MODIFICATIONS IN SERUM AND LIVER BIOCHEMICALS DURING THE CHEMICAL INDUCTION OF CIRRHOSIS. N.Mihail[1], C.Nistor[2], A.Cacoveanu[2] and Klara Makkay[3]. [1]Centre for Biological Research, Cluj Napoca, Romania. [2]Oncological Institute, Cluj Napoca, Romania. [3]Faculty of Chemistry, Cluj Napoca, Romania.

The modifications in a series of biochemical parameters in the serum and liver were determined during the chemical induction of cirrhosis. Modification in the following were measured: the enzymes E.C. 3.1.3.1, E.C. 2.6.1.1, E.C. 2.6.1.2 and E.C. 3.1.1.8, bilirubin, total protein, calcium, magnesium, phosphorus, iron, copper, nitrogen and glucose.

We observed during the induction of cirrhosis increases of 150-200% in enzyme activities and 320% in bilirubin levels in the serum and a 410% increase in the bilirubin level in the liver. Modifications of between 40-100% were noted in the levels of the other parameters measured as compared with the levels in the serum and livers of normal animals.

CYTOTOXICITY AND MODE OF ACTION OF N, N'-bis (ALKYLMETHYL)-1,6-HEXANEDIAMINE DIOXIDES M.Miko, Department of Microbiology and Biochemistry, Slovak Polyt. University, 812 37 Bratislava, Janska 1, Czechoslovakia.

The cytotoxic activities of newly synthesized compounds mentioned above have been studied. The efficiency of the compounds was measured by determining the incorporation rate of ^{14}C-precursors (adenine, valine, thymidine, uridine) into appropriate macromolecules of Ehrlich's ascites carcinoma (EAC) cells. At the same time the effects on aerobic glucose utilization, lactic acid formation, content of SH-groups, respiration and levels of ATP have been compared. Cytotoxicity is a consequence of the cytolytic activity of the compounds mentioned above. Membranous effects were demonstrated by the measuring of marker enzyme activities lactate dehydrogenase (EC 1.1.1.27), malate dehydrogenase (EC 1.1.1.37), protein concentration in EAC cells and in the culture medium, as well as by morphological examination. It is evident that the biological membranes which, after interaction with amine oxides, undergo changes in molecular organization, osmotic and permeability properties, are the site of action.

CIRCADIAN DEPENDENT AND PROTRACTED EFFECT OF METHOTREXATE ON G1 CELLS STUDIED IN VIVO IN A KERATINIZED EPITHELIUM BY FLOW CYTOMETRY. U.Møller, J.K.Larsen, N.Keiding[1] and I.J.Christensen. The Finsen Laboratory and [1]Statistical Research Unit, University of Copenhagen, Copenhagen, Denmark.

In the partially synchronized cell system of the hamster cheek pouch epithelium, bolus injections of Methotrexate (Mtx) both in lethal and non-lethal dosage were found to inhibit cell cycle progression primarily by impairing the G1/S transition. These results were assessed by flow cytometric DNA analysis. The inhibitory effect of Mtx materialized as a relative decrease in S-fraction, was maintained for more than one 24 hr period, and was both circadian dependent and dose dependent. The bolus injection of Mtx was given either at 12.00 hr (minimal number of cells in S phase) or at 02.00 hr (maximal number of cells in S phase). The maximal cumulative decrease in S-fraction was seen with the Mtx bolus injection at 12.00 hr. The time of the decrease in S-fraction was independent of the time of Mtx injection, but was correlated to the time of the diurnal flux from G1 to S phase. In earlier toxicological studies the survival of hamsters was dependent on the time of injection, and was highest after injection at 12.00 hr. Thus maximal cytokinetic effect on epithelial cells was found by a time schedule which had minimal lethal effect on the individual.