Alberta Health Services

Newborn Metabolic Screening

Information for Health Professionals

Citrullinemia (CIT)

(metabolic condition: amino acid disorder)

Also known as:

- citrullinuria
- argininosuccinate synthetase deficiency
- argininosuccinic acid synthetase deficiency

What are amino acid disorders?

Amino acid disorders are a group of inherited metabolic conditions in which certain amino acids cannot be broken down. This leads to an accumulation of toxic metabolites in the body which can cause serious health problems.

What is CIT?

CIT is a urea cycle defect. Many amino acids are broken down through the urea cycle which is a means of removing excess nitrogen from the body. When the urea cycle enzymes are not functioning well (urea cycle defect) a toxic buildup of ammonia (hyperammonemia) may occur.

What causes CIT?

CIT is caused by mutations in the gene for argininosuccinic acid synthase (ASA synthase) resulting in absent or decreased enzyme activity. This results in defective function of the urea cycle and accumulation of citrulline and ammonia.

How common is CIT?

The incidence of CIT is about 1 in every 60,000 infants born in Canada.

What are the clinical features of CIT?

CIT usually presents in the newborn period with hyperammonemia. The clinical features include poor appetite, lethargy and vomiting with progression to seizures, hypothermia, coma and death. In children who survive the newborn period, episodes of hyperammonemia may occur during a minor illness or after a large protein meal. A small number of patients present later and have a less severe course.

What is the screening test for CIT?

An increased concentration of citrulline is detected on the newborn blood spot screen. Newborn blood spot screening is not 100% perfect. Infants with clinical symptoms need timely assessment and diagnostic testing even if their screen result is normal.

How is the diagnosis confirmed?

The diagnosis of CIT is confirmed by measurement of amino acids in blood and plasma ammonia. Citrulline is increased and several other amino acids may also be abnormal. Orotic acid excretion in urine may be increased. Specialists at the clinics listed below will arrange diagnostic testing.

How is CIT treated?

Prevention of hyperammonemia is an essential factor in the treatment of CIT. Treatment consists of a diet low in protein, arginine supplementation and a special formula. Medications to assist in removing ammonia from the body may also be prescribed. Parent education is an important component of treatment, including advising parents on actions to be taken when their child develops a minor illness. Metabolic crises may occur during a minor illness or following a high-protein meal and require prompt treatment with intravenous fluids of glucose and lipids, together with medications to reduce ammonia levels. The treatment is lifelong. In some cases, a liver transplant may be indicated.

What is the outcome of treatment for CIT?

Neurological damage may occur in the newborn period if the diagnosis is delayed, as ammonia is very toxic to the brain. Early recognition before symptoms occur provides the best outcome for the condition, although neurological impairment and developmental delay may occur.

Is CIT inherited?

CIT is inherited as an autosomal recessive trait. Parents of a child with CIT are carriers of the condition and have a 1 in 4 chance of having another affected child in each subsequent pregnancy. CIT carriers are healthy. Genetic counselling and prenatal testing is available to all families with CIT.

For additional resources, please call:

Clinical & Metabolic Genetics Program (Edmonton)

8-53 Medical Sciences Building
8440 – 112 St. NW
Edmonton, AB T6G 2H7
Phone: 780-407-7333
Fax: 780-407-6845

Emergency consultations:
Phone 780-407-8822 and ask for the specialist on call for metabolic diseases.

Clinical & Metabolic Genetics Program (Calgary)

Alberta Children's Hospital
28 Oki Drive NW
Calgary, AB T3B 6A8
Phone: 403-955-7587
Fax: 403-955-3091

Emergency consultations:
Phone 403-955-7211 and ask for the specialist on call for metabolic diseases.