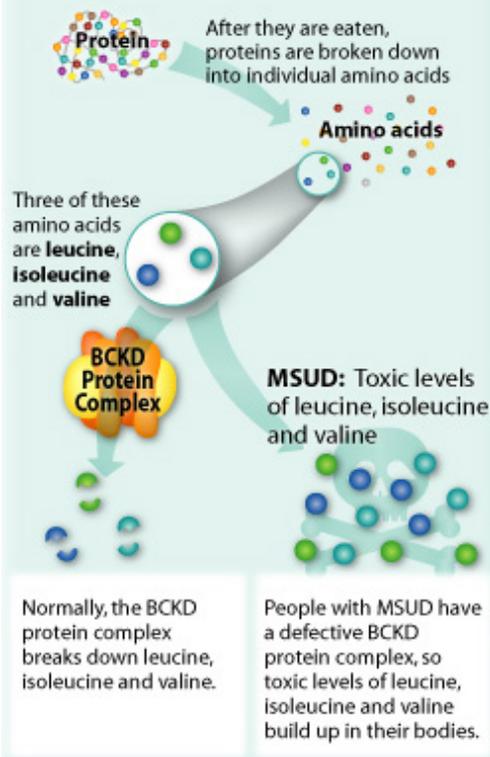




MAPLE SYRUP URINE DISEASE INFORMATION FOR PARENTS/CARERS

People with MSUD Have a Defective BCKD Protein Complex



Maple Syrup Urine Disease, or MSUD (also called branched-chain ketonuria), is a genetic disorder. The name comes from the characteristic odour of the urine of affected infants.

MSUD is a potentially deadly disorder that affects the way the body breaks down three amino acids, leucine, isoleucine, and valine. When they're not being used to build a protein, these three amino acids can be either be recycled or broken down and used for energy. They are normally broken down by six proteins that act as a team and form a complex called BCKD (branched-chain alpha-ketoacid dehydrogenase).

Therefore, they can't break down leucine, isoleucine, and valine. They end up with dangerously high levels of these amino acids in their blood, causing the rapid degeneration of brain cells and death if left untreated.

What are the symptoms of MSUD?

There is a classic form of MSUD and several less common forms. Each form varies in its severity and characteristic features. However, all subtypes of the disorder can be caused by mutations in any of the 6 genes used to build the BCKD protein complex.

A baby who has the disorder may appear normal at birth. But within three to four days, the symptoms appear. These may include: loss of appetite, fussiness, and sweet-smelling urine. The elevated levels of amino acids in the urine generate the smell, which is reminiscent of maple syrup. This is how MSUD got its name. If left untreated, the condition usually worsens. The baby will have seizures, go into a coma, and die within the first few months of life.

How do doctors diagnose MSUD?

All babies need to be screened for MSUD within 24 hours after birth. A blood sample taken from the baby's heel is analyzed for high leucine levels.

How is MSUD treated?

Treatment involved dietary restriction of the amino acids leucine, isoleucine, and valine.



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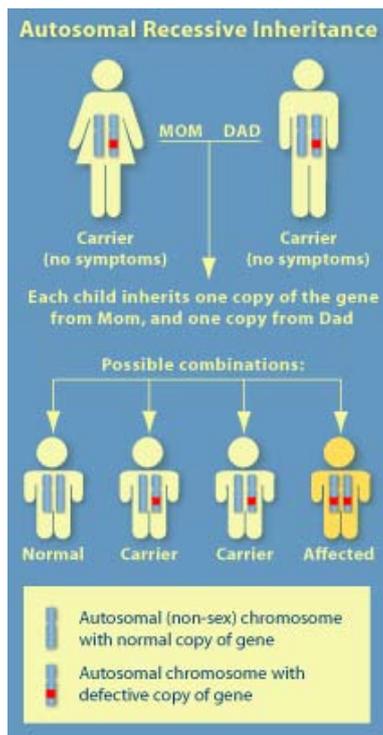
This treatment must begin very early to prevent brain damage. Babies with the disease must eat a special formula that does not contain the amino acids leucine, isoleucine, and valine. As the person grows to adulthood, he or she must always watch their diet, avoiding high protein foods such as meat, eggs, and nuts.

If levels of the three amino acids still get too high, patients can be treated with an intravenous (given through a vein) solution that helps the body use up excess leucine, isoleucine, and valine for protein synthesis.

A few patients have been described with milder variants of maple syrup urine disease. These mild variant patients may respond to the B vitamin thiamine, but this treatment is not useful in the usual form of MSUD.

Gene therapy is also a potential future treatment for patients with MSUD. This would involve replacing the mutated gene with a good copy, allowing the patient's cells to generate a functional BCKD protein complex and break down the excess amino acids.

How do people get MSUD?



MSUD is inherited in an autosomal recessive pattern. For a child to get the disease, he or she must inherit a defective copy of the gene from each parent. If both parents carry the MSUD gene, each of their children has a 25 percent chance of getting the disorder, and a 50 percent chance of being a carrier.

How many people have MSUD?

About one in every 200,000 babies is born with MSUD

If MSUD is not treated, what problems occur?

There are a number of different forms of MSUD. The most common form, "classic MSUD", can be life-threatening and must be treated promptly to prevent serious health problems. Other forms, including 'intermediate' and 'intermittent' forms of MSUD, are less severe. These milder forms are less common. This fact sheet contains information on classic MSUD.

