### Disease name
**Maple syrup urine disease**

### Alternate name(s)
Branched chain ketoaciduria, Branched chain alpha-keto dehydrogenase deficiency

### Acronym
MSUD type 1A, BCKD deficiency

### Disease classification
Organic Acid Disorder

### Variants
Yes

### Variant name
MSUD type 1B, MSUD Type II, Intermittent branched-chain ketoaciduria, Intermediate branched-chain ketoaciduria, Thiamine responsive MSUD

### Symptom onset
Neonatal with some variability

### Symptoms
Lethargy progressive to coma and possible death, vomiting, difficulty feeding, opisthotonic posturing, hypoglycemia, possible high pitched cry.

### Natural history without treatment
Neurologic abnormalities and profound mental retardation.

### Natural history with treatment
Normal IQ and development may be expected if treatment is initiated before first crisis, but development is delayed in the severest cases.

### Treatment
Dietary restriction of the branched chain amino acids and supplementation with medical formula. Thiamine supplementation in thiamine responsive patients.

### Other
“Maple syrup”-like odor to urine (usually present during crisis)

### Physical phenotype
None

### Inheritance
Autosomal recessive

### General population incidence
1:200,000
**Ethnic differences**
Yes

**Population**
Mennonites, French-Canadians

**Ethnic incidence**
1/760 (Mennonites)

**Enzyme location**
Inner mitochondrial membrane; liver, kidney, leukocytes and fibroblasts.

**Enzyme function**
Catalyzes the decarboxylation of oxoacids.

**Missing enzyme**
Branched-chain ketoacid dehydrogenase (BCKAD). This enzyme is a multienzyme complex with 3 components – E1, E2 and E3.

**Metabolite changes**
Increased leucine, isoleucine and valine in plasma and urine, increased organic acids in urine.

**Gene**
Four genes are involved in formation of multicomplex enzyme.

**Gene location**
- E1alpha = 19q13.1-13.2
- E1beta = 6p21-22
- E2 = 1p31
- E3=7q31-32

**DNA testing available**
Yes

**DNA testing detail**
Common mutation present in Mennonites (Y393N-alpha) and comprehensive DNA mutation analysis.

**Prenatal testing**
Enzyme testing by CVS or amnio. If mutation is known, DNA testing may be available.

**MS/MS profile**
Leucine elevated, leucine to alanine ratio elevated.

**OMIM link**

**Genetests link**
www.genetests.org/servlet/access?prg=j&db=genestar&site=&fcn=d&id=12600&qry=22186&res=nous&res=nointl&key=hp5d0Ly2h80eI&show_flag=c

**Support group**
The MSUD Family Support Group
www.msud-support.org

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

National Coalition for PKU and Allied Disorders
www.pku-allieddisorders.org
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