ECFS Neonatal Screening Working Group

ISSUE 4 AUGUST 2013

NSWG CONTACTS

Dr Kevin Southern
Reader and Honorary Consultant in Paediatric Respiratory Medicine
Institute of Child Health
University of Liverpool
Alder Hey Children's Hospital
Eaton Road
Liverpool L12 2AP
United Kingdom
Email; kwsouth@liv.ac.uk

Victoria Winters
ECFS NSWG Administrator
Address as above
Email; v.winters@liv.ac.uk

UPCOMING EVENTS

The 37th ECFS Conference will take place in, Gothenburg, Sweden
11-14 June 2014

Introduction

This newsletter outlines ECFS standards for the performance of newborn screening for CF, which are soon to be published. These standards were developed by the Core Group using Delphi methodology and will be part of a larger ECFS document that includes standards for a wide variety of CF care issues.

The standards are self-explanatory and the aim is to drive up quality. Programmes achieving these standards should not be complacent and should continue to examine strategies to improve performance. The standards represent minimum levels of expectation. Statement 3 refers to repeat sampling and this reflects the importance of good quality dried blood samples for IRT measurement.

The final statement refers to the management of infants with equivocal diagnosis after NBS. This is timely as the Working Group is currently undertaking a consensus project to better determine the management of these infants. Again, we are employing a Delphi methodology, reflecting the lack of evidence base on which to base these guidelines. The first stage of this process is underway and we would appreciate your input. The deadline for phase 1 is the 6th September. You should have already received an invitation to take part in the project; if not, please contact Vicki Winters via email on v.winters@liv.ac.uk.

Kevin Southern

Newborn Screening and Access to Specialist Care from Early Life

Kevin Southern (UK), Anne Munck (F), Nataliya Kashirskaya (Rus), The ECFS Neonatal Screening Working Group (Core Committee)

There is clear evidence to support newborn screening for CF, with early recognition providing the foundation for future management and preventing the diagnostic odyssey that has affected so many families[1]. Protocols should be designed to reflect the population and minimise potential negative impacts. Please refer to the ECFS guidelines on newborn screening and on the management of young infants with CF diagnosed through screening[2, 3].

1. What population and socio-geographical characteristics validate screening newborn infants for cystic fibrosis?

Health authorities need to balance the benefit / risk ratio of screening newborns for CF in their population. If the incidence of CF is less 1/7000 births, careful evaluation is required as to whether NBS is valid. The protocol must be shown to be causing the minimum negative impact possible on the population.

2. What health and social resources are minimally acceptable for newborn screening to be a valid undertaking?

Infants identified with CF through a NBS programme should have prompt access to specialist CF care that achieves ECFS standards. A NBS programme may be a mechanism to better organise CF services, through the direct referral of infants for specialist CF care. Countries with limited resources should consider a pilot study to assess the validity of NBS in their population.

3. What is an acceptable number of repeat tests required for inadequate dried blood samples for every 1000 infants screened?

The number of requests for repeat dried blood samples should be monitored and should be less than 0.5%. More than 20 repeats for every 1000 infants is unacceptable (2%).

4. What is an acceptable number of false positive NBS results (infants referred for clinical assessment and sweat testing)?

Programmes should aim for a minimum positive predictive value of 0.3 (PPV is the number of infants with a true positive NBS test divided by the total number of positive NBS tests).

5. What is an acceptable number of false negative NBS results? These are infants with a negative NBS test that are subsequently diagnosed with CF (a delayed diagnosis).

Programmes should aim for a minimum sensitivity of 95%. Sensitivity is the number of true positive NBS results as a percentage of the total CF population (true positive and false negatives). Mechanisms should be in place for the collection of reliable long-term false negative data.

6. What is the maximum acceptable delay between a sweat test being undertaken and the result given to the family?

The sweat test should be analysed immediately and the result reported to the family on the same day.

7. What is the maximum acceptable age of an infant on the day they are first reviewed by a specialist CF team following a diagnosis of CF after NBS?

The majority of infants with a confirmed diagnosis after NBS should be seen by the Specialist CF team by 35 days of age (no later than day 58). Programmes that are consistently missing these targets should undertake a protocol review and consider alternative strategies.

8. What is the minimum acceptable information for families of an infant recognised to be a carrier of a CF causing CFTR mutation after NBS?

a. *Families should receive a verbal report of the result. They should also receive written information to refer to. Information should also be sent to the family Primary Care Physician.*

b. *The information should be clear that:*
   - i. *The infant does not have CF.*
   - ii. *The baby is a healthy carrier.*
   - iii. *Future pregnancies for this couple are not free of risk of CF and the parents may opt for genetic counselling.*
   - iv. *here are implications that could affect reproductive decision making for extended family members and the infant when they are of child bearing age.*

9. What are the minimum acceptable standards for reporting a CF diagnosis following NBS to the family?

a. A CF Specialist should discuss the result in person with the parents.
b. The family should receive written information to read after the consultation. Information should also be sent to the family Primary Care Physician.
c. The family should have a clear understanding of short and long term plans with respect to the child's management.

10. What are the minimal acceptable standards for the recognition and management of infants with an equivocal diagnosis following NBS?*

a. The infant should be reviewed by a CF Specialist.
b. This may be in a CF clinic or a non-CF clinic, if local circumstances are appropriate.
c. Extended gene sequencing should be undertaken when one or no mutations are recognised.
d. Sweat testing should be repeated in a centre with considerable experience (>150 sweat tests per annum) and sweat chloride measured by a standard method.
e. Families should receive clear verbal and written information about the infant and have a clear understanding of what to expect with respect to progress and possible symptoms. Information should also be sent to the family Primary Care Physician.

**definition; an infant with a repeatedly intermediate sweat test result, or an infant with two CFTR gene mutations (one of which has unclear phenotypic outcome) and a normal or intermediate sweat test result. An intermediate sweat test result is a sweat chloride value between 30-59 mmol/L[4].*

REFERENCES

1. Southern KW, Mérelle MME, Dankert-Roelse JE, Nagelkerke A. Newborn screening for cystic fibrosis. Cochrane Database Syst Rev 2009: Issue 1. Art. No.: CD001402. DOI: 10.1002/14651858.CD001402.pub2.

2. Castellani C, Southern KW, Brownlee K, et al. European best practice guidelines for cystic fibrosis neonatal screening. J Cyst Fibros 2009; 8(3): 153-73.

3. Sermet-Gaudelus I, Mayell SJ, Southern KW. Guidelines on the early management of infants diagnosed with cystic fibrosis following newborn screening. J Cyst Fibros 2010; 9(5): 323-9.

4. Mayell SJ, Munck A, Craig JV, et al. A European consensus for the evaluation and management of infants with an equivocal diagnosis following newborn screening for cystic fibrosis. J Cyst Fibros 2009; 8(1): 71-8.

If you have anything you wish to add to the next ECFS NSWG Newsletter please email v.winters@liv.ac.uk or kwsouth@liv.ac.uk.