

SA Neonatal Screening Centre Bulletin

Report of the activity for the period February 1999 to February 2000

Introduction

The Department of Chemical Pathology at the Women's and Children's Hospital introduced tandem mass spectrometry into front-line newborn screening in February 1999 as part of an Expanded Neonatal Screening Programme. This new technology has had a significant impact on the provision of neonatal screening service with the ability to identify over 30 different inborn error of metabolism (IEM). This was in addition to the standard screening for congenital hypothyroidism, galactosemia and cystic fibrosis.

The Expanded Neonatal Screening Programme in the first year of operation has identified a number of disorders of fatty acid oxidation, organic acidurias and aminoacidopathies.

ACHIEVEMENTS

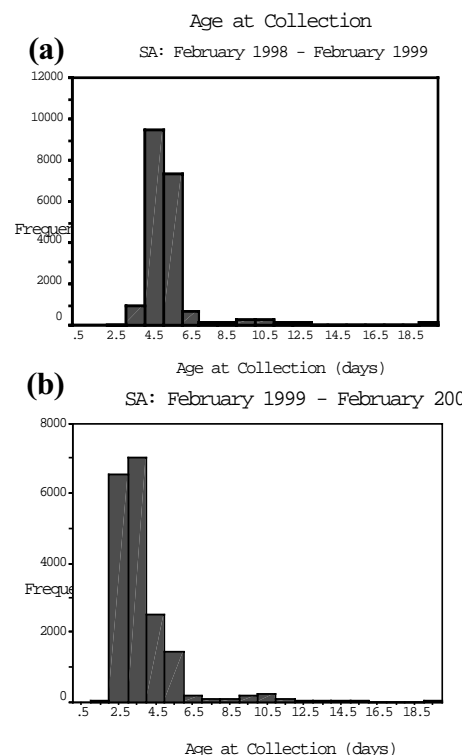
In the 12 month period of operation 19,942 neonatal blood-spot screening tests have been analysed from the South Australian newborn population. The analysis was performed using tandem mass spectrometry in which an acylcarnitine profile identified fatty acid oxidation defects and organic acidurias and an aminoacid profile is used to identify aminoacidopathies. In addition to this, standard techniques were employed for the screening of congenital hypothyroidism, galactosemia and cystic fibrosis.

Some infants have been screened on more than one occasion, the majority of these were premature infants in whom repeat testing at various ages is accepted protocol. As usual, some samples were inadequate for analysis and repeat samples were requested; this proportion was no different from that seen in previous years. Other infants had repeat samples requested because of transient abnormal profiles detected on their blood-spot screening tests. There was a ~3-4% overall recall rate for poor specimen, inappropriate collection time, multiple collection for premature infants and repeat testing.

A clinical interpretation software was developed in collaboration with Professor A Roscher from the Munich Paediatric Hospital. The software enables the interpretation of the 93 individual analytical results produced by the tandem mass spectrometer in order to make a provisional diagnosis of an IEM. Confirmation of a "high risk" infant identified by screening was performed by routine metabolic testing using blood and urine.

Routine screening at 48 hours of age has now become accepted practice in South Australia with greater than 80% of infants having a collection at 2 days of age. Figure 1a and b shows the change towards earlier collection from 4 to 5 days of age in 1998 to 2 to 3 days with the introduction of tandem mass spectrometry. This has meant that almost all collections are performed prior to discharge reducing greatly the risk of a "missed collection". The new collection cards provides for the required additional information of date and time of birth and collection in addition to details regarding feed type to be documented.

Figure 1



Outcomes

Using tandem mass spectrometry the SA Neonatal Screening Programme has detected 4 babies with metabolic abnormalities, who would not have been detected using our previous screening methods. These were detected with abnormal acylcarnitine profiles diagnostic for medium chain acyl-CoA dehydrogenase deficiency (MCAD), isovaleric acidemia (IVA), 3-methyl crotonyl CoA carboxylase deficiency (3MeCoACD) and a case of carnitine deficiency. There was an additional MCAD detected in December 1998 during the pilot phase. Tandem mass spectrometry screening using an acylcarnitine and aminoacid profile has detected 9 infants overall, giving an incidence of 1 in 2055 using this technology. The specific diagnoses are listed in Table 1.

Table 1

Detection using Tandem Mass Spectrometry		
Disorder	Number	Incidence
PKU Hyperphenylalaninemia	4 1	1: 4,985 1: 19,942
MCAD IVA 3-MeCCoACD (maternal)	1 1 1	1: 6,647
Carnitine Deficiency	1	1: 19,942
Incidence rate per child screened	9	1 in 2,055

In order to make these diagnoses, 118 infants had repeat neonatal screening tests requested: 33 for abnormal amino acid profiles and 85 for abnormal acylcarnitine profiles (0.43% of all babies screened). Thirteen infants had persistently abnormal results and were recalled for counseling and further metabolic testing, of whom 9 have received a diagnosis of an inborn error of metabolism. In some infants the acylcarnitine marker metabolites were grossly elevated and a direct request for a formal metabolic screen was made without the need for a repeat blood-spot collection. In addition, fifteen infants were diagnosed by other screening methods to have congenital hypothyroidism (8 infants), galactosemia (2 infants) and cystic fibrosis (5 infants) (table 2). The collective incidence is one infant identified in every 771 births in the SA population.

Table 2

Disorders Screened by Traditional Methods		
Disorder	Number	Incidence
Congenital Hypothyroidism	8	1: 2,492
Galactosemia	2	1: 9,971
Cystic Fibrosis	5	1: 3,988

Conclusion

The SA Expanded Neonatal Screening Programme using tandem mass spectrometry has been successfully introduced in SA. This has enabled the identification, within 2 days of age, of four infants with an IEM that would have otherwise not been detected.