<table>
<thead>
<tr>
<th><strong>Disease name</strong></th>
<th>Methylmalonic acidemia, Vitamin B-12 responsive</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alternate name(s)</strong></td>
<td>Methylmalonic acidemia, Vitamin B-12 responsive, due to defect in adenosylcobalamin, cblA complementation type; Methylmalonic acidemia, cblA type; Methylmalonic acidemia, Vitamin B-12 responsive, due to defect in synthesis of adenosylcobalamin, cbl B complementation type</td>
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<tr>
<td><strong>Acronym</strong></td>
<td>MMA, MMAA/MMAB</td>
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<tr>
<td><strong>Disease classification</strong></td>
<td>Organic Acid Disorder</td>
</tr>
<tr>
<td><strong>Inheritance</strong></td>
<td>Autosomal recessive</td>
</tr>
<tr>
<td><strong>Variants</strong></td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Variant names</strong></td>
<td>Methylmalonic acidemia, Vitamin B-12 non-responsive; Combined deficiency of methylmalonyl-CoA mutase and homocysteine</td>
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<tr>
<td><strong>Symptom onset</strong></td>
<td>Variable. Ranges from the first days of life to completely asymptomatic.</td>
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<tr>
<td><strong>Symptoms</strong></td>
<td>Episodic ketoacidosis with vomiting accompanied by lethargy and coma which can lead to death. Survivors can have developmental delays, growth retardation, spastic quadripareisis, dystonia and seizures. Neutropenia, thrombocytopenia and osteoporosis are common complications.</td>
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<tr>
<td><strong>Natural history without treatment</strong></td>
<td>Variable depending on the enzyme defect. Some will die in the newborn period, others will survive with deficits and others will be asymptomatic.</td>
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<tr>
<td><strong>Natural history with treatment</strong></td>
<td><strong>CblA</strong>: Good prognosis with injections of hydroxy-cobalamin (OH-cbl) which reverses biochemical and clinical abnormalities in about 90% of patients.</td>
</tr>
</tbody>
</table>
**CblB:** Equal fractions of affected patients are alive and well, alive and impaired, or deceased. The age of onset of symptoms can help prognosticate outcome – those patients with a later onset of symptoms have a more benign course. Approximately 40% of patients will respond with a drop in MMA level when given OH-cbl injections.

### Treatment
Protein restricted diet, OH-cbl injections, carnitine supplementation, oral antibiotic therapy to decrease propionate and medical foods. Liver transplant or combined liver/kidney transplant may increase metabolic control, but may not prevent neurologic complications.

### Other
N/A

### Physical phenotype
Minor facial dysmorphisms including high forehead, broad nasal bridge, epicanthal folds, long, smooth philtrum and triangular mouth. A variety of skin lesions can be seen in patients due to moniliasis.

### Inheritance
Autosomal recessive

### General population incidence
1:48,000

### Ethnic differences
No known population at increased risk

### Population
N/A

### Ethnic incidence
N/A

### Enzyme location
Mitochondria

### Enzyme function
Production of adenosylcobalamin

### Missing enzyme
Cobalamin A (cblA) deficiency: cobalamin reductase
Cobalamin B (cblB) deficiency: cobalamin adenosyltransferase

### Metabolite changes
Elevated glycine in urine

### Gene
MMAA (cobalamin A disease)  
MMAB (cobalamin B disease)

### Gene location
MMAA: 4q31.1-q31.2  
MMAB: 12q24
**DNA testing available**
Sequencing available internationally

**DNA testing detail**
N/A

**Prenatal testing**
Possible via enzyme assay on amniocytes or CVS

**MS/MS profile**
Elevated C3 propionyl carnitine, elevated C4 DC methylmalonyl carnitine.

**OMIM link**

**Genetests link**
www.genetests.org/servlet/access?prg=j&db=genetests&site=gt&id=8888891&fcn=c&qry=22174&res=nous&res=nointl&key=ya10OD5WOSqMG&show_flag=c

**Support Group**
Organic Acidemia Association
www.oaanews.org

Save Babies through Screening Foundation
www.savebabies.org

Genetic Alliance
www.geneticalliance.org

Fatty Oxidation Disorder (FOD) Family Support Group
www.fodsupport.org

Organic Acidemia Association
www.oaanews.org

Save Babies through Screening Foundation
www.savebabies.org

Genetic Alliance
www.geneticalliance.org

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**Reviewed by**
HI, CA, OR and WA metabolic specialists

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**Update on**
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