470* Newborn screening for CF in the Czech Republic: results from a pilot study

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According to epidemiologic/genetic studies the incidence of CF in our country is 1:2700 newborns. Thus, given the current birthrate ~35 new cases of CF should annually be detected. However, registry data demonstrated that 1/3 of CF patients remains clinically undiagnosed and that the age at diagnosis has markedly increased (prior to 1998 median: 0.58; between 1999–2005: 1.2 years).

Therefore, in II/2006 we started two tier (IRT/DNA) pilot CF neonatal screening project (NSCF) comprising Bohemian regions, representing ~2/3 of our population. Altogether 45,453 newborns were examined during the initial 9 month period. In 545 cases (1.2%), who had IRT concentration above the continuously adjusted cut off level, we examined the most common *CFTR* mutations.

The diagnosis of CF was established in 5 newborns (2× F508del/F508del; 2× F508del/G551D; 1× F508del/R117H-7T – mild CF) and these children were subsequently referred to CF Centres. Furthermore, we detected 42 newborns with 1 CFTR allele (35× F508del, 2× CFTRdele2.3/21kb/, 2× N1303K, 1× G551D, 1× I507del and 1× I148T). Until now 27 follow up sweat tests (ST) were performed (26× <30 mmol/L, 1× 30–40 mmol/L). IRT recall was carried out in 14 children with IRT >200 ng/mL and with a non-detectable CFTR allele – 11 children had negative IRT recall and 1 child was positive (ST negative).

From these results the incidence of CF can preliminarily be adjusted to 1:9090 newborns. However, these results can be skewed due to lower number of newborns tested, effect of prenatal diagnosis and/or false negativity of NSCF.

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471 Increased age at diagnosis justifies CF neonatal screening

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CF care in Czech R. (CZ) has notably improved during the past decade, with patient prognosis reaching that of other EU countries. On the other hand we are observing an increased number of late diagnoses. We assume that this is due to changes in postgraduate practician education within long-term health care system transformation.

We analyzed age at diagnosis (ADG) in 357 patients clinically diagnosed before 1998 and in 87 patients diagnosed between 1999–2005. Before 1998 the median ADG was 0.58 years (60.2% of cases were diagnosed <1 year), while after 1999 the median ADG increased to 1.2 years (47.1% of cases were diagnosed by age 1; $p=0.036$). Furthermore, increasingly patients are diagnosed between ages 2 and 6 (27.6% vs. 16.5%; $p=0.03$). Although 45.8% of these patients are carriers of a Class IV-V ("mild") and/or unknown CFTR allele associated with pancreatic sufficiency, more than half of them diagnosed after the age of 2 years have pancreatic insufficiency (PI) and present with severe malnutrition/irreversible lung disease.

Our longitudinally monitored patients with PI diagnosed after age 1 have poorer lung functions at the age of 8 years compared to those diagnosed before the age of 1 year (FEV1 71.7±22.9 vs. FEV1 84.5±21.8%, predicted value; $p=0.01$).

In the light of these observations we initiated in II/2005 pilot neonatal screening project comprising Bohemian regions of the CZ (2/3 of our population). We hope that it will help us to ascertain all CF infants with PI and most patients with mild CFTR alleles, and perhaps even older siblings with moderate disease phenotypes.

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472 Incidence of Cystic Fibrosis in high-risk Egyptian children and CFTR mutation analysis

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Background: Knowledge about Cystic Fibrosis (CF) in Egypt is limited. The objective of this study was to screen for CF in Egyptian children with suggestive clinical features and identify causative genetic mutations.

Methods: Sixty-one patients from the Chest Unit, Cairo University Children's Hospital, Egypt, were included. Subjects presented with persistent or recurrent respiratory symptoms, failure to thrive, diarrhea and/or steatorrhea and unexplained persistent jaundice. Patients were screened using the CF Indicator™ sweat test system (PolyChrome Medical, Inc, Brooklyn Ctr, MN). A quantitative sweat testing was conducted on 10 of 12 positive patients. Seven probands and one sibling underwent molecular analysis by direct DNA sequencing of the coding region and of the intronic sequences adjacent to the 27 exons of the CFTR gene.

Results: Of 61 patients, 12 (20%) had positive sweat chloride screening. Ten of the 12 patients underwent quantitative sweat testing and were positive. Eight CFTR sequence changes were identified in seven affected probands and two were confirmed in one sibling by direct DNA sequencing

Conclusion: The study results suggest that CF is more common in Egypt than previously anticipated. Larger studies are warranted to identify the incidence, molecular basis and clinical pattern of CF in the Egyptian population.

473 Diagnosing and managing of Cystic Fibrosis patients in Western Ukraine

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Every year about 250 Cystic Fibrosis (CF) children are expected to be born in Ukraine. There are differences between the CF patients' management possibilities in miscellaneous region of Ukraine. CFTR gene mutation analysis is performed in two centers only. Results of 10 years activities of non-formal Western Ukrainian CF team are examined.

CFTR mutations are studied by PCR, RFLP, heteroduplex analysis, agarose or polyacrylamide gel electrophoresis.

Since 1994 101 CF probands were detected. Eleven different CFTR gene mutations were found with the following frequencies: F508del (54.5%), W1282X (2.5%), CFTRdele2,3(21kb) (2.5%), N1303K (2.0%), G542X (2.0%), 1898–1G>A (1%), 3849+10kbC>T (0.5%), R334W (0.5%), 2721del11 (0.5%), 1717–1G>A (0.5%), R553X(0.5%). Thirteen prenatal diagnostics were performed. Five cases of CF were confirmed.

The evaluation of possible exocrine pancreatic insufficiency is determined by faecal elastase-1 level which can also serve as a method for rapid and effective therapy adjustment in CF patients.

CF patients, we monitor, receive effective pancreatic enzymes, mucolytics, antibiotic, bronchodilators, and individualized physiotherapy. Pancreatic enzymes only are free of charge for CF patients. Often patients have to pay the drugs costs of the themselves.

The majority of patients are physically and socially adapted. We progress in decreased of mortality rate and improved survival of CF patients. In 1997 association DZVIN was found by CF children parents. It renders social and psychological aid for such families.

In Ukraine adequate CF patients' healthcare requires creation of the CF National Program and regional CF centers.