70.

PROGNOSTIC RELEVANCE OF CLINICAL STAGES AND HISTOLOGIC SUBGROUPS IN CHILDHOOD NON-HODGKIN LYMPHOMA (NHL). M.Gasparini, F.Lombardi, C.Gianni, F.Fossati-Bellani. Istituto Nazionale per lo Studio e la Cura dei Tumori, 20133 Milan, Italy.

A series of 79 consecutive children treated for NHL with the same intensive treatment regimen (polichemotherapy + bulky tumor site radiotherapy + CNS prophylaxis) was retrospectively evaluated to assess the prognostic value of histologic subtypes and of patterns of clinical presentation. Treatment response (97% complete remission rate) was not affected by histology or clinical stage. Burkitt type NHL was diagnosed in 35 of 79 (44%) and showed a peculiar clinical behaviour compared to the other histologic subtypes, and a significantly different survival rate. The staging system proposed by Ziegler and Magrath (Pathobiol.Ann.,1974) applied to burkitt type NHL showed some usefulness in predicting the final outcome. For what concerns the 44 children belonging to the other histologic subgroups, 26 were diagnosed as having convoluted cell type NHL, and 6 as lymphoblastic unspecified NHL. Four children belonged to rarer histologic subgroups, and 8 could not be properly classified. No differences in terms of relapse-free survival and survival were observed among these histologic subgroups. The clinical stage we adopted permitted to distinguish subsets with different prognosis. We concluded that Burkitt type NHL are a unique disease which deserves a particular treatment strategy. As far as NHL belonging to other histologic subgroups are concerned, treatment should be differentiated according to the clinical stage.

71.

RATIONALS, CONCEPT AND EARLY RESULTS OF THE ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) THERAPY STUDY BFM 81. G.Henze, H.-J.Langermann, H.Riehm, for the BFM study group. Dept.of Pediatrics, Free University, D-1000 Berlin, FRG.

Multiparametric analysis of patient data from study BFM 70/76 revealed indicators of the leukemic cell mass (peripheral leukemia cell count <LCC>, liver <L> and spleen <S> enlargement in cm below costal margin) to be most relevant prognostic factors. A risk factor

$$RF = 0.2 \times \log (LCC + 1) + 0.06 \times L + 0.04 \times S$$

with weighted contribution of these parameters forms the basis for patients' (pts) stratification in respect to therapeutic intensity. Because of their poor response to commonly used ALL-therapy pts with B-ALL are treated with an experimental protocol and therefore excluded from stratification by RF. The expected distribution of pts in 3 risk groups: standard risk (SR:= RF < 1.2), median risk (MR:= 1.2 <= RF < 1.7) and high risk (HR:= RF >= 1.7), is 65 : 25 : 10. Questions of the study are:

1. Is adaptation of treatment intensity capable of producing similar continuous complete remission (CCR) rates (about 80%) for all risk groups (retrospective test)?
2. Will in SR pts combined I.T. and intermediate dose I.V. methotrexate (500 mg/m^2) replace irradiation of the central nervous system (CNS) without any disadvantage (randomisation 1 : 1)?
3. Will shortening of the total duration of therapy from 24 to 18 months be possible for all pts (randomisation 1 : 1)?

Between April 1, 1981, and April 30, 1982, 259 pts aged 0 - 18 years from 34 institutions have been registered on study. Four pts died before onset of treatment. 155 (63%), 73 (30%), and 18 (7%) pts were allocated to groups SR, MR, and HR. B-ALL was diagnosed in 9 pts. 5/246 non-B-ALL pts died during remission induction. Six pts died in CCR. One pt did not respond to therapy and none relapsed in this group. In B-ALL pts 1 pt did not achieve remission, one died in CCR and 3 relapsed, two of them in the CNS and 1 in the bone marrow. These results have to be confirmed by longer observation periods.

72.

GRANULOCYTE AND PLATELET SUPPORT DURING INDUCTION THERAPY OF CHILDHOOD ALL. W.Schmidmeier†, P.Höcker†, H.Gadner†, M.Kundi×+St.Anna Children's Hospital, A-1090 Vienna, *Intensive Blood Bank, University of Vienna, ×Institute of Enviromental Hygiene

The platelet and granulocyte transfusion requirements of 49 patient with ALL during induction therapy (BFM-protocol) were studied. 31 children (63 %) required support of platelets and/or granulocytes. Indication for platelet support was a platelet count below 20.000/µl with supposed or manifest hemorrhage. Granulocyte concentrates were given below 200/µl, when bacterial infection was proven or strongly suspected. Comparing the support group with the no-support group (18 Pts.), the following differences were found: patients in the support group - predominantly females with c-ALL - had significantly higher initial leucocyte and blast cell counts. Their platelet counts were significantly lower. A discriminance analysis was performed. Taking into account sex and age, immunological subtype, initial cell counts, spleen and liver size, a prediction regarding transfusion requirements could be made in 76 %.

73.

CHILDHOOD PRE-B CELL LEUKEMIA RESPONDS LESS WELL TO THERAPY. W. Crist, M. Roper, J. Jackson, J. Pullen, B. Humphrey, J. Boyett, R. Metzgar, J. van Eys, J. Falletta, M. Cooper for the Pediatric Oncology Group, St. Louis, MO., USA.

Clinical and laboratory features were analyzed for a large group of newly diagnosed pediatric patients with acute lymphocytic leukemia (ALL). ALL of pre-B phenotype, characterized by lymphoblasts (>10%) containing cytoplasmic IgM but undetectable surface immunoglobulin, was diagnosed in 83 such patients. The incidence of pre-B cell leukemia in 311 completely studied ALL patients was 18.3%. Mean age, presenting WBC count, male/female ratio and incidence of mediastinal mass in patients with pre-B leukemia were not significantly different from these parameters in patients with non-B non-T cell disease (n=208), but were significantly lower than in patients (n=75) with T-cell disease (>40% rosetting blasts and/or peripheral T antigen positivity). A significantly higher percentage of pre-B as compared to null cell patients were black (p=.04), and the incidence of pre-B cell leukemia was significantly increased in blacks (p=.02). PAS negativity and acid phosphatase paranuclear staining occurred more often in T cell than in non-B non-T or pre-B patients (p<.01). Morphologic classification by FAB criteria was not discriminatory. Common ALL and HLA-DR antigens were detected on most pre-B and non-B non-T leukemias. Forty-one pre-B patients had successful Giemsa banding and none had the 14q+ or other distinguishing cytogenetic abnormality. Initial response to therapy was excellent for all groups, but disease-free survival was significantly poorer, even after adjusting for age and WBC, for pre-B as compared to non-B non-T patients treated in the same manner (p=.02). These results suggest that, although pre-B and non-B non-T ALL are indistinguishable by clinical and most laboratory tests, the recognition of the pre-B phenotype permits identification of a significant subgroup of common ALL that appears to have a worse prognosis.

74.

POOR PROGNOSIS IN INTERMEDIATE PRE-B/B-ALL. ˆP.Paolucci, ˆG.Paolucci, ˆF.Munizza, ˆV.Vecchi, ˆF.Vivarelli, ˆA.Mancini, ˆ=M. Gobbi, for ˆSection of Haematology/Oncology, Department of Pediatrics and ˆInstitute of Haematology, University of Bologna, Italy. Supported by CNR, PFCCN n.80.01605.96 115.12574-Rome.

We describe one case of ALL having, at the onset, both pre-B leukaemic cells(30%) and an additional subpopulation(28%), identical in cytoplasmic µ staining characteristics, but smaller in size and bearing amounts of surface µ. The leukaemia cells expressed DR antigens(80%), had low levels of nuclear Tdt, were negative for HuTLA, OKT3, sheep-E rosettes and expressed little c-ALLA(10%). No mediastinal mass and CNS involvement were present, but enlargement of lymph nodes, liver and spleen were observed. As the WBC count was 10×10^5/mmc. and the age of one year she was placed on a high risk leukaemia chemotherapy intensive protocol(AIEOP 7903 A). She achieved complete remission at the 14th day, but relapsed in treatment after two months and the blood and bone marrow leukaemia cells expressed the same phenotype we observed at the onset of the disease, with a greater proportion of pre-B cells(38%) and of intermediate pre-B/B cells(50%). One month later she died without achieving second remission. The poor prognosis of this case greatly differs from the cases reported by Vogler et al.(1981), suggesting that intermediate pre-B/B ALL may also express stages of maturation closer to B ALL than to common ALL and require more intensive therapy. Interestingly, virtually no sIgM, sIgG, sIgA, sIgD and light chains were present when the cells were analised in suspension preparations, but sIgM$^+$cells were clearly identifiable when surface-stained cells were sedimented onto glass slide by cytocentrifugation.