

June 5, 2020 Barth Syndrome Foundation Roundtable Discussion (via Zoom)

**Strength, stamina and fatigue in Barth syndrome, with special guest speaker Brittany DeCroes Hornby, PT, DPT, PCS from the Department of Physical Therapy, Kennedy Krieger Institute.**

Brittany is a physical therapist involved with many individuals with Barth syndrome at the multi-disciplinary Barth syndrome clinic within Kennedy Krieger Institute and has also engaged with families and affected children and adults at BSF conferences since 2014. Based on her observations through research studies at the conferences and sessions within the clinic, Brittany and the team noticed that people with Barth syndrome of all ages demonstrate and report struggles with strength, stamina and fatigue. As a result, Brittany has become more interested in quantifying and describing those struggles over the last several years.

**Do people with Barth syndrome have more weakness and more fatigue than other people?**

A [dynamometer](#) is a device used in physical therapy to measure how strong a muscle group is in pounds to provide an objective measure of strength. Using this device, Brittany has found in prior research that ALL boys and men with Barth syndrome have shown significantly impaired lower extremity (specifically at hips and knees) muscle strength (in comparison to people without Barth syndrome, called “normative values”). At the 2014 BSF conference, Brittany found that the most impaired muscle group in the Barth boys and men was the knee extensors, or the quadricep muscles which are used when a person straightens his leg. In addition, when normalized to body weight, Brittany found that weakness was significant which implies an impairment in functional strength as well. This is important because the quad muscles are the powerhouse of the legs and make everyday movement such as walking, standing and stepping possible.

In typical populations, adults are stronger than children in this type of testing. However, it turns out this is not the case in people with Barth syndrome. By testing a group of the same 11 people with Barth syndrome over six years at three BSF conferences (2014, 2016 and 2018), Brittany discovered that there was actually not a statistically significant change in leg strength (when normalized for body weight) over time. In other words, regardless of age, the average leg strength is always significantly lower than normal in people with Barth syndrome.

While handheld dynamometry is one measure of strength, there are other more functional assessments of strength and stamina that can be used. For example, Brittany has used the “5 times sit to stand” (FTSST, a functional assessment of strength) test and a six-minute walk test (6MWT, a measure of functional exercise capacity) in her physical assessments of people with Barth syndrome. The FTSST test is performed exactly as it sounds; a person is asked to sit in a chair and then stand up (ideally without using his or her hands or other assistance) five times in a row. Brittany has found a strong correlation between increased age and difficulty with the FTSST test. In fact, some older people with Barth syndrome cannot do this task without using their hands for support. This test is in alignment with the experience of weakness and fatigue that most people with Barth syndrome and also suggests that there is weakness not only in the large quadricep muscles but also in other muscle groups (such as the hip extensors, etc.).

### **What are some PT recommendations for people with Barth syndrome at home?**

Telehealth for home exercise programs and for PT support at home can be an excellent option, especially while many people are at home due to COVID-19. Brittany notes that there are some surprising benefits to telehealth physical therapy. One benefit is the opportunity for the therapist to “see” virtually what an individual has at home so that he/she can make individualized recommendations using materials and tools (stairs, hand weights, a stool, etc.) that are already at home. In addition, it may be possible for some people who cannot travel to an institution such as KKI to be able to have PT support virtually via telemedicine. As the laws surrounding this vary state to state, Brittany advises contacting your PT provider or her if you are interested ([Hornby@Kennedykrieger.org](mailto:Hornby@Kennedykrieger.org)).

Regardless of whether or not you have access to a PT via telehealth or in person, Brittany suggests being active for at least 10 minutes every single hour if possible. In fact, she suggests that the research supports the benefits of intermittent activity (such as climbing the stairs and doing one or two sets of 10 bridge exercises several times a day). A sedentary lifestyle (sitting most of the time) is associated with a number of risk factors and diseases in healthy people and consequently is also detrimental to the health and stamina of people with Barth syndrome. Therefore, Brittany recommends moving as much as possible in short pockets of time and suggests that this may also help combat the overwhelming “rebound fatigue” that some people with Barth syndrome experience when they have done too much physical activity for too long.

### **Fatigue, Weakness and Age**

Normally, in people without Barth syndrome, the distance a person can walk during a six-minute time period increases with age. This makes sense since people usually get taller and stronger with age and therefore can go a longer distance. However, in the Barth syndrome population that Brittany has studied, that has not been the case. She has found that, regardless of age, the vast majority of the boys and men with Barth syndrome in her studies can walk somewhere between 350-400 meters during a 6MWT, a distance that is significantly less than most other people in any age group. She also notes that when there is a variation from that distance (for example a Barth individual can walk further than 400 meters or cannot complete 350 meters), she has usually found that to correlate with some change in lifestyle or a significant medical event.

Fatigue is difficult to capture and quantify, especially in the snapshot of a 60-minute clinic appointment. In general, fatigue correlates with performance on assessments such as the FSST and 6MWT. In addition, Brittany has found that people with Barth syndrome who use significant effort to go a greater distance in these tests report significant fatigue when they are finished. Adults with Barth syndrome have reported that working, walking and exercise are the most impacted by fatigue in their lives, while middle school age kids also add cognitive fatigue to their description. Stamina also comes into play as a factor contributing to increased fatigue as seen when individuals with Barth syndrome are asked to repeat an assessment several times in a row. In that circumstance, Brittany has noticed a marked change in ability and fatigue with each repeat trial.

### **Additional Insight from Dr. Richard Kelley and Dr. Peter Barth:**

Dr. Kelley adds that there are metabolic abnormalities that contribute to weakness and fatigue in Barth syndrome. Dr. Kelley suggests that prealbumin is the single best measure of new protein synthesis, which is inadequate in many children and adults with Barth syndrome and is a cause of Barth-related cardiomyopathy. In neuromuscular diseases with similar degrees of weakness, such as spinal muscular atrophy types 2 and 3, progressive muscle weakness can occur when protein synthesis is normal. However, in children with Barth syndrome, the major cause of muscle weakness is inadequate protein synthesis because of an insufficient supply of amino acids required in much larger-than-normal amounts in Barth syndrome. In this case, Dr. Kelley notes that strength can be improved by treating common amino acid deficiencies, such as arginine and methionine, and associated vitamin insufficiencies, such as vitamin B6 and vitamin C. Anecdotally, Dr. Kelley shares that he has seen several Barth patients with profound skeletal muscle weakness but normal heart function, implying that the weakness is not uniform across all muscle types. After puberty, inadequate protein synthesis is less common, yet weakness persists, at least in part because of intrinsic underdevelopment of type I (postural) muscle. In addition, the impaired physical abilities of young men with Barth syndrome conspire to limit the muscle-building effect that exercise provides.

Dr. Barth concurs with both clinicians, and additionally observes that neuromuscular weakness has been the most neglected symptom of Barth syndrome in prior literature and research, perhaps because cardiomyopathy and neutropenia are more severe and also life-threatening. Nonetheless, Dr. Barth notes with confidence that this element of Barth syndrome is already and will likely continue to warrant more attention in the future.

### **Summary**

Based on research studies evaluating strength, stamina and fatigue in a consistent population of boys and men with Barth syndrome, physical therapist Brittany Hornby from Kennedy Krieger Institute has found that these individuals experience weakness, especially in the lower extremities, in a way that is statistically significant. More importantly, these symptoms, as shared by many individuals at BSF's Patient-Focused Drug Development Meeting in 2018, have a profound impact on an individual's functional abilities and quality of life. Insight from assessments such as the FSST and 6MWT in addition to self-reported patient data can help improve our understanding of weakness and fatigue in Barth syndrome. The opportunity for more research and correlational studies exists and will continue to be a focus of research and study.