



Genetic Fact Sheets for Parents

Organic Acid Disorders

Screening, Technology, and Research in Genetics is a multi-state project to improve information about the financial, ethical, legal, and social issues surrounding expanded newborn screening and genetic testing – [http:// www.newbornscreening.info](http://www.newbornscreening.info)

Disease name: Beta ketothiolase deficiency
Acronym: BKD

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This fact sheet has general information about BKD. Every child is different and some of these facts may not apply to your child specifically. Certain treatments may be recommended for some children but not others. All children with BKD should be followed by a metabolic doctor in addition to their primary doctor.

What is BKD?

BKD stands for “beta ketothiolase deficiency”. It is one type of organic acid disorder. People with BKD have problems breaking down an amino acid called isoleucine from the food they eat.

Organic Acid Disorders:

Organic acid disorders (OAs) are a group of rare inherited conditions. 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.

The symptoms and treatment vary between different organic acid disorders. They can also vary from person to person with the same organic acid disorder. See the fact sheets for each specific organic acid disorder.

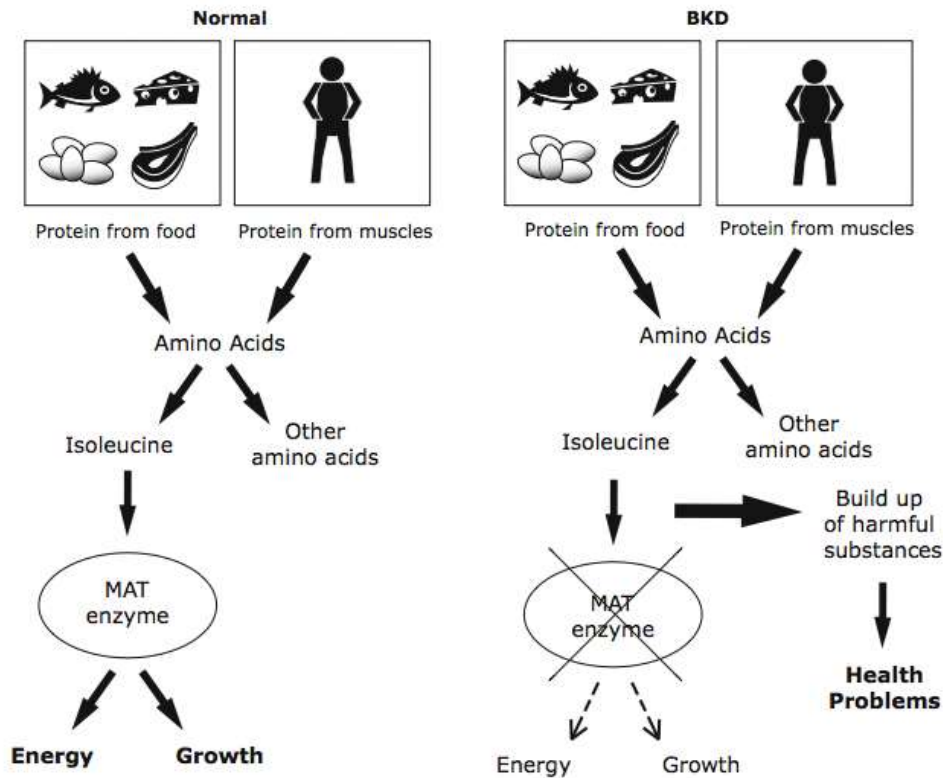
Organic acid disorders are inherited in an autosomal recessive manner and affect both males and females.

What causes BKD?

In order for the body to use protein from the food we eat, it is broken down into smaller parts called amino acids. Special enzymes then make changes to the amino acids so the body can use them.

BKD occurs when an enzyme, called “mitochondrial acetoacetyl-CoA thiolase” (MAT), is either missing or not working properly. This enzyme’s job is to help break down the amino acid isoleucine. When a child with BKD eats food containing isoleucine, harmful substances called organic acids build up in the blood and cause problems. Isoleucine is found in all foods that contain protein.

Beta Ketothiolase deficiency (BKD)



If BKD is not treated, what problems occur?

Each child with BKD has slightly different effects. The first symptoms often start around age one, although babies can show signs either earlier or later than this. Some people with BKD never develop symptoms.

BKD can cause episodes of illness called metabolic crises. Some of the first symptoms of a metabolic crisis are:

- extreme sleepiness or lack of energy
- vomiting
- diarrhea
- fever
- poor appetite
- ketones in the urine (substances created during the breakdown of fat)

Other symptoms then follow:

- increased levels of acidic substances in the blood, called metabolic acidosis
- low blood sugar, called hypoglycemia
- coma, sometimes leading to death

Episodes of metabolic crisis can be triggered by:

- going too long without food
- illness or infection
- eating too much protein

Other long-term effects of untreated BKD can include:

- intellectual disabilities
- enlarged heart with irregular heart beat
- poor growth
- abnormal muscle tone (too floppy or too rigid)
- jerky uncoordinated movements
- low platelets
- low level of white blood cells (increasing the risk of infection)

Some people with BKD never have symptoms and are only found to be affected after a brother or sister is diagnosed.

What is the treatment for BKD?

Your baby's primary doctor will work with a metabolic doctor and a dietician to care for your child.

Prompt treatment is needed to prevent metabolic crises and the health effects that follow. When necessary, treatment is usually needed throughout life.

The following are treatments sometimes advised for babies and children with BKD:

1. Medication

Some children may be helped by taking L-carnitine by mouth. This is a safe and natural substance that helps body cells make energy. It also helps the body get rid of harmful wastes. Your doctor will decide whether or not your child needs L-carnitine supplements. Unless you are advised otherwise, use only L-carnitine prescribed by your doctor. Do not use any medication without checking with your metabolic doctor.

Children with symptoms of a metabolic crisis need to be treated in the hospital. During a metabolic crisis, your child may be given medications such as bicarbonate by IV to help reduce the acid levels in the blood. In addition, glucose is often given by IV to prevent the breakdown of body stores of protein. Ask your metabolic doctor if you should carry a special travel letter with medical instructions for your child's care.

2. Avoid going a long time without food

Some infants and young children with BKD need to eat frequently to prevent a metabolic crisis. Your metabolic doctor will tell you how often your child needs to be fed. Your doctor will also give you a 'sick day' plan, tailored to your child's needs, for you to follow during illnesses or other times when your child will not eat.

Your metabolic doctor will continue to advise you on how often your child should eat as he or she gets older. When they are well, many teens and adults with BKD can go without food for up to 12 hours without problems. The other treatments usually need to be continued throughout life.

3. Low-protein diet

Some children may be able to eat normal amounts of protein, but others will need to be on a low-protein diet.

Foods high in protein that may need to be limited include:

- milk and dairy products
- meat and poultry
- fish
- eggs
- dried beans
- nuts and peanut butter

Eating large amounts of these foods can cause protein levels to become too high, causing illness. However, do not remove all protein from the diet. Children with BKD need a certain amount of protein to grow properly.

If it is necessary for your child to eat a low-protein diet, your dietician can help you create a food plan that meets your child's needs. Any diet changes should be made under the guidance of a dietician.

4. Tracking ketone levels

Periodic urine tests to test the level of ketones may be necessary. This can be done at home or at the doctor's office. Ketones are substances formed when body fat is broken down for energy. This happens after going without food for long periods of time, during illness, or during periods of heavy exercise. Ketones in the urine may signal the start of a metabolic crisis.

5. Call your doctor at the start of any illness

In some children, even minor illness can lead to a metabolic crisis. In order to prevent problems, call your doctor right away when your child has any of the following:

- loss of appetite
- vomiting
- diarrhea

- infection or illness
- fever

When your child is ill, he or she needs extra fluids and carbohydrates to prevent a metabolic crisis. Whenever your child becomes ill, it is important to restrict protein and give him or her extra starchy or sugary foods.

What happens when BKD is treated?

If treatment is started early and metabolic crises do not occur, your child is likely to have normal growth and intelligence. Even with treatment, some children still have repeated episodes of metabolic crises, which can cause brain damage. This can result in learning disabilities, intellectual disabilities or other problems.

Between episodes of metabolic crisis, people with BKD are usually healthy. Metabolic crises tend to happen less often as a child gets older. They are rare in children older than 10.

What causes the MAT enzyme to be absent or not working correctly?

Genes tell the body to make various enzymes. People with BKD have a pair of genes that do not work correctly. Because of the changes in this pair of genes, the MAT enzyme either does not work properly or is not made at all.

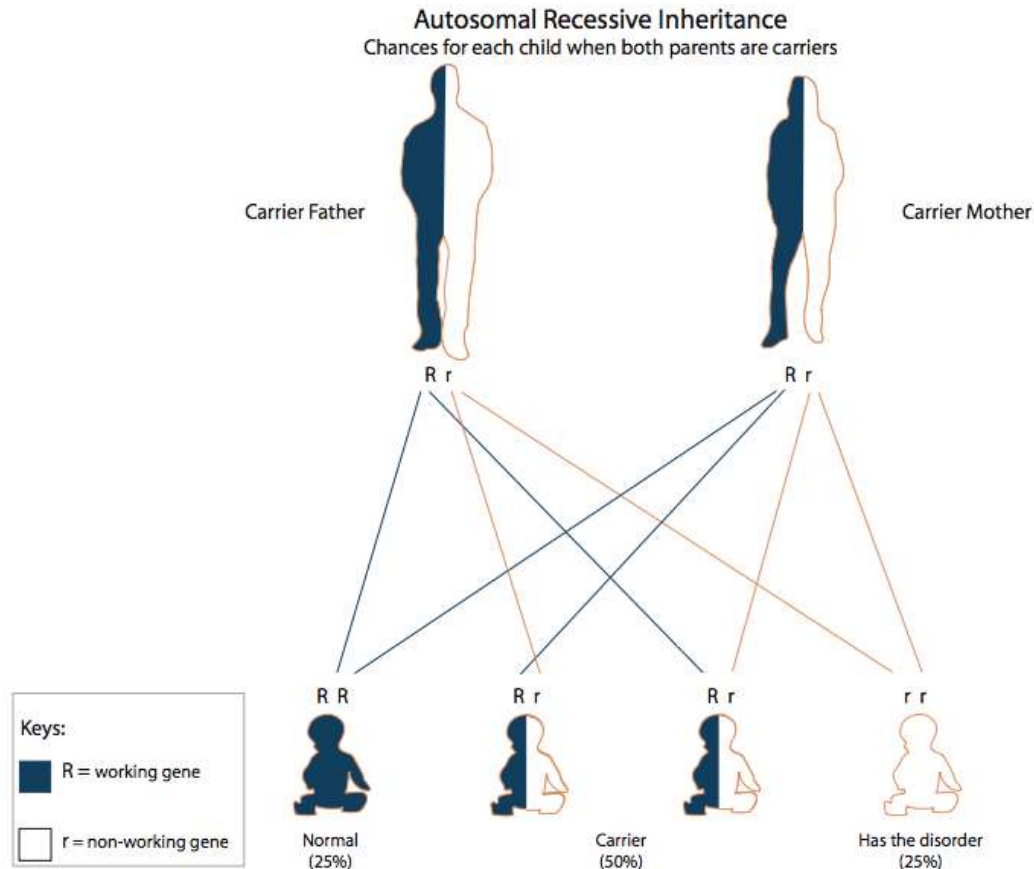
How is BKD inherited?

BKD is inherited in an autosomal recessive manner. It affects both boys and girls equally.

Everyone has a pair of genes that make the MAT enzyme. In children with BKD, neither of these genes works correctly. These children inherit one non-working gene for the condition from each parent.

Parents of children with BKD rarely have the condition themselves. Instead, each parent has a single non-working gene for BKD. They are called carriers. Carriers do not have BKD because the other gene of this pair is working correctly.

When both parents are carriers, there is a 25% chance in each pregnancy for the child to have BKD. There is a 50% chance for the child to be a carrier, just like the parents. And, there is a 25% chance for the child to have two working genes.



Genetic counseling is available to families who have children with BKD. Genetic counselors can answer your questions about how the condition is inherited, choices during future pregnancies, and how to test other family members. Ask your doctor about a referral to a genetic counselor.

Is genetic testing available?

Genetic testing for BKD is available. Genetic testing, also called DNA testing, looks for changes in the pair of genes that causes BKD. Talk with your genetic counselor or metabolic doctor if you have questions about DNA testing.

DNA testing is not necessary to diagnose your child. It can be helpful for carrier testing or prenatal diagnosis, discussed below.

What other testing is available?

Special tests on urine, blood or skin samples can be done to help confirm BKD. Talk to your doctor or your genetic counselor if you have questions about testing for BKD.

Can you test during pregnancy?

If both gene changes have been found in your child, DNA testing can be done during future pregnancies. The sample needed for this test is obtained by either CVS or amniocentesis.

Parents may choose to have testing during pregnancy or wait until birth to have the baby tested. A genetic counselor can talk to you about your choices and answer questions about prenatal testing or testing your baby after birth.

Can other members of the family have BKD or be carriers?

Having BKD

Older brothers and sisters of a baby with BKD may have a small chance of being affected, even if they haven't had symptoms. Finding out whether other children in the family have BKD is important because early treatment may prevent serious health problems. Talk with your metabolic doctor or genetic counselor about testing your other children.

BKD carriers

Brothers and sisters who do not have BKD still have a chance to be carriers like their parents. Except in special cases, carrier testing should only be done in people over 18 years of age.

Each of the parents' brothers and sisters has a 50% chance to be a carrier. It is important for other family members to be told that they could be carriers. There is a small chance they are also at risk to have children with BKD.

All states offer newborn screening for BKD. However, when both parents are carriers, newborn screening results are not sufficient to rule out BKD in a newborn baby. In this case, special diagnostic testing should be done in addition to newborn screening.

Can other family members be tested?

Diagnostic testing

Brothers and sisters can be tested using blood, urine or skin samples.

Carrier testing

If both gene changes have been found in your child, other family members can have DNA testing to see if they are carriers.

If DNA testing is not possible or is not helpful, other methods of carrier testing may be available. Your metabolic doctor or genetic counselor can answer your questions about carrier testing.

How many people have BKD?

BKD is thought to be rare. The actual incidence is unknown.

Does BKD happen more frequently in a certain ethnic group?

No, BKD does not happen more often in any specific race, ethnic group, geographical area or country.

Does BKD go by any other names?

BKD is also sometimes called:

- Ketone utilization disorder
- Alpha-methylacetoacetic aciduria
- 2-methyl-3-hydroxybutyric acidemia
- Mitochondrial acetoacetyl-CoA thiolase deficiency
- MAT deficiency
- T2 deficiency
- 3-oxothiolase deficiency
- 3-ketothiolase deficiency
- 3-KTD deficiency

Where can I find more information?

Organic Acidemia Association

<http://www.oaaneews.org>

CLIMB (Children Living with Inherited Metabolic Diseases)

<http://www.climb.org.uk>

Save Babies through Screening Foundation
<http://www.savebabies.org>

Baby's First Test
<http://www.babysfirsttest.org>

Ketone Utilization Disorder: A Guide for Parents (PacNoRGG publication)
http://westernstatesgenetics.org/archives/pacnorgg/PDFs_all-081409/ketone_util_eng.pdf

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