

THIS IS AN EXAMPLE OF AN ACTUAL GA2 MOM'S TREATMENT- If you wanted to create your own protocol please insert your own specifics and Drs' names and numbers etc

Hospital Protocol for: Mother & Infant

Please review prior to delivery to ensure proper management.

Indicated for: Labor, Delivery, Postpartum Care
H/O variant of Glutaric Aciduria type II / Mitochondrial Disease
Affected Mother and possible affected infant.
Infant due date ...

Delivering Mother: Name
SS#
DOB:

Spouse: Name

Blood Type:

Obstetrician: Name and Phone
Off site PCP: Name and Phone

Please see separately attached Emergency Protocol letter.

No Lactated Ringers

Allergy: list all allergies

Do NOT administer **Lactated Ringers** in any form (through bolus or hanging fluids) for mother or infant.

History

Allergies: list drugs, etc

Known **Paradoxical** reactions to:

Metabolizes most medications rapidly and requires **much** less than recommended dose. Paradoxical reactions are unpredictable. **Proceed with caution.**

Have taken with success:

Blood pressure medication of choice:

Because Cardiomyopathy (enlarged heart) is associated with some fatty acid oxidation defects and mitochondrial disease, care should be taken with use of OTC cold medications and interactions with antibiotics like erythromycin or any of its related family of drugs

History of **HELLP syndrome & severe preeclampsia**, which can be manifestations of underlying disease in mother and/or infant, if affected.

Blood glucose levels should **NOT** be totally relied on as the **ONLY** indicator of a possible crisis. Other levels such as Free Fatty Acids, Organic Acids, Amino Acids, etc. may be rising BEFORE you see a drop in glucose or elevation in Ammonia, CPK, Lactic acid, etc. ~ All of which, can be Neurologically Toxic and or fatal to mother and baby.

Signs of altered mental status, hypertension, increased muscle weakness or sudden change in overall status may indicate impending crisis.

Mother's typical blood pressure runs ----- .

Patient has trouble with ----- .

Cardiac: list specifics if have cardiac issues.

Potential for cardiomyopathy or cardiac autonomic dysfunction under stress.

Contact Dr. -----, for consult as needed: Phone, Cell, Pager #

Experiences severe muscle weakness, including respiratory muscles – weakness may cause difficulty breathing. **Use caution with medications that Relax the muscles**

History of very low blood pressure during pregnancy (often low as 85/40) so a rise of blood pressure, even borderline high may be indicative of stress or preeclampsia.

Mother has history of Metabolic Stroke (compare to previous brain MRI's at (list hospital) and ischemic events via EKG. Proceed with brain MRI with MRS and EKG as needed.

Mother should remain inpatient until fully stable.

THIS IS AN EXAMPLE OF AN ACTUAL GA2 MOM's TREATMENT During a Pregnancy - If you wanted to create your own protocol please insert your own specifics and Drs' names and numbers etc

Current Home Management & Medications (patient has PICC line)

- 18 hour IV Dextrose 10% with half normal saline at 56/hr (1000ml total)
- 3000mg IV **Carnitor** daily (3000mg added to bag – infused over 18 hrs)
- 500mg Riboflavin/Vitamin B2 daily – 250mg twice daily
- 100 mg CoEnzymeQ10 daily
- 34-68 grams Miralax daily (2-4 divided doses)
- Colace stool softener
- Cal-Nate prenatal vitamin
- 100mg Omega 3 Fatty Acids
- Full source nutrition from Peptinex DT (by Novartis)

During hospitalization

- Switch IV fluids to 24 hr D10%, half normal saline at 83cc/hr.
Never turn **off D10% without tapering down first.**
- 3000mg IV **Carnitor** should be given over 24 hr period, in fluids – approx 1500mg per 1000ml bag - if using 2, 1000ml bags per 24 hrs.
- New IVF rate & should be maintained until oral intake is sufficient; patient is under less stress from delivery and recovery and/or until laboratory testing is normal.
- Continue to administer Regular Home PO meds as indicated
- Patient needs IV antibiotics at time of delivery – see chart

It is important to provide this higher rate of Dextrose infusion to help meet sufficient Energy demands for proper cellular function (i.e., increasing the body's ability to perform and recover). Fat & protein metabolic pathways are broken and will not allow for patient to generate enough energy without an Extra amount of Carbohydrates, which is provided in the Dextrose solution.

Upon discharge, patient should continue with PICC line IVF infusions with - previous home care supplies and orders (unless they change) until at least 6 week postpartum checkup.

Please ensure appropriate fluids and all medications/supplements are administered throughout hospitalization.

Appropriate labs should be drawn throughout delivery and post partum recovery,

Note: metabolic changes can change rapidly, which means you may need to draw labs more often.

1. CMP
2. CBC w/diff.
3. Lactate & Pyruvate, L:P ratio
4. Ammonia
5. CK & cardiac enzymes
6. LDH
7. PT/PTT
8. Peripheral Smear for signs of Hemolysis
9. Fibrinogen
10. Blood gases as needed

Urine: Protein

Any abnormal, onsite testing for Mother should be reported immediately to (hospital's) metabolic specialist, in addition to patient's Metabolic Geneticist, for consultation.

Infant Testing & monitoring:

Collect Cord blood for Viacord (patient has kit)

Infant should be monitored closely for signs of MADD/GAI1 by neonatal team.

Check infant's blood glucose **before** initial feed and randomly prior future feeds before discharging. Do check **post prandial** glucose if found to be low initially. Continue to monitor until stable.

We will treat the infant as if **Affected**, until laboratory test proves otherwise. There is thought to be at least a 50% chance of inheritance for the infant.

Infant should intake regular formula unless symptoms of intolerance appear or laboratory tests indicate a problem.

Avoid Fasting – feed every 2 hours or as needed.

Appropriate labs should be drawn (ASAP) to evaluate for metabolic acidosis, including:

1. CMP
2. CBC w/diff. (family history of bone marrow suppression in affected sibling)
3. Lactate & Pyruvate, L:P ratio
4. Ammonia
5. CK & cardiac enzymes
6. LDH
7. Blood gases as needed

Repeat the above labs as needed and/or before discharge from hospital, with 48 hour newborn metabolic testing.

At approximately 48 hours of age, other labs for disease detection should be drawn. Including:

Newborn Screening Card/heel stick. *Screening Company should be made aware of family history and should expedite results to hospital. *

Metabolic Screening - Blood

1. Acylcarnitines, Quantitative
2. Amino Acids, Quantitative
3. Carnitine Levels

Urine

1. Acylglycines, Quantitative
2. Organic Acids
3. Acyl Carnitine Profile
4. Carnitine Levels
4. Amino Acids, Quantitative

Systemic Tests

1. Echo,
2. EKG
3. Audiology Testing

4. Brain & Abdominal MRI – as warranted

In preparation, please review labs and call **Mayo Laboratories (or other requested Lab)** to ensure minimum necessary amount of blood is drawn, the possibility of expedition of results and the appropriate fasting times for a newborn is established. Mayo Client Service Representatives: 800-533-1710.

Skin Fibroblast Testing for Richards Infant

Skin from circumcision, will be collected under the supervision of **Dr. -----** of Pediatrics.

Send skin to the -----**lab** for storage and cell growth.

Lab telephone: Phone

Lab fax:

Test:

Skin Fibroblast Acyl-Carnitine Profile

Skin cells should be grown and sent to:

List name, address, phone, fax, email address of person/Lab

Please contact ----- lab for proper collecting and shipping instructions.

For the infant: Signs of disease manifestation and are not limited to:

Hypoglycemia, lethargy, acidosis, hypotonia, vomiting, Diarrhea, Reyes Like Syndrome
Seizures, Small for gestational age/low birth weight, Jaundice, Respiratory distress, Club feet
Abdominal hernias, Rocker bottom feet, Autonomic dysfunction

▶ systemic anomalies

- neonatal acidosis
- "sweat-sock" odor
- hypoglycemia
- sweaty feet odor
- stale breath odor
- neonatal death frequent
- lipid accumulation in liver, heart, and renal tubular epithelium

▶ craniofacial anomalies

- facial dysmorphism
- macrocephaly
- cerebral pachygyria
- cerebral gliosis
- large anterior fontanel
- high forehead
- flat nasal bridge

- telecanthus
- cataract
- malformed ears

▶ cardiac anomalies

- cardiomyocytic steatosis

▶ hepatic anomalies

- hepatocytic steatosis
- hepatomegaly
- Hepatic periportal necrosis

▶ hypoplasia of pancreatic ductules

▶ thymic involution

▶ thymic atrophy

▶ hypoglycemic coma

▶ muscular anomalies

- lipid storage myopathy
- vacuolar myopathy with lipid accumulation

▶ pancreatic anomalies

- acute pancreatitis
- recurrent pancreatitis

▶ thoracic anomalies

- pulmonary hypoplasia (respiratory distress)
- pulmonary alveolar proteinosis (2082330)
- bilateral 13 ribs

▶ renal anomalies

- selective proximal tubular damage
- renal cortical cysts (glomerulocysts)
- renal multicystic dysplasia
- polycystic kidneys (renal cystic disease)
- renal medullary dysplasia
- tubular cell steatosis
- lipid accumulation in renal tubular epithelium

▶ genital defects

- hypospadias
- cryptorchidism

▶ cerebrospinal anomalies

- cerebral pachygyria

- agenesis of the cerebellar vermis
- hypoplastic temporal lobes
- immature brain with white matter gliosis
- symmetric warty dysplasia of cerebral cortex
- spongiosis and gliosis of the spinal cord (2082330)

▶ placenta anomalies (12007026)

- delayed maturation
 - large-for-gestational-age size
 - abundant immature intermediate villi with cellular syncytiotrophoblast
 - persistent villous cytotrophoblast
 - decreased syncytial knots
- immature intermediate villi showed exaggeration of lacunar interstitial spaces consistent with non-hydropsic villous edema
- marked lipid accumulation within extravillous trophoblasts of placental septa and cell islands
- light lipid accumulation in fibroblasts of stem villi

**** Infant may appear perfectly well, even if affected ****
Previous affected children have no anomalies.

AVOID FASTING – AVOID FASTING – AVOID FASTING

GAI/Glutaric Aciduria II or MADD/Multiple Acyl CoA Dehydrogenase Deficiency

is a FAOD/Fatty Acid Oxidation Disorder, organic academia & mitochondrial disease.

GAI/MADD is a genetic, metabolic deficiency in which the body is unable to oxidize (breakdown) fatty acids & proteins to make energy because an enzyme is either missing or not working correctly. The main source of energy for the body is a sugar called **glucose**. Normally when the glucose runs out, fat is broken down into energy. However, that energy is not readily available to children/ adults with an **FOD**. **If undiagnosed and untreated**, these disorders can lead to serious complications affecting the liver, heart, eyes and general muscle development, and possibly death. There is a **wide variation in presentation of FODs, even within the same family**. Manifestations of this disorder place infant at risk for metabolic acidosis.

Mitochondrial diseases result from failures of the mitochondria, specialized compartments present in every cell of the body except red blood cells. Mitochondria are responsible for creating more than 90% of the energy needed by the body to sustain life and support growth. When they fail, less and less energy is generated within the cell. Cell injury and even cell death follow. If this process is repeated throughout the body, whole systems begin to fail, and the life of the person in whom this is happening is severely compromised. Diseases of the mitochondria appear to cause the most damage to cells of the brain, heart, liver, skeletal muscles, kidney and the endocrine and respiratory systems. Depending on which cells are affected, symptoms may include loss of motor control, muscle weakness and pain, gastro-intestinal disorders and swallowing difficulties, poor growth, cardiac disease, liver disease, diabetes, respiratory complications, seizures, visual/hearing

problems, lactic acidosis, developmental delays and susceptibility to infection.

Avoidance of Physiologic "Stress" Physiologic stress is triggered by external factors that may result in worsening the metabolic situation, which may result in temporary , or in sometimes, permanent worsening of the condition.

Cold Stress is extremely important. Thermal regulation (temperature control) is not always normal in people with mitochondrial diseases and exposure to cold can result in severe heat loss and trigger an energy crisis. Over bundling can be a problem too .

Heat Stress can be a problem in some people. This is especially true of those with an inability to sweat normally. Heat exhaustion and heat stroke may occur on hot days.

Starvation — avoid fasting.

Avoid fasting. This is perhaps the most important part of the treatment for most people with metabolic disorders. Fasting means "not eating" and avoiding fasting means avoid prolonged periods without a meal (even an overnight "fast" from 8 pm to 8 am may be dangerous in some patients). In some patients an unintended fast resulting from an illness that causes vomiting or loss of appetite (like the flu) should be hospitalized to ensure continuous nutrition (intravenous glucose for example). In order to ensure adequate frequent nutrition, sometimes a feeding tube needs to be placed in order for the person to receive feeding at night.

Lack of sleep may also be harmful.

Vitamins and cofactors are compounds that are required in order for the chemical reactions, which make energy, to run efficiently. By definition, a cofactor can be made by the body, whereas a vitamin cannot, and therefore must be eaten. For most people, a regular diet contains all the vitamins one could possibly need and their bodies can make as much of any specific cofactor that it needs.

For those with mitochondrial disorders, added vitamins and cofactors may be useful.

Please see <http://www.umdf.org/site/c.dnJEKLNqFoG/b.3042175/#Toxins>

For more information on treatments and thereapies for Mitochondrial Disease.

Copied to:

List every person/Lab/hospital that this info was sent to

Mother's Primary Geneticist: List name, address, phone etc

Mother's local consult/Geneticist and affected children's geneticist:

List name, address, phone etc