To the parent/guardian: Regarding the newborn screening test 英語版

The purpose of the newborn mass screening test is to detect and prevent diseases which may be life-threatening if left undetected and untreated. Currently in Japan, 20 types of disease present at birth are targeted, and other diseases have also been studied.

At this time, a study on the screening test for the following diseases has started: **severe combined immunodeficiency, lysosome disease (Pompe disease, Fabry disease, and mucopolysaccharidosis type I and type II), spinal muscular atrophy (SMA), and adrenoleukodystrophy**. Screening test for some diseases, including adrenoleukodystrophy, are only available for boys.

Severe combined immunodeficiency is an abnormality in immunity from birth, where the body cannot protect itself from harmful pathogens and the person suffers repeated infections, resulting in a high risk of death. Although this can be life-threatening, it is possible to live a healthy life after early detection and treatment such as bone marrow transplantation.

Lysosomal disease is a general term for diseases where enzyme activity to dissolve substances which are no longer needed such as fats and sugars decreases, and these substances accumulate in the cells in various parts around the body causing symptoms. As early detection as soon as possible after birth and starting treatment such as enzyme replacement therapy can reduce the progression of symptoms, screening testing for Pompe disease, a type of lysosomal disease, Fabry disease, and Mucopolysaccharidosis type I and type II has started in Aichi prefecture.

● **Pompe disease**: Pompe disease is a congenital muscle disorder. In the most severe infantile-onset type, weakening muscle strength leads to enlargement of the heart and respiratory disorder during infancy. This requires an artificial respirator, and life may be lost due to heart failure. In a milder form called the late-onset type, symptoms such as loss of muscle strength occur in late childhood or after. Infantile-onset is rarer than late-onset. By mass screening and early detection soon after birth, disease progression may be stopped or delayed. Mass screening can sometimes detect the late-onset type which does not need immediate treatment.

● **Fabry disease**: Abnormal substances accumulate in blood vessels throughout the body, causing pain in the hands and legs, complications in the kidney, heart, cerebral blood vessels, or eyes. Since the disease is a sex chromosome genetic disease, symptoms mainly appear in male infants, but it may be observed in women after adulthood. Symptoms appear after 5-6 years, so even if identified by mass screening, treatment will not be started immediately. When to begin the treatment will be decided according to close observation of symptom conditions. For girls, even if the test results from the mass screening are normal, symptoms may appear after puberty or adulthood. For this reason, girls are not subject to screening testing for this disease. This disease can be treated by enzyme replacement therapy, and in some patients, success with oral medication can be expected.

● **Mucopolysaccharidosis type I and type II**: This is a progressive disease where abnormal substances called "mucopolysaccharides" accumulate throughout the whole body. Symptoms include inflammation of the inner ear, joint contracture, peculiar facial features, cataracts (not observed in type II), respiratory disorders, heart valve disease, and growth/developmental disorders. Although there are no differences between the sexes for type I, type II is a sex chromosome genetic disease and almost exclusively affects male infants. By early detection and enzyme replacement therapy or hematopoietic stem cell transplant, prevention of disease progress can be expected. Early detection and treatment is possible with the mass screening test, and mild cases appearing after adulthood are sometimes detected.

Adrenoleukodystrophy (ALD) is one type of peroxisomal disorder that mostly appears only in boys. There are several known types of the disease, but severe Childhood Cerebral ALD causes degeneration of nerve cells and nerve fibers in the brain and other organs, and abnormalities in the adrenal glands, which produce essential hormones for body. This results in a rapid deterioration of intelligence, behavioral abnormalities, and deterioration of motor skills and vision. Without treatment, the patient will become bedridden within one to two years of the appearance of symptoms, but early treatment, such as bone marrow transplantation, can prevent or reduce symptoms. Since the disease progresses if the symptoms are not diagnosed until after the onset of the disease, the new newborn mass screening test is used to diagnose the disease in advance, and periodical MRI scans are performed to check for the disease's onset. However, abnormalities may not appear even if the disease is diagnosed. Note that girls are not included in the mass screening tests.

Spinal muscular atrophy (SMA) is a degeneration of the nerve cells in the spinal cord that allow the body to move, causing muscle atrophy and progressive muscle weakness. The trunk, arms, and legs also lose strength as the muscles weaken. The disease is classified into Type I, Type II, Type III, and Type IV based on the age at which symptoms begin to appear and the following conditions. Type I symptoms begin by about six months of age. The baby cannot sit without support, has difficulty swallowing milk or food, and has difficulty breathing. Therefore, patients must wear a ventilator or have nutritional supplements injected into their stomachs through a tube to live. Nevertheless, with the development of gene therapy and new therapeutic agents, symptoms may be prevented or alleviated if diagnosed earlier and treatment initiated.

This test is already widely carried out overseas, and has saved many lives.

This test is not provided by the government or local municipality, but is carried out as part of a clinical study by Fujita Health University and Nagoya University. Receiving the test is voluntary, not mandatory. In addition, due to the testing system, it is not possible to test only for a specific ailment.

A circumstance in which the interests of participants in the research have the potential to conflict with the interests of the researchers or company is known as 'a conflict of interest.' A member of this study, Jun Natsume, is a teacher in the developmental disability medicine course at the Nagoya University Graduate School of Medicine, which is run on donations from Aichi Prefecture, so has a potential conflict of interest with Aichi Prefecture. However, this study does not use any donations provided by Aichi Prefecture, and Aichi Prefecture has had no involvement whatsoever in the evaluation of design or creation of the research plan, nor in the assessment of statistical analysis of its data.

Cost of the test

The cost for this test shall **be personally covered by the individual who takes the test**. Please check with the healthcare provider where the baby was born for details.

Test method and notification of the results

At the time of mass screening, a very minute amount of blood will be drawn from the bottom of the foot. The drawn blood will be sent from the healthcare provider to Aichi Health Promotion Public Interest Foundation for the test.

This test poses no danger.

Please receive an explanation from the attending physician of the healthcare provider regarding the results of the test. In case of no abnormality, the explanation method and time varies, so please check with your healthcare provider. If an abnormality is suspected, you will be immediately informed via the healthcare provider which drew the blood. When a detailed examination is needed, please follow the instructions of the attending physician at the provider that conducted the test, and immediately visit the detailed examination institution.

Points to keep in mind

Personal information obtained for the implementation of this test will only be used for the purpose of this test. The blood collected on filter paper is preserved in a way so that a specific individual cannot be identified, and can be used for a new newborn mass screening study. Due to the characteristics of this test, even if an abnormality is not detected in this test, the disease cannot be completely ruled out.

This test is performed as a clinical study by Fujita Health University and Nagoya University. In order to improve test accuracy and methods, the sample after completion of the test may be used in this study, and the results may be presented at academic conferences. Even in such cases, full consideration is given to personal information, and such information will be used anonymously. In the event consent is not given, no disadvantage will be incurred. And even after consent has been given, such consent can be withdrawn. This study has obtained approval from the ethical review committee of Fujita Health University/Nagoya University Hospital.

Contact: Metabolic disorders examination room, Aichi Health Promotion Public Interest Foundation
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Consent Form

Principal investigator: Dr. Tetsuya Ito, Department of Pediatrics, Fujita Health University

I have received a written explanation on the "Study on the expansion of diseases covered by newborn screening," and fully understand the following items (please check the box that applies after receiving and fully understanding the explanation from the following sentences):

- ☐ Purpose of this study, significance, implementation method, and predicted danger.
- ☐ Cost for this test shall be borne by the individual.
- ☐ Refusal to participate in this study shall not result in any disadvantage in the future medical care.
- ☐ Participation can be withdrawn at any time, even after providing consent.
- ☐ Full consideration is given to the protection personal information.
- ☐ Test result notification method.
- ☐ Policy regarding sample storage and use after completion of the test.

Will you participate in this study and provide consent to receive the new mass screening test?

☐ Yes. ☐ No.

Date _____

Name (parent/guardian) _____ (relationship _____)

Address _____

Name of the healthcare provider where the baby was born

_____

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Consent Withdrawal Form

Principal investigator: Dr. Tetsuya Ito, Department of Pediatrics, Fujita Health University

Name of the study: "Study on the expansion of diseases covered by newborn screening"

I withdraw consent for participation in this study.

Date _____

Name (parent/guardian) _____ (Date of birth _____)

Address _____

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