

survival and patterns of relapse. The DFP was 65 months for the Tonsillar and 92 for the non-Tonsillar group. The median survival was 86 months for the first, while it has not reached yet in the second group. The most common site of relapse was GI tract in the Tonsillar group (7 out of 21 cases) and CNS in the non-Tonsillar NHL (4 out of 14 cases).

**Conclusion:** The most common site of HN-NHL is tonsil. The vast majority of HN-NHL are presented in early stages and belong to aggressive histology. Tonsillar NHL have rather different clinical behaviour and should be considered as distinctive and separate entity.

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POSTER

### Primary gastrointestinal lymphoma: Long-term follow-up of 75 patients treated in 2 German centers

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The gastrointestinal tract is the most common site of extranodal lymphomas. We present long-term follow-up data of 75 patients with primary gastrointestinal Non-Hodgkin's lymphoma (GI-NHL) treated in two German centers. The median age was 63 years, range 28–85. 60% of patients had high-grade NHL. The median tumor diameter was 9 cm. Major treatment options were limited surgery and/or radiotherapy in localized low-grade GI-NHL with or without chemotherapy. The mainstay of the treatment was chemotherapy in all stages of high-grade GI-NHL. 10-year overall survival rate was 57%. Patients with gastric lymphoma had a better prognosis (10-year survival rate 73%) than patients with lymphoma of other sites of the gastrointestinal tract (10-year survival rate 44%). Bleeding or perforation rarely occurred during chemotherapy without lethal consequences. Patients with high-grade as well as low-grade gastric lymphoma had an excellent prognosis if they achieved a complete remission at any time of their treatment (10-year overall survival rate >90%). Patients who could not achieve a complete remission had a much worse prognosis (4-year overall survival rate 14%) irrespective of the malignancy grade of their lymphoma. These results suggest that GI-NHL have a different clinical course than their nodal counterparts and the achievement of a complete remission should be a therapeutic goal even in low-grade GI-NHL.

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POSTER

### Secondary tumors in longsurvival patients with Hodgkin (HDK) disease

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**Purpose:** We report our experience of secondary tumors in the series of patients seen in our hospital between January 1967 and December 1995.

**Methods:** We review the medical records of 486 patients with HDK followed in our hospital and the type of secondary tumor, period of presentation and mortality of the group were analyzed.

**Results:** Forty six second tumors were found. Leukemia and myelodysplastic

Tumor type	N° (%)	<5 years	5–10 years	>10 years	Mortality
Leukemia/MDS	12 (26)	4/4	6/6	2/2	12/12
Lymphoma	7 (15)	1/3	2/2	1/2	4/7
Lung ca	7 (15)	0/1	3/3	1/3	4/7
Breast ca	7 (15)	–	1/1	2/6	3/3
Sarcoma	6 (14)	2/2	2/3	0/1	4/6
Others	7 (15)	1/2	1/3	1/2	3/7
Total	46 (100)	8/12 (35%)	16/18 (36%)	7/18 (38%)	31/46 (67%)

syndrome (MDS) were the most commonly observed (33%) during the period of 10 years following diagnosis; after the 10th year, leukemia and MDS represented only 12% of the total at that period and breast and lung carcinoma reached the 56%.

**Conclusion:** Prolonged follow-up of HDK patients shows a steady rate of secondary tumors. Breast and lung Ca. screening must be recommended in this group of patients

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POSTER

### Serum L-Selectin and P-Selectin levels in lymphomas

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**Purpose:** Adhesion of lymphocytes to endothelium is essential in lymphocyte trafficking. Lymphoma cells represent immortalized counterparts of normal lymphocytes. Altered expression patterns of adhesion molecules appear to be involved in the spread of lymphoid malignancies. In this study, serum levels of soluble L-Selectin and P-Selectin were determined in patients with Hodgkin's (HL) and non-Hodgkin's lymphoma (NHL) and in normal healthy individuals.

**Methods:** The study group consisted of 17 patients (10 NHL, 7 HL; 11 men, 6 women; median age 35 years, range 19–70) and 15 healthy volunteers (11 men, 4 women; median age 49 years, range 36–67). Serum L-Selectin and P-Selectin levels were determined with ELISA (Bender MedSystems, Vienna, Austria). Data are presented as mean ± SD. Unpaired t-test was used for statistical analysis.

**Results:** Serum soluble L-Selectin and P-Selectin levels were significantly elevated in patients with both Hodgkin's and non-Hodgkin's lymphoma (table).

Patients (n)	L-Selectin (ng/ml)	P-Selectin (ng/ml)	p
HL (7)	1140 ± 498	875 ± 370	0.0082
NHL (10)	1137 ± 428	610 ± 211	0.0023
Controls (15)	625 ± 159	178 ± 48	

**Conclusion:** Differential expression of these adhesion molecules may account for distinct patterns of growth and dissemination in lymphomas. The study of adhesion molecule expression and function may allow a better understanding of the malignant behavior of lymphomas.

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POSTER

### Non Hodgkin lymphoma (NHL) & hepatitis C in Egypt: Prevalence, clinical characteristics & response to therapy in a randomized controlled trial

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Hepatitis C is associated with chronic B cell stimulation, mixed cryoglobulinemia, and is implicated as a causative factor in the development of NHL. Whether the clinical characteristics of HCV associated NHL differ from HCV–ve is not known. The response to therapy has not been compared in the 2 groups, and the value of adding interferon (IFN) to treatment has not been assessed.

**Aim:** This study aimed at assessing the prevalence of HCV antibodies in patients with NHL in an area of Egypt with high prevalence for HCV infection, and comparing it to HCV antibody prevalence in other malignancies and to normal individuals. We also aimed at assessing the clinical characteristics of HCV associated NHL, and assessing its response to therapy using standard CHOP or CHOP+IFN compared to HCV–ve NHL in a randomized controlled manner.

**Patients and Methods:** Sixty consenting patients with intermediate and high grade NHL (40 males), 60 patients with other malignancies, and 60 normal asymptomatic matched controls were included. Patients and control sera were tested for anti-HCV by 2nd generation ELISA. Patients with NHL were categorized according to anti-HCV status, and the disease severity and clinical characteristics were assessed. Anti-HCV+ve patients were randomized to receive CHOP or CHOP+IFN 5 MU/day for 5 days with CHOP cycles and tiw in the interim.

**Results:** Forty two NHL patients were anti-HCV+ve (70%) (33 males) compared to 24 patients (40%) with other malignancies, and 22 controls (36.7%), (both  $p < 0.0001$ , Risk Ratio 4.03, 95% CI 1.9–8.6). Males with NHL were more likely to be anti-HCV+ve ( $p < 0.005$ ). Clinical characteristics including stage, number of sites involved, bulkiness of disease, B symptoms, bone marrow involvement, and elevated LDH were not different in the 2 NHL groups. Complete remission (CR) was achieved in 61% of HCV–ve patients and 52% of HCV+ves ( $p > 0.05$ ). Twenty HCV+ve patients received CHOP+IFN and 22 standard CHOP. CR was achieved in 60% and 46% respectively ( $p = 0.34$ ). Side effects were comparable in the two groups, but significant liver dysfunction occurred in 1/18 of the anti-HCV–ves, and in 10/22 of the CHOP group and 3/20 of the CHOP+IFN group ( $p < 0.05$ ).

**Conclusion:** The prevalence of HCV infection in NHL is higher than the general population and patients with other malignancies, and HCV infection

appears to increase the risk for NHL. HCV associated NHL has similar clinical characteristics to HCV-negative disease. The response to therapy is the same, with CR achieved equally. The addition of IFN to standard CHOP did not significantly increase the response rate, but decreased significantly hepatic side effects. Further cohort studies are needed to evaluate the risk of development of NHL in the natural history of HCV infection.

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POSTER

### Thyroid toxicity after treatment of Hodgkin's disease

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**Purpose:** Thyroid disease, especially hypothyroidism, is a possible late toxicity after therapy for Hodgkin's disease (HD). We analysed the thyroid function of patients (pts) who were treated for HD according to the protocols of the German Hodgkin Study Group between 1970 and 1994 at two University centres.

**Methods:** 177 pts (92 men and 85 women) with median age of 38 years (range 18–74) and median time after therapy of 6 years (range 1–20) were studied. 35 pts (20%) were treated with chemotherapy alone (mainly COPP/ABVD), 44 (25%) with radiotherapy alone and 98 (55%) received combined modality. All pts were without evidence of HD for at least one year. They were evaluated for symptoms of thyroid disorder, biochemical thyroid-parameters and ultrasound imaging.

**Results:** Overall 48 pts (27%) were found to have subclinical (20%) or overt (7%) hypothyroidism. None of the pts with chemotherapy alone developed hypothyroidism, but 36% of pts with supradiaphragmatic radiotherapy and 34% of pts with combined supradiaphragmatic radiotherapy and chemotherapy. All pts with infradiaphragmatic radiation alone were euthyroid except one patient with hemithyroidectomy.

**Conclusions:** Supradiaphragmatic radiation is associated with a distinctively increased risk of hypothyroidism, chemotherapy neither alone nor in combined modality seems to enhance the risk of hypothyroidism.

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PUBLICATION

### Prognostic factors in low grade NHL (A multivariate analysis)

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During the period between January, 1970 and December, 1989 inclusive 278 newly diagnosed low grade NHL patients were treated and followed up at the RMH, England. The median survival and PFS was 8.75 years and 2.5 years respectively (median follow up = 8 years).

By univariate analysis, age (60 years), stage (III and IV), more than 2 sites of disease, extranodal disease, anaemia, B-symptoms, bone marrow involvement, ESR > 40 mm/h and chemotherapy treatment were adverse prognostic factors affecting survival.

By multivariate analysis, more than 2 sites of disease, age (60 years) and anaemia remained as significant adverse prognostic factors. For PFS, old age, advanced stage, more than 2 sites of disease, extranodal disease, bone marrow involvement, liver involvement, anaemia and chemotherapy treatment were univariate adverse prognostic factors.

By multivariate analysis more than 2 sites of disease and extranodal disease remained significant.

Treatment modality does not have any further significance as a prognostic factor. A pattern of continuous late relapse has been characteristic of low grade NHL.

Potentially curative treatment strategies are needed and require prospective evaluation. Only with designed clinical trials can a significant survival plateau be realized.

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PUBLICATION

### Importance of surgery in the treatment of non-Hodgkin's lymphoma of the stomach

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**Purpose:** Although rising incidence of non-Hodgkin's lymphoma (NHL) of the stomach could be obtained worldwide in the last years optimal treatment options remain controversial, above all the role and extent of surgery in low as well as in high grade malignancies.

**Methods:** Between 1969 and 1996 the postoperative course of 105 pts was analyzed retrospectively in regard to the complication rate and long term survival depending on tumor stages as well as multimodality treatment.

**Results:** The overall incidence of NHL-pts who underwent surgical treatment was 4.2% (105/2475 pts); increasing to 8% in the last decade. In 93.3% (98/105 pts) total or subtotal distal gastrectomy could be carried out with an operative mortality of 7%. The pathohistological staging determined CSI = 49, CSII = 31 and CSIV = 25; 5-year survival rate obtained for these stages was 94%, 64% and 35% resp. (p = 0.002). Compared to surgical treatment alone no statistically improved benefit was obvious after post-operative radio- and/or chemotherapy.

**Conclusion:** Based on the data obtained the most reliable therapy of gastric NHL is still surgery. Nevertheless, promising results of anti-H. pylori therapy of superficial low grade malignant NHL or chemo-/radiotherapy in CSI/II high grade malignant NHL must be investigated in further trials.

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PUBLICATION

### Treatment of relapsing and refractory non-Hodgkin's lymphoma with a combination of dexamethasone, Ara-C, ifosfamide and cisplatin (DAIP)

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**Purpose:** To evaluate the efficacy and toxicity of a novel combination of dexamethasone (D), Ara-C (A), ifosfamide (I) and cisplatin (P) – DAIP – in patients (pts) with non-Hodgkin's lymphoma (NHL) previously treated with both adriamycin and etoposide.

**Methods:** All medications were given over 4 consecutive days. D (40 mg/day), I (max. daily dose 1,200 mg/m<sup>2</sup>) and P (max. daily dose 20 mg/m<sup>2</sup>) were given by IV bolus. A (max. daily dose 75 mg/m<sup>2</sup>) was given by 1 hr IV infusion. Cycles were repeated every 3 wks. Adequate hydration and mesna were given.

**Results:** 30 pts (23 aggressive NHL, 6 low-grade NHL, 1 mantle cell) were entered in the study. Median age was 50 yrs (range, 19–69). The most common prior therapy was ProMACE/MOPP (18 pts). Nine pts received ≥ 2 prior combinations. Consolidation with high-dose chemotherapy (HDCT) was given to 6 pts. Complete response (CR) was achieved in 10 pts (33%) and partial response (PR) in 6 (20%). Median duration of PR was 4 mos; that of CR was not reached. Three pts were disease-free at 6+, 47+ and 55+ months. CR rate was higher in relapsing pts than in refractory pts (9/13 vs 1/17). Median WBC nadir was 1,050 mm<sup>3</sup> and median platelets nadir was 26,000/mm<sup>3</sup>. Neutropenic fever developed in 13 pts (43%) and platelets transfusions were required in 6 (20%). There was one treatment-related death with sepsis and GIT bleeding.

**Conclusion:** DAIP is an active combination in relapsing NHL following prior exposure to adriamycin and etoposide and may be used before HDCT. Myelosuppression is the dose-limiting toxicity.

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PUBLICATION

### Inverse relationship between apoptotic fraction and volume weighted mean nuclear volume in childhood Burkitt's versus diffuse B/T large cell lymphoma

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**Purpose:** Nuclear apoptosis results in nuclear size reduction and if present may cause the average nuclear appearance in histological sections to vary within lesions of the same lineage, complicating morphological classification. The accurate apoptotic fraction in most lesions is presently not appreciated.

**Methods:** We studied diagnostic pre-treatment tissue samples of 28 consecutive, unselected childhood MNHL (13 Burkitt's, mean age 8 y, range 4 y 2 m–14 y, 7 M, 6 F; 15 diffuse large cell lesions, mean age 9 y 9 m, range 1 y 5 m–16 y 8 m, 10 M, 5 F) for volume weighted mean nuclear volume by image analysis (Quantimet 570C) and for mean apoptotic fraction using Frag-EL DNA in-situ labelling (CalBiochem, USA). Lesions were typed as B-T cell using either immuno-cytochemistry, flow cytometry or immunoglobulin/T-cell receptor gene re-arrangements.

**Results:** Volume weighted mean nuclear volume of Burkitt's lymphoma (mean 250, range 134–411 μm<sup>3</sup>) was smaller than that of large cell diffuse lesions (mean 285, range 168–489 μm<sup>3</sup>). However this difference is based on selective increase of B-cell lesions only (n = 7, mean 350, range 260–489 μm<sup>3</sup>) in contrast to T-cell lesions (n = 8, mean 228, range 168–350 μm<sup>3</sup>). Conversely, mean apoptotic fraction of large cell, B-cell lesions (40.2, range