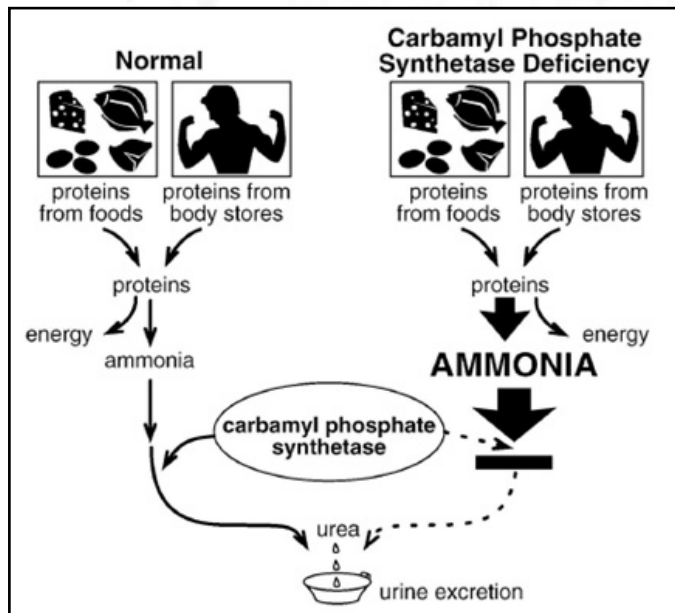




CITRULLINEMIA INFORMATION FOR PARENTS/CARERS

What is Citrullinemia?



This fact sheet contains general information Citrullinemia. Citrullinemia results from a defect in argininosuccinate synthetase (ASS), the third step in the urea cycle, that result when a baby's body cannot remove certain waste products from the blood. Without treatment, progressive brain damage and death occur. Under normal circumstances, citrulline is condensed with aspartic acid to form argininosuccinic acid (ASA), which is a reaction mediated by the argininosuccinic acid synthase enzyme. Participation of aspartate in the reaction fixes a second waste nitrogen atom into the reaction product, ASA; the first waste nitrogen molecule derives from free ammonia in the carbamyl phosphate synthetase (CPS) reaction. ASA synthase

deficiency leads to accumulation of citrulline, a condition known as citrullinemia.

How Does Citrullinemia Affect a Child?

Babies with citrullinemia and ASA can not process ammonia, a by-product of the proteins we eat, into a harmless product called urea. This causes ammonia to build up in their blood. High levels of ammonia are toxic (poisonous) and cause the symptoms of citrullinemia and ASA .

What are the signs and symptoms of Citrullinemia?

These symptoms in babies include:

- poor appetite;
- vomiting;
- lethargy;
- increased intracranial pressure;
- apnea;
- seizures;
- coma, possibly leading to death; and
- lab findings:
 - hyperammonemia;
 - elevated citrulline; and
 - absent argininosuccinic acid.



**Symptoms of the milder form in children may include:**

- poor growth,
- poor appetite,
- vomiting,
- headaches,
- learning disabilities,
- behavior problems,
- hyperactivity,
- balance and coordination problems, and
- spasticity.

Is There a Test for Citrullinemia?

Yes. Babies can be tested through newborn screening for Citrullinemia before they leave the hospital. The baby's heel is pricked and a few drops of blood are taken. The blood is sent to the newborn screening laboratory to find out if it has more than a normal amount of citrulline. The finding of elevated Citrulline in a dried blood spot upon newborn screening suggests one of two metabolic defects: 1) Citrullinemia I, 2) Argininosuccinic acidemia; 3) Citrullinemia II (citrin deficiency) 4) Pyruvate carboxylase deficiency.

How are Citrullinemia and ASA treated?

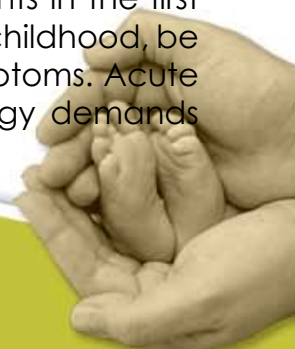
Newborns are placed on a special formula to restrict protein. Certain supplements and medicines may be given. Kidney dialysis may be needed for some children.

- As in all hyperammonemic states, immediately restrict dietary protein in patients with citrullinemia. Emphasize other nonprotein caloric sources to compensate.
- Intravenous sodium benzoate, sodium phenylacetate, and arginine are important therapeutic avenues for reduction of blood ammonia levels. Intravenous benzoate and phenylacetate are investigational new drugs. In severe cases, hemodialysis may be indicated to rapidly reduce the blood ammonia level.
- Long-term management requires close dietary monitoring and oral administration of sodium phenylbutyrate and arginine.

In every case, a biochemical geneticist should administer definitive short- and long-term treatment with sufficient laboratory backup to obtain rapid ammonia and amino acid levels

If Citrullinemia is not treated, what problems occur?

With treatment preventing serious hyperammonemic episodes, normal IQ and development are possible. Without treatment, classical citrullinemia type I generally presents in the first week after establishing a normal protein diet. Less acute forms may present in childhood, be asymptomatic, or present during pregnancy or postpartum with severe symptoms. Acute symptoms may occur during prolonged fasting, periods of increased energy demands



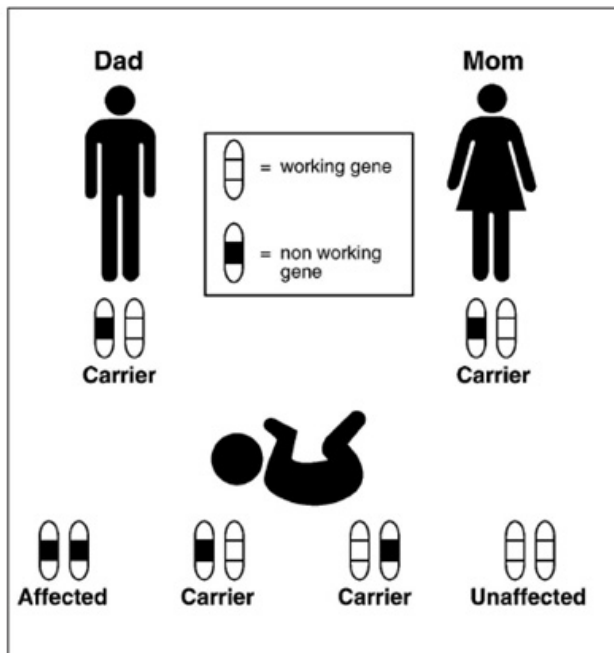


(fever, stress, lack of sleep), and after meals high in protein.

How common is Citrullinemia?

Citrullinemia affects at least about 1/250,000 live births worldwide.

How is Citrullinemia inherited?



This condition is inherited in an autosomal recessive manner. It affects both boys and girls equally. Everyone has a pair of genes that make the enzyme. In children with citrullinemia, neither of these genes works correctly. These children inherit one non-working gene for the condition from each parent. Parents of children with citrullinemia rarely have the condition themselves. Instead, each parent has a single non-working gene for citrullinemia. They are called carriers. Carriers do not have the condition 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 citrullinemia. 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 this condition. Genetic counselors can answer your questions about how it is inherited, options during future pregnancies, and how to test other family members. Ask your doctor about a referral to a genetic counselor.

