

infiltrate. Occasionally OTL was limited to a single lobule. Rarely only small numbers of lymphoblasts were identified, typically grouped around capillary vessels. The latter findings support extension of the biopsy-taking to several sites rather than the single testicular biopsy(bilateral) now taken. Overt TR occurred 8-26 mos. in 6 boys after negative testicular biopsies at 3 yrs. of CCR. More extensive biopsying may have permitted earlier recognition of OTR. Very little evidence of therapy-induced changes in either the interstitial or tubular components was found in this study.

80.

**HANDMIRROR CELLS AND CENTRAL NERVOUS SYSTEM RELAPSE IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA.**  
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Handmirror cell (HMC) percentages of washed lymphoblasts were counted in cyto centrifuge-preparations of thirty-three children with acute lymphoblastic leukemia (ALL). Nine children developed a central nervous system (CNS) relapse; all nine had a HMC-percentage less than 10 %. From the other twenty-four children without such a relapse only nine had a HMC-percentage less than 10 %. This difference is statistically significant (Wilcoxon:  $p < 0.001$ ). CNS-relapse was also correlated with a high initial white bloodcell count ( $p < 0.01$ ) and T-ALL ( $p < 0.05$ ). It appears that HMC-percentage in cyto centrifuge-preparations is more reliable than in bone-marrow smears. Our conclusion is that a HMC-percentage less than 10 % in ALL might be a prognostic factor for the development of a CNS-relapse.

81.

**CHANGES IN THE MONAMINE METABOLITES IN THE CEREBRAL SPINAL FLUID OF CHILDREN WITH ALL**

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A pilot study was carried out to investigate Monoamine metabolites in CSF of children with ALL. The main objectives of this study were:

- 1) To examine inpatient and outpatient's variations in the Monoamine metabolites (5-HIAA and HVA).
- 2) To study the correlation between the behavior status of these patients and the metabolites levels in the CSF.
- 3) To examine the relationship between the clinical status of the patient and the CSF level of metabolites.

#### Methods and Results

The CSF samples were collected under identical conditions by LP. The samples were analyzed by High Performance Liquid Chromatography using electro-chemical detector. A reverse phase C<sub>18</sub> (5 $\mu$ ) column was used for the analysis. The CSF samples were run directly on the column using 50  $\mu$ l or 100  $\mu$ l depending on the concentration.

Over 50 cerebral spinal fluids have been analyzed so far and wide variations between subjects are seen as also variations between samples from the same patient collected at different intervals. In view of the postulated role for catecholamine in learning, memory, affect and emotional behavior in man and animal, it appears from the preliminary data that the study may be of potential value in understanding the biochemical changes in these patients. It may also help to correlate with the behavior and intellectual functions. A prospective study is being undertaken at the present time.

82.

**SERUM COPPER AND ZINC VALUES AND COPPER/ZINC RATIO IN ACUTE LEUKEMIA AND RELATION TO PROGNOSIS**  
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Serum Cu and Zn levels and Cu/Zn ratio were measured in 69 cases with acute leukemia. The mean

serum Cu level of the controls was  $178.2 \pm 55.0$   $\mu$ g %; it was  $275.8 \pm 76.0$   $\mu$ g % in acute lymphoblastic leukemia (ALL) and it was  $220.8 \pm 39.3$   $\mu$ g % in acute myelomonoblastic leukemia (AMML). The mean serum level of Cu in untreated leukemic children was significantly higher than the controls ( $P < 0.01$  and  $P < 0.001$ ). Serum Cu levels decreased to normal values in ALL and in AMML in remission. These concentrations were significantly lower than values in untreated stage ( $P < 0.001$ ). The mean serum Zn level of the controls was  $112.7 \pm 26.5$   $\mu$ g %, it was  $81.5 \pm 28.0$   $\mu$ g % in ALL and it was  $79.5 \pm 30.7$   $\mu$ g % in AMML. The mean serum level of Zn was significantly lower in untreated leukemic children than the control group ( $P < 0.001$ ). Serum Zn levels reached to normal values in remission. The mean Cu/Zn ratio in controls was  $1.7 \pm 0.8$ . The mean Cu/Zn ratio in ALL and in AMML were  $3.80 \pm 1.50$  and  $3.12 \pm 1.31$  respectively. The mean Cu/Zn ratio decreased in remission  $1.4 \pm 0.4$  in ALL and  $1.86 \pm 0.5$  in AMML ( $P < 0.001$ ). The relationship between serum Cu and Zn levels and prognosis was also investigated. The patients who have normal serum Cu levels in pretreatment stage have good prognosis. Patients with serum Zn levels lower than 70  $\mu$ g % seem to have shorter survival rate in ALL.

83.

**SIGNIFICANCE OF CYTOGENETIC STUDIES IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA (ALL).** M. WYSS, Ch. WERNER-FAVRE, Ch. CABROL, J.-F. BABEL, V. von FLIEDNER, from the Clinic of Pediatrics and the Institute of Medical Genetics, University of Geneva (Switzerland).

Cytogenetic studies were performed in 22 children with ALL (October 1979 to April 1982). 20 cases were classified by immunological markers. 3 high risk ALL patients over 22 had striking chromosomal abnormalities, 2 at diagnosis and relapse, the third one only at relapse.

Case 1: non B non T ALL - 47,XY,-9,+8,inv(5),+mar.  
Case 2: pre-B ALL - 47,XY,-8,-11,+X,+i(8q),+mar.  
Case 3: non B non T ALL - 46,XX,ring 1/-18

These 3 patients had early hematological relapses.

2 ALL children showed a congenital chromosome abnormality. In the first case, a pericentric inversion of chromosome 11: inv(11)(p15q13) was seen and discovered to be present in 5 other members of the family over two generations. In the second case, the presence of a congenital ring chromosome 21: 46,XX,r(21) was considered to result from a "de novo" mutation. The possible relation between congenital chromosome anomalies and a predisposition to neoplasia raises the question as to whether the association is fortuitous or has causal implications. No chromosome abnormalities were seen in the karyotypes of the 17 remaining patients.

These data seem to corroborate recent works showing that the karyotype alone, may have prognostic value.

84.

**TREATMENT OF ACUTE NON LYMPHOCTIC LEUKEMIA (ANLL) WITH HIGH DOSE CYTOSINE ARABINOSIDE (AC) AT MAXIMUM RECRUITMENT INTERVALS.** J.A.J.M.Taminiau, L.A.Smetts, H.Behrendt, P.A.Voûte, Emma Kinderziekenhuis and Netherlands Cancer Institute, Spinozastraat 51, 1018 HJ Amsterdam, The Netherlands.

5 patients with acute non lymphocytic leukemia were treated with AC  $1000 \text{ mg/m}^2$  i.v. push at 12 consecutive days at maximum S-phase following recruitments. Recruitment time was estimated by flow cytometry and varied between 24-36 hours in individual pats. Bone marrow aspirates were done at expected time intervals after one AC dose estimated on initial % S-phase cells. A straight line could be drawn correlating the initial S-phase cells with the maximum of recruitments induced by the first injection. AC was followed by 1 or 2 Adriamycin (AC) doses  $40 \text{ mg/m}^2$  i.v. to turn off recruitment as expected to be initiated after each AC dose and to kill residual cells unresponsive to AC treatment.

Total expected tumour burden:  $10^{12}$  would be eliminated in 12 doses (1 log each dose). All primary patients went into haematological remission: 1 patient with myelofibrosis who did not respond to AC but to AD died; 1 patient had a first relapse (relapse 5+ months) when entering this protocol. Bone marrow aplasia persisted for 2-3 weeks with full recovery and maintained remission for 6-7 months, with repeated half treatment courses (6 x AC, 1 x AD) every 6 weeks. Duration of bone marrow aplasia after each treatment course was 1-2 weeks. We conclude: complete remission can be obtained with one treatment course and maintained with full haematology recovery and good physical performances.