

## Abstracts of doctoral theses defended at the Department of Pediatrics

### SUMMARY

#### 1. PALII Ina

**Title:** *"The syndrome of heart failure at children with congenital heart diseases and pulmonary arterial hypertension: pathophysiological, clinic-evolutive, therapeutic and prognostic particularities"*.

PhD thesis in medicine. Chisinau 2012.

**Aim of research:** The evaluation of the pathophysiological, clinic-evolutive and therapeutics particularities of children with the syndrome of heart failure due to congenital heart disorders and pulmonary arterial hypertension.

**Objectives of research:** To elucidate the pathophysiological mechanisms, the clinical-evolutive and paraclinical particularities, the predictors of the severity and riskiness of the evolution of the syndrome of CHF secondary to CHD depending on the grade of PAH. To evaluate the circulated levels of CHF's biomarkers - endothelin 1, NT-proBNP, nitric oxide; of the proinflammatory cytokines - TNF-alpha, IL-1, IL-6 and to estimate the role of the oxidative stress in the pathophysiology, diagnosis and evolution of the syndrome. A complex clinical study of the sildenafil's efficacy in the treatments of children with PAH and CHF as well as the elaboration of the optimised therapeutic management program.

**Novelty and originality of research:** For the first time the pathophysiological mechanisms (neuroendocrine activation, cytokine and oxidative stress) involved in the evolution of the CHF with the background of CHD and PAH of different grade are elucidated.

**Theoretical significance:** It is emphasized and completed the concept of neuroendocrine, cytokine and oxidative stress activation concerning the heart failure pathogenesis.

**Applied value:** The proper diagnosis is favored and correct management is elucidated with the aim to prevent severe complications and to ameliorate the quality of life of the children with CHF secondary to CHD and PAH.

#### 2. ROMANCIUC Lilia

**Title:** *„The estimation of heart rate variability and efficiency of beta-blockers at children with functional heart disturbances and mitral valve prolapsed,,*.

Doctoral thesis in medicine. Chi in u, 2012

**The purpose:** an estimation of heart rate variability as basic marker of vegetative regulation and efficiency selective beta-blocker bisoprolol at children with mitral valve prolapse and functional heart disturbances.

**Objectives of research:** assessment of clinical, paraclinical and haemodynamic features; studying of changes of vegetative nervous system; assessment of heart rate variability; an effect estimation beta-bloker selective bisoprolol on clinical, haemodynamic indicators and parametres of heart rate variability in children with mitral valve prolapse and functional heart disturbances.

**Novelty and originality of research:** clinico-haemodynamic and vegetative features at children with symptomatic mitral valve prolapse, spectral and statistical parametres of heart rate variability on Holter monitoring ECG have been defined. Development arrhythmic risk factors are revealed. The effect of treatment with bisoprolol on heart rate variability is studied.

**The theoretical importance:** results of research have proved the importance of definition of heart rate variability at children with mitral valve prolapse and estimation of risk of development arrhythmia.

**Applied value:** results of research gave reason for necessity and information value uses Holter monitoring ECG at patients with mitral valve prolapse.

### 3. DRU CA Angela.

**Title:** „*Juvenile idiopathic arthritis: clinical features-evolutionary, systems endogenous oxidation/antioxidant, nitric oxide and curative management effectiveness*”.

PhD thesis in medicine, Republic of Moldova, Chisinau City, 2012.

**The purpose of the study:** assessing the role of endogenous lipid peroxidation system, antioxidant protection, pathogenetic mechanisms of nitric oxide in JIA and assessment of antioxidant efficacy in different types of JIA evolution.

**Study objectives:** to determine the clinical, paraclinical particularities of JIA in different stages of disease; to assess the state of the endogenous systems of the lipid peroxidation and antioxidant protection in patients with JIA in dependence with its evolving character and in different stages of the disease, assessing the correlation between nitric oxide level and the progression of the JIA, the influence of various treatment programs on indices of lipid peroxidation, antioxidant system and nitric oxide in patients with JIA.

**The scientific novelty and originality** was to reveal clinical and diagnostic importance in determining radiological scores – Steinbrocker and Sharp in the JIA, the identification of favorable and unfavorable prognostic factors for the development of JIA; it was determined the important role of oxidative stress in the pathogenesis of JIA.

**The important scientific problem solved in the thesis.** It was elucidated the role of oxidative stress and NO in the pathogenesis of JIA. The antioxidant preparation influenced positive on the prooxidant indexes and halted the joint damage.

**The theoretical and practical importance** of the study was to reveal the clinical features of JIA, endogenous systems of oxidation/antioxidant, nitric oxide in the JIA and the effectiveness of various treatment programs on indices of lipid peroxidation, antioxidant system and nitric oxide in patients with JIA, we help early diagnosis of disease and therapeutic approach allows us to improve the efficiency and quality of life.

### 4. TURCU Oxana

**Title:** „*Etiopathogenic, clinical and therapeutic peculiarities of the digestive system disturbances in children with cystic fibrosis*”.

PhD thesis, Chisinau, 2011.

**Aim of the study:** assessment of digestive system disturbances in children with cystic fibrosis correlated with the gene mutations for optimization of the therapeutic programs.

**Purpose:** identification of CFTR mutations spectrum in patients with CF from the geographical area of Republic of Moldova; assessment of elastase-1 value for determining pancreatic insufficiency and the correlation with CFTR mutations in children with CF; assessment of nutritional status, clinical signs, imaging-endoscopic and histological peculiarities of digestive system lesions depending on genotype in children with CF; research of nutritional disorders impact on the bone mineralization in CF; optimization of pancreatic enzyme replacement therapy in accordance with the degree of pancreatic insufficiency in children with CF.

**Scientific novelty and originality.** For the first time in Moldova has been realized a clinical controlled complex trial of a representative group of patients with CF, which formed the basis for the National Register of Cystic Fibrosis. The molecular examination to identify mutations responsible for CF development, allowed the determination of CFTR mutations spectrum characteristic for the geographical area of Moldova. The study confirmed the high correlation of genotype-phenotype of pancreatic function in children with CF and that F508del mutation is responsible for the high frequency and severe degree of exocrine pancreatic insufficiency. Elastase-1 study results have argued the need for pancreatic enzyme replacement therapy in

children with CF only, if exocrine pancreatic insufficient; estimation of clinical and explorative criteria in time showed that diagnosis age is a prognostic factor of the disease severity.

The **theoretical significance** of the work was to determine the frequency and characteristics of the digestive system modifications in children with CF, which allowed the elucidation of etiopathogenical mechanisms in disease evolution.

**Applicative value** of the research is the determination of the peculiarities of the digestive system modifications for early suspicion and confirmation of CF in children. Assessment of fecal elastase-1 levels is recommended as a reference index in the diagnosis of exocrine pancreatic insufficiency in patients with CF. The body mass index has been proposed for the nutritional status evaluation in these children. It was proposed the use of clinical-radiological score in the disease severity assessment.

## **5. PÂRTU Lucia**

**Title:** *"Aspects of clinical course and risk factors of arterial hypertension in children".*

PhD thesis in medicine. Chisinau, 2012.

**Purpose:** Estimation of risk factors and clinical features of evolution in hypertension in children to improve the quality of care to these patients.

**Study objectives:** Estimating the prevalence of pre- and hypertension in children in three areas of the Republic of Moldova, finding risk factors in order to determine the impact of hypertension in children, highlighting the clinical course of arterial hypertension in children, assessing the frequency of left ventricular hypertrophy and indicators that could it determine.

**Novelty and originality of research.** For the first time in the country there were studied the risk factors of arterial hypertension in children based on the geographical area and living environment. The investigation process included a category of children with higher blood pressure values that are admissible for age and are considered as physiological, but which have high risk for developing hypertension. There were identified the clinical features of disease, the presence of comorbidities, the determining prognostic indicators in target organ damage.

**Scientific problem solved in the dissertation.** It was evaluated the clinical features and evolution of hypertension in children and highlight the repercussions of risk factors in occurrence of hypertension in childhood.

**The theoretical importance.** It was demonstrated the importance of risk factor elucidating in children's arterial hypertension, comorbidities, assessing blood pressure variability, pulse pressure, which are indices with prognostic value in the development of left ventricular hypertrophy.

**Applicative value.** Based on the results it will be developed a strategy to combat cardiovascular disease in children with primary health warning on the importance of measuring blood pressure values in children, selecting risk groups, initiating a strategy for promoting a healthy lifestyle in childhood.

## **6. Cirstea Olga.**

**Title:** *„Genetic substrate underlying the onset and evolution of asthma phenotype in childhood”.*

PhD thesis in medicine, Chisinau, 2013.

**Aim of the study:** to investigate the association of genetic and environmental risk factors with asthma onset and evolution in children and, based on the obtained results, to elaborate prognostic methods for the disease development and progression assessment.

**Objectives:** to evaluate peculiarities of functionally compromised alleles and genotypes spread of the GSTT1, GSTM1, GSTP1, NAT2, IL-4, IL-4R, TNF, CC16 and NOS1 genes in the general population sample of Moldovans; to assess the frequencies of alleles and genotypes

of the genetic polymorphisms in xenobiotic metabolizing genes, immune mediators genes, and NOS1 and CC16 genes in children with asthma and healthy controls; to study the association of genetic polymorphisms with asthma phenotypes; to evaluate the risk of childhood asthma development under the influence of the gene-environment interactions; to develop prognostic methods for the asthma onset and clinical evolution assessment in children.

**Novelty and scientific originality:** particular genetic variants of the asthma candidate genes in Moldovan children were assessed; the role of genetic factors and gene-gene interactions in the asthma development was determined; unfavorable genetic variants for the asthma development and evolution in native population were identified.

**The theoretical significance of the study.** The study findings reveal aspects of the pathogenetic mechanisms of multifactorial disease development in ethnic Moldavians.

**Applicative value of the study.** The elaborated prognostic algorithm allows identifying high risk subjects for atopy and asthma development.

## **7. Adam Ianos.**

**Title:** „*Gastroesophageal reflux disease in children with asthma: interrelationships, risk factors, clinical manifestations and evolution aspects*”. PhD thesis in medicine, Chisinau, 2013.

**Aim of the study:** to evaluate clinical and pathogenetic interrelationships between the gastroesophageal reflux disease (GERD) and childhood asthma in order to optimize therapeutic management and clinical care of patients.

**Objectives:** to assess the pattern and impact of risk factors in children with gastroesophageal reflux disease associated with asthma; to study the variability of digestive and extra-digestive manifestations in children with GERD associated with asthma; to evaluate particular features of the endoscopic, pH metric and morphologic examinations of the esophagogastric area in children with GERD associated with asthma; to assess functional respiratory and immunological indices in children with asthma associated with GERD; to evaluate the role of the gastroesophageal reflux disease in the persistence of bronchial hyperresponsiveness; to study the efficacy of the antisecretory medication for the complex treatment of GERD associated with asthma in children in order to optimize therapeutic management and clinical care of patients.

**Novelty and scientific originality:** to estimate the role of predisposing risk factors for GERD development in children with asthma; to evaluate the effectiveness of the antisecretory medication (proton-pump inhibitors, PPIs) for treatment of children with GERD associated with asthma assessed by clinical symptomatology and the Paediatric Asthma Quality of Life Questionnaire (PAQLQ).

**The theoretical significance of the study.** The study results represent a scientific background in understanding and evaluation of complex interrelationships between gastroesophageal reflux disease and bronchial asthma in children.

**Applicative value of the study.** The research contributed to the development of effective preventive measures aimed to improve the diagnosis, clinical care and appropriate therapeutic management of GERD associated with asthma in children.