

FACT SHEET
Healthcare Provider

Classic Citrullinemia (CIT)
Citrullinemia Type I

Description:

Citrullinemia is a rare autosomal recessive disorder caused by a missing or poorly functioning enzyme, argininosuccinate synthetase (ASS) enzyme activity. Argininosuccinate synthetase is one of six enzymes that play a role in the breakdown and removal of waste nitrogen from the body, a process known as the urea cycle. The lack of this enzyme results in excessive accumulation of citrulline and nitrogen, in the form of ammonia (hyperammonemia), in the blood.

Symptoms:

Most patients present with symptoms early in the neonatal period but there may be later onset. Infants are generally well for the first 24-72 hours but then may demonstrate lethargy, poor feeding, vomiting, grunting respirations, tachypnea, hypothermia, progressing to opisthotonus, seizures, cerebral edema, coma, apnea, and death if not treated. Infants with the severe form who are treated promptly may survive for an indeterminate period of time but may have neurological deficit. Milder variants, asymptomatic individuals and intra-family variability have been reported.

Incidence in General Population:

1:57,000 live births worldwide

Diagnosis:

Newborn screening—Tandem mass spectrometry:

- Citrulline—very elevated.
- Arginine—low/undetectable.

A second dried-blood-spot filter paper card may be requested by the Newborn Screening Laboratory if the initial screening result is above the normal range. Infants with presumptive positive screening (critical) results require prompt follow up. If this occurred, the clinician would be contacted by the Metabolic Treatment Center. When notified of these results, the clinician should immediately check on the clinical status of the baby and facilitate referral to the Metabolic Treatment Center. The Metabolic Treatment Center will provide consultation and assistance with diagnostic testing.

Monitoring:

- When informed of an infant with a presumptive positive screening test result, the clinician should immediately check on the clinical status of the baby and facilitate referral to a metabolic consultant.
- Metabolic Treatment Center will provide the appropriate monitoring and follow up of a patient with Citrullinemia.
- It is important for the primary care provider and the Metabolic Treatment Center staff to develop an ongoing collaborative relationship in caring for these patients.

Treatment:

Rescue of an infant from hyperammonemic encephalopathy may be possible with aggressive hemodialysis and specialized care. Maintenance treatment consists of a protein-restricted diet, ammonia disposal drugs, arginine supplementation, and aggressive intervention for recurrent bouts of hyperammonemia. Infants with severe hyperammonemia require prompt treatment, which may include hemodialysis or the use of intravenous medications that help reduce the ammonia level. Liver transplantation is an effective treatment. Lifelong dietary management is necessary and requires the services of a metabolic nutritionist.

Illness:

- Patients with Citrullinemia must be monitored closely during times of illness.
- Infectious diseases, such as colds and flu, can be very serious and even life threatening in these children.
- A sick-day plan should be formulated with the Metabolic Treatment Center.
- During illness, it is recommended that dietary protein be further reduced or eliminated and consumption of high carbohydrate drinks is advised in order to maintain hydration. The patient will need to be seen by his/her physician.
- Should hospitalization be necessary, treatment may consist of medications that help the body dispose of waste nitrogen. Hemodialysis may be required to help rid the body of excess ammonia during episodes of severe hyperammonemia.
- Consult with the Metabolic Treatment Center within 24 hours of the onset of an illness or at the time of hospitalization.

Immunizations:

Immunizations must be kept current.

Surgical/Surgical Procedures:

Major stresses, such as surgery or accidents, can be complicated for these patients. Extreme care is required to avoid problems during such periods.

Growth and Development:

- It is crucial to closely monitor citrullinemia patients. Despite optimum treatment, they are prone to periodic bouts of hyperammonemia, which can be life threatening and damaging.
- There is a direct correlation between the length of time a patient is in hyperammonemic coma and IQ. While early diagnosis and treatment may be lifesaving, neurologic damage is not usually prevented.
- In some patients, chronic hepatic dysfunction results in cirrhosis and liver failure, and a liver transplant may be indicated despite adequate treatment and metabolic control.



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November 2005