Fatty Acid Disorders

(aka Fatty Acid Oxidation Disorders or FAO Disorder)

In these metabolic disorders, enzymes necessary for fatty acid breakdown are unavailable or have reduced activity. Breakdown, or oxidation, of fatty acids is necessary for energy production when glucose levels are low. Without this energy supply, some individuals may have recurring incidences of low blood sugar levels. Consequently, most fatty acid disorders do not surface until a fasting challenge has been encountered sometime after birth. In newborns, a "fasting state" can be produced in as little as four hours without feeding. Fasting states can also be caused by illnesses such as ear infections or flu. Depending on the situation and the disorder involved, an affected infant could develop symptoms and suffer metabolic crisis anywhere from within 24 hours after birth up to sometime during early childhood when they begin sleeping through the night or switch over to solid food. Affected individuals may show vomiting, diarrhea, lethargy, seizures or coma. Failure to diagnose fatty acid disorders may also result in excessive fat buildup in the liver, heart and kidneys. This buildup can cause a variety of symptoms, ranging from hepatic failure, encephalopathy, heart and eye complications to general problems with muscle development. Many of these clinical symptoms can lead to death. Many deaths due to fatty acid disorders have been misdiagnosed as Sudden Infant Death Syndrome (SIDS) or Reye's Syndrome in the past. Fatty acid disorders are autosomal recessive.

As of July 1st, 2005, the Missouri Newborn Screening Program has been screening every newborn for several fatty acid disorders using tandem mass spectrometry. The fatty acids from the infant's blood are of different carbon chain lengths and are called "acyl" groups. They are covalently bound to the endogenous amino acid, carnitine. These acylcarnitine molecules of various forms and chain lengths are stable in the dried blood spot sample. The acylcarnitnes are abbreviated with a "C" for carbon, followed by the number of carbons in their chain. For example: C8 stands for octanoylcarnitine on our lab reports. These acylcarnitines serve as metabolic markers, as each disorder has its own profile of acylcarnitines that elevate in the infant's blood from the result of a disabled or missing enzyme in the fatty acid oxidation pathway. Most fatty acid disorders are named in reference to the deficient enzyme involved. Due to the length of the enzyme names, their acronyms are more commonly used.

The list of fatty acid disorders that we screen for are:

Carnitine acylcarnitine translocase deficiency (CACT)
Carnitine uptake defect (CUD, carnitine transport defect) *****
Carnitine palmitoyl transferase deficiency I (CPT-1a)
Carnitine palmitoyl transferase deficiency II (CPT-II)
Dienoyl-CoA reductase deficiency (DE-RED)
Glutaric acidemia type II (GA-II, multiple acyl-CoA dehydrogenase deficiency)
Long-chain hydroxyacyl-CoA dehydrogenase deficiency (LCHAD)
Medium-chain acyl-CoA dehydrogenase deficiency (MCAD)
Medium-chain ketoacyl-CoA thiolase deficiency (MCKAT)
Medium/Short chain L-3-hydroxy acyl-CoA dehydrogenase deficiency (M/SCHAD)
Short-chain acyl-CoA dehydrogenase deficiency (SCAD)
Trifunctional protein deficiency (TFP)
Very long-chain acyl-CoA dehydrogenase deficiency (VLCAD)

* There is a lower probability of detection of this disorder during the immediate newborn period.

Prevalence: 1: 10,000 (This is the projected, combined prevalence of all the FAO disorders).

Analytes Measured: The list of acylcarnitine markers and ratio markers that we monitor in each dried blood spot sample to screen for these fatty acid disorders are:

Disorder	Marker	Abnormal Range
CUD	Free Carnitine (C0)	< 12 umol/L
	C2	< 12 umol/L
CPT-1a	Free Carnitine (C0)	> 110 umol/L
	C16	<0.30 umol/L
	C0 / C16+C18	> 90
SCAD	C4	> 1.30 umol/L
	C4/C3	> 0.75
	C4/C2	> 0.05
GA-II	C4	> 1.30 umol/L
	C5	> 0.70 umol/L
	C5DC	> 0.32 umol/L
M/SCHAD	C4OH	> 1.00 umol/L
	C6OH	> 0.45 umol/L
MCAD and MCKAT	C8	> 0.40 umol/L
	C8/C10	> 3.0
	C6	>0.24 umol/L
	C10:1	>0.30 umol/L
DE-RED	C10:2	> 0.15 umol/L
VLCAD	C14:1	> 0.65 umol/L
	C14:1 / C12:1	> 3.0
	C14:1/C16	>0.20
	C14	>0.70 umol/L
	C14:2	> 0.15 umol/L
CACT and CPT-II	C16	> 7.8 umol/L
	C18:1	> 3.5 umol/L
LCHAD and TFP	C16-OH	> 0.15 umol/L
	C18-OH	> 0.10 umol/L
	C16OH / C16	> 0.08

Reported Abnormal Ranges may change slightly with reagent kit lot changes.

Feeding Effect: The marker analytes usually spike to a certain degree immediately after birth in affected newborns. This can be especially noticeable in infants that are breast fed only due to the longer fast that is imposed until the mother's milk production begins. As the infant feeds regularly for a few days, the marker analytes will lower in concentration, but usually continue to remain above the established cutoffs.

Timing Effect: The recommended collection time between 24 and 48 hours after birth is adequate. Waiting too many days after birth to collect a newborn screening sample could jeopardize the detection of some fatty acid disorders. It is recommended that samples for confirmatory testing of abnormal fatty acid disorder screens be drawn immediately before a feeding time.

We have special sample collection guidelines for premature, sick, low birth-weight, and NICU infants in regards to minimizing interferences from factors causing false positives in that population; while at the same time upholding prompt identification of true disorders (see NICU guidelines on this web-site).

Confirmation: Screening results that indicate a low risk for a fatty acid disorder require only a prompt repeat newborn screening test. This means that only a slight elevation of one of the markers was detected on the initial screening test, and that specific diagnostic testing does not appear necessary. Our cutoffs are set low enough so that some normal infants (sometimes carriers of the disorder) will be flagged for retesting. If, however, the infant is sick or displays signs of metabolic distress, the physician may wish to conduct diagnostic testing instead of, or in addition to the repeat screen.

Screening results that indicate a moderate to high risk for a fatty acid disorder are considered "presumptive positive" and are immediately phoned and faxed to the physician of record. The doctor is then referred to our contracted genetic referral centers for expert advice on the disorder in question and is informed on what confirmatory diagnostic testing should be done to rule out the disorder, and what precautionary measures should be taken until the confirmatory results are completed.

Treatment: Treatment for MCAD and some other FAO disorders is extraordinarily simple once the diagnosis is made. Avoidance of fasting, particularly as infants and young children, is the primary treatment. When the infant reaches the age that he may sleep through the night, this may require feeding before bedtime and waking him up during the night and administering some form of fluid calories. Carnitine supplementation is used to provide a pathway for removal of toxic intermediate metabolites. Patients with these disorders may require glucose IV support during intercurrent infections or illnesses in which the infant is too sick to feed until oral feeding can be resumed. With appropriate continued treatment, hepatic, cardiac and muscular complications can be reduced or eliminated. Outcomes for some FAO disorders are unknown, and unfortunately even with screening, some infants with FAO disorders may develop a metabolic crisis before results are available.