The results of a series of experimental trials using rats with toxic liver cirrhosis are given. After 12 hours, and in 1, 3, 5 and 7 days after the pathological condition simulation, blood erythrocytes in animals as well as homogenates of liver parenchyma and pancreatic lipid peroxidation were determined by calculation of concentration of lipoperoxidation intermediates and the activity of antioxidant enzymes. The findings suggest that the course of experimental cirrhosis is accompanied by sharp intensification of lipid peroxidation and associated inhibition of the enzymatic activity and non-enzymatic antioxidant protection units, as noted in 5 days with a maximum severity on the day 3. There was shown the involvement of erythrocytes in mediating the pathological process, as well as the liver parenchyma and pancreas. The authors conclude that the complex pathogenetic therapy of liver cirrhosis should include the administration of preparations with expressed antioxidant properties.

Keywords: experimental cirrhosis, lipid peroxidation, antioxidant defence, blood, erythrocytes, liver, pancreas, complex pathogenetic therapy.

Conference participants, National championship in scientific analytics

![Image](http://dx.doi.org/10.18007/gisap.msp.v0i9.1267)
- superoxide dismutase (SOD), glutathione peroxidase and glutathione reductase. The content of LP products was determined by the method described [12, 13]. SOD activity was determined by the level of NBT reduction inhibition in the presence of NADH and phenazine methosulfate. [14] Glutathione peroxidase activity was determined by the glutathione oxidation rate in the presence of tertiary butyl hydroperoxide [15], the activity of glutathione-NADRH – by the oxidized glutathione reduction rate in the presence of NADRH [16].

MDA and DC content in the rat blood plasma and red blood cells was determined as described [12, 13]. SOD activity was determined by the method of [14]. Activity of general glutathione was determined by the method of [16]. The α-tocopherol content was determined as described [17] in the modification [18].

The results were processed statistically using One Way Analysis of Variance Criteria. Differences were considered significant at p < 0.5.

Results and discussion.
There was a significant accumulation of MDA and DC in the blood of rats with ELC, absolute indices and concentrations of which reached 2.69 ± 0.18 nmol/l and 0.70 ± 0.07 mmol/l, respectively in 12 hours of the process, which was 1.9 times (p < 0.01) and 1.7-fold (p < 0.1) higher than in the control cases (Table 1). Later on, the value of MDA and DC continued to increase, reaching a maximum on the 3rd day of the pathological process when the value of the indices studied exceeded those in the controls by 3.1 times and 2.4 times (in both cases p < 0.01). Subsequently, there was a slight decrease in the value of MDA and DC, the concentration if which remained significantly higher than in controls (p < 0.5, Table 1) on the 7th day.

Under these conditions, the blood of rats showed a significant reduction in the activity of antioxidant enzymes – catalase, SOD, glutathione and

Note: in all Tables * - p < .05, ** - p < .01, and *** - p < .001 - significant differences of the studied indices compared to those values in the control group (ANOVA statistical test)

<table>
<thead>
<tr>
<th>Indices under study</th>
<th>Control group, n=9</th>
<th>Values of the studied indices during different periods after reproduction of ELC (M±m), n = 10</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>in 12 hours</td>
<td>in 24 hours</td>
</tr>
<tr>
<td>Malon dialdehyde, mmol / l</td>
<td>1.4±0.11</td>
<td>2.69±0.18***</td>
</tr>
<tr>
<td>Diene conjugates, mmol / l</td>
<td>0.41±0.05</td>
<td>0.70±0.07**</td>
</tr>
<tr>
<td>Catalase, cond. u</td>
<td>1.92±0.13</td>
<td>1.31±0.13***</td>
</tr>
<tr>
<td>SOD units / ml</td>
<td>2.79±0.17</td>
<td>1.68±0.16***</td>
</tr>
<tr>
<td>Total glutathione mM</td>
<td>20.1±0.6</td>
<td>15.7±1.1**</td>
</tr>
<tr>
<td>a-tocopherol, (mmol / ml)</td>
<td>51.8±3.7</td>
<td>38.9±3.8*</td>
</tr>
</tbody>
</table>

Table 1.

The concentration of lipid peroxidation products and antioxidant enzyme activity in the blood of rats in different periods after reproduction of liver cirrhosis

<table>
<thead>
<tr>
<th>Indices under study</th>
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<tbody>
<tr>
<td></td>
<td>in 12 hours</td>
<td>in 24 hours</td>
</tr>
<tr>
<td>Malon dialdehyde, mmol / l</td>
<td>2.0±0.2</td>
<td>3.2±0.3*</td>
</tr>
<tr>
<td>Diene conjugates, mmol / l</td>
<td>3.1±0.3</td>
<td>4.2±0.4***</td>
</tr>
<tr>
<td>Catalase, cond. u</td>
<td>2.9±0.2</td>
<td>2.0±0.2**</td>
</tr>
<tr>
<td>SOD units / ml</td>
<td>2.5±0.2</td>
<td>1.6±0.2**</td>
</tr>
<tr>
<td>Glutathione peroxidase, mmol/min/l</td>
<td>3.3±0.3</td>
<td>2.0±0.2*</td>
</tr>
<tr>
<td>Glutathione reductase, mkat NADPH /l</td>
<td>1.4±0.1</td>
<td>0.9±0.1*</td>
</tr>
</tbody>
</table>

Table 2.
α-tocopherol, indices of the absolute activity were minimal during 1 - 3 days since the moment of ELC reproduction (p < 0.1). Subsequently the activity of the studied enzymes did not restore until the 7th day of the experiment (p <0.5, Table 1).

A concentration of the intermediate products of lipid peroxidation in the red blood cells had a similar tendency: intense pathobiological changes in the red blood cells were revealed during 1-5 days of the ELC course with the highest concentration of MDA and DC on the 3rd day of the pathological process, when the studied indices exceeded those in control cases (p < 0.01, Table 3). The maximum expression of the intermediate products of lipid peroxidation accumulation was observed on the 1st day of ELC (p < 0.01) with a slight decrease in the studied indices on the 3rd (p < 0.01) and 5th (p < 0.5) days of the experiment. On the 7th day of the experiment the values of the studied indices did not differ in the experimental and control groups (p> 0.5).

Thus, our results after a critical analysis allow us formulate the following basic points concerning the pathophysiological mechanisms of ELC. First, the ELC course is accompanied by the increased lipid peroxidation manifested in the accumulation of intermediate products of lipid peroxidation and decreased enzymatic activity, and non-enzymatic antioxidant protection units. These facts

<table>
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</tr>
</thead>
<tbody>
<tr>
<td>Malon dialdehyde, mcmol / l</td>
<td>2.87±0.19</td>
<td>4.82±0.33 *** 4.59±0.29 ** 3.61±0.21 * 3.14±0.23</td>
</tr>
<tr>
<td>Diene conjugates, mcmol / l</td>
<td>0.47±0.05 ***</td>
<td>0.85±0.08 ** 0.92±0.08 ** 0.67±0.09 * 0.55±0.08 0.43±0.04</td>
</tr>
<tr>
<td>SOD units / ml</td>
<td>1.79±0.17</td>
<td>1.05±0.08 * 0.98±0.08 ** 1.29±0.08 * 1.44±0.12 1.74±0.14</td>
</tr>
<tr>
<td>Glutathione peroxidase, units/g</td>
<td>2.71±0.19 **</td>
<td>1.47±0.12 *** 1.31±0.11 *** 1.82±0.13 * 2.04±0.16 2.30±0.18</td>
</tr>
<tr>
<td>Glutathione reductase, units/g</td>
<td>2.59±0.14 **</td>
<td>1.67±0.12 *** 1.43±0.12 *** 1.71±0.13 * 2.19±0.17 2.54±0.21</td>
</tr>
</tbody>
</table>
are consistent with the known views [19-21] on the pathogenetic role of intensification of lipid peroxidation in a number of pathological processes and inflammation under the action of heat, radiation factor and other alternating influences. Secondly, the data obtained demonstrates the involvement of the blood cell unit, namely erythrocytes, in pathogenetic mechanisms of the hepatocellular destruction; there is increased concentration of lipid peroxidation products and reduction of the antioxidant enzyme activity in the erythrocytes unidirectional with the blood plasma. Summing up these results and suggestions it becomes obvious that there is generalization of the pathological process in liver cirrhosis, which explains both its acceleration and magnitude of the abnormal cell changes, that should necessarily be taken into account in the clinical conditions when determining the appropriate treatment strategy for these patients.

Thirdly, we have shown the accompanying processes of accelerated lipid peroxidation and inhibition of antioxidant protection expression, which take place directly in the liver tissue. In our opinion this data explains the rapid development of large volume and, as a rule, irreversibility of the pathological process of the cellular destruction in liver cirrhosis. And finally, fourthly, taking into account the anatomical proximity, common physiological functioning and disorders similar to the liver parenchyma, which were manifested in shifting the dynamic equilibrium in the "POL-antioxidant system" towards the increased lipid peroxidation, we were able to clearly register the accumulation of lipid peroxidation products and inhibition of the antioxidant protection processes expression in the parenchyma of the pancreas somewhat less pronounced than in the liver tissue.

Summarizing the data, pathophysiological mechanisms of development of multiple organ dysfunction syndrome in liver cirrhosis, the development of liver fibrosis, portal hypertension and/or liver failure become obvious. Taking into account the facts of intensification of lipid peroxidation and resulted inhibition of antiradical protection activity, inclusion of drugs with antioxidant properties facilitating and/or preventing the process of the hepatocellular destruction is important for making up schemes of complex pathogenetic reasonable pharmacotherapy of liver cirrhosis. It may also provide crucial protective effect in preventing the development of hepatic insufficiency.

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