

However, in chronic myocarditis the evolution of the autoimmune disorders are clearly evident. These results are of interest for the treatment of human myocarditis suggesting the avoidance of immunosuppressive therapy in the initial stages of chronic ongoing myocarditis with viral persistence to prevent a direct cytopathic effect in the absence of an effective immune system. However, in the setting of a chronic myocarditis having the marked autoimmune disorders and no viral sequences, immunomodifiers or/and immunosuppressive drugs seem to be effective and safe. It is thus important to reduce the level of viremia very early during the infection using, e.g. INFs for CMV3-positive patients, thereby reducing the incidence of virus-mediated heart damage and autoimmunity, and later on immunosuppression for autoimmune, virus-negative patients with a cellular infiltrate.

#### 497 Chronic hepatic C virus infection and evolution with lymphoma: case-control study of 58 lymphoma patients

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**Background:** The risk of non-Hodgkin lymphomas (NHL) occurrence in chronic hepatitis C virus infection (CHCVI) is well established.  
**Aims:** To study the impact of CHCVI on NHL histology, mean age and stage at diagnosis, 5-year evolution and association with immune markers.  
**Design:** Case control study of 58 patients (pts.) with NHL: 29 pts. with CHCVI preceding by 14.8 ± 2.3 years the diagnosis of NHL - Gr. A, and 29 NHL pts. without CHCVI - Gr. B. The groups were compared for sex ratio, mean age and stage at NHL diagnosis, NHL histology, 5-year evolution with relapses and mortality, persistent elevated titres of monoclonal component, type I and II cryoglobulins, anti-nuclear, antierythrocyte and antiplatelet autoantibodies and rheumatoid factor.

**Results:** Results are presented in the table.

Parameters	Gr. A	Gr. B
Sex ratio (male/female)	11/18	12/17
Mean age ± SD (years)	36.52 ± 2.5	57.32 ± 1.9
NHL histology: high grade	19 pts.*	3 pts.
Ann Arbor NHL stage: IVB	25 pts.*	1 pts.
5-year evolution		
Relapses	20 pts.	18 pts.
Mortality	27 pts.*	7 pts.
Immune markers		
Monoclonal component	18 pts.*	4 pts.
Cryoglobulins	20 pts.*	3 pts.
Autoantibodies	18 pts.*	1 pts.

\* 0.05 for group A compared to group B.

**Conclusion:** In association with chronic hepatitis C virus infection non-Hodgkin lymphomas appear at younger ages and in an advanced stage, have an aggressive histology type and evolve with increased autoimmunity and 5-year mortality.

#### 498 Is it possible nowadays to predict development of autoimmune pathologies using immunogenetic and immunologic markers?

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Type I diabetes is an autoimmune pathology where roles of its immunogenetic and immunologic markers (HLA and antibodies to beta cells, respectively) is significantly studied. Molecular-genetic typing of HLA-allelic variations introduced an entirely new opportunity to determine individual risk for type I diabetes development to the disease clinic. The method is implied among 'clinical healthy' members of families where at least one parent is type I diabetic patient. Among 26 families where 26 parents were type I diabetic patients, 23 of them (88.5%) were revealed to bear type I diabetes + associated HLA-alleles and variations in the genotypes. Type I diabetes-associated genetic susceptibility was determined among 89% children of the families where one parent was type I diabetic patient. Besides 81% children inherited entire type I diabetes-associated genotypes. The latter refer them to the high-risk group for the disease development. However, some 8% children did not bear any type I diabetes + associated HLA-allele markers of the disease in their HLA genotypes. It suggests their relative risk level to correspond to that within the population. Specific glutamate-decarboxylase antibody markers of type I diabetes preclinical manifestations were determined among 8% children, and their genotypes bore type I diabetes-associated HLA-alleles too. The possible role of type I diabetes-negative-associated HLA-alleles among the given families are considered in regard to the disease development.

#### J 499 Peptides bound to MHC class I molecules induce signal transduction by these molecules

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Earlier we have found out that peptides extracted from peptide-binding groove of MHC class I and II molecules possess their own physiological activity. This physiological activity is directed to antigen presentation and other cell functions. We have extracted tissue-specific MHC class I peptides from thymus,

spleen, kidney, liver, heart and blood vessels. These peptide complexes had therapeutic activity during autoimmune pathology by the changing of some cell metabolic processes. Thus, we investigated the ability of MHC I peptides to induce the signal transduction through MHC class I molecules. MHC class I molecules localized on peripheral blood mononuclears were immunoprecipitated by anti-HLA-A,B,C monoclonal antibody. Peptides bound to these molecules were extracted from the immunoprecipitate by trifluoroacetic acid and ultrafiltrated. The influence of MHC I peptides on the expression of lymphocyte membrane molecules (CD3, CD4, CD8, CD22, HLA-Dr and HLA-A,B,C) was investigated by a fluorescent microscopy. Proteins associated with MHC I molecules and the changing of its phosphorylation under the action of MHC I peptides were investigated by immunoblotting with antiphosphotyrosine antibody. Dot immunoblotting was used to investigate the expressions of bcl-2 and p53. We characterized cell apoptosis process by a nuclear morphology, an electrophoretical DNA fragmentation and an annexin V binding. *In vitro* treatment of donor blood by MHC I peptides increased expression and clustering of CD3, CD4, CD8, HLA-Dr and HLA-A,B,C (but not CD22) on blood lymphocytes. These data suggest that MHC I peptides rearrange the lymphocyte membrane receptors. The immunoprecipitation shows that five proteins with molecular weight about 40, 50-60, 70 and 80-90 kDa were associated with MHC class I molecules. The treatment of the cells by MHC I peptides led to the increase of phosphorylation of 50-60 and 70 kDa proteins. MHC I peptides increased the expression of bcl-2 and decreased the level of apoptosis. MHC I peptides rearranged the lymphocyte membrane receptors and transduced a signal through MHC class I molecules. Perhaps, this MHC-I-mediated signal transduction involved the protein phosphorylation.

#### 500 Complex cryopathy in the patients with system diseases of connecting tissue

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**Background:** The purpose of our research was the establishment of clinical and laboratory criteria of cryopathological complex in the patients with different diseases of connecting tissue.

**Method:** We surveyed 128 patients with rheumatoid diseases. Forty-seven (36.7%) patients had clinical attributes of cryopathy: overcooling and change of skin colour on the extremities, various elements of skin rash, itching, paresthesia, disturbance of sensation. The condition of vessel system was estimated with the help of microscopic research of a hair vessel and