Lym 04**RECOGNITION OF RELAPSES OF PATIENTS WITH MALIGNANT LYMPHOMAS: EFFICIENCY OF DIFFERENT METHODS**
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The study is based on the observation of 584 patients (pts) with malignant lymphomas (Morbus Hodgkin 248, Non Hodgkin Lymphoma of favorable histology 203, of unfavorable histology 133), who had regular follow up's from 1974-1983. 315 of these pts attained a complete remission (169, 64,82 respectively). 108 pts suffered from a relapse (61,22,25). 68% of these pts had symptoms directing to the relapse (62,77,76%). 33% palpated the tumor themselves (36,41,20%). 20% showed specific symptoms like local pain or lymphedema (13,13,44%). 15% suffered from general symptoms like B-symptoms (13,13,12%). Regarding the 32% of the pts without symptoms: the relapse was diagnosed by clinical examination in 10% (11,9,8%). The routinely taken chest x ray showed the relapse in 8% (10,9,4%), the sonography in 7% (10,5,4%). In 6% the relapse was discovered by other investigations (7,0,8%). At the time of the relapse the following laboratory findings were striking: 49% of pts with M. H. had a leucocytosis, in 70% an elevated ESR, in 58% the alpha-2-globulin fraction was increased over 10%. Pts with unfavorable NHL showed in 60% an elevated ESR and LDH, in 46% the alpha-2-globulin fraction was increased. Our study shows that the history and the clinical examination are the most important parameter recognizing a relapse. Chest x ray and sonography show only in 8 or 7% the relapse. The laboratory findings are less important except the ESR, the LDH and the alpha-2-globulin fraction.

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Lym 05**ROSETTE INHIBITING FACTOR (RIF) PRODUCED BY HODGKIN-CELL LINES**

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Decreased SRBC-rosette formation of peripheral T-cells is a well known phenomenon in Hodgkin's disease. From extracts of involved spleens of Hodgkin's disease (HD)-patients a rosette inhibiting factor (RIF) has been detected and related to the low-density lipoprotein (LDL)-fraction (Bieber et al., Clin. Exp. Immunol. 29 (3), 365, 1977). We could demonstrate a similar RIF-activity in the supernatant of the in vitro HD-tumor-cell-line L428 (Schaadt et al., Int. J. Cancer 26, 723, 1980). Peripheral T-cells from healthy donors show a significant decrease (30-50%) in SRBC-rosette formation after preincubation (60 min, 37°C) with HD-cell supernatant. Rosetting of T-cells from HD-patients, which is impaired in comparison to normal T-cells, could not be further decreased by incubation with L428 supernatant.

Blocking-tests did not show interference of RIF with OKT 11 at the binding site. RIF is stable after 30' 56°C heating, by 100°C heating the activity is destroyed as well as after trypsin treatment. Stable storage of a RIF-solution is possible at -80°C, at higher temperatures the activity decreases. Lyophilisation did not affect the activity. Optimal inhibition could be shown at pH 7, at more acidic pH levels the activity decreased rapidly. After passage over a Biogel A 0,5 column RIF activity can be identified at 100 KD, 50 KD and 25 KD. By ion-exchange chromatography RIF activity appears at a concentration of 0,38-0,43 mol NaCl. By ultracentrifugation with and without addition of serum LDL we could demonstrate in contrast to the findings of Bieber and coworkers that RIF is not represented in the LDL-fraction, but is capable to bind to LDL.

We conclude from these data, that the rosette inhibiting activity generated by the in vitro HD-lines is very similar to that detected in HD-spleen extracts.

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Lym 06**REARRANGEMENTS OF T CELL RECEPTOR GENES AND EXPRESSION OF HIGH AFFINITY IL-2 RECEPTORS IN AN EBV TRANSFORMED B CELL LINE**

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An EBNA positive B-cell line (GL 134) was established from bone marrow cells of a 43-year-old patient with advanced Hodgkin's disease. These cells are EBV non-producers and express the B-cell marker B-1. In addition to a functional rearrangement of Ig-genes and expression of surface IgM/λ, GL 134 cells show rearrangement but no expression of the chain genes of the T cell antigen receptor. Thus, this cell line, although phenotypically a mature B-cell, has a mixed T/B cell genotype. Further, this cell line constitutively expresses low levels of IL-2 receptors. Treatment of GL 134 with PMA not only resulted in an increase of Tac-positive cells but also enhanced Tac-antigen density on cells already positive stained with anti-Tac MoAb. IL-2 treatment also enhanced the expression of Tac-binding sites on positive cells, whereas both interferon-γ and PHA had no effect. The expression of high affinity IL-2 receptors on GL 134 cells and the enhancement of IL-2 receptor by PMA was confirmed by 1.) specific binding of ¹²⁵I-IL-2; 2.) IL-2 absorption studies and 3.) Northern blot analysis. These data reveal that GL 134 expresses an average of 1000 and 3000 high affinity receptors/cell (kD = 10¹¹) when unstimulated and upon PMA-stimulation, respectively. Although GL 134 cells are capable to proliferate in the absence of IL-2, the enhanced growth rate in the presence of IL-2 indicates that IL-2 exerts functional activity.

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Lym 07**OLIGOCLONALITY OF NON-HODGKIN'S LYMPHOMA ESTABLISHED BY ANALYSIS OF IMMUNOGLOBULIN GENE REARRANGEMENTS**

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Rearrangements of immunoglobulin- (Ig) and T-cell receptor (TCR) genes have been shown to be specific and sensitive markers for lymphoid tumors of T- or B-cell lineage. We here report a case of a centrocytic-centroblastic Non-Hodgkin's lymphoma (NHL) with involvement of the liver and the bone marrow. Interestingly, focal conversion into a more aggressive centroblastic cell type was found in circumscribed areas of the spleen. We extracted the DNA from bone marrow and four macroscopically different sites of the spleen (A,B,C,D). The DNA was examined by Southern blot analysis using ³²P-labelled cDNA probes specific for the Ig heavy chain J region genes (J_H) and the TCR β-chain gene (T_β). Hybridization of EcoR I digested DNA with the J_H-probe DNA revealed the germline 17 kilobase pair (kb) fragment and one clonally rearranged fragment of 4.2 kb in all five biopsy specimen. Two additional bands were observed at 22.3 kb and 7.9 kb in A, indicating the existence of a second distinct neoplastic B-cell clone at this site. In D and in the bone marrow yet another additional 2.0 kb fragment occurred indicating a third entity type of B-cell tumor. The existence of 3 distinct B-cell tumors was confirmed by Southern blot analysis of Ig light chain gene rearrangements using C_κ and C_λ cDNA probes. In addition, using the T_β-chain cDNA probe we also observed clonal TCR gene rearrangements in all biopsy-sites investigated. These TCR rearrangements may either represent a separate neoplastic T-cell clone or, more likely, result from aberrant DNA rearrangements in the neoplastic B-cell clones.

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