

CYTOGENETIC AND ULTRASTRUCTURAL STUDIES IN THERAPY-RELATED LEUKAEMIA.

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Cytogenetic studies were performed on 12 myeloid disorders following intensive therapy for malignant diseases. These were breast cancer (9) plasmocytoma (1) non-Hodgkin lymphoma (1) and malignant melanoma (1). All the primary neoplasms were treated by local radiotherapy. Then, all the patients but one* received prolonged chemotherapy including at least one alkylating agent.

In all cases presenting with a clinical evolution and a morphological pattern of typical iatrogenic leukaemia, numerous clones of cells with multiple cytogenetic abnormalities were observed. Ultrastructural findings included: nuclear-cytoplasmic asynchrony, abnormal granules and bundles of micro-filaments in granulo-monocytic cell line, membrane-bound nuclear blebs and intra-nuclear clefts in erythroblastic cells and abnormal platelets. Multiple anomalies were noted on all marrow cell-lines, bearing out the extended involvement of the bone-marrow, so-called "panmyelosis".

In a single case* with a peculiar haematological pattern ("eosinophilic leukaemia"), the karyotype was found to be completely normal, leading to the hypothesis that this atypical disorder, which occurred a few weeks before the patient's death, was not due to the same therapy-induced bone-marrow damage.

DETECTION OF 2,3-DIHYDROXY-2-(7'-GUANYL)-3-HYDROXYAFLATOXIN B₁ (AFB-GuaI) IN HUMAN URINE.Herman Autrup, Johnstone Wakhisi¹, Abulkalam Shamsuddin and Kirsi Vahakangas. Laboratory of Human Carcinogenesis, National Cancer Institute, Bethesda, MD, USA;¹University of Nairobi, Kenya.

A possible role of aflatoxin B₁ (AFB) in the etiology of liver cancer has been suggested from several laboratory-epidemiological studies. In Murang'a District, a positive association between dietary intake of AFB and the incidence of liver cancer has been established. To further examine this hypothesis, we have tested urine samples collected at Murang'a District hospital for the presence of AFB-GuaI. Urine samples were collected at the out-patient clinic from patients without any known liver disorder. Urinary proteins were removed by precipitation with 2-propanol, and the urinary products were collected on a C₁₈ Sep-Pak. After elution with 80% methanol, the eluate was analyzed by high pressure liquid chromatography using a C₁₈ Bondapak column. Urine samples with compounds absorbing (365 nm) in the region of AFB-GuaI (elution time 14 min) were rechromatographed using an Ultrasil-Si column (retention time 6.0 min). Eight of 106 samples had a detectable level of AFB-GuaI; its identity was confirmed by synchronous fluorescence spectrophotometry with photon counting. Semiquantitative determinations indicate that the amount of AFB-GuaI in 25 ml of urine ranged from 0.3 to 3 pmoles. These results are an indication that metabolic activation of AFB and interaction between its ultimate carcinogenic form and cellular nucleic acid occurs in humans.

SEQUENTIAL CELLULAR CHANGES DURING CHEMICAL CARCINOGENESIS

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Carcinogenesis induced by chemical compounds in various experimental models has been studied sequentially by cytomorphological, cytochemical and morphometric methods. In a number of tissues early focal lesions with characteristic cellular changes have been detected by these methods. A sequence of qualitatively different cell populations seemed regularly to lead from the early foci to the tumours appearing weeks or months later. The findings support the view that the chemically induced neoplastic cell transformation is a slow process which takes place stepwise and differs from one tumour type to the other. The identification of putative preneoplastic and early neoplastic cell populations by morphological and cytochemical micromethods allows for the first time the dissection and subsequent detailed investigation of target cells of chemical carcinogens which are at a high risk of becoming cancer cells. The combination of cytochemical and biochemical micromethods seems to be the most useful tool for clarifying a number of important problems of carcinogenesis at present.