In order to study the pathogenetic mechanisms of vascular complications (peripheral angiopathy), 39 patients with type 1 diabetes mellitus were diagnosed with the phenomena of the beginning diabetic foot and changes in metabolism of different degrees of compensation: decompensated, subcompensated and compensated, and also on 20 healthy individuals. All patients received basic therapy with insulin preparations of short and intermediate action, and some patients with a subcompensated form received coenzyme Q10 simultaneously with hypoglycemic therapy. The parameters of lipid peroxidation and antioxidant system, concentration of total metabolites of nitric oxide, low density lipoproteins, activity of organo-specific enzymes: alanine aminotransferase, aspartate aminotransferase, gamma-glutamyl transpeptidase were determined. The change in blood flow in the vessels of the lower extremities (shin and foot segments) was judged by the rheovasogram determined by the "Valenta" diagnostic system. The obtained data testified to the presence of oxidative stress in patients with diabetes mellitus decompensated with subcompensated forms. At the same time, the concentration of nitric oxide and its bioavailability decreased due to an increase in the blood of atherogenic lipoproteins: low-density cholesterol and high-density cholesterol. These biochemical changes in the blood were accompanied by a violation of hemodynamics in the vessels of the shin and foot. Against the background of traditional treatment, there were positive changes in carbohydrate and lipid metabolism, but the indicators were significantly different from the control level, and hemodynamic changes in the segments of the shin and foot were preserved. Inclusion of coenzyme Q10 in the complex treatment of antioxidant led to a decrease in malonic dialdehyde content, an increase in the activity of antioxidant defense enzymes, and a concentration of total metabolites of nitric oxide. Bioavailability of nitric oxide also increased, due to a decrease in the concentration of low-density atherogenic lipoproteins. In the vessels of microcirculation, the tone of arterioles and precapillaries decreased, the modulus of elasticity increased, pulse blood filling increased in the segments of the shin and foot, and venous congestion decreased.
people with diabetes mellitus in the world, which is 6.6%. In the
genesis of vascular complications of type 1 diabetes mellitus,
endothelial dysfunction plays a pathogenetic role, which leads to
systemic hemodynamic disorders, including microangiopathies: nephropathy, retinopathy, diabetic foot, etc. Its role in the
development of vascular complications is caused by activation of
lipid peroxidation, disturbance of the metabolism of nitric oxide and non-enzymatic glycosylation of proteins [5-12]. Endothelial
dysfunction develops, the ability of endothelial cells to synthesize
nitric oxide - the most important vasodilator [13,14]. On the other
hand, the development of effective comprehensive methods for
treating type 1 diabetes mellitus with peripheral angiopathies is
topical and these questions are not enough in the literature.

The purpose of this study was to study the mechanisms of
endothelial dysfunction in patients with type 1 diabetes mellitus of
varying degrees of compensation and the effectiveness of complex
therapy with coenzyme Q₁₀.

Material and Methods
The investigations were carried out on the basis of the Republican
Endocrinology Dispensary of the Republic of North Ossetia-
Alania and the Department of Pathobiochemistry of IBMi VSC
RAS. The analysis was carried out in 39 patients with type 1
diabetes with duration of disease on average 1-35 years (aged 18
to 40 years) with the phenomena of peripheral diabetic angiopathy
and metabolic disorders of various degrees of compensation before, after basic and complex therapy and 20 healthy persons
without sugar Diabetes, constituting the control group. Among
the surveyed: men - 26, women - 13 patients with type 1 diabetes
mellitus. Assessment of the severity and phase of compensation for
type 1 diabetes mellitus was carried out according to clinical and
laboratory criteria recommended by the endocrinology research
center of the Russian Academy of Medical Sciences [15].

Patients were divided into 3 groups depending on the compensation
of metabolism:

• Decompensated patients - before treatment (n = 12 people).
• Patients with a subcompensated form of diabetes mellitus,
  who received basic therapy with insulin preparations - short-
  acting (actrapid) and intermediate action (protopid, monotard,
  actress, humulin) (n = 15 people).
• Patients with a subcompensated form of diabetes mellitus who
  received complex treatment: insulin preparations + coenzyme
  Q₁₀, 2 capsules 0.5 g each. (Evalar ZAO) per day with meals
  (n = 12).

Blood sampling for analysis was performed in the morning on
an empty stomach from the ulnar vein. Serum was obtained by
centrifugation at 4°C for 15 minutes at 2500 rpm. Glucoso E-D
(Vitale Diagnostics SPB), glycated Hb (HbAlc) colorimetry
method (Lachema kit), lipid peroxidation concentration by malonic
dialdehyde concentration (Asacawa T method) was determined
in blood by glucose oxidase method. [16], catalase activity by
the method of Korolyuk MA [17] and superoxide dismutase -
the autoxidation of epinephrine [18], the concentration of total
metabolites of nitric oxide [19], the activity of transaminases, the
content of total cholesterol ("Fluitest Chol", "Cholesterin Chool-
Papu", "Fluitest HOL-D Direct HOL-Cholesterol" Respectively,
the company "BIOKON".

The indices of diabetic angiopathy were changes in hemodynamics
in the segments of the shin and foot, determined using the
diagnostic system "Valenta". According to the rheovasogram, the
following indices were determined:
1. Rheographic index; B / p.
2. Modulus of elasticity; %.
3. Time of maximum systolic filling; Sec.
4. Diastolic index.
5. Venous outflow; %.

Statistical processing was carried out using the Microsoft Excel
program. The results are presented as the mean (Mean) and
the mean error (Sem). The reliability of the differences between these
patients with type 1 diabetes and the control group was checked
using Student's t-test, the level of statistical significance was
considered to be p <0.05.

Results and Discussion
The data presented in Table. 1 indicate that in patients with type 1
diabetes mellitus with decompensated and subcompensated forms,
there is a statistically significant increase in blood glucose and
glycated hemoglobin content, respectively, to 10.4 ± 0.71% and
8.6 ± 0.71% (p <0.001), in comparison with the control (HALAC,
5.3 ± 0.81%). Metabolic disorders, including glycated hemoglobin,
lead to activation of lipid peroxidation in patients in a state of
decompensation, which is accompanied by the accumulation
of malonic dialdehyde in the blood. The antioxidant system is
disrupted - the activity of superoxide dismutase decreases with
decompensated and subcompensated forms of type 1 diabetes
mellitus, and catalase activity rises. Oxidative stress develops,
against which there is a decrease in the content of total metabolites
of nitric oxide in the blood serum. The intensification of the
processes of free radical oxidation contributes to the disruption of
the activity of eNOS (NOS III), through the effect on the cofactors:
Tetrahydrobiopterin and Nicotinamide adenine dinucleotide
phosphate +.

The radical (O₂⁻) formed in this superoxideidion reacts with
NO, producing peroxynitrite, which has a damaging effect
on the vascular endothelium. Reducing the bioavailability of
NO contributes to the violation of cholesterol metabolism and
atherogenesis. In patients with type 1 diabetes mellitus, the content
of total cholesterol, triacylglycerides, low-density cholesterol
and high-density cholesterol decrease. These data indicate
the prevalence of athrogenic lipoproteins in the blood, also
contributing to the development of endothelial dysfunction and a
decrease in the bioavailability of NO, which is consistent with the
literature data [20-22]. All these patients had cardiopathy, arterial
hypertension, a decrease in the concentration of total metabolites
of NO and peripheral angiopathy of the lower extremities (Table
1).
the other part of the patients it did not differ significantly from the venous system increased in 37.8-45.9% of patients, while in the condition of the arterial network were accompanied by venous vessels and the nature of hemodynamics. These changes in the characterizing the state of the vascular wall of microcirculatory and almost reached the control level after 14-20 days of complex therapy with insulin preparations. The activity of superoxide dismutase increased against the background of complex therapy and almost reached the control level after 14-20 days of complex treatment, whereas the catalase activity decreased, but remained elevated compared to the control group. The concentration of total metabolites of NO - the main vasodilating factor was increased.

Analysis of data characterizing hemodynamic changes in the lower extremities showed that in patients with decompensated and subcompensated forms of type 1 diabetes mellitus, the pulse blood filling of the shank segments (left and right) and the foot (left and right) decreased, as a result of vascular elasticity, Arterial network of the lower leg and foot, as well as arterioles and precapillaries. In the process of statistical processing of rheovasogram indices in 51,3-70,3% of patients with decompensated and subcompensated forms of type 1 diabetes mellitus, the rheographic index (by 122% and 143%), respectively, characterizing the state of the vascular wall of microcirculatory vessels and the nature of hemodynamics. These changes in the condition of the arterial network were accompanied by venous congestion by 374.6% and the indicator subject to outflow through the venous system increased in 37.8-45.9% of patients, while in the other part of the patients it did not differ significantly from the level of normative indices. The maximum systolic filling rate was increased by 126.4% in 62.29-72.97% of patients; the diastolic index was increased by 196% in 70.3-86.5%. Comparing the nature of changes in the hemodynamics of the left segments of the shin, the foot with the right, asymmetry is often noted. Infringement of microcirculation of the lower extremities (shin, foot) is accompanied by hyperperfusion in the main arterial vessels and an increase in the value of arterial blood pressure by 131%.

Along with this, in patients with type 1 diabetes mellitus with cardiopathic disorders and angiopathies as a result of activation of lipid peroxidation, there is a violation of the permeability of cardiomyocyte cell membranes and an increase in the activity of transaminases: alanine aminotransferase (by 236.3%), aspartate aminotransferase (by 125%) And the membrane enzyme gamma-glutamyl transpeptidase 7-fold.

Chain reactions involving free radicals are the cause of endothelial dysfunction, accompanied by organ-systemic disorders in type 1 diabetes mellitus, which served as the basis for the use of complex antioxidant treatment with coenzyme Q_{10} [23]. This drug was taken by patients 2 capsules 1 time per day during meals for 14-20 days along with traditional therapy, including insulin preparations. All general clinical, biochemical and functional studies were performed 14-20 days after the beginning of the course of therapy, i.e. at an extract from a hospital. In contrast to the data obtained against the background of traditional therapy, complex treatment in combination with the antioxidant coenzyme Q_{10} showed a more statistically significant decrease in the final product of lipid peroxidation - malonic dialdehyde in the blood, the values of which remained statistically significantly elevated in patients with a subcompensated form of diabetes mellitus, Who received therapy with insulin preparations. The activity of superoxide dismutase increased against the background of complex therapy and almost reached the control level after 14-20 days of complex treatment, whereas the catalase activity decreased, but remained elevated compared to the control group. The concentration of total metabolites of NO - the main vasodilating factor was increased. Thus, after the course of treatment, complex therapy led to a significant positive shift in the lipid peroxidation system-antioxidant protection, there was a significant increase in superoxide dismutase activity and a decrease in catalase activity, i.e. an imbalance was eliminated in this system. Reduction of oxidation-reduction processes led to an increase in the nitrooxide-forming function of the endothelium: vessels and an increase in the serum concentration of total NO metabolites. Positive dynamics of metabolic and functional indices was detected in some patients with a subcompensated form of type 1 diabetes mellitus receiving complex therapy: hypoglycemic drugs and coenzyme Q_{10}. Against the background of complex treatment, peripheral hemodynamics normalized, due to the restoration of the elasticity of the microcirculation vessels, a decrease in the tone of arterioles and precapillaries, or an insignificant increase in the segments of the shin. These changes are indicated by a decrease in the rheographic index and the modulus of elasticity of the wall of arterioles and precapillaries. The tone of the venous network either fully recovered or the hypotension was negligible, in accordance with which the volume of venous outflow decreased. In the segments of the foot against the background of a hypoglycemic and metabolic correcting drug, there is also an improvement in pulse blood filling, due to a decrease in vascular tone, since the modulus of elasticity decreases. There is a decrease in the volume of venous outflow due to an increase in the tone of the venous network.

### Table 1:Change in biochemical parameters in peripheral angiopathy (diabetic foot) of different compensation of metabolism in patients with type 1 diabetes mellitus.

<table>
<thead>
<tr>
<th>Index</th>
<th>Control group</th>
<th>Decompensated form</th>
<th>Subcompensated form</th>
<th>Compensated form</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose, mmol/l</td>
<td>5.06 ± 0.1</td>
<td>14.6 ± 0.5</td>
<td>10.6 ± 0.2</td>
<td>7.133 ± 0.261</td>
</tr>
<tr>
<td>HbA1c, %</td>
<td>5.3 ± 0.81</td>
<td>10.4 ± 0.71</td>
<td>8.6 ± 0.71</td>
<td>5.3 ± 0.81</td>
</tr>
<tr>
<td>Low-density lipoprotein cholesterol, mmol/l</td>
<td>2.92 ± 0.13</td>
<td>4.61 ± 0.59</td>
<td>3.48 ± 0.59</td>
<td>3.08 ± 0.36</td>
</tr>
<tr>
<td>High-density lipoprotein cholesterol, mmol/l</td>
<td>1.42 ± 0.05</td>
<td>1.15 ± 0.04</td>
<td>1.24 ± 0.05</td>
<td>1.39 ± 0.06</td>
</tr>
<tr>
<td>Malonic dialdehyde, mmol/ml</td>
<td>2.93 ± 0.177</td>
<td>5.70 ± 0.80</td>
<td>4.20 ± 0.61</td>
<td>3.80 ± 0.32</td>
</tr>
<tr>
<td>Catalase, mcd/l</td>
<td>251.1 ± 42.8</td>
<td>564.8 ± 43.2</td>
<td>438.0 ± 34.4</td>
<td>329 ± 23.7</td>
</tr>
<tr>
<td>Superoxide dismutase, unit/act.</td>
<td>3.55 ± 0.156</td>
<td>2.45 ± 0.061</td>
<td>2.65 ± 0.045</td>
<td>3.15 ± 0.035</td>
</tr>
<tr>
<td>NO, mc/mol</td>
<td>53.64 ± 0.831</td>
<td>34.5 ± 1.208</td>
<td>41.9 ± 0.459</td>
<td>50.05 ± 1.39</td>
</tr>
</tbody>
</table>

Note: * - p (reliability) to the norm; ^ - to decompensated diabetes mellitus; " - to subcompensated diabetes mellitus. *** - p <0.001; ** - p <0.01; * - p <0.02; * - p <0.05.
Conclusion
Thus, coenzyme Q$_{10}$, regulating the function of the respiratory chain, inhibits the formation of free radicals, promotes the complete restoration of oxygen to the water molecule and energy formation. The effectiveness of the action of coenzyme Q$_{10}$ was confirmed by correlation analysis, a direct correlation was found between malonal dialdehyde and catalase activity ($r = +0.57$), negative correlation ($r = -0.46$) between the reduction level of malonic dialdehyde concentration and the increase of superoxide dismutase activity, the relationship between the concentration of NO and malonic dialdehyde ($r = -0.51$). Considering the dynamics of metabolic indicators against the background of complex treatment, more significant changes in the level of glycated hemoglobin, total cholesterol, and low and high density lipoprotein cholesterol were noted.

These biochemical changes were accompanied by restoration of the elasticity of the vessels of microcirculation, a decrease in the tone of arterioles and precapillaries, a modulus of elasticity and an increase in pulse blood filling in the segments of the shin and foot, and a decrease in venous stasis. Reduction of vascular resistance in the microcirculatory bed was accompanied by normalization of arterial pressure.

References