Christine Lysaght, Stroke Module Assignment B

Spinal muscular atrophy is an autosomal recessive genetic disease that results in muscle weakness and atrophy, biased to proximal and bulbar muscles, secondary to destruction of the alpha motor neuron in the ventral horn of spinal cord. [1] This damage is caused by lack of expression of the survival motor neuron (SMN1) protein. [1] Incidence of all types of SMA (I-IV) is 1 out 6,000-10,000 live births. [1] Type I is the most severe form of SMA accounting for approximately 12% of living SMA patients. [1] Children with SMA type I are unable to sit independently, experience difficulty with head control and typically require assistance with respiration. [2] Secondary osteoporosis is common in children with SMA Type 1. [3,4] The purpose of this paper is to briefly describe the etiology and treatment of osteoporosis in SMA and discuss the implications for physical therapy practice.

Osteoporosis is defined as "a systematic skeletal disorder characterized by low bone mass and micro-architectural deterioration of bone tissue with a consequent increase in bone fragility and susceptibility to fracture." [5] Secondary osteoporosis in children is due to the effects of a disease process or treatment that alters mobility, inflammatory cytokines, glucocorticoids, sex hormones or nutritional status or body weight. [5] Children with SMA type I have a higher risk of femoral and humeral fractures due to secondary osteoporosis. [3,6] Vestergaard et al. found that risk fracture increases 2-7 years after initial diagnosis of muscular dystrophy or spinal muscular atrophy. [6] No studies have specifically identified prevalence of osteoporosis in SMA type 1. However, Khatri et al. found that children with SMA (Types I-III) have the lowest bone mineral density when compared to children with muscular dystrophy. [4] Based on this on this data that patients with less disabling muscular dystrophy exhibit osteopenia or osteomalaica, children with SMA Type I would develop significantly greater loss of BMD especially in less active extremities and spine. This is similar to evidence in patients with spinal cord injury that develop site-specific bone changes. [7] Bone loss in SCI and SMA is thought to occur as a

consequence lack of ambulation and immobility. [6,7] However, recent studies implicate increased osteoclast activity mediated by decreased SMN1 proteins [8] and low lean body mass promote decreased bone mineral content, in conjunction with reduced load bearing. [4] Another associated factor in this population is reduced Vitamin D. [3]

Management of bone health for children with SMA type 1 is difficult due to muscle atrophy, weakness and inability to independently weight bear. Additionally, based on clinical observations children with SMA type 1 have difficulties managing their secretions when fully upright, even with adequate support from adapted equipment. Some evidence supports supplementation with Vitamin D and calcium to support bone health. [3] Pharmacological interventions aimed at maintaining and improving strength/lean muscle mass demonstrate limited success. [9] Empirically, increased muscle mass and use prolongs bone health as stated above.

How does this apply to physical therapists working with children with SMA type I? First and foremost, PTs need to understand that these children are prone to fracture, especially of the femur. This is crucial because these children are constantly transferred and handled by caregivers. Also this population develops joint contractures necessitating passive range of motion delivered by PTs, family members and nursing staff. Caregivers must be educated on safe handling and passive range of motion must be firm but gentle. Additionally, X-rays prior to initial standing in adaptive equipment is necessary to rule out hip dislocation and previous femoral fractures. Standers are recommended for children with SMA type I to provide load bearing on lower extremities and a static stretch to manage joint contractures. [10-13] However, there is lack of evidence that supported standing increases bone mineral density. [7] No studies specific to SMA type I exist.

Exercise and functional activities may maintain or improve lean body mass. Kang et al. hypothesize that collateral sprouting may occur during development to compensate for motor neuron

loss.[14] This supports the use of exercise and functional task specific training once thought to be detrimental individuals with neuromuscular disease [15] to positively impact bone mineral density. Aquatic therapy has also been found to improve function and strength in patients with SMA type III, further supporting the use of exercise to support muscle function. [16]

1. SMA Foundation. SMA overview. SMA Foundation Web site. http://www.smafoundation.org/wp-content/uploads/2012/03/SMA-Overview.pdf.

2. Stuberg WA. Muscular dystrophy and spinal muscle atrophy

 . In: Campbell S, Palisano R, Orlin M, eds. *Physical therapy for children.* 4th ed. St. Louis, Missouri: Elsevier Saunders; 2012:353-384.

3. Joyce NC, Hache LP, Clemens PR. Bone health and associated metabolic complications in neuromuscular diseases. *Phys Med Rehabil Clin N Am*. 2012;23(4):773-799. doi: 10.1016/j.pmr.2012.08.005; 10.1016/j.pmr.2012.08.005.

4. Khatri IA, Chaudhry US, Seikaly MG, Browne RH, Iannaccone ST. Low bone mineral density in spinal muscular atrophy. *J Clin Neuromuscul Dis*. 2008;10(1):11-17. doi: 10.1097/CND.0b013e318183e0fa; 10.1097/CND.0b013e318183e0fa.

5. Shaw NJ. Management of osteoporosis in children. *Eur J Endocrinol*. 2008;159 Suppl 1:S33-9. doi: 10.1530/EJE-08-0282; 10.1530/EJE-08-0282.

6. Vestergaard P, Glerup H, Steffensen BF, Rejnmark L, Rahbek J, Moseklide L. Fracture risk in patients with muscular dystrophy and spinal muscular atrophy. *J Rehabil Med*. 2001;33(4):150-155.

7. Giangregorio L, McCartney N. Bone loss and muscle atrophy in spinal cord injury: Epidemiology, fracture prediction, and rehabilitation strategies. *J Spinal Cord Med*. 2006;29(5):489-500.

8. Shanmugarajan S, Tsuruga E, Swoboda KJ, Maria BL, Ries WL, Reddy SV. Bone loss in survival motor neuron (smn(-/-) SMN2) genetic mouse model of spinal muscular atrophy. *J Pathol*. 2009;219(1):52-60. doi: 10.1002/path.2566; 10.1002/path.2566.

9. Frazin N. Valproic acid shows promise for treating spinal muscular atrophy. National Institute of Neurological Disorders and Strokes Web site. http://www.ninds.nih.gov/news_and_events/news_articles/news_article_sma_valproic.htm. Published February 18, 2004. Updated 2012. Accessed 10/10, 2013.

10. Glickman LB, Geigle PR, Paleg GS. A systematic review of supported standing programs. *J Pediatr Rehabil Med*. 2010;3(3):197-213. doi: 10.3233/PRM-2010-0129; 10.3233/PRM-2010-0129.

11. Skalsky AJ, McDonald CM. Prevention and management of limb contractures in neuromuscular diseases. *Phys Med Rehabil Clin N Am*. 2012;23(3):675-687. doi: 10.1016/j.pmr.2012.06.009; 10.1016/j.pmr.2012.06.009.

12. Gibson SK, Sprod JA, Maher CA. The use of standing frames for contracture management for nonmobile children with cerebral palsy. *Int J Rehabil Res*. 2009;32(4):316-323. doi: 10.1097/MRR.0b013e32831e4501; 10.1097/MRR.0b013e32831e4501.

13. Damcott M, Blochlinger S, Foulds R. Effects of passive versus dynamic loading interventions on bone health in children who are nonambulatory. *Pediatr Phys Ther*. 2013;25(3):248-255. doi: 10.1097/PEP.0b013e318299127d; 10.1097/PEP.0b013e318299127d.

14. Kang PB, Gooch CL, McDermott MP, et al. The motor neuron response to SMN1 deficiency in spinal muscular atrophy. *Muscle Nerve*. 2013. doi: 10.1002/mus.23967; 10.1002/mus.23967.

15. Anziska Y, Sternberg A. Exercise in neuromuscular disease. *Muscle Nerve*. 2013;48(1):3-20. doi: 10.1002/mus.23771; 10.1002/mus.23771.

16. Salem Y, Gropack SJ. Aquatic therapy for a child with type III spinal muscular atrophy: A case report. *Phys Occup Ther Pediatr*. 2010;30(4):313-324. doi: 10.3109/01942638.2010.493097; 10.3109/01942638.2010.493097.