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LONG TERM FOLLOW-UP OF PATIENTS WITH HODGKIN'S DISEASE TREATED WITH EXCLUSIVE RADIOTHERAPY (RT). F. SOUM , A. PONS , JM BACHAUD , N.DALY-SCHVEITZER - Radiation Dept. Centre Claudius Regaud - Toulouse - France.
Between Jan. 1975 to Dec. 1985, 67 patients with stage I or II were treated in our institution by exclusive RT. 56 pts were submitted to a laparotomy with splenectomy as part of their initial staging. RT was performed using Kaplan's technique up to 36 to 40 gy with daily dose from 2 to 2.5 gy. Ten pts received additional Waldeyer's ring irradiation because of initial involvement of those sites. Mean follow-up of this series is 136 months. 6 pts presented tumoral relapse (mean delay : 38 months), in sus-diaphragmatic areas (3 inside the fields, 1 marginal). 6 patients experienced tumoral relapse in sub-diaphragmatic areas, 2 of them with initial pathologic staging. Secondary treatment of these relapses allowed definitive cure in 9 of 12 pts. Disease free survival is respectively 85, 83, 80 % at 5, 10 and 15 years. Causes of death were : evolutive disease 2, severe herpes zoster 1, second cancer (NHL) 1, documented cardiac failure 1, "sudden death" 2, intercurrent disease 1. In addition one patient presented late radiation myelitis. Special analysis was performed in order to precise factors of tumoral failure and causes of therapeutic side effects.

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PHASE II STUDY OF WEEKLY ADMINISTRATION OF VINORELBINE IN HEAVILY PRETREATED HODGKIN'S DISEASE.
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From March 1992 to January 1993, 19 heavily pretreated patients (pts) with refractory Hodgkin's disease were given Vinorelbine at 30 mg/mq by weekly i.v. bolus. Characteristics of 16/19 evaluable patients, were: M/F: 7/9; median age: 30 yr (22-54); B symptoms: 8; extra ± nodal involvement: 12; All pts had received at least 3 regimens including MOPP, ABVD, CEP or MINE, 10 were given > 3 regimens including high-dose chemotherapy in 2 cases. Three complete responses (7+mos, 2 mos, 2 mos), 7 partial responses (1+- 6+mos), 5 stable disease (2 mos - 8 mos) were documented. Disease progression occurred in 1 case. As of January 1993, 6 pts were still on treatment and 13 were alive. Toxicity was evaluated according to the NCI classification. All cycles were administered at full dose but 84% of courses were delayed due to Grade 3 leukopenia/neutropenia. Anemia and thrombocytopenia were negligible. Nausea, vomiting and hair loss were never observed. Grade 3 infectious episodes were observed in only 3% of cycles. Grade 2 reversible peripheral neurotoxicity occurred in one patient after 10 doses. Grade 3 skin toxicity was detected to the injection site in the first 5 pts. Therefore in the following pts a central venous catheter was utilized. The conclusion of this phase II study are:1) Vinorelbine is active in heavily pretreated HD and is devoid of cross-resistance with vinca alkaloids, 2) toxicity is generally mild also in pretreated pts, 3) studies with different schedules and then inclusion of Vinorelbine in second line regimens are highly suggested.

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MOPP/EBVD +/- LOCAL RT FOR ADVANCED HODGKIN'S DISEASE
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Twenty-four pts affected by advanced Hodgkin's disease (M/F=15/9; Stage II bulky and/or B=9; Stage III=9; Stage IV=6; PL=5; SN=11; CM=8; median age=28 yrs, range,17-69) were given a median (range,4-8) of 8 cycles of MOPP/EBVD combination chemotherapy, monthly delivered: HN_2 6 mg/m^2 i.v. day 1, VCR 1.4 mg/m^2 i.v. day 1, PCZ 100 mg/m^2 p.o. days 1-7, PDN 40 mg/m^2 p.o. days 1-14, VLB 6 mg/m^2 i.v. day 8, EDX 30 mg/m^2 i.v. day 8, BLM 10 mg/m^2 i.v. day 8, DTIC 375 mg/m^2 i.v. day 8. Eleven pts presenting with bulky mediastinum (M/T>0.33) received also additional local RT (35 Gy). Twenty-three (96%) pts attained a CR and one had progressive disease. After 10-55 (median,24) mos the actuarial OS and FFP were 82% and 79% respectively. After 4-48 (median,17) mos the projected DFS was 72%. Two pts died at 10 and 34 mos and two pts relapsed at 6 and 36 mos. Toxicity included grade 1-3 alopecia (42%), vomiting (62%) and leukopenia (58%), grade 1-2 infection (46%) and paresthesias (25%). The median "average dose density" actually delivered was 0.86 for HN_2-PCZ and 0.83 for EDX-VLB. The median "average dose intensity" actually received in the first four cycles was 0.99 for HN_2-PCZ and 0.97 for EDX-VLB.
MOPP/EBVD +/- RT program for advanced Hodgkin's disease allows to deliver adequate doses of cytotoxic drugs. Moreover it is very effective to induce high CR, OS, FFP and DFS rates, with a moderate acute toxicity.

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PROGNOSTIC SIGNIFICANCE OF THE PATHOLOGICAL SUB-TYPES OF NS TYPE HODGKIN'S DISEASE

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Subclassification of the NS type Hodgkin's disease was introduced for the first time by the British National Lymphoma Investigation (NS type divided to NS1 subtype with good prognosis and NS2 subtype with poor prognosis). The aim of this study is an analysis of the prognostic significance of BNLI subclassification. We have investigated this subclassification with regard to their prognostic value for disease free survival and overall survival. 93 patients with NS type of Hodgkin's treated in Cancer Center in Warsaw between 1980 and 1985 were retrospectively reclassified to NS1 and NS2 group. Statistical analysis showed that NS1 subtype has important prognostic value as an independent good prognostic factor. Prognosis in NS2 patients was significantly worse especially if NS2 subtype was correlated with elevated ESR and "bulk" mediastinal disease. Our data confirmed the prognostic value of the BNLI sublassification of the NS type Hodgkin's disease.

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TITLE: INFRADIAPHRAGMATIC HODGKIN'S DISEASE
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INTRODUCTION: Exclusively infradiaphragmatic (ID) form accounts to 4-12% of all cases of Hodgkin's disease (HD) and has been traditionally considered having a worse outcome. Recommendations for treatment are difficult because of the scarce number of early stage-patients (ES) and the lack of uniform therapeutic approaches.
MATERIAL AND METHODS: We retrospectively studied 133 HD diagnosed patients between 1971 and 1992. We found 67 ES (50,3%); 8 (6%) ID, 4 stage I (2 IA and 2 IB) and 4 stage II (2 IIA and 2 IIB). Five were male, two female and the average age was 41 years (21-55). Groin was the most frequent involved site (80%). The histologic subgroups were 3 mixed cellularity, 2 nodular sclerosis, 1 lymphocyte depleted and in 2 cases classification was not possible.

TREATMENT RESULTS: Two patients (25%) were treated with radiotherapy (R) alone (inverted Y+spleen) one of them is alive and with no evidence of disease (NED) after 107 months (mo). The other relapsed in supradiaphragmatic location, the rescue was done with R and chemotherapy (Ch) and he died of non treatment or disease related problems. Two patients (25%) were treated with R+Ch, both NED after 250 and 258 mo respectively with severe gastric and bowel toxicity. Four patients (50%) were treated with Ch, NED after 49-101 mo. Five-year actuarial survival of ID HD is 86% while the global survival for the total series is 86%-79% for stage I and II respectively.
CONCLUSIONS: ID HD has similar prognosis than other HD presentations at the same stage. The combined therapy causes toxicity which may be considered excessive while exclusive Ch achieves good control of ID HD.

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DOSE-VOLUME HISTOGRAM ANALYSIS FOR MANTLE-FIELD IRRADIATION IN HODGKIN'S DISEASE.
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In order to obtain a quantitative assessment of the dose homogeneity for the mediastinal regions of interest and for organs at risk (heart) in mantle field irradiation of Hodgkin's disease, dose volume histograms were calculated based on a conventional treatment plan . An algorithm, developed at our institution was introduced into a CT-planning system (Mevaplan). Target structures were delineated on each axial CT slice by the radiotherapist. Dose distributions were calculated on each axial slice and a three dimensional dose matrix was therefor constructed. The influence of spinal-cord blocking (SCB) inserted after 19.8 Gy or 30.6 Gy, respectively, on the projected total dose 43 Gy (single dose 1.8 Gy) delivered by 8 MeV or Co-60 beam at a weighting of 1:1 and 2:1 (anterior to posterior field) was evaluated. Additionaly, the impact of the simultaneous use of a subcarinal block inserted at 30 Gy was determined.
The mean dose in the mediastinal target volume for 8 MeV photon beams without spinal cord blocking at a weighting of 1:1 was 88.4%, with SCB after 20 Gy 81.4%, and with SCB after 30 Gy 84.7% of the total dose. The additional subcarinal block at 30 Gy resulted in 79.3 Gy. At a weighting of 2:1 even without SCB the mean dose in the target volume decreased about 8%. The results with Co-beam at 80.2% without SCB were even worse. As a consequence a reduction of overall dose without SCB or insertion of SCB at a later stage might be indicated.