



## **Trifunctional Protein Deficiency Information for Health Professionals**

Trifunctional protein deficiency (TFP deficiency) is a fatty acid oxidation disorder. Individuals are lacking or have decreased function of trifunctional protein, leading to an inability to utilize certain dietary fats or fat stored in the body for energy.

### **✓ Clinical Symptoms**

The clinical severity and age of onset may vary among patients with TFP deficiency. Overall, TFP deficiency causes intermittent metabolic crises which usually occur after fasting, long periods of exercise, illness/infection, or physical stress. Symptoms of a metabolic crisis include lethargy, behavioral changes, hypotonia, poor appetite, fever, vomiting, hypoglycemia, and metabolic acidosis. Other clinical problems include cardiomyopathy, hepatomegaly, and rhabdomyolysis. If untreated, metabolic crisis can lead to breathing problems, seizures, coma, and death.

Women carrying a fetus with TFP deficiency are at a significant risk for developing medical problems including HELLP (hypertension, elevated liver enzymes, low platelets) syndrome and AFLP (acute fatty liver of pregnancy).

### **✓ Incidence**

TFP is considered a very rare disorder and occurs in less than 1 in 100,000 births.

### **✓ Genetics of trifunctional protein deficiency**

Mutations in the HADHA and HADHB genes cause TFP deficiency. Mutations result in inadequate levels of the enzyme complex trifunctional protein. This causes an inability to metabolize and process long chain fatty acids leading to metabolic crisis and hypoglycemia. Long-chain fatty acids and partially metabolized fatty acids can also buildup in the body causing hepatomegaly, cardiomyopathy and skeletal myopathy.

### **✓ How do people inherit trifunctional protein deficiency?**

Trifunctional protein deficiency is inherited in an autosomal recessive manner. Parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but do not show signs and symptoms of the condition. Each pregnancy between carrier parents has a 25% chance of producing a child affected with TFP deficiency, a 50% chance of producing an unaffected carrier child, and a 25% chance of producing a child who is unaffected and is not a carrier.

### **✓ Treatment**

Immediate diagnosis and treatment of TFP deficiency in the neonatal period is critical to normal brain development and physical growth. Recommended treatment is a lifetime diet that is low in long chain fatty acids and high in carbohydrates. Medium Chain Triglyceride oil is often included in this diet. L-carnitine supplementation may be recommended. During illness, children may need to be admitted for medical care to prevent hypoglycemia and metabolic crisis and fasting should always be avoided.

## ✓ Screening Methodology

Primary newborn screening for TFP deficiency utilizes tandem mass spectrometry. Individuals with a positive screen will have elevated levels of 3-hydroxypalmitoyl carnitine (C16-OH) and/or elevated levels of C18:1-OH and other long chain acylcarnitines.

## ✓ What to do After Receiving Presumptive Positive TFP deficiency Screening Results: **MEDICAL EMERGENCY - TAKE THE FOLLOWING IMMEDIATE ACTIONS:**

- 1) The clinician should immediately check on the clinical status of the baby.
- 2) Consultation with a metabolic specialist is essential.
- 3) Call KS Newborn Screening Program at 785-291-3363 with questions about results.
- 4) Report Clinical Findings to Newborn Screening Program at 785-291-3363.
- 5) Same birth siblings (twins, triplets) of infants diagnosed with TFP deficiency should be re-screened; additional testing of these siblings also may be indicated.

## ✓ Confirmation of Diagnosis

Plasma acylcarnitine and urine organic acid analysis are needed for confirmation. TFP deficiency and long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency (LCHADD) both have the same newborn screening profiles. Differentiation requires biochemical and molecular genetic testing using a skin biopsy.

## ✓ Communication of Results to Parents

**If a baby has a presumptive positive TFP deficiency newborn screening result, additional testing needs to be performed to confirm a diagnosis.** In accordance with Kansas Administrative Regulation 28-4-502, it is the responsibility of the attending physician or other birth attendant to obtain repeat specimens when needed to complete the screening process.

If a baby is diagnosed with TFP deficiency, the following points should be conveyed to parents:

- ***Parents should understand that treatment for TFP deficiency will be lifelong.***
- ***Parents should understand that treatment is not curative and that all morbidity cannot be prevented. Long-term management, monitoring, and compliance with treatment recommendations are essential to the child's well-being. A multidisciplinary approach is recommended and should include the following specialties: pediatrics, metabolic disease specialists, and dieticians. A cardiologist, ophthalmologist, and neurologist should also be consulted.***
- ***Genetic counseling services may be indicated. A list of counselors and geneticists, whose services are available in Kansas, should be given to the parents if they have not already seen a geneticist.***

For consultation, contact:

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