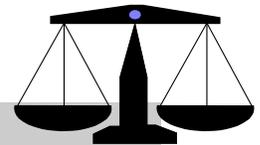


UNDERSTANDING HOMOCYSTINURIA

What is Homocystinuria?

Homocystinuria (HOMO-SISTIN-UREA) is genetic disorder that affects how protein is broken down in the body. It is a **metabolic** disorder. About 1 out of 200 000 babies are born with homocystinuria each year in Canada.

Homocystinuria can be treated with drugs, with diet or with a combination of both. One of the drugs used is **pyridoxine** or **vitamin B6**. About half the people affected by homocystinuria are very responsive to vitamin B6 and do not need any other special treatment. These people are said to be "**pyridoxine responsive**". There are 2 other groups of people with homocystinuria: those who partly respond to pyridoxine, and those who have no response to pyridoxine. Both these groups of people will need to take other medications and follow a special diet.



Amino acids are the building blocks of protein. Of the 20 amino acids found in body protein, 8 cannot be made by adults and must be obtained from foods. These are considered **essential** amino acids. Normally, the protein we eat is broken down or "metabolized" in our bodies into amino acids and used for growth and tissue repair.

People who are born with homocystinuria are unable to properly break down **methionine**, an amino acid found in food. In people not affected by homocystinuria, methionine is used by the body for growth and repair. Leftover methionine is changed to homocysteine and then to cysteine. Excess homocysteine is changed back to methionine. This balance is assisted by vitamins.



Most people with homocystinuria are missing **cystathionine B-synthetase**, the enzyme that changes **homocysteine** into **cysteine** in the liver. **Enzymes** can best be described as keys that unlock doors in the body.



Think of the food in our system as a person with a big delivery to make. As long as the person has all the keys, the load can be delivered and everyone gets their packages. When enzymes or keys are missing, the packages cannot be delivered and the delivery person is left with a big load, and no one gets the packages they need to do their job.

Food eaten is like the delivery. In homocystinuria, when the enzyme is missing, homocysteine cannot be made into cysteine. Cysteine therefore becomes an essential amino acid for people with homocystinuria and they must get it from their food. They are not receiving the delivery of raw material to make cysteine in their body.

Since homocysteine is not being changed into something useful for the body, it builds up in the blood, fluid around the brain and spinal cord, and urine. The name "homocystinuria" means homocysteine in the urine. When it builds up, some of it is changed back into methionine. It is like a person receiving packages they have no shelf room for; they give it back to the delivery person and the load is increased.

With untreated homocystinuria then, the balance is upset. There is too much homocysteine and methionine and not enough cysteine. This imbalance can cause:

- mental retardation,
- severe bone problems,
- osteoporosis, or thinning of the bones,
- dislocated lenses of the eyes,
- heart disease and blood clot formation.

Some people with homocystinuria can have all of these complications and be severely affected whereas others may have only a few complications or none at all.

How is homocystinuria treated?

Therapy needs to begin before complications occur because, once they develop, they are irreversible. Treatment must be started as soon as the disorder is diagnosed.

The type of homocystinuria determines the treatment. The following approaches are used alone or in combination.



MEDICATION

1. Pyridoxine (vitamin B6)

Pyridoxine or vitamin B6 is a natural substance found in the body. It helps to change homocysteine into cysteine. Some people with homocystinuria respond well to vitamin B6 supplements. This can be determined by a blood test that measures the homocysteine level after a trial of vitamin B6. Vitamin B6 is taken by mouth in pill form and is available at health food and drug stores.

2. Vitamin B12

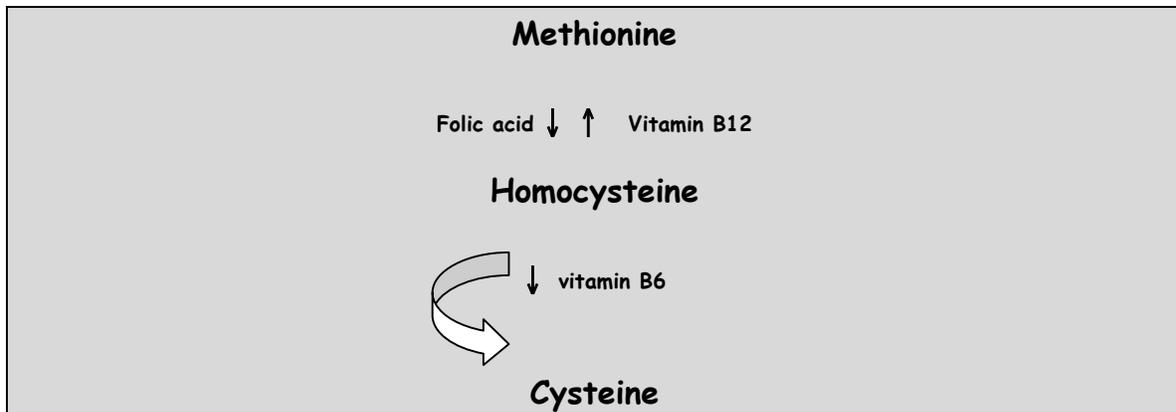
Vitamin B12 is also a natural substance found in the body. It helps to change the excess homocysteine back into methionine. Vitamin B12 is taken by mouth in pill form and is available at health food and drug stores.

3. Folic acid

Folic acid is another natural substance found in the body. It helps vitamin B12 to change homocysteine back into methionine. It is also taken in pill form and available at health food and drug stores.

4. Betaine

Betaine is a natural substance found in the body. For some people with homocystinuria, a betaine supplement helps to lower homocysteine levels by changing homocysteine back to methionine. It comes in a powder and is taken by mouth. Betaine is available by prescription only.



5. Other medications

There are other medications to treat symptoms and complications associated with homocystinuria. The most common medication that may be prescribed is an anticoagulant to prevent clots from forming in the blood. Blood clots may cause heart attacks or strokes and therefore need to be prevented from forming.

DIET



People who have homocystinuria and whose levels do not respond to vitamin B6 need to limit their intake of protein-containing foods. This is done with the help of a registered dietician. In order to meet the protein requirements for body growth and repair, the person must also drink special medical formula that is free of methionine but provides all other amino acids, vitamins and minerals. The amount of food and drink the person can consume is monitored by the dietician.

Examples of foods that must be eliminated from a low-methionine diet are those high in protein:

- milk and dairy products
- meat, fish, chicken
- nuts (including peanut butter)
- beans
- eggs

Eating high protein foods increases methionine levels leading to high homocysteine levels. This puts the person at risk for developing complications.

It is not unusual for someone on a methionine-restricted diet to have 2 kinds of vegetables and a baked potato for dinner. However, if these foods were all that the person ate, their diet would be lacking in protein, vitamins and minerals. That is where the special medical formula comes in. It provides all the protein and nutrients normally obtained from high-protein food. In order to prevent complications, the person must adhere to this diet for life.

How do people get homocystinuria?

Homocystinuria is an inborn error of metabolism. It is genetic. This means that the person has the disorder from the time they are conceived. At conception, the baby receives two sets of genetic material, one from the mother, and one from the father. This genetic material, called **DNA**, acts as a recipe for the baby's development.



DNA includes information about the baby's eye and hair colour, sex and even whether the baby will be right or left-handed. DNA comes in units called **genes**. Each pair of genes gives directions to a certain part of the body.

In homocystinuria, there is a problem with the genes that give information on how the body breaks down protein. The disorder is caused by getting two copies of the faulty gene that gives the wrong instructions. One copy comes from the mother and one comes from the father. If the child inherits only one copy of the gene, they are a carrier for homocystinuria but are not affected. There is a 1 in 4, or 25% chance that two carriers of the gene will have a baby with homocystinuria. Boys and girls are equally affected.

Children born to carriers have:

- a 25% chance of having homocystinuria,
- a 50% chance of being a carrier and
- a 25% chance of being unaffected.

With each pregnancy, there is the **same** 25% chance of having a child with homocystinuria. In some families, there may be only one child with homocystinuria, while in other families, multiple children may be affected.

Can adults with homocystinuria pass the disorder on to their children?

Because homocystinuria requires a carrier or recessive gene from each parent, the only way a person with homocystinuria can have an affected child is to have children with a carrier or another person with the disorder.



Homocystinuria and pregnancy

When a woman with homocystinuria decides to have a family, it is very important that she sees a metabolic team **in the planning stages**. To have the best outcomes, it is essential that she is closely monitored and appropriately treated **prior to conception** and **throughout pregnancy**.

How is Homocystinuria monitored?

Regular bloodwork is necessary to monitor changes in homocysteine levels which ideally should be under **30 micromol/L**. Visits to the metabolic clinic are needed to consult with the team and to make adjustments to medication and/or diet.

How can family and friends help?



Family and friends play a special role in supporting the person with homocystinuria. It may be very difficult for the person to remain motivated and committed to treatment regimes, especially if they require a protein-restricted diet. Family and friends can provide support through understanding and providing a listening ear to frustrations.

If the person is on a protein-restricted diet, learn to prepare some favourite special dishes. If you are having a person with homocystinuria over for a meal, ask them what they would like to eat and offer low-protein snack options such as:

- soda pop
- fruit juices
- vegetable sticks or pita with dips
- fruit plate
- bread sticks or corn chips with salsa