METABOLISM AND DNA BINDING OF AFLATOXIN B_1 (AFB_1) AND 2-ACETYLAMINOFLUORENE (AAF) IN HUMAN AND ANIMAL BLADDER AND TRACHEOBRONCHIAL TISSUES. F.Bernard Daniel, Herman A.J.Schut and Gary D.Stoner. Health Effects Research Laboratory, U.S.Environmental Protection Agency, Cincinnati, OH 45268 and Department of Pathology, Medical College of Ohio, Toledo, Ohio 43614, USA.

The metabolism, DNA binding and adduct formation was studied in cultured bladder (Bl) explants with AAF and AFB_1 as substrates, and in cultured tracheobronchial (Tb) explants with AFB_1 as the substrate. Tissues from the human, monkey, dog, hamster and rat were incubated in medium without serum in a 50% O_2-45% N_2-5% CO_2 atmosphere. DNA binding (μmol/mol deoxyribonucleotide) was measured after 24 hr incubation with 1 μM [^{3}H]AAF or 1 μM [^{3}H]AFB_1

Substrate (tissue)	Human	Monkey	Dog	Hamster	Rat
AFB_1(Bl)	1.5 ± 2.3	2.5 ± 1.1	5.2 ± 2.3	26.2 ± 13.3	3.8 ± 1.1
AFB_1(Tb)	2.2 ± 2.4		10.6 ± 6.6	134.6 ± 44.6	5.7 ± 2.4
AAF (Bl)	0.2 ± 0.2	0.4 ± 0.3	2.0 ± 1.0	1.1 ± 1.7	0.5 ± 0.4

The binding levels were not correlated with the relative susceptibilities of these species to AAF or AFB_1 induced tumours. In all cases, adduct analysis of AFB_1-DNA or AAF-DNA by HPLC showed the presence of adducts which were identical to those formed by the liver of various species. HPLC analysis of AAF metabolites in the medium showed that both ring-hydroxylated and N-hydroxylated metabolites were formed by bladder explants of all species, with the amounts of each varying with the species. It is concluded that both human and animal bladder and tracheobronchial tissues metabolize AAF and AFB_1 to products which are qualitatively similar to those formed in the liver, and that quantitative differences in these products may account for species differences in susceptibility to cancer induced by these agents.

AN EXPERIMENTAL STUDY ON THE CAUSAL RELATIONSHIP BETWEEN SCHISTOSOMA HAEMOTOBIASIS AND BLADDER CANCER. P.K.Das[1,2,3], H.Walvoort[2], H.Tubing[1] and G.Godges[4]. [1]Formerly: International Immunology Training and Research Center, Amsterdam, The Netherlands. [2]National Institute of Public Health, Bilthoven, The Netherlands. [3]Department of Pathology, University of Amsterdam, The Netherlands. [4]Imperial Cancer Research Fund, London, U.K.

Statistical evidence suggests an association between bladder cancer and schistosome haematobiasis (bilharziasis). This relationship does not, however, always prevail. Involvement of bilharzia in the genesis of bladder cancer remains essentially little studied at the experimental level and this has led to an in vitro investigation aimed at establishing whether the bilharziasis is a co-factor or a direct carcinogen.

In this preliminary study, hamster bladder organ cultures were treated with S. haematobium egg hatching fluid (HF) in combination with anti-HF antibody and complement, or anti-HF antibody and/or complement alone or HF alone. There was a significant urothelial response only when cultures were exposed to the first experimental combination and this could be suggestive of antibody dependent hypersensitivity reaction, particularly since a relationship between HF products of S.haematobium and the generation of bladder cancer has been suggested in the literature. Our preliminary data indicate that the organ culture model may serve as a valid system for further investigations on the role of such products, either alone or with carcinogenic compounds, in the development of bladder carcinoma.

PREVENTION AND/OR REVERSIBILITY OF CHEMICAL MUTAGENESIS BY PROSTAGLANDINS: A NEW CONCEPT. U.N. Das, Department of Genetics, Osmania University, Hyderabad-500007 and UND MedTech Centre, Yellareddyguda, Hyderabad-500873, India.

Earlier I proposed that most, if not all, mutagens and carcinogens imbalance the prostaglandin (PG) system in such a way that a deficiency of PGE1 and thromboxane A2(TXA2) and an excess of PGE2 and PGF2alpha occurs. Further, normal binding of PGE1 and TXA2 to DNA may regulate gene action, prevent mutagenesis and suppress the activation of oncogenes. If this concept is correct, methods designed to enhance PGE1 and TXA2 synthesis should be able to prevent/reverse mutagenesis.

In mice, using the micronucleus test and sperm head abnormality assay as markers, it was observed that colchicine, a PGE1 and TXA2 synthesis and action enhancer, prevents/reverses the mutagenic action of diphenylhydantoin and benzo(a)pyrene. These results suggest that possibly prostaglandin system has a role in mutagenesis and thus in carcinogenesis.