888 HEMOLYTIC ANEMIA (HA) IN A CHILD WITH ADENOSINE DEAMINASE (ADA) DEFICIENCY. J. Kurtzberg, M. Haas, T. McManus, R. Schiff, C. Ingold, R. Buckley and M. Hershfield, Depts. of Pediatrics, Medicine, and Physiology, Duke University, Durham, N.C.

Selective lymphopenia and immunodeficiency are known clinical consequences of ADA deficiency (ADA-D) which also causes biochemical abnormalities in RBC's, notably a marked accumulation of dATP. In reported cases, RBC ATP has been normal or elevated. Decreased RBC survival has not been described. We studied a 9 month old girl with ADA-D who, at diagnosis, also had a heinz body (+) HA, with reticulocytosis and shaptoglobinemia. Her RBC's showed an increased tendency to lyse spontaneously in vitro, which was not corrected by addition of glucose. RBC ATP, measured on four occasions, was 0.5-0.81 umol/ml (controls=1.42±0.35), and the level of dATP 1.0-1.53 umol/ml (normally <0.002), with a ratio of ATP:dATP of 0.46-0.67. We have previously defined a mechanism by which accumulation of dATP causes ATP catabolism in ADA inhibited lymphoid cells in vitro. Moreover, in vivo treatment with deoxycoformycin (dCF), a potent ADA inhibitor, can result not only in dATP accumulation, but also in ATP depletion in RBC's, and in hemolysis. The occurrence in a patient with genetic ADA-D of both very low ATP:dATP ratio and hemolysis establishes that hemolysis is a consequence of ADA-D per se, and not of some effect of dCF unrelated to its inhibition of ADA. We conclude that ADA-D is among the inborn errors of metabolism, including pyruvate kinase deficiency and massively increased RBC ADA activity, that can cause HA due to ATP depletion.

● 889 IN VIVO EFFECTS OF β-CAROTENE ON ACTIVATED NEUTROPHILS. Joan E. Lafuze, Robert L. Baehner. Indiana University School of Medicine, Indiana University Hospitals, Department of Pediatrics, Indianapolis, Indiana.

Patients with gram negative sepsis may suffer neutropenia and respiratory distress associated with activation of polymorphonuclear neutrophils (PMN). Infusion with the synthetic analog of the bacterial chemoattractant N-Formyl-Methionyl-Leucyl-Phenylalanine (FMLP) causes a dramatic but transient neutropenia, hypotension and respiratory distress in rabbits. Employing this rabbit model, we have shown previously that pretreatment with vitamin E (vit E) accelerates the return of the absolute granulocyte count (AGC) and mean blood pressure (MBP) toward normal at 10 min but not at 5 min after FMLP infusion. To test the effects of another antioxidant β-carotene (BC) on neutrophil activation in vivo we pretreated rabbits with BC to raise plasma levels (test 1.1±.8ug/ml vs control .05±.06ug/ml p=0.02). When 0.5ug FMLP was administered iv AGC decreased (at 2.5 min % change was 34±1.3 control vs 25±10 test p=ns). By 5 min there was a significantly greater return of PMN to the peripheral circulation in the BC treated animals (% change 39.6± vs 61±5 controls $p < 0.04$). There was not a significant difference in % change of MBP between test and control animals at any time over the 30 minutes of monitoring. Thus, BC appears to be more effective than vit E in accelerating the return of PMN to the peripheral circulation following activation and may have therapeutic potential in diseases associated with PMN activation.

890 ROUTINE ULTRASONOGRAPHY FOR OVARIAN INVOLVEMENT IN ACUTE LYMPHOCYTIC LEUKEMIA PATIENTS AFTER DISCONTINUATION OF THERAPY. Daniel M. Lane and Robyn L. Birdwell (Spon. by Jack Metcoff), Langston Medical Clinic, and The Oklahoma City Clinic, Dept. of Radiology, Oklahoma City, Oklahoma.

Extramedullary recurrence after discontinuation of therapy has become an increasingly difficult management problem in childhood acute lymphocytic leukemia. Gonadal recurrence in males has been extensively studied, but in females has only recently received attention. Since January, 1982, the authors have routinely followed all female leukemics who have completed therapy with routine ultrasonography (non-invasive, non-ionizing) of the ovaries at 6 month intervals. All patients remained asymptomatic with no clinical evidence of recurrence until November,1983 when one patient (D.W.) demonstrated an enlarged right ovary (2-3x's) on routine sonography compared with six months earlier. Surgical resection confirmed the presence of leukemic infiltrate in the right ovary and tube with no evidence of dissemination in the bone marrow or spinal fluid.

The authors conclude that:

1) ovarian recurrence can be detected by ultrasonography prior to its becoming symptomatic; 2) the ovary may be a pharmacologic sanctuary as is the testis; 3) ultrasonography of the ovaries should be part of the routine follow-up examination in female leukemics off therapy.

891 EMOTIONAL STRESS AND STRESS RELATED BEHAVIOR IN ADOLESCENT SIBLINGS OF PEDIATRIC CANCER PATIENTS-PILOT, Paul R. Lund, E. Omer Burgert, Jr., R. C. Colligan, M. E. Grobe, G. S. Gilchrist, W. A. Smithson, V. Duffney, C. A. McCarthy, J. R. O'Fallon, and D. L. Betcher, Mayo Medical School, Department of Pediatrics, Rochester, MN.

Emotional stress and behavioral effects in the pediatrics cancer patient are well known, but the impact on their healthy siblings is not well defined. This pilot study used standardized tests for adolescents (aged 13-20)-Minnesota Multiphasic Personality Inventory (MMPI), Achenbach Behavioral Checklist (ABC), and Achenbach Self Report (ASR). A new comprehensive questionnaire (interview) was developed and its use with adolescent siblings explores their understanding, behavior, misconceptions, and past and present feelings about having a brother or sister with cancer. Adolescent siblings were identified from three groups of pediatric cancer patients: 1) with controlled cancer on active therapy; 2) with probable cured cancer off all therapy; and 3) with death more than 12 months prior to testing. Preliminary data show that the MMPI, ABC, and ASR are useful as a general indicator of emotional difficulty and maladaptive behavior. The new questionnaire brings out specific fears and concerns which may be troubling the sibling. Further use of this questionnaire (interview) is necessary to ascertain its value for younger siblings. From the three cancer patient groups their adolescent siblings are compared in regard to their coping, especially fears, concerns, and emotional adjustment.

892 VARIABLE SUPPRESSION OF IN VITRO GRANULOPOIESIS BY β-LACTAM ANTIBIOTICS. D.H. Mahoney, Jr., D. Clark, D.C. Anderson, S.L. Kaplan (Spon. by K.A. Starling) Baylor College of Medicine, Department of Pediatrics, Houston.

The effects of a number of β-lactam antibiotics (βL-A) on in vitro granulocyte/macrophage colony formation (CFU_{GM}) in the agar culture system were studied. Normal bone marrow mononuclear cells (BM-MNC) (2×10^5/ml) were cultured in 0.3% agar with peripheral blood leukocyte (10^6) underlayers. Dilutions of antibiotics were prepared in phosphate-buffered saline. The drug (0.1 ml) or buffered saline (0.1 ml) as a control was added directly to BM-MNC and plated with 0.3% agar. Drug dose survival curves were obtained. Studies were done in at least duplicate.

Drug	LD_{50}[a]	Drug	LD_{50}
Moxalactam	108 ± 28	Cefotaxime	200
Cefoxitin	166 ± 58	Ticarcillin	>500
Cefatriaxone	320 ± 148	Methicillin	>400
Cefaperazone	200	Penicillin G	>1000
Cefamandole	100	Penicillin G[b]	250

[a] LD_{50} = mean drug dose (μgm/ml) at which ≥50% suppression of CFU_{GM}. [b] Penicillin G stored at room temperature x 5 days.

Further studies of Moxalactam, with overnight incubation followed by washing of BM-MNC and culture, indicate that suppression did not appear to result from direct cytotoxicity. Decreased colony formation with "aged" Penicillin G suggests that degradation by-products may be the principal cause of in vitro suppression with this and other βL-A. This may have significance for the evolution of clinical neutropenia.

† 893 SPLENECTOMY IN SPHEROCYTOSIS: IS IT WORTH THE RISK? Catherine S. Manno and Alan R. Cohen (Spon. by Elias Schwartz) U of Pennsylvania School of Medicine and Children's Hospital of Phila, Dept. of Pediatrics, Philadelphia.

Splenectomy reduces the incidence of gallstone formation in patients with hereditary spherocytosis (HS). However, this surgical procedure carries an operative risk as well as the risk of postsplenectomy sepsis (PSS). Furthermore, gallstones do not always cause symptomatic biliary tract disease. Using decision analysis, a quantitative approach to problem solving under conditions of uncertainty, we have examined the relative merits of two approaches to patients with mild HS: (1) routine splenectomy in childhood or (2) cholecystectomy for symptomatic gallstones in adulthood. Probability values for critical events were obtained from the medical literature; final outcome is recovery or death. The analysis shows the risk of death associated with the choice of splenectomy to be 40 times greater than the risk of cholecystectomy for symptomatic gallstones (.0245 vs .0006). Sensitivity and threshold analyses show that the decision to avoid splenectomy remains unaltered even if the risk of death from PSS (.022) is reduced four-fold or if the risk of developing gallstones (including symptomatic and silent stones) is increased from .43 to 1.0. The choices become equivalent only if the risk of developing symptomatic gallstones increases from .08 to .50 while the risk of PSS falls from .022 to .001. On the basis of the best data currently available, the preferable course for patients with HS and mild anemia is careful surveillance for symptomatic biliary tract disease rather than routine splenectomy to prevent gallstones.