lines, i.e. cells with an already altered phenotype. Whether these cells may be termed initiated and are thus the appropriate targets for promotion is not clear. Following recent observations phorbol esters interfere with intercellular communication processes and thus may well act not only on initiated cells but also on their normal surrounding cells, thus rendering the tissue permissive for the expression of the transformed phenotype and for the development of the initiated cells to visible tumors.

BLOOM'S SYNDROME : A DEFICIENCY IN THE DETOXIFICATION OF ACTIVE OXYGEN SPECIES ?

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Bloom's Syndrome (BS) is an autosomal recessive disease which is characterized clinically by growth retardation, skin sensitivity to sunlight, immunodeficiency and increased susceptibility for development of cancer. Increased frequencies of spontanenous chromosomal aberrations and sister chromatid exchanges have been observed on the cellular level. In studies of the near-ultraviolet photobiology of skin fibroblasts of BS patients we have investigated the survival of the colony forming ability and the formation of DNA single strand breaks following exposure to monochromatic light at 313 nm. Near-ultraviolet represents a major portion of the solar radiation which reaches the surface of the earth. Abnormal survival curves were observed in 6 of 7 BS strains, 4 strains being hypersensitive to the lethal action of 313 nm light. In 6 of 8 strains 313 nm light induced excessive DNA fragmentation. These abnormalities in the response of cultured BS fibroblasts to near-ultraviolet light may be reflection in vitro of the skin sensitivity of BS patients to sunlight.
Further insight into the pathology of BS was obtained in cytogenetic studies. A low molecular weight component was identified in concentrated media from 6 BS fibroblast strains which induces chromosomal aberrations in phytohemagglutinin stimulated lymphocytes from normal donors. The activity of this clastogenic factor could be decreased substantially by the addition of bovine CU-Zn superoxide dismutase. The clastogenic factor also induced sister chromatid exchanges in normal lymphocytes, albeit with low efficiency. In analogy to collagen diseases such as systemic lupus erythmatosus, Crohn's disease and periarteritis nodosa it is speculated that BS fibroblasts are deficient in the detoxification of active oxygen species ($O_2^{\cdot}$, $OH^{\cdot}$). On the basis of our photobiological and cytogenetic results a new hypothesis for the pathology of BS will be discussed.
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PROGNOSTIC FACTORS IN THE TREATMENT OF METASTATIC GERM CELL CANCER

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91 patients with metastatic germ cell cancer were classified as having either advanced disease (AD) or minimal disease (MD). Criteria for staging are given. All patients were treated similarly according to protocol 01/76 of the Swiss Group for Clinical Cancer Research (SAKK). Complete remission (CR) rates (95 % vs 35 %) and survival (84 % vs 33 %) were significantly better ($p < 0.001$) for the MD group than for the AD group. Disease sites did not influence the therapy results. Patients with MD had higher CR rates ($p = 0.003$ to 0.009) than AD patients at all sites (lung, abdomen or combined sites). The incidence of MD was higher in patients with embryonal cell carcinoma than in all other histology groups (54 % vs 31 %, $p = 0.026$). This was reflected in a higher CR rate (77 %) for the embryonal cell carcinoma patients than in the other histological groups (46 %, $p = 0.003$). The CR rate for patients with MD was the same in all histology groups (89 % to 100 %). In AD the 50 % CR rate for embryonal cell carcinoma patients versus the 28 % rate for other patients showed a definite trend but did not reach statistical significance. The dosages of chemotherapy given had no apparent effect upon CR rates. Relaps rates were significantly affected by dosage reduction, and in AD patients, by the number of chemotherapy cycles given.

LONG TERM SURVIVORS WITH SMALL CELL CARCINOMA OF THE LUNG

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Several authors have recently reported long term, disease-free survival in patients with small cell carcinoma of the lung (SCCL) after aggressive initial treatment. In an attempt to identify long term, potentially cured survivors with SCCL in Switzerland a questicnnaire was sent to all medical oncology centers throughout the country. 14 patients with SCCL were reported achieving disease-free survival for over 24 months after initial therapy. Median age was 61 (39 - 80), median performance status 0 (0 - 2), 2 were females and 12 were males. 13 patients were classified as limited

disease, 1 patients had extensive disease with boney metastases. 2 of the 13 patients with limited disease had a small peripheral nodule detected on routine chest films. Only 2 patients had weight loss in the 6 months prior to the diagnosis. 5 patients were treated with local therapy alone (surgery 3, radiotherapy 1, surgery plus radiotherapy 1), 9 patients received systemic treatment (chemotherapy 5, chemotherapy plus radiotherapy 4). Median duration of cytostatic treatment was 17 months (3 - 39) with 3 of 9 patients receiving chemotherapy for less than 6 months. Chest radiotherapy doses varied from 2000 rads over 1 week to 7000 rads over 7 weeks. Only 1 patient received prophylactic cranial irradiation. 3 patients relapsed after initial treatment (surgery 1, radiotherapy 1, radiotherapy plus chemotherapy 1) after 27, 34 and 54 months. Median survival is 56+ months (27+ - 81+). Patients have been off treatment for a median of 41+ months (2+ - 75+).
We conclude that long term, disease-free survival can be achieved in patients with limited disease SCCL even with relatively short inital treatment.

PHASE I CLINICAL TRIAL AND PHARMACOKINETIC STUDY OF 5'-DEOXY- 5-FLUOROURIDINE

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5'-deoxy-5-fluorouridine (DFUR) is a new fluorouridine analog lacking a 5'-hydroxyl group in the chemical structure of its pentose ring. Under the action of uridine phosphorylase, 5-fluorouracil (FU) is released. DFUR is thus acting probably as a prodrug. DFUR is active against several experimental animal tumors. Further, it has a higher therapeutic index compared to FU in animals. DFUR has been administered as a rapid intravenous bolus injection daily x 5 and repeated every 3 weeks. 21 patients were treated at various dose levels. The majority of patients were non pretreated and had gastro-intestinal adenocarcinoma or non small cell lung cancer. 2 courses of DFUR or more were administered to 15 patients. A minimum of 4 patients were entered at each dose level. Doses were escalated from 300 - 3000 mg/m2/day. Intrapatient dose escalation was not done. No significant leucopenia was detected, but occasional thrombopenia was seen at each dose level. There was no evidence of cumulative myelotoxicity on subsequent courses of DFUR. Anorexia and nausea was seen in 4 patients, without drug induced vomiting. 2 patients had discrete and 1 patient severe diffuse stomatitis. Precordial pain with reversible electrocardiographic changes or transient cardiac enzymatic elevations was observed in 2 patients. The maximal tolerated dose has not yet been reached. Pharmacokinetic data are available for 5 patients after administration of 1000 to 2100 mg of DFUR. The unchanged drug elimination has a mean $t_{1/2}\ \alpha$ of 5.6 min. (range 3 - 8.3 min.) and a mean $t_{1/2}\ \beta$ of 20.5 min. (range 14.5 to 30.8 min.). Distribution volume β is between 27 and 50 liters. Total plasmatic clearance lies between 0.8 and 1.8 liter/min. We conclude that DFUR can be given at higher doses than FU and that its clinical tolerance is good, at the dose levels tested.

PHASE I TRIAL OF α 1,3,5-TRIGLYCIDYL-S-TRIAZENETRIONE (TGT, NSC-296934)

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TGT is a new anticancer agent that was identified by random screening. It is a triepoxide derivative with alkylating properties. The drug is active against a wide variety of experimental murine tumors including P388 leukemia resistant to cyclophosphamide, intracerebrally implanted L1210 leukemia and ependymoblastoma. This ongoing phase I trial was designed to determine the maximum tolerated dose (MTD) in adult patient with solid tumors using daily treatments for 5 consecutive days. The therapy course is repeated every 3 weeks. The drug is given iv. bolus. A total of 33 patients have been entered in the trial with a median age of 59 (38 - 73) and a median performance status of 70 (40-90). All have received prior chemotherapy and had recovered from prior drug-induced side-effects. Patients had following tumors : 8 colo-rectal, 8 lung, 6 breast, 4 melanoma, 2 upper-GI, 2 headneck, 2 unknown origin, 1 sarcoma. The trial was initiated at a starting dose of 12 mg/m2/d corresponding to 1/10 LD10 in the mouse. To date, doses have been escalated up to 600 mg/m2/d (= level 13). Dose levels have been occasionally increased within the same patients when no toxicity was encountered in previous courses. So far not clearly dose-related toxic effects have been observed. Toxic manifestations include nausea-vomiting (6 patients), phlebitis (7 patients) and erratic myelo-suppression (5 patients). So far antitumor activity has not been detected. Since the MTD has not yet been clearly reached, the trial as well as pharmacokinetic studies are ongoing.