75.

RECEPTORS FOR PEANUT AGGLUTININ IN THE IMMUNOLOGICAL SUB-GROUPING OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA (ALL).
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Childhood ALL is composed of subgroups defined by immunologic markers and certain markers are known to have prognostic significance. Null cell ALL is the largest subgroup and additional markers are needed to identify patients at increased risk of early relapse within this non-T, non-B category. We have used a direct immunofluorescence assay to identify the presence of receptors for the lectin peanut agglutin (PNA) on blasts from 26/46 (63%) of our null cell ALL patients and have subsequently noted a high rate of relapse (17/26) in this PNA+ group. Relapse has occurred in only 5/20 patients whose blasts lacked the PNA receptor. The PNA+ and PNA- groups were comparable in clinical features (i.e., age, leukocyte count, follow-up times) and the striking difference in relapse rate was correlated only with the presence of receptors for the lectin ($p<0.01$). PNA receptors are commonly found on fetal thymocytes but not on mature peripheral lymphocytes except after neuraminidase treatment. SDS-PAGE analysis of NaB^3H_4-galactose oxidase labelled solubilized cell membrane extracts revealed a 68,000 dalton glycoprotein found only on PNA+ ALL lymphoblasts. Neither PNA- blasts nor PNA+ normal thymocytes expressed this component. The lectin PNA seems to define a high risk group of null cell ALL patients and to be associated with a specific cell membrane component.
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76.

NEWER MODES OF TREATMENT IN CHILDHOOD ALL.
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All children, suffering from leukaemia are treated in Hungary by one of the 10 centres participating in the Working Party. In the early 70-ies, treatment results improved as a result of CNS prophylaxis. No further improvement was seen however, despite efforts to establish new approaches. As from 1980 VCR-DR-Pred and daily Asp have been used in remission induction while CP and Ara-C in the consolidation phase. Remission rate rose and preliminary analysis of CCR is encouraging.

In 1981, 54 new patients with ALL were started on a new protocol, which in addition to the above cytostatics employs medium-dose MTX and for high-risk cases a 2 week combination of Ara-C and VM-26. Remission rate and early treatment results are promising, and so far the ratio of complications and side effects remains very low according to a close neurological survey of all patients.

77.

OUTCOME OF CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) IN INITIAL RELAPSE: RELATIONSHIP TO TYPE OF RELAPSE, PROGNOSTIC FACTORS, AND TREATMENT.
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From 1975-1981, the CCSG entered 3514 children with ALL into five treatment protocols. We recently reviewed the subsequent treatment and outcome of those children who had an initial relapse in the marrow (499), central nervous system (150) or testes (66) while still on therapy. The treatment for patients with relapse in the CNS or testes was local treatment to that site plus reinduction followed by reconsolidation and remaintenance chemotherapy. Patients who had an initial relapse in the marrow were treated on specific relapsing ALL protocols. Recently some patients with an initial marrow relapse and with a suitable sibling donor have received a bone marrow transplant (BMT). Comparing the outcome of those children with initial relapse in the marrow, testes and CNS, there is a highly significant difference ($p<.0001$). The life table survival at 3 years from time of initial relapse is: marrow-7%, testes-36%, CNS-39%. Within each of these groups there is heterogeneity of outcome that can be partially explained by prognostic factors. For marrow relapse, the duration of initial remission and age at diagnosis are the most important factors. For extramedullary sites, the important factors are duration of initial remission and these characteristics at the time of original diagnosis: age, white blood count, presence of mediastinal mass, and hemoglobin level. Outcome for the 21 children who received BMT shows that at one year from transplant the life table survival is 32% and at two years is 29%. Of the 5 children with current follow-up of one year or more from BMT, one has died. Longer follow-up will be necessary to assess whether a "cure rate" in the range of 20-25% is achieved with BMT. If so, this would be an improvement over conventional treatment of initial marrow relapse.

78.

FATE AFTER OCCULT TESTICULAR RELAPSE (OTR) IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA (ALL): THE ROLE OF TESTICULAR BIOPSY.
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Cessation of therapy after 3 years of continuous complete remission (CCR) is associated with a bone marrow (BM) relapse rate of 10-20%, higher in males than females, and a testicular relapse (TR) rate of 10-40%. In CCG 101/143, 15% of boys developed OTR off therapy, of whom 55% remained in BM remission with a median follow-up of 50 mos. The purpose of this study was to 1) determine the incidence of OTR after 3 yrs. of CCR; 2) identify males at risk of OTR off therapy; and 3) prolong subsequent disease-free survival of boys with OTR. Of 465 boys entered on CCG 141 between 1975 and 1977 and achieving CR, 261 (56.1%) were in CCR at 3 yrs. Two hundred thirty-five underwent open wedge testicular biopsy; 26 refused biopsy.

Isolated OTR was detected in 26 boys (11.1%). Two had concomitant BM relapse. None were in the poor prognostic group (initial WBC>$50x10^9/\ell$), and no other distinguishing clinical features (age, FAB morphology, lymphoma syndrome, massive splenomegaly, hemoglobin and immunoglobulin levels, day 14 BM) were associated with OTR. Treatment consisted of testicular radiation, systemic reinduction, CNS prophylaxis with intrathecal methotrexate, and maintenance therapy for 3 yrs. Of the 26, 20 (77%) are in CCR 12 to 34 mos. after OTR, 4 are alive after BM relapse, and 2 died 22 and 24 mos. after TR. Overt TR occurred 8-26 mos. off therapy in 6 boys (2.6%) with presumed negative biopsies at 3 yrs. of CCR; 3 were isolated, 3 had concomitant BM relapse. All were given local and systemic therapy and are alive 8-35 mos. after TR. In conclusion, open wedge testicular biopsy after 3 yrs. of CCR identified males with OTR which can be effectively controlled with local radiation, systemic reinduction and maintenance therapy, and CNS prophylaxis.

79.

MORPHOLOGIC FINDINGS IN OCCULT TESTICULAR RELAPSE IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA.
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Cessation of therapy after 3 years continuous complete remission (CCR) is associated with a testicular relapse (TR) rate of 10-40%. To determine the incidence of occult TR at the 3 year endpoint in CCG-141 all eligible boys were subjected to open wedge testicular biopsy. Occult TR was detected in 26 boys (11.1%) who subsequertly were effectively treated with testicular irradiation, further chemotherapy and CNS prophylaxis therapy.

The morphologic criteria for leukemic involvement applied in the CCG pathology review were derived from a systematic light and electron microscopic study of CCG-141 patients treated at Columbus Children's Hospital. No satisfactory accounts of the developmental changes in the prepubertal human testes were available. In particular, the origins of several immature-appearing cell populations within the interstitium were obscure and led in several early instances to an erroneous diagnosis of leukemic involvement. Ultrastructurally we have shown these cells to be components in the maturation sequence of the Leydig cell. Each has distinctive ultrastructural features and is distinguishable from a lymphoblastic cell.

Occult testicular leukemic (OTL) involvement in CCG-141 was present usually as a variably dense, diffuse interstitial