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Newborn Screening Programme *for* Inborn Errors of Metabolism

Department of Health
The Government of the Hong Kong Special Administrative Region

醫院管理局
HOSPITAL AUTHORITY

Newborn Screening for IEM at a Glance

1 Antenatal Visit

Antenatal health education related to IEM screening programme is provided by healthcare professionals.

2 Consent

With parent's written consent after delivery, majority of babies born after 24-72 hours and preferably have been milk- fed for 24 hours will receive heel pricking procedure for blood specimen collection.

3

Collection of blood specimen on a filter paper card.

4 Laboratory

Laboratory analysis

5 Screening results

Screening results within the scope of this screening programme available.

6 Report

Results will usually be available within 7 working days.

Normal results: Parents will not receive notification.

For abnormal or uncertain results: Parents will be informed early by phone. Babies will be referred to paediatricians for further evaluation.

What is Newborn Screening?

Newborn screening is a public health measure. Through the provision of screening test to newborn babies, it is intended to achieve early diagnosis of serious yet treatable genetic disorders which may not have obvious symptoms at the early stage, so as to reduce morbidity and mortality.

Newborn screening has over 30 years of history in Hong Kong. The Department of Health (DH) has been providing free cord blood screening of Congenital Hypothyroidism and Glucose-6-phosphate Dehydrogenase Deficiency for all babies born in public hospitals.

What is Inborn Errors of Metabolism?

Human being is a highly complex life form. Metabolism takes place at all times inside our body in order to keep us alive and to enable our diverse functions. Simple examples are like how food, after digestion and absorption, is converted into energy and various body tissues; how aged or damaged tissues are renewed and how the daily metabolic waste is disposed.

Inborn Errors of Metabolism (IEM) occurs because of inherent deficiency of a certain enzyme or co-factor, which in turn impairs normal metabolism. Accumulation of toxic substances or deficiency of essential metabolites may damage organs like the brain, the liver and the kidneys and, in the end, result in serious consequences of physical and mental disability.

Why is IEM screening important?

IEM are a diverse group of genetic disorders. Although any one disorder is very rare, the collective incidence of the whole group is not as rare. The incidence is about 1:4000 newborns in Hong Kong. As most IEM are recessively inherited, family history is often absent. Therefore, even if the parents and family members are all healthy, IEM can occur in any newborns.

Owing to the lack of obvious signs and symptoms at the early stage, IEM usually are not noticeable to parents and sometimes even medical professionals. Yet the appearance of obvious signs and symptoms may indicate the presence of organ damage or even at risk of death. The latest medical technologies enable early detection, diagnosis and treatment which may avoid or ameliorate serious consequences because of IEM.

What is the scope of this screening Programme?

Newborn screening for IEM is a public health programme. Its operation relies on the integration of organizational management, health education, medical testing technology and clinical management. The scope of screening is determined by considering the prevalence and seriousness of the diseases, the availability of reliable testing methods as well as the availability and effectiveness of the treatments. To this end, a Workgroup jointly formed by the DH and the Hospital Authority (HA) conducted an eighteen-month pilot study of newborn screening for Inborn Errors of Metabolism in Queen Elizabeth Hospital (QEH) and Queen Mary Hospital (QMH) from 1 October 2015 to 31 March 2017, to study the feasibility of launching a newborn screening programme for IEM within Hong Kong's public health care system. The pilot study has been proven effective. According to the Policy Address 2017, newborn screening for IEM is planned to be extended to all public hospitals in phases.

Given the diverse nature of IEM, not all metabolic diseases are included in the programme. After making reference to international practices and opinions of local experts, this newborn screening programme covers 26 IEM conditions (please refer to Appendix for details), including the following three major categories and other IEM:

- Amino Acid Disorders
- Organic Acid Disorders
- Fatty Acid Oxidation Disorders
- Other IEM

Is my baby eligible for this screening Programme?

All babies born at the implementing public hospitals are eligible for the screening programme, as long as a written consent is signed by a parent. The participation is voluntary and free of charge.

What is the screening process like?

The process of screening includes health education, blood sample collection, laboratory testing, confirmation of screen-positive (abnormal or uncertain) cases and referral for follow-up care.

Health education

The obstetrics departments of the implementing hospitals will provide antenatal and postnatal health education to expectant mothers who have delivery booking there. The healthcare professionals will explain the details to them.

Blood specimen collection and delivery

With the written consent from parents, babies who reach 24-72 hours after birth and preferably have been milk-fed for at least 24 hours will have heel pricking with a lancet for blood specimen collection. A small volume of blood will be dotted on a filter paper card. Usually only one DBS specimen is required. However, babies under the following conditions require additional blood specimens for testing* :

1. premature (less than 34 weeks of gestation), or
2. birth weight less than 2kg, or
3. being admitted into Neonatal Intensive Care Unit (NICU).

*Schedule of additional blood specimen collection		
1st specimen	2nd specimen	Remarks
To be collected at 24 to 72 hours of life.	To be collected at discharge or on day 28 of life whichever comes first.	If blood transfusion is required before the first specimen is collected, one more *pre-transfusion sample* would be collected.

Heel pricking is a safe blood collection method specific for newborn babies. The risks are small, including pain and bruising at the puncture site. Few babies have an infection as a result of the heel prick. Parents who find abnormal redness and swelling at the puncture site on their babies should inform the medical staff for management.

All blood samples are to be sent to the laboratory under HA for testing.

Screening results and follow-up

Screening Results		Follow-up Action
Normal	Risk of suffering from the screened metabolic diseases is very low.	Parents will not receive any notification.
Abnormal	Risk of suffering from the screened metabolic disease is high.	Hospital staff will notify parents by telephone within 7 working days. Babies will be referred to paediatricians for further diagnostic testing and management.
Uncertain	About 1% of the screened specimens will have uncertain results.	

All screening results and data will be made available to the Department of Health for data analysis.

Diagnostic testing

For abnormal or uncertain screening results, further evaluation and diagnostic testing is required. Diagnostic tests generally include blood, urine, and/or genetic testing, depending on which specific IEM condition is implicated by the screening results.

Treatment arrangement

Depending on the health condition of the babies, admission into their birth hospitals or consultation at the Specialist Clinic will be arranged. These services will be charged as admission or attendance at the specialist clinic under the HA accordingly.

How accurate is the screening test?

Although the accuracy of IEM screening is generally high, it is not 100% accurate. As a matter of fact, affected patients can escape detection by the screening (i.e. false negative). That is why a negative screening result only indicates a low risk instead of absolute normal. On the contrary, some normal babies are mistakenly identified as potential patients (i.e. false positive). This is why an abnormal or uncertain result does not necessarily mean the baby is affected; it only indicates that further follow-up assessment by paediatricians is necessary. The false positive and false negative rates vary between different IEM conditions.

It is also possible that incidental findings which are out of the scope of this screening programme may be detected. These incidental findings may or may not have clinical impact for your baby. Further follow-up assessment by specialist will be arranged.

Enquiries

For general queries, please call:

Tel: 2361 9979 (Clinical Genetic Service, Department of Health)
(till 30th June 2023)

Tel: 5741 4280 (Clinical Genetics Service Unit, Hospital Authority)
(from 1st July 2023)

For further enquiries about this Newborn Screening Programme for IEM, please approach your healthcare professionals when attending antenatal visits.

Appendix

Scope of the Newborn Screening for IEM

(Total 26 IEM conditions)

Disorders of Organic Acids (8 conditions)
Beta-ketothiolase deficiency
Glutaric acidaemia type I
Isovaleric acidaemia
Methylmalonic acidaemia (Methylmalonyl-CoA mutase deficiency)
Methylmalonic acidaemia and homocystinaemia (Cobalamin C deficiency)
Multiple carboxylase deficiency
Propionic acidaemia
3-hydroxy-3-methylglutaryl-CoA lyase deficiency

Disorders of Amino Acids (9 conditions)
Argininaemia
Argininosuccinic acidaemia
Citrullinaemia type I
Citrullinaemia type II
Classic phenylketonuria
Homocystinuria
Maple syrup urine disease
Tyrosinaemia Type I
6-pyruvoyl-tetrahydropterin synthase deficiency

Disorders of Fatty Acid Oxidation (6 conditions)
Carnitine-acylcarnitine translocase deficiency
Carnitine palmitoyltransferase II deficiency
Carnitine uptake deficiency
Glutaric acidaemia type II
Medium-chain acyl-CoA dehydrogenase deficiency
Very long-chain acyl-CoA dehydrogenase deficiency

Other IEM conditions (3 conditions)
Biotinidase deficiency
Classic galactosaemia
Congenital adrenal hyperplasia