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Potential Value of Biliary CEA Assay in Early Detection of Liver Metastases from Colorectal Carcinomas

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Elevation of the biliary CEA level in patients with liver metastases from colorectal carcinomas has been reported. The aim of this study is to determine the potential value of biliary CEA assay for the early detection of liver metastases. Biliary and serum CEA levels were determined in patients operated on for a colorectal cancer and in control groups. Among patients with liver metastases from colorectal carcinomas, biliary CEA levels were markedly elevated (>40 ng/ml) in 6/9, moderately elevated (6-40ng/ml) in 2/9 and normal (arbitrarly defined as <6ng/ml) in 1/9. Of 15 patients with primary colorectal carcinoma without detectable hepatic secondaries, there was no marked CEA elevation in the bile. Eight had moderate biliary CEA elevation and 5 had normal levels. Among 10 patients with other hepatobiliary pathology, there was 1 marked biliary CEA elevation, 4 moderate elevations and 5 normal levels. None of the 9 normal individuals had elevated biliary CEA levels. The follow-up of patients with a colorectal primary tumour presenting a biliary CEA elevation without evidence of hepatic secondaries is of particular interest. If subsequent appearance of liver metastases is confirmed in such cases, intra-operative biliary CEA assay could be considered a valuable detection test. Further studies will then have to prove the possible benefit of a specific treatment for these patients.

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FECAL HIGH BUTYRATE PRODUCTION OF CLINICAL RELEVANCE WITH PLANTAGO OVATA SEEDS (POS)

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Butyrate which supports differetiation of enterocytes can be used for the treatment of inflammatory bowel disease and may be important for colorectal cancer prevention. If a fibre is fermentable by the colonic flore, butyrate is a major metabolite. Therefore absolute and relative fermentative butyrate formation was measured with POS and compared another types of fibre.
Freshly ground POS were added to specimens of feces of healthy volunteers (n=18) or patients operated upon colorectal cancer (n=10) and incubated for 6-24h. The samples were analysed for total short chain fatty acids (SCFA: C2-C6) and for butyrate (B:C4) by gas chromatography.
In samples of heathly controls the production of SCFA and B was almost doubled in presence of POS. Plantago ovata husks (POH) or wheat bran (WB). In the cancer group, however, almost no change of B was observed with POH and WB, but an up to 10-fold increase of the fecal concentration of B after POS fermentation and the SCFA/B-radio became normalized as in healthly controls.
In conclusion, unlike other fibres, POS considerably enhances fermentative fecal formation of B. Therefore POS may be a special fibre preserving intestinal mucose, e.g. in ulcerative cottis patients. This is under clinical investigation.

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TOTAL RECTAL RESECTION, COLO-ANAL ANASTOMOSIS AND "J" RESERVOIR IN LOWER THIRD RECTAL CANCER

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A consecutive series of 73 patients (median age 61 years; range 30-79), 35 males and 38 females underwent radical rectal resection extended to the dentate line and colic J shaped pouch with handsewn colo-anal anastomosis, from March 1990 to November 1993. A temporary colostomy on the trasversum was associated in all cases and is to be removed in about 2 months. They were affected by lower third rectal cancer (19 pts Dukes A; 12 pts Dukes B; 30 pts Dukes C; 11 pts Dukes D; 4 pts villous adenoma with severe displasia and 5 pts anastomotic recurrence after Anterior Resection). The median distance from the lower margin of the tumour to the anal verge was 5.4 cm (range 2,5-8 cm) for 46 evaluable patients. Surgery was followed by chemotherapy (5 FU + Folonic Acid) in 25 pts (Dukes C/D) and radiotherapy in 41 pts (Dukes B/C/D). Only one patient died for MOF after surgical procedure; seventeen patients presented a radiological subclinical fistula and were treated with TPN for two weeks. No patients in our series claimed relevant impairment concerning anal sphincter or urinary functions. Median hospital postoperative stay was 17 days. The median follow-up of 16 months (range 1-45) detected seven (14%) local recurrence, but none to the anastomotic site. Two patients with synchronous liver metastases died of progressive disease the first 6 months and the second 10 months after surgery. The excellent quality of life, good cure rate and lack of major complications suggests that sphincter saving procedures are adequate in treatment of lower third rectal cancer.

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UKCCCR ANAL CANCER TRIAL

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Up until the 1980's surgery was the predominant treatment for cancer of the anus in the UK. Studies have shown that non-sugical treatment (radiation alone or combined with chemotherapy) can achieve comparable cure rates without the need for colostomy in the majority of cases. Use of historical controls makes interpretation of these results unreliable.

In order to fully address the question of whether the addition of chemotherapy to radiation confers any extra advantage, which outweighs the added morbidity that is likely to be produced by chemotherapy, the UKCCCR Anal Cancer Trial was opened in December 1987. Patients are randomised to receive radiotherapy (4500 cGy in 20 or 25 fractions) with or without chemotherapy (5FU and mitomycin C given during the first week of radiotherapy and 5FU only during the last week of radiotherapy).

By the end of September 558 patients had been randomised and a further 244 were registered, being unsuitable for the protocol. In 1992 about 45% of the UK incidence were registered or randomised into the trial. Although the original accrual target was reached on time, the trial remains open since insufficient events have yet been recorded to reliably answer the question. The data monitoring sub-committee regularly reviews the trial status. We suggest that monitoring of trials should not just be for stopping; continuation to provide sufficient power is an important aspect.

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ARTERIAL ENDOTHELIUM (ED) DAMAGE CAUSED BY 5-FLUOROURACIL (5-FU) INFUSION MAY RESPONSIBLE FOR ANGINA OF COLORECTAL CANCER PATIENTS --- ANIMAL MODEL STUDY. Lai G.M., Lau Y.T., Tsai C.C., Ho Y.S. Chang Gung Memorial Tumor Institute, Taipei 10591, Taiwan, CHINA

Prinzmetal angina, possibly due to coronary arterial spasm caused by high dose 5-FU infusion, became troublesome in colorectal cancer patients receiving chemotherapy. The mechanism is still unknown. We postulate the infusion of 5-FU may cause ED damage, impair endothelium-derived relaxing factor release and thereby lead to vasospasm. Wistar rats of 250-300 gm weight were cannulated and fixed by a swivel in a metabolic cage. After 5-FU infusion for few days, abdominal aorta was harvested for electron microscope (EM) examination and measurement of vascular tone in organ chamber. After a plateau of contraction reached by norepinephrine, relaxation response to acetylcholine were compared between control (C), mechanical damage (M) by cotton rod and 5-FU (200 mg/kg/d x 3 days) treated (T). The degree of ED damage showed by EM, e.g. swelling, vacuolization and detachment, was clearly dose related. The % of relaxation was 81-90 vs 10-14 vs 13-24 of C vs M vsT, respectively. In case of two bolus of weekly dose (360 mg/kg) of 5-FU, the % of relaxation was 42-51, which was quite smiliar to that of partial mechanical damage (44-53%). We conclude 5-FU infusion may cause endothelium damage in a dose response manner, by which the vessel intend to maintain higher vascular tone. Such findings may explain a part why angina occurred in patients receiving 5-FU treatment.

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ADJUVANT POSTOPERATIVE RADIOTHERAPY IN CANCER OF THE RECTUM. REPORT ON 146 CASES WITH 3-YEAR MINIMUM FOLLOW UP.

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From Jan. 1980 to June 1990, 146 pts with cancer of the rectum in pathological stage B2-B3 or C according to the Astler-Coller classification, were referred to our Institute after radical surgery.
Surgery was AP resection in 94, anterior resection in 47, transanal excision in 5.
Stage: 72 B2-B3, 74 C1-C3; histological grade: 4 G1, 103 G2, 7 G3, colloid 21, not specified 11; sex: 88 males, 48 females.
Distance from anal margin: 33<=4 cm, 53 5-9 cm, 41>=10 cm, 14 not specified
Lenght of follow up: 123>5 yrs, 14=5 yrs, 2=4 yrs, 7=3 yrs.
Radiotherapy: 50 Gy in 25 sessions; box technique.
In 42 cases a flash dose of 5 Gy was given the same day of surgery. Twelve pts (8.2%) relapsed in the irradiated area, 44 (30%) in a distant site, 4 (2.7%) had both events.
The local recurrence rate was not affected by the histotype, by the stage (B2-B3 8.3%, C 13.4%) and by the type of surgery (APR 10.6%, AR 10.6%); a lower recurrence rate (6%) was found in pts with tumor located below 5 cm from anal margin and given APR.
Distant met. rate was affected by the stage (B2-B3 23.6%; C 41.8%). Less dist.met. were also found in pts receiving the preop. flash (19%) than in those not receiving the preop. flash (39.4%). A considerable incidence of side effects (25.3%) occurred including 13 cases of death after surgery for late small boxel occlusion (8.9%); most of the fatal events occurred in the first period of the study in pts who were not immediately referred to us at the first appearance of subocclusive symptoms, and who received an emergency operation in other hospitals.
Because of the problem of side effects, our present policy is to give preoperative radiotherapy with concomitant 5FU and folinic acid.