Announcement of diagnosis and quality approach in CF

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The announcement of a diagnosis is always a critical period for the patient-caregiver relationship, in particular concerning CF. It’s an announcement of an asymptomatic but serious and incurable illness which requires intensive treatment. This announcement is always traumatic, but the method of announcement can aggravate or alleviate the trauma. The announcement must not be improvised and must be an issue of constant concern in order to improve it. Neonatal screening already allows for improvement of the context: the stress and resentment due to a diagnostic delay are reduced; the possibility of early treatment reassures the parents; the non-urgent context permits better preparation of the first meeting between the physician and the family. Neonatal screening is extended to all of France since 2003. We will examine how a process of constant improvement of quality, as described by Deming, has been engaged:

- Plan: identification of the specific problematic to announce an asymptomatic but incurable illness;
- Do: description of an action plan in the shape of recommendations;
- Study: evaluation (examine the implementation of these measures and the analyze the deviations);
- Act: proposition of corrective measures and innovative actions.

The steps involved for the child, parents and concerned professionals, present

procedure and present a document entitled “report on telephone conversation with

Procedure

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The 2 first steps have been accomplished and now, we have to cross the next 2 steps. We will comment on how the different actors can join their reflections for an innovative and federating project: Evaluation of CF announcement practices (after neonatal screening) in relation with the recommendations.

Procedure for diagnostic announcement of Cystic Fibrosis by a multidisciplinary team

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In France, systematic screening at birth for CF is carried out since 2003. Announcing the diagnosis is one of the main tasks of the CRCM (CF Resource and Treatment Centre). At the CRCM, ROSCOFF (Brittany), announcement of diagnosis began at the end of 2004. In preparation for this new activity, the multidisciplinary team set up a quality-oriented procedure to announce the diagnosis of CF, adapting national recommendations to the specific work conditions. This procedure applies only to newborns for whom the 2 mutations are identified at screening. We describe the procedure and present a document entitled “report on telephone conversation with the parents in preparation for a consultation to confirm diagnosis of CF”. The different steps involved for the child, parents and concerned professionals, present at the consultation are also described.

Severe and mild CFTR genotypes: age and presenting symptoms in patients diagnosed through newborn screening versus clinical symptoms

A. Munck1, C. Sahler1, J.P. Farriaux, AFDPHE. Paris, France

Newborn screening (NBS) for CF has been implemented on a nation wide basis in France in 2002.

Aim: according to the genotype severe/mild (http://www.genet.sickkids.on.ca/cftr, 2 mutations from the CF-30 kit), to quantify the diagnosis saving time and identify the main presenting symptoms in CF patients diagnosed through NBS/clinical symptoms (CS).

Patients: CS group from the French National Observatory ONM 1999-2001 (exclusion: familial CF, antenatal dg, regional NBS, meconium ileus (MI)). NBS group from the French Association for Neonatal Screening data AFDPHE 2002-2004 (exclusion: antenatal dg, MI, false negative). Four cohorts in each group were defined according to the CF mutation data base S/S (class I, II, III), S/508/508, S/SM (class IV, V), R117H/other.

Methods: the median age at diagnosis and the main presenting symptoms (failure to thrive, digestive and respiratory).

Results:

<table>
<thead>
<tr>
<th>NBS Age (m)</th>
<th>Thrive (%</th>
<th>Digestive (%)</th>
<th>Respiratory (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S/S</td>
<td>148/221</td>
<td>16/1.1</td>
<td>35/22</td>
</tr>
<tr>
<td>P508/508</td>
<td>106/144</td>
<td>12/1.1</td>
<td>35/33</td>
</tr>
<tr>
<td>S/M</td>
<td>15/56</td>
<td>26/1.2</td>
<td>13/7.5</td>
</tr>
<tr>
<td>R117H/other</td>
<td>4/36</td>
<td>280/1.5</td>
<td>50/0</td>
</tr>
</tbody>
</table>

CF patients S/S have been diagnosed on CS at a mean age of 16 m, 63% already had a clinical pulmonary involvement meanwhile it concerned only 15% of the NBS. Patients with S/M have been diagnosed on CS during the second decade of life due to a milder symptomatology, though NBS might be questionable for them.

Conclusion: Up to 85% of the NBS neonates with a severe genotype started their follow up in CF centres before a clinical pulmonary involvement and should benefit of the optimal preventive treatment whereas two thirds of the ones diagnosed on CS at 16 m had pulmonary symptoms at diagnosis already.

CF screened newborns with at least one R117H mutation: immunoreactive trypsineogen (IRT) and sweat test values, polyT and clinical symptoms

A. Munck1, C. Sahler1, J.P. Farriaux, AFDPHE, Paris, France

Newborn screening (NBS) for CF has been implemented over France (2002-early 2003). The program uses an immunoreactive trypsineogen (IRT)/DNA testing for positive samples (kit Elucigen CF-30 Orchid ARMS) on dried blood spots at day 3. A controversy exists regarding the detection of the R117H as the natural history of these patients is not clearly defined. Small cohorts demonstrate CF phenotypes from normal to moderate mostly during the second decade of life.

Aim: estimation of the incidence, IRT, sweat chloride (SC) levels and parameters at diagnosis of screened CF with R117H in comparison to CF without R117H.

Subjects and Methods: to date 2002-October 2005, we detected 569 CF NBS, among them 48 had at least one R117H. Were evaluated the median IRT (cut off initially 60 then 65 µg/L), SC (borderline 30-50 mEq/L) values, median age and symptoms (failure to thrive, digestive, respiratory) at diagnosis in both groups and the R117H/poly T.

Results: see the table.

<table>
<thead>
<tr>
<th></th>
<th>NBR</th>
<th>IRT (µg/L)</th>
<th>Diagnosis</th>
<th>SC (mEq/L)</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>CF without R117H</td>
<td>521</td>
<td>138</td>
<td>34</td>
<td>98</td>
<td>281 (54%)</td>
</tr>
<tr>
<td>R117H/poly T</td>
<td>48</td>
<td>88</td>
<td>42</td>
<td>31</td>
<td>3 (8%)</td>
</tr>
</tbody>
</table>

Over 8.4% of the NBS CF infants had at least one R117H. Only 1/48 was associated with 5T, he was asymptomatic, SC < 35, 3/4 were R117H/R117H all asymptomatic, SC = 35, 30, 29. Among the 47 T/T, 21 with borderline SC were asymptomatic, the others had normal SC but 2 had respiratory symptoms (bronchiolitis, atelecstasis).

Conclusion: We conclude that CF infants with one R117H detected through NBS are mostly asymptomatic at diagnosis, nevertheless 50% had either an abnormal or a borderline SC. They should be all monitored in a CF center (one refusal) with repeated SC and clinical evaluation. Only long term follow up will help physicians to better understand this cohort. Discussion around the R117H withdrawal from the CF-30 kit may be questionable but perhaps too premature.

We thank the maternities, laboratories, regional associations and the CF centers who participated in this study.