Newborn Screening

Missouri State Public Health Laboratory

Patrick Hopkins; Newborn Screening Laboratory Manager

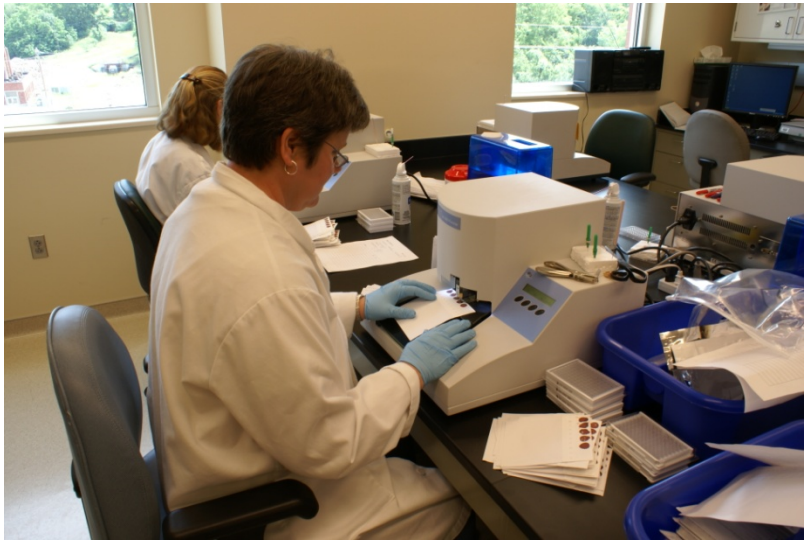

STOP

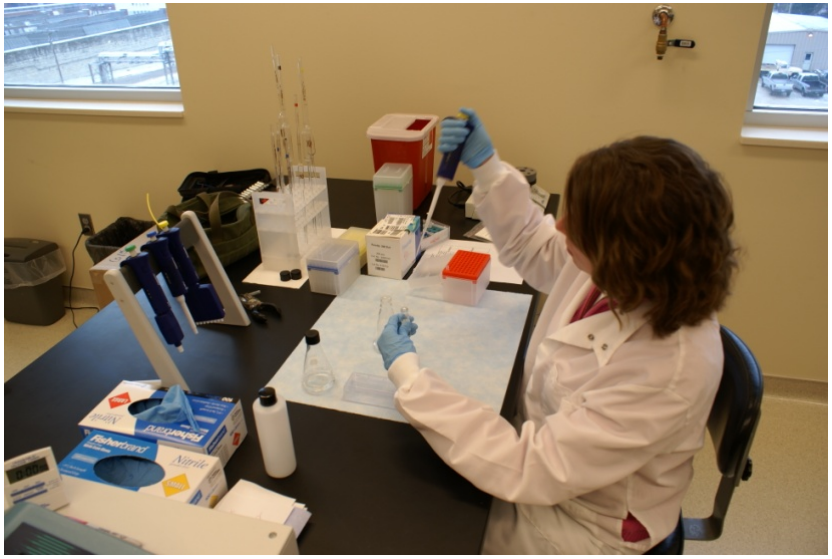
Newborn Screening Laboratory

- 81,030 babies screened in 2008
- Average of 400 specimens tested per working day
- Staff of 15 scientists and 4 office support
- 67 disorders screened all newborns
- 150 confirmed disorders detected in 2008
- Saved a baby every other working day!

Accuracy and Efficiency!

We Understand the Importance of Our Job

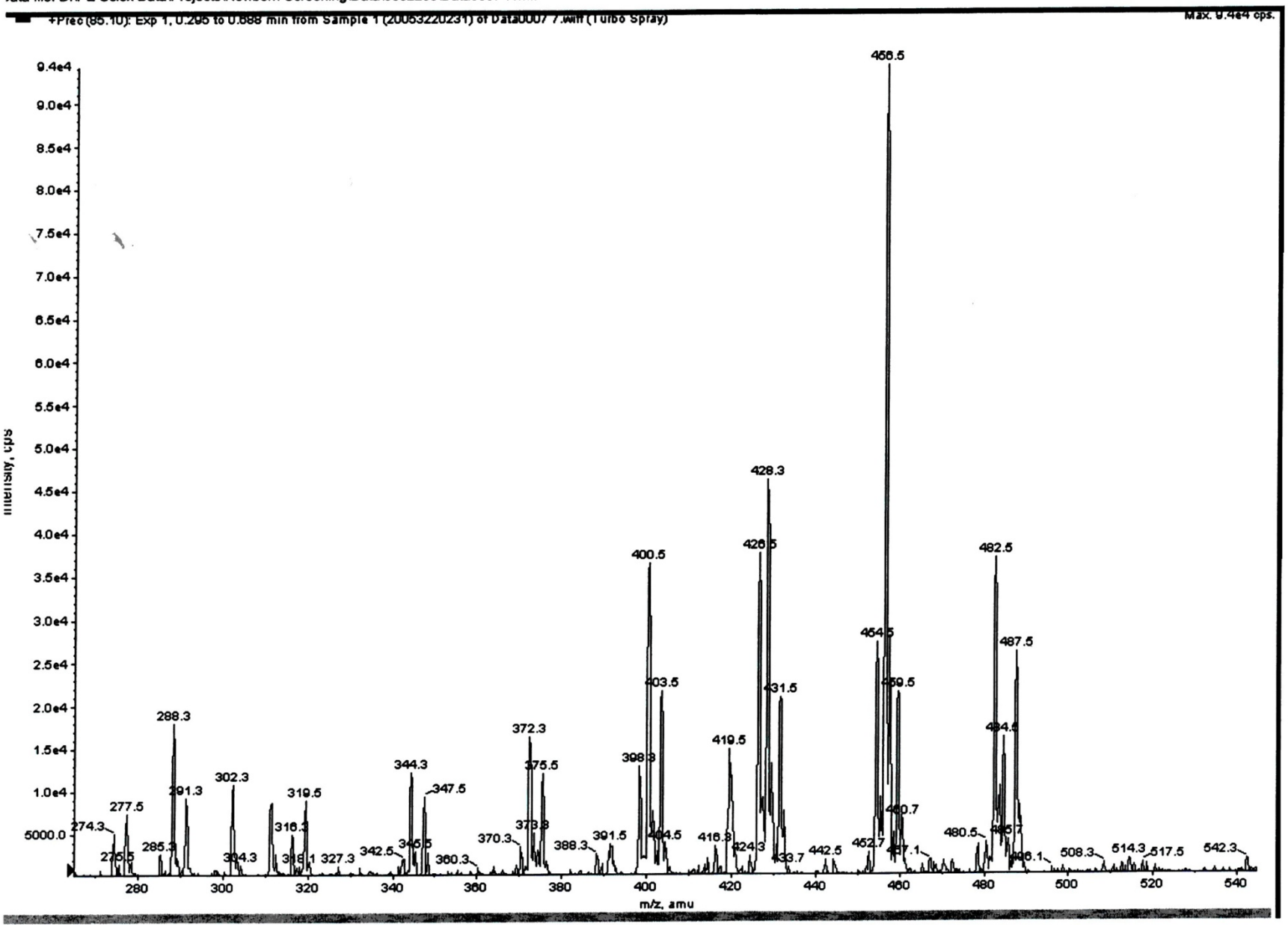




Technology Has Greatly Improved!

Sample ID: 20053220231 Plate: 0532205

Data file: D:\PE Sciex Data\Projects\Newborn Screening\Data\0532205\Data0007 7.wiff



Printed: 11/9/04 10:06:34 AM

Sample ID: OHIO009 Plate: Ohio 1, 9-16-04

PKU

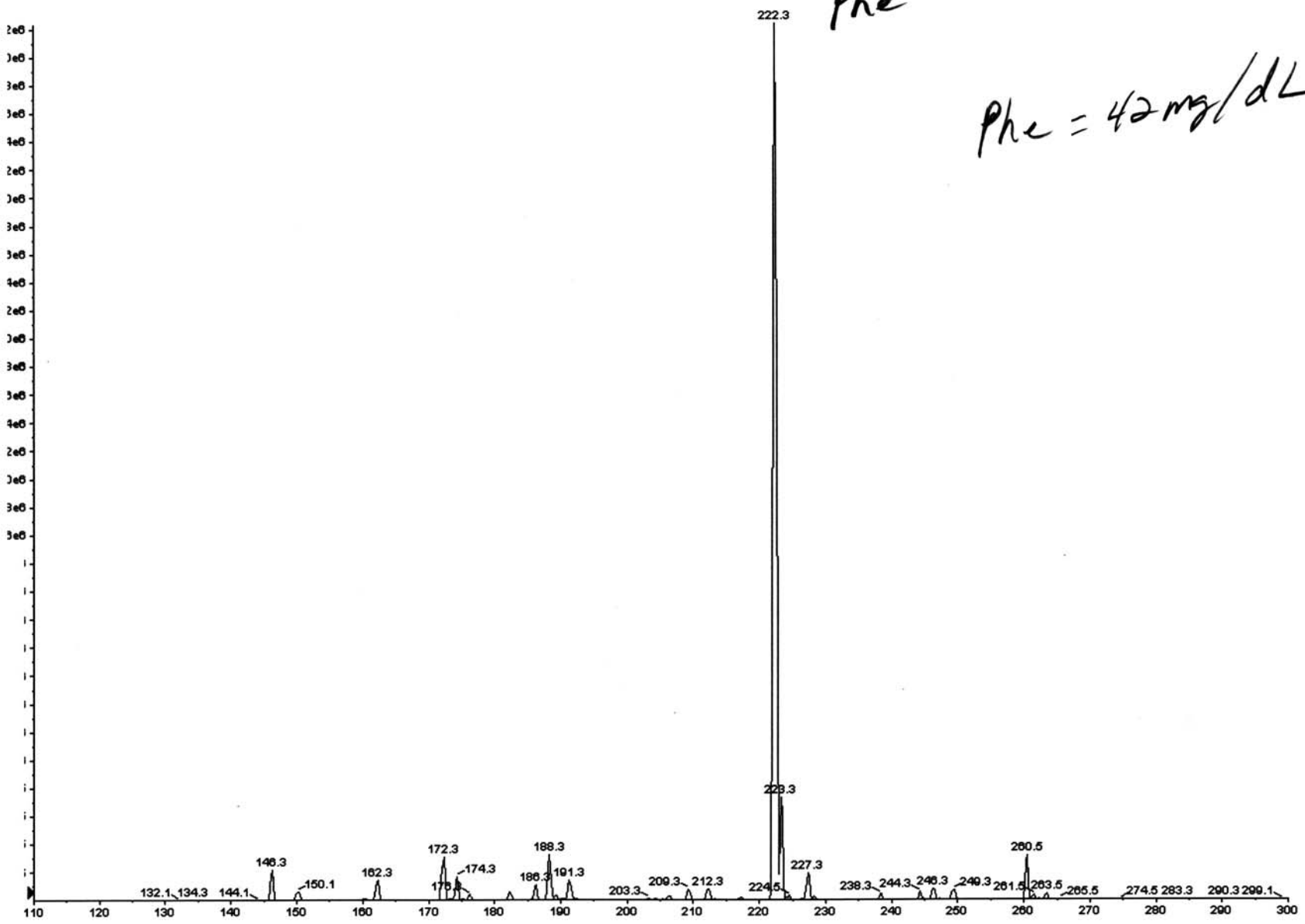
Data file: D:\PE Sciex Data\Projects\Newborn Screening\Data\Ohio 1, 9-16-04\Data0009 9.wiff

+NL (102.00): Exp 2, 0.303 to 0.557 min from Sample 1 (OHIO009) of Data0009 9.wiff (Turbo Spray)

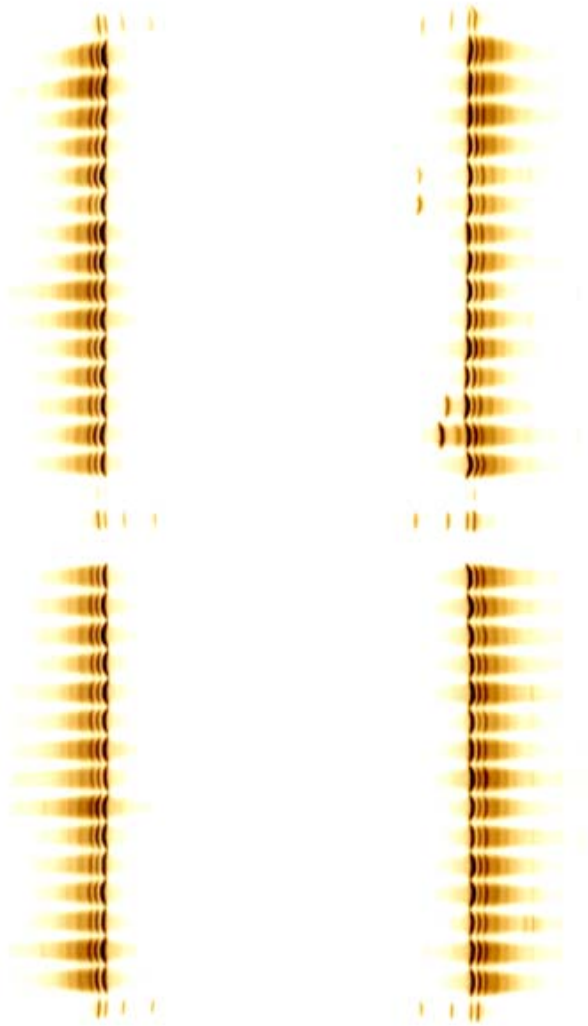
Max. 6.2e6 cps.

Phe

Phe = 42 mg/dL



19 Hemoglobin Disorders Can Be Detected



The Missouri NBS List

Biotinidase Deficiency (BIO)
Classical galactosemia (GALT)
Congenital adrenal hyperplasia (CAH)
Congenital primary hypothyroidism (CH)
Cystic fibrosis (CF)

Amino Acid Disorders
- Argininemia (ARG, arginase deficiency)
- Argininosuccinate acidemia (ASA, argininosuccinase)
- Citrullinemia type I (CIT-I, argininosuccinate synthetase)
- Citrullinemia type II (CIT-II, citrin deficiency)
- Defects of biopterin cofactor biosynthesis (BIOPT-BS)
- Defects of biopterin cofactor regeneration (BIOPT-RG)
- Homocystinuria (HCY, cystathionine beta synthase)
- Hyperphenylalaninemia (H-PHE)
- Hypermethioninemia (MET)
- Maple syrup urine disease (MSUD, branched-chain ketoacid dehydrogenase)
- Phenylketonuria (PKU, phenylalanine hydroxylase)
- Tyrosinemia type I (TYR-1, fumarylacetoacetate hydrolase) *
- Tyrosinemia type II (TYR-II, tyrosine aminotransferase)
- Tyrosinemia type III (TYR-III, hydroxyphenylpyruvate dioxygenase)

Fatty Acid Disorders
- Carnitine acylcarnitine translocase deficiency (CACT)
- Carnitine uptake defect (CUD, carnitine transport defect) *
- Carnitine palmitoyl transferase deficiency I (CPT-1a)
- Carnitine palmitoyl transferase deficiency II (CPT-II)
- Dienoyl-CoA reductase deficiency (DE-RED)
- Glutaric acidemia type II (GA-II, multiple acyl-CoA dehydrogenase deficiency)
- Long-chain hydroxyacyl-CoA dehydrogenase deficiency (LCHAD)
- Medium-chain acyl-CoA dehydrogenase deficiency (MCAD)
- Medium-chain ketoacyl-CoA thiolase deficiency (MCKAT)
- Medium/Short chain L-3-hydroxy acyl-CoA dehydrogenase deficiency (M/SCHAD)
- Short-chain acyl-CoA dehydrogenase deficiency (SCAD)
- Trifunctional protein deficiency (TFP)
- Very long-chain acyl-CoA dehydrogenase deficiency (VLCAD)

Organic Acid Disorders
- 2-Methyl-3-hydroxybutyric aciduria (2M3HBA)
- 2-Methylbutyryl-CoA dehydrogenase deficiency (2MBG, SBCAD)
- 3-Hydroxy 3-methylglutaric aciduria (HMG, 3-Hydrox 3-methylglutaryl-CoA lyase)
- 3-Methylcrotonyl-CoA carboxylase deficiency (3-MCC)
- 3-Methylglutaconic aciduria (3MGA, Type I hydratase deficiency)
- Beta ketothiolase (BKT, mitochondrial acetoacetyl-CoA thiolase, short-chain ketoacylthiolase)
- Glutaric acidemia type I (GA-1, glutaryl-CoA dehydrogenase)
- Isobutyryl-CoA dehydrogenase deficiency (IBG)
- Isovaleric acidemia (IVA, Isovaleryl-CoA dehydrogenase)
- Malonic acidemia (MAL, malonyl-CoA decarboxylase)
- Methylmalonic acidemia (CBL A,B; vitamin B12 disorders)
- Methylmalonic acidemia (CBL C,D)
- Methylmalonic acidemia (MUT, methylmalonyl-CoA mutase)
- Multiple carboxylase deficiency (MCD, holocarboxylase synthetase)
- Propionic acidemia (PROP, propionyl-CoA carboxylase)

Hemoglobinopathies
- Sickle cell disease (Hb S/S)
- Sickle hemoglobin-C disease (Hb S/C)
- Sickle beta zero thalassemia disease
- Sickle beta plus thalassemia disease
- Sickle hemoglobin-D disease
- Sickle hemoglobin-E disease
- Sickle hemoglobin-O-Arab disease
- Sickle hemoglobin Lepore Boston disease
- Sickle HPFH disorder
- Sickle "Unidentified"
- Hemoglobin-C beta zero thalassemia disease
- Hemoglobin-C beta plus thalassemia disease
- Hemoglobin-E beta zero thalassemia disease
- Hemoglobin-E beta plus thalassemia disease
- Hemoglobin-H disease
- Homozygous beta zero thalassemia disease
- Homozygous-C disease
- Homozygous-E disorder
- Double heterozygous beta thalassemia disease

Others
- Hearing

* There is a lower probability of detection of this disorder during the immediate newborn period.

The Missouri Newborn Screening Laboratory's goal is to identify infants at risk and in need of diagnostic testing for the above disorders. A normal screening result does **NOT** rule out the possibility of an underlying metabolic/genetic disease.

The NBS Lab is Measuring Analytes

TSH
- Hypothyroidism

C4
-SCAD
-IBG

C3
-PROP
-MUT
-Cbl A,B,C,D

FS
– S / S Disease
– S / Beta-Thal
– S / HPFH
– S / ? Variant

C5
-IVA
-2MBG
-Pivalic Acid Interference

C5OH
– 3MCC
– HMG
– BKT
– MCD
– 3MGA
– 2M3HBA
– BIO

One Disorder Can Have Several Analyte Markers

-The primary markers elevate first and highest in true disorders

-The secondary markers elevate next and add to the risk

- MSUD elevates Leucine and Valine
- ASA elevates ASA and Citrulline
- MCAD elevates C8, C6, C10:1, C8/C10, C8/C2
- LCHAD elevated C16-OH, C18-OH, C18:1-OH
- VLCAD elevates C14:1, C14:2, C14, C14:1/C12:1
- GA-II elevates C4, C5, C5DC, C6, C8, C10, C12, & C14

The NBS Lab Makes Risk Assessments

- Low Risk / Borderline Risk
  - A primary marker analyte is slightly out of range
  - Usually just requires a repeat screen
  - PCP can pursue diagnostics if they wish
- Moderate Risk
  - One or more marker analytes are moderately out of range
  - Physician of record is phoned and faxed by the NBS laboratory
  - Referred to genetic referral center for evaluation and further testing to rule out a disorder
- High Risk
  - One or more marker analytes are highly out of range
  - Physician of record is phoned and faxed by the NBS laboratory
  - Referred urgently to the referral centers for advice and confirmatory testing
  - Possible prophylactic treatment until diagnostic testing is finished

NBS Laboratory Report

Newborn Screening Laboratory
Phone: 573-751-2662 Fax: 573-522-8155

Dr. John Mathewson, Laboratory Director

Missouri Department of Health & Senior Services
State Public Health Laboratory
P.O. Box 570
Jefferson City, MO 65102

(Duplicate)
LABORATORY REPORT

Lab ID Number: **20083270002**
Form ID Number: **B11111111**

Submitter: CAPITAL REGION MEDICAL CENTER
Address: 1125 SOUTH MADISON
JEFFERSON CITY , MO 65101

Physician: DOUGLAS BOUDREAU MD
Address: 1125 MADISON ST
JEFFERSON CITY , MO 65102-1128

Baby's Name: **BOB, BILLY**
Date of Birth: **11/19/2008@12:00**
Sex: M Race: W
Med Rcd# 123456
Birth Weight: 2500 gms
Gestation Age: 39 wks
Feeding Type: Non-Lactose Formula

Specimen Type: **Repeat**
Age @ Collection: **1 day(s) 3 hour(s)**
Date Collected: 11/20/2008@16:00
Date Received: 11/20/2008
Date Reported: 12/08/2008
Copy Printed: 12/08/2008

Mother: **BOB, SUE**
DIRT ROAD
HAPPY TRAILS , MO 65101
Phone: (573) 123-4567
Med Rec: 7891011

DISORDER	SCREENING RESULT
Congenital Hypothyroidism (CH)	Normal
Congenital Adrenal Hyperplasia (CAH)	Normal
Hemoglobinopathy	Normal
Biotinidase Deficiency	Normal
Galactosemia	Normal
Fatty Acid Disorders	Normal
Organic Acid Disorders	Normal
Amino Acid Disorders	Normal
Cystic Fibrosis	Normal

*The above screening results are meant to identify infants at risk and in need of diagnostic testing. A normal screening result does **NOT** rule out the possibility of an underlying metabolic/genetic disease.*

NBS Laboratory Report

Newborn Screening Laboratory
Phone: 573-751-2662 Fax: 573-522-8155

Dr. John Mathewson, Laboratory Director

Missouri Department of Health & Senior Services
State Public Health Laboratory
P.O. Box 570
Jefferson City, MO 65102

LABORATORY REPORT (Duplicate)

Lab ID Number: **20083270001**
Form ID Number: **B08008817**

Submitter: CAPITAL REGION MEDICAL CENTER
Address: 1125 SOUTH MADISON
JEFFERSON CITY , MO 65101

Physician: CAPITAL REGION MEDICAL CENTER
Address: 1125 SOUTH MADISON
JEFFERSON CITY , MO 65101

Baby's Name: **DOE, NP**
Date of Birth: **11/18/2008@12:00**
Sex: M Race: W
Med Rcd# 123456
Birth Weight: 3250 gms
Gestation Age: 42 wks
Feeding Type: Breast

Specimen Type: **Initial**
Age @ Collection: **1 day(s) 2 hour(s)**
Date Collected: 11/19/2008@14:00
Date Received: 11/20/2008
Date Reported: 12/08/2008
Copy Printed: 12/08/2008

Mother: **DOE, JANE**
123 HAPPY AVE
SUNSHINE , MO 65101
Phone: (573) 123-4567
Med Rec: 7891011

*NP = Not Provided

DISORDER	SCREENING RESULT	EXPECTED RANGE
Congenital Hypothyroidism (CH)	Normal	
Congenital Adrenal Hyperplasia (CAH)	Normal	
Hemoglobinopathy	Normal	
Biotinidase Deficiency	Normal	
Galactosemia	Normal	
Fatty Acid Disorders	**ABNORMAL**	
C8	**19.63 µmol/L**	< 0.40 µmol/L
C6	**1.74 µmol/L**	< 0.24 µmol/L
C10:1	**0.71 µmol/L**	< 0.30 µmol/L
C8/C10	**16.64 Ratio**	< 3.0
C8/C2	**0.65 Ratio**	< 0.03
Organic Acid Disorders	Normal	
Amino Acid Disorders	Normal	
Cystic Fibrosis	Normal	

Comments

ABNORMAL FATTY ACID SCREEN: Test shows a highly elevated C8 level with an elevated C6, C10:1 or C8/C10 ratio indicating a HIGH RISK for MCAD (Medium Chain Acyl-CoA Dehydrogenase) deficiency. Immediate contact with a referral center for consultation, diagnosis, and treatment is needed.

*The above screening results are meant to identify infants at risk and in need of diagnostic testing. A normal screening result does **NOT** rule out the possibility of an underlying metabolic/genetic disease.*

NBS Referral Centers

- Children's Mercy Hospital in Kansas City
- University Hospitals and Clinics in Columbia
- Cardinal Glennon Children's Hospital in St. Louis
- St. Louis Children's Hospital

Recent Changes in the NBS Process

- Collect the newborn screen between 24 and 48 hours of life… (*see regulation 19 CSR 25-36.010)*

  (A) A specimen shall be taken from all infants before being discharged from the hospital or birthing facility regardless of age. A specimen collected between 24 and 48 hours of life is considered optimum for newborn screening. A second, or repeat, specimen shall be required within 14 days of life if the initial specimen was collected before 24 hours of life.

- Sick or premature infants require two screens

  (B) Initial specimens from ill or premature infants shall be collected before a blood transfusion or between 24 to 48 hours of life. All ill or premature infants shall have a repeat screen collected between 7 to 14 days of life.

Recent Changes in the NBS Process

Early Collections will get “NO RESULT” for:

- Congenital Hypothyroidism
- Congenital Adrenal Hyperplasia
- Organic Acid Disorders
- Amino Acid Disorders
- Cystic Fibrosis

If a “High Risk” result is found then the No Result will be overridden.

Biotinidase, Hemoglobin, Galactosemia, and Fatty Acid Disorder results will be reported in early collects.

Newborn Screens Collected Early

Newborn Screening Laboratory
Phone: 573-751-2662 Fax: 573-522-8155

Dr. John Mathewson, Laboratory Director

Missouri Department of Health & Senior Services
State Public Health Laboratory
P.O. Box 570
Jefferson City, MO 65102

LABORATORY REPORT (Duplicate)

Lab ID Number: **20090950001**
Form ID Number: **B1234567**

Submitter: CAPITAL REGION MEDICAL CENTER
Address: 1125 SOUTH MADISON
JEFFERSON CITY , MO 65101

Physician: BRIAN CONLEY MD
Address: 3348 AMERICAN AVE
JEFFERSON CITY , MO 65109-1079

Baby's Name: **BOY, BABY**
Date of Birth: **04/01/2009@12:00**
Sex: M Race: W
Med Rcd# 123456789
Birth Weight: 3250 gms
Gestation Age: 43 wks
Feeding Type: Breast

Specimen Type: **Initial**
Age @ Collection:
Date Collected: NP@NP
Date Received: 04/06/2009
Date Reported: 04/06/2009
Copy Printed: 04/06/2009

Mother: **BOY, MOMMA'S LITTLE**
PACIFIER LANE
DIAPERVILLE , MO 65101
Phone: (573) 999-9999
Med Rec: 987654321

*NP = Not Provided

DISORDER	SCREENING RESULT	EXPECTED RANGE
Congenital Hypothyroidism (CH)	**NO RESULT**	
Congenital Adrenal Hyperplasia (CAH)	**NO RESULT**	
Hemoglobinopathy	Normal	
Biotinidase Deficiency	Normal	
Galactosemia	Normal	
Fatty Acid Disorders	Normal	
Organic Acid Disorders	**NO RESULT**	
Amino Acid Disorders	**NO RESULT**	
Cystic Fibrosis	**NO RESULT**	

Comments

No Results: Results for primary congenital hypothyroidism, congenital adrenal hyperplasia, organic acid disorders, amino acid disorders, and cystic fibrosis are not reliable in specimens collected before 24 hours of age. This sample was either collected before 24 hours of age or not enough information was provided on the newborn screening collection form to determine the age at collection. A Repeat Specimen is required after 24 hours of age.

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More Changes in the NBS Process

- Biotinidase Deficiency screening went live in December of 2008.
  - Found 8 Partial Deficiencies already, with 4 pending.
  - The Wolf home-brew method is working nicely.

- The T4 analyte measurement has been dropped from the Hypothyroidism screen.
  - We have been relying only on the TSH for referring CH cases to follow-up for quite some time.
  - T4 screening has not produced any additional CH cases that TSH missed.

Future Possibilities in NBS

- Lysosomal Storage Disorders (LSD)
  - Krabbe, Pompe, Gaucher, Fabry, Niemann-Pick, MPS, MLD and others.
  - Over 40 LSDs
  - Must be treated in the first few weeks of life before symptoms present.
- Severe Combined Immunodeficiency (SCID)
  - SCID is often called “bubble boy disease”. David Vetter lived for 12 years in a plastic, germ-free bubble.
  - Wisconsin has been screening for SCIDs for a year.
  - SCID can be cured if diagnosed early enough.

Important Things to Remember

- Don’t wait too long to collect the newborn screen.
- Get it to your courier pickup site as soon as it is completely dried.
- Remember to fill in the collection date and time on the form.
- This is a Screening Test.
- We have an email notification list for important announcements from the NBS Lab.

Missouri NBS Laboratory Team

We See The Babies Behind the Specimens

Because We Are Parents Too!

How to Contact Us

- Telephone: 573-751-2662
- Agency Web Site: www.dhss.mo.gov (click State Laboratory, then Newborn Screening)
- Laboratory Web Site: www.dhss.mo.gov/Lab/index.html
- Mailing Address: Missouri State Public Health Laboratory, PO Box 570, Attn: Newborn Screening, Jefferson City, MO 65102