What's New in Montana's Newborn Screening Program or Why I can't call it "the PKU test" anymore

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Montana Perinatal Meeting April 30, 2010

MONTANA
Department of Public Health & Human Services

Objectives

- Discuss the **Administrative Rules of Montana** defining Newborn Screening practices
- Describe proper collection procedures, unsatisfactory specimens and transport of specimens to the Montana Public Health Laboratory
- Define **Newborn Screening partners** and clinical resources

Purpose of Newborn Screening

- **Public health program** to screen for congenital and heritable disorders
- These disorders may cause severe mental retardation, illness, or death if not treated early
- If treated, infants may live relatively normal lives
- Results in savings in medical costs over time

According to the ACMG (American College of Medical Genetics), screened conditions should:

- be **identifiable at 24 to 48 hours** after birth (prior to clinical symptoms).
- Have incidence > 1 in 100,000 and cause significant morbidity/ mortality untreated
- have an **available test** with appropriate sensitivity and specificity (at suitable cost).
- demonstrate **benefits of early detection**, timely intervention, and efficacious treatment.

Newborn Screening is a system

- Screening (includes **pre-analytical**)
- **Follow-up** of initial abnormal results to normal repeat or referral as screen positive
- Diagnostic testing to confirm cases
- Treatment and long-term management
- Program evaluation and improvement
- **Education** of providers and families

Montana Screening History

- 1961: Microbiologist Dr. Robert Guthrie developed bloodspot test for PKU, by 1966 26 states had PKU testing
- 1973: Montana mandated PKU and hypothyroidism testing (performed in Oregon)
- 1985: Montana PHL began testing
- 2002: Montana offered optional expanded testing through Wisconsin State lab
- 2003: Montana mandated hemoglobinopathy and galactosemia testing
- 2006: ACMG/ AAP recommends 28 core conditions
- 2008: Montana begins mandated expanded panel

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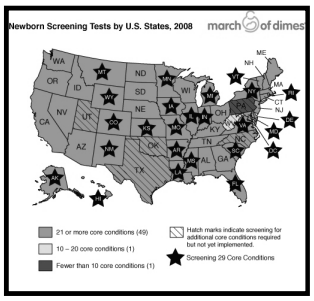
Montana earns a Star in 2008!



Source: http://marchofdimes.com/aboutus/22684_51920.asp

Three Hemoglobinopathies

- HbSS – Sickle cell anemia
- Hb S/Th – Hb S/ Beta-thalassemia
- Hb S/C – Hb S/C disease

Five Other Disorders

- CH – Congenital hypothyroidism
- BIOT – Biotinidase deficiency
- CAH – Congenital adrenal hyperplasia
- GALT – Galactosemia
- CF – Cystic Fibrosis

Five Fatty Acid Oxidation Disorders

- MCAD – Medium-chain acyl-CoA dehydrogenase deficiency
- VLCAD – Very long-chain acyl-CoA dehydrogenase deficiency
- LCHAD – Long-chain L-3-OH acyl-CoA dehydrogenase deficiency
- TFP – Trifunctional protein deficiency
- CUD – Carnitine uptake defect

Six Amino Acid Metabolism Disorders

- PKU – Phenylketonuria
- MSUD – Maple syrup urine disease
- HCY – Homocystinuria
- CIT – Citrullinemia
- ASA – Argininosuccinic acidemia
- TYR I – Tyrosinemia type I

Nine Organic Acidemia Disorders

- IVA - Isovaleric acidemia
- GA I – Glutaric acidemia type I
- HMG – 3-OH-3-methylglutaryl-CoA lyase def
- MCD – Multiple carboxylase deficiency
- MUT – Methylmalonic acidemia (mutase def)
- 3MCC – 3-Methylcrotonyl-CoA carboxylase deficiency
- Cbl A,B – Methylmalonic acidemia
- PROP – Propionic acidemia
- BKT – Beta-ketothiolase deficiency

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Montana's Newborn Screening Law

Montana Code Annotated - 2007

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50-19-203. Newborn screening and followup for metabolic and genetic disorders. (1) A person in charge of a facility in which a child is born or a facility in which a newborn is provided care or a person responsible for the registration of the birth of a newborn shall ensure that each newborn is administered tests designed to detect inborn metabolic and genetic disorders as required under rules adopted by the department.

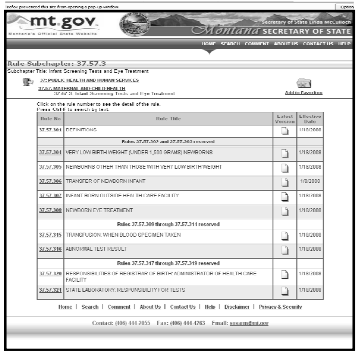
(2) The tests must be done by an approved laboratory. An approved laboratory must be the laboratory of the department or a laboratory approved by the department.

(3) The department shall contract with one or more providers qualified to provide followup services, including counseling and education, for children and parents of children identified with metabolic or genetic disorders to ensure the availability of followup services.

History: En. Sec. 2, Ch. 227, L. 1973; R.C.M. 1947, 69-6711; amd. Sec. 1, Ch. 401, L. 2007.

Provided by Montana Legislative Services

Montana's Administrative Rules (A.R.M.) for Newborn Screening Updated 1/18/08



Question #1

You are having trouble getting a large enough drop of blood to fill each circle on the card so…

- ☐ You touch the baby's heel multiple times to the card until a circle is filled.
- ☐ You use a capillary to collect the blood and apply to the card even though there are some clots.
- ☐ You warm the baby's heel first (to 42 degrees) to increase blood flow.

Question #2

You notice that a NBS sample for sendout has hardly any blood in each spot and….

- ☐ Send it as usual because you're not an expert.
- ☐ Notify the nursery and provider that results will be delayed if a repeat specimen is not obtained now.
- ☐ Add a note that this is all the blood you could get so do the screen anyway.

Question #3

You are responsible for sending bloodspots to the PHL so you…

- ☐ Close the card immediately after obtaining the specimen and rush to get it in the shipping envelope.
- ☐ Save the hospital money by sending batched specimens only twice a week.
- ☐ Send specimens every day by mail or courier if possible.

Question #4

The Public Health Lab calls to say a specimen was unsatisfactory so you

- ☐ Assume the provider will see the unsatisfactory report when it arrives and repeat the screen.
- ☐ Leave a message for the provider listed in your system and assume he will call the family and repeat the screen.
- ☐ Call the listed provider and make sure he can contact the family.

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A.R.M. 37.57.320 RESPONSIBILITIES OF REGISTRAR OF BIRTH: ADMINISTRATOR OF HEALTH CARE FACILITY

- The person in charge of health care facility or birth attendant must be **certain the specimen is adequate prior to discharge.**
- Cause specimen to be forwarded to Public Health lab **within 24 hours of collection** by first class mail or equivalent.
- **Record on the newborn's chart** the date of collection and the results of the screen.

Valid specimen:

"Unsatisfactory" because….

- "**LAYERED SPECIMEN** DUE TO APPLYING BLOOD TO A PARTIALLY OR COMPLETELY DRIED AREA. FILL ONE CIRCLE COMPLETELY BEFORE FILLING ANOTHER."
- "**INCOMPLETE SATURATION** OF FILTER PAPER."
- "FILTER **PAPER DAMAGED** DURING APPLICATION OF BLOOD. CAPILLARY TUBE MUSTNOT TOUCH THE FILTER PAPER."
- "**INSUFFICIENT SAMPLE** TO COMPLETE TESTING."
- "BLOOD **CLOTS** ON SURFACE"

Why does bloodspot quantity and quality matter?

- **Quantitative results depend on a standard serum volume per 1/8 inch (3.2 mm) punch.** Per CLSI, mean serum volume per punch should be 1.54 ± 0.17 microliters from spot of 100 microliters of intact RBC's at 55% hematocrit.
- Public Health Labs try to use the "best" spots, but sometimes not sufficient to do all tests.
- **Screening rule:** an unsatisfactory specimen is assumed to have an abnormal result until a satisfactory repeat specimen is tested.

Impact of expanded panel on Unsatisfactory Specimens

- In 2007 and before:
  - 4 mandated tests
  - Manual punching in one laboratory
  - **Less than 0.2% unsatisfactory**
- In 2008:
  - 13 tests for 28 mandated conditions
  - Manual and automated punching in 2 labs
  - **2.4% unsatisfactory overall**

Question #5

A baby is discharged home about 12 hours after delivery. The hospital should …

- ☐ Assume the baby's provider will collect later, since the newborn screen is not valid before 24 hours.
- ☐ Tell the parents they must bring the baby back the next day for collection.
- ☐ Obtain the screen immediately before discharge and ask the parents to assume responsibility to repeat the screen within 2 weeks.

Why require repeat if collected at less than 24 hours?

- Early collection may produce **false positive and negative results** for TSH (CH screen), 17-hydroxyprogesterone (CAH screen), and IRT (CF screen).
- **Normal amino acid levels are not reliable** for specimens drawn at less than 24 hours.
- Early collection **increases** the chance of detection of a fatty acid oxidation disorder (catabolic state)

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A.R.M. 37.57.305 NEWBORNS OTHER THAN THOSE WITH VERY LOW BIRTH WEIGHT

- The health care facility must obtain the required blood specimen **between 24 and 72 hours of age.**
- If the newborn is discharged before 24 hours, **take the specimen immediately before discharge** AND take another specimen day 4 to 14.
- The **health care facility** must explain why the repeat is needed and ensure parent assumes responsibility to bring baby for repeat.
- If medically contraindicated, obtain specimen as soon as the medical condition of the newborn permits.

Question # 6

You are collecting blood for discharge testing on a preemie, and notice no newborn screen was ordered so…

- ☐ You don't worry because the baby had a screen in the first week after birth.
- ☐ You remember that the hospital is required to repeat the screen if less than 1500 g at birth.
- ☐ You assume the discharge note will ask the family doc to repeat the screen.

Question # 7

If a baby is sick or premature, the best time to collect the initial newborn screen is….

- ☐ After the baby has received total parenteral nutrition and gained weight
- ☐ After the baby has received a transfusion and has more blood
- ☐ Upon admission to the NICU before any treatment

A.R.M. 37.57.304 VERY LOW BIRTH WEIGHT (UNDER 1,500 GRAMS) NEWBORNS

- If very low birth weight (<1,500 grams), collect specimen between 24 hours of age and 7 days of age.
- If medically contraindicated, collect as soon as the infant's medical condition permits.
- If the newborn is hospitalized more than 14 days, **repeat the screen at discharge or 1 month** (if hospitalized longer than 1 month).

Transfusion and Newborn Screen

- Normal donor RBC's can cause false negative screens for **Sickle Cell Disease and Galactosemia** for the life of the donor cells (120 days).
- **Extracorporeal Life Support** "ECMO" involves large amounts of donor blood and invalidates all NBS tests for the duration and varying times afterward.

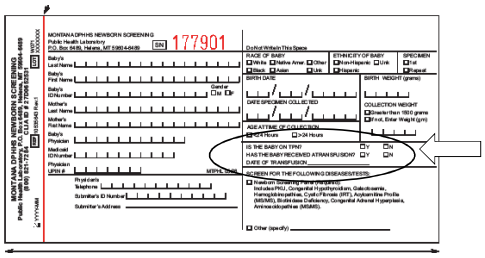
A.R.M. 37.57.315 TRANSFUSION: WHEN BLOOD SPECIMEN TAKEN

- If a newborn needs a transfusion, blood specimens for the tests required by this subchapter must be taken before the transfusion takes place.

TPN and Newborn Screen

- **Amino acids** may be elevated: Leucine, Methionine, Phenylalanine, Tyrosine, Citrulline
- **Acylcarnitines** may be elevated, especially if fatty acids supplemented
- **Comment on NBS report**: "The newborn screening specimen on this infant was collected while on Total Parental Nutrition (TPN). The TPN caused one or more of the amino acids or acylcarnitines to be elevated. A repeat specimen is required after the TPN has been discontinued."

Is the baby on TPN? Was the baby transfused?



Sick/ Premature Newborns

- **NICN babies account for 40% of "possible abnormal" results** but almost all are normal on repeat. Many of these abnormalities are treatment-related
- Challenge: Optimize the timing, minimize the number of blood spot collections for NICN babies.
- CLSI released new standards in 2009.

Future rule changes for Sick/ Premature Newborns?

	Proposed CLSI	Current MT rule
Bloodspot collection	1st: NICU admit, 2nd: 48-72 hrs 3rd: 28 days (<2000 g)	<1500 g: 1st by day 7, 2nd by 28 days or discharge
Out of range results	Most abnormals on 1st normalize on 2nd or 3rd	Repeat within 48 hours of notification
Transfusion	Collect prior	Collect prior
Transfer	Collect at NICU admit	Receiving collects
Special cases	If pre-treatment sample not obtained.	No current rule

Question # 8

A baby delivered at home by a midwife is transferred to your hospital and you

- ☐ Remember that the birth attendant is responsible for collecting the screen so you assume it was done.
- ☐ Tell the family to ask the midwife to collect the screen after discharge.
- ☐ Collect a newborn screen on any transferred baby.

A.R.M. 37.57.306 TRANSFER OF NEWBORN INFANT

- In the event of transfer … **the specimen required must be taken and submitted by the receiving health care facility** unless a sample was taken and submitted by the transferring health care facility or other responsible person.
- A receiving health care facility must take specimens as necessary for follow-up tests .

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A.R.M. 37.57.307
INFANT BORN OUTSIDE HEALTH CARE FACILITY

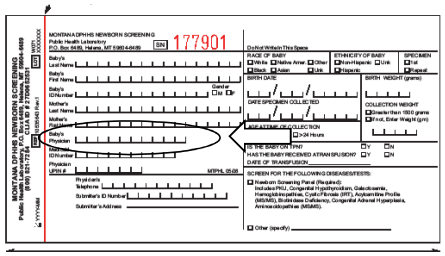
- When an infant is born outside of a health care facility and is not subsequently transferred to a health care facility , **it is the responsibility of the birth attendant or person who registers the birth** to collect the newborn screen.
- Difficult to enforce unless the birth attendant is licensed (direct entry midwives, etc)

Question #9

The PHL calls to say a specimen has a possible abnormal result and needs to be repeated immediately, so you

- ☐ Assume the provider will see the abnormal report when it arrives and repeat the screen.
- ☐ Make sure the PHL is able to contact a provider who is seeing the baby.
- ☐ Tell the PHL it's not you problem because the baby has been discharged.

Who is the provider responsible for follow-up?



Newborn Screening Results

- **Screen negative:** No further screening required
- **Unsatisfactory:** Repeat the screen as soon as possible.
- **"Possible Abnormal"** mildly out of range result: Repeat the screen as soon as possible (48 hours)
- **"Probable abnormal"** significantly out of range result: Depending on condition, perform diagnostic testing, consult a specialist, evaluate the baby clinically. May also repeat screen.

A.R.M. 37.57.316
ABNORMAL TEST RESULT

- Initial test result outside the normal range will be reported to the attending physician or midwife, who **must submit a repeat specimen within 48 hours.**
- If a repeat is also abnormal, the provider must obtain a specimen for diagnostic testing ("quantitative analysis")
- Diagnostic test records must be submitted to the NBS program.

Babies identified by NBS in Montana 2008-09

- **14** babies with congenital hypothyroidism
- **2** babies with galactosemia variant
- **1** baby with phenylketonuria
- **1** baby with sickle cell anemia
- **6** babies with cystic fibrosis
- **3** babies with rare fatty acid oxidation disorders
- **5** babies with an organic acidemia

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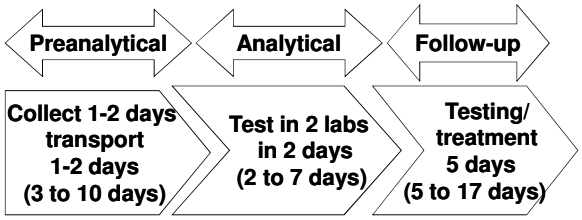
How soon is soon enough to get screen results and start treatment?

- Congenital hypothyroidism patients should be treated within **1-2 weeks** or IQ drops.
- Babies with classic galactosemia can die of sepsis in the **first week**
- Some fatty acid oxidation disorders can be fatal in **days to weeks.**
- Isovaleric acidemia can cause serious illness or death **within 1 week**
- Babies with PKU should be on special diet within **1-2 weeks** or IQ drops

Can we do better in Montana?

- More than 90% of screens are collected within **3 days (but some are missed)**
- 88% of screens have results by **2 to 4 days** after delivery to the PHL (up to 7 days)
- 74% of screens are delivered to the PHL in **3 days** or less (but some take more)
- Time to PHL receipt not necessarily correlated with distance from Helena

Montana: best case scenario is 5 days from birth to result



What happens if…

- The specimen is unsatisfactory and needs to be re-collected?
- The hospital **batches** specimens for several days before shipping?
- The specimen is collected on a weekend?
- The specimen arrives at the PHL on Friday?

Perinatal Professionals are Newborn Screening Partners !

- Help make sure you submit **satisfactory bloodspot specimens** in a timely manner
- Make sure the **NBS requisition** is filled out clearly (ALL CAPITALS) and completely and includes the name of the baby's provider
- Explain that newborn screening is much more than **"the PKU test"**

Perinatal Professionals are Newborn Screening Partners !

- Help providers to repeat unsatisfactory specimens or "possible abnormals"
- Help expedite provider notification and diagnostic testing for "probable abnormals"
- Tell us how we can make the program better

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Montana NBS Program Partners and Resources

- Montana Public Health Laboratory
  Newborn Screening Section (Denise or Linda Beischel)
  1-800-821-7284
- Montana Medical Genetics Program at Shodair Hospital
  Contracted to provide expert medical consultation to providers and follow-up after diagnosis (Anne Seliskar)
  1-406-202-2954

The Newest Montanans Thank You!