University of Massachusetts Medical School

UMASS

COMMONWEALTH OF MASSACHUSETTS
DEPARTMENT OF PUBLIC HEALTH

NEWBORN SCREENING in Massachusetts:

Information for You and Your Baby

New England Newborn Screening Program

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A Program of the Massachusetts Department of Public Health

Available in other languages:
http://nensp.umassmed.edu

Dear Parent,

Here is some information about a service that is required by law to be provided to your baby and to all other babies in Massachusetts. The service is called newborn screening.

Each year in Massachusetts, about 160 babies are born with some rare disorder that is found with required newborn screening. The only way to find most of the babies who need help is with a newborn screening laboratory test because most of these babies look just like all other babies. These babies can then be helped. After newborn screening, the babies with rare disorders can get the early treatment that they need. The first time laboratory testing was done to find a rare disorder among babies was in Massachusetts in 1962. At that time, screening looked to find just one disorder. Since then, newborn screening looks for many more disorders, and required newborn screening has become a standard of care, worldwide.

Newborn screening is a public health service. It is designed to prevent bad outcomes from rare disorders that some babies may have. When it is ***known*** *that bad outcomes can be prevented by newborn screening for a disorder, newborn screening for that disorder is required for all babies.*

When it is ***thought*** *that newborn screening for a new disorder will help to find more babies who need help, we need to prove whether newborn screening will prevent bad outcomes. Massachusetts has been a leader in studies to know if screening can or should be done for more disorders. Until it is known that newborn screening can prevent bad outcomes for that new disorder, testing is voluntary and called a "pilot study."*

You should expect that your baby will be screened for required newborn screening disorders and that your baby's healthcare provider will ask you if you want your baby to be screened for disorders in the current Massachusetts pilot study. *To help with your decision about the pilot study, we include a colored insert to this brochure that shows two lists of disorders: those that are required and those that are in the voluntary pilot study. The colored insert also includes a description of the current pilot study. After you respond with your decision, you will get a copy of the form that is sent to us, which is a record of your answer (please see example on the next page).*

We wish you and your baby the very best!

Sincerely,

The Staff of The New England Newborn Screening Program

EXAMPLE FORM
PARENT'S COPY

Pilot Study Decision: Consents | Refuses

LAB ID # 100001

Recorder's initials: _____

BABY'S NAME (Last) (First)

Dear Parent
This sheet is your record to show that a small blood specimen was taken from your baby for required newborn screening. This required service ensures that your baby will be screened for treatable disorders as mandated by the Massachusetts Department of Public Health.

In addition, this sheet shows the instructions that were sent to the New England Newborn Screening Program after you decided whether you wanted to take part in the current newborn screening pilot study.

- If the Consent box at the top right is marked with an **X**, then your baby WILL be tested for all disorders that are in the current pilot study (list is provided in colored insert).
- If the Refuse box is marked with an **X**, or if neither box has an X, then your baby will be NOT be tested for any disorders in the current pilot study.

New England Newborn Screening Program, University of Massachusetts Medical School
377 Plantation St., Worcester, MA 01605 774-455-4600

SUMMARY

Newborn Screening helps to prevent bad outcomes from certain treatable disorders.

- Babies with some disorders need treatment in early infancy to prevent severe disease.
- Newborn screening helps to find the babies who have these disorders.
- Most likely, your baby does NOT have one of these disorders.

Newborn Screening works by testing *all* babies who are born in Massachusetts.

- Testing all babies is important, because most babies appear healthy at birth, even the babies who have the disorders that need treatment.
- The testing for newborn screening is done on a few small drops of blood that are collected when your baby is one or two days old.
- If testing shows that your baby has signs of one of these treatable disorders, your baby's doctor will call you to arrange care for your baby.

REQUIRED NEWBORN SCREENING

- In Massachusetts, REQUIRED NEWBORN SCREENING is done for disorders that have treatments that are known to be more effective if the disorder is found in the newborn period.
- Under Massachusetts' law, it is a requirement that *all* babies born in Massachusetts be screened for laboratory markers of these treatable disorders unless parents object on the basis of religious beliefs.

VOLUNTARY NEWBORN SCREENING (Pilot Study)

- Massachusetts also offers some newborn screening services that are voluntary.
- The VOLUNTARY NEWBORN SCREENING allows Massachusetts to study new disorders for newborn screening.
- The statewide pilot study is research that is valuable for future babies and that may be of benefit to your baby.
- ***There is no extra cost and no extra blood required for your baby to participate.***
- Under Massachusetts' guidelines, after your baby is born, you will be asked whether you want to take advantage of the NEWBORN SCREENING pilot study.
- If, for some reason, you decide that you do not want to participate in the VOLUNTARY program, your baby will still have all the benefits of REQUIRED NEWBORN SCREENING.

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REQUIRED NEWBORN SCREENING

What is the purpose of the Newborn Screening Program?

The purpose of the Newborn Screening Program is to test all newborns in Massachusetts for early signs of a number of treatable disorders (as mandated by Massachusetts Department of Public Health Regulations 105 CMR 270.000).

What is the chance my baby has a disorder that can be detected by required newborn screening?

The chance that your baby will have one of these disorders is very small. In the rare cases when a disorder is found, early diagnosis and treatment can usually prevent the problems associated with these disorders.

Newborn screening tests provide an early opportunity to detect certain disorders — before symptoms appear. However, we know that even the best screening cannot always detect a disorder. If your baby does not seem well, talk to your baby's doctor as soon as possible.

How are the newborn screening tests done?

Between 24 and 48 hours after birth, or just before your baby is discharged from the hospital, a few drops of blood will be taken from your baby's heel.

Your baby's birth hospital then sends the blood samples to the New England Newborn Screening Program. Special tests for small blood samples are done and reported to your baby's healthcare provider.

Important! Babies who are born outside of hospitals should also be tested, preferably between 24 and 48 hours after birth. Parents should arrange with a doctor, hospital, or midwife to have the screening done.

Who decides which disorders are included in Newborn Screening?

The Commissioner of Public Health is responsible for deciding on the list of disorders. An Advisory Board, made up of doctors, nurses, scientists, ethicists, and parents, advises the Commissioner which disorders to include. For a disorder to be included in the list, the following must be true: 1) the disorder is treatable, 2) there is a good test, and 3) early medical intervention would benefit the infant.

May I refuse the newborn screening tests for my baby?

In Massachusetts, you may refuse newborn screening for religious reasons. If you wish to refuse the required newborn screening for your baby, all of your baby's legal guardians will have to sign a refusal form. This form relieves your doctor of liability for damages that result from a disorder that could have been detected by screening.

How can I get information about the results of my baby's newborn screening tests?

Your baby's newborn screening results will be reported to the hospital where your baby was born and to the pediatrician who is listed for your baby. These reports include results of all required testing and results of any voluntary (pilot) testing your baby had.

In addition, if your baby's test results indicate that further attention is needed (see below), we will notify the hospital where your baby was born or your baby's doctor.

My baby's doctor says that I need to bring my baby in because of newborn screening. Does that mean that my baby has a disorder?

Not always. There are several reasons why your baby's doctor may have asked you to bring your baby in. Some reasons are named below:

Unsatisfactory specimen: There is not enough blood on the sample that was sent to us or the sample does not work for other reasons and we were not able to complete all of the required newborn screening tests. Another specimen is needed.

"Too Early" specimen: If the blood specimen was collected before your baby was 24 hours old, a second sample should be taken as soon as possible. The best time for a specimen to be collected is between 24 and 48 hours after birth.

Out-of-Range Test Result: An out-of-range test result means that further evaluation is needed to know if your baby has a disorder. Sometimes this means that another specimen is needed, sometimes this means that the baby will have to be seen and tested by a specialist within a few days, and sometimes it means that the baby should be seen by a specialist as soon as possible. Your baby's doctor will let you know what is recommended.

Note: Premature or low birth weight newborns are more likely to have out-of-range test results on the first specimen even if a disorder is *not* present.

What disorders are included in REQUIRED NEWBORN SCREENING?

A detailed list of disorders included in screening is provided on the colored insert.

What is known about the disorders that are included in REQUIRED NEWBORN SCREENING?

We know that the disorders included in REQUIRED NEWBORN SCREENING are thought to be treatable.

> For some of these disorders, there is a good deal of information about the outcomes of babies who have the disorders. This may be because there are many babies with the disorder, or may be because the screening has been in place for many years, or both.
>
> For other disorders, there is enough information to know that babies with the disorder will do better if they are found and treated early, but we do not yet have full information to know what to predict for their future. This may be because there are very few babies with the disorder, or because the screening is new, or because there is a new treatment.

In order to ensure that we can provide the best information for care and for decision-making, the Newborn Screening Program collects information about how the patients with these disorders are doing.

> The kinds of information collected depend on the disorder, and includes information about whether the patients are alive and well, and whether they see a specialist regularly. Other information collected helps the Newborn Screening Program to provide knowledge about the disorder to babies' health care providers and to families.

NEWBORN SCREENING QUALITY ASSURANCE AND IMPROVEMENTS

Newborn screening programs need to know that they are working well and how to improve. This means that programs need to know whether the screening results match diagnostic results. This also means that programs need to know how well babies are doing after they are diagnosed with newborn screening disorders, and whether they continue to get the care they need. Information on diagnoses and outcomes is collected for program-wide improvements.

Your baby's leftover blood may be stored for up to 16 years. Sometimes, your baby's information or leftover blood will be used to make sure that newborn screening tests are working well. Sometimes the information or leftover blood will be used to make better tests for the Newborn Screening Program. Other times, the information or leftover blood will be used for health studies.

Release of your baby's information for health studies:

When the state offers voluntary screening services to all newborns in a pilot study, your spoken permission is needed before we provide those services to you and your baby.

For any other health studies, additional written permission will be needed from you before we release your baby's name to any researcher. If any information or leftover blood is going to be used for a study, the study has to be approved by two groups of people who make sure that your baby's rights are protected. These groups of people are called "Human Subjects Review Committees." One Human Subjects Review Committee is at the Department of Public Health, and the other is at the University of Massachusetts Medical School. The Federal Government sets the rules and regulates each Committee. As stated above, for any study that would use your baby's name, we would need to have your written permission before including your baby's information or leftover blood. For other studies that would not use your baby's name, the Human Subject's Review Committee would decide whether your baby's identity is protected and then decide the level of permission needed, if any. If you so desire, it is possible to prevent your baby's specimen from being used in any health study.*

*If you do not want your baby's specimen to be used for any health research studies, you must send your request in writing to the Director, with cc to the Deputy Director and Chief Medical Officer, of The New England Newborn Screening Program, University of Massachusetts Medical School, 377 Plantation St, Worcester, MA 01605. When residual specimens are excluded from research, the NENSP may still use such specimens for non-research purposes, including Laboratory Quality Assurance.

Contacting you: We know that for many reasons, parents change health care providers and may change the name of their baby. If your baby has been diagnosed with a newborn screening disorder, or is being followed to find out if your baby has a newborn screening disorder, you may receive a letter from the New England Newborn Screening Program to ensure that your baby's information is up-to-date.

VOLUNTARY NEWBORN SCREENING

Research studies of new tests (pilot studies)

The Massachusetts Department of Public Health may authorize and direct research studies of new tests in the Newborn Screening Program. Research studies of new tests, called pilot studies, are done when the Department of Public Health expects they could benefit both individuals and the public health. *No additional blood will be taken from your baby*, but these tests will screen for a number of disorders in addition to the required newborn screening testing already described.

Results from pilot study tests are reported with required screening results. As with required newborn screening, if there were to be an out-of-range result, your baby's doctor would work with the right specialists to manage any special care that your baby might need.

What pilot study is being conducted now?

Please see the colored insert.

Why is newborn screening for some disorders being offered as a voluntary pilot study rather than being required by mandate?

The Massachusetts Department of Health has determined that there is not yet enough evidence to require (mandate) newborn screening for the disorders included in the pilot study. They need more information on one or more of the following questions:

1. What is the extent of benefit from newborn screening for these disorders? (Does it save lives? Does it prevent serious life-compromising outcomes? Do the treatments work as expected?)
2. How often do these disorders occur in Massachusetts?
3. How good are the laboratory tests used to screen for these disorders?

Can any newborn participate in the pilot study?

Yes, any newborn who would be included in required newborn screening may participate.

May I refuse to participate in the pilot study?

Yes. You may refuse your baby's participation in the current pilot study, for any reason. If you refuse, your baby will NOT be tested for any of the disorders in the current pilot study. If you refuse, your baby will still have all the advantages of required newborn screening.

How do I enroll? Or, how do I refuse to participate?

After your baby is born, you will be asked whether you want your baby to be screened for the disorders in the pilot study.

Important! You will be asked to give your response before your baby's specimen is sent to the screening lab.*

Your answer will be indicated on the newborn screening collection form. When your answer is recorded on your baby's specimen collection form, you will be given a copy to keep for your records. A sample of the copy you will receive is shown in the beginning of this brochure. (Note: you may be reading a non-English translation of this brochure. However, the actual copy for your records would be in English.)

*Specimens are ideally obtained between 24 and 48 hours after birth, or prior to discharge if discharge is earlier than 24 hours. In order to ensure that required newborn screening of your baby for the mandated disorders is not delayed, the specimen must be collected and transported promptly.

What are the general benefits and risks associated with the pilot study?

Possible Benefits

- The most important individual benefit for your baby is the following:
  If your baby does have one of the disorders included in the study, your baby will have the earliest opportunity for detection of the disorder.
- Other benefits may include your own satisfaction that you are helping to answer important questions that may help other babies.

Possible Risks

- The most important individual risk for your baby is rare:
  If your baby does have one of the disorders included in the study and the study testing does not detect your baby's disorder, there could be a delayed diagnosis. This is always a risk with any screening. Not detecting a disorder should be an unusual event, whether the testing is tried and true or still being studied. If your baby does not seem well, or does not seem right, talk with your baby's health care provider.
- Other risks include the possibility that the screening will show information that your baby has a disorder or a condition that we were not looking for, but that showed up as a by-product of the screen. Some believe this to be a benefit and for others, it is a risk. Finding by-products can happen with most any testing. Such results are reported to your baby's health care provider.
- The most common risk is that an out-of-range screening result may require additional testing and may cause you to worry, even if it turns out that your baby does not have a newborn screening disorder.

  Note: **All of newborn screening services (required and voluntary) are performed in compliance with Massachusetts and Federal rules and regulations that protect personal information and minimize the risk of a breach of confidentiality. Participation in a pilot study does not include any additional risk.**

Where can I find out more about the current pilot study?

See the colored insert and the section entitled "More about the current pilot study."

I have some suggestions or I have some comments. How can I be sure that my comments will be considered?

You should address your written comments to any of the following committees or programs, and the Department's Newborn Screening Advisory Committee or a representative will review them:

Chairperson
Newborn Screening Advisory Committee
Massachusetts Department of Public Health
250 Washington St.
Boston, MA 02108-4619

Commissioner of Public Health
Massachusetts Department of Public Health
250 Washington St.
Boston, MA 02108-4619

Director
New England Newborn Screening Program
University of Massachusetts Medical School
Biotech 4, 2nd Floor
377 Plantation Street
Worcester, MA 01605-2300

University of Massachusetts Medical School

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New England Newborn Screening Program

January 2018

ADDITIONAL INFORMATION FOR PARENTS ABOUT NEWBORN SCREENING DISORDERS AND STUDIES

Effective January 2018

List of disorders included in REQUIRED NEWBORN SCREENING mandated by MA DPH:

Your baby will be screened for laboratory markers of the following 32 disorders:

1. Argininemia (ARG)
2. Argininosuccinic acidemia (ASA)
3. ß-Ketothiolase deficiency (BKT)
4. Biotinidase deficiency (BIOT)
5. Carbamoylphosphate synthetase deficiency (CPS)
6. Carnitine: acylcarnitine translocase deficiency (CACT)
7. Carnitine uptake defect (CUD)
8. Citrullinemia (CIT)
9. Congenital adrenal hyperplasia (CAH)
10. Congenital hypothyroidism (CH)
11. Congenital toxoplasmosis (TOXO)
12. Cystic fibrosis (CF)
13. Galactosemia (GALT)
14. Glutaric acidemia type I (GAI)
15. Homocystinuria (HCY)
16. 3-hydroxy-3-methyl glutaric aciduria (HMG)
17. Isovaleric acidemia (IVA)
18. Long-chain L-3-OH acyl-CoA dehydrogenase deficiency (LCHAD)
19. Maple syrup disease (MSUD)
20. Ornithine transcarbamylase deficiency (OTC)
21. Phenylketonuria (PKU)
22. Sickle cell anemia (Hb SS)
23. Hb S/C disease (Hb SC)
24. Hb S/ß-thalassemia (Hb S/ßTh)
25. Medium-chain acyl-CoA dehydrogenase deficiency (MCAD)
26. Methylmalonic acidemia: mutase deficiency (MUT)
27. Methylmalonic acidemia: cobalamin A, B (Cbl A,B)
28. Methylmalonic acidemia: cobalamin C,D (Cbl C,D)
29. Propionic acidemia (PROP)
30. Severe Combined Immunodeficiency (SCID)
31. Tyrosinemia type I (TYR I)
32. Very long-chain acyl-CoA dehydrogenase deficiency (VLCAD)

Screening for the required 32 disorders listed above may reveal information about the following disorders and conditions (such information is a by-product of mandatory screening):

a. Atypical cystic fibrosis (includes CBAVD)
b. 2-Methyl 3-hydroxy butyric aciduria (2M3HBA)
c. 2-Methylbutyryl-CoA dehydrogenase deficiency (2MBG)
d. 3-Methylcrotonyl-CoA carboxylase Deficiency (3MCC)
e. 3-Methylglutaconic aciduria (3MGA)
f. Benign hyperphenylalaninemia (H-PHE)
g. Carnitine palmitoyltransferase IA deficiency (liver) (CPT IA)
h. Carnitine palmitoyltransferase II deficiency (CPT II)
i. Citrullinemia type II (CIT II)
j. Defects of biopterin cofactor biosynthesis (BIOPT BS)
k. Defects of biopterin cofactor regeneration (BIOPT Reg)
l. Galactokinase deficiency (GALK)
m. Galactose epimerase deficiency (GALE)
n. Glutaric acidemia type II (GA2)
o. Hypermethioninemia (MET)
p. Isobutyryl-CoA dehydrogenase deficiency (IBG)
q. Medium-chain ketoacyl-CoA thiolase deficiency (MCKAT)
r. Multiple carboxylase deficiency (MCD)
s. Non-SCID primary immunodeficiencies or other conditions associated with low T cells
t. Short-chain acyl-CoA dehydrogenase deficiency (SCAD)
u. Trifunctional protein deficiency (TFP)
v. Tyrosinemia type II (TYR II)
w. Tyrosinemia type III (TYR III)
x. Variant Hb-pathies (Var Hb)
y. Carrier status of any of the conditions listed in 1-32 or a-x.

Descriptions of Disorders in REQUIRED NEWBORN SCREEENING

Disorders included in required newborn screening can be grouped according to the cause or treatment of the disorder.

- **Amino Acidopathies:** Babies and patients with these disorders cannot break down one of the amino acids found in regular food. As their bodies cannot use regular food, they are given special food. A metabolic specialist or a biochemical geneticist usually treats these babies.
- **Congenital Infectious Diseases:** Babies with these disorders are infected with a kind of bacteria, virus, or parasite. The infection of the baby can occur during pregnancy or at birth. An expert in infectious disease usually treats these babies.
- **Cystic Fibrosis (CF):** Babies and patients with this genetic disorder cannot make an effective component needed for cells in the lungs and gut. Without the effective component, the lungs develop a layer of thick sticky mucus, making a home for lung infections. Likewise, mucus in the gut causes problems with absorbing food. A pulmonologist or a CF specialist at a CF Center typically treats these babies.
- **Endocrinopathies:** Babies and patients with these disorders cannot make one of the body's hormones. If a baby's body cannot make a hormone, the baby needs help and is usually given medicine containing the necessary hormone. These babies are usually treated by an endocrinologist or by a pediatrician who is working with an endocrinologist.
- **Enzyme Deficiencies for Vitamins and Sugars:** Babies and patients with these disorders cannot process some sugars, vitamins, or other nutrients. A metabolic specialist or a biochemical geneticist typically treats these babies.
- **Fatty Acid Oxidation Disorders:** Babies and patients with these disorders cannot use the fats that they have stored in their body for emergency energy. When a person with such a disorder does not eat for a while, there is a risk that important functions of their body will stop working. A metabolic specialist or a biochemical geneticist usually treats these babies.
- **Hemoglobinopathies:** Babies and patients with these disorders have a change in their red blood cells that causes problems such as sickle cell disease. It means the baby is more likely to have anemia, episodes of pain, strokes, and life-threatening infections. Treatment with penicillin may prevent serious infections in early childhood. These patients are usually treated by a hematologist.
- **Organic Acid Disorders:** Babies and patients with these disorders cannot process some amino acids found in regular food called branched chain amino acids or lysine. The patient needs help and is usually given special food and other treatment. These patients are usually treated by a metabolic specialist or a biochemical geneticist.
- **SCID, or Severe Combined Immunodeficiency:** A disorder that severely affects the immune system. Unless treated, babies with this disorder will die at a few months of age because they cannot fight off the usual infections that all babies get. With treatment, most babies live. Treatment for a SCID baby includes a bone-marrow transplant. This allows the baby to live because it can make T cells that untreated SCID babies cannot make. These patients are usually treated by pediatric immunologists and transplant specialists.
- **Urea Cycle Disorders:** Babies and patients with these disorders are unable to remove nitrogen from their bloodstreams. These patients have high levels of toxic ammonia in their blood and need immediate help. These patients are usually treated by a metabolic specialist or a biochemical geneticist.

More about the CURRENT PILOT STUDY

List of disorders included in VOLUNTARY NEWBORN SCREENING offered by MA DPH:

You will be asked whether you want your baby to be included in the current MA pilot study. If you say yes, your baby will be screened for laboratory markers of the following 8 disorders:

1. **Dienoyl-CoA reductase deficiency (DE RED):** Patients with this condition cannot change certain fats in the food we eat into energy and depend completely on glucose. Babies and children with this disorder may become very ill when the glucose is not available (as in fasting) or when higher amounts of energy are required (as during infections). It is believed that early treatment may be able to prevent death and disability in some cases. These patients are usually treated by a metabolic specialist or a biochemical geneticist.
2. **Hyperornithinemia, Hyperammoninemia, Homocitrullinemia Syndrome (HHH):** Patients with HHH are unable to remove nitrogen from their bloodstreams. As a result, ammonia in the blood may rise to toxic levels. Patients may become very sick without immediate treatment. These patients are usually treated by a metabolic specialist or a biochemical geneticist.
3. **Malonic acidemia (MAL):** Patients with MAL are not able to produce fatty acids as needed or utilize the fats present in food properly. This may cause a low blood sugar, enlarged heart, poor muscle tone, vomiting, diarrhea, dehydration, or seizures. These patients are usually treated by a metabolic specialist or a biochemical geneticist.
4. **Medium/short-chain L-3-OH acyl-CoA dehydrogenase deficiency (M/SCHAD):** Patients with this condition cannot change certain fats in the food we eat into energy and depend completely on glucose. Babies and children with this disorder may become very ill when the glucose is not available (as in fasting) or when higher amounts of energy are required (as during infections). It is believed that early treatment may be able to prevent death and disability in some cases. These patients are usually treated by a metabolic specialist or a biochemical geneticist.
5. **Mucopolysaccharidosis Type I (MPS I):** Patients with MPS I, cannot recycle the waste materials from the breakdown of large complex sugars. When the waste materials build up in the body, they cause health problems in many parts of the body including a change in appearance, developmental delay and sometimes death. There are severe, moderate and milder forms of MPS1; most identified by newborn screening will be severe. These patients are usually treated by a diverse team of specialists including metabolics and genetics.
6. **Pompe Disease, infantile onset (Pompe):** Patients with Pompe disease cannot break down stored sugar. As a result, the stored sugar builds up in the body, especially the muscles, and causes serious health problems such as heart disease and muscle weakness that restricts mobility. Infantile onset is severe and adult onset may be mild. These patients are usually treated by a team including a pediatric cardiologist, and a geneticist or a neurologist.
7. **Spinal Muscular Atrophy (SMA):** Patients with SMA suffer a progressive loss of nerve cells that are needed to develop and maintain healthy muscles. There are generally four types of SMA, the most severe form appears in young infants, who have little muscle control. The milder forms appear in teens and sometimes in adults, whose muscles will become weak. Patients are usually treated by a pediatric neurologist and geneticist.
8. **X-linked Adrenoleukodystrophy, childhood onset (X-ALD):** Patients with X-ALD have a buildup of fatty acids and over time, damage is done to the adrenal glands, the brain and the spinal cord. The worst form appears in boys between the ages of 4 and 10, beginning with behavioral issues. Blindness, deafness, seizures, loss of muscle control and progressive dementia follow. Patients are usually treated by a team of pediatric geneticists, neurologists, and endocrinologists.

Screening for laboratory markers of the 8 disorders listed above may reveal information about the following disorders and conditions:

a. Pseudodeficiency for the IDUA enzyme associated with MPS I
b. Late-onset Pompe Disease
c. Pseudodeficiency for the GAA enzyme associated with Pompe
d. Zellweger syndrome and other peroxisomal disorders (by-product of screening for X-ALD)
e. Klinefelter syndrome and other conditions associated with X aneuploidy (by-product of screening for X-ALD)
f. Carrier status of any of the 8 disorders

Descriptions of CURRENT PILOT STUDIES

These pilot studies are being done because the Massachusetts Newborn Screening Advisory Committee determined that there is some potential for benefit. All 8 pilot studies seek to answer the same general questions: Is newborn screening for a particular disorder clinically beneficial and do the benefits of screening outweigh the harms of screening? In addition each group of studies has a specific purpose:

- **Ongoing Study of Screening for 4 Inborn Errors of Metabolism:** Screening for the first four disorders on the Voluntary list has been in place since at least 2009. Patients with these disorders are usually treated by a metabolic specialist or a biochemical geneticist. We know that newborn screening can find infants with these disorders and that it can be done with limited implications for infants who do not have these disorders. However, the first four disorders on the list are so rare that we still have to ask if there is proven benefit to screening. The purpose of the study is to continue data collection to know whether there is benefit.

- **Study of Screening for Two Lysosomal Storage Diseases, MPS1 and Pompe:** There are preliminary data from clinical trials in older children indicating that early detection of these two disorders may be beneficial, allowing early treatment with enzyme therapy and stem cell transplants. However, we also know that newborn screening for these disorders is not reliably able to provide information about whether the baby was born with a severe or mild form of the disease or whether the baby will show symptoms as an infant or as an adult. Knowing when to start treatment may be uncertain for some and such uncertainty can cause harm. Patients with these disorders are usually cared for by a team of pediatric geneticists and neurologists. The purpose of the study is to find out how well the screening works, whether we can improve the focus of the screen to those best served by early treatment, and whether the benefit of screening and treatment outweighs the harms.

- **Study of Screening for SMA:** There are data from clinical trials in infants and older children indicating the potential to change the course of the disease or to stop its progression if the treatment is begun early enough. However, despite the recent FDA approval of a drug for SMA, the data from such clinical trials are new and the long-term outcomes from the treatment, which may include harms, have not yet been documented. Patients with these disorders are usually cared for by a team of pediatric geneticists and neurologists. The purpose of the study is to find out how well the screening works, whether we can make it better, whether the treatment is as promising as hoped and whether the benefit of screening and treatment outweighs any harms.

- **Study of Screening for X-ALD:** Early detection of X-ALD allows monitoring of infants who have X-ALD so that they can begin treatment as soon as the monitoring indicates the need, thus leading to better treatment. Patients with X-ALD disorders are usually cared for by a team of pediatric geneticists, neurologists and endocrinologists. Although there is a clear standard for what to look for to know that treatment should begin, the time from diagnosis to treatment will be at least one year and may be several years. The purpose of the study is to determine whether we can find good indicators of those babies who need the earliest help, and whether the benefit of screening and treatment outweighs the harms.