INTRODUCTION

Worldwide, obstructive respiratory dysfunction (ORD) represents a major health problem, with economic consequences and significant disturbance of the patient's quality of life. In the speciality literature, it is emphasised that the recovery of pulmonary not only means educational – fizical – kinetic program, but involves complex issues, essentially one of which is the assessment patient (initial and ongoing), through which can be appreciated the results achieved through the pulmonary rehabilitation program.

Cystic fibrosis (CF) is condition the most recently recognized of major chronic diseases of man, being the most prevalent inborn error of the caucasian race. It is characterised by generalised dysfunction of mucous and seroase (e.g. sweat glands) exocrine glands: secretions from the majority of organs and systems will be poor water containing, viscous, adherent to epithelia excretory ducts, difficult to eliminate the outside, the primary abnormality being CF gene. In the absence of early diagnosis in the newborn period or during the first years of life, and a treatment correctly applied, the chances of survival do not exceed the age of preschool. In our
country, this affection is still little known despite some quite persevering and is completely ignored in adult pathology. Although CF is a multisystem distress, respiratory suffering (*chronic obstructive pulmonary disease*) is the main element in terms of patient outcome and are the leading cause of morbidity and mortality. The goal of CF lung recovery is to delay the development of respiratory disease for a longer period of time, and to preserve lung function and physical capacity. It is a proactive treatment that includes an appropriate combination between:

- inhalation therapy,
- respiratory clearance techniques (RCT),
- exercise and physical activity,
- continuing education about the disease and its treatment.

Frequency evaluation, review and continuous optimization of therapeutic programs are essential for effective and efficient daily treatment in time to prevent or at least slowing the progression of lung disease. Increased survival expectancy contributes to patients with CF and their families to be recipients of current research and future progress in the field of modern therapies, especially gene therapy that has as main objective cure.

**OBJECTIVES**

1. Complex assessment of patients with CF and identify those clinical and paraclinical parameters through periodic tracking of which we can assess correctly the effects of the treatment and to adapt our ongoing treatment at the individual needs of patients.

2. Finding meaningful indicators in individual monitoring of prognosis and in particular identify those that can be influenced through therapy, in order to slow down the progression of the disease and increase the life expectancy of such children, thus increasing the chances of them being the beneficiaries of the current and future research progress in the field of modern therapies, including gene therapy, only the main purpose of healing.

3. Tracking the effects of a sustained program at home of increased regular physical activity level on the lung volumes and flows, and recognition of potential clinical factors that influence these effects.

**MATERIAL AND METHODS**

We used a retrospective, multicenter, cross-sectional study, conducted on a group of patients diagnosed with CF, aged between 3 months and 29 years old, which are found in the records of the II Pediatric Clinic of Emergency County Hospital from Craiova, Maria Sklodowska Curie Children’s Emergency Hospital and Alfred D. Rusescu Institute for
Maternal and Child, both from Bucharest, in 2009. Initially the lot included a number of 105 patients. Nine patients were excluded from the study because they presented either altered general condition, requiring specialist care in the intensive care department, either had a single admission in this year, on this occasion was suspicionat diagnosis of CF. Five of them died by the end of 2009. Thus, the group included 96 patients with certain diagnosis of CF.

For patients who could cooperate to spirometric testing (more than six years), I performed a prospective study, which I follow the evolution of the lung volumes and flows forward (last rating of 2008) and a year after implementing a program at home of increased regular physical activity level, which coincided with the assessment for the whole group of patients, in 2009.

Patients and their families receive the necessary information about the use of medical data for this study, obtaining their agreement in this regard.

I have included in the study patients who have had certain diagnosis by CF. Suspected diagnosis of CF was based on characteristic clinical and anamnestic criteria: chronic cough, recurrent wheezing, chronic diarrhea and steatorrhea, growth failure despite a good appetite and nutritional intake accordingly, and was confirmed by two positive sweat tests and to some patients by genetic test.

Patients received comprehensive treatment, according to management guidelines in CF.

For all patients, educational-physical-kinetic treatment included: inhalation therapy (antibiotics and mucolytics) and respiratory clearance techniques (RCT) - an appropriate combination between respiratory kinetotherapy, postural drainage, percussion, vibration and education cough. Cooperating patients, what they could participate in spirometric testing (more than 6 years), in addition to rehabilitation treatment described above were included in a sustained exercise program at home to increase regular physical activity level, since the last assessment of 2008, while one year. Note that these patients (more than 6 years) showed no signs of acute respiratory failure, chronic pulmonary heart disease (CPHD) or the coexistence of decompensated heart disease, respiratory disease independent but aggravated by it.

The used clinical, paraclinical and functional parameters

- General characteristics of patients: current age (in years), sex, age he had a patient at the time of diagnosis of CF (in years), patient age at the start of the aerosol mucolytic treatment with Alfa-dornasa (Pulmozyme ) and duration of therapy with inhaled
Pulmozyme (in years), significant family history and number of days of hospitalization per patient in 2009.

- **Genotype**
- **Anthropometric indicators:** weight (W), height (H) and body mass index (BMI) – Zscore.
- **Spirometric indices:** vital capacity (VC), forced expiratory volume in first second (FEV1), forced expiratory flow between 25 and 75% of forced vital capitation (FEF25-75%) and report FEV1/VC (bronchial permeability index - BPI).
- **Degree dyspnoea** during normal physical activities - MRC scale.
- **Bacteriological examination of sputum**
- **Complications:** allergic bronchopulmonary aspergillosis (ABPA), atelectasis and bronchiectasis, clubbing digital, arthritis, pancreatic insufficiency, diabetes associated with CF, impaired hepatobiliary, gastroesophageal reflux.
- **Cooperman score**

**Indicators and statistical tests**

The data collected have been stored on a database compiled in Microsoft Access. Data were expressed as number of cases (proportion) and I used the following statistical indicators: average, standard deviation (SD) and coefficient of variation (CV). Graphics were made using Microsoft Excel. For processing of data, I used the following statistical tests: Student test, ANOVA test, chi squared test (level of statistical significance was set at p <0.05), the relative risk (RR) and odds ratio (OR), Pearson correlation coefficient (r) and correlation coefficient squared (R²).

**RESULTS AND DISCUSSIONS**

**Useful indicators of assessment and their implications for evolution of cystic fibrosis**

1. **Sex:** female gender was a factor of unfavorable prognostic; thus, although the proportion of male patients with CF was greater than that of female patients (58.33% versus 41.67%), girls had significantly more advanced pulmonary dysfunction (p <0.05), (at least until around age of 18 years), a significantly more severe degree of dyspnoea (p = 0.023), digital clubbing (indicator of chronic hypoxemia) in a significantly higher percentage (53.85%, p = 0.009) and significantly more reserved prognosis (p = 0005); benefits of sustained physical activity program at home on lung function were more important in boys than girls, for young patients.

2. **Age:** older age were associated with marked deterioration in lung function (inverse correlation with age), the presence of Pseudomonas aeruginosa, complications such as diabetes associated with CF,
hepatobiliary damage and prognosis (score Copeman) more serious (r = -0.541); as shown in specialty literature, despite the efforts of treatment, the disease progressed with age.

3. Genetic type: ΔF508 homozygous genotype was associated with more severe degrees of pulmonary impairment (p <0.05), according to some studies.

4. For the group studied, early diagnosis and consequently prompt and correct treatment of the disease had a positive influence on the pulmonary function and were decisive prognostic factors (r =- 0.255).

5. Nutritional status: Pearson correlation coefficient values showed that optimal nutritional status (especially optimal weight) was beneficial both respiratory parameters and quality of life, patients with good nutritional status were making the usual daily activities without difficulty; therefore, proper nutrition and respectively dietary advices were important links in the treatment of CF.

6. Type of germs that affects the respiratory tract: colonization itself was a negative factor, especially when the Pseudomonas aeruginosa was involved, which was associated with presence of bronchiectasis (p = 0.00073), severe respiratory dysfunction (p = 0.040), high degree of dyspnoea (p = 0.002) and the reserved prognosis (p <0.0001).

7. Spirometric indices: FEV1, VC, FEF25-75% and FEV1/VC report were found as important prognostic factors (direct correlation with Cooperman score); FEV1 had a stable marker value in terms of prognosis (r = 0.688); the practical utility is that FEV1 measurement can be useful in making a decision for a particular therapy (eg. considering the optimal timing for heart-lung transplantation).

8. The existence and nature of complications: diabetes associated with CF and impaired hepatobiliary were associated in all cases studied with poor nutritional status and severe respiratory dysfunction.

9. Digital clubbing was found an important indicator of the presence of bronchiectasis, (p ~ 0) – conclusion of practical utility, which highlight the importance of general clinical examination to assess structural changes of lungs, in CF.

10. Alfa-dornasa (Pulmozyme): treatment precocity (small age) led to beneficial effects on lung function (inverse correlation), the degree of dyspnea (r = 0.352), nutritional status (r =- 0.321) and prognosis (r =- 0.513); thus, despite its high acquisition cost, being a product of genetic engineering, I consider that the clinical benefits should take priority over economic considerations.
Effects of increasing the level of regular physical activity at home, on pulmonary function, in cystic fibrosis
(The study findings were published in “Jurnalul Pediatrului”, no. 53-54/2011)

The introduction in the treatment plan of patients with CF, of the recommendation of moderate or grater intensity physical activity (depending on the degree of endurance of the physical effort by the patient), at least 3 times a week, with a duration of at least 30 minutes, was intended to prevent, improve or at least slow the progression of pulmonary dysfunction, during a year of study. The effects depended on age and gender, with significant benefits on spirometric indices in children (6-12 years) and in males; significant improvement in FEV1 (p<0.05) for all patients, regardless of gender, in the age group 6-12 years, suggested that the pulmonary function may improve at least until that age, in CF.

Table 1. Spirometry indices at one year after the implementation of a physical activity program at home for female patients of the age group 6-12 years

<table>
<thead>
<tr>
<th>Variable</th>
<th>Initial value (mean±SD)</th>
<th>Final value (mean±SD)</th>
<th>Student test p</th>
</tr>
</thead>
<tbody>
<tr>
<td>VC (percent of predicted value)</td>
<td>68.22±20.13</td>
<td>70.68±19.67</td>
<td>0.06126</td>
</tr>
<tr>
<td>FEV1 (percent of predicted value)</td>
<td>49.41±23.26</td>
<td>60.45±19.54</td>
<td>0.01116</td>
</tr>
<tr>
<td>FEF25-75% (percent of predicted value)</td>
<td>42.52±27.50</td>
<td>48.90±22.00</td>
<td>0.14107</td>
</tr>
<tr>
<td>FEV1/VC</td>
<td>0.67±0.13</td>
<td>0.68±0.11</td>
<td>0.28361</td>
</tr>
</tbody>
</table>

Table 2. Spirometry indices at one year after the implementation of a physical activity program at home, for male patients of the age group 6-12 years

<table>
<thead>
<tr>
<th>Variable</th>
<th>Initial value (mean±SD)</th>
<th>Final value (mean±SD)</th>
<th>Student test p</th>
</tr>
</thead>
<tbody>
<tr>
<td>VC (percent of predicted value)</td>
<td>70.98±18.80</td>
<td>80.24±15.69</td>
<td>0.00833</td>
</tr>
<tr>
<td>FEV1 (percent of predicted value)</td>
<td>60.11±21.54</td>
<td>78.11±16.28</td>
<td>0.00001</td>
</tr>
<tr>
<td>FEF25-75% (percent of predicted value)</td>
<td>53.31±29.92</td>
<td>66.66±23.98</td>
<td>0.00023</td>
</tr>
<tr>
<td>FEV1/VC</td>
<td>0.73±0.10</td>
<td>0.77±0.09</td>
<td>0.00011</td>
</tr>
</tbody>
</table>

For older patients (≥13 years), increasing physical activity level helped maintain pulmonary functional status, with insignificant variations in spirometric indices, regardless of gender (p>0.05), one year after baseline.

As a result, I appreciate that such a recommendation is appropriate for all patients with CF (except those with contraindications to physical effort), with the possibility of prevention or improvement of respiratory
dysfunction for a period of time, unless it is done from a small age as possible.

CONCLUSIONS
1. **The pattern of decline in lung function** for this group was similar to that observed in other studies: initially the predominant small airway obstructive disease, with reduced FEF25-75%, before the usual indicators of obstruction FEV1 and IPB to change, and VC impairment later, with the installation of lung fibrosis (inverse correlation with age); compared with results of studies conducted in England, Canada and the U.S., where cystic CF is granted special attention (material and logistics) and patients are treated in specialized centers, tracking and treatment for CF, in the studied group, pulmonary dysfunction appeared at a younger age and was higher intensity.

2. **Parallel evolution** of VC and FEV1 ($R^2 = 0.7539$) pleaded for mixed damage bronchoalveolar nature, at least in stages when bronchial barrier has been overcome. The practical importance of this strong correlation is the measurement of VC as an indicator of bronchoalveolar damage in younger children who can not cooperate for the determination of FEV1.

3. **FEF25-75%** analysis allowed the identification of respiratory disorders in 5 patients, initially classified as having normal lung function, therefore I appreciate that in CF is necessary to measure FEF25-75% for early recognition of the changes in peripheral airways.

4. **Deterioration of lung function** has increased the number of days of hospitalization during one year (inverse correlation). As a result, economic costs related to useful therapies to improve lung function may be partially offset by the earnings saved by reducing hospitalization days/year and antibiotics, and consequently decrease the number of absences from school or work.

5. **Cooperman score** was a simple tool by which I evaluated the prognosis. In this study, I highlighted the importance score for lung functional status, with strong direct correlations (results are amended in the same sense) between the value of this score (a high value meaning a good prognosis) and spirometric indices values (CV: $r = 0.690$, FEV1: $r = 0.688$, FEF25-75%: $r = 0.574$, FEV1/VC: $r = 0.599$).

6. **Precocity inhalation therapy with Alfa-dornasa (Pulmozyme)** (young age of patient at the start of this treatment) resulted in beneficial effects on lung function (inverse correlation with spirometric indices values), degree of dyspnoea ($r = 0.352$), nutritional status ($r = -0.321$) and Cooperman score ($r = 0.513$); thus, although this mucolitic has a high acquisition cost, being a product of genetic engineering, I consider that the clinical benefits should take priority over economic considerations.
7. The introduction of exercise and physical activity recommended in the treatment plan was meant to prevent, improve or at least slow the progression of lung disease for a period of time; the effects depended on age and sex: most important benefits to infants and in males; significant improvement in FEV1 (p<0.05) for all patients regardless of gender, observed in the age group of 6-12 years old, suggested that, at least up to age, not every change in lung function is permanent, resulting in the opportunity as early introduction of such recommendation as a life style of patients with CF.

8. Educational measures: adequate nutrition and therefore optimum growth rate and an active lifestyle, beginning as early as possible in an environment poor in pollutants, have proved important aspects of treatment, with beneficial implications, proven in this study, on the lung function, responsible for the greatest morbidity and mortality, in CF.

9. Results obtained in this thesis on monitoring and prognostic indicators, and influencing some of them by some interventional measures, do not contradict the findings of recent studies, but bring an spore of knowledge by features of the study group, which substantiates and complements in scientific and original way, the management of cystic CF (evaluation and treatment), in our country.

10. Taking into account the clinical and paraclinical correlations found, I could make the profile of the patient with CF and pulmonary function as close to normal parameters: male patient, young age (under 11 years old), genotype non ∆F508/∆F508, with early diagnosis and specific treatment (under 1 year of age), therapy with inhaled Alfa-dornasa of age as close to the time of diagnosis, optimum weight, an active lifestyle, to which primary and secondary preventive measures against bacterial infections of respiratory tract (especially Pseudomonas aeruginosa infection) were effective, without digital clubbing, diabetes associated and hepatobiliary damage.

11. Achieving this thesis, I draw a useful conclusion today, with implications in a future time: involvement of physician of rehabilitation and physical medicine in the management of CF (evaluation and treatment), as a member of the team care of patients with this type of pathology, and development of controlled studies, composed according to a rigorous methodology, to determine optimal treatment scheme for recovery of respiratory distress for each stage of CF evolution. Note that in our country, in the specialty Physical medicine and rehabilitation, CF is a disease rarely mentioned only theoretically, and not wrong saying that in our rehabilitation clinics are not treating patients with this disorder; therefore no studies in this regard.
SELECTIVE BIBLIOGRAPHY


3. Lazăr J, Popescu R, Lazăr L. Spirometric assessment in a lot of patients with cystic fibrosis, following implementation of a program for increasing outpatient usual physical activity level. *Jurnalul Pediatrului* 2011; 53-54: 3-9;


CURRICULUM VITAE

1. Forename: Janine
2. Surname: Lazăr
3. Date and place of birth: 19.01.1976, Craiova
4. Citizenship: roumanian

5. Education:

<table>
<thead>
<tr>
<th>Period</th>
<th>Institution</th>
<th>Degrees and diploma</th>
<th>Institution</th>
<th>Degrees and diploma</th>
</tr>
</thead>
<tbody>
<tr>
<td>1982-1987</td>
<td>General School number 12, Craiova</td>
<td>Baccalaureate degree</td>
<td>University of Medicine and Pharmacy from Craiova</td>
<td>University degree, Physician Diploma</td>
</tr>
<tr>
<td>1987-1990</td>
<td>General School number 21, Craiova</td>
<td></td>
<td>“Nicolae Bălcescu” (Carol I) National College, Craiova, mathematical-physical section</td>
<td></td>
</tr>
<tr>
<td>1990-1994</td>
<td>“Nicolae Bălcescu” (Carol I) National College, Craiova, mathematical-physical section</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1994-2000</td>
<td>University of Medicine and Pharmacy from Craiova, Faculty of Medicine</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

6. Cultural education:

<table>
<thead>
<tr>
<th>Period</th>
<th>Institution</th>
<th>Degrees and diploma</th>
<th>Institution</th>
<th>Degrees and diploma</th>
</tr>
</thead>
<tbody>
<tr>
<td>2002-2005</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

7. Scientific title: preparing for a doctor’s degree in medical sciences

8. Professional experience:

<table>
<thead>
<tr>
<th>Period</th>
<th>Location</th>
<th>Institution</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>2001</td>
<td>Physical medicine and rehabilitation clinic</td>
<td>Emergency County Hospital from Craiova</td>
<td>Physician in training</td>
</tr>
<tr>
<td>2002-2006</td>
<td>Physical medicine and rehabilitation department</td>
<td>Recovery Hospital from Iași and Emergency County Hospital from Craiova</td>
<td>Resident physician, Rehabilitation, physical medicine and balneology</td>
</tr>
<tr>
<td>From 2007 to present</td>
<td>CF Hospital Craiova, Outpatient Department</td>
<td>Specialist physician, Rehabilitation, physical medicine and balneology</td>
<td></td>
</tr>
</tbody>
</table>
9. Scientific works published during doctoral studies of the Ph.D. thesis:
   - 3 articles in *extenso* (first author for 2 and co-author for 1) in internationally accepted journals \((B +)\);
   - 2 scientific works published *in summary* form in a national journal.

10. **Cultural activities:** Member of the Choir of the University of Medicine and Pharmacy from Craiova, since 1997

11. **Foreign languages:** English, French