proceed towards the fully transformed malignant phenotype.

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Biomonitoring of exposure to genotoxic agents and tumoral markers in uremic patients undergoing hemodialysis

A higher incidence of malignancies in uremic patients receiving long-term dialysis has been established through epidemiological studies. The present work was carried out to determine whether patients suffering from renal insufficiency who undergo hemodialysis are more highly exposed to genotoxicity. In 30 patients and 30 age-matched healthy volunteers three cytogenetic tests with different endpoints have been determined: sister-chromatid exchanges (SCE), chromosome aberrations (CA) and proliferating rate indices (PRI), as well as tumoral markers, such as carcinoembryonic antigen, α-fetoprotein and tissue polypeptide antigen. SCE frequency and CA were higher in patients ($p < 0.05$) who also showed enhanced values of tumoral markers. Cytogenetic and tumoral markers were more elevated in cases of pyelonephritis. With regard to the composition of the membranes used in the dialyzers, increased values of CA were associated with cuprophan and those of SCE with polyacrylonitrile. The endogenous and exogenous factors possibly involved in the production of the cytogenetic alterations are discussed.

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Liquid-holding experiments on G0 human lymphocytes exposed to methylmercury chloride

The capacity of human lymphocytes to repair structural and numerical damages induced by methylmercury chloride (MMC) was evaluated after treatment in the G0 phase of the mitotic cycle. The cultures were treated with MMC (0–25 $\times 10^{-6}$M) for 24 h and structural (CA) and numerical (AN) aberrations were scored in metaphases I and II. Moreover, the variation of proliferation index (IP) was assessed. The frequency of sister-chromatid exchanges (SCEs) was evaluated in 25 second metaphases. MMC induced chromosomal and chromatid aberrations in a dose-related manner and the lymphocytes showed a low repair capacity after 48 h of liquid holding. AN induced in the G0 phase reached a significant level only at the highest tested dose. When the AN frequency was compared to that induced by vinblastine (VB), used as a positive control under same conditions, important differences were observed in the occurrence of AN. Therefore, by considering the liquid holding effect, it may be inferred that MMC induced either reparable or stable damage of DNA and of other cellular structures, and these may subsequently yield chromosomal aberrations in the following cellular cycles.

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Comparative (geno)toxicity assessment of organic mercury compounds in human lymphocytes and in rat tissues in vitro and in vivo

The potential of methylmercury chloride (MMC) and dimethylmercury (DMM) to induce DNA damage was investigated by means of the microgel electrophoresis assay. This rapid and efficient method allows measurement of single-stranded DNA damage and alkali-sensitive lesions at the individual cell level. Human and rat lymphocytes (HL, RL), rat gastric mucosa cells (RGM) and rat hepatocytes (RH) were treated in suspension culture in vitro for 1 h with different

concentrations of MMC and DMM and were then subjected to electrophoresis. The cytotoxicity of the two compounds was also assessed by dye exclusion using aliquots of the treated cell suspensions. MMC and DMM were both genotoxic in vitro but MMC resulted in an about 10-fold higher degree of damage. The extent of damage in the three cell types HL, RL and RGM was similar for each compound, but in RH MMC exhibited a lower potency of genotoxic activity. In most cases, the induced DNA damage was comparable to the degree of induced cytotoxicity. An analysis of repair kinetics following exposure to 2 μg/ml MMC was carried out in HL. The bulk of DNA repair occurred after 90 min and it was about complete by 120 min after discontinuation of exposure. The degree of viability (76%) remained constant during the experiment. Finally the genotoxic effects of MMC were analysed in RL and RGM following 1 h and 6 h in vivo exposure of the donor animals (5 mg/kg; p.o.). So far low levels of DNA damage seemed to be detectable in RL (6 h exposure). Presently higher doses are being analysed to better define the potential in vivo genotoxicity of MMC.

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Effect of smoking on plasma oncoprotein levels and cytogenetic parameters in humans

The measurement of serum oncoprotein levels has been proposed as a method for assessing carcinogenic risk from exposure to chemicals. It has been proposed that the correlation of an increase in these levels with such exposure could suggest a greater carcinogenic risk for an exposed population. As part of an on-going research project designed to investigate the suitability of plasma oncoprotein levels as an end-point for population monitoring, 20 smokers (averaging 16 per day for an average 16.8 years) and 20 non-smokers were examined. They were pair-matched for a range of endogenous and exogenous life style factors and were not known to have been exposed to any other specific chemical hazard. Simultaneously, chromosome preparations from their lymphocytes were examined for the incidence of chromosome aberrations, sister-chromatid exchanges and proliferative rate index of the cells measured. Plasma samples from each individual were examined for the presence of *ras* protein. In agreement with previous work from this laboratory, no effect of smoking was found on any of the cytogenetic parameters, although a small, statistically non-significant, increase in sister-chromatid exchange was seen. No *ras* protein was found in any of the plasma samples (but was detected in the plasma spiked with low amounts of purified recombinant *ras* protein used as a positive control). It was concluded that smoking did not induce detectable increases in plasma oncoprotein levels in this study. Therefore it may not be a confounding factor in human monitoring studies using plasma oncoprotein levels as an end-point.

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Paracetamol inhibits the repair of DNA damage induced by some mutagens in mammalian cells in vitro

Chronic exposure to high doses of the analgesic paracetamol (pHAA) has been reported to cause cancer in rodents, and the drug is genotoxic in a number of in vitro test systems. pHAA interferes with DNA synthesis in vitro, and inhibits ribonucleotide reductase as demonstrated recently. In the present in vitro study we have investigated the effects of pHAA on the repair of DNA damage in mammalian cells of various origin. Resting human peripheral lymphocytes were exposed to low doses of 254-nm UV (3 J/m^2), post-incubated in the presence or absence of pHAA, and assayed for SSBs (single-strand breaks + alkali-labile sites) with alkaline elution. Therapeutically relevant concentration of pHAA (0.3 mM) increased the maximum level of SSBs