These preliminary results suggest that IAC with CDDP appears to be a sufficiently safe and effective therapy and should be considered in the treatment of various, large, unoperable pediatric tumors.

90.

ACTION OF METHOTREXATE (MTX) ON 5,10-METHENYL-TETRAHYDROFOLATE CYCLOHYDROLASE IN CELLS. F.Tzortzatou-Stathopoulou, M.Ziva-Petropoulou, S.Haidas, S.Grafacos, N.Matsaniotis, for the Oncology Unit of First Department of Paediatrics, University of Athens, Aghia Sophia Childrens Hospital Goudi, Athens, Greece.

The enzyme 5,10-methenyl-tetrahydrofolate cyclohydrolase is very important in the conversion of 5,10-methenyl-tetrahydrofolate to 10-formyl-tetrahydrofolate. This folate derivative plays a significant part in the biosynthesis of purines. A cytochemical method has been used to study a) the enzyme in cells of peripheral blood and bone marrow of patients with acute leukaemia and b)the action of MTX in vivo on the activity of the enzyme in leucocytes. The enzymatic activity of the myeloid cell line increased with maturation of the cells and was strongly positive in polymorphonuclear leucocytes and eosinophils. Blast cells were weakly positive or negative. These cells would be expected to contain more enzyme activity than was found as they are engaged in the active synthesis of DNA. Probably the enzyme appears in the blast cells at some stage of the cell cycle. On remission two populations of lymphocytes were found:One with low enzyme activity and a second with no enzyme activity. A reduction of enzyme activity was observed in the leucocytes of some patients treated with combination chemotherapy including MTX. MTX appears to be the cause of the diminution of the activity of this enzyme since the other cytotoxic drugs were shown not to influence the enzyme activity. The enzyme is a target for the action of MTX. Further investigation in necessary to determine the clinical significance of these findings.

91.

L-ASPARAGINASE INDUCED ANTITHROMBIN III AND ANTIPLASMIN DEFICIENCY AND HYPOFIBRINOGENEMIA IN CHILDREN WITH ALL DURING INDUCTION THERAPY
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Bleedings and thrombotic complications are a known side effect of asparaginase (asp) therapy.
20 children with newly diagnosed ALL received asp (E.coli; 3000 U/kg body weight) IV over 60 minutes four times q 3 days as phase II of the current induction protocol having completed four weeks of daily prednisone and weekly vincristine and adriamycin. The following coagulation tests were performed prior and 30 min. post each asp infusion: partial thromboplastin time (PTT), Quick's prothrombin time (Quick), thrombin time (TT), factors I, II, V and VII, fibrin degradation products (FDP's), antithrombin III (AT III), antiplasmin (AP) and heparin activity.
Under asp therapy there was a marked and increasing drop in plasma fibrinogen, AP and AT III activity. The other coagulation tests remained unchanged. On average the fibrinogen level was 100 mg/dl and the AT III activity 50% following the fourth asp infusion. This may explain sufficiently the increased bleeding and thrombotic complications seen under asp therapy.
As all patients were in remission when asp was applied the coagulation disturbance can only be explained by direct asp effect.

92.

CHANGES IN PLATELET FUNCTION INDUCED BY INTRAVENOUS GAMMAGLOBULIN IN PATIENTS WITH ALL IN REMISSION. H.Jürgens, R.vonKries, V.Wahn, A.András, U.Göbel, Pediatric hospital, University of Duesseldorf, Moorenstr. 5, D-4000 Duesseldorf, West Germany

To minimize the risk of viral infections a trial of intravenous gammaglobulin 150 mg/kg body weight every four weeks was performed with 45 children with ALL in initial remission under conventional maintenance therapy.
Reported here are changes in platelet function induced by intravenous gammaglobulin.
The following pattern of tests was performed in 15 patients with ALL under maintenance therapy prior and 15 minutes post a 45 minute infusion of intravenous gammaglobulin 150 mg/kg body weight: platelet count, thrombelastography, platelet retention to glassbeeds, ADP-, thrombin-, collagen- and ristocetin induced platelet aggregation, platelet factor 3 release, partial thromboplastin time, thromboplastin time, thrombin time, fibrinogen, factors II, V and VII, IgG, IgA and IgM.
No influence was seen on the plasmatic coagulation system. There was a minor drop in platelet count following intravenous gammaglobulin in some patients. Changes in platelet function test results were variable. One third of patients showed improved platelet function following intravenous gammaglobulin, a few patients developed a marked impairment of ADP and thrombin induced platelet aggregation whereas the remaining patients showed no notable changes. The observed changes in platelet function tests seemed to correlate with the serum IgG level. Patients with very low IgG levels tended to show improved platelet function following intravenous gammaglobulin, patients with higher IgG levels had disturbed platelet function following infusion.
