<table>
<thead>
<tr>
<th>Disease Name</th>
<th>MAPLE SYRUP URINE DISEASE (MSUD)</th>
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<tbody>
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<td>(BRANCHED-CHAIN KETOACIDURIA; BRANCHED-CHAIN ALPHA-KETO ACID DEHYDROGENASE DEFICIENCY; MSUD; KETO ACID DECARBOXYLASE DEFICIENCY)</td>
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<tr>
<td>Classification:</td>
<td>Organic aciduria</td>
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### Genetic Information

| Inheritance: | Autosomal recessive.. |
| Population Incidence: | Worldwide frequency is 1:185,000 births |
| Ethnic Incidence: | Old Order Mennonite frequency is 1:176 births. Ashkenazi Jews 1:113 births. Increased incidence among the aboriginal tribes in Taiwan. |

| Gene & Location: | E1α. located on 19q13.1-q13.2  
E1β. located on 6p21-p22  
E2- located on 1p31  
E3- located on 7q31-q32 |

| Common Mutation: | More than 63 mutations in all four genes. Mennonite population has a common mutation of the Type IA phenotype- Y393N-α. Ashkenazi Jewish common mutation- R183P-E1β. Austronesian tribes with a common E2 gene 4.7kb deletion. Founder mutation among Filipino population- E2 gene deletion. |

| OMIM # | *248600; *248611; *248610; *246900 |

### Disease Information

| Symptom Onset: | Variable onset, usually by two years of age. Neonatal classic disease onset is most severe and most common. |
| Symptoms: | Classic form infants appear normal at birth and develop symptoms between four to seven days of life. Lethargy and poor suck are first signs followed by alternating hyper and hypotonia, irritability and dystonia. Progress to severe ketoacidosis, hyperammonemia, with seizures and coma leading to death if untreated. Hypoglycemia is not a prominent feature. Pseudotumor cerebri is occasionally observed. Infants with milder forms may only present with episodic acidosis during intercurrent illnesses or other stressors and labs may be normal between episodes. |
| Physical Findings: | No particular dysmorphisms do have prominent neurological findings when ill. Cerumen, urine or sweat may smell faintly of maple syrup. |
| Treatment: | Dietary management with decreased leucine in diet and limited isoleucine and valine. Aggressive management of acute metabolic events. |

### Natural History

**without treatment:** The classic form progresses to coma and death if untreated. The intermediate form develops neurological damage and bouts of metabolic decompensation. The intermittent form has normal development with intermittent episodes of metabolic decompensation. Even without metabolic decompensation, a chronic high level of BCAA has been shown to cause demyelination.

**with treatment:** Age of diagnosis and metabolic control are the most important determinants of long-term outcome. Patients with classical disease started on treatment after 14 days of life rarely achieve normal intellect. Early treatment has improved outcome, but there can be complications. Even with treatment some have died from brain edema. Depending on severity of metabolic events, neurological outcome varies.

### Metabolic Information

| Missing Enzyme & Location: | Branched-chain alpha-keto acid dehydrogenase is a multi-enzyme complex loosely associated with the inner membrane of the mitochondria responsible for the breakdown of the branched chain amino acids. |
| **MS/MS profile:** | Leucine- elevated.  
Leucine to alanine ratio – elevated. |
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<td><strong>Prenatal testing:</strong></td>
<td>Prenatal diagnosis is possible by enzyme assay or if mutations known can do molecular diagnosis.</td>
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<td><strong>Miscellaneous Information:</strong></td>
<td>E3 gene deficiency causes a defect in dihydrolipoyl dehydrogenase with resultant defects in branched chain metabolism, pyruvate dehydrogenase and alpha ketoglutarate dehydrogenase and typically a more severe, progressive course and later onset of symptoms.</td>
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<tr>
<td><strong>Credit:</strong></td>
<td>Prepared by the North West Regional Newborn Screening Program Judith Tuerck, RN, MS, and Lorinda Paradise at Oregon Health Services University in Portland, Oregon and by Sara Copeland MD, Iowa Neonatal Metabolic Screening Program.</td>
</tr>
</tbody>
</table>
| **Sites of Reference:** | Dietary Specialties - Low Protein Foods [www.dietspec.com/](http://www.dietspec.com/)  
Maple Syrup Urine Disease (MSUD) [www.doh.wa.gov/EHSPHL/PHL/Newborn/msud.htm](http://www.doh.wa.gov/EHSPHL/PHL/Newborn/msud.htm)  
MUMS - National Parent-to-Parent Network [www.netnet.net/mums/](http://www.netnet.net/mums/)  
| **Support Groups:** | MSUD Family Support Group  
24806 SR119  
Goshen, IN 46526  
[www.msud-support.org/](http://www.msud-support.org/)  
(219) 862-2992  
Fax: (219) 862-2012  
Contact: Joyce Brubacher  
[msud-support@juno.com](mailto:msud-support@juno.com)  
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[steve@climb.org.uk](mailto:steve@climb.org.uk)  
[www.climb.org.uk](http://www.climb.org.uk)  
National Coalition for PKU & Allied Disorders  
P.O. Box 1244  
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[www.pku-allieddisorders.org/](http://www.pku-allieddisorders.org/)  
Contact: Trish Mullaley  
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