430. Cystic fibrosis: clinical and laboratory studies

P4287
Pulmonary function preservation with targeted antibiotic use in infants with CF
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We hypothesized that in CF infants microbiologic surveillance with targeted antibiotic intervention preserves pulmonary function. Our program follows a standardized protocol with microbiologic surveillance performed at every visit by oropharyngeal sampling for culture. Positive cultures are treated based on antibiotic susceptibility regardless of clinical status. First detection of Pseudomonas aeruginosa (PA) is treated with a 6 week course of ciprofloxacin and 6 months of inhaled Colistin. Pulmonary function (PFT) is assessed by raised-volume rapid thoracoabdominal compression (RVRTC) and multi-breath washout (MBW). Nutritional status is monitored by weight for length Z-score (WLZ). Twenty four CF infants have participated since 2008. Mean age at diagnosis was 6.8 weeks, 16 are female. On average, 75% of the cultures per patient were positive. Only 6 of the infants had at least one positive culture for PA. In contrast 75% of the infants had at least one positive culture for S. aureus. By RVRTC parameters only 4 infants had evidence for significant obstruction. However by MBW almost all had evidence for mild ventilatory inhomogeneity (mean LCT 8.5±1.1). No correlation was found between RVRTC and MBW parameters. We did find an inverse correlation between WLZ and LCI (r=-0.46). Further, we found no relationship between microbiologic results and PFT parameters. Patients with positive cultures, including those with PA, had comparable PFT results to those not infected. Thus, despite airway colonization with CF pathogens, there was no evidence for significant detrimental changes in lung function. We propose that frequent monitoring and targeted use of antibiotics preserves lung function in infants with CF.

P4288
KL-6 serum levels in adult cystic fibrosis patients
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Introduction: Cystic fibrosis (CF) is a chronic lung disease with a typical obstructive pulmonary pattern. KL-6 is a high molecular weight glycoprotein, whose serum level are related to alveolar epithelium damage particularly in interstitial lung diseases; its role is not clear in CF patients.

Objective: To compare C-reactive protein (CRP) and KL-6 levels in adult CF patients requiring intravenous antibiotic therapy or pulmonary exacerbation.

Methods: Prospective observational study of adult CF patients admitted with pulmonary exacerbation to CF Adult Unit of Policlinico Hospital, Milan between November 2009 and February 2010. KL-6 and CRP serum levels were measured on admission, at day 7 and day 14 of intravenous therapy. Clinical and functional data were collected.

Results: 13 patients were analyzed (mean age 33 yrs, range 24-44, 6 women). Mean FEV1 was 49% of predicted (range 25-70). KL-6 levels seemed to show a trend similar to CRP’s during hospitalisation, with early increase and late decrease of the mean values.

Conclusion: These preliminary data show that KL-6 could be a useful biomarker in the follow-up of pulmonary exacerbation of adult CF patients. Further studies in greater cohorts are needed in order to confirm these data.

P4289
Six minute walk test in children, adolescents and young adults with and without cystic fibrosis
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Background: The six minute walk test (6MWT) analyses tolerance to submaximal effort. It’s important to compare Cystic Fibrosis (CF) patients with healthy controls to better understand their responses to physical exercise.

Objective: To evaluate patients with CF submitted to 6MWT and compare them to a control group (CG).

Methods: Transversal, prospective study comprising patients from a Brazilian CF reference centre. 6MWT was applied in a group of CF patients and in healthy controls accordingly to ATS guidelines and repeated after 30 minutes of rest. Respiratory frequency (RF), heart rate (HR), oxygen saturation (SpO2), dyspnea index, nutritional status and spirometry values were analyzed. Patients on pulmonary exacerbation were excluded from the research. Spearman’s correlation and ANOVA for repeated measures were used. p<0.05.

Results: Fifty-five CF patients and 185 healthy individuals participated (12.2±4.3 and 11.3±4.3 years, respectively). CG walked a greater distance than the CF patients in both tests (610.3±53.4m x 547.2±80.6m and 616.2±58.0m x 552.2±82.1m; p<0.0001). Walked distance correlated with age, weight and height. Both groups achieved similar distances in both tests, although CF patients had better performance in the first test. Learning effect was not seen. The ICC calculated between the two tests was 0.81 and 0.77 (CF and CG, respectively). The SpO2 maintained stable during the test, with an increase in HR and RF (p<0.0001) in all individuals.

Conclusion: CF patients presented functional impairment when compared to control group. Repeating 6MWT may represent an unnecessary effort for patients with chronic pulmonary disease.

P4290
Exhaled breath temperature in adult cystic fibrosis
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Cystic fibrosis (CF) is characterized by chronic airway infection and inflammation, which accounts for most morbidity and deaths. It has been suggested that inflamed airways may increase the exhaled breath temperature (EBT), however, patient with Cystic Fibrosis (CF) may have of the opposite effects. The aim of this study was to measure exhaled breath temperature in adults CF patients by comparison with healthy controls. Fifteen adults CF patients examined (8 female, mean age 28.6±7 years, VEF1% 44±21%) and 15 healthy persons (7 female, mean age 34±3 years) were recruited for the control group. The measurements of exhaled breath temperature (EBT) were performed with a second generation hand-held device (X-Halo, Delmedical Investments LTD Singapore) using an antibacterial filter (Clear Advantage, Creative Biomedics, Inc). Mean value of EBT in controls was 33.8±0.05°C and EBT mean value in adults CF patients was 33.5±0.7°C, the difference was not significant (p=0.05). We conclude that patients with CF had EBT similarly to healthy people, contrary to the asthmatics patients, possible due to chronic epithelial cell damage, increased mucosal barrier and the reduce of the vascularity.

Conclusion: These preliminary data show that KL-6 could be an useful biomarker in the follow-up of pulmonary exacerbation of adult CF patients. Further studies in greater cohorts are needed in order to confirm these data.

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P4291
Detection of volatile hydrogen cyanide released by *Pseudomonas aeruginosa* with cavity ring down spectroscopy
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*Pseudomonas aeruginosa* (Pa) produces hydrogen cyanide (HCN) which discriminates from other common CF lung pathogens. HCN production is supposedly increased under microaerobic conditions, which characterizes the habitat of Pa in vivo. This implies a potentially interesting marker in detecting *Pa* respiratory infections. Laser-based cavity ring down spectroscopy (CRDS) offers high sensitivity and molecular specificity in detecting trace gases and is suitable for incorporation in handheld devices. In this *in vitro* study we aimed to assess the feasibility and reproducibility of measuring HCN production through CRDS, and to determine the optimal oxygen concentration for cyanogenesis from Pa cultures on agar media.

A state-of-the-art CRDS was used to assess HCN online concentrations from the head space of Pa grown in petri dishes. Twenty-four hours prior to the experiments Pa was grafted on Muller Hinton media and grown in ambient air at 37°C. From start of the experiment, cultures were flushed with adjustable flow of 0.01%, 1%, 10% and 21% O₂, diluted in pure nitrogen.

HCN production was measured well above the detection limit from Pa cultures using CRDS (table1).

<table>
<thead>
<tr>
<th>Headspace oxygen (%)</th>
<th>N</th>
<th>Median HCN release [range]</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.01</td>
<td>38</td>
<td>399 [11-1227]</td>
</tr>
<tr>
<td>1</td>
<td>50</td>
<td>44 [9-778]</td>
</tr>
<tr>
<td>10</td>
<td>21</td>
<td>10 [2-37]</td>
</tr>
<tr>
<td>21</td>
<td>12</td>
<td>11 [1-80]</td>
</tr>
</tbody>
</table>

HCN may serve as a sensitive marker for presence of these bacteria, well above the detection limit. Intra-experimental variation coefficient was 21%. HCN production was higher in low oxygen concentrations (p<0.001). HCN production can be measured using CRDS, and is affected by oxygen concentration. HCN may serve as a sensitive marker for presence of these bacteria.

P4292
Achromobacter xylosoxidans: Friend or foe?
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Background: Despite increasing prevalence of Achromobacter xylosoxidans (AX) in cystic fibrosis (CF), it is still unclear what its pathogenicity is. Most studies suggest AX is a colonizer of damaged lungs rather than a pathogen. We looked at prevalence of chronic colonization of AX in our CF population and investigated impact on clinical progression.

Methods: In a cross-sectional analysis of 307 CF patients, we compared the group of once only infected (OI) to chronically colonized (CC). We analyzed differences in age, lung function and BMI z-score. Subanalysis included hospitalization rate and evolution of lung function in ten CC patients.

Results: Of the 307 patients, 22% showed positive culture for AX during at least 1 follow-up with 6% being CC, 9% and 7% with intermittently positive cultures. In 2009, the prevalence of a positive culture was 8%. No difference was detected between the OI and the CC group for age (p=0.16), FEV1% (p=0.24), FVC% (p=0.4) and BMI z-score (p=0.64). Subanalysis showed no impact of colonization on lung function decline and BMI z-score, though subanalysis showed significantly more hospitalizations (0.8 vs 1.6, p=0.049) during two years after diagnosis of colonization compared to two years before. Chronically infected patients had higher prevalence of *Pseudomonas aeruginosa* (PA) with only one of 19 patients acquiring AX. AX may serve as a sensitive marker for presence of these bacteria, well above the detection limit from Pa cultures using CRDS (table1).

Conclusion: A small subset of CF patients (6%) and not all patients with acquisition of AX (less than 1 in 3) become CC with AX. CC with AX was associated with increase in hospitalization rate, but did not affect lung function decline nor BMI evolution. Further data, e.g. case-control studies to exclude time-effect, are necessary to clarify clinical relevance of AX in CF.

P4293
Impact of *stentrophomonas maltophilia* in cystic fibrosis: A retrospective analysis
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Introduction: *Stenotrophomonas maltophilia* (SM) has been isolated more frequently in cystic fibrosis patients (CF) the past few years but the real significance of its presence remains to be elucidated. We investigated the impact of a positive sputum culture with SM on lung disease morbidity in our CF population.

Methods: Patients from the CF database were reviewed for presence of SM. Lung function and BMI data were analyzed at 1 year before, at acquisition, at 6 months, and 2 years after acquisition. We compared data between three groups: patients intermittently colonized with SM (IC), chronically colonized (CC) patients and a control group (CG) of CF patients that never acquired SM in their sputum and were matched for gender, age, *Pseudomonas* status and pancreas insufficiency.

Results: Median age was 18 y (IQR 12-25). FEV1% was significantly different between three groups: with lower values in the CC and IC 6 months (p=0.013) before and at time of acquisition (p=0.003). There was no significant difference in lung function evolution between three groups (FEV1% p=0.34, FVC% p=0.24, PEFR% p=0.33), but a trend was seen for BMI evolution (p=0.06) with worse BMI over the time in the IC (p=0.04) and CC (p=0.06). There was significant increase in # hospitalizations and number of IV courses with antibiotic use after acquisition of SM with highest increase in CC (p=0.034).

Conclusion: CF patients with positive sputum culture with SM had worse lung function not only at time of acquisition but also in preceding months. Acquisition of SM was not associated with accelerated FEV1 decline but BMI decreased in patients with SM and exacerbation rate and number of IV antibiotic courses increased after acquisition of SM.

P4294
The role of serum *pseudomonas aeruginosa* antibodies in diagnosis and follow-up of patients with cystic fibrosis
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In cystic fibrosis (CF), if *Pseudomonas aeruginosa* (Pa) infection is not diagnosed and treated early, chronic colonization in lungs may later lead to rapid decline in pulmonary functions. The aim of this study was to evaluate Pa antibodies, to compare them with Pa culture results, to determine their role in early diagnosis and follow-up, to correlate them with severity of disease and to determine factors which cause antibody positivity. Ninety CF patients were included; they were divided into chronic, intermittent, control and mucoid Pa groups according to their airway cultures. They were evaluated in every 3-6 months in total 4 visits in a follow-up period of 2 years. In each visit, Pa antibodies against exotoxin, elastase and alkaline protease were determined in blood by ELISA method. The presence of at least one antibody had the highest sensitivity. Among the antibodies, alkaline protease had the highest specificity and elastase had the highest sensitivity. All antibodies were highest in mucoid group followed by the chronic group. Antibodies were higher in the chronically colonized patients than the noncolonised ones. Elastase was highest in the chronic and lowest in the mucoid Pa group. The presence of antibodies were much higher than positive Pa cultures in patients younger than 5 years of age. Only in mucoid group, there was a negative correlation between FEV1 and alkaline protease. In CF, Pa antibodies can be considered as early markers for diagnosis especially in young children who can not expectorate, however, anti-Pa antibodies should be used together with sputum cultures for long term follow-up and treatment.

P4295
*Stenotrophomonas maltophilia* and *acrobacter xylosoxidans* in cystic fibrosis patients
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Introduction: In recent years there has been an increasing number of recognized emerging pathogens like *Stenotrophomonas maltophilia* (SM) and *Achromobacter xylosoxidans* (AX) but their effect in CF lung disease is yet unknown. Aims: 1) to assess the prevalence of SM and AX and 2) to compare the lung function, clinical symptoms at first isolation, CT scan and colonization with *Pseudomonas aeruginosa* (PA) between the two groups.

Methods: Retrospective cohort study using the CF Database of the CF Center of Catalonia (Spain): Data were collected at first isolation and after one year. Results: 130 patients were included in this study, 44 of whom (33.8%) had a positive culture to SM and 11 (8.4%) to AX at some time. Mean age at acquisition of SM was 6±4.6 years and of AX was 6.5±3.3 years. In the SM group 36% of patients were under 4 years in comparison with 9% in the AX group. No significant difference in symptoms at acquisition (56% and 63% respectively), FEV1 (75% and 84%), bronchiectasis (47% and 36%) and PA colonization (79% and 91%) were found between the SM and AX groups. After specific ATB therapy, chronic colonization was higher in AX (36%) in comparison with the SM group (9%).

Conclusions: The prevalence of SM colonisation was higher than AX. Patients colonized with SM were younger but chronic infection was more associated with AX.
P4296
Preventable deaths and better outcomes in CF: Need for organising care at European standards in developing countries
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Advances in research and treatment changed the outlook for CF patients in developed countries.
Aims: Evaluation of actual standards of CF care and identification of opportunities for changing the outcome of Romanian CF patients.
Methods: Analysis of clinical outcomes of CF patients (0-17 years) followed up in a Regional Center over 12 years (1998-2011) correlated with standards of care and level of funding.
Results: 45 children with CF followed up over the study period, 90% diagnosed before the age of 1 year (10/45 with meconium ileus, all underwent surgery and had complications). Mean age at diagnosis was 1.3 years, 36/45 were genotyped with 66% prevalence of del F508. 15 deaths were encountered, 67% before 2004 when the Ministry of Health provided funding. 66% of deaths before the age of 3 years, were influenced by poor socio-economic status, undernutrition and reduced level of understanding of the nature of the disease. 65% of patients developed premature severe lung disease related to poor nutrition and early acquisition of P aeruginosa. CF related conditions as ABPA, CFRLD, diabetes in 6/45 patients represented risk factors for poorer outcomes. In 55% of patients malnutrition was correlated with poverty. The level of funding represented only 50% of the needs and the lack of a staffed CF unit was a major barrier to proper care of patients.
Conclusions: Clinical outcomes were adversely impacted by lack of funding and complexity of factors that characterise transition to European standards in a developing country. Development of programmes aimed to increase knowledge and motivation for being involved in CF care are needed in order to offer better outlooks for CF patients.

P4297
Genotype-phenotype correlation in cystic fibrosis patients bearing a novel complex allele
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Objective: The genotype-phenotype relationship in cystic fibrosis (CF) patients bearing a novel transmembrane conductance regulator (CFTR) complex allele was investigated.
Cases report: During the genetic characterization of 289 CF Caucasian patients [MF ratio 0.9:1, median age 16 years (range 1-46)] we found a new complex allele [H939R,H949L] in five unrelated male patients (age range 15-25 years). They carried two CF-associated mutations, H939R and B494L, on the same exon 13 of CFTR gene in one allele, and had R242T, G542X, 1259insA, G1349D and F508del, respectively, in the other allele. All subjects had abnormal sweat chloride test values. The patient with R242T/H939R,H949L genotype showed CF-related symptoms restricted exclusively to hepatopathy with high levels of transaminases, but a good nutritional status and pancreatitis. The other four patients had signs of classic CF, including chronic lung and sinus disease, recurrent respiratory infections, failure to thrive and pancreatic insufficiency. Particularly, patient with 1259insA/H939R,H949L genotype presented with meconium ileus, and the subject bearing F508del/H939R,H949L showed the most severe pulmonary manifestations with abnormal values on tests of lung function.
Conclusion: Our findings suggest that the allele [H939R,H949L] greatly reduces the residual function of CFTR if on the other allele is present a severe mutation (i.e. G542X, 1259insA, G1349D and F508del), determining a very low residual function of the compound, the combined effect being an overall reduction of CFTR function; on the contrary, when the other allele carries a mild mutation, such as R242T, the overall effect is a cumulative better CFTR functioning.

P4298
Twenty years of care for CF patients in Moscow region of Russia
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Objectives: The aim of the study was to assess the median survival age of the patients in Moscow region of Russia, followed in children and adult CF Centers of Moscow during the period 1991-2000 and 2001-2010, the proportion of adults and gender differences in the survival, if any.
Methods: A database of CF patients was started in 1990. The diagnosis of CF was confirmed by positive sweat test and/or genetic analysis, or neonatal screening. During 2001-2010 of 371 patients, 45 (12.1%) had died (26 males, the age of death ranging from 4 months to 40 years: the mean age at death was 16.8±8.4 yrs); 326 patients were alive (mean age 13.2±4.9 yrs). The median survival age increased significantly - 35.71 years (p=0.045). There was no significant gender difference in the survival rate. 32.6% of adult patients – a significant difference since 1991-2000 (p<0.05).
Conclusion: A large increase in the Moscow Region CF patients’ survival and improvement of quality of life was observed during 9 years of specialized treatment, performed in Moscow centers, pointing out a survival advantage of specialized care.

P4299
Phenotype and genotype in adult patients with cystic fibrosis in Uruguay
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There is insufficient knowledge on Cystic Fibrosis (CF) in many countries; patients are often treated inadequately. Life expectancy is consequently far below than could be attainable with adequate treatment. Therefore it is very important to train Centers to concentrate clinical experience on diagnosis and management of disease. In June 2010, the Uruguayan Parliament created the First National Reference Center for Diagnosis and Treatment of Patients with Cystic Fibrosis.
Objective: To describe genotypic and phenotypic characteristics of patients at the time of first encounter at a CF Center for adults in Uruguay.
Methods: CF patients over 14 years were evaluated with medical history, spirometry and sweat studies.
Results: 41 adults entered the center. Mean age was 23.9±8.4, mean age at diagnosis was 14.2±11.3 years. Colonized patients showed differences with non- colonized in: mean age (25.8 vs. 22.0, p<0.01), mean age at diagnosis (13.1±1 vs. 14.4±1, p<0.01), lung function: FVC (84% vs. 95%, p<0.01); FEV1 (68% vs. 88%, p=0.05) and history of hemoptysis. Genetic mapping for 30 patients indicated that: 30% had two CFTR mutations, 36% a single mutated allele detected and in 35% no mutations detected. The most common mutation was AF508. The remaining mutations were substantially heterogeneous. In all, we had 3 alleles mutation class 1, 13 class 2, 3 class 4, and 1 class 5.
Conclusions: Colonized patients were diagnosed earlier in life, showed significant deteriora- tion in spirometric measures and more frequent hemoptysis. Our population had different types of CFTR mutations. The mutation AF508DEL was the most common and present in 16%. 33% of CFTR mutations were not detected.

P4301
The peculiarities of basic metabolism in cystic fibrosis patients
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Object: The study of a basic metabolism dependence on the disease state and infection process in cystic fibrosis patients in Saint-Petersburg.
Materials and methods: 23 patients with mixed forms of cystic fibrosis confirmed by the genetic examination were recorded in this clinical research study. The examination of basic metabolism in the children with cystic fibrosis was performed by the apparatus “Fit mate PRO, Cosmed, Italy”. The basic metabolism rate is calculated as a percentage of target values and depends on inspired O2 volume in ml/min, sex, age and height and body weight. The examinations were performed within 15 minutes at a comfortable ambient temperature (18-20°C) in the lying position, in an emotionally resting condition 12-16 hours later of the last meal without considering of daily stresses.
Results: The basic metabolism in the all examined cystic fibrosis patients exceeds the respective age norm by 30-90%. The statistic evaluation by the Mann-Whitney test confirmed by the Mann-Whitney test the basic metabolism appeared to be significantly higher in the patient group with the chronic pseudomonas infection (p<0.0167).
In 8 patients an oxygen intake volume during the maximal physical stress was determined. In all these patients it was considerably reduced.
Conclusion: The direct dependence of the basic metabolism on the state severity of cystic fibrosis (with the increase of severity) and the clear dependence on the infection process (the basic metabolism increase with the addition of pseudomonas infection) were revealed. The very low training of cystic fibrosis patients in Saint-Petersburg (on the base of oxygen intake rates) should be noted.
**P4302**
Evaluation of disease knowledge in children with cystic fibrosis and their families

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**Introduction:** Increasing the disease knowledge of patients with cystic fibrosis (CF) and their families is important for treatment adherence.

**Aim:** To determine the knowledge levels and associated factors in CF patients and their families.

**Methods:** Parents of 82 CF patients and 39 children >10 years followed at Paediatric Pulmonology Division were included in the study. Knowledge levels were evaluated with a standardized questionnaire which assesses 3 domains of knowledge: respiratory, digestion, and nutrition. Knowledge was compared with demographic features and disease severity determined by Shwachman-Kulczycki Scores (SKS) and pulmonary function tests (FEV1%).

**Findings:** 82 patients were included to the study (44 girls; median age: 9.5 years [25-75 percentiles: 5.1-14.1]). Median follow up was 8.0 years (25-75 percentiles: 4.6-11.4). Median SKS was 75、“good” (25-75 percentiles: 55-85）”good”. Mean FEV1% was 66.6±28.0. Disease knowledge was 65.8±14.7 for children and 69.9±14.6 for families. Children’s knowledge increased with age (p<0.04), but there was no relation with children’s age and family knowledge. Although no correlation was found with children’s knowledge and socio-economic status (SES), families’ knowledge was related with SES (p<0.04). There was no relation with disease severity and children’s or families’ knowledge. Knowledge level was higher for patients who were followed for longer period at our clinic (p<0.04). Knowledge of caregiving families and children was related. Knowledge level at presentation and at disease follow-up was significantly higher compared to the initial presentation (p<0.001).

**Conclusion:** CF patients’ and their families’ knowledge are fairly good but needs improvement. Families’ knowledge is associated with SES. Knowledge of children increases with age and follow up time, but is independent from family knowledge and SES.

**P4303**
An audit to assess the value of the MDT approach in patients in a UK CF unit

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**Background:** It is widely accepted that in CF best patient and family care should involve a well-coordinated multidisciplinary service. However, the interdisciplinarity effectiveness of the team, including the patient’s perception of their team is rarely measured.

**Aims:** We performed this study in order to evaluate the performance of our local CF MDT from an objective and patient perspective.

**Methods:** “On the spot” questionnaires were distributed to MDT members, who had worked with the unit for over one year. Questions were related to the knowledge of 15 randomly selected CF patients regarding their microbiology, FEV1, transplant status, social history, portacath, compliance issues and insulin therapy.

**Results:**

<table>
<thead>
<tr>
<th>1st, Doctors</th>
<th>83%</th>
<th>2nd, CF nurses</th>
<th>83%</th>
<th>3rd, Dieticians</th>
<th>80%</th>
<th>4th, Physiotherapists</th>
<th>75%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average scores and ranking</td>
<td></td>
<td></td>
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Questionnaires were simultaneously distributed to the same patients for anonymous completion requiring them to rank the MDT members according to perceived importance in their care and their relationship with each.

**Table 2. Overall ranking by patients**

| Most important member of MDT | 1st, Doctors 2nd, CF nurses 3rd, Dieticians & Physiotherapists 4th, Others |
|-------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|
| Personal ranking | | | | | | | | |

**Conclusions:** Results confirmed CF patients often form close rapport with specialist nurses and associate Consultants with important decision making related to their care. Interestingly, doctors and CF nurses scored equally well in patient knowledge and only marginally above others. These results suggest an effectively functioning MDT whilst highlighting the often under-recognised value of individual specialties.

**P4304**
Improved turn around time for molecular genetic analysis for cystic fibrosis: The Irish experience

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**Introduction:** Ireland’s Cystic Fibrosis (CF) newborn screening programme is due to commence later in 2011 using immune reactive trypsinogen & genetic analysis for the detection of cystic fibrosis transmembrane regulator protein (CFTR) mutations. The National Centre for Medical Genetics screens for 11 CFTR mutations & further analysis for rarer mutations is currently performed in Manchester (using gene sequencing & multiplex ligation-dependent probe amplification (MLPA) testing). Prior to 2008 this further analysis was performed in Exeter & subsequently in Brest.

**Aim:** To identify the turn-around time for genetic analysis results for children with suspected CF.

**Methods:** A 16 year retrospective study of genetic analysis results for CFTR mutations was performed. The turn-around time was defined as the number of days from sending DNA until reports were received. Descriptive statistics were used.

**Results:** Overall, the median time to receive genetic analysis results was 23 days, range 1-2434 days (n=91). The median turn-around time for the identification of 2 positive CFTR mutations was 21 days, range 1-1973 days. The most common identified mutation, Phe508del/Phe508del, had the shortest median turn around time of 18 days, range 1-107 days. Three patients initially suspected of having CF & with 2 positive sweat tests, did not have any CFTR mutations identified (median time 2252 days, range 229-2434 days).

**Conclusion:** Recent technological advancements allow for more detailed genetic analysis to be performed, identifying newer CFTR mutations over a shorter time period. The introduction of newborn screening & extended CFTR genetic analysis will ensure that the time to CF diagnosis is greatly improved.

**P4305**
Validation of the Spanish version of the Leicester cough questionnaire in children with cystic fibrosis

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**Antecedents:** Cystic Fibrosis (CF) patients present chronic inflammation with a mucus thickness and decrease ciliar mobility, causing chronic cough, bacterial colonization and respiratory infections. Cough is one of the most important symptoms for CF and it is directly related to exacerbations. Also, represents an upshot that affects quality of life and social relations.

**Objective:** Validate the Spanish version of the Leicester Cough Questionnaire (LCQ) in CF.

**Methods:** After the adaptation to Spanish, the sample was selected by 58 CF patients from Corporacio Parc Taulí and Asociacion Madrileña Contra la Fibrosis Quística, Spain. The questionnaire was administered twice in stable disease patients in order to contrast the results.

**Results:** Patients characteristics: age 11.7 (3.1) years, BMI of 19 (13) kg/m2. Total LCQ: 18.46 (2.4) vs LCQ2: 18.69 (2.3) (p=0.769). Cough alpha coefficients were: LCQtoral (0.86) and for the domains: LCQphysiol (0.76); LCQpsychosocial (0.79) and LCQsocial (0.78). The ICC was: LCQphysiol (0.82), LCQpsychosocial (0.75), LCQtoral (0.63) and LCQsocial (0.83). We observed moderate correlations with specific quality of life questionnaire (CFQ-R: respiratory symptoms CFQ-R14 (r=0.51) and CFQ-R4Child (r=0.67) (p<0.01), both) and with pulmonary function. FVC and FVE1: LCQphysiol (0.42 and 0.48); LCQpsychosocial (0.60 and 0.62) and LCQtoral (0.55 and 0.58), all significative (p<0.05).

**Conclusion:** The Spanish version of the LCQ is reliable and valid for CF patients, in which it has observed relations between quality of life and pulmonary functions. Sponsord by: Proyecto AVANZA, TSI-00110-2009-431. Ministerio de Industria Turismo y Comercio, Spain.