KETONE UTILIZATION DISORDER (BETA-KETOTHIOLASE DEFICIENCY)

A Guide for Parents

Sponsored by PacNoRGG
The Pacific Northwest
Regional Genetics Group

This booklet contains general information about ketone utilization disorder, previously called beta-ketothiolase deficiency.

As every child with this disorder is different, the information in this booklet may not apply to your child specifically.

Please share this booklet with anyone who cares for your child, such as health providers, nutritionists, and other health care workers, school professionals, child care providers, and members of your family.

Feel free to ask your child's health provider any questions you may have about the enclosed information.

For your reference, a glossary of medical terms is included in the back of the booklet.

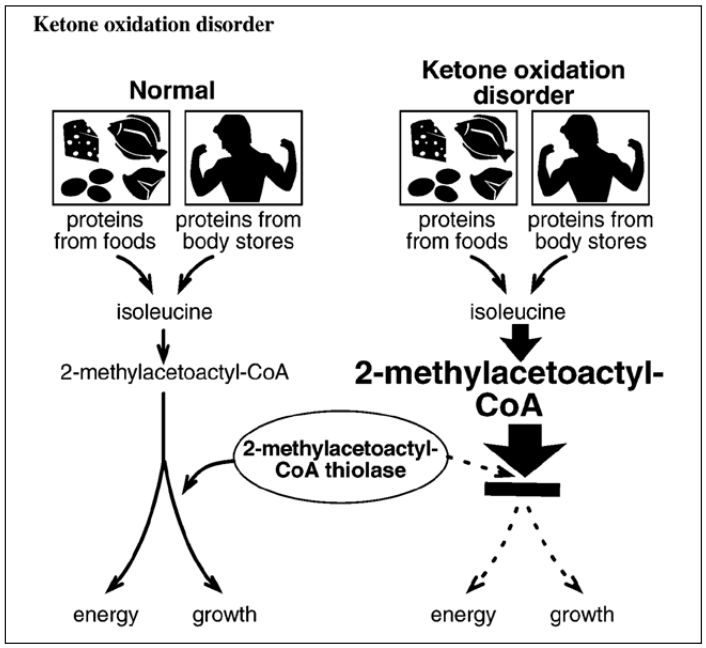
Ketone Utilization Disorder (Beta-Ketothiolase Deficiency)

Ketone utilization disorder, previously known as beta-kethothialase deficiency (pronounced bate-a key-toe thi-o-lase), is a generic term for a deficiency of a group of enzymes, one of which is called 2-methylacetoacetyl-CoA thiolase (pronounced 2-meth-el-a-see-toe-a-see-til-ko-A thi- o-laze). Sometimes this disorder is called by the complete name of the missing enzyme, 2- methylacetoacetyl-CoA thiolase deficiency.

An enzyme is a substance in the body that enables chemical reactions to occur. The enzyme missing in ketone utilization disorder would normally help the body break down proteins from foods, and proteins stored in the body. Since children with this disorder lack this enzyme, they are unable to completely break down proteins, causing toxic build-up in body tissues. (See Diagram 1.)

Ketone utilization disorder is an inherited metabolic problem. Children born with this disorder must follow a strict food pattern (another term for diet) limiting protein in order to stay healthy.

Diagram 1.
The metabolic defect in ketone utilization disorder.



Most proteins are eventually broken down to 2- methylacetoacetyl-CoA. In ketone utilization disorder, because the enzyme 2- methylacetoacetyl-CoA thiolase is inactive, protein cannot be completely broken down, and 2-methylacetoacetyl-CoA levels can build-up to result in illness.

Symptoms of Ketone Utilization Disorder

Normally, protein is used to provide energy for cell functions and growth, and to repair tissues. Often we eat more protein than the body needs. The extra protein in the body is chemically changed by enzymes into other compounds, and is stored in the body or used for energy. Since individuals with ketone utilization disorder are missing the enzyme for normal protein breakdown, the excess eaten in foods accumulates in the body and can cause severe illness.

Each child with ketone utilization defect will be affected slightly differently. But symptoms can include severe vomiting, diarrhea, and fever. With severe episodes, acidosis (the build up of harmful acids in the body) and even coma can occur.

The harmful effects of the ketone utilization disorder may be lessened if the child begins a low protein food pattern at the time of diagnosis and maintains this pattern throughout life. A low protein food pattern is the only way to keep amino acid levels in the blood at safe levels. At these levels the brain can function normally, and a child can grow and develop at the same rate as other children.

In addition, these children have difficulty using energy stored in the body during times of fasting. Thus, the food pattern includes avoidance of long periods of fasting by ensuring that not too much times passes between meals and snacks.

Treatment

There are three parts to successful treatment of ketone utilization defect:

1. A low protein food pattern.

The most effective treatment for ketone utilization disorder is a food pattern low in protein. This is *not* a protein-free food pattern. The body needs small amounts of protein to function properly. The amount of protein which can be tolerated ranges from child to child. Frequent visits to the health provider and/or nutritionist are recommended to be sure the food pattern is appropriate for your child. Meals and snacks should not be delayed or skipped.

2. Supplemental forms of carnitine and/or bicitra.

Carnitine is essential for muscle energy production and helps transport fat to cells where it can be converted into energy. Bicitra is a compound which helps your child maintain what is called an acid-base balance in the blood. These compounds also help decrease harmful by-products of normal protein breakdown.

Contact your health provider to see if these medications are needed for your child.

3. Immediate contact with your child's health provider when illness occurs.

All children become ill at times, whether or not they have ketone utilization disorder. Sometimes they catch a cold, the flu, or something more severe. Your child with ketone utilization disorder will need to take special precautions during these times.

Typical childhood illnesses may cause the body to break down its own sources of protein, causing toxic protein build-up.

To prevent this, give your child fluids and foods with extra energy, but no protein. Extra energy foods, such as sugar, will decrease the amount of protein broken down by the body. Feeding an ill child can sometimes be difficult, as sick children often have very little appetite. Encourage drinking of fluids as much as possible. Many children enjoy popsicles or drinks which are frozen, then chipped into ice chunks.

Always call the health provider when your child is vomiting, has diarrhea, has an infection, or has a fever of more than 101 degrees Fahrenheit.

Nutrition and Dietary Guidelines

The food pattern for ketone utilization disorder is low in protein. High protein foods that should be limited include milk and dairy products, meat, fish, chicken, eggs, beans, peanut butter, and nuts. Eating large quantities of these foods will cause protein levels to become too high, causing illness.

Again, it is important to remember that your child needs small amounts of protein for normal growth and development. Protein should not be completely eliminated from the food pattern. A nutritionist can help you create a specific food and supplement pattern to ensure your child will be well-nourished.

Many foods contain protein, and each one contains different amounts of protein. For this reason some foods should be limited because they contain too much protein. Other foods may be eaten in moderate amounts, and still others may be eaten freely.

The Low Protein Food Pattern

A. Low protein foods which can be included:

Cereals and Grains: (1/2 cup serving has about 2 grams protein)

cold cereals
hot cereals
bagels
breads
pasta noodles
croutons
english muffins
rice rolls
buns
wheat germ
pita bread
tortillas
animal crackers
graham crackers
crackers
popcorn
corn
potatoes
lentils
sweet potatoes
yams

Vegetables: (1/2 cup serving has about 1 gram protein)

broccoli
green beans/peas
asparagus
cauliflower
vegetable juices
carrots
lettuce
cabbage
onions
mushrooms
squash
spinach
radishes

Fruits: (1/2 cup serving has a trace of protein)

apples
oranges
fruit cocktail
apricots
grapes
berries
cherries
peaches
pears
fruit juices
raisins
pineapples
kiwi
tomatoes
bananas

B. High protein foods which should be limited:

(1 oz meat, 1 egg, or 8 oz milk each contain 7-10 grams protein)

meats
all forms of milk
nuts, seeds, and their products
poultry
cheeses
fish
yogurt
peanut butter
eggs
dairy products
dried peas and beans
ice cream

C. Foods with NO protein which provide extra energy

gum drops
hard candy
Kool-aid
jams and jellies
pure sugar
popsicles
sodas
suckers
margarine
oils
low protein pastas and breads

You may have questions regarding the amounts of protein in each food, and the following books may be good references for you to have. Your nutritionist should be able to tell you how they can be purchased.

Low Protein Food List for PKU
by Virginia Schuett
Dietary Specialties, Inc
PO 227, Rochester, NY
1-800-544-0099

Bowes & Church's Food Values of Portions Commonly Used, 17th ed.
by Jean AT Pennington
JB Lippincott

Your nutritionist will create a meal plan specifically designed to meet your child's unique needs for growth and development. Each child will be able to eat different amounts of protein. The nutritionist can introduce you to a wide variety of special low protein foods which can offer more food choices and variety.

For infants and children, a special formula (sometimes called a medical food) is often prescribed to provide the nutrients and energy your child may not be able to get from low protein foods alone. Ask your health provider or nutritionist if this is needed for your child.

Because your child will be limiting certain foods, the food pattern may not always have enough vitamins and minerals to meet your child's growing needs. **A general multivitamin and mineral supplement that includes calcium and iron is essential.**

Length of Treatment and Medical Visits

Ketone utilization disorder does not go away. The low protein food pattern must be continued throughout life to maintain health. Stopping the food pattern may lead to nervous system damage or even death, no matter how old your child is. However, as your child matures and develops, larger amounts of protein may be tolerated. Your child's nutritionist will be able to modify the food pattern when necessary.

Because your child has a life-long condition that could harm growth and development if left untreated, your child should be followed closely by your health provider and nutritionist.

Medical visits offer many advantages for children with ketone utilization disorder. The medical team will want to learn how your child gets along with parents, siblings, and friends, and work with you to solve problems. The goal is to help your child develop skills needed to take responsibility for managing his or her own condition. The staff knows this will not be easy, and wants to provide as much support as they can to you and your family. Most importantly, these visits offer you an opportunity to ask questions and get answers.

At a medical visit, you and your child can expect any of the following:

What to expect:	How it will help:
Discussion of medical history since last appointment	To determine if treatment is working, and to see if changes are needed; To talk about concerns at home, at school, with friends and/or with caregivers
Physical exam	To look at neurological status and other measures of physical well-being
Record of height, weight, and head size	To monitor child's growth and treatment
Food records	To look at food choices, assess the amounts of fats and proteins eaten, and adjust as needed
Developmental exam	To assess child's learning and development
Blood draw	To measure levels of amino acids and other compounds in the blood

Organizing Your Information

You may want to buy a 3-ring notebook binder with tab dividers to record information, questions, and food patterns. Here you can collect treatment plans, growth and medication records, questions, articles, food lists, recipes, and other information that may be useful to you. One section might hold food records, and another a graph of your child's growth and development. Make a list of questions as you think of them, so you'll remember them at your next medical visit.

Social Concerns

Every child is different, and will be affected by ketone utilization defect to a different degree. Some children will display physical or learning disabilities, while some may not. Your child will be tested periodically to assess these factors, and community resources are available to help you address the challenges of raising a child with special needs.

The family plays a very important role in your child's treatment. Children in the family, including the child with the disorder, should be taught about the low protein food pattern as soon as they are able to understand it. Encourage the other children to help feed your child with ketone utilization disorder so they become familiar with foods that are allowed and foods that are not allowed. Explain the disorder to everyone who will participate in the care of your child (relatives, day care providers, baby-sitters, friends, teachers, etc.) so they become familiar with the food pattern. Be sure to emphasize the importance of the special food pattern for normal growth and development. Teach siblings and relatives not to feel sorry for the child with the disorder because he or she cannot eat certain foods.

Treat your child with ketone utilization disorder as normally as possible. Despite efforts to make your affected child feel good about himself or herself, there may come a time when your child becomes aware of his or her uniqueness and simply wants to be like everyone else. Be sure to help your child celebrate his or her individuality and realize that every person is different in some way.

Genetics

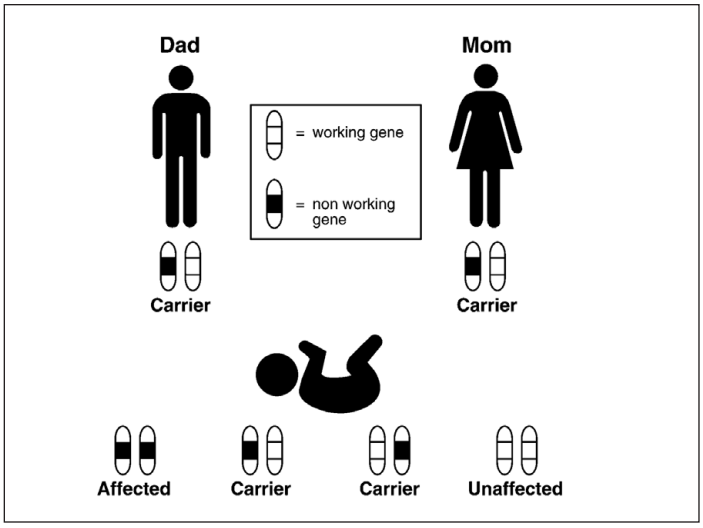
Within each child there are two copies of every gene; one copy from the mother and the other copy from the father. Most often, genes work normally. Sometimes however, a gene is changed from its original form. This is called a mutation. Mutations usually cause genes not to work correctly.

The gene change that causes ketone utilization disorder is inherited in what is called an autosomal recessive pattern. This means that one copy of the changed, or non-working, gene must be inherited from each parent for a child to be affected with the disorder. The parents' health is not affected because their other copy of the gene is working correctly. Therefore, each parent is called a gene "carrier." It is important to remember that all people carry several of these "hidden" recessive genes. Also, it is no one's fault that your child was born with ketone utilization disorder, and both boys and girls can have the problem.

The chance that two parents who carry the same changed gene will have a child with the disorder is one in four, or 25% with each pregnancy. The chance these parents will have a child that is healthy, but a carrier, is one in two, or 50% with each pregnancy. There is also a one in four, or 25% chance that these parents will have a child who is neither affected nor a carrier. (See Diagram 2.)

For affected individuals planning to have children, a consultation with a genetic counselor is recommended. The genetic counselor can explain the chances and risks of any future children being affected with the disorder, and can also explain options for testing.

Diagram 2.
Autosomal recessive inheritance



The chance that two parents who carry the same changed gene will have a child with the disorder is one in four, or 25% with each pregnancy.

Resources

Following is a list of agencies that may be helpful to you. Each agency specializes in different areas, such as health care, physical or mental development, support groups, or general information. Since each child is affected differently, not all agencies may be useful to you.

The ARC of the United States National Headquarters Office
1010 Wayne Ave, Ste 650
Silver Spring MD 20910
301/565-3842
Fax: 301/565-5342
info@thearc.org
http://www.TheArc.org

Genetic Alliance, Inc.
4301 Connecticut Ave NW Ste 404
Washington DC 20008
202/966-5557; 800/336-GENE (4363)
info@geneticalliance.org
http://www.geneticalliance.org

Metabolic Information Network
PO Box 670847
Dallas TX 75367-0847
214/696-2188; 800/945-2188
Fax: 214/696-3258
mizesg@ix.netcom.com

MUMS: National Parent-to-Parent Network
150 Custer Court
Green Bay Wisconsin 54301-1243
920/336-5333
Fax: 920/339-0995
mums@netnet.net
http://www.netnet.net/mums

National Center for Learning Disabilities
381 Park Ave S Ste 1401
New York NY 10016
212/545-7510; 888/575-7373
Fax: 212/545-9665
http://www.ncld.org

National Parent Network on Disabilities (NPND)
1130 - 17th Street NW Ste 400
Washington DC 20036
202/463-2299
Fax: 202/463-9405
npnd@mindspring.com
http://www.npnd.org

National Society of Genetic Counselors
233 Canterbury Drive
Wallingford PA 19086-6617
610/872-7608
nsgc@aol.com
http://www.nsgc.org

NORD: National Organization for Rare Disorders
PO Box 8923
New Fairfield CT 06812
203/746-6518; 800/999-6673
Fax: 203/746-6481
orphan@rarediseases.org
http://www.rarediseases.org

Organic Acidemia Association
13210 35th Ave. North
Plymouth, MN 55441
763-559-1797
Fax: 763-694-0017
http://www.oaanews.org
http://www.pafoundation.com

Washington State Parent-to-Parent Program
4738 - 172nd Court SE
Bellevue WA 98006
425/641-7504; 800/821-5927
statep2p@earthlink.net
http://www.arcwa.org

ALASKA

PARENTS: Parents as Resources Engaged in Networking and Training
4743 Northern Lights
Anchorage AK 99508
907/337-7678
Fax: 907/337-7671
parents@parentsinc.org
http://www.parentsinc.org/

IDAHO

Idaho Parents Unlimited
4696 Overland Road Ste 568
Boise ID 83705
208/342-5884; 800/242-4785 (ID only)
Fax: 208/342-1408
ipul@rmci.net
http://home.rmci.net/ipul

MONTANA

PLUK: Parents, Let's Unite for Kids
516 N 32nd Street
Billings MT 59101
406/255-0540; 800/222-7585
Fax: 406/225-0523
plukinfo@pluk.org
http://www.pluk.org

OREGON

Coalition in Oregon for Parent Education (COPE)
999 Locust Street NE
Salem OR 97303
503/581-8156; 888/505-COPE (2673)
Fax: 503/391-0429
orcope@open.org
http://www.open.org/~orcope/index.htm

WASHINGTON

Washington PAVE
6316 S 12th
Tacoma WA 98465
253/565-2266; 800/572-7368 (WA only)
Fax: 253/566-8052
wapave9@washingtonpave.com
http://www.washingtonpave.org

Treatment Plan

Prescribed food pattern:

Vitamin and/or mineral supplement: _____

Specific foods to be avoided:

Medication _____ Dose _____ Schedule _____

_____ _____ _____

Important names and phone numbers:

Health Care Provider:

Nutritionist:

Hospital:

Genetic Counselor:

To Schedule Clinic Appointments:

Public Health Nurse:

Remember

Raising a child with a rare metabolic disorder can be challenging and often confusing. Your health care providers are there to help you, and can answer the questions you will have along the way. Please do not hesitate to call upon them as you make the many changes necessary for successful treatment of your child's disorder.

Glossary

Acidosis - the build up of harmful acids in the body.

Autosomal recessive inheritance - one copy of the changed gene must be inherited from each parent.

Bicitra - citrate solution used to maintain acid-base balance.

Carrier - a person who carries one non-working (mutated) gene in a pair of genes. Carriers do not have the disorder, they simply carry one gene for it.

Carnitine - a non-toxic, natural chemical which helps decrease the harmful by-products of normal protein breakdown.

Enzyme - a substance in the body that enables chemical reactions to occur.

Food pattern - another term for diet. A food pattern consists of foods and beverages to be included or avoided on a daily basis.

Gene - the smallest unit of hereditary material.

Genetics - the study of heredity.

Mutation - occurs when a gene is changed from its original form.

Protein - the building blocks of body tissues.

Scientific References:

1. Altintas B, Tezic T, Coskun T, Ozalp I, Kukner S, and Kaya A, "Beta-ketothiolase Deficiency: A Case Report," The Turkish Journal of Pediatrics, Vol. 34, 1992, pp. 43-46.

2. Frerman FE and Goodman SI, "Nuclear-encoded defects of the mitochondrial respiratory chain, including glutaric acidemia, type II." Scriver CR, Beaudet Al, Sly WS, and Valle D, eds. The Metabolic and Molecular Bases of Inherited Disease, 7th ed. new York, McGraw Hill, 1995.

3. Sabetta G, Bachmann C, Giardini O, Castro M, Gambara M, Bartlett K, and Middleton B, "Case Report. Beta-ketothiolase Deficiency with Favourable Evolution," Journal of Inherited Metabolic Disease, Vol. 10, 1987, pp. 405-406.

4. Middleton B, Gray R, and Bennett M, "Two Cases of Beta-Ketothiolase Deficiency: A Comparison," Journal of Inherited Metabolic Disease, Vol. 7, Suppl. 2, 1984, pp. 131-132.

5. Bennett M, Littlewood J, MacDonald A, Pollitt R, and Thompson J, "Case Report: A Case of Beta-Ketothiolase Deficiency," Journal of Inherited Metabolic Disease, Vol. 6, 1983, p. 157.

6. Schutgens R, Middleton B, Blij J, Oorthuys J, Veder H, Vulina T, and Tegelaen W, "Beta-ketothiolase Deficiency in a Family Confirmed by in vitro Enzymatic Assays in Fibroblasts," European Journal of Pediatrics, Vol. 139, 1982, pp. 39-42.

7. Holton JB, ed., The Inherited Metabolic Diseases, 2nd ed, Longman Singapore Publisher, Pte, Ltd, Singapore, 1994, pp. 138-141.

8. Sweetman LS, Williams JC, "Branched Chain Organic Acidemias," in Scriver CR, Beaudet Al, Sly WS, Valle D, eds. The Metabolic and Molecular Basis of Inherited Disease, 7th ed. New York, McGraw Hill, 1995, pp. 1387.

Christine Cavanaugh, MS, RD

Cristine M Trahms, MS, RD, FADA Department of Genetics and Development and Center on Human Development and Disabilities University of Washington, Seattle

Robin Bennett, MS, CGC, Department of Genetics University of Washington, Seattle

And the PacNoRGG Education Committee, with special thanks, to Johanneke Smith, MS, CGC; Susie Ball, MS, CGC; Rebecca Zacharias, MS, CGC; and Diane Plumridge, MSW.

Reviewed 2002

This project was partially funded by project #6 H46 MC 00091-15 SI of the Maternal and Child Health Bureau, Department of Health and Human Services. An equal opportunity affirmative action institution.

Project Administrator and Regional Coordinator:
Kerry Silvey, MA, CGC
Project Director: Jonathan Zonana, MD
Administrative Assistant: Denise Whitworth

Copies of this booklet are available on the PacNoRGG web site:
http://mchneighborhood.ichp.edu/pacnorgg

Design & Production: Northwest Media, Inc.