

ORGANIC ACID DISORDERS

Organic Acid Disorders

Organic acid disorders are a group of inherited metabolic conditions, each associated with a specific enzyme deficiency that causes the accumulation of organic acids in blood and urine. The accumulated compounds or their metabolites are toxic, resulting in the clinical features of these disorders.

Organic Acid Oxidation Disorders Screened in Kansas

The newborn screening program in the State of Kansas is designed to screen for nine different organic acid disorders. These disorders include:

- Isovaleric Acidemia (IVA)
- Glutaric Aciduria Type I (GA-I)
- 3-hydroxy-3-methylglutaryl CoA Lyase Deficiency (HMG)
- Multiple Carboxylase Deficiency (MCD)
- Methylmalonic Acidemia/Methylmalonyl-CoA Mutase (MUT)
- Methylmalonic Acidemia/Vitamin B12 Disorders (Cbl A,B)
- 3-methylcrotonyl-CoA Carboxylase Deficiency (3MCC)
- Propionic Acidemia (PROP)
- Beta Ketothiolase Deficiency (BKT)

Clinical Features in Children with Untreated Organic Acid Disorders

Infants with organic acid disorders often appear normal for the first few days of life, but then may develop lethargy, vomiting, hypotonia and poor feeding. If left untreated, these disorders can progress to more serious complications such as seizures, coma and death.

Laboratory Screening Tests

Organic acid disorders are screened using a tandem mass spectrophotometer (MS/MS). MS/MS technology tests for certain analytes which are present in the baby's blood sample. If a particular analyte is abnormal, the MS/MS instrument will flag that sample to indicate the abnormal result. The instrument will interpret positive samples as either low risk (LR), moderate risk (MR) or high risk (HR). Often, secondary markers are taken into consideration when determining the risk level. These secondary markers may be actual analyte levels or the ratio of two analytes. All results are reviewed by trained technicians prior to being reported.

The cutoffs values for MS/MS analytes are reviewed periodically, as more data is collected. Cutoffs are adjusted as needed, which can reduce false positive and false negative results.

Confirmatory Testing

Infants with low or moderate risk results for organic acid disorders on the initial newborn screening need to have the screening promptly repeated. If the initial results are high risk, consultation with a metabolic specialist and diagnostic testing should be promptly scheduled.

Treatment

For many organic acid disorders, early diagnosis and treatment can significantly change the outcome of the patient. Improved outcome is noted in most cases when the infant is provided a low-protein diet and carnitine supplementation. For some organic acid disorders, additional dietary supplements and/or vitamins are recommended. Aggressive treatment during metabolic crises, including glucose administration, is recommended.

Screening Practice Considerations

The newborn screening sample should be collected between 24 and 48 hours after birth.

Protein feeding is helpful in detecting these conditions as it challenges the metabolic pathways involved and causes the identifying markers to elevate above the normal cutoff levels in affected infants.

If the baby was transfused, repeat the screening on day 4 after transfusion.

Medical Consultant

A medical consultant is available to provide consultation for the follow-up, evaluation and long-term management of children with organic acid disorders. Please contact:

Dr. Majed Dasouki
KU Medical Center
Kansas City, KS
Office 913-588-6326

It is strongly recommended that prior to repeating the newborn screen practitioners should confer with the consultant. The consultant may recommend repeating the state newborn screen, or may suggest labs to draw and analyze in a practitioner's local lab. The consultant may wish to see the newborn in the office and do the lab work and assessment there. Whatever the case, we want to prevent unnecessary lab draws or inappropriate testing on these infants. In summary, please contact the consultant prior to drawing the repeat blood work.

**Overview of Follow-up Procedure
Abnormal Newborn Screening for Organic Acid Disorders**

- 1) Newborn Screening follow-up team reviews the laboratory reports that are faxed overnight from the lab or records the information provided per telephone call from the laboratory on a white phone information sheet.
- 2) If the result is considered **normal**.
 - a) Follow-up team does not receive results.
 - b) Lab will fax or mail results to doctor listed on NBS card.
- 3) If the result is **Low Risk (LR)** or **Moderate Risk (MR)**:
 - a) Lab will contact follow-up team via phone and/or email with baby's information and test results. Follow-up team will document information on white phone slip.
 - b) Follow-up team will print out baby's information from DHEL database on a yellow sheet of paper, attach the white phone slip and write the appropriate abnormal test and the result on yellow sheet.
 - c) If test results are emailed, follow-up team will print results and attach to yellow paper.
 - d) Follow-up team will enter infant's demographic data and reported test results into Access database under Organic Acid Disorders.
 - e) Follow-up team will call healthcare provider listed on report and:
 - i) Verify that they are seeing the baby.
 - ii) Inform them of results.
 - iii) Ask them to get a repeat NBS card submitted to the KS lab.
 - iv) Confirm doctor's fax number.
 - v) Inform them that a letter will be faxed to their office with the results and instructions.
 - f) Follow-up team will print appropriate organic acid low risk or moderate risk letter and fax (or mail, if no fax) to healthcare provider.
 - g) Follow-up team will print organic acid parent letter and organic acid parent information sheet and mail to baby's parents to inform them that their child has an abnormal result. NOTE: If infant is in the NICU, no parent letter is sent.
 - h) Follow-up team will enter data into Excel spreadsheet "Presumptive Totals" located on the "H" drive.
 - i) Lab will fax or mail results to doctor listed on NBS card. Lab will fax results to follow-up team. Report is attached to yellow sheet.
 - j) Follow-up team will enter lab information into WebIZ and set a follow-up reminder for 1 month from date of letter. NOTE: Name changes are documented on the copy of the lab report. Surname changes are also documented in WebIZ as an alias.
 - k) When complete, paperwork is filed by infant's date of birth.
- 4) If the results are considered **High Risk (HR)**:
 - a) Lab will contact follow-up team via phone and/or email with baby's information and test results. Follow-up team will document information on white phone slip.
 - b) Follow-up team will print out baby's information from DHEL database on a green sheet of paper, attach the white phone slip and write the appropriate abnormal test and the result on green sheet.
 - c) If test results are emailed, follow-up team will print results and attach to green paper.

- d) Follow-up team will enter infant's demographic data and reported test results into Access database under Organic Acid Disorders.
- e) Follow-up team will call healthcare provider listed on report and:
 - i) Verify that they are seeing the baby.
 - ii) Inform them of results.
 - iii) Ask them to notify parents and arrange appointment with specialist.
 - iv) Confirm doctor's fax number.
 - v) Inform them that a letter will be faxed to their office with the results and instructions.
- f) Follow-up team will print appropriate organic acid high risk letter and physician report form and fax (or mail, if no fax) to healthcare provider.
- g) Follow-up team will print organic acid parent letter and organic acid parent information sheet and mail to baby's parents to inform them that their child has an abnormal result. NOTE: If infant is in the NICU, no parent letter is sent.
- h) Follow-up team will enter data into Excel spreadsheet "Presumptive Totals" located on the "H" drive.
- i) Lab will fax or mail results to doctor listed on NBS card.
- j) Lab will fax results to follow-up team. Report is attached to green sheet.
- k) Follow-up team will enter lab information into WebIZ and set a follow-up reminder for 1 month from date of letter. NOTE: Name changes are documented on the copy of the lab report. Surname changes are also documented in WebIZ as an alias.
- l) When complete, paperwork is filed by infant's date of birth.



NEWBORN SCREENING ACT SHEET

SCREEN FOR: ELEVATED C5-OH ACYLCARNITINE

CONDITION: ORGANIC ACIDEMIAS (3MCC, HMG, BKT & MCD)

DIFFERENTIAL DIAGNOSIS: Most likely 3-methylcrotonyl-CoA carboxylase (3MMC) deficiency (**infant or mother**); may be 3-hydroxy-3-methylglutaryl (HMG)-CoA lyase deficiency; β -ketothiolase (BKT) deficiency; or multiple carboxylase (MCD) deficiency including biotinidase deficiency.

METABOLIC DESCRIPTION: Each of the disorders is caused by a deficiency of the relevant enzyme. In most of the disorders, the substrate, for which the enzyme is named, accumulates along with its potentially toxic metabolites.

MEDICAL EMERGENCY - ACTION TO BE TAKEN IMMEDIATELY:

- Contact family to inform them of the newborn screening results and ascertain clinical status (poor feeding, vomiting, lethargy).
- Consult with pediatric metabolic specialist.
- Evaluate the newborn (hypoglycemia, ketonuria, metabolic acidosis). If any of these parameters are abnormal or the infant is ill, initiate emergency treatment as indicated by metabolic specialist and transport IMMEDIATELY to tertiary center with metabolic specialist.
- Initiate timely confirmatory/diagnostic testing as recommended by specialist.
- Educate family about signs, symptoms and need for urgent treatment of metabolic acidosis (poor feeding, vomiting, lethargy).
- Report findings to newborn screening program.

CONFIRMATION OF DIAGNOSIS: Confirmatory tests include urine organic acids on infant and mother, plasma acylcarnitine analysis, and serum biotinidase assay. The organic acids analysis on infant and mother should clarify the differential except for biotinidase deficiency (clarified by biotinidase assay).

CLINICAL EXPECTATIONS: The neonate is usually asymptomatic in 3MMC deficiency. However, episodic hypoglycemia, lethargy, hypotonia and mild developmental delay can occur at any time from the neonatal period through childhood for any of these disorders. There is beneficial treatment that is specialized to each condition.

REPORTING: Report diagnostic result to family and Kansas NBS program.

SPECIALIST:

Dr. Majed Dasouki
KU Medical Center
Kansas City, KS

Office: 913-588-6326
FAX: 913-558-6288



NEWBORN SCREENING ACT SHEET

SCREEN FOR: ELEVATED C5-DC ACYLCARNITINE

CONDITION: GLUTARYL-COA DEHYDROGENASE DEFICIENCY (GA-I)

DIFFERENTIAL DIAGNOSIS: Glutaric aciduria (GA-I)

METABOLIC DESCRIPTION: GA-I is caused by a defect of glutaryl-CoA dehydrogenase which limits the metabolism of glutaryl-CoA to crotonyl-CoA, resulting in increased glutaric acid (toxic) and its metabolites.

ACTION TO BE TAKEN IMMEDIATELY:

- Contact family to inform them of the newborn screening result.
- Consult with pediatric metabolic specialist.
- Evaluate the newborn for macrocephaly and muscle hypotonia. Initiate confirmatory/diagnostic testing as recommended by metabolic specialist.
- Refer to metabolic specialist to be seen as soon as possible but not later than three weeks.
- Educate family about diagnostic possibilities, complexity of diagnostic work-up and the possibility of neurodegenerative crisis with an intercurrent infectious illness.
- IMMEDIATE treatment with IV glucose is needed for intercurrent infectious illness.
- Report findings to newborn screening program.

CONFIRMATION OF DIAGNOSIS: Urine organic acid analysis will reveal **elevated glutaric acid** and **3-hydroxyglutaric acid**. Testing should be ordered promptly and is often diagnostic. If urine organic acids don't confirm the diagnosis, the metabolic specialist will consider analyzing glutarylcarnitine in urine and 3-hydroxyglutaric acid in blood and CSF, enzyme assay in fibroblasts, and molecular analysis of the GCDH gene.

CLINICAL EXPECTATIONS: The neonate with glutaric aciduria type I is usually macrocephalic but otherwise asymptomatic. Later signs include metabolic ketoacidosis, failure to thrive and sudden onset of dystonia and athetosis due to irreversible striatal damage. With appropriate treatment, 60-70% of patients will not suffer neurodegenerative disease.

REPORTING: Report diagnostic result to family and Kansas NBS program.

SPECIALIST:

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NEWBORN SCREENING ACT SHEET

SCREEN FOR: ELEVATED C5 ACYLCARNITINE

CONDITION: ISOVALERIC ACIDEMIA (IVA)

DIFFERENTIAL DIAGNOSIS: Isovaleric acidemia (IVA)

METABOLIC DESCRIPTION: IVA results from a defect in the metabolism of the branched chain amino acid, leucine (isovaleryl-CoA dehydrogenase in IVA). Specific metabolites accumulate and are potentially toxic.

MEDICAL EMERGENCY - ACTION TO BE TAKEN IMMEDIATELY:

- Contact family to inform them of the newborn screening result and ascertain clinical status (poor feeding, vomiting, lethargy, tachypnea, odor of sweaty feet).
- Consult with pediatric metabolic specialist.
- Evaluate the newborn; if infant is ill, initiate emergency treatment as indicated by metabolic specialist and transport **IMMEDIATELY** to tertiary center with metabolic specialist.
- Initiate timely confirmatory/diagnostic testing as recommended by specialist.
- Educate family about signs, symptoms and need for urgent treatment of metabolic acidosis (poor feeding, vomiting, lethargy, tachypnea, odor of sweaty feet).
- Report findings to newborn screening program.

CONFIRMATION OF DIAGNOSIS: Plasma acylcarnitine analysis confirms the increased C5. Urine organic acid analysis will show isovalerylglycine in IVA. Urine acylglycine and acylcarnitine analysis may also be informative.

CLINICAL EXPECTATIONS: Isovaleric acidemia presents in the neonate with metabolic ketoacidosis, a "sweaty feet" odor, dehydration, hyperammonemia, ketonuria, vomiting, hypoglycemia, and failure to thrive. Milder variants without neonatal illness exist. Long term prognosis of IVA with appropriate therapy is good.

REPORTING: Report diagnostic result to family and Kansas NBS program.

SPECIALIST:

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KU Medical Center
Kansas City, KS

Office: 913-588-6326
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NEWBORN SCREENING ACT SHEET

SCREEN FOR: ELEVATED C3 ACYLCARNITINE

CONDITION: PROPIONIC ACIDEMIA (PROP) AND
METHYLMALONIC ACIDEMIA (MUT, Cbl A & B)

DIFFERENTIAL DIAGNOSIS: Propionic acidemia (PROP); Methylmalonic acidemias (MUT) including defects in B12 synthesis and transport; severe maternal B12 deficiency.

METABOLIC DESCRIPTION: PROP is caused by a defect in Propionyl-CoA carboxylase which converts propionyl-CoA to methylmalonyl-CoA; MUT results from a defect in methylmalonyl-CoA mutase which converts methylmalonyl-CoA to succinyl-CoA or from lack of the required B₁₂ cofactor for methylmalonyl-CoA mutase (cobalamin A,B,C,D and F).

MEDICAL EMERGENCY - ACTION TO BE TAKEN IMMEDIATELY:

- Contact family to inform them of the newborn screening result and ascertain clinical status (poor feeding, vomiting, lethargy, tachypnea.)
- Consult with pediatric metabolic specialist.
- Evaluate the newborn; check urine for ketones and, if elevated or infant is ill, initiate emergency treatment as indicated by metabolic specialist and transport immediately to tertiary center with metabolic specialist.
- Initiate timely confirmatory/diagnostic testing as recommended by specialist.
- Educate family about signs, symptoms and need for urgent treatment of hyperammonemia and metabolic acidosis (poor feeding, vomiting, lethargy, tachypnea).
- Report findings to the newborn screening program.

CONFIRMATION OF DIAGNOSIS: Plasma acylcarnitine confirms the increased C3. Blood amino acid analysis may show increased glycine. Urine organic acid analysis will demonstrate increased metabolites characteristic of propionic acidemia or increased methylmalonic acid characteristic of methylmalonic acidemia.

CLINICAL EXPECTATIONS: Patients with PROP and severe cases of MUT typically present in the neonatal period with metabolic ketoacidosis, dehydration, hyperammonemia, ketonuria, vomiting, hypoglycemia, and failure to thrive. Long-term complications are common; early treatment may be lifesaving and continued treatment may be beneficial.

REPORTING: Report diagnostic result to family and Kansas NBS program.

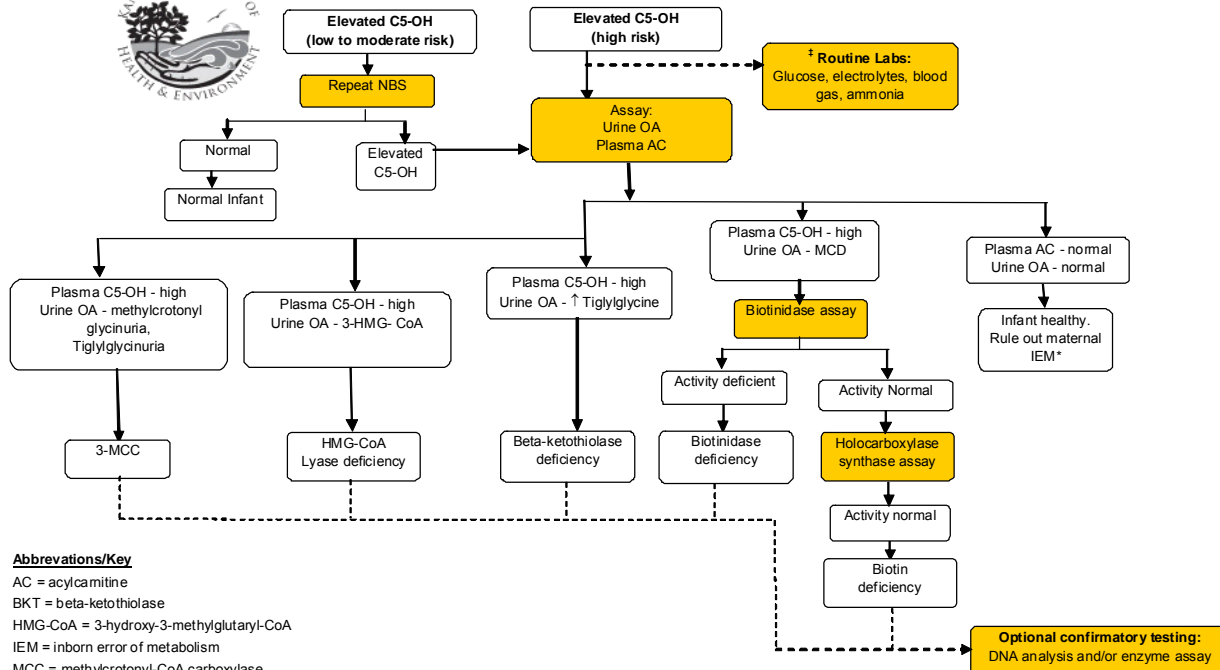
SPECIALIST:

Dr. Majed Dasouki
KU Medical Center
Kansas City, KS

Office: 913-588-6326
FAX: 913-588-6288



ELEVATED C5-OH



Abbreviations/Key

AC = acylcarnitine
 BKT = beta-ketothiolase
 HMG-CoA = 3-hydroxy-3-methylglutaryl-CoA
 IEM = inborn error of metabolism
 MCC = methylcrotonyl-CoA carboxylase
 MCD = multiple carboxylase deficiency
 NBS = Newborn Screening
 OA = organic acid

Action steps are shown in gold (shaded) boxes; results are in plain boxes.
 Dash lines indicate optional steps

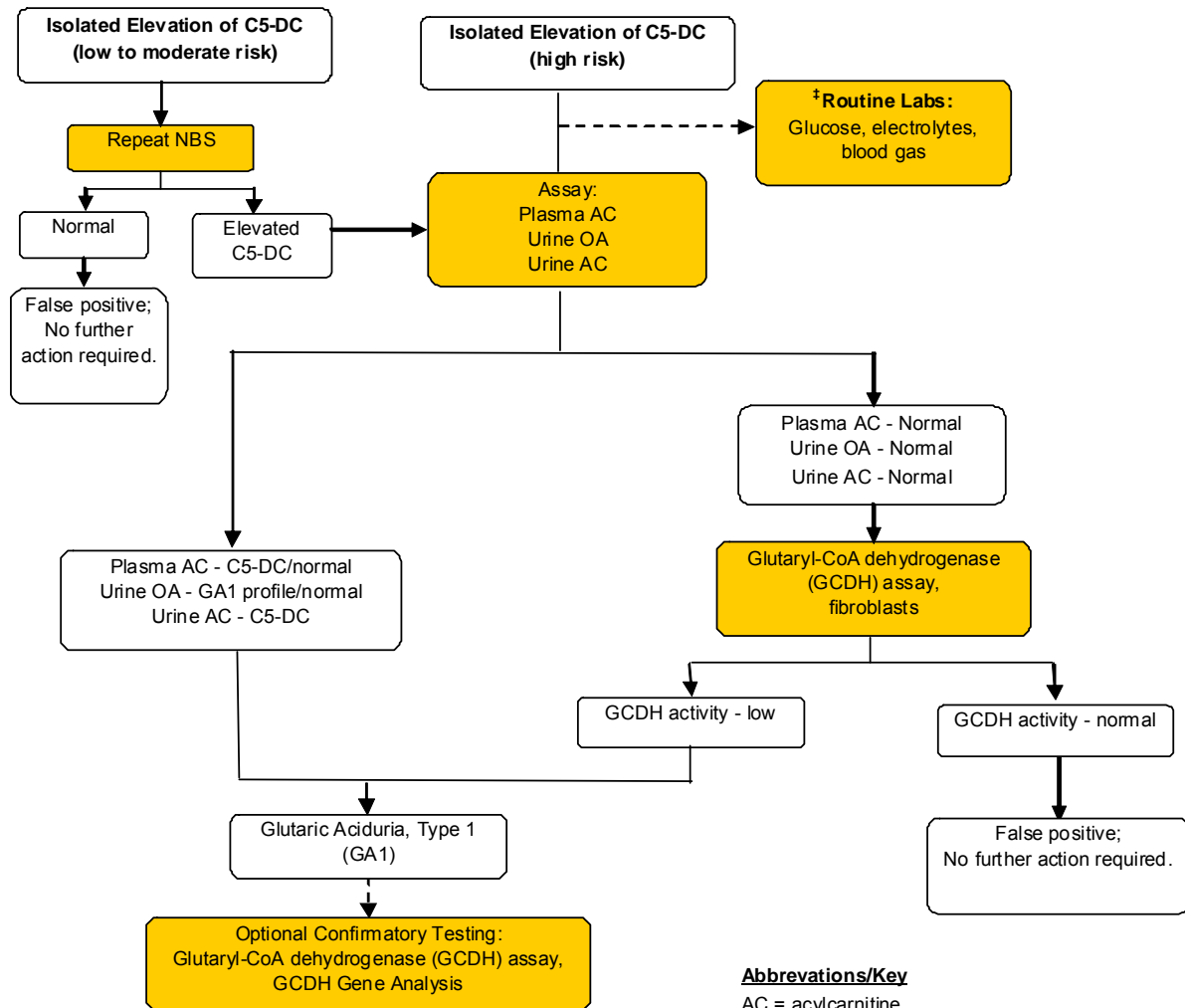
* = Maternal MCC and holocarboxylase deficiency have been reported as having been identified in newborn screening.

‡ = When the positive predictive value of screening is sufficiently high and the risk to the newborn is high, some initiate diagnostic

DISCLAIMER: These algorithms and guidelines were adapted from the American College of Medical Genetics algorithm sheets. They are designed primarily as an educational resource for physicians to help them provide quality medical services. Adherence to these standards and guidelines does not necessarily ensure a successful medical outcome. These standards and guidelines should not be considered inclusive of all proper procedures and tests or exclusive of other procedures and tests that are reasonable directed to obtaining the same results. In determining the propriety of any specific procedure or test, the healthcare provider should apply his or her own professional judgment to the specific clinical circumstances presented by the individual patient or specimen. It may be prudent, however, to document in the patient's record the rationale for any significant deviation from these standards and guidelines



ELEVATED C5-DC (ISOLATED)



Action steps are shown in gold (shaded) boxes; results are in plain boxes.
Dash lines indicate optional steps

Abbreviations/Key

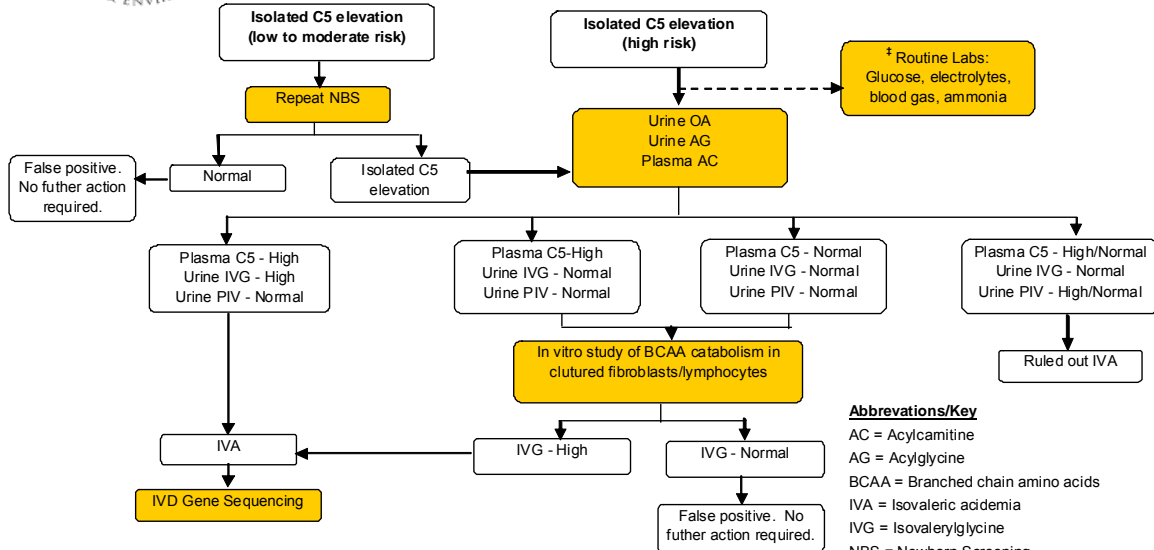
AC = acylcarnitine
DC = dicarboxylic
GA = glutaric acid
GCDH = glutaryl-CoA dehydrogenase
NBS = Newborn Screening
OA = organic acid

† = When the positive predictive value of screening is sufficiently high and the risk to the baby is high, some initiate diagnostic studies at the same time as the confirmation of screening result is done.

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ELEVATED C5 (ISOLATED)



Abbreviations/Key

AC = Acylcamitine
 AG = Acylglycine
 BCAA = Branched chain amino acids
 IVA = Isovaleric acidemia
 IVG = Isovalerylglycine
 NBS = Newborn Screening
 OA = Organic Acid
 PIV = Pivalic acid (antibiotic)

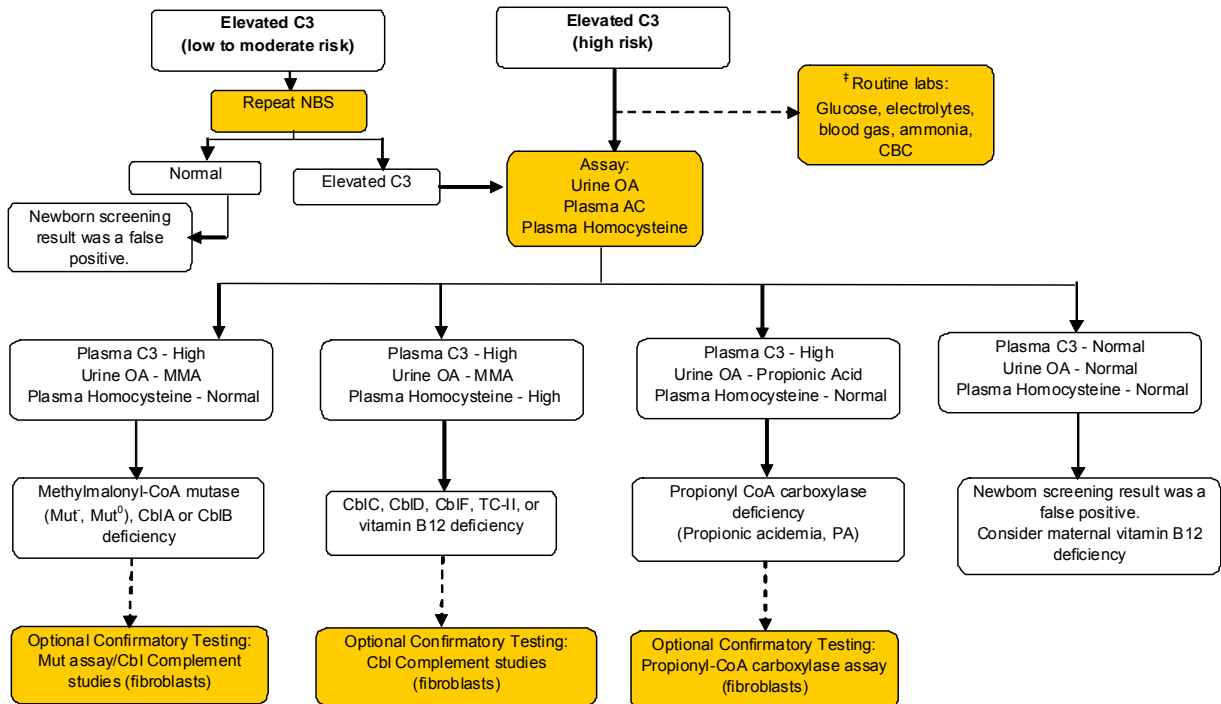
† = When the positive predictive value of screening is sufficiently high and the risk to the infant is high, some initiate diagnostic studies that are locally available at the same time as confirmation of the screening result is done.

Action steps are shown in gold (shaded) boxes; results are in plain boxes.
 Dash lines indicate optional steps

DISCLAIMER: These algorithms and guidelines were adapted from the American College of Medical Genetics algorithm sheets. They are designed primarily as an educational resource for physicians to help them provide quality medical services. Adherence to these standards and guidelines does not necessarily ensure a successful medical outcome. These standards and guidelines should not be considered inclusive of all proper procedures and tests or exclusive of other procedures and tests that are reasonable directed to obtaining the same results. In determining the propriety of any specific procedure or test, the healthcare provider should apply his or her own professional judgment to the specific clinical circumstances presented by the individual patient or specimen. It may be prudent, however, to document in the patient's record the rationale for any significant deviation from these standards and guidelines.



ELEVATED C3 (isolated)



Abbreviations/Key

AC = acylcarnitine
 CBC = complete blood count
 Cbl = cobalamin
 MMA = methylmalonic acidemia
 Mut = mutase
 OA = organic acid
 TC-II = transcobalamin II

Action steps are shown in gold (shaded) boxes; results are in plain boxes.
 Dash lines indicate optional steps

‡ When the positive predictive value of screening is sufficiently high and the risk to the infant is high, some initiate diagnostic studies that are locally available at the same time as confirmation of the screening result is done.

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EXAMPLE OF 1ST LETTER TO PHYSICIAN'S FOR LOW RISK ORGANIC ACID DISORDERS



Mark Parkinson, Governor
Roderick L. Bremby, Secretary

DEPARTMENT OF HEALTH
AND ENVIRONMENT

www.kdheks.gov

**Elevated C5 Lab Report
Kansas Newborn Screening Program**

Date

Doctor's Name
Address Line 1
Address Line 2

RE: Baby's Name
DOB: xx/xx/xxxx

MOTHER'S NAME: Mother's Name
PHONE NUMBER: xxx-xxx-xxxx

Specimen date: xx/xx/xxxx

C5: Result $\mu\text{mol/L}$
Expected range: $< 0.71 \mu\text{mol/L}$

The newborn screening result above is consistent with a **low** risk for isovaleric acidemia. This C5 level is considered to be indeterminate because isovaleric acidemia cannot be ruled out. Increased analyte levels may be seen if the specimen is collected from an infant less than 24 hours of age; a premature infant; or an acutely ill infant.

The final newborn screening lab report will be sent when all testing is completed.

RECOMMENDATION:

Repeat the screening test within 1 to 3 days of receiving this notice, and send the specimen to the State lab for analysis. (If the baby was transfused, repeat the screening on day 4 after transfusion). If the repeat screen is positive or indeterminate, additional testing and consultation with a specialist will be required.

In accordance with Kansas Administrative Regulation 28-4-502, it is the responsibility of the attending physician or other birth attendant to obtain repeat specimens when needed to complete the screening process.

For consultation, please contact:

Dr. Majed Dasouki
KU Medical Center
Kansas City
Office 913-588-6326
Pager 913-917-3647

Additional information is available on the Kansas Newborn Screening Website at:
http://www.kdheks.gov/newborn_screening/info_professionals.htm.

You may contact the Newborn Screening Program at (785) 291-3363 or 1-800-332-6262 if you have any questions or concerns.

EXAMPLE OF 1ST LETTER SENT TO PHYSICIAN FOR MODERATE RISK ORGANIC ACID DISORDERS



Mark Parkinson, Governor
Roderick L. Bremby, Secretary

DEPARTMENT OF HEALTH
AND ENVIRONMENT

www.kdheks.gov

**Elevated C5 Lab Report
Kansas Newborn Screening Program**

Date

Doctor's Name
Address Line 1
Address Line 2

RE: Baby's Name
DOB: xx/xx/xxxx

MOTHER'S NAME: Mother's Name
PHONE NUMBER: xxx-xxx-xxxx

Specimen date: xx/xx/xxxx

C5: Result $\mu\text{mol/L}$
Expected range: $< 0.71 \mu\text{mol/L}$

The newborn screening result above is consistent with a **moderate** risk for isovaleric acidemia. This C5 level is considered to be indeterminate because isovaleric acidemia cannot be ruled out. Increased analyte levels may be seen if the specimen is collected from an infant less than 24 hours of age; a premature infant; or an acutely ill infant.

The final newborn screening lab report will be sent when all testing is completed.

RECOMMENDATION:

Repeat the screening test within 1 to 3 days of receiving this notice, and send the specimen to the State lab for analysis. If the baby was transfused, repeat the screening on day 4 after transfusion. If the repeat screen is positive or indeterminate, additional testing and consultation with a specialist will be required.

In accordance with Kansas Administrative Regulation 28-4-502, it is the responsibility of the attending physician or other birth attendant to obtain repeat specimens when needed to complete the screening process.

For consultation, please contact:

Dr. Majed Dasouki
KU Medical Center
Kansas City
Office 913-588-6326
Pager 913-917-3647

Additional information is available on the Kansas Newborn Screening Website at:
http://www.kdheks.gov/newborn_screening/info_professionals.htm.

You may contact the Newborn Screening Program at (785) 291-3363 or 1-800-332-6262 if you have any questions or concerns.

EXAMPLE OF 1ST LETTER SENT TO PHYSICIAN FOR HIGH RISK ORGANIC ACID DISORDERS



Mark Parkinson, Governor
Roderick L. Bremby, Secretary

DEPARTMENT OF HEALTH
AND ENVIRONMENT

www.kdheks.gov

**Elevated C5 Lab Report
Kansas Newborn Screening Program**

Date

Doctor's Name
Address Line 1
Address Line 2

RE: Baby's Name
DOB: xx/xx/xxxx

MOTHER'S NAME: Mother's Name
PHONE NUMBER: xxx-xxx-xxxx

Specimen date: xx/xx/xxxx

C5: Result $\mu\text{mol/L}$
Expected range: $< 0.71 \mu\text{mol/L}$

The newborn screening result above is **highly suggestive** of isovaleric acidemia. Isovaleric acidemia presents in the neonate with metabolic ketoacidosis, a "sweaty feet" odor, dehydration, hyperammonemia, ketonuria, vomiting, hypoglycemia and failure to thrive.

The final newborn screening lab report will be sent when all testing is completed.

RECOMMENDATION:

Immediate consultation with the consultant listed below is essential for diagnostic testing and genetic counseling. Please call to arrange an immediate appointment.

In accordance with Kansas Administrative Regulation 28-4-502, it is the responsibility of the attending physician or other birth attendant to obtain repeat specimens when needed to complete the screening process.

For consultation, please contact:

Dr. Majed Dasouki
KU Medical Center
Kansas City
Office 913-588-6326
Pager 913-917-3647

PLEASE COMPLETE AND RETURN THE ENCLOSED PHYSICIAN REPORTING FORM WHEN FOLLOW UP IS COMPLETE.

Additional information is available on the Kansas Newborn Screening Website at:
http://www.kdheks.gov/newborn_screening/info_professionals.htm.

You may contact the Newborn Screening Program at (785) 291-3363 or 1-800-332-6262 if you have any questions or concerns.

EXAMPLE OF LETTER TO PHYSICIANS FOR MULTIPLE LOW OR MODERATE RISK MS/MS RESULTS



Mark Parkinson, Governor
Roderick L. Bremby, Secretary

DEPARTMENT OF HEALTH
AND ENVIRONMENT

www.kdheks.gov

**Multiple Elevated MS/MS Analytes Lab Report
Kansas Newborn Screening Program**

Date

Doctor's Name
Address Line 1
Address Line 2

RE: Baby's Name
DOB: xx/xx/xxxx

MOTHER'S NAME: Mother's Name
PHONE NUMBER: xxx-xxx-xxxx

Specimen date: xx/xx/xxxx

The above infant has multiple MS/MS analyte results that are within the low-moderate risk range. The elevated results may be due to TPN or other supplements, but further testing is required to identify any true positive results.

Analyte	Result (µmol/L)	Expected Range (µmol/L)	Associated Disorder
Phenylalanine	Result	< 128	PKU
Leucine	Result	< 250	MSUD
Methionine	Result	< 79	HCY
Tyrosine	Result	< 260	TYR I
Argininosuccinic Acid	Result	< 0.60	ASA
Citrulline	Result	< 53	CIT
C8	Result	< 0.38	MCADD
C14:1	Result	< 0.66	VLCADD
C16-OH	Result	< 0.12	LCHAD/TFP
C0	Result	> 14.5	CUD
C5	Result	< 0.71	IVA
C5DC	Result	< 0.32	GA-1
C5-OH	Result	< 0.61	3MCC, HMG, BKT AND MCD
C3	Result	< 6.6	PROP, MUT, Cbi A&B

NR = No Result reported at this time

RECOMMENDATION:

Infant should be off TPN or other dietary supplements for 48 hours prior to retest. Repeat the screening test and send the specimen to the State lab for analysis. (If the baby was transfused, repeat the screening on day 4 after transfusion). If the repeat screen is positive or indeterminate, additional testing and consultation with a specialist will be required.

In accordance with Kansas Administrative Regulation 28-4-502, it is the responsibility of the attending physician or other birth attendant to obtain repeat specimens when needed to complete the screening process.

Additional information is available on the Kansas Newborn Screening Website at:
http://www.kdheks.gov/newborn_screening/info_professionals.htm.

You may contact the Newborn Screening Program at (785) 291-3363 or 1-800-332-6262 if you have any questions or concerns.



Mark Parkinson, Governor
Roderick L. Bremby, Secretary

DEPARTMENT OF HEALTH
AND ENVIRONMENT

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**Elevated C5-OH Lab Report
Kansas Newborn Screening Program**

Date

Doctor's Name
Address Line 1
Address Line 2

RE: Baby's Name
DOB: xx/xx/xxxx

MOTHER'S NAME: Mother's Name
PHONE NUMBER: xxx-xxx-xxxx

1st specimen date: xx/xx/xxxx
2nd specimen date: xx/xx/xxxx

C5-OH: Result $\mu\text{mol/L}$
C5-OH: Result $\mu\text{mol/L}$
Expected result: $< 0.61 \mu\text{mol/L}$

The newborn screening results above are **suggestive** of an organic acid disorder, including 3-methylcrotonyl-CoA carboxylase (3MCC) deficiency, 3-hydroxy-3-methylglutaryl (HMG)-CoA lyase deficiency, beta-ketothiolase (BKT) deficiency, multiple carboxylase (MCD) deficiency or biotinidase deficiency. A neonate affected with an organic acid disorder is usually well at birth and for the first few days of life. The usual clinical presentation is that of toxic encephalopathy and includes vomiting, poor feeding, neurologic symptoms such as seizures and abnormal tone, and lethargy progressing to coma.

The final newborn screening lab report will be sent when all testing is completed.

RECOMMENDATION:

The repeat newborn screen is elevated. Consultation with the consultant listed below is essential for diagnostic testing and genetic counseling. Please call to arrange an immediate appointment.

In accordance with Kansas Administrative Regulation 28-4-502, it is the responsibility of the attending physician or other birth attendant to obtain repeat specimens when needed to complete the screening process.

For consultation, please contact:
Dr. Majed Dasouki
KU Medical Center
Kansas City, KS
Office 913-588-6326
Pager 913-917-3647

PLEASE COMPLETE AND RETURN THE ENCLOSED PHYSICIAN REPORTING FORM WHEN FOLLOW UP IS COMPLETE.

Additional information is available on the Kansas Newborn Screening Website at:
http://www.kdheks.gov/newborn_screening/info_professionals.htm.

You may contact the Newborn Screening Program at (785) 291-3363 or 1-800-332-6262 if you have any questions or concerns.

EXAMPLE OF 3MCC/HMG/BKT/MCD PHYSICIAN'S REPORTING FORM



Mark Parkinson, Governor
Roderick L. Bremby, Secretary

DEPARTMENT OF HEALTH
AND ENVIRONMENT

www.kdheks.gov

**ELEVATED C5-OH (Possible 3MCC / HMG-CoA Lyase/ BKT / MCD/Biotinidase Deficiency)
NEWBORN SCREENING
PHYSICIAN REPORTING FORM**

****Return this form When Follow-Up is Complete ****

Date

Doctor's Name
Address Line 1
Address Line 2

If this infant is not a current patient of this practice, record name and contact information for Primary Care Physician and return this form.

RE: Baby's Name
DOB: xx/xx/xxxx

Baby's name if different than listed

DIAGNOSIS EXCLUDED: Date Excluded: _____

Baby does **NOT** have 3MCC deficiency, HMG-CoA lyase deficiency, beta ketothiolase deficiency, multiple carboxylase deficiency or biotinidase deficiency

DIAGNOSIS CONFIRMED: Date Diagnosis Confirmed: _____

Baby has (circle one):
3MCC deficiency / HMG-CoA lyase deficiency / BKT deficiency / MCD /
Biotinidase deficiency

Lab Results: (please fill in and attach a copy of specialist's report)

Acylcarnitine profile: _____

Urine organic acids: _____

Additional lab results: _____

Date treatment began: _____

Baby referred to specialist (please attach copy of specialist's report)

Name of specialist: _____

FORM CONTINUES ON BACK

EXAMPLE OF GA-1 PHYSICIAN'S REPORTING FORM



Mark Parkinson, Governor
Roderick L. Bremby, Secretary

DEPARTMENT OF HEALTH
AND ENVIRONMENT

www.kdheks.gov

**ELEVATED C5-DC (Possible GA-I)
NEWBORN SCREENING
PHYSICIAN REPORTING FORM**

****Return this form When Follow-Up is Complete ****

Date

Doctor's Name
Address Line 1
Address Line 2

If this infant is not a current patient of this practice, record name and contact information for Primary Care Physician and return this form.

RE: Baby's Name
DOB: xx/xx/xxxx

Baby's name if different than listed

DIAGNOSIS EXCLUDED: Date Excluded: _____

Baby does **NOT** have Glutaric Aciduria Type I

DIAGNOSIS CONFIRMED: Date Diagnosis Confirmed: _____

Baby has Glutaric Aciduria Type I

Lab Results: (please fill in and attach a copy of specialist's report)

Acylcarnitine profile: _____

Urine organic acids: _____

Additional lab results: _____

Date treatment began: _____

Baby referred to specialist (please attach copy of specialist's report)

Name of specialist: _____

FORM CONTINUES ON BACK

EXAMPLE OF IVA PHYSICIAN'S REPORTING FORM



Mark Parkinson, Governor
Roderick L. Bremby, Secretary

DEPARTMENT OF HEALTH
AND ENVIRONMENT

www.kdheks.gov

**ELEVATED C5 (Possible IVA)
NEWBORN SCREENING
PHYSICIAN REPORTING FORM**

****Return this form When Follow-Up is Complete ****

Date

Doctor's Name
Address Line 1
Address Line 2

If this infant is not a current patient of this practice, record name and contact information for Primary Care Physician and return this form.

RE: Baby's Name
DOB: xx/xx/xxxx

Baby's name if different than listed

DIAGNOSIS EXCLUDED: Date Excluded: _____

Baby does **NOT** have Isovaleric Acidemia

DIAGNOSIS CONFIRMED: Date Diagnosis Confirmed: _____

Baby has Isovaleric Acidemia

Lab Results: (please fill in and attach a copy of specialist's report)

Acylcarnitine profile: _____

Urine organic acids: _____

Additional lab results: _____

Date treatment began: _____

Baby referred to specialist (please attach copy of specialist's report)

Name of specialist: _____

FORM CONTINUES ON BACK

EXAMPLE OF PROP/MUT/CBL A,B PHYSICIAN'S REPORTING FORM



Mark Parkinson, Governor
Roderick L. Bremby, Secretary

DEPARTMENT OF HEALTH
AND ENVIRONMENT

www.kdheks.gov

**ELEVATED C3 (Possible PROP / MUT / CBL A,B)
NEWBORN SCREENING
PHYSICIAN REPORTING FORM**

****Return this form When Follow-Up is Complete ****

Date

Doctor's Name
Address Line 1
Address Line 2

If this infant is not a current patient of this practice, record name and contact information for Primary Care Physician and return this form.

RE: Baby's Name
DOB: xx/xx/xxxx

Baby's name if different than listed

DIAGNOSIS EXCLUDED: Date Excluded: _____

Baby does **NOT** have Propionic Acidemia or Methylmalonic Acidemia due to Mutase or Cobalamin A or B deficiencies

DIAGNOSIS CONFIRMED: Date Diagnosis Confirmed: _____

Baby has PROP or MMA mutase deficiency or MMA Cbl A or B deficiency (circle one)

Lab Results: (please fill in and attach a copy of specialist's report)

Acylcarnitine profile: _____

Urine organic acids: _____

Additional lab results: _____

Date treatment began: _____

Baby referred to specialist (please attach copy of specialist's report)

Name of specialist: _____

FORM CONTINUES ON BACK



3MCC Deficiency Information for Health Professionals

3-Methylcrotonyl-CoA Carboxylase deficiency (3MCC deficiency) is an organic acid disorder in which individuals are unable to process leucine.

✓ Clinical Symptoms

Symptoms start after 3 months of age in some individuals; others will never have symptoms. 3MCC deficiency can cause metabolic crises, particularly after fasting, illness/infection, or high protein intake. Symptoms of a metabolic crisis include feeding difficulties, vomiting, behavioral changes, hypotonia, lethargy, hypoglycemia, metabolic acidosis, increased ketones in urine, and high levels of ammonia in the blood. If untreated, the crisis can lead to breathing problems, liver failure, seizures, coma, and death. Repeat crises can cause brain damage.

Even without a metabolic crisis, symptoms may include poor growth and development, and hypotonia or spasticity. Adulthood symptoms include weakness and lethargy.

✓ Incidence

3MCC deficiency occurs in greater than 1 in 75,000 births.

✓ Genetics of 3MCC deficiency

Mutations in the MCCC1 and MCCC2 genes cause 3MCC deficiency. Mutations in these genes prevent or reduce the production of the enzyme 3-methylcrotonyl-CoA carboxylase, which is necessary for the processing of leucine. Mutations, therefore, cause a buildup of the byproducts of leucine processing in the body.

✓ How do people inherit 3MCC deficiency?

3MCC deficiency is inherited in an autosomal recessive manner. Parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but do not show signs and symptoms of the condition. Each pregnancy between carrier parents has a 25% chance of producing a child affected with 3MCC deficiency, a 50% chance of producing an unaffected carrier child, and a 25% chance of producing a child who is unaffected and is not a carrier.

✓ Treatment

Many children identified through newborn screening will not require treatment. If individuals show symptoms of 3MCC deficiency, treatment is necessary for normal growth and development. Individuals may need a diet low in leucine and protein. L-carnitine supplementation may be beneficial and individuals should avoid fasting.

✓ **Screening Methodology**

Primary screening for 3MCC deficiency utilizes tandem mass spectrometry. Individuals who screen positive for 3MCC deficiency will have elevated levels of C5-OH (3-hydroxyisovaleryl carnitine). False positive and false negative results are possible with this screen.

✓ **What to do After Receiving Presumptive Positive 3MCC Deficiency Screening Results**

- 1) The clinician should immediately check on the clinical status of the baby.
- 2) Consultation with a metabolic specialist is essential.
- 3) Call KS Newborn Screening Program at 785-291-3363 with questions about results.
- 4) Report clinical findings to the Newborn Screening Program at 785-291-3363.
- 5) Same birth siblings (twins, triplets) of infants diagnosed with 3MCC deficiency should be re-screened; additional testing of these siblings also may be indicated.
- 6) Consider testing older siblings of affected individuals. Many individuals may have no symptoms of this condition and may be undiagnosed. Maternal 3MCC deficiency may also need to be excluded.

✓ **Confirmation of Diagnosis**

The diagnosis of 3MCC deficiency is confirmed through urine organic acid analysis and plasma acylcarnitine analysis.

✓ **Communication of Results to Parents**

If a baby has a presumptive positive 3MCC deficiency newborn screening result, additional testing needs to be performed to confirm a diagnosis. In accordance with Kansas Administrative Regulation 28-4-502, it is the responsibility of the attending physician or other birth attendant to obtain repeat specimens when needed to complete the screening process.

If a baby is diagnosed with 3MCC deficiency, the following points should be conveyed to parents:

- ***If treatment is required, it is likely to be life long.***
- ***Parent should understand that treatment is not curative and that all morbidity cannot necessarily be prevented. Long-term management, monitoring, and compliance with treatment recommendations are essential to the child's well-being. A multidisciplinary approach is recommended and should include pediatrics, metabolic specialists, and a dietician.***
- ***Genetic services may be indicated. A list of geneticists and counselors, whose services are available in Kansas, should be given to the parents if they have not already seen a geneticist.***

For consultation, contact:

Dr. Majed Dasouki
KU Medical Center
Kansas City, KS
913-588-6362

11/24/08



Beta Ketothiolase Deficiency Information for Health Professional

Beta ketothiolase deficiency (BKT) is an organic acid disorder that results from an inability to process the amino acid isoleucine.

✓ Clinical Symptoms

Symptoms usually begin around one year of age. Individuals with beta ketothiolase deficiency are at an increased risk of developing metabolic crises, particularly after fasting, illness/infection, or high protein intake. Metabolic crises can cause the following symptoms: lethargy, feeding difficulties, ketosis, fever, diarrhea, vomiting, metabolic acidosis, hypoglycemia, coma, and death. Long-term effects in untreated individuals include cardiomegaly, prolonged QT interval, neutropenia, thrombocytopenia, failure to thrive, abnormal muscle tone, ataxia, and mental retardation.

✓ Incidence

Beta ketothiolase deficiency occurs in less than 1 in 100,000 births.

✓ Genetics of beta ketothiolase deficiency

Mutations in the ACAT1 gene cause beta ketothiolase deficiency. Mutations in this gene reduce or eliminate the activity of the enzyme mitochondrial acetoacetyl-CoA thiolase. This enzyme is necessary to process isoleucine. When an affected individual consumes proteins and fats, toxic byproducts accumulate in the body causing the symptoms of this condition and resulting in ketoacidosis.

✓ How do people inherit beta ketothiolase deficiency?

Beta ketothiolase deficiency is inherited in an autosomal recessive manner. Parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but do not show signs and symptoms of the condition. Each pregnancy between carrier parents has a 25% chance of producing a child affected with beta ketothiolase deficiency, a 50% chance of producing an unaffected carrier child, and a 25% chance of producing a child who is unaffected and is not a carrier.

✓ Treatment

Immediate diagnosis and treatment of beta ketothiolase deficiency is critical to normal growth and development. L-carnitine supplementations may be beneficial. During a metabolic crisis, glucose and bicarbonate via IV may be necessary. Individuals should avoid fasting. Some children may need a low-protein diet. Urine tests to check ketone levels are periodically needed.

✓ **Screening Methodology**

Newborn screening for beta ketothiolase deficiency utilizes tandem mass spectrometry. Elevated C5-OH (3-hydroxyisovaleryl carnitine) indicates the possibility of beta ketothiolase deficiency. False positive and false negative results are possible with this screen

✓ **What to do After Receiving Presumptive Positive BKT Screening Results**

- 1) **The clinician should immediately check on the clinical status of the baby.**
- 2) **Consultation with a metabolic specialist is essential.**
- 3) **The specialist may request urine organic acid analysis and other labs on the baby.**
- 4) **Call KS Newborn Screening Program at 785-291-3363 with questions about results.**
- 5) **Report clinical findings to the Newborn Screening Program at 785-291-3363.**
- 6) **Same birth siblings (twins, triplets) of infants diagnosed with BKT should be re-screened; additional testing of these siblings also may be indicated.**
- 7) **Consider testing older siblings. Some individuals may be affected, but show no symptoms of the condition.**

✓ **Confirmation of Diagnosis**

The diagnosis of beta ketothiolase deficiency is confirmed through urine organic acid analysis and plasma acylcarnitine analysis.

✓ **Communication of Results to Parents**

If a baby has a presumptive positive beta ketothiolase deficiency newborn screening result, additional testing needs to be performed to confirm a diagnosis. In accordance with Kansas Administrative Regulation 28-4-502, it is the responsibility of the attending physician or other birth attendant to obtain repeat specimens when needed to complete the screening process.

If a baby is diagnosed with BKT deficiency, the following points should be conveyed to parents:

- ***Parents should understand that treatment for beta ketothiolase deficiency will be lifelong.***
- ***Parents should understand that treatment is not curative and that all morbidity cannot necessarily be prevented. Long-term management, monitoring, and compliance with treatment recommendations are essential to the child's well-being. A multidisciplinary approach is recommended and includes pediatrics and a metabolic specialist.***
- ***Genetic counseling may be indicated. A list of counselors and geneticists, whose services are available in Kansas, should be given to the parents if they have not already seen a geneticist.***

For consultation, contact:

Dr. Majed Dasouki
KU Medical Center
Kansas City, KS
913-588-6326

11/24/08



HMG-CoA Lyase Deficiency Information for Health Professionals

3-hydroxy-3-methylglutaryl-CoA lyase deficiency (HMG-CoA lyase deficiency) is an organic acid disorder.

✓ Clinical Symptoms

Symptoms begin in about 1/3 of patients during the neonatal period and the rest develop symptoms between 3 and 11 months. HMG-CoA lyase deficiency causes periods of metabolic crisis, which are generally triggered by illness or infection, high protein intake, or fasting. Metabolic crises cause lethargy, behavioral changes, hypotonia, fever, nausea, vomiting, diarrhea, hypoketotic hypoglycemia, metabolic acidosis, hyperammonia, hepatomegaly, and if untreated can lead to breathing problems, seizures, coma, and death. In approximately 20% of untreated patients, the first metabolic crisis causes death. Repeated episodes of metabolic crisis can lead to white matter changes, mental retardation, and epilepsy. Possible long-term effects include: cardiomyopathy with arrhythmia, pancreatitis, nonprogressive deafness, retinitis pigmentosa, learning disabilities or mental retardation.

✓ Incidence

This condition occurs in less than 1 in 100,000 births.

✓ Genetics of HMG-CoA lyase deficiency

Mutations in the HMGCL gene cause HMG-CoA lyase deficiency. Mutations in this gene reduce or eliminate the activity of the enzyme HMG-CoA lyase. This enzyme is necessary for processing leucine, as well as for producing ketones from fats.

✓ How do people inherit HMG-CoA lyase deficiency?

HMG-CoA lyase deficiency is inherited in an autosomal recessive manner. Parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but do not show signs and symptoms of the condition. Each pregnancy between carrier parents has a 25% chance of producing a child affected with HMG-CoA lyase deficiency, 50% chance of producing an unaffected carrier child, and a 25% chance of producing a child who is unaffected and is not a carrier.

✓ Treatment

Immediate diagnosis and treatment of HMG-CoA lyase deficiency is critical to normal growth, development, and survival. Individuals should follow a low-leucine, high carbohydrate diet, which generally requires medical foods and formulas, and should avoid fasting. L-carnitine supplementation may be recommended. During periods of illness, children may need to be admitted for medical care to prevent a metabolic crisis.

✓ Screening Methodology

Primary newborn screening for HMG-CoA lyase deficiency utilizes tandem mass spectrometry. Elevated levels of C5-OH (3-hydroxyisovaleryl carnitine) indicate the possibility of HMG-CoA lyase deficiency. False positive and false negative results are possible with this screen.

✓ What to do After Receiving Presumptive Positive HMG-CoA Lyase Deficiency Screening Results

- 1) The clinician should immediately check on the clinical status of the baby.
- 2) Consultation with a metabolic specialist is essential.
- 3) The specialist may request urine organic analysis or plasma acylcarnitine analysis on the baby.
- 4) Call KS Newborn Screening Program at 785-291-3363 with questions about the results.
- 5) Report clinical findings to the Newborn Screening Program at 785-291-3363.
- 6) Same birth siblings (twins, triplets) of infants diagnosed with HMG-CoA lyase deficiency should be re-screened; additional testing of these siblings also may be indicated.
- 7) Consider testing older siblings of an affected individual. Some people may have no symptoms and may go undiagnosed.

✓ Confirmation of Diagnosis

The diagnosis of HMG-CoA lyase deficiency is confirmed through urine organic acid analysis and plasma acylcarnitine analysis.

✓ Communication of Results to Parents

If a baby has a presumptive positive HMG-CoA lyase deficiency newborn screening result, additional testing needs to be performed to confirm a diagnosis. In accordance with Kansas Administrative Regulation 28-4-502, it is the responsibility of the attending physician or other birth attendant to obtain repeat specimens when needed to complete the screening process.

If the baby is diagnosed with HMG-CoA lyase deficiency, the following points should be conveyed to parents:

- ***Parents should understand that treatment for HMG-CoA lyase deficiency will be lifelong.***
- ***Parent should understand that treatment is not curative and that all health problems and morbidity cannot necessarily be prevented. Long-term management, monitoring, and compliance with treatment recommendations are essential to the child's well-being. A multidisciplinary approach is recommended and should include pediatrics, dieticians, and a metabolic disease specialist.***
- ***Genetic counseling services may be indicated. A list of counselors and geneticists, whose services are available in Kansas, should be given to the parents if they have not already seen a geneticist.***

For consultation, contact:

Dr. Majed Dasouki
KU Medical Center
Kansas City, KS
913-588-6326

11/24/08



Multiple Carboxylase Deficiency Information for Health Professionals

Multiple carboxylase deficiency, or holocarboxylase synthetase deficiency, is an organic acid disorder caused by a reduction or lack of the enzyme holocarboxylase synthetase activity.

✓ Clinical Symptoms

Many individuals present with symptoms within hours of birth, and most will have symptoms by two years of age. Multiple carboxylase deficiency can cause episodes of metabolic crisis. Symptoms of a crisis include feeding difficulty, lethargy, behavior changes, hypotonia, and severe eczema. Laboratory findings include hypoglycemia, low platelets, ketoacidosis, metabolic acidosis, and mild hyperammonemia. If untreated, a metabolic crisis may lead to tachypnea, seizures, brain swelling, coma, and possibly death.

Even without experiencing a metabolic crisis, untreated children can develop skin rashes, alopecia, vision/hearing loss, failure to thrive, developmental delays, spasticity, ataxia, and seizures. Death usually occurs if untreated.

✓ Incidence

Multiple carboxylase deficiency occurs in less than 1 in 100,000 births with no increased incidence based on sex or race.

✓ Genetics of multiple carboxylase deficiency

Mutations in the HLCS gene cause multiple carboxylase deficiency. Mutations prevent the production of or reduce the activity of the enzyme holocarboxylase synthetase (HCS). Normally, this enzyme activates multiple carboxylases by attaching the B vitamin, biotin, to the carboxylases. Deficiency of these carboxylases impairs fat, carbohydrate and protein metabolism.

✓ How do people inherit multiple carboxylase deficiency?

Multiple carboxylase deficiency is inherited in an autosomal recessive manner. Parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but do not show signs and symptoms of the condition. Each pregnancy between carrier parents has a 25% chance of producing a child affected with multiple carboxylase deficiency, a 50% chance of producing an unaffected carrier child, and a 25% chance of producing a child who is unaffected and is not a carrier.

✓ Treatment

Immediate diagnosis and treatment of multiple carboxylase deficiency is critical to normal growth and development. Treatment is usually effective if started early. Recommended treatment is daily supplementation of biotin. Biotin can prevent symptoms and may reverse some health problems.

✓ **Screening Methodology**

Primary newborn screening for multiple carboxylase deficiency utilizes tandem mass spectrometry. Elevated C5-OH (3-hydroxyisovaleryl carnitine) indicates the possibility of multiple carboxylase deficiency. False positive and false negative results are possible with this screen.

✓ **What to do After Receiving Presumptive Positive MCD Results**

- 1) The clinician should immediately check on the clinical status of the baby.
- 2) Consultation with a metabolic specialist is essential.
- 3) The specialist may request urine organic acid analysis and other labs for the baby.
- 4) Call KS Newborn Screening Program at 785-291-3363 with questions about results.
- 5) Report clinical findings to the Newborn Screening Program at 785-291-3363.
- 6) Same birth siblings (twins, triplets) of infants diagnosed with MCD should be re-screened; additional testing of these siblings also may be indicated.

✓ **Confirmation of Diagnosis**

The diagnosis of multiple carboxylase deficiency is confirmed through urine organic acid analysis, plasma acylcarnitine analysis, and serum biotinidase assay.

✓ **Communication of Results to Parents**

If a baby has a **presumptive positive multiple carboxylase deficiency newborn screening result, additional testing needs to be performed to confirm a diagnosis.** In accordance with Kansas Administrative Regulation 28-4-502, it is the responsibility of the attending physician or other birth attendant to obtain repeat specimens when needed to complete the screening process.

If a baby is diagnosed with MCD, the following points should be conveyed to parents:

- ***Parents should understand that treatment for multiple carboxylase deficiency will be life long.***
- ***Parents should understand that treatment is not curative and that all morbidity cannot necessarily be prevented. Long-term management, monitoring, and compliance with treatment recommendations are essential to the child's well-being. A multidisciplinary approach is recommended and includes pediatrics and a metabolic specialist.***
- ***Genetic counseling may be indicated. A list of counselors and geneticists, whose services are available in Kansas, should be given to the parents if they have not already seen a geneticist.***

For consultation, contact:

Dr. Majed Dasouki
KU Medical Center
Kansas City, KS
913-588-6326

11/24/08



Glutaric Aciduria, Type 1

Information for Health Professionals

Glutaric aciduria, type 1 is an organic acid disorder where individuals cannot metabolize the amino acids lysine, hydroxylysine and tryptophan. Deficiency of the enzyme Glutaryl-CoA dehydrogenase causes this form of glutaric aciduria.

✓ Clinical Symptoms

Symptoms generally begin between two months and four years of age, though some infants may be born with macrocephaly. Isolated macrocephaly can be a benign familial trait. Glutaric aciduria, type 1 causes periods of metabolic crisis. Early symptoms of a crisis include feeding difficulties, irritability, vomiting, lethargy, and hypertonia. If untreated, symptoms include muscle spasms, spasticity, metabolic acidosis, dystonia, seizures, subdural hematomas, coma, and death. Metabolic crises can be triggered by illness/infection, fever, or fasting. Crises are less common as the child ages.

Even without a metabolic crisis, symptoms may include: failure to thrive, hepatomegaly, hypotonia, progressive spasticity, dystonia, fevers, developmental delay, learning delays or mental retardation, and speech problems.

✓ Incidence

Glutaric aciduria, type 1 occurs in greater than 1 in 75,000 Caucasian live births. There is an increased incidence in the Amish, the Ojibway population of Canada, and people with Swedish ancestry.

✓ Genetics of glutaric aciduria type 1

Mutations in the GCDH gene cause glutaric aciduria, type 1. Mutations in this gene reduce or eliminate the activity of glutaryl-CoA dehydrogenase. This enzyme is necessary in breaking down glutaryl-CoA, which is produced during the metabolism of the amino acids lysine, tryptophan, and hydroxylysine. This causes the accumulation of glutaric acid in the blood and results in the symptoms of this condition. This accumulation is especially damaging to the basal ganglia, which causes the movement symptoms seen in this condition.

✓ How do people inherit glutaric aciduria, type 1?

Glutaric aciduria, type 1 is inherited in an autosomal recessive manner. Parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but do not show signs and symptoms of the condition. Each pregnancy between carrier parents has a 25% chance of producing a child affected with glutaric aciduria, type 1, a 50% chance of producing an unaffected carrier child, and a 25% chance of producing a child who is unaffected and is not a carrier.

✓ Treatment

Immediate diagnosis and treatment of glutaric aciduria, type 1 is critical for normal growth and development. Affected individuals should follow a diet that is low in lysine and tryptophan, which generally requires medical foods and formulas. L-carnitine and riboflavin supplementation may be recommended. Symptoms of a metabolic crisis require immediate medical treatment, which may require IV medications such as glucose, carnitine, and others. Individuals should avoid fasting and have regular blood and urine tests to measure amino acid levels.

✓ **Screening Methodology**

Primary newborn screening for glutaric aciduria, type 1 utilizes tandem mass spectrometry. Elevated C5-DC (glutaryl carnitine) indicates the possibility of glutaric aciduria, type 1. False positive and false negative results are possible with this screen.

✓ **What to do After Receiving Presumptive Positive GA-1 Screening Results**

- 1) **The clinician should immediately check on the clinical status of the baby.**
- 2) **Consultation with a metabolic specialist is essential.**
- 3) **The specialist may request urine organic acid analysis and other labs on the baby.**
- 4) **Call the KS Newborn Screening Program at 785-291-3363 with questions about results.**
- 5) **Report clinical findings to the Newborn Screening Program at 785-291-3363.**
- 6) **Same birth siblings (twins, triplets) of infants diagnosed with glutaric aciduria, type 1 should be re-screened; additional testing of these siblings also may be indicated.**
- 7) **Consider testing older siblings. Some individuals may show no symptoms and will go undiagnosed.**

✓ **Confirmation of Diagnosis**

The diagnosis of glutaric aciduria, type 1 is confirmed through urine organic acid analysis revealing elevated glutaric acid and 3-hydroxyglutaric acid. If this is not confirmatory, 3-hydroxyglutaric acid in blood and CSF, urine glutarylcarnitine, enzyme analysis using fibroblasts, or molecular analysis can diagnose this condition.

✓ **Communication of Results to Parents**

If a baby has a presumptive positive glutaric aciduria, type 1 newborn screening result, additional testing needs to be performed to confirm a diagnosis. In accordance with the Kansas Administrative Regulation 28-4-502, it is the responsibility of the attending physician or other birth attendant to obtain repeat specimens when needed to complete the screening process.

If a baby is diagnosed with glutaric aciduria, type 1 the following points should be conveyed to parents:

- ***Parents should understand that treatment for glutaric aciduria type 1 will be lifelong.***
- ***Parents should understand that treatment is not curative and that all morbidity cannot necessarily be prevented. Long-term management, monitoring, and compliance with treatment recommendations are essential to the child's well-being. A multidisciplinary approach is recommended and should include pediatric, metabolic specialists, and dieticians.***
- ***Genetics counseling services may be indicated. A list of counselors and geneticists, whose services are available in Kansas, should be given to the parents if they have not already seen a geneticist.***

For consultation contact:

Dr. Majed Dasouki
KU Medical Center
Kansas City, KS
913-588-6362

12/17/08



Isovaleric Acidemia Information for Health Professionals

Isovaleric acidemia is an organic acid disorder in which individuals cannot metabolize leucine.

✓ Clinical Symptoms

Symptoms of isovaleric acidemia can begin shortly after birth through childhood. Isovaleric acidemia causes periods of metabolic crisis. Early symptoms of a crisis include: feeding difficulty, lethargy, hypothermia, and a “sweaty feet” odor. If untreated, symptoms include: metabolic acidosis, ketonuria, thrombocytopenia, neutropenia, hyperammonemia, seizures, cerebral hemorrhage, coma, and death. Survivors of repeated metabolic crisis can have brain damage. In individuals who do not show symptoms until childhood, metabolic crisis can be triggered by illness, infection, or high protein intake.

Some children still have metabolic crises, even when treated, though crises occur less frequently as the child ages.

✓ Incidence

Isovaleric acidemia occurs in less than 1 in 100,000 births.

✓ Genetics of isovaleric acidemia

Mutations in the IVD gene cause isovaleric acidemia. Mutations in this gene reduce or eliminate the activity of the enzyme isovaleryl-CoA dehydrogenase. This enzyme is necessary for breaking down isovaleryl-CoA, which is produced during the metabolism of the amino acid leucine. This causes the accumulation of isovaleric acid in the blood, which causes symptoms of this condition.

✓ How do people inherit isovaleric acidemia?

Isovaleric acidemia is inherited in an autosomal recessive manner. Parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but do not show signs and symptoms of the condition. Each pregnancy between carrier parents has a 25% chance of producing a child affected with isovaleric acidemia, a 50% chance of producing an unaffected carrier child, and a 25% chance of producing a child who is unaffected and is not a carrier.

✓ Treatment

Immediate diagnosis and treatment of isovaleric acidemia is critical to normal development and survival. Individuals should follow a low-leucine, low-protein diet, which generally requires medical foods and formulas. L-carnitine supplementation and glycine may be recommended. Symptoms of a metabolic crisis require immediate medical treatment which may require IV medications, such as bicarbonate and glucose.

✓ **Screening Methodology**

Primary newborn screening for isovaleric acidemia utilizes tandem mass spectrometry to determine the levels of C5 acylcarnitine (isovaleryl/ 2-methylbutyryl carnitine). Elevated levels of C5 indicate the possibility of isovaleric acidemia. False positive and false negative results are possible with this screen.

✓ **What to do After Receiving Presumptive Positive IVA Screening Results**

- 1) The clinician should immediately check on the clinical status of the baby.
- 2) Consultation with a metabolic specialist is essential.
- 3) The specialist may request confirmatory lab tests on the baby.
- 4) Call KS Newborn Screening Program at 785-291-3363 with questions about results.
- 5) Report Clinical Findings to Newborn Screening Program at 785-291-3363.
- 6) Same birth siblings (twins, triplets) of infants diagnosed with isovaleric acidemia should be re-screened; additional testing of these siblings also may be indicated.

✓ **Confirmation of Diagnosis**

The diagnosis of isovaleric acidemia is confirmed through plasma acylcarnitine analysis revealing elevated C5. Urine organic acid analysis will show isovalerylglycine in most cases of isovaleric acidemia.

✓ **Communication of Results to Parents**

If a baby has a presumptive positive isovaleric acidemia newborn screening result, additional testing needs to be performed to confirm a diagnosis. In accordance with the Kansas Administrative Regulation 28-4-502, it is the responsibility of the attending physician or other birth attendant to obtain repeat specimens when needed to complete the screening process.

If a baby is diagnosed with isovaleric acidemia, the following points should be conveyed to parents:

- ***Parents should understand that treatment for isovaleric acidemia will be life long.***
- ***Parents should understand that treatment is not curative and that all morbidity cannot necessarily be prevented. Long-term management, monitoring, and compliance with treatment recommendations are essential to the child's well-being. A multidisciplinary approach is recommended and should include the following specialties: pediatrics, metabolic disease specialist, and dietician.***
- ***Genetic counseling services may be indicated. A list of counselors and geneticists, whose services are available in Kansas, should be given to the parents if they have not already seen a geneticist.***

For consultation, contact:

Dr. Majed Dasouki
KU Medical Center
Kansas City, KS
913-588-6326

11/24/08



Methylmalonic Acidemia (Cbl A,B) Information for Health Professionals

Methylmalonic acidemia (MMA) is an organic acid disorder. MMA can generally be classified into two types; vitamin B12 non-responsive and vitamin B12 responsive. Vitamin B12 responsive forms include Cobalamin A (CblA) and Cobalamin B (CblB) deficiencies.

✓ Clinical Symptoms

Most newborns do not have symptoms at birth. Symptoms generally occur during the first few months or years of life. Individuals will develop feeding problems, failure to thrive, developmental delay, and hypotonia. Some individuals will have protein aversion and infants are at an increased risk for a metabolic crisis.

✓ Incidence

MMA (Cbl A,B) occurs in less than 1 in 100,000 births with no increased incidence based on sex or race. Vitamin B12 responsive forms account for approximately half of the cases of MMA.

✓ Genetics of methylmalonic acidemia

Mutations in the MMAA or MMAB genes can cause methylmalonic acidemia. These genes produce cobalamin reductase and cobalamin adenosyltransferase. The MMAA protein is necessary for transportation of Cbl for use in adenosylcobalamin synthesis and the MMAB protein is an adenosyltransferase.

✓ How do people inherit methylmalonic acidemia?

Methylmalonic acidemia is inherited in an autosomal recessive manner. Parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but do not show signs or symptoms of the condition. The recurrence risk for carrier parents is 25% with each pregnancy.

✓ Treatment

Immediate diagnosis and treatment of methylmalonic acidemia is critical to normal growth and development. Individuals should follow a low-protein, high carbohydrate diet, which generally requires medical formulas and foods that restrict isoleucine, valine, threonine, and methionine. L-carnitine supplementation may be recommended. Liver and kidney transplantations are not curative, but may be beneficial. During periods of illness, children may need to be admitted for medical care to prevent a metabolic crisis.

✓ Screening Methodology

Primary newborn screening for MMA utilizes tandem mass spectrometry to determine the C3 levels. Elevated C3 (propionylcarnitine) indicates the possibility of MMA or Propionic acidemia. Additional testing is needed to distinguish them. False positive and false negatives are possible with this screen.

✓ **What to do After Receiving Presumptive Positive Methylmalonic Acidemia Screening Results**

- 1) The clinician should immediately check on the clinical status of the baby.
- 2) Confirmatory labs should be performed with direction from the metabolic specialist.
- 3) Call KS Newborn Screening Program at 785-291-3363 with questions about results.
- 4) Report Clinical Findings to Newborn Screening Program at 785-291-3363.
- 5) Same birth siblings (twins, triplets) of infants diagnosed with MMA should be re-screened; additional testing of these siblings also may be indicated.

✓ **Confirmation of Diagnosis**

The diagnosis of methylmalonic acidemia is confirmed through organic acid analysis of urine or plasma revealing elevated methylmalonic acid. To establish the specific form of methylmalonic acidemia, additional studies must be done. These include vitamin B12 responsiveness, complementation analysis, C14 propionate tracer assay, and cobalamin distribution.

✓ **Communication of Results to Parents**

If a baby has a presumptive positive methylmalonic acidemia newborn screening result, additional testing needs to be performed to confirm a diagnosis. In accordance with Kansas Administrative Regulation 28-4-502, it is the responsibility of the attending physician or other birth attendant to obtain repeat specimens when needed to complete the screening process.

If a baby is diagnosed with MMA, the following points should be conveyed to parents:

- ***Parents should understand that treatment for methylmalonic acidemia will be lifelong.***
- ***Parents should understand that treatment is not curative and that all morbidity cannot necessarily be prevented. Long-term management, monitoring and compliance with treatment recommendations are essential to the child's well-being. A multidisciplinary approach is recommended and should include the following specialties: pediatrics, metabolic genetics and nutrition. Periodic blood and urine analysis is needed.***
- ***Genetic counseling services may be indicated. A list of counselors and geneticists, whose services are available in Kansas, should be given to the parents if they have not already seen a geneticist.***

For consultation, contact:

Dr. Majed Dasouki
KU Medical Center
Kansas City, KS
913-588-6326

03/18/09



Methylmalonic Acidemia (MUT) Information for Health Professionals

Methylmalonic acidemia (MMA) is an organic acid disorder. MMA can generally be classified into two types; vitamin B12 non-responsive and vitamin B12 responsive. Two types of MMA that are non-responsive to vitamin B12 and caused by mutations in the MMA-CoA mutase (MUT) gene are referred to as mut^0 and mut^- .

✓ **Clinical Symptoms**

Most newborns do not have symptoms at birth, but will soon develop lethargy, vomiting, and dehydration. Other findings can include mental retardation, movement disorders, metabolic stroke, failure to thrive, hepatomegaly, encephalopathy, and hyperammonemia.

✓ **Incidence**

MMA (MUT) occurs in greater than 1 in 75,000 births with no increased incidence based on sex or race.

✓ **Genetics of methylmalonic acidemia**

Approximately half of methylmalonic acidemia cases are caused by mutation the MUT gene. Many mutations in the MUT gene have been identified. Mutations prevent the production of or reduce the activity of methylmalonyl CoA mutase, resulting in impaired catabolism of fatty acids as well as some amino acids. This results in an accumulation of methylmalonyl CoA which causes the symptoms of methylmalonic acidemia.

Mutations that do not allow production of functional enzyme are designated mut^0 . Mutations that cause a change in the structure of the enzyme but allow it to remain partially functional are designated mut^- , and this form is typically less severe and more clinically variable than the mut^0 form. Both forms are referred to as “vitamin B12 non-responsive”.

✓ **How do people inherit methylmalonic acidemia?**

Methylmalonic acidemia is inherited in an autosomal recessive manner. Parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but do not show signs or symptoms of the condition. Each pregnancy between carrier parents has a 25% chance of producing a child affected with MMA, a 50% chance of producing an unaffected carrier child, and a 25% chance of producing a child who is unaffected and is not a carrier.

✓ **Treatment**

Even with early diagnosis, mortality rates remain high. This is particularly true in vitamin B12 non-responsive methylmalonic acidemia. Affected individuals should follow a low-protein, high carbohydrate diet, which generally requires medical formulas and foods that restrict isoleucine, valine, threonine, and methionine. L-carnitine supplementation may be recommended. During periods of illness, children may need to be admitted for medical care to prevent a metabolic crisis. Combined liver and kidney transplantation may be curative in patients with MMA and renal insufficiency.

✓ Screening Methodology

Primary newborn screening for MMA utilizes tandem mass spectrometry to determine the propionylcarnitine (C3) level. Elevated propionylcarnitine, and occasionally methylmalonyl carnitine (C4DC), indicates the possibility of MMA. False positives and false negatives are possible with this screen.

✓ What to do After Receiving Presumptive Positive Methylmalonic Acidemia Screening Results

- 1) The clinician should immediately check on the clinical status of the baby.
- 2) Consultation with a metabolic specialist is essential.
- 3) The specialist may request urine organic acid analysis and other labs on baby.
- 4) Call KS Newborn Screening Program at 785-291-3363 with questions about results.
- 5) Report Clinical Findings to Newborn Screening Program at 785-291-3363.
- 6) Same birth siblings (twins, triplets) of infants diagnosed with MMA should be re-screened; additional testing of these siblings also may be indicated.

✓ Confirmation of Diagnosis

The diagnosis of methylmalonic acidemia is confirmed through organic acid analysis of urine or plasma revealing elevated methylmalonic acid. To establish the specific form of methylmalonic acidemia, additional studies must be done. These include vitamin B12 responsiveness, complementation analysis, C14 propionate tracer assay, and cobalamin distribution.

✓ Communication of Results to Parents

If a baby has a presumptive positive methylmalonic acidemia newborn screening result, additional testing needs to be performed to confirm a diagnosis. In accordance with Kansas Administrative Regulation 28-4-502, it is the responsibility of the attending physician or other birth attendant to obtain repeat specimens when needed to complete the screening process.

If a baby is diagnosed with MMA, the following points should be conveyed to parents:

- ***Parents should understand that treatment for methylmalonic acidemia will be lifelong.***
- ***Parents should understand that treatment is not curative and that all morbidity cannot necessarily be prevented. Long-term management, monitoring and compliance with treatment recommendations are essential to the child's well-being. A multidisciplinary approach is recommended and should include the following specialties: pediatrics, metabolic genetics and nutrition. Periodic blood and urine analysis is needed.***
- ***Genetic counseling services may be indicated. A list of counselors and geneticists, whose services are available in Kansas, should be given to the parents if they have not already seen a geneticist.***

For consultation, contact:

Dr. Majed Dasouki
KU Medical Center
Kansas City, KS
913-588-6326

11/24/08



Propionic Acidemia Information for Health Professionals

Propionic acidemia is an organic acid disorder in which individuals are lacking or have reduced activity of the enzyme propionyl-CoA carboxylase, leading to propionic acidemia.

✓ Clinical Symptoms

Symptoms generally begin in the first few days following birth. Metabolic crisis can occur, particularly after fasting, periods of illness/infection, high protein intake, or during periods of stress on the body. Symptoms of a metabolic crisis include lethargy, behavior changes, feeding problems, hypotonia, and vomiting. If untreated, metabolic crises can lead to tachypnea, brain swelling, cardiomyopathy, seizures, coma, basal ganglia stroke, and death. Many babies die within the first year of life. Lab findings during a metabolic crisis commonly include urine ketones, hyperammonemia, metabolic acidosis, low platelets, low white blood cells, and high blood ammonia and glycine levels.

Long term effects may occur despite treatment and include developmental delay, brain damage, dystonia, failure to thrive, short stature, spasticity, pancreatitis, osteoporosis, and skin lesions.

✓ Incidence

Propionic acidemia occurs in greater than 1 in 75,000 live births and is more common in Saudi Arabians and the Inuit population of Greenland.

✓ Genetics of propionic acidemia

Mutations in the PCCA and PCCB genes cause propionic acidemia. Mutations prevent the production of or reduce the activity of propionyl-CoA carboxylase, which converts propionyl-CoA to methylmalonyl-CoA. This causes the body to be unable to correctly process isoleucine, valine, methionine, and threonine, resulting in an accumulation of glycine and propionic acid, which causes the symptoms seen in this condition.

✓ How do people inherit propionic acidemia?

Propionic acidemia is inherited in an autosomal recessive manner. Parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but do not show signs and symptoms of the condition. Each pregnancy between carrier parents has a 25% chance of producing a child affected with propionic acidemia, a 50% chance of producing an unaffected carrier child, and a 25% chance of producing a child who is unaffected and is not a carrier.

✓ Treatment

Immediate diagnosis and treatment of propionic acidemia in the neonatal period is critical to normal development and survival. Treatment is more effective the earlier it begins. Individuals should follow a low-protein diet which restricts leucine, valine, threonine, and methionine. Medical foods and formulas may be required. Certain medications, such as L-carnitine, antibiotics, and biotin, may be recommended. Regular blood and urine tests are needed to check ketone and amino acid levels. During illness, children may need to be admitted for medical care to prevent a metabolic crisis and fasting should always be avoided.

✓ **Screening Methodology**

Primary newborn screening for propionic acidemia utilizes tandem mass spectrometry. Elevated levels of C3 indicate the possibility of propionic acidemia. Elevated C3 (propionylcarnitine) is also a marker for methylmalonic acidemia. Additional metabolic studies are needed to distinguish between these two disorders. False positives and false negatives are possible with this screen.

✓ **What to do After Receiving Presumptive Positive PROP Screening Results**

- 1) **The clinician should immediately check on the clinical status of the baby.**
- 2) **Consultation with a metabolic specialist is essential.**
- 3) **Urine organic acid analysis and other labs may be recommended.**
- 4) **Call KS Newborn Screening Program at 785-291-3363 with questions about results.**
- 5) **Report clinical findings to the Newborn Screening Program at 785-291-3363.**
- 6) **Same birth siblings (twins, triplets) of infants diagnosed with PROP should be re-screened; additional testing of these siblings also may be indicated.**

✓ **Confirmation of Diagnosis**

The diagnosis of propionic acidemia is confirmed through plasma acylcarnitine analysis revealing increased C3. Urine organic acids should show propionic aciduria. An increase in glycine may be present on blood amino acid analysis.

✓ **Communication of Results to Parents**

If a baby has a presumptive positive propionic acidemia newborn screening result, additional testing needs to be performed to confirm a diagnosis. In accordance with Kansas Administrative Regulation 28-4-502, it is the responsibility of the attending physician or other birth attendant to obtain repeat specimens when needed to complete the screening process.

If a baby is diagnosed with PROP, the following points should be conveyed to parents:

- ***Parents should understand that treatment for propionic acidemia will be lifelong.***
- ***Parents should understand that treatment is not curative and that all morbidity cannot necessarily be prevented. Long-term management, monitoring, and compliance with treatment recommendations are essential to the child's well-being. A multidisciplinary approach is recommended and should include pediatrics, metabolic specialists, and dieticians.***
- ***Periodic blood and urine analysis is needed.***
- ***Genetic counseling services may be indicated. A list of counselors and geneticists, whose services are available in Kansas, should be given to the parents if they have not already seen a geneticist.***

For consultation contact:

Dr. Majed Dasouki
KU Medical Center
Kansas City, KS
913-588-6362

11/24/08



Mark Parkinson, Governor
Roderick L. Bremby, Secretary

DEPARTMENT OF HEALTH
AND ENVIRONMENT

www.kdheks.gov

Date

Mother's Name
Address Line 1
Address Line 2

RE: Baby's Name DOB: xx/xx/xxxx

Dear Parent:

Best wishes on the birth of your baby! Shortly after your baby was born, a small blood sample was taken for a test called the Newborn Screen. This test helps parents find out if their baby has certain health problems. A baby can look healthy, but may have a harmful illness that can be found by doing this blood test.

The result of your baby's blood test shows that more testing needs to be done for an organic acid disorder. ***This does not necessarily mean your child is ill.***

THIS IS WHAT YOU NEED TO DO NOW:

1. Call your baby's doctor. Say that you have received a letter stating that your baby's Newborn Screen test was not normal. Set up a time for your baby to have a second test done as soon as you can.
2. We have < Doctor's Name > listed as your baby's doctor, and we have notified him/her of your baby's test result. If this is NOT your baby's doctor, please call the Newborn Screening Program at 785-296-0109 so we can contact the right doctor.

DO NOT DELAY. YOUR BABY'S HEALTH DEPENDS ON YOU.

If your baby does not have a doctor, or if you have questions about this letter, please call Kansas Newborn Screening at 785-296-0109.

Sincerely,

A handwritten signature in black ink that reads "Jamey Kendall".

Jamey Kendall BSN, RN
Kansas Newborn Screening
Follow-up Coordinator

A handwritten signature in black ink that reads "Linda A. Williams".

Linda A. Williams, MT(ASCP)
Kansas Newborn Screening
Follow-up Coordinator



Organic Acid Disorders Information for Parents

➤ Overview

Organic acid disorders are a group of rare, inherited conditions that affect infants from birth. They are caused by enzymes that do not work properly. A number of enzymes are needed to process protein from the food we eat for use by the body. Problems with one or more of these enzymes can cause an organic acid disorder. People with organic acid disorders cannot break down protein properly. This causes harmful substances to build up in their blood and urine. These substances can affect health, growth and learning.

➤ Kansas Newborn Screening for organic acid disorders

The newborn screening program in the State of Kansas is designed to screen for nine different organic acid disorders. These disorders include:

- Isovaleric Acidemia (IVA)
- Glutaric Aciduria type I (GA-I)
- Multiple carboxylase deficiency (MCD)
- Propionic Acidemia (PA)
- Beta ketothiolase deficiency (BKT)
- 3-methylcrotonyl-CoA carboxylase deficiency (3MCC)
- 3-hydroxy-3-methylglutaryl CoA lyase deficiency (HMG)
- Methylmalonic acidemia - mutase deficiency (MUT) or vitamin B12 disorders (Cbl A, Cbl B)

➤ Why is newborn screening done for organic acid disorders?

Newborn screening is done for organic acid disorders so that babies with these conditions can be diagnosed and treated quickly. Immediate diagnosis and treatment of organic acid disorders is important for normal development and health. Without prompt diagnosis and treatment, infants with organic acid disorders will develop varying degrees of developmental delay or mental retardation, medical complications and may even experience death.

➤ Does a positive result from the Kansas Newborn Screening Lab mean that my baby has an organic acid disorder?

No, not necessarily. Newborn screening identifies babies at increased risk for having one of these disorders. Additional tests will need to be done to determine if the baby actually has an organic acid disorder.

➤ What are the signs and symptoms of organic acid disorders?

The age that symptoms start and the types of symptoms that a person has vary. A newborn affected with an organic acid disorder is usually well at birth and for the first few days of life. If the condition is not treated, babies usually develop vomiting, poor feeding, neurologic symptoms such as seizures and abnormal muscle tone (floppy or stiff), and excessive sleepiness. This can progress to coma and death.

➤ Is there a cure for organic acid disorders?

No, there is no cure for organic acid disorders. However, the outcome is best in infants who are treated early and continue with lifelong treatment. Treatment usually consists of a special diet and sometimes medications or supplements.

➤ Where can I get additional information?

Kansas Newborn Screening at www.kdheks.gov/newborn_screening/info_parents.htm
Save Babies Through Screening Foundation at www.savebabies.org
Screening, Technology and Research in Genetics at www.newbornscreening.info

11/24/08



3MCC Deficiency Information for Parents

➤ Overview

3-Methylcrotonyl-CoA Carboxylase deficiency is commonly known as 3MCC deficiency. This condition affects infants from birth (congenital) and results from an inability of the body to break down certain parts of food.

➤ What is 3MCC deficiency?

Our bodies break down protein from the food we eat into smaller parts called amino acids. Certain chemicals in our bodies, called enzymes, make changes to these amino acids so the body can use them. 3MCC deficiency occurs when the enzyme that breaks down an amino acid, called leucine, is missing or is not working correctly. This causes harmful substances to build up in the body and causes health problems.

➤ Why is newborn screening done for 3MCC deficiency?

Newborn screening is done for 3MCC deficiency so that babies with this condition can be diagnosed and treated quickly if need be. Immediate diagnosis and possible treatment gives babies the best opportunity for normal growth and development.

➤ Does a positive result from the Kansas Newborn Screening Lab mean that my baby has 3MCC deficiency?

No, not necessarily. Newborn screening tests for elevated levels of the compound C5-OH (3-hydroxyisovaleryl carnitine) in a baby's blood. Additional tests will need to be done to determine if a baby has 3MCC deficiency or not.

➤ How common is 3MCC deficiency?

3MCC deficiency affects greater than 1 in every 75,000 infants.

➤ Is 3MCC deficiency inherited?

3MCC deficiency is inherited in an autosomal recessive manner. This means that both parents of the affected child are carriers of the condition, but they do not have the disease. Each pregnancy between carrier parents has a 25% chance of producing a child affected with 3MCC deficiency, a 50% chance of producing an unaffected carrier child, and a 25% chance of producing a child who is unaffected and is not a carrier.

➤ **What are the signs and symptoms of 3MCC deficiency?**

Babies with 3MCC deficiency are healthy at birth. Symptoms may never occur, but if they do, usually begin after 3 months of age. 3MCC deficiency can cause periods of severe illness, called metabolic crises. These episodes can be caused if the child goes too long without food, eats large amounts of protein, or is sick. Symptoms of a metabolic crisis include extreme sleepiness, poor appetite, changes in behavior and mood, muscle weakness, and vomiting. If left untreated, the crisis can cause breathing problems, liver failure, seizures, coma, and possibly death. If babies survive repeated episodes of metabolic crisis, learning difficulties and mental retardation can occur.

Some children do not have metabolic crises, but can have poor growth and problems with their muscles (such as “floppy” muscles or tight muscles). Other people may not have symptoms until they are adults.

➤ **How is 3MCC deficiency diagnosed?**

False positive and false negative results are possible with this screening. If C5-OH (3-hydroxyisovaleryl carnitine) is elevated, additional confirmatory blood and urine tests will be necessary.

➤ **Is there a cure for 3MCC deficiency?**

No, there is no cure for 3MCC deficiency. However, some individuals may never need treatment. In individuals that do, the outcome is usually good in infants who are treated early and continue with lifelong treatment.

➤ **How is 3MCC deficiency treated?**

- Treatment sometimes includes a diet that is low in leucine and protein, which may include medical foods and formulas. These foods contain the right types of nutrients the child needs for growth and development.
- Supplements of the substance L-carnitine may be prescribed. This substance helps the body make energy and get rid of wastes.
- If the child is ill or is not eating, they may need treatment at a hospital to prevent a metabolic crisis.

➤ **Where can I get additional information?**

Organic Acidemia Association at www.oaanews.org

Children Living with Inherited Metabolic Disorders at www.climb.org.uk

11/24/08



Beta Ketothiolase Deficiency Information for Parents

➤ Overview

Beta ketothiolase deficiency (BKT) is a condition that affects infants from birth (congenital). Babies have difficulties processing certain parts of food in a way that their body can use them for energy and nutrients.

➤ What is beta ketothiolase deficiency?

Our bodies break down protein from the food we eat into smaller parts, called amino acids. Certain chemicals in our bodies, called enzymes, make changes to these amino acids so the body can use them. One enzyme called mitochondrial acetoacetyl-CoA thiolase breaks down the amino acid isoleucine. Beta ketothiolase deficiency occurs when this enzyme is missing or is not working properly.

➤ Why is newborn screening done for beta ketothiolase deficiency?

Newborn screening is done for beta ketothiolase deficiency so that babies with this condition can be diagnosed and treated quickly. Immediate diagnosis and treatment of beta ketothiolase deficiency gives babies the best opportunity for normal development and growth. Without prompt diagnosis and treatment, infants with beta ketothiolase deficiency will develop varying degrees of mental retardation and may experience death.

➤ Does a positive result from the Kansas Newborn Screening Lab mean that my baby has beta ketothiolase deficiency?

No, not necessarily. Newborn screening tests for elevated levels of the compound C5-OH (3-hydroxyisovaleryl carnitine) in a baby's blood. Additional tests will need to be done to determine if a baby has beta ketothiolase deficiency or not.

➤ How common is beta ketothiolase deficiency?

Beta ketothiolase deficiency occurs in less than 1 in 100,000 births.

➤ Is beta ketothiolase deficiency inherited?

Beta ketothiolase deficiency is inherited in an autosomal recessive manner. This means that both parents of an affected child are carriers of the condition, but they do not have the disease. Each pregnancy between carrier parents has a 25% chance of producing a child affected with beta ketothiolase deficiency, a 50% chance of producing an unaffected carrier child, and a 25% chance of producing a child who is unaffected and is not a carrier.

➤ **What are the signs and symptoms of beta ketothiolase deficiency?**

Most infants with beta ketothiolase deficiency appear normal at birth and symptoms often start around the age of one. Beta ketothiolase deficiency can cause periods of serious illness, called metabolic crises. Metabolic crises are caused if the child goes for a long time without food, is ill, or eats food that is high in protein. Symptoms of a metabolic crisis include extreme sleepiness, irritable mood, poor appetite, vomiting, fever, diarrhea, acidic substances in the blood, low blood sugar (hypoglycemia), coma, or death. If beta ketothiolase deficiency is untreated, symptoms can include heart problems, mental retardation, poor growth, uncontrolled movements, problems with muscle tone (they could appear “floppy” or rigid), and other laboratory findings, such as low platelets and white blood cells.

➤ **How is beta ketothiolase deficiency diagnosed?**

False positive and false negative results are possible with this screening. If C5-OH (3-hydroxyisovaleryl carnitine) is elevated, additional confirmatory tests using blood or urine will be ordered.

➤ **Is there a cure for beta ketothiolase deficiency?**

No, there is no cure for beta ketothiolase deficiency. However, the outcome is usually good in infants who are treated early and continue with lifelong treatment.

➤ **How is beta ketothiolase deficiency treated?**

- Life long treatment is required. You doctor may prescribe supplementation of L-carnitine. This substance helps the body make energy and get rid of harmful wastes.
- Individuals with beta ketothiolase deficiency need to eat frequently and should avoid going long times without food. If your child is ill or is not eating, they may need to be treated at a hospital to prevent a metabolic crisis.
- Some children may need to be on a diet that is low in protein.
- Periodic urine tests are needed.

➤ **Where can I get additional information?**

Organic Acidemia Association at www.oaanews.org

Children Living with Inherited Metabolic Diseases at www.climb.org.uk

Ketone Utilization Disorder: A Guide for Parents at http://mchneighborhood.ichp.edu/pacnorgg/media/Metabolic/ketone_util_eng.pdf

11/24/08



Glutaric Aciduria, Type 1 Information for Parents

➤ Overview

Glutaric aciduria, type 1, is a condition that affects infants from birth (congenital). Babies with this condition have difficulty breaking down certain parts of food in a way that their body can use them for nutrients and energy.

➤ What is glutaric aciduria, type 1?

Our bodies break down the protein from the food we eat into smaller parts called amino acids. Certain chemicals in our bodies, called enzymes, make changes to these amino acids so our body can use them. When the amino acids lysine, tryptophan, and hydroxylysine are broken down, a substance called glutaryl-CoA is produced. Glutaric aciduria, type 1 occurs when the enzyme that helps get rid of glutaryl-CoA is missing or is not working correctly.

➤ Why is newborn screening done for glutaric aciduria, type 1?

Newborn screening is done for glutaric aciduria, type 1 so that babies with this condition can be diagnosed and treated quickly. Immediate diagnosis and treatment of glutaric aciduria, type 1 gives babies the best opportunity for normal brain development and health. Without prompt diagnosis and treatment, infants with glutaric aciduria, type 1 will develop varying degrees of mental retardation and may experience serious health complications.

➤ Does a positive result from the Kansas Newborn Screening Lab mean that my baby has glutaric aciduria, type 1?

No, not necessarily. Newborn screening tests for elevated levels of the compound C5-DC (glutaryl carnitine) in a baby's blood. Additional tests will need to be done to determine if a baby has glutaric aciduria, type 1 or not.

➤ How common is glutaric aciduria, type 1?

Glutaric aciduria, type 1 affects greater than 1 in every 75,000 Caucasian infants. It is more common in certain populations, such as the Amish, the Ojibway population, and in people with Swedish ancestry.

➤ Is glutaric aciduria, type 1 inherited?

Glutaric aciduria, type 1 is inherited in an autosomal recessive manner. This means that both parents of an affected child are carriers of the condition, but they do not have the disease. Each pregnancy between carrier parents has a 25% chance of producing a child affected with glutaric aciduria, type 1, a 50% chance of producing an unaffected carrier child, and a 25% chance of producing a child who is unaffected and is not a carrier.

➤ **What are the signs and symptoms of glutaric aciduria, type 1?**

Most babies with glutaric aciduria, type 1 appear normal at birth, though they may have a slightly larger head. Symptoms usually begin when the child is between 2 months and 4 years old. Glutaric aciduria, type 1 can cause periods of severe illness, called metabolic crises, which are usually caused if the child goes for a long time without food, is sick, or has a fever. Symptoms of a metabolic crisis are a poor appetite, extreme sleepiness, vomiting, “floppy” weak muscles, and irritability or jitteriness. If the crisis is not treated, more serious problems can occur, such as muscle contractions, poor balance, increased levels of acidic substances in the blood, seizures, swelling or bleeding in the brain, coma, and possibly death. Even without a metabolic crisis, children can have symptoms such as a large liver, poor growth, movements that they can’t control, delays in walking, learning delays or mental retardation, and problems with speech.

➤ **How is glutaric aciduria, type 1 diagnosed?**

False positive and false negative results are possible with this screening. If C5-DC (glutaryl carnitine) is elevated, additional confirmatory urine tests will be ordered. If this test doesn’t confirm a diagnosis, but the diagnosis is still suspected, blood tests, genetic tests, or other special tests may be ordered.

➤ **Is there a cure for glutaric aciduria, type 1?**

No, there is no cure for glutaric aciduria, type 1. However, the outcome is usually good in infants who are treated early and continue with lifelong treatment.

➤ **How is glutaric aciduria, type 1 treated?**

- Lifelong treatment is required. The primary treatment for glutaric aciduria, type 1 is a diet that is low in lysine and tryptophan, which usually requires special medical foods and formulas. Medical formulas contain the right type of nutrients your child needs for growth and development.
- Supplementation of the vitamin riboflavin or the substance L-carnitine may be prescribed. These substances may help the body get rid of harmful wastes.
- Individuals with glutaric aciduria, type 1 need to eat frequently and should not go long periods of time without food. If your child is ill or is not eating, they may need to be treated at the hospital.
- Immediate treatment in a hospital is necessary if the child shows any symptoms of a metabolic crisis.

➤ **Where can I get additional information?**

Organic Acidemia Association at www.oaaneews.org

International Organization of Glutaric Acidemia at www.glutaricacidemia.org

Children Living with Inherited Metabolic Disorders at www.climb.org.uk

11/24/08



HMG-CoA Lyase Deficiency Information for Parents

➤ Overview

HMG-CoA lyase deficiency is the common name given to the disorder 3-hydroxy-3-methylglutaryl-CoA lyase deficiency. HMG-CoA lyase deficiency is a condition that affects infants from birth (congenital). Babies have problems breaking down certain parts of food which causes harmful substances to build up in the body.

➤ What is HMG-CoA lyase deficiency?

Protein from the food we eat is broken down into smaller parts, called amino acids. Certain chemicals in our bodies, called enzymes, process the amino acids so that our body can use them. Enzymes also help break down fat and turn it into energy. The enzyme HMG-CoA lyase helps break down the amino acid leucine. This enzyme also makes ketones during the breakdown of fats for energy. HMG-CoA lyase deficiency occurs if this enzyme is missing or is not working properly.

➤ Why is newborn screening done for HMG-CoA lyase deficiency?

Newborn screening is done for HMG-CoA lyase deficiency so that babies with this condition can be diagnosed and treated quickly. Immediate diagnosis and treatment of HMG-CoA lyase deficiency gives babies the best opportunity for normal brain development and growth. Without prompt diagnosis and treatment, infants with HMG-CoA lyase deficiency will develop varying degrees of mental retardation and may experience death.

➤ Does a positive result from the Kansas Newborn Screening Lab mean that my baby has HMG-CoA lyase deficiency?

No, not necessarily. Newborn screening tests for elevated levels of the compound C5-OH (3-hydroxyisovaleryl carnitine) in a baby's blood. Additional tests will need to be done to determine if a baby has HMG-CoA lyase deficiency or not.

➤ How common is HMG-CoA lyase deficiency?

HMG-CoA lyase deficiency occurs in less than 1 in 100,000 births.

➤ Is HMG-CoA lyase deficiency inherited?

HMG-CoA lyase deficiency is inherited in an autosomal recessive manner. This means that both parents of the affected child are carriers of the condition, but they do not have the disease. Each pregnancy between carrier parents has a 25% chance of producing a child affected with HMG-CoA lyase deficiency, a 50% chance of producing an unaffected carrier child, and a 25% chance of producing a child who is unaffected and is not a carrier.

➤ **What are the signs and symptoms of HMG-CoA lyase deficiency?**

Most infants with HMG-CoA lyase deficiency appear normal at birth. About 1/3 of children will have symptoms shortly after birth (the first 2-5 days) and the rest will have symptoms between 3 and 11 months of age. HMG-CoA lyase deficiency can cause periods of serious illness, called metabolic crises, which are often triggered by going for long periods of time without food, illness, or by eating large amounts of protein. Signs of a metabolic crisis include extreme sleepiness, poor appetite, an irritable mood, vomiting, fever, diarrhea, muscle weakness, high levels of ammonia in the blood, or hypoglycemia (low blood sugar). Without treatment, serious health consequences can result, such as breathing problems, seizures, coma, or death.

Even if a child does not have a metabolic crisis, long-term effects, such as hearing and vision loss, an enlarged heart, inflammation of the pancreas, or learning disabilities or mental retardation, can occur.

➤ **How is HMG-CoA lyase deficiency diagnosed?**

False positive and false negative results are possible with this screening. If C5-OH (3-hydroxyisovaleryl carnitine) is elevated, additional confirmatory tests using blood or urine will be ordered.

➤ **Is there a cure for HMG-CoA lyase deficiency?**

No, there is no cure for HMG-CoA lyase deficiency. However, the outcome is usually good in infants who are treated early and continue with lifelong treatment.

➤ **How is HMG-CoA lyase deficiency treated?**

- Lifelong treatment is required. The primary treatment for HMG-CoA lyase deficiency is a diet that is low in leucine and high in carbohydrates, which usually requires special medical foods and formulas. Medical formulas contain the right types of nutrients your child needs for growth and development.
- Individuals with HMG-CoA lyase deficiency need to eat frequently and should avoid going long times without food. If your child is ill or is not eating, they may need to be treated at a hospital.
- Supplementation of the substance L-carnitine may be prescribed. This may help prevent a metabolic crisis.

➤ **Where can I get additional information?**

Organic Acidemia Association at www.oaanews.org

Children Living with Inherited Metabolic Disorders at www.climb.org.uk

GeneTests at www.genetests.org

11/24/08



Isovaleric Acidemia Information for Parents

➤ Overview

Isovaleric acidemia is a condition that affects infants from birth (congenital). Babies with this condition have problems breaking down certain parts of food in a way that their body can use them for nutrients and energy.

➤ What is isovaleric acidemia?

Our bodies break down protein from the food we eat into smaller parts, called amino acids. Certain chemicals in our bodies, called enzymes, make changes to these amino acids so our body can use them. When the amino acid leucine is broken down, a substance called isovaleryl-CoA is produced. Isovaleric acidemia occurs when the enzyme that helps get rid of isovaleryl-CoA is missing or is not working correctly.

➤ Why is newborn screening done for isovaleric acidemia?

Newborn screening is done for isovaleric acidemia so that babies with this condition can be diagnosed and treated quickly. Immediate diagnosis and treatment of isovaleric acidemia gives babies the best opportunity for normal brain development and physical growth. Without prompt diagnosis and treatment, infants with isovaleric acidemia may develop varying degrees of mental retardation, or may experience serious health complications, including death.

➤ Does a positive result from the Kansas Newborn Screening Lab mean that my baby has isovaleric acidemia?

No, not necessarily. Newborn screening tests for elevated levels of the compound C5 (isovaleryl/2-methylbutyryl carnitine) in a baby's blood. Additional tests will need to be done to determine if a baby has isovaleric acidemia or not.

➤ How common is isovaleric acidemia?

Isovaleric acidemia affects less than 1 in 100,000 infants.

➤ Is isovaleric acidemia inherited?

Isovaleric acidemia is inherited in an autosomal recessive manner. This means that both parents of an affected child are carriers of the condition, but they do not have the disease. Each pregnancy between carrier parents has a 25% chance of producing a child affected with isovaleric acidemia, a 50% chance of producing an unaffected carrier child, and a 25% chance of producing a child who is unaffected and is not a carrier.

➤ What are the signs and symptoms of isovaleric acidemia?

Most babies with isovaleric acidemia appear normal at birth. Symptoms can begin anytime from shortly after birth through childhood. Isovaleric acidemia can cause periods of illness, called metabolic crisis, which commonly occur if the child is sick, has an infection, or eats a lot of protein. Symptoms of a metabolic crisis include a poor appetite, extreme sleepiness, vomiting,

problems staying warm, and a “sweaty feet” odor. If the crisis is not treated, many serious health problems can occur, including seizures, swelling or bleeding in the brain, coma, and possibly death. Repeated metabolic crisis can lead to learning problems or mental retardation.

About half of babies with isovaleric acidemia will show symptoms of this condition shortly after birth. Others will develop symptoms in late infancy or childhood.

➤ **How is isovaleric acidemia diagnosed?**

False positive and false negative results are possible with this screening. If C5 (isovaleryl/2-methylbutyryl carnitine) is elevated, additional confirmatory blood tests will be ordered that measure C5. Urine tests may also be performed.

➤ **Is there a cure for isovaleric acidemia?**

No, there is no cure for isovaleric acidemia. However, the outcome is usually good in infants who are treated early and continue with lifelong treatment.

➤ **How is isovaleric acidemia treated?**

- Lifelong treatment is required. The primary treatment for isovaleric acidemia is a diet that is low in leucine and protein, which usually requires special medical foods and formulas. Medical formulas contain the right type of nutrients your child needs for growth and development.
- Supplementation of the amino acid glycine and L-carnitine may be prescribed. These substances may help prevent a metabolic crisis and help the body get rid of harmful wastes.
- Immediate treatment in the hospital is necessary if the child shows any symptoms of a metabolic crisis.

➤ **Where can I get additional information?**

IVA Support Group at ivasupport.org

Organic Acidemia Association at www.oaanews.org

Children Living with Inherited Metabolic Disorders (CLIMB) at www.climb.org.uk

Isovaleric Acidemia: A Guide for Parents at http://mchneighborhood.ichp.edu/pacnorgg/media/Metabolic/isovaleric_eng.pdf

11/24/08



Multiple Carboxylase Deficiency Information for Parents

➤ Overview

Multiple carboxylase deficiency (MCD), also known as holocarboxylase synthetase deficiency, is a condition that affects infants from birth (congenital). Babies have problems making changes to certain parts of food (fats, proteins and sugars) in a way that their body can use them for energy.

➤ What is multiple carboxylase deficiency?

Our bodies break down the food we eat into nutrients and energy that our body needs. Certain chemicals in our bodies, called enzymes, help with this process. One of these enzymes is holocarboxylase synthetase. Multiple carboxylase deficiency occurs if this enzyme is missing or is not working properly. As a result, certain harmful substances can build up in the body and cause health problems.

➤ Why is newborn screening done for multiple carboxylase deficiency?

Newborn screening is done for multiple carboxylase deficiency so that babies with this condition can be diagnosed and treated quickly. Immediate diagnosis and treatment of multiple carboxylase deficiency gives babies the best opportunity for normal development and growth. Without prompt diagnosis and treatment, infants with multiple carboxylase deficiency will develop varying degrees of mental retardation and may experience death.

➤ Does a positive result from the Kansas Newborn Screening Lab mean that my baby has multiple carboxylase deficiency?

No, not necessarily. Newborn screening tests for elevated levels of the compound C5-OH (3-hydroxyisovaleryl carnitine) in a baby's blood. Additional tests will need to be done to determine if a baby has multiple carboxylase deficiency or not.

➤ How common is multiple carboxylase deficiency?

Multiple carboxylase deficiency affects less than 1 in every 100,000 infants. It affects boys and girls equally and does not occur more often in a specific race or ethnic group.

➤ Is multiple carboxylase deficiency inherited?

Multiple carboxylase deficiency is inherited in an autosomal recessive manner. This means that both parent of an affected child are carriers of the condition, but they do not have the disease. Each pregnancy between carrier parents has a 25% chance of producing a child affected with multiple carboxylase deficiency, a 50% chance of

producing an unaffected carrier child, and a 25% chance of producing a child who is unaffected and is not a carrier.

➤ **What are the signs and symptoms of multiple carboxylase deficiency?**

Many babies with multiple carboxylase deficiency will have symptoms during the first few days of life. Symptoms usually begin before 2 years of age.

Multiple carboxylase deficiency can cause periods of serious illness, called metabolic crises. Signs of a metabolic crisis include extreme sleepiness, irritable mood, poor appetite, vomiting, low muscle tone or “floppy” muscles, a skin rash, and certain laboratory findings. Without treatment, serious health consequences can result, such as breathing problems, seizures, brain swelling, coma, or death.

Even if babies don’t have a metabolic crisis, they will still have symptoms if they are not treated. These include skin rashes, learning disabilities or mental retardation, convulsions or seizures, poor growth, hearing/vision loss, hair loss, delays in walking, and problems with movement.

➤ **How is multiple carboxylase deficiency diagnosed?**

False positive and false negative results are possible with this screening. If C5-OH (3-hydroxyisovaleryl carnitine) is elevated, additional confirmatory tests using blood or urine will be ordered.

➤ **Is there a cure for multiple carboxylase deficiency?**

No, there is no cure for multiple carboxylase deficiency. However, the outcome is usually good in infants who are treated early and continue with lifelong treatment.

➤ **How is multiple carboxylase deficiency treated?**

Lifelong treatment is required. The main treatment for multiple carboxylase deficiency is supplementation of a type of B vitamin called biotin. This supplement can help prevent symptoms and reverse some health problems.

➤ **Where can I get additional information?**

Organic Acidemia Association at www.oaaneews.org

Children Living with Inherited Metabolic Disorders at www.climb.org.uk

11/24/08



Methylmalonic Acidemia (Cbl A, B) Information for Parents

➤ **Overview**

Methylmalonic acidemia (Cbl A, B), is a condition that affects infants from birth (congenital). Babies have difficulty breaking down food and fat in a way that their body can use for nutrients and energy.

➤ **What is methylmalonic acidemia?**

Our bodies break down the food we eat into nutrients that our body needs. Certain chemicals in our bodies, called enzymes, help with this process. One of these enzymes is called methylmalonyl CoA mutase (MUT). Cbl A and Cbl B normally work as helpers for MUT to carry out its normal function. If there is deficiency of Cbl A or B, then MUT won't be able to work correctly which then causes methylmalonic acidemia.

➤ **Why is newborn screening done for methylmalonic acidemia?**

Newborn screening is done for methylmalonic acidemia so that babies with this condition can be diagnosed and treated quickly. Immediate diagnosis and treatment of methylmalonic acidemia give babies the best opportunity for normal brain development and physical growth. Without prompt diagnosis and treatment, infants with methylmalonic acidemia may develop varying degrees of mental retardation, as well as other health complications.

➤ **Does a positive result from the Kansas Newborn Screening Lab mean that my baby has methylmalonic acidemia?**

No, not necessarily. Newborn screening tests for elevated levels of certain compound known as C3 in a baby's blood. Additional tests will need to be done to determine if a baby has methylmalonic acidemia or not.

➤ **How common is methylmalonic acidemia?**

Methylmalonic acidemia (Cbl A, B) affects less than 1 out of every 100,000 infants. It affects boys and girls equally and does not occur more often in a specific ethnic group or race.

➤ **Is methylmalonic acidemia inherited?**

Methylmalonic acidemia is inherited in an autosomal recessive manner. This means that both parents of the affected child are carriers of the condition, but they do not have the disease. Each pregnancy between carrier parents has a 25% chance of producing a child affected with methylmalonic acidemia, a 50% chance of producing an unaffected carrier child, and a 25% chance of producing a child who is unaffected and is not a carrier.

➤ **What are the signs and symptoms of methylmalonic acidemia?**

Most infants with this form of methylmalonic acidemia appear normal at birth. Symptoms often begin during the first few months or years of life. Early signs of methylmalonic acidemia include

feeding problems, poor growth, and low muscle tone. Some infants may vomit after eating food with high protein content. Methylmalonic acidemia can cause periods of serious illness, called metabolic crises, which are often triggered by going for long periods without food, illness, or by eating large amounts of protein. Signs of a metabolic crisis include extreme sleepiness, irritable mood, poor appetite, vomiting, fever, diarrhea, vomiting, muscle weakness, or hypoglycemia (low blood sugar). Without treatment, more serious problems can occur, including seizures, stroke, coma, or death.

Even if a child does not have a metabolic crisis, long-term effects, such as poor growth, developmental delay, mental retardation, skin rashes, and liver and kidney problems, can be caused if the child is untreated.

➤ **How is methylmalonic acidemia diagnosed?**

False positive and false negative results are possible with this screening. If C3 (propionylcarnitine) is elevated, additional confirmatory blood tests will be ordered.

➤ **Is there a cure for methylmalonic acidemia?**

No, there is no cure for methylmalonic acidemia. Early and lifelong treatment gives children the best chance for normal development; however, not all medical problems can be prevented.

➤ **How is methylmalonic acidemia treated?**

- Lifelong treatment is required. Your child will likely need a diet that is low in protein and high in carbohydrates, which may include special medical foods and formulas. Medical formula contains the right types of nutrients your child needs for growth and development.
- Individuals with methylmalonic acidemia need to eat frequently and should avoid going long times without food. If your child is ill or is not eating, they may need to be treated at a hospital.
- Supplementation of L-carnitine may be prescribed. This substance helps the body make energy and get rid of harmful wastes.
- Liver or kidney transplants are sometimes given to children with methylmalonic acidemia.

➤ **Where can I get additional information?**

Organic Acidemia Association at www.oaanews.org

CLIMB (Children Living with Inherited Metabolic Disorders) at www.climb.org.uk

GeneTests at www.genetests.org

03/23/09



Methylmalonic Acidemia (MUT) Information for Parents

➤ **Overview**

Methylmalonic acidemia (MUT), also known as methylmalonyl CoA mutase deficiency, is a condition that affects infants from birth (congenital). Babies have difficulty breaking down food and fat in a way that their body can use them for nutrients and energy.

➤ **What is methylmalonic acidemia (MUT)?**

Our bodies break down the food we eat into nutrients that our body needs. Certain chemicals in our bodies, called enzymes, help with this process. One enzyme called methylmalonyl CoA mutase helps break down proteins and fats. Methylmalonic acidemia (MUT) occurs if this enzyme is missing or is not working properly. As a result, certain harmful substances can build up in the body and cause health problems.

➤ **Why is newborn screening done for methylmalonic acidemia?**

Newborn screening is done for methylmalonic acidemia so that babies with this condition can be diagnosed and treated quickly. Immediate diagnosis and treatment of methylmalonic acidemia gives babies the best opportunity for normal brain development and physical growth. Without prompt diagnosis and treatment, infants with methylmalonic acidemia will develop varying degrees of mental retardation and may experience death.

➤ **Does a positive result from the Kansas Newborn Screening Lab mean that my baby has methylmalonic acidemia?**

No, not necessarily. Newborn screening tests for elevated levels of a certain compound called C3 in a baby's blood. Additional tests will need to be done to determine if a baby has methylmalonic acidemia or not.

➤ **How common is methylmalonic acidemia?**

Methylmalonic acidemia (MUT) affects greater than 1 in every 75,000 infants. It affects boys and girls equally and does not occur more often in a specific ethnic group or race.

➤ **Is methylmalonic acidemia inherited?**

Methylmalonic acidemia is inherited in an autosomal recessive manner. This means that both parents of the affected child are carriers of the condition, but they do not have the disease. Each pregnancy between carrier parents has a 25% chance of producing a child affected with methylmalonic acidemia, a 50% chance of producing an unaffected carrier child, and a 25% chance of producing a child who is unaffected and is not a carrier.

➤ **What are the signs and symptoms of methylmalonic acidemia?**

Most infants with methylmalonic acidemia appear normal at birth, though symptoms often begin shortly after birth. These symptoms include lethargy, vomiting, and dehydration. Methylmalonic acidemia can cause periods of serious illness, called metabolic crises, which are often triggered

by going for long periods without food, illness, or by eating large amounts of protein. Signs of a metabolic crisis include extreme sleepiness, irritable mood, poor appetite, vomiting, fever, diarrhea, muscle weakness, or hypoglycemia (low blood sugar). Without treatment, serious health consequences can result, such as seizures, stroke, coma, or death.

Even if a child does not have a metabolic crisis, long-term effects, such as poor growth, developmental delay, mental retardation, skin rashes, and liver and kidney problems, can result if the child is untreated.

➤ **How is methylmalonic acidemia diagnosed?**

False positive and false negative results are possible with this screening. If C3 (propionylcarnitine) is elevated, additional confirmatory blood tests will be ordered. Elevated C3 may be due to methylmalonic or propionic acidemia, which have similar symptoms. Additional testing will be needed to distinguish them.

➤ **Is there a cure for methylmalonic acidemia?**

No, there is no cure for methylmalonic acidemia. Treatment that is started early, and continued for a lifetime, is the best way to prevent complications. However, not all medical problems can be prevented by early treatment.

➤ **How is methylmalonic acidemia treated?**

- Lifelong treatment is required. Your child will likely need a diet that is low in protein and high in carbohydrates, which may include special medical foods and formulas. Medical formula contains the right types of nutrients your child needs for growth and development.
- Individuals with methylmalonic acidemia need to eat frequently and should avoid going long times without food. If your child is ill or is not eating, they may need to be treated at a hospital.
- Supplementation of L-carnitine may be prescribed. This substance helps the body make energy and get rid of harmful wastes.
- Liver or kidney transplants are sometimes given to children with methylmalonic acidemia.

➤ **Where can I get additional information?**

Organic Acidemia Association at www.oaanews.org

CLIMB (Children Living with Inherited Metabolic Disorders) at www.climb.org.uk

GeneTests at www.genetests.org

11/24/08



Propionic Acidemia Information for Parents

➤ **Overview**

Propionic acidemia is a condition that affects infants from birth (congenital) and results from an inability of the body to break down certain parts of food. It is an example of an organic disorder.

➤ **What is propionic acidemia?**

Our bodies break down the protein from the food that we eat into smaller parts, called amino acids. Certain chemicals in our bodies, called enzymes, make changes to these amino acids so that the body can use them. Propionic acidemia occurs when the enzyme that breaks down certain amino acids is missing or not working correctly. This causes propionic acid to build up in the body and results in health problems.

➤ **Why is newborn screening done for propionic acidemia?**

Newborn screening is done for propionic acidemia so that babies with this condition can be diagnosed and treated quickly. Immediate diagnosis and treatment of propionic acidemia gives babies the best opportunity for normal brain development and physical growth. Without prompt diagnosis and treatment, infants with propionic acidemia will develop varying degrees of mental retardation and may experience death.

➤ **Does a positive result from the Kansas Newborn Screening Lab mean that my baby has propionic acidemia?**

No, not necessarily. Newborn screening tests for elevated levels of the compound C3 (propionyl carnitine) in a baby's blood. Additional tests will need to be done to determine if a baby has propionic acidemia or not.

➤ **How common is propionic acidemia?**

Propionic acidemia affects greater than 1 in every 75,000 infants. It is more common in Saudi Arabians and the Inuit population of Greenland.

➤ **Is propionic acidemia inherited?**

Propionic acidemia is inherited in an autosomal recessive manner. This means that both parents of the affected child are carriers of the condition, but they do not have the disease. Each pregnancy between carrier parents has a 25% chance of producing a child affected with propionic acidemia, a 50% chance of producing an unaffected carrier child, and a 25% chance of producing a child who is unaffected and is not a carrier.

➤ **What are the signs and symptoms of propionic acidemia?**

Most babies with propionic acidemia will begin to have symptoms within the first few days after birth. Propionic acidemia can cause periods of illness, called metabolic crises, which are more common if the baby goes for long periods of time without food, eats a lot of protein, or is sick. Symptoms of a metabolic crisis include extreme sleepiness, changes in behavior, a poor appetite, vomiting, and “floppy” muscles. If not treated, a metabolic crisis can lead to breathing problems, swelling of the brain, seizures, coma, stroke, and even death.

Propionic acidemia can cause long-term effects, such as inflammation of the pancreas, poor growth, delays in walking, learning difficulties or mental retardation, and rigid muscles.

➤ **How is propionic acidemia diagnosed?**

False positive and false negative results are possible with this screening. If C3 (propionyl carnitine) is elevated, additional confirmatory blood and urine tests will be ordered. Another organic acid disorder called methylmalonic acidemia looks the same on the newborn screening test.

➤ **Is there a cure for propionic acidemia?**

No, there is no cure for propionic acidemia. However, the outcome is usually good if infants are treated early and continue with lifelong treatment.

➤ **How is propionic acidemia treated?**

- Lifelong treatment is required. The primary treatment for propionic acidemia is a diet that is low in the amino acids leucine, methionine, valine, and threonine. The diet may require special medical foods and formulas. Medical formulas contain the right type of nutrients your child needs for growth and development.
- Individuals with propionic acidemia need to eat frequently and should avoid going long times without food. If your child is ill or is not eating, they may need to be treated at a hospital.
- Supplementation of L-carnitine may be prescribed. This substance helps the body make energy and get rid of harmful wastes. Children may also be given antibiotics and/or biotin supplements.

➤ **Where can I get additional information?**

Propionic Acidemia Foundation at www.pafoundation.com

Organic Acidemia Association at www.oaanews.org

Children Living with Inherited Metabolic Disorders at www.climb.org.uk

11/24/08