

# Living with a cobalamin cofactor metabolism defect

What you should know about cbl defects that cause homocystinuria

## The ABCs of cobalamin (cbl) defects

### Cobalamin cofactor metabolism defects = cbl defects

Many different cbl defects cause homocystinuria. (And a few do not.) Each type is named with a letter of the alphabet.

**A B C s**

### Combined disorders

homocystinuria and methylmalonic acidemia

cbIC defect

cbID defect

cbIF defect

cbIJ defect

cbIX defect

### Single disorders

homocystinuria

cbID defect (variant 1)

cbIE defect

cbIG defect

Not actual patients or caregivers



Marcus has cbIC defect



Shayna has cbIG defect

# A cbl defect can affect health in many ways



Cbl defects impair the body's ability to metabolize or break down an amino acid called **homocysteine**. The body makes homocysteine during the metabolism of **methionine**, another amino acid. Most foods contain methionine. Different forms of **cobalamin**, also known as **vitamin B12**, are also involved in the methionine metabolic process.

If someone has a **combined disorder**, then both **homocysteine and methylmalonic acid** can build up in their blood. If someone has a **single disorder**, then only **homocysteine** may build up in their blood. In both types of disorders, serious health problems may develop.

## Symptoms of combined disorders

The most common cbl defect is cblC defect. Like Marcus, most people with cblC defect begin to develop **symptoms before they are a year old**. This is the **early-onset form of cblC defect**. As a baby, Marcus was often fussy and didn't want to eat. Among other symptoms that developed over time, Marcus's parents began to notice that his eyes wandered.



### BRAIN & SPINAL CORD

**Common signs:** drowsiness, floppy muscles and joints, seizures, developmental delay



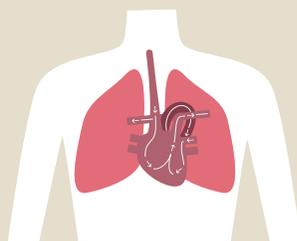
### GROWTH & FEEDING

**Common signs:** feeding problems, reduced growth



### EYES

**Common signs:** unusual eye movements, vision problems



### HEART & BLOOD

**Common signs:** inherited heart disease, megaloblastic anemia, blood clots

People with **late-onset cblC defect** may not develop symptoms until later in life – from childhood to adulthood. Late-onset symptoms may be milder than early-onset symptoms. Although there is some overlap, people with late-onset cblC defect may develop blood clots, muscle stiffness, an unusual way of walking, learning problems, and/or mental health problems.

## Other combined disorders

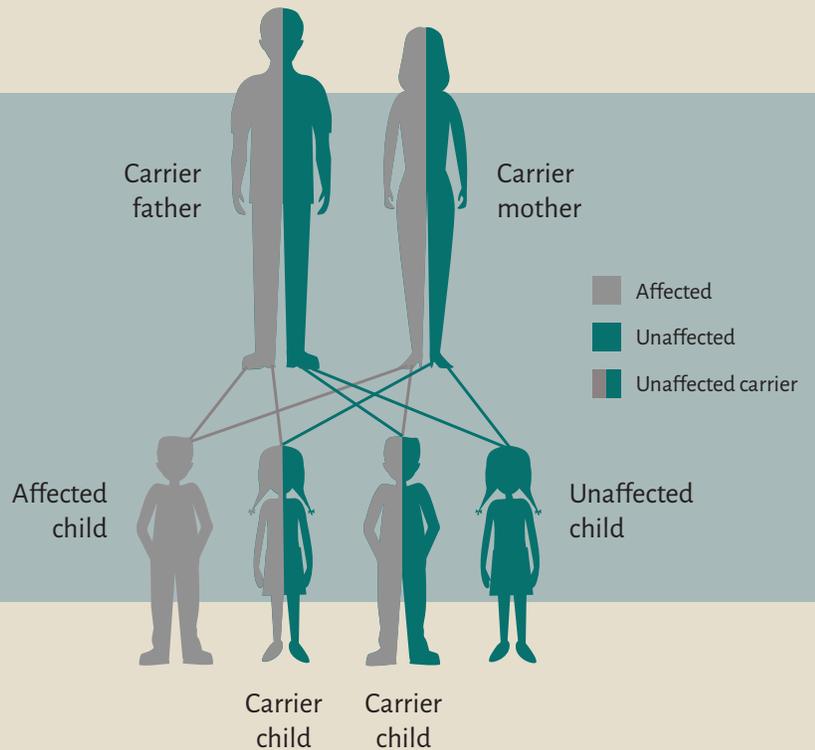
Other combined disorders – cblD defect, cblF defect, cblJ defect, or cblX defect – may cause some of the same symptoms as cblC defect.

# Symptoms of single disorders



Single disorders such as *cb1D* defect (variant 1), *cb1E* defect, and *cb1G* defect may cause some of the same symptoms as *cb1C* defect. Shayna had episodes of megaloblastic anemia during her first year of life. Occupational and physical therapy helped her sit up, crawl, stand, and walk.

## Cbl defects are genetic disorders



Marcus's parents are **carriers** of a *cb1C* defect because each has one normal and one abnormal *cb1C* gene.

Marcus has *cb1C* defect because he inherited an abnormal *cb1C* gene from each parent. And Shayna has *cb1G* defect because she inherited an abnormal *cb1G* gene from each parent. None of the parents have any symptoms.

When both parents are carriers, each child in the family has a 25% chance of having homocystinuria due to the specific *cbl* defect, a 50% chance of being a carrier, and a 25% chance of having no abnormal *cbl* genes.

**All *cbl* defects except *cb1X* defect are inherited in this manner.**

***CblX* defect** is caused by an abnormal gene on the X chromosome. Males who inherit an abnormal *cb1X* gene will develop symptoms, while females who inherit an abnormal *cb1X* gene are not likely to develop symptoms.

# Diagnosing cbl defects

Marcus's cbl defect was suspected after standard newborn screening test results. Shayna wasn't tested until she began having symptoms. (CblG defect is currently not included in newborn screening.) In both cases, specific blood tests were done to diagnose their homocystinuria. DNA testing was then done to identify the gene causing the particular cbl defect.



## Working with a healthcare team to prevent or reduce symptoms



"Shayna was slow to crawl, but she was always determined to get her light-up piano." —Shayna's mom

Both Marcus and Shayna see a healthcare team that includes a **metabolic specialist**. A metabolic specialist is a doctor who specializes in treating genetic conditions that involve the body's metabolism.

Both children also follow a personalized **treatment plan** every day. Treatment for most people with a cbl defect includes medication and a form of vitamin B12. Periodic blood tests are done to see how well someone's treatment plan is working.

And both children see **other healthcare professionals**, including therapists, as needed. Marcus also sees an eye doctor because of his vision problems. Shayna also sees a hematologist because of her history of megaloblastic anemia.

The goal of treatment is to prevent or reduce symptoms by keeping homocysteine, methionine, and methylmalonic acid (MMA) levels in the blood as close to normal as possible. Doctors may call this "having good metabolic control."

# Looking ahead

Cbl defects are lifelong disorders. But by maintaining good metabolic control, people with homocystinuria due to a cbl defect may be able to reduce or even prevent some symptoms.



## Find out more

To learn more about cbl defects that cause homocystinuria, check out these organizations:

- HCU Network America (<https://hcunetworkamerica.org/>)
- Organic Acidemia Association (<https://www.oaanews.org/>)

