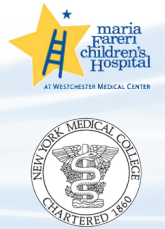


# Collaboration of the Metabolic Service, Caregiver and Home Nutrition Support Team in the Management of a Complex Home Nutrition Support Consumer

Robin Nagel, RD, CNSC, Coram Specialty Infusion Services, Plainview, NY. Shideh Mofidi, MS, RD, CSP; David Kronn, MD, Maria Fareri Childrens Hospital & Department of Pediatrics, New York Medical College, Valhalla, NY. Karen Sexton-Hamilton, MS, RD, LD, CNSC, Coram Specialty Infusion Services, Denver, CO.

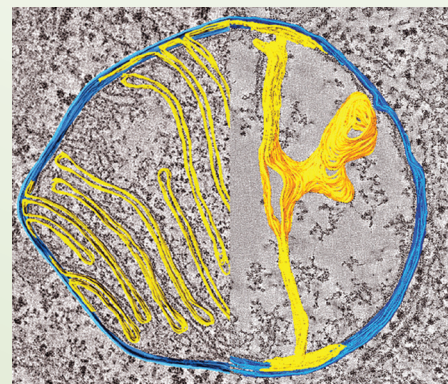


## Introduction

Synergy between the Metabolic Service, caregiver and Home Nutrition Support Team (HNST) is pivotal in providing optimal nutritional management of consumers, with complex metabolic alterations, who require long-term specialized nutrition support.

This case involves a young male with Barth Syndrome (BTHS) a rare, x-linked mitochondrial disorder. Less than 500 cases of BTHS have been reported worldwide. BTHS is caused by a mutation in the tafazzin gene (TAZ) located at Xq28. This defect results in abnormal modeling of cardiolipin, an essential phospholipid component of mitochondrial membranes that is important in energy metabolism.

As a result, mitochondrial structure and membrane recognition sites are altered leading to impaired function of the mitochondria. BTHS presents with a wide array of manifestations including cardiomyopathy, neutropenia, hypotonia and muscle weakness, fatigue and lack of stamina, growth delay, 3-methylglutaconic aciduria, and an abnormal cardiolipin profile.



Segmented electron microscopy tomograms of mitochondria from healthy (left) and Barth Syndrome (right) lymphoblasts. Images were scaled to the same magnification to compare and contrast two mitochondria halves in one chimera mitochondrion. - Image courtesy of Michael Schlame, MD.

There is no specific treatment for BTHS. Cardiac failure and severe infections are common causes of death in affected individuals. Cardiomyopathy is the cardinal manifestation in BTHS and is usually of the non-compact variety. Medicines help control varying degrees of cardiomyopathy; however, in many older BTHS patients, transplantation has been necessary. Neutropenia renders the individual more susceptible to infection and diarrheal illnesses. Bacterial infections can often be effectively treated with antibiotics. Granulocyte colony stimulating factor (G-CSF) is often used to stimulate white cell production by the bone marrow and help fight infections.

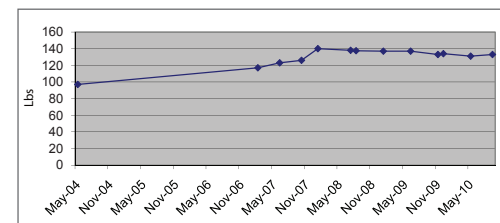
Throughout the growth continuum there are numerous nutritional concerns that arise. Painful oral aphthous ulcers may reduce intake. Reduced muscle mass, in addition to exercise intolerance, reduces caloric requirements and places the consumer at risk for overfeeding. Careful dietary monitoring is the only way to ensure proper caloric and nutritional intake.

**References**  
 Schlame M. Cardiolipin synthesis for the assembly of bacterial and mitochondrial membranes. *J Lipid Res.* 2008; 49(8): 1607-1620.  
 Schlame M, Ren M. The role of cardiolipin in the structural organization of mitochondrial membranes. *Biochim Biophys Acta.* 2009; 1788(10): 2080-2083.  
 Houtkooper RH, Turkenburg M, Poll-The BT, Karall D, Pérez-Cerdá C, Morroni A, et al. The enigmatic role of tafazzin in cardiolipin metabolism. *Biochim Biophys Acta.* 2009; 1788(10): 2003-2014.  
 Joshi A S, Zhou J, Gohil V M, Chen S, Greenberg M L. Cellular functions of cardiolipin in yeast. *Biochim Biophys Acta.* 2009; 1793(1): 212-218.  
 Hauff K D, Hatch G M. Cardiolipin metabolism and Barth syndrome. *Progress in Lipid Research.* 2006; 45: 91-101.

## Case Summary

At age 18, a male with BTHS was referred by an Inherited Metabolic Disease Center for home enteral nutrition (HEN). The HNST Registered Dietitian (RD), the Metabolic RD and mother conferred regarding the patient's medical and nutritional status. Consistent with BTHS, the patient had experienced growth delay as a child and had undergone an accelerated growth rate during later puberty. Despite this pronounced increase in linear growth, the patient was significantly underweight and malnourished. A very conservative HEN prescription was initiated via gastrostomy (GT) with consideration for potential refeeding sequelae. HEN was continued for two years until the feeding tube had to be removed as a result of recurrent infections. The patient was able to manifest improvement in his nutritional status during HEN despite these recurring medical obstacles, including development of superior mesenteric artery (SMA) syndrome and multiple viral illnesses. Once the feeding tube was removed, his feeding issues remained and his nutritional status further deteriorated. At that point, a decision was made to initiate total parenteral nutrition in the hospital requiring insertion of a lifoport. When stable, this was converted to home parenteral nutrition (HPN).

The preliminary goal of HPN institution was to achieve cautious weight gain of not greater than one pound per week, with a target weight of 140 pounds (20 percent lower than IBW for non-BTHS males). The weight goal for this patient was to maintain a target weight below IBW to prevent cardiac stress. Additional objectives were to: reduce chronic fatigue related to malnutrition; prevent catheter infections and complications; correct micronutrient deficiencies and nutritionally optimize for potential cardiac transplantation. Simultaneous medical management of chronic pain, nausea and vomiting and stabilization of cardiomyopathy were also essential.



The Metabolic and HNST RDs worked collaboratively over the next several months as the HPN was titrated up to goal. Clinical monitoring occurred during titration, and continues on-going. Various lab assays were obtained in relation to clinical status and in anticipation of the possibility and potential for developing nutrient deficiencies due to overt malnutrition. Although this patient received a conservative formulation to gradually promote weight gain without cardiac stress, MVI-13 and MTE-5C were provided daily with the TPN formulation. Challenged by multiple infections and hospitalizations associated with his diagnosis, the patient was able to achieve a net weight gain of 30 pounds with the assistance of home nutrition support therapy.

Imperial use of a specialized amino acid profile containing supplemental Arginine and Cysteine was implemented based on observations of low Arginine levels in BTHS subjects. It is postulated that Arginine in conjunction with Cysteine may be beneficial in reducing the profound fatigue associated with BTHS. The male did report mild improvement of fatigue and improvement of quality of life in conjunction with this customized amino acid profile.

Date	Home Nutrition Support Regime	Comments
5-04	Isotonic enteral GT feeding: Calories: 1000; Protein: 44 grams (23 cal/kg, 1 gm Pro/kg)	Weight: < 3rd percentile Height: 75-90 percentile BMI 13.3 kg/m2: < 3rd percentile
7-04	Transferred to alternate provider due to insurance	
3-06		Diagnosis with gastroenteritis and SMA syndrome
7-06	Removal of GT and closure of stoma	Infection: <i>Staphylococcus Aureus</i>
8-06	No HEN - nausea, vomiting, digoxin toxicity	Reaction to antibiotic treatment for GT site infection
12-06	No HEN - diarrhea, weight loss, osteoporosis	BTHS subject to reduced bone density based on a Dexa scan.
1-07 to 4-07	Acute episodes of vomiting, diarrhea and dehydration	Diagnosis with pancreatic insufficiency
4-07	Port-A-Cath® placement for TPN. TPN started in hospital.	
5-07	Return to initial home infusion company for TPN. TPN calories: 1100; Protein: 46 grams; Volume: 1000 mls over 20 hours (20 cal/kg, .8 gm Pro/kg, 18 mls/kg)	Goal: Rate of weight gain not > 1 lb/week. Limited volume due to cardiac considerations. Concentrated amino acid solution (15%) used to accommodate volume restriction.
	Iron replacement (Ferrolecit); Increase in lipid to .75 gm/kg	Fe Panel: Fe deficiency - TPN does not contain Fe source. Oral intake minimal. Oral Fe supplement instituted after IV Fe repletion dose complete; EFA Profile: EFAD
	Pancreatic enzymes	Patient has a history of SMA Syndrome due to lack of visceral fat stores. SMA syndrome predisposes individuals to pancreatic enzyme deficiency as duodenal occlusion limits passage of pancreatic enzymes through the gastrointestinal tract.
	Reduction in TPN potassium content	Hypotonia in BTHS results in limited potassium muscle reservoir for storage. GI illness result in significant potassium loss. Great caution with intravenous potassium supplementation is necessary to avoid rebound hyperkalemia.
6-07	Oral vitamin D supplementation (50,000 IU) - oral	25-hydroxy vitamin D level < 30 ng/ml
	Zinc supplementation	Decreased taste perception
	Poly-Vi-Sol™ 1-2 drops/d	Supplemental vitamin A and E
	Infusion hours reduced to 18 hours	Enhancement of quality of life
	TPN calories: 1450; Protein: Increased to 55 gms; Lipids: Increased to 55 gms; Volume: 1000 mls (26 cal/kg, 1 gm Pro and lipid/kg)	Declining Pre-albumin. Due to delicate cardiac status, fluid maintained at 1 liter. Further increase in substrates not considered due to volume constraints.
7-07 to 10-07		Four hospitalizations due to viral illness/infection
10-07		Net 5 lb weight increase over five months despite multiple hospitalizations
1-08	Attempt at TPN weaning. TPN protein and calories reduced by ~ 25-30%. Volume reduced to 800 mls over 15 hours.	Goal weight based on height and diagnosis BTHS achieved.
8-08	Baseline amino acid profile obtained. Metabolic team prescribed oral Arginine supplementation. Target total Arginine intake = 15 gms/day.	Theorized to improve chronic fatigue. Assists with wound healing.
1-09	Recent prolonged hospitalization due to diarrhea and electrolyte imbalance	Oral Arginine discontinued due to mouth sores which are common in immunocompromised BTHS patients.
10-09	Trace element and vitamin assays by Metabolic Team. Selenium increased to 90 mcg. Consideration of MVI - 12 (without vitamin K).	Low Selenium level. Elevated vitamin K level. Level to be repeated.
2-10	TPN regime increased by 20%	Multiple hospitalizations resulting in weight loss. Limited oral intake.
4-10	Addition of parenteral Arginine and Cysteine (2 gms each)	Unsuccessful attempts at oral Arginine supplementation. Arginine believed to work synergistically with Cysteine.
5-10 to 6-10	Decreased serum Amino Acid levels. Protein titrated up to 1.5 gm/kg (=90 gms).	Non-protein calorie: nitrogen ratio reducing. In BTHS patients that have a stable weight, an increase percentage of protein calories is desirable as the mitochondria prefer protein as a superior fuel source.

## Conclusion

The collaboration of the Metabolic Service, HNST and caregiver can foster optimal nutrition care planning and monitoring, as well as facilitate use of the latest advances in HEN and HPN therapy. This alliance serves to promote optimal care and better outcome for the home nutrition support patient with specialized complex metabolic conditions.

## Resources

- www.barthysndrome.org
- www.ninds.nih.gov/disorder/barth/barth.htm
- www.kennedykrieger.org/kki\_diag.jsp?pid=2170
- www.hopkinsmedicine.org/cmsl/Barth\_Summary.html