

# 10. Newborn screening

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## 10.1 Key points

### What is newborn screening?

- Newborn screening aims to detect babies who may be at risk of certain severe or life threatening conditions prior to the onset of symptoms, with the goal of reducing morbidity and mortality through earlier treatment.
- Newborn screening is a free test provided for all babies. A sample of blood is collected by heelprick onto a Guthrie card 48 to 72 hours after birth.
- Less than 0.1% of babies tested will be diagnosed with a medical condition as a result of newborn screening.
- Approximately 2% of babies will require further tests.
- Newborn screening does not detect all affected babies, therefore any symptomatic child should be investigated.

### What conditions are screened?

- Cystic fibrosis.
- Over 20 metabolic conditions, including phenylketonuria (PKU), are tested as part of the expanded newborn screening program (see Appendix 1).
- Congenital hypothyroidism.

### Why are these conditions tested?

**Disorders are selected for testing if they meet the following criteria:**

- They are potentially serious.
- Early treatment/intervention is beneficial.
- A cost-effective, reliable screening test is available.

Other disorders are evaluated for inclusion into the screening program as medical and scientific advances are made.

## Results

- The time taken for results to be available depends on the test. Metabolic test results may be available two to three days after the sample is received by the laboratory, while cystic fibrosis testing results may take up to six weeks to become available.
- Health care professionals can obtain results by contacting either the newborn screening liaison person at the relevant hospital or the Newborn Screening Laboratory on (03) 8341 6272. *The laboratory is unable to provide results to parents.*

### Normal results

- Ninety-eight per cent of babies will have normal results from testing of the Guthrie card.
- Not all affected babies will be detected.
- The laboratory does not directly inform parents if the results are normal. Results are sent to the centre named on the collection form.

### Where further testing is required

- Generally, newborn screening identifies babies requiring further testing. Where possible, the GP is contacted and informed of the need for further testing. The Newborn Screening Program will coordinate further testing and appointments.
- The majority of babies requiring further testing receive normal results on repeat or subsequent diagnostic testing.
- For metabolic conditions and congenital hypothyroidism, a rapid response to the screening result is required as delay in diagnosis increases morbidity.
- Feedback from families indicates that, where a diagnosis has been made, most families prefer to be contacted by someone they know, such as their GP or obstetrician.
- Treatment, counselling and support are provided free of charge by the services associated with the Newborn Screening Program.

## Role of the GP

### The role of the GP is to:

- Provide information about newborn screening to parents prior to delivery.
- Liaise with testing services if further testing is required or a condition is suspected.

## 10.2 Background

### Cystic fibrosis

See Part 9 *Cystic fibrosis* for more detailed information.

#### What is cystic fibrosis?

- Cystic fibrosis is primarily a respiratory disorder affecting approximately one in 3000 Victorian babies (Riley & Halliday 2000).
- Cystic fibrosis results from an altered synthesis of a protein involved in the transport of chloride ions.
- Cystic fibrosis is an autosomal recessive condition. Carriers are healthy.

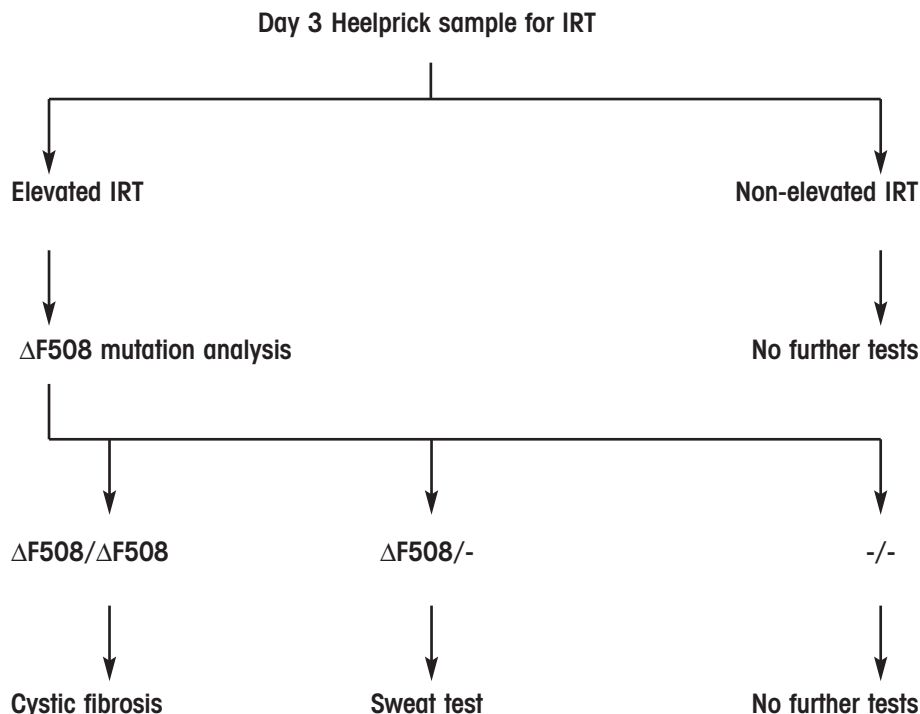
#### Common clinical features

- Cystic fibrosis primarily affects the respiratory system, digestive system (pancreas and sometimes liver) and reproductive system.
- Production of thickened mucous secretions results in frequent respiratory tract infections and difficulties digesting food properly.
- Babies with cystic fibrosis may have loose stools and gain weight poorly.

#### Test

- Neonatal screening for cystic fibrosis is a three-step process. See Figure 1.:
- Affected babies and babies requiring sweat tests will be informed of results within six weeks.

Figure 1. Newborn screening for cystic fibrosis



Source: Massie, J 2001, 'How to treat cystic fibrosis', *Australian Doctor*, 18 May

## Treatment

- Treatment includes physiotherapy, a high calorie diet and, often, pancreatic enzyme replacement.
- Early treatment aims to slow the progress of the disease.

## Implications for other family members

- Parents of a child with cystic fibrosis have a one in four risk of recurrence for each pregnancy. Prenatal testing is often available.
- Relatives of a person with cystic fibrosis may be carriers and should be referred to a genetic service for carrier testing; for example, healthy siblings of a person with cystic fibrosis have a two in three chance of being carriers.
- Relatives of people found to be carriers may themselves be carriers, and should consider carrier testing.

See Part I *Cystic fibrosis* for more information on carrier testing.

## Phenylketonuria (PKU)

### What is PKU?

- PKU is one of the most common metabolic disorders. Approximately one in 14,000 Victorian babies have PKU (Riley & Halliday 2000).
- PKU is caused by the absence of a fully active form of a liver enzyme (phenylalanine hydroxylase) that is responsible for the conversion of the amino acid phenylalanine to tyrosine.
- This results in an accumulation of phenylalanine in blood and tissues that damages the brain.
- PKU is an autosomal recessive condition. Carriers are healthy.

### Clinical features

Babies with PKU are asymptomatic at birth.

#### If untreated, PKU causes:

- Severe, progressive intellectual disability
- Motor retardation
- Microcephaly and seizures
- Growth problems.

### Test

- Nowadays, levels of phenylalanine in the blood spot are determined using a tandem mass spectrometer.
- Diagnosis requires confirmation of levels and a full metabolic screen on a blood sample.
- Results are usually available within 48 hours of receipt of the Guthrie card at the laboratory

## Treatment

- A strictly monitored low-protein diet with special supplements to provide tyrosine and essential amino acids is necessary to avoid the complications of PKU. This diet is maintained at least until the central nervous system has matured (usually early teens). The period of time the diet should be adhered to beyond this point is the area of current research.
- Monitoring of blood phenylalanine is an important aspect of dietary management. It is an essential amino acid and levels must be sufficient for the body's requirements, but low enough that damage to the central nervous system does not occur.
- Compliance with the highly restrictive diet is critical for the affected child to reach maximum potential.

## **Implications for other family members**

- A woman with PKU planning a pregnancy must be on a comprehensive diet before conception. Phenylalanine levels must be monitored frequently to prevent the teratogenic effects of accumulation of phenylalanine in the fetal central nervous system.
- Parents of a child with PKU have a one in four risk for each pregnancy of having another child affected by PKU.

## **Rare metabolic conditions**

- The expanded Newborn Screening Program now includes screening for over 20 metabolic disorders (see Appendix 1 for list).
- Approximately nine babies a year will be detected with a rare metabolic condition as a result of the Newborn Screening Program.
- Most metabolic disorders are inherited in an autosomal recessive fashion, however some are X-linked. Cause and inheritance will be discussed with the family and clinician by the Metabolic Unit of Genetic Health.

## **What types of conditions can be detected?**

Three groups of disorders can be detected.

### *Disorders of fatty acid oxidation.*

These are defects in the 'burning' of fatty acids. The most common of these is MCAD deficiency, which might be life threatening but is easily treated. Children with this condition are usually well but may suffer metabolic decompensation if fasting. They may present with altered breathing pattern and neurological status. Management usually consists of avoiding fasting and taking special measures when the child has an intercurrent infection. Newborns should be offered feeds four hourly in the first four days of life. The type of feed is not important.

### *Organic acidaemias/acidurias.*

These are the results of defects in the metabolism of, mainly, amino acids. They are rare but can be life threatening. Treatment consists of a low-protein diet, supplements and medications. Early treatment is associated with reduced mortality and morbidity.

### *Other amino acidopathies.*

These are the results of other defects in the metabolism of amino acids in which organic acids are not produced. They may result from a defect in a transporter or an enzyme of amino acid metabolism. They are also rare but can also be life threatening. Treatment consists of a low-protein diet, supplements and medications. Early treatment is associated with reduced mortality and morbidity.

## **Test and results**

- A specialised machine (tandem mass spectrometer) detects changed levels of metabolites in the blood spot on the Guthrie card.
- Altered metabolite levels can be due to enzyme or transporter deficiencies. The result may be diagnostic or indicate a need for further testing.
- Screening results are usually available within 24 to 48 hours of sample receipt at the laboratory. Diagnostic test results are usually available within 24 hours.
- In some cases, the baby may present in crisis prior to diagnosis by newborn screening.

## **Congenital hypothyroidism**

### ***What is congenital hypothyroidism?***

- Congenital hypothyroidism is due to an absent, ectopic or malfunctioning thyroid gland.
- Congenital hypothyroidism is not usually inherited, but occurs spontaneously. Other family members are not at increased risk.
- Approximately one in 4100 Victorian babies have congenital hypothyroidism (Riley & Halliday 2000).

### ***Clinical features***

- Newborns may be asymptomatic at birth. Early neonatal signs are non-specific: delayed passage of meconium, temperature instability, prolonged jaundice, umbilical hernia, feeding problems. Later there may be cool mottled skin, nasal discharge, coarse hair and skin.
- Without treatment, severe intellectual disability, growth problems, deafness and classical signs of hypothyroidism may occur.

### ***Test***

- Thyroid stimulating hormone (TSH) is assayed by an immunological method.
- Elevated levels of TSH are an indication of primary hypothyroidism.
- Further serum thyroid function tests are required for diagnosis. In addition, a thyroid scan and audiology are performed in most tertiary centres.
- Screening results are usually available within 48 hours of receipt at the laboratory.

### ***Treatment***

- Thyroxine taken orally for life.

## Appendix 1: Metabolic conditions detectable by expanded newborn screening

### *Fatty acid oxidation disorders*

#### Deficiencies of:

- Short-chain acyl-coA dehydrogenase (SCAD)
- Short-chain hydroxyacyl-coA dehydrogenase (SCHAD)
- Medium-chain acyl-coA dehydrogenase (MCAD)
- Long-chain acyl-coA dehydrogenase (LCAD)
- Very-long-chain acyl-coA dehydrogenase (VLCAD)
- Long-chain hydroxyacyl-coA dehydrogenase (LCHAD)
- Carnitine-palmitoyl-coA acyltransferase I (CPTI)
- Carnitine-palmitoyl-coA acyltransferase II (CPTII)
- Carnitine-acylcarnitine translocase
- Carnitine transporter.

### *Organic acidurias*

- Propionic acidaemia (PA)
- Methylmalonic aciduria (MMA)
- 3-methylcrotonyl-CoA carboxylase deficiency (3-MCC)
- Isovaleric acidaemia (IVA)
- Glutaric aciduria type 1 (GA1)
- Hydroxymethylglutaryl-CoA lyase deficiency (HMG-CoA lyase def)
- Beta-ketothiolase deficiency
- 2-methyl-3-hydroxybutyric aciduria
- Vitamin B12 deficiency (maternal and hence infant) and related disorders
- Holocarboxylase synthetase deficiency
- Multiple acyl-CoA dehydrogenase deficiency (MADD)
- Congenital lactic acidosis due to disorders of pyruvate dehydrogenase or oxidative phosphorylation.

### *Amino acid disorders*

- Phenylketonuria (several forms, including disorders of bipterin metabolism) (PKU etc)
- Tyrosinaemia (more than one type)
- Maple syrup urine disease (MSUD)
- Hypermethioninaemia
- Homocystinuria
- Citrullinaemia
- Argininosuccinic aciduria
- Non-ketotic hyperglycinaemia.

## 10.3 Patient and further information

### Support groups

#### *Cystic fibrosis*

Cystic Fibrosis Victoria  
80 Dodds Street, Southbank 3006  
PO Box 3036  
South Melbourne 3205  
Call: (03) 9686 1811  
Fax: (03) 9686 3437  
Freecall: 1800 633 685  
Email: [admin@cfv.org.au](mailto:admin@cfv.org.au)  
Website: <http://www.cfv.org.au>

#### *Metabolic disorders (including PKU)*

Metabolic Dietary Disorders Association  
Kerri Carboon, 57 Gordon Avenue  
Montrose 3765  
Call: (03) 9728 5510

#### *Congenital hypothyroidism*

Thyroid Australia Limited  
PO Box 2575, Fitzroy Delivery Centre 3065  
Call: 9561 2483  
Fax: 9561 4798  
Email: [support@thyroid.org.au](mailto:support@thyroid.org.au)  
Website: <http://www.thyroid.org.au>

### Websites

Better Health Channel: <http://www.betterhealth.vic.gov.au>  
Relevant topic: 'Newborn Screening'

Expanded Newborn Screening:  
<http://www.genetichealthvic.net.au/pages/news&views/NewbornScreening.html>  
<http://www.genetichealthvic.net.au/pages/diagnosis/metablicscreen.html>

HGSA Newborn Screening policy and policy on storage of Guthrie cards: <http://www.hgsa.com.au/>



## 10.5 References

Riley, M & Halliday, J 2000, Birth defects in Victoria 1983–1998, Perinatal Data Collection Unit, Victorian Government Department of Human Services, Melbourne.

