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**THE EFFECT OF PRENATAL ACETYL SALICYLIC ACID (ASA) INGESTION ON MATERNAL AND NEONATAL HEMOSTASIS.** M.J. Stuart, S.J. Gross, J.E. Graeber, F.R. Davey, M.T.

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The effect of prenatal ASA ingestion on hemostasis was investigated in 59 maternal-neonate pairs. Group I consisted of 36 control pairs in whom a negative ASA drug history was substantiated by normal maternal and neonatal platelet aggregations and values for the prostaglandin byproduct malonyldialdehyde (MDA). Group II consisted of 16 pairs in whom a positive history for maternal ASA ingestion was confirmed by the expected abnormalities in platelet aggregations and MDA. Group III comprised 7 maternal-neonate pairs where maternal ASA ingestion occurred within 6 hours post partum. All groups were evaluated for hemostatic abnormalities. Maternal blood loss was considered excessive, if a drop of >10% between initial and discharge hemoglobin occurred (vaginal delivery), or >25% (C section). In Group I, no maternal hemostatic abnormalities were noted, although 1/34 neonates demonstrated facial ecchymoses. In 10/16 Group II pairs where maternal ASA ingestion had occurred 0-5 days prior to delivery, clinical evidence of bleeding occurred in 90% (9/10) of the infants, and 60% (6/10) of the mothers. In contrast, in 6/16 Group III pairs, where ASA ingestion had occurred 6-10 days prior to delivery, no abnormalities were found. Group III infants were normal, although 57% (4/7) mothers in this group bled abnormally. ASA ingested in the 5 days prior to delivery, or immediately post partum, is associated with hemostatic abnormalities in both mother and neonate.

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**THE ROLE OF EOSINOPHILES IN GRANULOPOIESIS.** Kamran Tebbi, Adel Mahmoud and Samuel Gross, Case Western

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The role of eosinophiles in hematopoiesis is not clear. Despite the presence of eosinophilia in a variety of parasitic and other conditions, the leukocyte counts frequently are not elevated. This suggests a possible inhibitory effect of eosinophiles on granulopoiesis. This study was undertaken to examine the effects of eosinophiles on granulocytic colony forming units in culture (CFU-C) of mice bone marrow (BM). Marrow of normal as well as eosinophilic inbred C-57 black mice infected with *Trichinella spiralis* was cultured in semi-solid media with 1) anti-eosinophilic sera produced against mice eosinophiles in rabbit (AES), 2) the addition of purified eosinophiles, 3) colony stimulating activity (CSA), 4)  $\alpha$ -culture media, 5) normal rabbit serum, 6) eosinophilia extracts, and 7) irradiated eosinophiles. Each of the above experiments was repeated with and without added CSA. Addition of AES to BM cultures containing CSA sharply increased CFU-C levels in eosinophilic mice compared to CSA and rabbit serum (controls) alone ( $P < 0.01$ ), but had no effect on normal BM. Addition of increased numbers of eosinophiles significantly decreased the number of CFU-C in normal and eosinophilic mice ( $P < 0.01$ ). CSA was necessary to promote colony production and to enhance the effects of AES in eosinophilic mice. The results of this experiment suggest that eosinophiles have a suppressive effect on production of granulopoietic colonies and may indicate an inhibitory effect of these cells on total granulopoietic activity. This inhibitory effect of eosinophiles may be due to their high content of Prostaglandin E.

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**RECURRENCE OF PNEUMOCYSTIS CARINII PNEUMONIA IN PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA.** Kamran Tebbi and Samuel Gross, Dept. of Peds., CWRU,

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Patients receiving immunosuppressive therapy are at increased risk for pneumocystis carinii pneumonitis (PCP). However, recurrence of PCP is seldom documented. This report concerns recurrence of PCP in 2 patients with acute lymphoblastic leukemia (ALL) in continuous remission on maintenance therapy. An 8-year old girl, now 5 years post diagnosis, developed pneumonia on 6 occasions beginning 16 months post diagnosis. Lung biopsies x2 were diagnostic of PCP. A 14-year old girl developed 2 episodes of PCP, proven by open lung biopsy, at 19 and 36 months following diagnosis. One year later, she relapsed and died. Post mortem examination failed to show evidence of PCP. In both cases, PCP recurred despite adequate therapy of each episode and complete radiological clearing of the lungs. In the 8-year old, pulmonary function tests showed a decrease in all volume components, suggestive of a restrictive pattern without obstruction, presumably a sequelae of recurrent pneumonitis. On daily prophylaxis she remains disease-free. With combination chemotherapy and irradiation, many patients survive for extended periods of time. In children with ALL in continuous remission, PCP is a major cause of death due to infection (16-35% in various studies). Recurrent pneumonitis in immunosuppressed patients should raise a high index of suspicion of PCP, which, if identified following lung biopsy, should be treated and followed with continuous prophylaxis.

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**EB VIRUS AND HODGKIN'S DISEASE.** R.W. Veltri, W.C. Klingberg, J.E. McClung, B. Jones and P.M. Sprinkle,

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Two siblings with Epstein-Barr virus (EBV), heterophil negative lympho-proliferative disease are described. The sister presented first with heterophil negative infectious mononucleosis which was virologically confirmed EBV and which progressed to a fatal outcome. Cervical node biopsy revealed lymphocytes containing both EBV nuclear antigen (EBV-EBNA) and EBV early antigen (EBV-EA). At autopsy, there was widespread infiltration of spleen, lymph nodes, lungs and heart with lymphocytes demonstrating both of these EBV-coded antigens. Subsequently, her brother presented with a picture of disseminated lympho-proliferative disease which was serologically and virologically confirmed as due to EBV. T&A and cervical node biopsy were shown to harbor numerous EBV-EBNA and EBV-EA lymphocytes. A short period of improvement occurred to be followed by recurrence leading ultimately to re-evaluation. Cervical node biopsy followed by staging laparotomy demonstrated Stage III-B mixed cellular Hodgkin's Disease. In these specimens, there was again confirmation of the presence of EBV. X-ray therapy and multiple agent chemotherapy has been followed by remission of the Hodgkin's Disease. Concurrent studies of EBV serology reflects this fact also.

Details of the pathologic studies and EBV virus studies will be presented. It is postulated that in this child EBV virus can be implicated etiologically in his Hodgkin's Disease in a prospective study.

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**INCREASED COLONY STIMULATING ACTIVITY IN THE PLASMA OF A PATIENT WITH LYMPHOEPITHELIOMA METASTATIC TO THE LIVER.** Kamran Tebbi and Samuel Gross, Case Western

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Leukocytosis with predominance of polymorphonuclear leukocytes occurs in a variety of primary or metastatic hepatic tumors without apparent explanation. A 17-year-old male with lymphoepithelioma developed marked leukocytosis following the onset of liver metastases. In order to gain insight into the origin of the leukocytosis, granulopoietic colony stimulating activity (CSA) of patient's plasma and leukocytes were examined and compared to control. Leukocyte conditioned media (LCM) was prepared by the double layer culture method. The assay consisted of non-adherent marrow cells from normal individuals cultured in methylcellulose, fetal calf serum and  $\alpha$ -media. With the various CSA sources in this system, the number of granulocytic colony forming units (CFU-C) is proportional to the amount of CSA present and therefore allows for quantitative comparisons. The number of CFU-C produced with the patient's plasma was significantly higher ( $P < 0.001$ ) than those obtained from the patient's LCM or from control plasma or LCM. The size and distribution of colony type was similar irrespective of the source of CSA. Major sources of CSA in man are macrophages and monocytes. Thus identification of a stronger stimulatory activity in plasma as compared to LCM indicates the presence of a major new source of CSA in this patient. The fact that leukocytosis paralleled the onset of liver metastases suggests that a CSA derived from tumor products or secondary to hepatocellular damage may be responsible for this finding.

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**SUCCESSFUL BONE MARROW TRANSPLANTATION (BMT) FOR APLASTIC ANEMIA WITH AN HLA-MLC NON-IDENTICAL PARENT DONOR.** Phyllis Warkentin, Mark Nesbit, Peter Coccia,

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Successful BMT was performed in a 9 yr. old black female with severe idiopathic aplastic anemia from her HLA-MLC non-identical father. Initial Hgb.=3.8 gm.%, retic. count=0.1%, WBC=700 cmm., platelets=10,000 cmm.; bone marrow biopsy was markedly hypocellular with 85% non-hematopoietic elements. Tissue typing showed the patient to be HLA A-1 B-8, A-26 B-7; the father was HLA A-1 B-8, A-3 B-7. In mixed leukocyte culture (MLC), there was low but significant bidirectional (10%; 16%) stimulation. Cell mediated lympholysis demonstrated no significant killing. Pre-transplant preparation included Procarbazine 15 mg/kg/day x 3 days, antithymocyte globulin (ATG) 15 mg/kg/day x 3 days, and 750 rads of total body irradiation by linear accelerator. Cells from the donor ( $6.9 \times 10^8$ /kg) were infused intravenously. Graft versus host (GVH) prophylaxis following BMT consisted of IV Methotrexate weekly x 100 days and ATG and corticosteroids on days 7-21. By day 28 post BMT, cells of donor HLA type were present and marrow chromosomes were 100% XY. On days 29-31 mild GVH developed with fever, rash and slight liver enzyme elevations. Skin biopsy was consistent with GVH. Skin GVH resolved with Prednisone treatment. At 7 months post BMT peripheral counts are normal, however liver enzyme elevations persist. Marrow engraftment with minimal GVH in this patient should encourage further trials of BMT in patients without HLA-MLC identical siblings.