

# *Michigan Newborn Screening Program*



Revised  
April 2008

# *Newborn Screening Goals*



- Quick identification of newborns with rare, serious, but treatable disorders
- Early diagnosis and treatment of affected infants resulting in normal growth and development
- Reduction of significant human and financial costs for families and society

# *Criteria for Disorder*



- Michigan follows U.S. Department of Health and Human Services, Health Resources and Services Administration (HRSA) and the American College of Medical Genetics (ACMG) guidelines for additions to the screening panel.

# *Newborn Screening Law*



## **MCL 333.5431**

- No informed consent required
- Department may require that the tests be performed by the department
- Violation is a misdemeanor
- Fee for testing
- Annual increase in fee based on the CPI
- Allows blood specimens to be used for medical research during the retention period
- Parents can request second specimen to keep

# *Newborn Screening Law*

Senate Bill No. 794 – Effective 02/23/06

10 member Quality Assurance Advisory Committee  
created in the Department

- Meets annually to review the list of newborn screening tests
- Conducts a financial review of any recommended changes
- Submits a written report to the Department
- Recommendations submitted to the Legislature
- Recommendations considered approved if not rejected by the Legislature

# Michigan Newborn Screening History

- 1965
  - Phenylketonuria
- 1977
  - Congenital Hypothyroidism
- 1984
  - Galactosemia
- 1987
  - Biotinidase Deficiency
  - Maple Syrup Urine Disease (MSUD)
  - Hemoglobinopathies
- 1993
  - Congenital Adrenal Hyperplasia (CAH)
- 2003
  - Medium-Chain Acyl-Coenzyme A Dehydrogenase Deficiency (MCAD)
- 2004
  - Citrullinemia
  - Homocystinuria
  - Argininosuccinic Aciduria (ASA)
- 2005
  - Expanded Screen Pilot
- 2006
  - Screen for more than 48 metabolic disorders
- 2007
  - Cystic Fibrosis

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- The Newborn Screening Laboratory screens all infants born in Michigan for forty-eight disorders
  - Hearing Screening done in Hospitals

# *Amino Acid Disorders*



- A specific enzyme is missing or not functioning properly
- The body is not able to break down protein in food
- Toxic chemicals build up in the body causing damage to organs

# *Amino Acid Disorders -Continued*

- Autosomal recessive disorder
- Untreated:
  - Brain damage
  - Mental retardation
  - Vision problems
  - Liver damage
  - Coma and death

# *Amino Acid Disorders* - *Continued*



- Treatment (Lifelong):
  - Use of special formula and low protein foods
  - May require medication to help the body get rid of harmful toxins
- Special Needs:
  - Primary care physician, pediatric metabolic specialist, and a dietician

# *Amino Acid Disorders -Continued*



Phenylketonuria (PKU)  
Benign hyperphenylalaninemia (H-PHE)  
Biopterin cofactor biosynthesis (BIOPT (BS))  
Defects of biopterin cofactor regeneration (BIOPT(Reg))  
Maple Syrup Disease (MSUD)  
Homocystinuria (HCY)  
Hypermethioninemia (MET)  
Citrullinemia (CIT)  
Citrullinemia Type II (CIT II)  
Argininosuccinic acidemia (ASA)  
Tyrosinemia Type I (TYR I)  
Argininemia (ARG)

# *Fatty Acid Oxidation Disorders*

- A specific enzyme is missing or not functioning properly
- The body cannot use stored fat for energy

# *Fatty Acid Oxidation Disorders-*

*Continued*

- Autosomal recessive disorder
- Untreated:
  - Vomiting
  - Sleepiness
  - Seizures
  - Liver damage
  - Coma and death

# *Fatty Acid Oxidation Disorders-*

*Continued*

- Treatment (Lifelong):
  - Frequent meals
  - Do not fast
  - Medication may be needed to help the body use energy
- Special Needs:
  - Primary care physician, a pediatric metabolic specialist, and a dietician

# *Fatty Acid Oxidation Disorders-*

*Continued*



Carnitine: acylcarnitine translocase deficiency (CACT)  
Carnitine palmitoyltransferase II deficiency (CPT II)  
Carnitine uptake defect (CUD)  
Carnitine palmitoyltransferase IA def. (liver) (CPT IA)  
Short-chain acyl-CoA dehydrogenase deficiency (SCAD)  
Glutaric acidemia type II (GA II)  
Med.-chain acyl-CoA dehydrogenase deficiency (MCAD)  
Long-chain L-3-OH acyl-CoA dehydrogenase deficiency (LCHAD)  
Trifunctional protein deficiency (TFP)  
Very long-chain acyl-CoA dehydrogenase deficiency (VLCAD)  
Med.-chain ketoacyl-CoA thiolase deficiency (MCKAT)  
Med./short-chain L-3-OH acyl-CoA dehydrogenase deficiency (M/SCHAD)  
Dienoyl-CoA reductase deficiency (DE RED)

# *Organic Acid Disorders*



- A specific enzyme is missing or not functioning properly
- The body is not able to break down protein in food
- Toxic chemicals can build up in the body and cause damage to organs

# *Organic Acid Disorders - Continued*



- Autosomal recessive disorder
- Untreated:
  - Vomiting
  - Feeding difficulties
  - Liver and kidney damage
  - Mental retardation
  - Death

# *Organic Acid Disorders - Continued*



- Treatment (Lifelong):
  - Restrict certain proteins that the body has difficulty breaking down
  - May require medication to help the body get rid of harmful toxins
- Special Needs:
  - Primary care physician, a pediatric metabolic specialist, and a dietician

# *Organic Acid Disorders - Continued*



Isovaleric acidemia (IVA)  
2-Methyl butyryl-CoA dehydrogenase deficiency (2MBG)  
3-Methylcrotonyl-CoA carboxylase deficiency (3MCC)  
3-OH 3-CH<sub>3</sub> glutaric aciduria (HMG)  
3-Methylglutaconic aciduria (3MGA)  
Beta-ketothiolase deficiency (BKT)  
Glutaric acidemia type I (GA I)  
Propionic acidemia (PA)  
Methylmalonic acidemia (mutase deficiency) (MUT)  
Methylmalonic acidemia (Cbl A,B)  
Methylmalonic acidemia (Cbl C,D)  
Multiple carboxylase deficiency (MCD)  
2-Methyl 3 hydroxy butyric aciduria (2M3HBA)  
Malonic acidemia (MAL)  
Isobutyryl-CoA dehydrogenase deficiency (IBG)

## *Endocrine Disorders:*

Congenital Adrenal Hyperplasia (CAH)

Congenital Hypothyroidism (CH)

## *Enzyme Disorders:*

Galactosemia (GALT)

Biotinidase Deficiency (BIOT)

## *Hemoglobinopathies:*

Sickle cell anemia (Hb SS)

Hb S/C Disease (Hb S/C)

Hb S/Beta-thalassemia (Hb S/Beta-Th)

Variant Hb-pathies (Var Hb)

# *Congenital Adrenal Hyperplasia (CAH)*



- Autosomal recessive disorder
- Decrease or absence of certain adrenal hormones
- Untreated:
  - Sex misassignment in females
  - Adrenal Crisis
  - Death
- Treatment (Lifelong):
  - Hormone replacement therapy

# *Congenital Hypothyroidism (CH)*

- Approximately 10% are genetically inherited
- Inadequate or absent production of thyroid hormone
- Untreated:
  - Mental retardation
  - Poor growth and development
- Treatment (Lifelong):
  - Daily oral thyroid replacement

# *Galactosemia (GAL)*



- Autosomal recessive disorder
- Failure to metabolize the milk sugar galactose
- Untreated:
  - Cataracts
  - Cirrhosis of the liver
  - Mental retardation
  - Death
- Treatment (Lifelong):
  - Exclusion of galactose from the diet

# *Biotinidase Deficiency (BIO)*



- Autosomal recessive disorder
- The enzyme is missing or not functioning properly
- Untreated:
  - Seizures
  - Hearing loss
  - Neurological impairment
  - Death
- Treatment (Lifelong):
  - Daily oral biotin supplements

# *Hemoglobinopathies (Sickle Cell Disease)*

- Autosomal recessive disorder
- Blood vessels become “clogged”
- Untreated:
  - Severe pain
  - Sickle cell crisis
  - Death from pneumococcal sepsis
- Treatment:
  - Penicillin prophylaxis until at least six years of age

# *Michigan Newborn Screening Facts*

- Approximately 126,000 births per year
  - Of which approximately 13,000 are NICU births
- 94 birthing hospitals

## *Disorders Identified via Newborn Screening Michigan Residents, 1965-2006*

<b>Type of Disorder Classification (Year Screening Began)</b>	<b>Cases in 2006 (N)</b>	<b>Cases Through 2006 (N)</b>	<b>Cumulative Detection Rate*</b>
<b>Galactosemia (1985)</b>	<b>11</b>	<b>116</b>	<b>1: 24,850</b>
<b>Biotinidase Deficiencies (1987)</b>	<b>20</b>	<b>148</b>	<b>1: 16,928</b>
<b>Amino Acid Disorders (1965)</b>	<b>16</b>	<b>590</b>	<b>1: 9,901</b>
<b>Organic Acid Disorders (2005)</b>	<b>8</b>	<b>10</b>	<b>1: 12,752</b>
<b>Fatty Acid Oxidation Disorders (2003)</b>	<b>11</b>	<b>39</b>	<b>1: 9,951</b>
<b>Congenital Hypothyroidism (1987)</b>	<b>59</b>	<b>1,394</b>	<b>1: 1,870</b>
<b>Congenital Adrenal Hyperplasias (1993)</b>	<b>3</b>	<b>103</b>	<b>1: 16,819</b>
<b>Hemoglobinopathies (1987)</b>	<b>63</b>	<b>1,336</b>	<b>1: 1,951</b>

*\*Note: Denominators, the number of live births eligible to have been screened, are calculated from the year screening began onward; thus, if screening commenced other than at the start of the year the denominator will be slightly larger than the true denominator. Galactosemia includes both classical cases and Duarte variants (DG) since 2004. Biotinidase Deficiency includes both partial and profound biotinidase deficiency.*

# 2006

**Total Initial Specimens by Birth Date: 125,600**  
**Total Confirmed Cases All Disorders: 191**  
**Combined Incidence: ~1 per 658 births**



# *Program Funding*



- Hospitals are charged for first sample “blue” cards (\$85.61)
- All repeat test “pink” cards supplied at no additional cost
- Funding supports
  - Laboratory
  - Follow Up program
  - Medical Management programs

# *Medical Management*



- Children's Hospital of Michigan - Metabolic Clinic (CHMMC) (313) 745-4513
- University of Michigan - Endocrine Follow up program (EFUP) (734) 647-8938
- Sickle Cell Disease Association of America (SCDAA), Detroit Chapter (313) 864-4406

# *Hospital NBS Coordinator*



- Monitor hospital NBS process to ensure that NBS cards are filled out accurately and completely
- Monitor that the NBS specimen is submitted in a timely manner
- Receive the NBS Quality Report and NBS Update for distribution in the hospital
- Receive NBS Program updates for distribution in the hospital

# Screening Recommendations



- Obtain initial screen at 24-36 hours of age
- Always test before discharge or transfer regardless of age
  - Follow directions on Early Specimen letter from the State Laboratory regarding repeat specimens
- Always test before transfusion of red blood cells or the administration of TPN

# *NICU Screening Guidelines*



- Purpose: to detect CH in premature newborns
- Obtain initial NBS on admission to the NICU
- Ensure that initial NBS is obtained prior to the administration of TPN and/or RBC
- Obtain second NBS at 14 days or discharge
- Obtain third NBS at 30 days or discharge

# *Completing the Card*



- Accurate information is vital
  - Identification/location of infants for follow up of abnormal results
    - Inaccurate information could cause a life-threatening delay for affected infants
  - Age (in hours) and weight (in grams) are critical to provide accurate screening results

# *Completing the Card*



- Remove hearing slip before blood collection
- All information should be accurate, legible and complete

**The sample submitter is legally responsible for the accuracy and completeness of the information on the newborn screening card**

# Completing the Card

## Critical Demographic Information



*Press Firmly with Pen*

Baby's last name  
Mother's first and last name  
Mother's social security #  
Date and time of birth  
Birth weight in grams  
Gestational age  
Date and time of specimen collection  
Date of transfusion (red blood cells)  
TPN feeding Yes or No

# *Screening Cards*



## Features of the card

- Submitter copy
- Date/time of birth and date/time of specimen collection
- Space for initials of person collecting specimen
- Overlay flap to protect filter paper before collection

# Newborn Screening Card

<b>BABY</b>	LAST NAME				FIRST NAME				GENDER <input type="radio"/> MALE <input type="radio"/> FEMALE	
	BIRTH DATE MM DD YY		BIRTH TIME (Military) HH MM		BIRTH WT. (gms)		WKS GESTATION		BIRTH ORDER A B C D	
	SPECIMEN DATE MM DD YY		COLLECTION TIME (Military) HH MM		NICU/ SPECIAL CARE? <input type="radio"/> NO <input type="radio"/> YES		ANY RBC TRANSFUSION? <input type="radio"/> NO <input type="radio"/> YES		ANTIBIOTICS? <input type="radio"/> NO <input type="radio"/> YES	
	MEDICAL RECORD #				Collected By: (initials)		ANY TPN FEEDING? <input type="radio"/> NO <input type="radio"/> YES		DATE MM DD YY	
<b>MOTHER</b>	LAST NAME				FIRST NAME				MOM/BABY STERIOD TX? <input type="radio"/> NO <input type="radio"/> YES	
	ADDRESS								PHONE	
	CITY		STATE		ZIP		SOCIAL SECURITY NUMBER			
	MEDICAL RECORD #				BIRTH DATE MM DD YY		HEPATITIS B SURFACE ANTIGEN (HBsAg) TEST DATE MM DD YY			
<b>PHYSICIAN</b>	LAST NAME				FIRST NAME				RESULT <input type="radio"/> POSITIVE <input type="radio"/> NEGATIVE	
	PHONE				FAX				<b>FIRST SAMPLE</b>	
	SUBMITTER NAME									
<b>SUBMITTER</b>	ADDRESS								PHONE	
	CITY		STATE		ZIP					
	BIRTH HOSPITAL (if different from submitter)								MDCH use only	

**MDCH USE ONLY**

MI Dept. of Comm. Hlth.  
By Authority of Act 568  
P.A. MCLA 333.5431

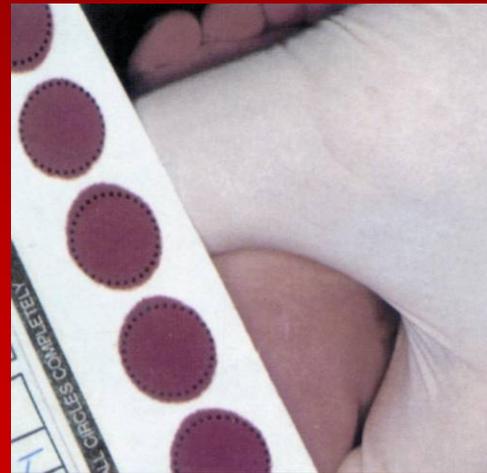
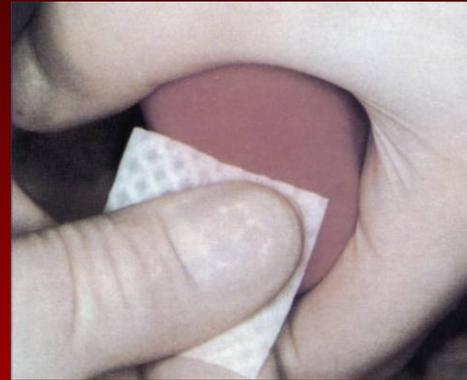
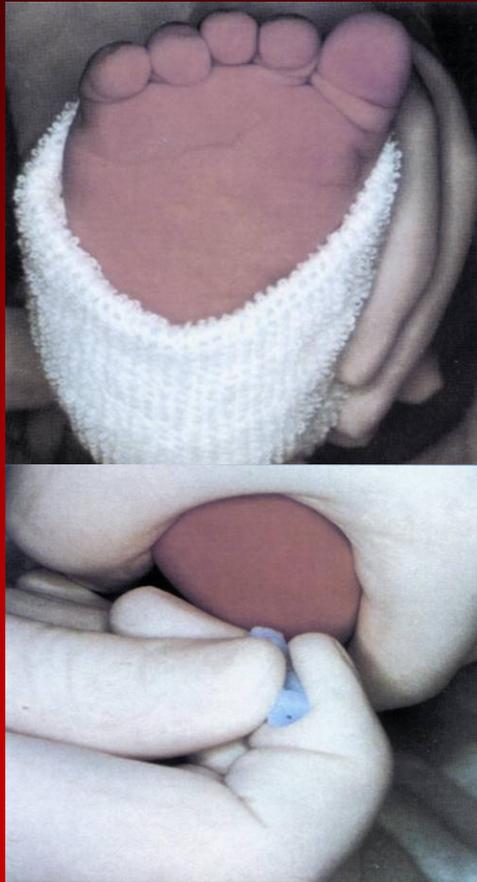


# *Collection Procedure*



- The Michigan Department of Community Health (MDCH) follows the recommendations of the Clinical and Laboratory Standards Institute, (CLSI), (formerly NCCLS) for collecting an acceptable specimen
  - “Blood Collection on Filter Paper for Neonatal Screening Programs; Approved Standard- Fifth Edition”

# *Newborn Screening Specimen*

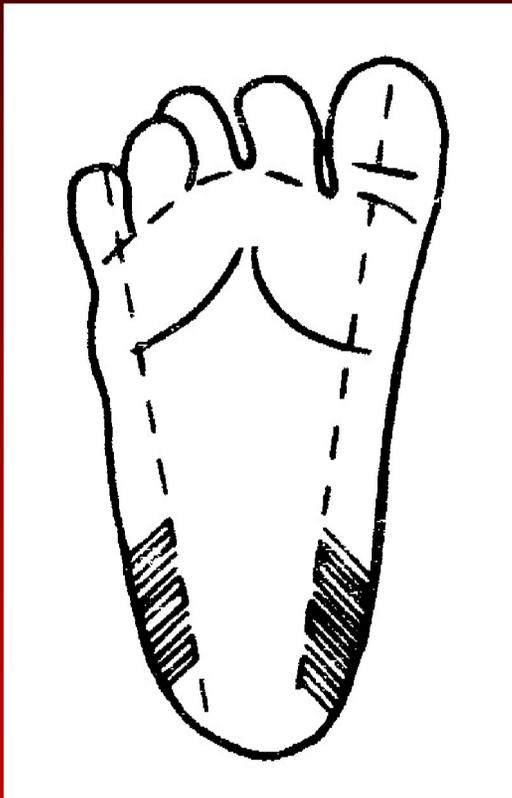


# *Collection Procedure*



- Use capillary blood from heelstick
- Fill in all five circles
- Apply blood to **only one side** of the filter paper
- Dry Flat at least 3 hours
- Mail to state laboratory within 24 hours of collection

# Collection Procedure



- Warm foot for 3 – 5 minutes to increase blood flow
- Cleanse site with alcohol prep
- Air dry or wipe dry with sterile gauze pad
- See picture for recommended puncture site

# *Collection Procedure*

- Puncture heel with lancet of no more than 2.0 mm in depth
- Wipe away first drop of blood
- Apply gentle pressure to allow a large drop of blood to form
- Lightly touch filter paper to large drop of blood
- Allow blood to soak through to completely fill the circle

# *Indwelling Line Procedure*



- Do not draw from intravenous lines where TPN or blood is being infused
- For other types of IV fluid, make sure the line has been thoroughly flushed
- Avoid the use of syringes with additives
- Spot the card immediately after collection

# *Feeding/Antibiotic/TPN Issues*



- Feeding status is less of a factor with technologies currently used in the MDCH Newborn Screening Laboratory
- Antibiotics have less effect on the NBS with current laboratory testing methods
- TPN may cause false positive screening tests for PKU, MSUD, and other amino acid and acylcarnitine disorders
  - Screening results should return to normal in unaffected babies when TPN discontinued

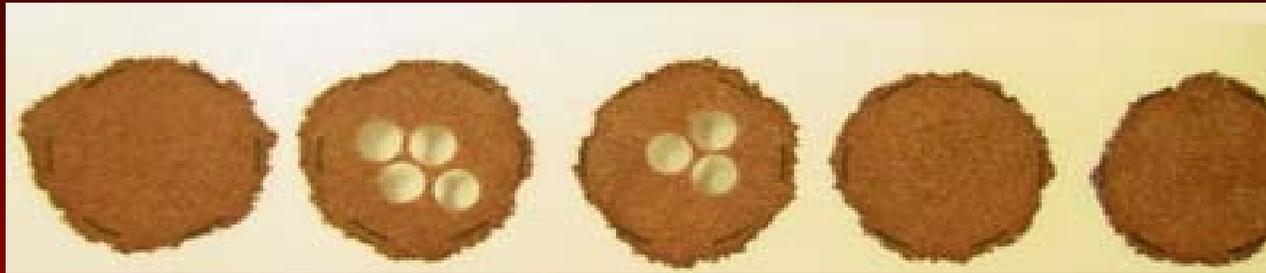
# *Things to Avoid*

## **DO NOT**



- Apply blood to both sides of the filter paper
- Apply “layers” of blood onto the same circle
- Apply excessive amounts of blood (circles should not touch one another)
- Allow filter paper to come in contact with other substances

# *Satisfactory Specimens*



Front



Back

Note the even penetration of blood that indicates a single large drop of blood was applied to the filter paper. The circle should look the same when viewing the card front or back.

# *Unsatisfactory Specimens*



- Failure to follow correct procedures will likely result in an unsatisfactory sample.
  - These samples will not yield reliable results
  - repeat test will be necessary

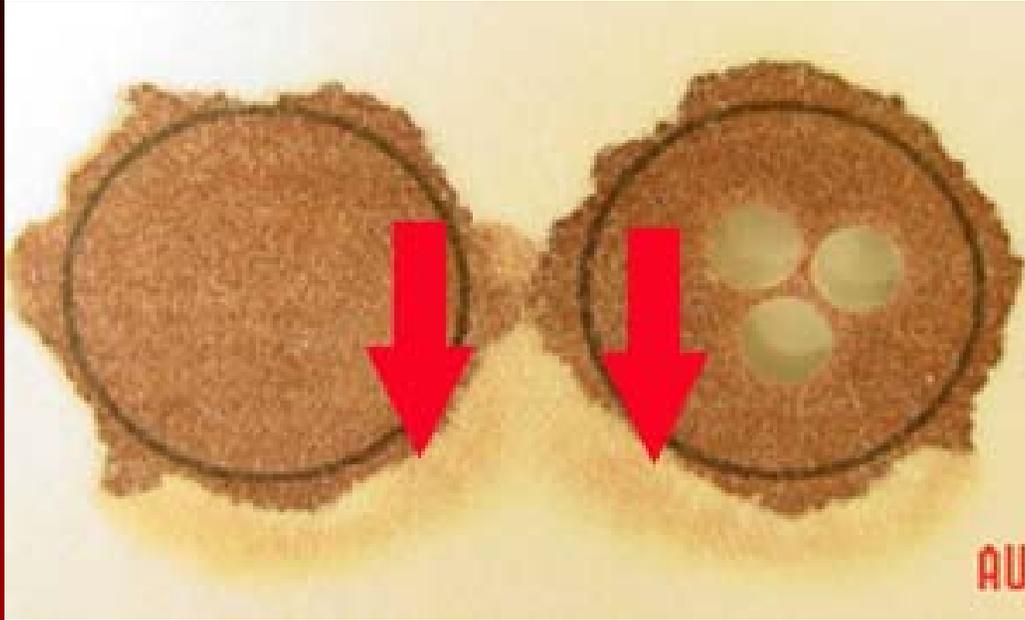
The delay caused by an unsatisfactory sample could be life-threatening to an affected child.

# Clotted Specimens



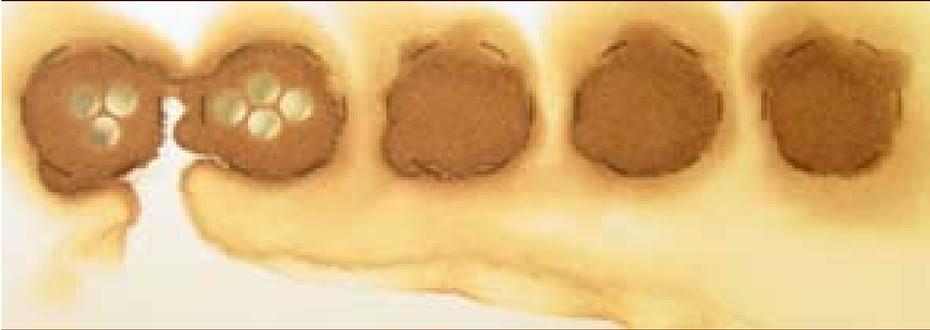
- Causes
  - Waiting too long to apply blood to the filter paper
  - Improper use of capillary tubes
  - Syringe used for blood collection
- Prevention
  - Warm heel to assure good blood flow
  - Follow MDCH guidelines for capillary tube collection
  - Avoid application of excessive amounts of blood

# *Serum Rings*



- **Causes**
  - Milking or squeezing around puncture site
  - Improper drying of specimen (up on side)
- **Prevention**
  - Wipe away first drop of blood (contains tissue fluid)
  - Protect from excessive heat
  - Dry in horizontal (flat) position

# *Contaminated Specimens*



- Causes
  - something spilled on the filter paper or it was set on a wet surface prior to or after the application of blood
- Prevention
  - protect the filter paper from coming in contact with hands or other substances before and after blood collection

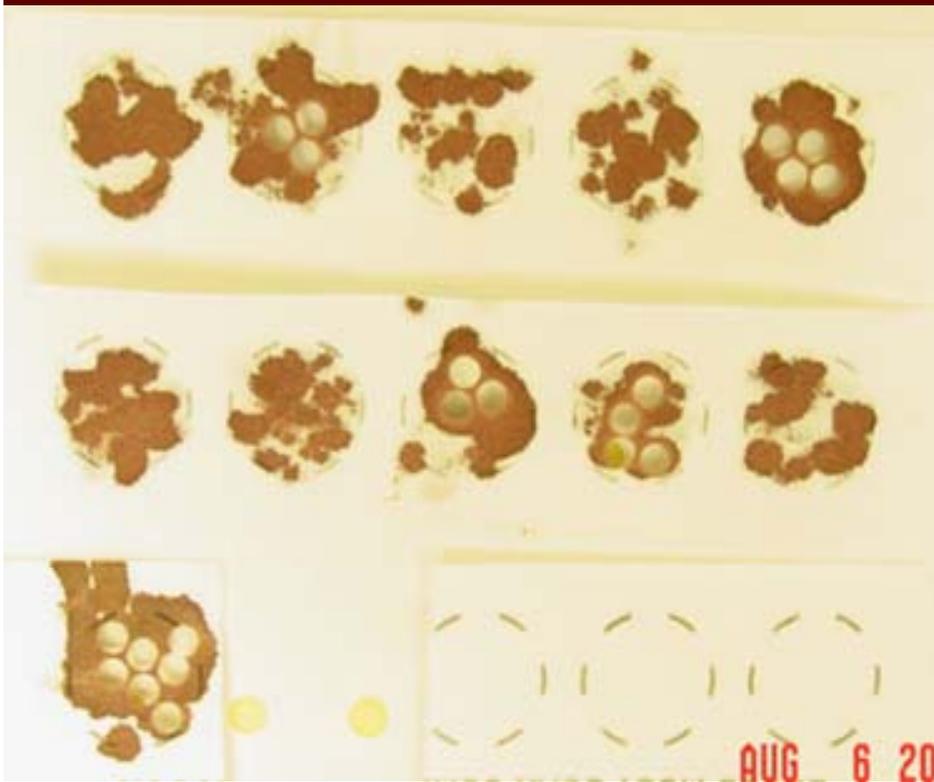
# *Insufficient Specimens*

- Causes

- Poor blood flow
- Lancet did not make good puncture
- All circles not filled
- Entire circle not filled
- Blood did not soak through filter paper

- Prevention

- Warm heel before blood collection
- Use lancet that makes a wound 2.0mm deep
- Fill all circles



# *Diluted Specimens*

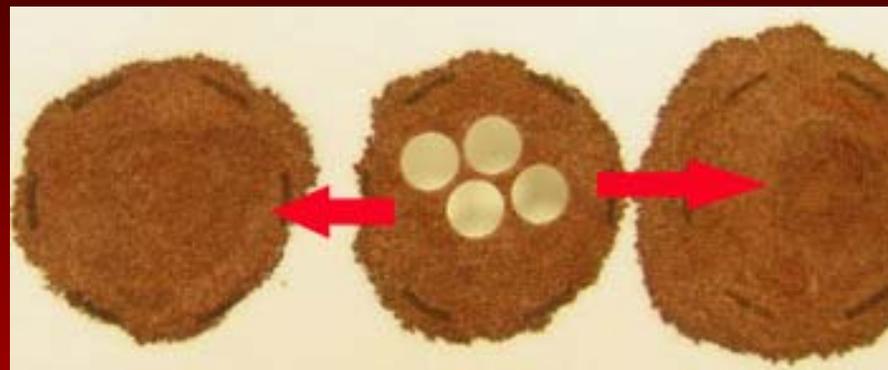


- Causes
  - Blood collected from an indwelling line that was not cleared prior to obtaining the specimen
- Prevention
  - Draw appropriate amount of blood (e.g. 2 to 2.5cc) from the line before sample is obtained.

# *Layered Specimens*

- Causes

- Multiple applications of blood to the same circle
- Blood applied to both sides of the filter paper
- Unevenly distributed blood
- Circles of blood touch or overlap



- Prevention

- Allow one large drop to soak through and fill the entire circle
- Apply blood to only one side
- Apply blood in circle only



# *Scratched or Damaged Specimens*



- Causes

- Improper use of capillary tubes and other collection devices
- Pressing the heel against the filter paper when obtaining the screening sample.

- Prevention

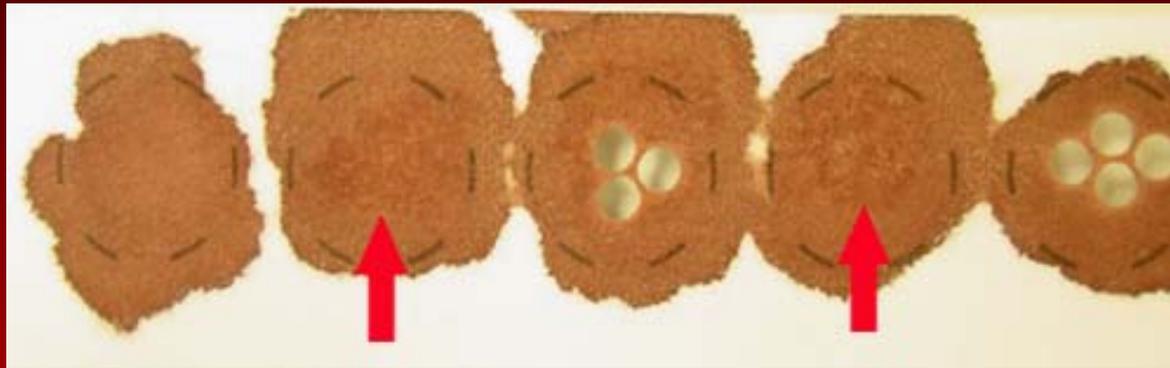
- Follow MDCH guidelines for capillary tube collection
- Avoid touching the filter paper with heel or collection device

# *Over Saturated Specimens*



- Causes
  - Application of excessive amounts of blood to the filter paper
  - Circles should not touch
- Prevention
  - Apply blood in the preprinted circles only

# *Stuck to Backing*



- Causes
  - Back of card not folded away during drying of blood spots
- Prevention
  - Do not allow the flap/backing to come in contact with the blood spots until dry.

# *Defective Form*



This specimen was collected on a defective or damaged form. Note the areas indicated by the arrows where the blood did not adhere to the form. When this happens, the process should be repeated on a new form.

# Drying/Mailing Instructions



- Air dry specimen FLAT for at least 3 hours
  - Keep away from heat and direct sunlight
- Mail specimens within 24 hours of collection
  - Do not hold specimens for bulk mailing
  - Pre-addressed envelopes are available for prompt mailing
- MDCH is implementing a courier service for same day specimen delivery.

# *Laboratory Procedures*



- Specimens are tested the day they are received
  - Up to 736 Specimens each day
- Preliminary results same day for life threatening disorders
- Unsatisfactory specimens reported the same day they are received
  - All tested and positives reported

# Laboratory Procedures - *continued*



# *Follow Up*



- Positive results are followed up with a repeat screening test or prompt referral to medical management
- Telephone/fax notification with instructions to local physician
- Negative results sent to hospital
  - Hospital forwards to local physician

# *Supplemental Screening*



Parents can obtain kit from supplemental screening lab (Pediatrix, Baylor, Mayo, University of CO)

- Blood is collected at same time as state test
- No follow-up component

# *Issues of Concern*

- Unscreened Infants
  - Match hearing screens to metabolic
  - Match NBS to birth certificates
  - Transfers and early discharge - Birth hospital is responsible for obtaining the initial screen

**Do not assume no news is good news, it may mean not done!**

# *Issues of Concern*



- “Late” Specimens: > 5 days from birth date to punch date in NBS Lab
  - Causes
    - Specimens drawn > 36 hours of age
    - Batching of specimens
    - Mailroom delays
    - Weekends
    - Insufficient postage

# *Strategies for Improvement*



- Quarterly Quality Assurance Reports
- “Newborn Screening Update”
- Site Visits
- Web based educational program
  - [www.training.mihealth.org](http://www.training.mihealth.org)
- Website
  - [www.michigan.gov/newbornscreening](http://www.michigan.gov/newbornscreening)

# Replacement Blue Cards



OOPS!

If blue cards (initial test) are “damaged” by:

- Improper specimen collection
- Mishandling
- Errors in recording patient or hospital information

Replacement cards can be obtained at no charge.

# *Replacement Procedure*



- **Only the top blue copy is needed for replacement**
- **Remove the filter paper portion if it contains blood (very important)**
- **Complete “Newborn Screening Card Replacement Form”**
  - Forms available on the NBS webpage or from NBS Accountant, Valerie Klasko at (517) 241-5583

# *Michigan Newborn Screening Program Brochure*



- Newborn Screening brochures are available to assist in discussing the NBS screening process with parents and prospective parents
- Brochures contain information on 11 of the disorders currently being screened
- Brochures are available in English, Spanish, and Arabic from NBS Accountant, Valerie Klasko (517) 241-5583

# *Free Online Program for Newborn Screening Education*

- Go to [www.training.mihealth.org](http://www.training.mihealth.org)
- Follow the directions to log in – free
- Select Newborn Screening
- Take the course

You can take the whole course or one part at a time. Average completion time is one hour or less. A certificate and 1.2 nursing contact hours are provided if a passing score is received on the final quiz, the evaluation is completed, and the appropriate information is provided.

# *It's Not Just PKU!*



The current newborn screening panel tests for more than 49 disorders including hearing screening. To avoid confusion, it is important to use correct terminology when referring to newborn screening tests.

**Please make every effort to call the test “Newborn Screen” rather than “PKU”**

# Contact Information

Newborn Screening Program

Telephone: 517-335-9205

Fax: 517-335-9419

Email:

[mdch-newbornscreening@michigan.gov](mailto:mdch-newbornscreening@michigan.gov)

Website:

[www.michigan.gov/newbornscreening](http://www.michigan.gov/newbornscreening)

William Young, Director

Newborn Screening Follow-up Program

Telephone 517-335-8938

Email: [youngw@michigan.gov](mailto:youngw@michigan.gov)

Harry Hawkins, Manager

Newborn Screening Laboratory

Telephone 517-335-8095

Email: [hawkinsh@michigan.gov](mailto:hawkinsh@michigan.gov)

