Newborn Screening for CF

PRP Branch
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Screening Newborns for CF

- The evidence in favour of newborn screening for CF is not overwhelming
- It is imperative therefore that we do it well, causing minimum harm

Processing a positive result

issues to be resolved

1. What is a positive screening result
2. Sweat tests; when, how and who?
3. DNA analysis
4. Clinical investigations
5. Appropriate follow up and management
6. Alternative physiological tests

1) What is a positive screening result?

- Biochemical
  - Second IRT test (21-28 days) above threshold
    - UK; set at 10 ng/ml below IRT-1 (99.5th centile)
- IRT-DNA
  - Recognition of two CF-associated CFTR gene abnormalities
  - One CF-associated CFTR gene abnormality

To be resolved

- IRT-2 threshold
- Genetic diagnosis

2) Sweat tests

- After positive screen
  - 5-6 weeks
- Method
  - Gibson Cooke
  - Capillary (macroduct)
- Recognised centre (>50 per year)
  - Experience balanced with geography
    - J Paed and Child Health, 2006;42:160-4

Positive sweat test result

- Chloride > 40 mmol L^{-1}
  - Australian data
    - Massie et al, Pediatr Pulmonol 2000;29:452-6
  - Wisconsin data
    - Farrell and Koscik, Pediatrics 1996;97:524-8
  - Normal data, Jayaraj et al. poster 479
    - Mean, 10.8 mmol L^{-1}; 97.5th centile, 22
- Conductivity
  - Nanoduct system

To be resolved

- Consensus on
  - When to sweat test
  - Reference range for sweat Cl-
  - Method
  - Necessary experience

3) DNA analysis

- At what point in the protocol
- Which mutations as a first screen (minimising carrier recognition)
- Further DNA analysis when one mutation found
- Methods to reduce sweat testing
- One mutation and positive sweat test

4) Clinical investigations

- Growth
  - Evidence of fat malabsorption
    - Fecal fats
    - Fecal elastase
- Respiratory condition
  - CXR if symptomatic; ? baseline
  - ? Routine respiratory cultures

5) Appropriate follow up and management

- Positive sweat test/ one mutation
  - CF clinic, standard management
  - Continue DNA analysis (extent?)
- Unusual genotype (for example R117H on a 7T background) with equivocal or normal sweat test
  - ? outpatient review (? frequency)
  - Monitor for respiratory symptoms/poor weight
  - Information/time for families

6) Role of further electrophysiology

- Nasal PD
  - Challenging in infants
  - Often equivocal
- Intestinal current measurements
  - More practical
- Both experimental at moment

Group members

- Kevin Southern
- Anne Munck
  - Carlo Castellani
  - Anne Green
  - Isabelle Sermet
  - Chris Taylor
  - Martin Schwartz
  - Giovanni Taccetti

Timescale

- Email correspondence; define individual tasks
- Complete draft proposals
  - September 2006
- Meeting
  - Ratify draft proposals
- Write consensus document
  - December 2006
- Ratify consensus document
  - March 2007