0.65). The higher ratios in the milder group may represent a milder β thal gene or the co-inheritance of an α thal gene, either one of which reduces the severity of homozygous β thal. We conclude that the study of peripheral blood globin chain synthesis in prospective parents with β thal trait may be extremely useful for estimating the potential severity of homozygous β thal in their offspring.

Phototherapy in ABO hemolytic disease of newborn. EUGENE KAPLAN, FRITZ HERZ, ELSIE SCHEYE, and LAWRENCE ROBINSON, JR. *Sinai Hosp. of Baltimore, Inc., Baltimore, Md.*

In hyperbilirubinemia of ABO hemolytic disease of newborn (ABO-HDN), phototherapy is less effective in lowering bilirubin concentrations than in hyperbilirubinemia of prematurity or nonhemolytic disorders of newborns. Nevertheless, phototherapy does alter patterns of serum bilirubin in ABO-HDN, as seen in a comparison of 29 treated infants with 144 untreated infants.

In ABO-HDN, recognizable patterns of serum bilirubin result from variations in the *severity of onset* in the 1st day of life, and in the time, extent, and duration of *maximum serum bilirubin* concentrations. A severe onset is seen in ⅓ of infants with ABO-HDN, serum bilirubin increasing at a rate of 0.5 mg/hr or greater. Peak bilirubin levels are noted on day 1 (10% of infants), day 2 (30%), day 3 (40%) and day 4 or 5 (20%). The peak bilirubin concentration is less than 16 mg% in ⅓ of the infants; between 16 and 19 mg% in ⅓ and exceeds 20 mg% in the remaining ⅓. In ⅓ of infants the maximum bilirubin concentration remains unchanged for at least 24 hrs. before decreasing.

On phototherapy, the bilirubin levels in 20% of infants with ABO-HDN continue to rise, remain unchanged in 40% and decrease in 40%. Light is least effective in infants with severe onset during the 1st day of life. However, in no infant on phototherapy does bilirubin reach its peak after the 3rd day of life and the maximum bilirubin concentration exceeds 20 mg% in only 10% of treated infants.

In-vitro chromosomal radiosensitivity in Fanconi's anemia. MAKOTO HIGURASHI and PATRICK E. CONEN (Intr. by Bernard Laski). *Univ. of Toronto and Hosp. for Sick Children, Toronto, Ont., Canada.*

Peripheral blood samples and fibroblast cultures from 5 children with Fanconi's anemia and 4 controls were irradiated with 10 and 100 rads; other controls were non-irradiated duplicate cultures. Blood cultures were harvested at 52 and 72 hours. Fibroblast cultures were irradiated 24 hours before fixation. Radiation break frequencies were calculated by subtracting figures for non-irradiated samples from those for irradiated samples. The number of chromosome-type breaks per cell per rad *in irradiated controls* was 0.0025 $\pm$ 0.0005 (52 hour cultures) and 0.0017 $\pm$ 0.005 (72 hour cultures) in lymphocytes, and 0.0059 $\pm$ 0.0016 in fibroblasts, and *in irradiated cells from Fanconi's anemia* was 0.0103 $\pm$ 0.0016 (52 hour cultures) and 0.0074 $\pm$ 0.0036 (72 hour cultures) in lymphocytes, and 0.0103 $\pm$ 0.0034 in fibroblasts. The number of dicentrics and rings per cell was significantly greater in the Fanconi's anemia samples than controls at 100 rads. We concluded that, in-vitro, chromosomes of cells from children with Fanconi's anemia were significantly more radiosensitive than those of controls ($P < 0.01$).

Microlymphocyte transformation (MLT) determinations of peripheral blood and marrow aspirates from children with acute lymphocytic leukemia. DAVID M. MUMFORD, JORDAN R. WILBUR, RACHID A. CHEEMA, CAROLYN A. BOUTTE, and DONNA L. RAUMAKER. *M. D. Anderson Hosp. and Tumor Institute, and Baylor Coll. of Med., Houston, Tex.* (Intr. by George W. Clayton).

Utilizing an 0.1 cc whole blood in vitro microlymphocyte transformation technique (MLT) previously described (Mumford, *Fed. Proc.* 29: 369, 1970), human peripheral blood white cells from acute lymphocytic leukemic (ALL) patients have been tested for immune responsiveness (triplicate runs) in 30 children during various stages and treatment of their disease. A mitogen (PHA) and selected common specific antigens were employed. Concurrent MLT runs (duplicate) on bone marrow aspirates taken at the same time were performed. While some MLT kinetics differ slightly from "macro" lymphocyte transformation studies (esp. optimum day of harvest), sensitivity approximates the "macro" test. Responses were considered positive when the ratio of positive stimulated cultures were greater than twice the control val-

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. JORDAN R. WILBUR, WATARU W. SUTOW, MARGARET P. SULLIVAN, JOSEPH R. CASTRO, HERBERT KAIZER, and H. GRANT TAYLOR. *M. D. Anderson Hospital and Tumor Institute, Houston, Tex.* (Intr. by Robert E. Greenberg).

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, Co^{60} radiation 5000–6000 rads tumor dose, and VAC chemotherapy. Surgery was subsequently utilized when feasible. The chemotherapy consisted of VCR 2 mg./M^2 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. DONALD P. PINKEL, JOSEPH V. SIMONE, H. OMAR HUSTU, and RHOMES J. AUR. *St. Jude Children's Res. Hosp., Memphis, Tenn.*

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