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PALLIATIVE THERAPY OF DUCTAL PANCREATIC CANCER.
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Since 1977 we perform a prospective study to test the sensitivity of p.ca. to palliative chemotherapy. Diagnosis was confirmed by histology/cytology, follow-up was done by sonography/CT, body weight, clinical symptoms and laboratory data including CA 19-9, CA 125 and CEA. The terms CR, PR, MR, SD were used as usually. Results: 0/74 CR, 11/74 SD, 10/74 PR or MR for all the drug regimens tested as well as for the single drug regimens: 5-FU+BCNU (20), FAM (14), 5-FU+MTX (14), 5-FU+M-C (10) were performed according to Kovach et al., Schein et al., Hermann et al., Buroker et al., M-C (16) was given every week (10mg) for 3 weeks in 6 weeks intervals. However, the responder (SD+PR/MR) showed a significantly longer survival: median: 3,5 months (progress); 7,5 months (SD); 11 months (PR/MR).

To our opinion these unsatisfactory results are mainly due to a too late diagnosis, a heterogeneous behaviour of the individual p.ca. to the drugs tested and possibly to a dose-dependency of cytostatic effectivity. That would mean, that the new tumor markers as well as pretherapeutic test models (nude mice, cell culture) might ameliorate this situation.

Consequently, we started a prospective clinical study in resected patients with follow-up in short time intervals by tumor markers, sonography, CT, immunoscintigraphy and others, and establishment of the human tumors in cell culture and nude mice to test the individual sensitivity. We also try to involve immunotherapy in this study (Mab and immunostimulants).

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RESULTS OF SURGICAL THERAPY FOR AMPULLARY CANCER
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From 1974 to 1983 52 patients with ampullary cancer were treated at the Department of General Surgery of Münster University. The sex ratio was 1,3:1 (29 male, 23 female patients). Ampullary cancer occurred most frequently in the age-group from 60 to 70 years. In 51 cases (98,1%) a positive histologic diagnosis could be obtained by pre- or intraoperative biopsies. Resection for cure was possible in 82,7% for the whole series and in all patients admitted during 1983 (n=10). 39 Whipple operations and four Total Pancreatectomies were performed. Among the palliatively treated patients, three T-tubes were inserted, and twice the bile ducts were drained by a biliodigestive anastomosis. In three cases only an exploratory laparotomy was done; one patient because of general contraindications was treated endoscopically. Usually the disease was locally limited. According to the Münster-TNM-Classification for pancreatic and ampullary cancer 25 patients belonged to the T1NoMo/T2NoMo group. In-hospital-mortality was 7,7% for the Whipple operation. The main symptoms in patients with ampullary cancer were weight loss (59,6%) and jaundice (55,8%). Approximately 60% of our patients were treated during the first three months after the onset of symptoms. A 5-year survival rate of 36,3% was calculated for the whole series with a median survival time of 46,2 months. 80,7% survived the first year after the operation. In T1NoMo/T2NoMo cases the 5-year survival rate amounted to 55,9%; pointing out that the Whipple operation is a curative procedure at least for limited disease.

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Col 01

POLYCLONALITY IN MALIGNANT TUMORS AS IDENTIFIED BY DNA FLOW CYTOMETRY

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Although it is generally accepted that most malignant tumors arise from a single transformed cell and are hence of monoclonal origin, features of polyclonality are detected in a considerable proportion of tumors upon their clinical presentation. The present study was performed in 163 untreated tumors to determine the degree of polyclonality as expressed by multiple DNA stemlines and to relate these findings to histo-pathology.

	n	DNA aneuploidy	polyclonal DNA stemlines
large bowel carcinoma	88	72 (82%)	29 (33%)
lung cancer	54	45 (83%)	20 (44%)
osteosarcoma	21	18 (86%)	11 (52%)
	163	135 (83%)	60 (37%)

In large bowel carcinomas well differentiated tumors expressed polyclonal stemlines more often than moderately or poorly differentiated cases. In lung cancer the frequency of polyclonal DNA stemlines was significantly higher in squamous cell carcinomas than in the other histologic subtypes. A similar relation was not detected in osteosarcomas.

These data indicate a high frequency of polyclonal DNA stemlines reflecting a considerable degree of genetic variability. Since polyclonal DNA stemlines probably represent secondary chromosomal aberrations which are considered to determine the biological characteristics of malignant cell populations, these data might have substantial impact on the prognosis and the clinical management of patients with malignant tumors.

Col 02

VARYING EXPRESSION OF KERATIN POLYPEPTIDES IN GASTROINTESTINAL TUMORS - MONOCLONAL KERATIN ANTIBODIES AS DIAGNOSTIC TOOLS

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Keratins are the most complex class of intermediate filament proteins. 19 different keratins have been identified on two-dimensional gels, and it has been shown that expression of these keratins depends on the epithelium under study, as well as on the degree of cellular differentiation. An alternative method of studying keratin complexity in different epithelia is to isolate and characterize monoclonal antibodies that are specific either to a single keratin or a subgroup of keratins. In this study we have investigated normal tissue of gastrointestinal tract and the corresponding tumors with different monoclonal keratin antibodies, which are specific for the keratin polypeptides 7, 8, 18, 19 respectively. Our results indicate that the keratin polypeptide pattern of the cell of origin is maintained in the corresponding tumors. The immunohistochemical determination of keratin polypeptide pattern is therefore of value for diagnostic purpose especially in metastasis, because large bowel carcinomas and stomach carcinomas can be distinguished from ductal pancreas carcinoma, and in primary carcinomas of liver a clear distinction between hepatocellular and cholangiocellular differentiation is possible.

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