866 RELATIVE EFFECT OF BLOOD OXYGEN (O_2) TRANSPORT CHARACTERISTICS ON OPTIMAL OXYGEN DELIVERY TO THE TISSUES. Linda M. Sacks, Daniel Isaacman, Gary Frishman and Maria Delivoria-Papadopoulos. University of Pennsylvania School of Medicine, Philadelphia, PA.

The present study investigates the relative importance of altering O_2 content and/or hemoglobin O_2 affinity (P_{50}) in changing cardiac output (C.O.) and O_2 delivery to the tissues. 18 newborn (NB) lambs were divided into 3 groups. Blood gases, [Hb], P_{50} (mm Hg), regional blood flow (ml/min/100g tissue) and C.O. (ml/min/kg) were measured before and 2 hrs after alteration of O_2 affinity and/or content by means of exchange transfusing the lambs with fetal or maternal blood of varying Hct. O_2 content was increased 38% in Gr 1 (n=6) with no change in P_{50}. O_2 content and P_{50} were increased 9% and 32% in Gr 2 (n=5), and 38% and 32% in Gr 3 (n=7), respectively. C.O. decreased 39% (364-221), 45% (324-177) and 48% (318-166) in groups 1,2 and 3, respectively. Systemic O_2 delivery decreased 22% in Gr 2 (52.9-32.4) and 26% in Gr 3 (45-33) and was unchanged in Gr 1. PVO_2 increased in Gr 2 from 31.8 to 34.6 and in Gr 3 from 23.4 to 32.3. O_2 consumption was unchanged in all groups. These data suggest that in the NB lamb an increased P_{50} associated with increased Hct provides the same reduction of C.O. as a 4-fold increased Hct without change in P_{50}. Higher increase in O_2 content provides no further reduction in C.O. but a greater increase in PVO_2, suggesting enhanced O_2 availability to the tissues. These data suggest that the combined effect of increased P_{50} and increased O_2 content achieves optimal O_2 delivery, presumably at the greatest economy of the cardiovascular system.

867 THERAPY OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) USING ADRIAMYCIN (ADR) WITH OR WITHOUT HIGH DOSE ASPARAGINASE (ASP). Stephen E. Sallan, Sidney Farber Cancer Institute, Boston, MA.

We initiated a protocol for non-T-cell childhood ALL that used q 3 weekly ADR. A random half of patients (pts) also received high dose ASP q 1 week for 6 months. All patients received cranial radiation and intrathecal methotrexate (MTX). After completing ADR, q 3 weekly pulses of MTX and 6-mercaptopurine were begun. Therapy was electively discontinued after the completion of 30 months. Seventy-four pts entered remission between 1977 and 1979. After randomization there were two 36-pt groups: A) ADR without ASP; B) ADR with ASP. The groups were comparable in age and white blood count. However, Grp A had 11/13 patients whose lymphoblasts lacked the common ALL antigen. In Grp A 16/36 pts had failed compared to Grp B 9/36. The median time to failure for Grp A was 28 months and disease-free survival in Grp B is 62%. The difference between the groups is not statistically significant, but the trend is apparent. Of the failures in Grp A, 15/16 relapsed; 11 in the bone marrow (BM) only, 1 in the central nervous system (CNS) and 3 in the BM/CNS. Of the 9 Grp B failures, 6 were relapses (3 BM, 1 testicle, 2 CNS). Four children died in remission: 3 of adriamycin cardiomyopathy and 1 of sepsis. Efforts to decrease toxicity involve prediction of cardiac toxicity by the measurement of the myocardial contractile state (methoxamine stress testing) and pharmacologic studies of ADR/ASP interactions. Further trials of therapy using high dose ASP for prolonged periods of treatment in childhood ALL appear warrented.

868 SPLENIC HYPOFUNCTION OF PATIENTS UNDERGOING BONE MARROW TRANSPLANTATION (BMT) Fredric T. Serota, Barbara Greenbaum, Sidney Heyman, Hasina Thawerani, Penelope A. Koch and Charles S. August, The Children's Hospital of Philadelphia, Department of Medicine, Philadelphia PA 19104

Five recipients of BMT at the Children's Hospital of Philadelphia developed late bacterial infections. This prompted us to review our clinical experience seeking evidence for splenic hypofunction in those and other patients (pts). Accordingly, we sought Howell-Jolly bodies (HJB) in peripheral blood smears of 29 pts; performed liver-spleen scans (LSS) in 9 pts with chronic graft-vs-host disease (CGVHD) and/or infection; and reviewed the spleens of 7 pts who died and had autopsies. In our series as a whole, 12 pts developed GVHD (5 acute; 2 chronic; 5 acute and chronic). 7/29 pts developed HJB; 4 of these had GVHD. Four pts receiving LSS showed decreased or absent splenic function; 3 had GVHD. The incidence of HJB or decreased function on LSS was not related to underlying diagnosis or preparative regimen. Lymphoid depletion was evident on all 7 spleens whose histopathology was reviewed: 2 showed total; 3 marked; and 2 moderately depleted lymphoid tissue. Our retrospective data suggest that splenic hypofunction is fairly common in the recipients of BMT, especially in pts with GVHD. Prospective studies performed at regular intervals after BMT will be necessary to define the true incidence of this condition and identify those pts who may need prophylactic antibiotic therapy.

869 FAMILIAL HISTIOCYTOSIS IN OFFSPRING OF ARTIFICIALLY INSEMINATED PREGNANCIES. David N. Shapiro and Raymond J. Hutchinson (Spon. by Ruth Heyn). Univ. of Michigan Medical School, Dept. of Pediatrics, Ann Arbor.

With new technology now available for "artificially" inducing pregnancy, responsibilities for the outcome of these pregnancies arise. We report the occurrence of fatal malignant histiocytosis in 2 siblings, the products of pregnancies resulting from insemination by the same sperm donor. The first, a female, became ill at 3 months of age with a constellation of clinical findings including fever, hepatosplenomegaly, pancytopenia, CSF pleocytosis and seizures, dying at 16 months of age. The second, a male, was conceived during his sib's illness which was felt not to be inherited. His illness, beginning at 2 months, was characterized by fever, hepatosplenomegaly, pancytopenia, CSF pleocytosis, and type IV hyperlipoproteinemia. Death occurred at 4 months from Pseudomonas sepsis. Viral cultures from multiple sites in both children were negative. Autopsies demonstrated massive hepatosplenomegaly and lymphohistiocytic meningeal infiltrates in each. The second sib had notable lymphohistiocytic infiltrate in liver and erythrophagocytosis in liver, spleen, and bone marrow. Both are thought to be cases of familial erythrophagocytic lymphohistiocytosis, a rare and frequently fatal disease, presumably transmitted in an autosomal recessive fashion. These cases illustrate the necessity of caution in utilizing the same sperm donor when one sib is affected with an unknown disorder, even if the problem is presumed not to be inherited. Until a diagnosis can be made with certainty, it may be more prudent to delay repeat insemination or to select a different donor.

870 CATHETER RELATED BACTEREMIA IN ONCOLOGY PATIENTS WITH INDWELLING BROVIAC CATHETERS. Eugene D. Shapiro, Kenneth N. Spiegelman, Ellen R. Wald, Kathy A. Nelson (Spon. by R.H. Michaels) Univ. of Pittsburgh School of Medicine, Children's Hospital of Pittsburgh, Dept. of Pediatrics, Pittsburgh

Nineteen children (median age 2 yrs) undergoing chemotherapy for malignancies had indwelling silastic Broviac catheters (BC) placed in the superior vena cava to provide vascular access. The BC were in place for a total of 85 patient-months (mean 4.5 mos/patient). There were 8 episodes of BC-related bacteremic infections (1 episode/10.6 patient-months). The infections occurred from 3wks-6 mos after BC insertion (median 7 wks). Presenting symptoms included fever in all cases (often associated with irrigation of the BC), chills, and peripheral vascular instability. The bacteremia was not associated with neutropenia or other foci of infection. The infecting organisms were Klebsiella pneumoniae (2), Staphylococcus epidermidis (2), Staphylococcus aureus, Pseudomonas aeruginosa, E. coli, Enterobacter cloacae, Candida tropicalis, and an unidentified gram-negative rod. Cultures drawn from the BC were positive in all cases and those drawn from a peripheral vein in 6/8 (75%). Antimicrobial therapy (Rx) alone without BC removal successfully cured the infection in 5 of 6 cases (83%). The one medical failure had bacteremia with 3 different organisms which cleared only after BC removal. One child with Candida infection had BC removal without antimicrobial Rx. One child had BC removal for reasons unrelated to infection. There were no other infection related complications. Most BC infections may initially be treated with antimicrobial Rx alone without BC removal.

871 ACYCLOVIR THERAPY OF PRIMARY VARICELLA IN LEUKEMIA. Stanford Shulman, Ram Yogev, Ron Keeney, and Elaine Morgan (spon. by Henry Nadler). Children's Memorial Hosp., Northwestern Univ. Medical School, Chicago, and Burroughs Wellcome Co., Research Triangle Park, North Carolina.

Acyclovir [9-(2-hydroxyethoxymethyl)guanine] is an acyclic nucleoside analogue with in vitro activity against herpesviruses including varicella-zoster virus. Acyclovir has had little toxicity except for occasional bullae secondary to drug extravasation. We report our uncontrolled experience with this agent in four children with acute lymphocytic leukemia in remission and disseminated primary varicella with involvement of liver, lungs, CNS, and evidence of myelosuppression and coagulopathy. Progressive organ dissemination of varicella was present in each patient, with new skin lesions in 2, despite three daily infusions of adenine arabinoside (Ara-A). Ara-A was discontinued and IV acyclovir begun at the dose of 500 mg/M^2 every 8 hours. Clinical improvement beginning within 24 hours of initiation of acyclovir with subsequent complete recovery following 7-10 days of drug occurred in 3 of 4 patients. The remaining patient, who manifested the most severe CNS, hepatic, and pulmonary dysfunction, ceased developing new skin lesions after acyclovir was begun but showed continued CNS and pulmonary deterioration with DIC, and died after three days. We observed no toxicity except for cutaneous bullae in one patient. This experience suggests that acyclovir may play a role in the treatment of disseminated primary varicella in immunocompromised hosts. Further controlled therapeutic trials with this agent are indicated.