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## AGE-RELATED PROGNOSTIC FACTOR ANALYSIS IN NON-HODGKIN'S LYMPHOMA (NHL)

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Age is known to have an important influence on median survival time (MST) in NHL. To investigate this observation, we reviewed the frequency of other known prognostic variables, outcome of treatment and survival of 251 patients (pts)  $\geq 65$  years of age compared to 256 younger pts registered between 1980-89, with the following findings:

Clinical Feature	Age $\geq 65$	Age $< 65$	Significance (P)
High Grade (%)	47	37	.05
† LDH level (%)	29	20	.06
Bulky disease (%)	38	33	NS (.23)
"B" symptoms (%)	37	34	NS (.54)
Stage III + IV (%)	62	67	NS
CR (%)	38	56	< .001
Remission (mos)	29	40	NS (.11)
2° Response (CR+PR)	45	66	< .001

The MST for older pts was 24 mos compared to  $> 120$  mos for younger pts ( $P < .001$ ). The difference is partly accounted for by a higher proportion of high-grade tumours, a lower response rate to therapy and a poorer response to salvage therapy compared to younger pts; however, multivariate analysis confirmed age to be an independent negative factor influencing survival.

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## CHOP IN THE UNITED KINGDOM: A SURVEY OF DOSE-INTENSITY

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CHOP (Cyclophosphamide 750mg/m<sup>2</sup> day 1; Adriamycin 50mg/m<sup>2</sup> day 1; Vincristine 1.4mg/m<sup>2</sup> day 1; Prednisolone 100mg/m<sup>2</sup> days 1-5; cycle length 21 days) has recently re-emerged as acceptable standard therapy for patients with aggressive non-Hodgkin's lymphoma. We surveyed 35 UK oncology centres and found 22 different CHOP regimens in use. 8 centres used  $> 1$  regimen; one centre used 4 different regimens. Average relative dose-intensity (ARDI) varied from 0.80 to 1.53, median 1.09. Adriamycin RDI was bimodally distributed; 0.75, corresponding to a day 1 + 8 regimen, and 1.0 (standard CHOP). Similarly the Vincristine RDI was 1.5 (day 1 + 8 regimen) or 1.0 (day 1 regimen). Cyclophosphamide RDI varied more but most regimens had RDI of either 1.5 (day 1 + 8) or 1.0 (day 1). There was marked heterogeneity in prednisolone dosage: RDI 0.2 to 2.4; median 0.6. It is disconcerting to discover such wide variations in what should be a standard regimen. 25% of protocols have ARDI  $< 0.92$ ; 75% of protocols have prednisolone RDI  $< 0.6$ . The day 1 + 8 regimen has a lower adriamycin RDI than standard CHOP but the RDI's for cyclophosphamide and vincristine are higher - this may impair efficacy and increase toxicity. CHOP as used in many UK centres differs significantly from standard CHOP as used in recent randomised trials. This has implications for the applicability of these trial results to UK practice: pruned CHOP will prune survival.

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## GASTRO-DUODENAL LYMPHOMA - AIDS RELATED

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The incidence of Gastro-duodenal malignant Non-Hodgkin's Lymphomas (NHL) - related to HIV infection in Puglia has been established in our study about 3.6% (from November 1985 273 cases of AIDS were diagnosed). The gastric lesions may cause significant bleeding but are less likely the obstruction. Imaging studies available for evaluation of suspected lesions included barium contrast studies, endoscopic with biopsy, abdominal ultrasonography, computed tomography, scanning and magnetic resonance imaging. The luminal lesions may have characteristic appearances suggesting malignancy, however tissue easily biopsied with standard endoscopic forceps is required. Endoscopic biopsies have been usually positive, even though the neoplastic tissue has been predominantly sub-mucosal. A total gastrectomy was not performed in all cases. Adjuvant chemotherapy was offered. The natural history of NHL in our series shows a close association with AIDS and the Epstein-Barr virus infection has been implicated in the pathogenesis.

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## THE REARRANGEMENT OF BCL-2 GENE IN CHINESE CASES OF FOLLICULAR LYMPHOMA

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According to data collected over the past 5 years in our hospital, the incidence of follicular lymphoma is very low, accounting for only 7.5% (16/220) of all NHL cases. Using probes for the breakpoint cluster region of bcl-2 gene, genomic DNAs from B cell lymphoma of 16 patients were analyzed. Eight of 16 cases (50%) with follicular lymphoma showed bcl-2 gene rearrangement. Seven cases with bcl-2 rearrangement had the breakpoints located within the mbr region; the remaining one within the mcr region. Restrictive DNA fragments of bcl-2 were found to comigrate with JH genes in all the follicular lymphoma which had bcl-2 rearrangement located with mbr. Our data showed that in spite of the lower incidence of follicular lymphoma in Chinese, the incidence of bcl-2 gene involvement in follicular lymphoma was higher than those in the reports of Japan and Hong Kong.

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## THE TREATMENT OF EARLY STAGE GASTRIC LYMPHOMA

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The treatment of early stage gastric lymphoma is still in controversy. This retrospective analysis reported on the outcome of 24 patients (26 treatments) treated in our institution in the last 3 decades. Fourteen patients had stage Ia, one patient had IaB, 8 patients IIa and 3 patients had stage IIb non Hodgkin's lymphoma (NHL). Diffuse large cell intermediate grade NHL was diagnosed in 18 patients, diffuse small cleaved cell in 4 patients, and diffuse mixed large and small cell, "lymphosarcoma", low grade B cell lymphoma and unclassified lymphoma in one patient each. Sixteen patients underwent surgery (surg), 22 had radiation therapy (XRT) and 10 patients received chemotherapy (chemo). Surg+XRT were given to 9 patients, XRT alone was delivered to 5 patients, surg+XRT+chemo and XRT+chemo were in use in 4 patients each. Surg alone was the initial treatment in 2 patients who subsequently relapsed and were treated with combined modalities (surg+XRT and surg+chemo). Surg+chemo and chemo alone were given to one patient each. Following treatments 22/24 achieved a complete response. During a mean follow up of 72.7 months (range 1-285) 5 patients relapsed. Two patients who treated with surg alone developed local recurrence. The third patient developed retroperitoneal lymphadenopathy, noted 2 months following completion of XRT to a small gastric field, the forth developed cervical adenopathy and in the fifth the site of relapse is unknown. At 10 years the actuarial survival of the 15 patients with stage I disease was 58% and for stage II it was 55% (Gehan P value 0.41). Freedom from relapse (FFR) was 61% and 58% respectively (P value 0.68). No significant statistical differences in terms of survival and FFR were noted in patients treated with surg, chemo or XRT. The outcome of 4 patients treated with the 3 modality treatments (surg+XRT+chemo) was similar to the patients treated with 2 modality treatment (surg+XRT in 9 patients and XRT+chemo in 4 patients) and to the 5 patients treated with XRT alone. Gender, age, presenting symptoms, depth of tumor through the gastric wall and the stage were not statistically significant for prediction of either survival or FFR. We conclude that both surg+XRT and chemo+XRT are effective in the treatment of early stage gastric disease. XRT alone is equally effective as two or three modality treatments in subset of patients with early stage gastric lymphoma.

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## EARLY STUDY OF CLINICAL EFFECTS OF RH TUMOR NECROSIS FACTOR IN PATIENTS WITH NON HODGKIN'S LYMPHOMA

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In our study recombinant human Tumor Necrosis Factor alpha (rhTNF) was administered to 17 patients with NHL (stadium IIIB, IVA, B) who developed a resistance on standard chemotherapy. Therapy consisted of 30-minute intravenous infusion for 5 consecutive days every 2 weeks. This cycles was repeated 3 times. Daily doses of rhTNF ranged from 25 µg/m<sup>2</sup> to 200 µg/m<sup>2</sup>. Rigors, fever, nausea, vomiting, headache were observed in 95%, 80%, 62%, 48%, and 23% respectively. All toxicities were reversible within 12 hours. No major changes in liver or renal function, coagulation or blood lipids were observed. Therapeutic findings: one patient fulfilled the traditional criteria for a objective regression (200 days). 5 patients had a stable course of this disease overage during 4,5 months. 6 subjects developed not significant remission. Only five of treated persons have progress in course of disease. TNF seems to be effective in NHL.