Monthly variation in newborn screening immunoreactive trypsinogen concentrations [IRT]

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Aim: To audit monthly variations in [IRT] corresponding to the 98, 99 and 99.9% newborn screening cut-off values using two methods.

Methods: [IRT] was analyzed from newborn dried blood spots using the enzyme immunoassay Quantanse Neonatal IRT Screening Assay® (Bio-Rad Laboratories, Europe Ltd, Perth, Scotland, UK). The number of newborns identified for follow-up using [IRT] correlating to the top 2, 1 and 0.1% were calculated on a monthly basis then compared to a fixed cut-off value corresponding to the cumulative results for one year.

Results: For the 98% threshold, monthly [IRT] ranged from 66 to 86 μg/L whereas the fixed cut-off was 76 μg/L. These approaches both resulted in the identification of 326 newborns. Monthly [IRT] ranged from 76 to 112 μg/L whereas the fixed cut-off was 94 μg/L for the 99% threshold resulting in the identification of 166 and 155 newborns, respectively. At the 99.9% threshold, monthly [IRT] ranged from 110 to 230 μg/L whereas the fixed cut-off was 157 μg/L, which resulted in the identification of 21 and 13 newborns, respectively. No seasonal variation was noted.

Conclusion: The number of newborns identified for follow-up is influenced by the method used to calculate the newborn screening thresholds for [IRT].

Newborn screening in the Czech Republic: an effective tool for early detection of CF

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After 1998 an increasing number of newly diagnosed CF cases led us to initiate a pilot newborn screening (NBS) project in the Czech Republic (II/2005-XII/2006). The aim of our study was to compare clinical development of 41 patients diagnosed by NBS with the cohort of 95 patients diagnosed clinically. Both groups have been followed-up at Prague CF Centre (1999–2006). We have analysed age at diagnosis, CFTR genotype, nutritional status, lung function and lung radiological changes. Within the clinically diagnosed group median age at diagnosis (MADg) was 1.5 years. Body height (SDS) at diagnosis was −1.0±1.0 SD and body weight −1.27±1.1 SD. Nutritional status was worse in children diagnosed during the first year of life (median weight −2 SD). Although due to intensive treatment mean FEV1 at the age of 5 years was favourable (92.7±18.7% p. v.), 17% of patients were diagnosed late, i.e. with obstruction of the airways and irreversible lung damage. In the NBS group MADg was 37 days. Interestingly, 4 cases were simultaneously diagnosed clinically elsewhere. Two patients were compound heterozygotes for F508del with a mild (Class IV-V) mutation: I336K; 384K→10kb C→T. Body height at diagnosis was −0.8±0.6 SD and body weight −0.6±0.6 SD. Further development of the screened patients is favourable with mean weight at 6 months and 1 year (−0.3 SD) promising an overall better outcome in these cases. Although, our data are preliminary these results suggest that NBS in the conditions of the Czech Republic is an effective tool for early CF detection. According to our experience it may improve the course of the disease at least in 17% of Czech CF patients.

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Cystic fibrosis newborn screening in the Czech Republic: overview of a pilot study

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CF is the most common autosomal recessive, potentially lethal disorder, affecting approximately ~1:2700 newborns in the Czech Republic (CZ). A significant delay of the age at diagnosis (ADg) in our country (ADg prior to 1998:median: 0.58 years; significantly increased from 1999 to 2005 (median 1.2 years)), p = 0.036 led us to initiate a pilot newborn screening (NBS) for CF (II/2005 – XI/2006) covering 62% of all Czech newborns. The major aim of the two-tier (IRT/DNA) NBS was to assess its feasibility and efficacy in the conditions of our country. The level of immunoreactive trypsinogen (IRT) was measured in 76,438 Guthrie cards. Concentration of IRT above the adjusted cut off level of 75 ng/ml was found in 800 cases (1.05% of the total). In these high risk cases we examined the most common, population specific mutations, of CFTR gene covering approximately 84% of all CF alleles. A total of 12 cases with CF were identified, with the median ADg of 38 days. Furthermore, we detected 53 newborns with 1 CFTR allele. These were subjected to follow-up sweat tests. Thus far, 45x were negative – unaffected heterozygotes and one was borderline, which requires long-term monitoring. The ascertained incidence of 1: 6369 newborns, using NBS data only, was significantly lower than the epidemiologically established incidence. Nevertheless, when respective prenatal diagnosis data were taken into consideration an adjusted incidence increased to 1:3500 newborns. Overall, our study proved that NBS is a feasible and efficacious tool for uniform and early diagnosis of CF.

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Newborn screening in the Czech Republic: an effective tool for early detection of CF

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Cystic fibrosis newborn screening in Russian Federation

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Objective: Total screening of newborns has become one of the important methods of cystic fibrosis (CF) early detection, which allows timely start the treatment that, in turn, increases the life span and the quality of life of the patients.

Methods: Since June 2006, the screening of newborns has been conducting in several regions of Russian Federation (RF). At the first stage of examination, the immuno-reactive trypcine content in the dried blood spot is determined. If the sweat test is positive (≥70 mmol/L), repeated determination is made during the fourth week of life. If the retest is also positive (>40 ng/ml), the newborn is forwarded to the CF Center. Proof of the diagnosis is based on the sweat test. If the sweat test is positive (>60 mmol/L in classical test or >80 mmol/L using determination of the sweat conductivity by Nanoduct, Macroduct-Sweat-Check (Wescor) systems) the CF diagnosis is considered to be confirmed. If the result of the sweat test is border-line (40–60 mmol/L and 60–80 mmol/L, respectively) the DNA test is conducted at 23 widespread in RF CF mutations.

Results: From June to December 2006, 63082 newborns were examined in Moscow. 408 had neonatal hypertrypcinemia. Repeated test was positive in 41 cases. Based on the sweat test, CF was confirmed in 5 cases. The signs of pancreatic deficiency were noticed in 5, and respiratory syndrome in 4 cases. Three families denied the examination at the CF Center.

Discussion: Since Jan 2007 the screening program will be performed in all regions of RF. It will allow (i) determine the true frequency of the disease in various regions, (ii) provide in time diagnostics, (iii) improve CF progress and prognosis. Our data proves the frequency of CF in RF which has been previously determined to be 1:12300 newborns.