

CARBAMYL PHOSPHATE SYNTHETASE DEFICIENCY: CPSD

A Guide for Parents



Sponsored by the
Pacific Northwest
Regional Genetics Group (PacNoRGG)

This booklet contains general information about carbamyl phosphate synthetase 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, childcare 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.

Carbamyl Phosphate Synthetase Deficiency

Carbamyl phosphate synthetase deficiency (pronounced car-ba- mill fos-fate sin-the-tase) is a rare, inherited disorder.

People with this disorder lack an enzyme called carbamyl phosphate synthetase. An enzyme is a substance in the body which enables chemical reactions to occur. Normally, this enzyme helps metabolize ammonia, which is toxic to the body.

Ammonia is a normal waste product from many of the body's chemical reactions. For example, when a person eats protein, the body breaks it down for many different purposes, and as a result, ammonia is formed. Normally ammonia is converted to a substance called urea, and then safely excreted in the urine. (See Diagram 1.)

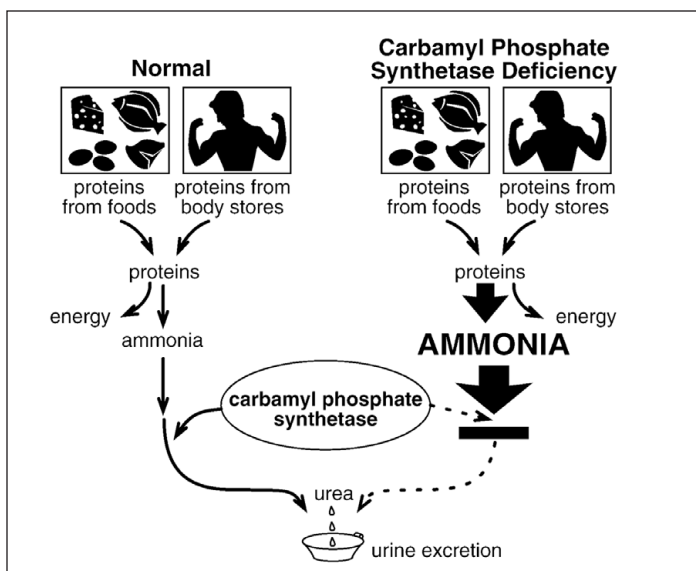
Symptoms of Carbamyl Phosphate Synthetase Deficiency

If ammonia is not converted to urea, it begins to build up in the blood and can be very harmful. If ammonia levels stay high for too long, severe brain damage can occur. High levels can cause vomiting, weakness, seizures, or neurological damage, and may even lead to coma or death.

But the harmful effects of this disorder can be lessened if treatment begins immediately upon diagnosis, and if a low protein food pattern (another term for diet) is started early and maintained throughout life.

Diagram 1.

The metabolic defect of carbamyl phosphate synthetase deficiency.



Proteins are broken down for many different purposes, and as a result ammonia is formed. Normally, ammonia is safely metabolized and excreted in the urine. For people with this disorder, the enzyme carbamyl phosphate synthetase does not work properly, so normal ammonia conversion to urea does not occur. This causes ammonia in the blood to build up to harmful levels.

Amino acids - the building blocks of proteins

Metabolism - Chemical processes in the body that

1) break down complex molecules into simpler ones and 2) consume energy to build complicated molecules from simpler ones.

Treatment

There are four parts to successful treatment of carbamyl phosphate synthetase deficiency:

1. A low protein food pattern and/or specialized medical food (formula).

The body naturally produces small amounts of ammonia. However, if there is too much ammonia, problems can occur.

The way to keep from forming too much ammonia is to avoid foods high in protein. When protein is broken down in the body to ammonia, this excess ammonia can't be cleared away because your child lacks the enzyme needed for ammonia breakdown.

A special medical food (formula) may be prescribed for your child. Medical foods supply protein without the amino acids which are not metabolized in carbamyl phosphate synthetase deficiency. However, these amino acids are required for growth so they are added back in small amounts of infant formula or cow's milk.

It should be noted that this is *not* a protein-free food pattern. Your child needs small amounts of protein for normal growth and development. All protein will not be completely eliminated from the food pattern. A nutritionist can help you create a specific food pattern to ensure your child will be well-nourished.

2. Preventing ammonia build-up in the blood with medication.

The body is always making ammonia, even if protein is avoided. Your child needs a way to help the body clear ammonia away. Sodium benzoate and phenylacetate

are oral medications which combine with ammonia to make it less harmful and help the body clear it away. Your health provider can tell you whether these medications are needed for your child.

3. Supplemental forms of arginine and/or carnitine.

Each child with carbamyl phosphate synthetase deficiency will be affected to a different degree. For some, the system that normally clears away ammonia won't work at all. For others, it may work better. Depending on your child, your health provider may prescribe arginine and/or carnitine.

Arginine is a natural amino acid (a building block of protein) which helps the body grow and repair tissues. Children with carbamyl phosphate synthetase deficiency may be low in arginine and may require arginine supplements.

Carnitine is a safe, natural chemical which helps the body produce muscle energy. It also combines with ammonia to make it less harmful.

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

All children become ill at times, whether they have carbamyl phosphate synthetase deficiency or not. Sometimes they catch a cold, the flu, or something more severe. Your child with carbamyl phosphate synthetase deficiency will need to take special precautions during these times. Typical childhood illnesses can cause the body to break down its own sources of protein, creating excess ammonia build-up.

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 fluid intake as much as possible. Many children enjoy drinks which are frozen, then chipped into ice chunks.

Always call your child's 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 most effective treatment for carbamyl phosphate synthetase deficiency is a low protein food pattern. Many high protein foods must be limited to reduce sources of amino acids. Milk and dairy products, meat, fish, chicken, eggs, beans, peanut butter, and nuts are all high protein foods and should be limited. Eating these foods can cause ammonia to build up and result in severe illness.

Remember, your child needs small amounts of protein for growth and development. Protein will not be completely eliminated from the food pattern. Your nutritionist can help you create a specific food and medication pattern to ensure your child will be well-nourished.

Many foods contain varying amounts of protein. Some foods should be eliminated entirely because they contain too much protein, while others may be eaten in moderate amounts, and still others may be eaten freely.

The Low Protein Food Pattern

Medical foods (formula): If a medical food is needed, a prescribed amount of formula and a recipe for its preparation will be provided. This recipe may change frequently based on the child's growth, development, and blood levels.

A. Lower protein foods which can be included:

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

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

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

corn	cauliflower
potatoes	cabbage
asparagus	spinach
lentils	yams
green beans and peas	sweet potatoes
carrots	mushrooms
broccoli	lettuce
vegetable juices	squash
onions	radishes

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

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

B. High protein foods to be avoided or used only in prescribed amounts:

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

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

C. Foods with NO protein which provide extra energy

- | | |
|------------------|-------------------------------|
| gum drops | popsicles |
| hard candy | sodas |
| Kool-aid | margarine |
| jams and jellies | oils |
| sugar | 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 can introduce you to a wide variety of special low protein foods which can offer more food choices and add variety. 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 contains calcium and iron is essential.**

Length of Treatment and Medical Visits

Carbamyl phosphate synthetase deficiency does not go away. Treatment must continue throughout life to maintain health.

Because your child has a lifelong condition that can

harm growth and development, your child should be followed closely by your health provider and nutritionist. Medical visits offer many advantages for children with carbamyl phosphate synthetase deficiency such as developmental, physical, and neurological assessments.

The medical team will want to learn how your child is getting along with parents, siblings, and friends, and work with you to solve problems. Their goal is to help your child develop the skills needed to take responsibility for managing his or her own condition. The staff knows this will be no easy task, 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

The family plays a very important role in your child's treatment. Other children in the family, as well as the child with the disorder, should be taught about the low protein food pattern. Encourage the other children to help feed your child with the disorder in order to become familiar with foods that are allowed and not allowed. Explain carbamyl phosphate synthetase deficiency to everyone who will participate in the care of your child (relatives, teachers, child-care providers, friends, baby-sitters, and others). They need to become familiar with the foods allowed and excluded, and they must understand the importance of the strict food pattern for growth and development. Also teach siblings and relatives not to feel sorry for the child with the disorder because he or she can't eat certain foods.

Treat your child with carbamyl phosphate synthetase deficiency 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.

Even with the most careful treatment, many children with carbamyl phosphate synthetase deficiency have had some degree of damage to their brain because of high levels of blood ammonia. Some children are more affected than others. The degree of mental and developmental delay varies from one child to the next depending on the severity of the disorder and how high ammonia levels have risen. There are community resources available, listed in the back of this booklet, to help you face the challenges of raising a child with special needs.

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.

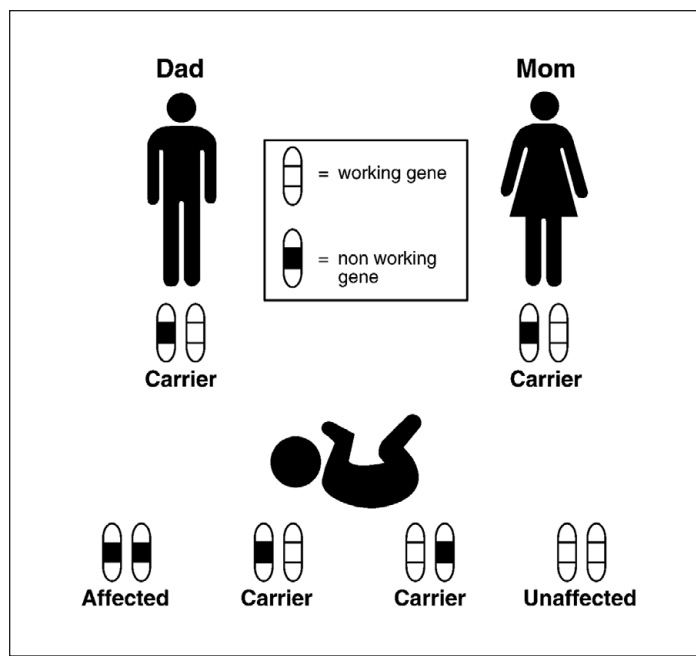
The gene change that causes carbamyl phosphate synthetase deficiency is inherited in what is called an autosomal recessive pattern. This means that one copy of the changed, or non-working, gene must be inherited from each parent for a child to be affected with the disorder. The parents' health is not 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 carbamyl phosphate synthetase deficiency, and both boys and girls can have the disorder.

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.

NATIONAL

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.ncl.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

National Urea Cycle Disorders Foundation
4841 Hill Street
LaCanada, CA 91011
800/386-8233
INFO@nucdf.org
http://www.nucdf.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

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: 406/255-0523
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

Ammonia - an acid which results from the normal breakdown of proteins, either from foods or body stores.

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

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.

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.

Sodium benzoate - a commonly prescribed medication which combines with ammonia and makes it less harmful.

Scientific References:

1. Brusilow SW and Horwich AL, "Urea Cycle Enzymes," In: Scriver CR, Beaudet AL, Sly WS, and Valle D, eds. *Metabolic and Molecular Bases of Inherited Disease* 1995, New York, McGraw Hill.
2. Trahms CM, "Nutritional Care in Metabolic Disorders." In: Mahan, LK and Escott-Stump S, eds., *Food, Nutrition, and Diet Therapy*, 9th edition, WB Saunders Co, Philadelphia, PA.
3. Tuchman M, Mauer S, Holzkecht R, Summar M, and Vnencak-Jones C, "Prospective Versus Clinical Diagnosis and Therapy of Acute Neonatal Hyperammonemia in Two Sisters with Carbamyl Phosphate Synthetase Deficiency," *Journal of Inherited Metabolic Disease*, Vol. 15, 1992, pp. 269-277.
4. Ampola MG, *Metabolic Diseases in Pediatric Practice*, Little, Brown and Co, 1982, Boston, pp. 144-145.
5. Brusilow SW, "Phenylacetylglutamine May Replace Urea as a Vehicle for Waste Nitrogen Excretion," *Pediatric Research*, Vol. 29 (2), 1991, pp. 147-151.
6. Granot E, "Partial Carbamyl Phosphate Synthetase Deficiency, Simulating Reye's Syndrome, in a 9-year-old-girl," *Israel Journal of Medical Sciences*, Vol. 22, 1986, pp. 463-465.
7. Jaeken J, Devlieger H, Bachmann C, Van Aerde J, Corbeel L, and Eggermont E, "Carbamyl Phosphate Synthetase Deficiency with Lethal Neonatal Outcome," *European Journal of Pediatrics*, Vol. 139, 1982, pp. 72-75.
8. Kline J, Hug G, Schubert W, and Berry H, "Arginine Deficiency Syndrome: Its Occurrence in Carbamyl Phosphate Synthetase Deficiency," *American Journal of Diseases of Children*, Vol. 135, May, 1981, pp. 437-442.

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

Project Administrator: Kerry Silvey, MA, CGC

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 can be obtained from the PacNoRGG website:
<http://mchneighborhood.ichp.edu/pacnorgg>

Design & Production: Northwest Media Inc.

