weeks). Seventy-nine pts were treated with a 2-field technique, 66 pts with a 4-field technique and 2 pts with a direct perineal field. Median treated volume was 4.4 liters (1.2–9.4). One hundred and twenty pts were treated with X25 MV, the other 27 pts with 1.25 Mev ^{60}Co. All irradiated rectal tumors have been reanalyzed by the same pathologist in order to quantify tumor sterilization. Three groups were individualized according to the residual tumor cell density (RTCD): absence or low, intermediate and high.

All pts underwent surgery in a median delay of 4 weeks. Fifty-five tumors (37%) showed no (9/147) or low (46/147) RTCD; 51 (35%) showed an intermediate RTCD and 39 (27%) a high RTCD. The distribution of the pts according to age, tumor stage, tumor location, delay before surgery and RT parameters (total dose, fractionation, duration of treatment, 2 or 4-field technique, treated volume, X25 MV or 1.25 Mev ^{60}Co photons) was not statistically different in the 3 groups. Five-year actuarial survival rates were 100% in the group of pts with no RTCD, 54% in the group with low RTCD, 44% in the group with intermediate RTCD and 53% in the group with high RTCD. The difference did not reach significance, probably because of the small number of sterilized tumors. These results suggest however that tumor sterilization is a favorable prognostic factor after preoperative RT in rectal cancer.

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IL-8 INVOLVEMENT IN IMMUNE DISREGULATION OF CANCER PATIENTS

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The mechanisms for the recruitment of immune cells to sites of inflammation have not been fully elucidated. In order to understand the mechanisms of IL-8 a potent chemotactic and activating chemokine, during immune response, we examined in colon cancer patients and controls, serum levels of IL-8, IL7, IL-6, IL-4, TNF-α, IFN-γ IL-2, sIL-2R: IL-8 production in supernatants of PBMC with and without activation agents: PBMC phenotype (CD3, CD4, CD8, CD16, CD56, CD57, CD25): PBMC proliferative responses to IL-2, IL-4, anti-CD3. Our results show that IL-8 serum levels in patients (p) were higher than in controls (c) (n.p = 65, n.c = 51 $P = 0.007$) and this was significant only at stage II (n.p = 25 n.c = 51 $P = 0.01$) and III (n.p = 8 n.c = 51 $P = 0.03$). It is of great interest to note that our preliminary data of IL-8 production from: PBMC (n.p = 14 n.c = 4 $P = 0.0002$), plus PHA (n.p = 15 n.c. = 3 $P = 0.008$), plus anti-CD3 (n.p = 3 n.c = 3 $P = 0.03$) show that levels in patients are significantly lower than in controls. Correlation between IL-8 serum levels and other serum cyokines evidenced no significant values, but at stage I (n.p = 9 $P < 0.00001$), II (n.p = 23 $P < 0.00001$) and IV (n.p = 5 $P < 0.00001$) correlations with TNF-α levels were found. The phenotypic analysis showed only a positive correlation between IL-8 serum levels and CD8 expression (n.p = 34 $P = 0.01$). PBMC proliferative responses of patients showed no significant correlations with all examined agents. Analysing our data, it seems that in cancer patients there is a disregulation in IL-8 production. It is to note that in the serum, in this situation are involved the stage II and III, where principally are regulated the mechanisms for lymphonodal infiltration and host invasion. In this contest, the positive correlation between IL-8 and CD8 expression can be interesting information. So, our results support the hypothesis that IL-8 can be an active participant in the disregulation of immune response which allows the tumor to locate and progress in the host.

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COLON CANCER: SIL-2R AND CORRELATED MECHANISMS

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The current research has still not clarified why serum levels of sIL-2R increase in cancer patients. In order to establish whether this could be an independent event or there are correlated mechanisms, in colon cancer patients and controls we examined the level of this soluble receptor in correlation with phenotype of PBMC; serum levels of IL-6, TNF-α, IL-4, IFN-γ, IL-2; changes of HLA-I and HLAII antigen expression on tumor tissue respect to normal mucosa; PBMC proliferative response to IL-2, IL-4, anti-CD3. Correlations with the disease progression were evaluated. Our results show that sIL-2R level of patients (p) was higher than in controls (c) (n.p = 72, n.c = 79 $P < 0.0001$). There were no significant correlations between sIL-2R and the expression of CD3, CD4, CD8, CD16, CD56, CD57, CD25 antigens on PBMC of both patients and controls. In patients compared to controls, even if the serum levels showed an increase of IL-6 (n.p = 56, n.c = 49 $P = 0.0001$), IFN-γ (n.p = 73, n.c = 43 $P = 0.003$), IL-4 (n.p = 24, n.c = 33 $P < 0.0001$) and a decrease of IL-2 (n.p = 42, n.c = 27 $P < 0.0001$), sIL-2R level showed only a positive correlation with IL-4 (n.p = 19 $P = 0.033$). Moreover, from the evaluation of HLA antigens it is possible to note that when the expression of HLAI is the same in tumor tissue and normal mucosa (situation more often present at stage I: 66.7%), sIL-2R of patients was higher than controls ($P = 0.018$). With regard to the correlations with the proliferative response, merely a positive association with IL-2 plus anti-CD3 was determined (n.p = 29 $P = 0.013$). So, from our overall results, as IL-4 is produced by CD4$^+$TH2 cells and the anti-CD3 addition to IL-2 is well-known to be discriminant for the activation of these cells, it seems that the increase of sIL-2R in serum of cancer patients is an event dependent on CD4$^+$TH2 cells. This hypothesis is confirmed by the fact that when HLAI antigen expression was lower than normal, the HLAII antigens was higher, supporting an inflammatory situation.

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CANCER ESTABLISHMENT AND PROGRESSION

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Immunological evaluations on cancer patients provide informations to understand the disregulations which allow the tumor to locate and progress in the host. In colon cancer patients and controls we examined the serum levels of various cytokines and the proliferative response of PBMC to IL-2, IL-4, anti-CD3mAb. Our results show that in patients there was a significant serum increase of IFNγ, IL-4, IL-6, whereas IL-2 significantly decreases. This situation is indicative for the functional presence of inflammatory CD4$^+$TH2 cells. In patients it is possible to note a negative correlation between the proliferative response to IL-2 and stage of the disease ($^*P = 0.0024$), which changes into positive when anti-CD3 is added ($^*P = 0.007$) (indicative for a functional increase of CD4$^+$TH2 cells with the disease progression). Moreover in patients the proliferative response to IL-2 + anti-CD3 was comparable to controls ($\S P = 0.42$), whereas in the former there was a significant reduction after IL-4 addition ($\S P = 0.005$). This effect of IL-4 on IL-2 + anti-CD3 starts at stage II, whereas at stage I the response is still comparable to controls and there is a greater response to IL-2 alone ($\S P = 0.0035$). Analysing our data, it seems that the start of the immunological response in patients is of inflammatory type and it degenerates because IL-4, which raises with the disease progression, interferes with IL-2 mechanisms.

Serum levels	patients compared to controls				*stage correlations	
§ IFN-γ	n = 73	P = 0.003	n = 43	n = 63	r = 0.19	P = 0.14
§ IL-4	n = 24	P < 0.0001	n = 33	n = 24	r = 0.89	P < 0.0001
° IL-6	n = 56	P = 0.0001	n = 33	n = 55	r = 0.21	P = 0.12
° TNFα	n = 56	P = 0.1	n = 33	n = 51	r = 0.35	P = 0.014
§ IL-2	n = 42	P < 0.0001	n = 27	n = 41	r = −0.56	P = 0.0004

*Spearman rank correlations; §Student's t-test; °Mann-Whitney test

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INTRAHEPATIC CHEMOTHERAPY WITH FLOXURIDINE (FUDR) L-LEUCOVORIN (LV), DESAMETAZONE (D) IN CONTINUOUS INFUSION AND BOLUS MYTOMICIN C (MMC) IN HEPATIC METASTASES FROM COLORECTAL CANCER: A PHASE II STUDY

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Intrahepatic continuous infusion FUDR induces 50% response rate (RR) in patients (pts) with hepatic metastases from colorectal cancer (CRC). Lower RR are observed in pretreated pts. The combination of FUDR + LV has given over 70% RR with high hepatic toxicity. The use of D can decrease the hepatic toxicity. In a randomized study Kemeny *et al.* have observed an increase in RR and a decrease in hepatic toxicity in the group of pts treated with FUDR + D compared to the group receiving FUDR only. Moreover the combination of MMC, Carmustine and FUDR is effective also in pretreated pts. On these premises since July 1993 we have treated 22 pts affected by unresectable hepatic