Physical therapy management of Pompe disease

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Pompe disease (Glycogen storage disease type II, GSDII, or acid maltase deficiency) is an autosomal recessive disorder characterized by deficiency of acid α -glucosidase resulting in intra-lysosomal accumulation of glycogen and leading to progressive muscle dysfunction. The natural history of infantile-onset Pompe disease is characterized by hypertrophic cardiomyopathy and profound generalized weakness presenting in the first few months of life, with rapid progression and death usually occurring by one year of age. Late-onset Pompe disease is characterized by onset of symptoms after one year of age, less severe or absence of cardiac involvement and slower progression, with symptoms primarily related to progressive dysfunction of skeletal muscles and respiratory muscle involvement. Recent clinical trials of enzyme replacement therapy have begun to allow greater opportunity for potential improvement in motor status, function, and survival than ever before, with hopes of moving toward maximizing physical function for individuals with Pompe disease. Children are living longer with some achieving independent sitting, creeping, and walking—milestones typically never achieved in the untreated natural history of the disorder. With increased survival, clinical management based on an understanding of the pathology and pathokinesiology of motor function gains importance. This article reviews current knowledge regarding the motor system in Pompe disease and provides an overview of physical therapy management of Pompe disease, including management strategies for individuals on enzyme replacement therapy.

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Pompe disease (Glycogen storage disease type II, GSDII, or acid maltase deficiency) is an autosomal recessive disorder characterized by deficiency of acid α -glucosidase (GAA) resulting in intra-lysosomal accumulation of glycogen.^{1,2} Glycogen accumulates in various tissues, most significantly muscle, including cardiac, skeletal, and smooth muscle.^{1,2} The natural history of infantile-onset Pompe disease is characterized by hypertrophic cardiomyopathy and profound generalized weakness presenting in the first few months of life, with rapid disease progression and death usually occurring by one year of age.^{1,2} Late-onset Pompe disease (juvenile and adult onset) is characterized by onset of symptoms after one year of age, less severe to no cardiac involvement, and slower progression, with symptoms primarily related to progressive dysfunction of skeletal and respiratory muscles.^{1,3,4} The advent of enzyme replacement therapy (ERT) has begun to allow greater opportunity for potential improvement in motor status, function, and survival than ever before, with the hope of moving toward maximizing physical function for individuals with Pompe

disease.^{5–10} In this article the pathology and pathokinesiology of motor function in Pompe disease, and an overview of physical therapy (PT) management of Pompe disease, are provided. Studies have not previously been published on the use of PT with individuals with Pompe disease, therefore recommendations in this article are based on expert opinion, experience, and evidence from other neuromuscular disorders that have clinical features in common with Pompe disease.

OVERVIEW OF MOTOR INVOLVEMENT

Pathology of muscle weakness

Myopathy in Pompe disease results from intra-lysosomal accumulation of glycogen in muscle.¹ Glycogen accumulates primarily in muscle (cardiac, skeletal, and smooth) and the liver, but also in the central nervous system (including anterior horn cells, motor nuclei of the brain stem, and spinal ganglia) and other tissues.¹ Glucose metabolism is normal.^{1,2} Muscle involvement begins with enlargement of muscle fibers as glycogen accumulates in intact lysosomes,¹¹ later followed by muscle wasting, the precise mechanisms of which are unclear.¹² Glycogen accumulation in lysosomes is followed by lysosomal leakage or rupture with accumulation of glycogen in cytosol as well as lysosomes.¹¹ Lysosomal leakage or rupture also releases hydrolytic enzymes believed to have a role in muscle destruction¹¹ with degradation of myofibrils adjacent to glycogen accumulation in the cytosol.¹² Skeletal muscle contraction may cause lysosomes to rupture in muscle more than in other cell types, contributing to the greater relative involvement of muscle.¹¹ Lipofuscin-mediated

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apoptosis has been hypothesized to contribute to muscle wasting.¹² With disease progression, endstage fibers are left containing empty fluid-filled space with remnants of myofibrillar and sarcoplasmic material.¹³ Large vacuoles are evident in muscle fibers on MRI.¹⁴ Protein catabolism and abnormal protein metabolism may occur, due to or exacerbated by poor nutrition, with more rapid clearance of branched chain amino acids that normally have a role in muscle protein synthesis.^{15–18} Muscle function may be impaired by loss of contractile mass, decreased contractile function due to clusters of non-contractile material (glycogen) impeding force transmission by interrupting or displacing myofibrils,^{12,19,20} decreased oxidative capacity resulting in decreased adenosine-5'-triphosphate (ATP) availability for contraction, and impaired innervation.²¹

Clinical presentation and distribution of muscle weakness

Weakness in Pompe disease is greater in proximal muscles than distal, greater in lower extremities (LE's) than upper extremities (UE's), and generally symmetrical but imbalanced across joints.¹ Muscles may feel firm or hypertrophic despite profound weakness,^{1,2} especially calf musculature, and sometimes quadriceps, deltoids, and paraspinal muscles.

In the infantile form, progressive, profound, and generalized weakness occurs in neck, trunk, extremities, and facial and oral musculature, with macroglossia (Table 1).^{1,2} MRI shows diffuse hypertrophy of muscle groups with large vacuoles but without evidence of fatty infiltration.¹⁴ Cardiac involvement is severe with early hypertrophic cardiomyopathy progressing later to dilated cardiomyopathy.^{1,2} Respiratory involvement occurs early due to weakness in diaphragm, intercostals, and accessory muscles of respiration,² with ineffective cough due to weakness in abdominals. Paradoxical breathing with sternal and intercostal retraction during inspiration may occur due to weakness in abdominal and intercostal muscles.²² (See Pompe Disease Diagnosis and Management Guideline in this issue for respiratory details).

In the late-onset form, progressive proximal myopathy occurs with greater variation in distribution, extent, and rate of progression of weakness, even within families.^{1,3,4,23,24} Patterns of muscle involvement are listed in Table 2.^{1,3,4,23,25–27} With progression, weakness can become profound.⁷ CT and MRI of muscles in adults with Pompe disease show atrophy, fatty infiltration, and degeneration.^{25–27} Cardiac involvement is not typical in late-onset disease but respiratory involvement may be relatively more severe than skeletal muscle involvement and can be the presenting feature, with apparent selective involvement of the diaphragm.^{1,4}

Pathokinesiology of motor function and disease progression

Pathokinesiology in Pompe disease, as in all motor unit diseases, is characterized by a self-perpetuating cycle in which progressive imbalanced muscle weakness, compensatory movement patterns and postural habits, and the influence of gravity interact in the progression of disability.^{28,29} Weakness in Pompe disease evolves from the primary progressive myopathy described above,^{1,2} with possible contribution from anterior horn cell in-

Table 1
Clinical motor and musculoskeletal presentation in infantile-onset Pompe disease^{1,2}

Weakness: "floppy baby" appearance
Profound, progressive, symmetrical weakness
Proximal muscles weaker than distal muscles
Lower extremities weaker than upper extremities
Neck and trunk weakness profound
Facial and oralmotor weakness with myopathic facies
Respiratory involvement includes weakness in: diaphragm, intercostals, accessory muscles of respiration, abdominals
Hypertrophic cardiomyopathy progresses to dilated cardiomyopathy
Positional tendencies:
Hip flexion, abduction, external rotation
Knee flexion
Plantarvarus at feet and ankles
Spinal kyphosis at thoracic and lumbar levels in supported sitting
Head propped back into extension or falling forward in flexion in supported sitting
Forearm pronation, wrist flexion, finger flexion
Sternal and intercostal retraction from paradoxical breathing
Potential secondary musculoskeletal impairments:
Muscle tightness (hypoextensibility)/contracture:
Iliotibial bands (initially seen as lateral thigh groove)
Hip abductors and external rotators
Hip flexors
Hamstrings
Plantarflexors
Plantar fascia
Elbow flexors or extensors (position dependent)
Forearm pronators
Wrist/finger flexors-hypoextensibility over several joints sometimes accompanied by contracture or hypermobility at individual joints
Joint contractures:
Hip flexion, knee flexion, ankle plantarflexion
Elbow flexion or extension (position dependent), wrist and finger flexion
Deformity:
Rib cage flattened in anterior–posterior dimension with:
Sternal retraction (pectus excavatum)
Lower rib flaring
Spinal deformity: kyphosis, scoliosis, lordosis
Pelvic asymmetry with lateral pelvic obliquity, horizontal pelvic rotation, and posterior or anterior pelvic tilt
Hip subluxation/dislocation
Plagiocephaly, brachycephaly, or scaphocephaly
Osteopenia/osteoporosis/fracture

Table 2Clinical motor and musculoskeletal presentation in late-onset Pompe disease^{1,3,4,23,25–27}

Progressive proximal myopathy
Distribution of weakness variable, but:
Proximal muscles generally weaker than distal
Lower extremities generally weaker than upper
Weakness common in:
Pelvic girdle musculature (hip flexors, extensors, abductors, adductors)
Scapular stabilizers
Shoulder girdle musculature (including deltoids)
Spinal extensors (paraspinals)
Neck flexors more than extensors
Abdominals
Hamstrings
Quadriceps
Diaphragm
Weakness may progress to include: biceps brachii, triceps, tongue, and other musculature
Selective early involvement of hip adductors (especially adductor magnus), paraspinals, psoas, semi-membranosus, ventrolateral trunk muscles, rectus abdominus, gluteals, vastus medialis
Later involvement of the long head of the biceps femoris, semi-tendinosus, and anterior thigh muscles
Respiratory involvement may be more severe than skeletal muscle involvement, with early involvement of diaphragm
Relative sparing of tensor fascia lata, sartorius, short head of the biceps, gracilis, vastus lateralis, rectus femoris
Risk of secondary musculoskeletal impairment depends on patterns of weakness and compensation and is usually less than in infantile-onset, but scoliosis and lordosis may occur

involvement. Patterns of weakness have been described in Pompe disease^{1–4,23,24,30} and pathokinesiology has been studied in other disorders in which proximal weakness is greater than distal, such as Duchenne muscular dystrophy (DMD),^{28,31} a primary progressive myopathy, and spinal muscular atrophy (SMA),³² an anterior horn cell disease. Positioning, postural tendencies, and compensatory patterns of movement in these motor unit diseases are initially determined by the interaction between weakness and gravity, further compromised later by secondary musculoskeletal impairments.²⁸ Compensations are effective in maximizing function but, used persistently, can lead to contracture and deformity that contribute to increasing weakness and disability.²⁸ Compensations can also limit the use of existing strength by placing muscles at a mechanical disadvantage, compromise length-tension relationships, and limit opportunities to increase or maintain strength, leading to additional disuse atrophy.³³ Proportional increases in weakness may occur with growth due to biomechanical disadvantage as height, weight, or mass increase without the ability of the muscles to cope with the increased workload, as in DMD and SMA.³² Respiratory involvement, and cardiac involvement, if

present, can further compromise function and endurance as in other disorders,^{1,2,34} as can undernutrition due to feeding problems from oral-motor weakness.¹⁵ Detailed descriptions of pathokinesiology in infantile and late-onset disease are included in the electronic version of this article.

Secondary musculoskeletal impairments

Secondary musculoskeletal impairments occur in accordance with principles of biomechanics and developmental biomechanics³⁵ in which the application of small forces over time has powerful effects, especially during periods of rapid growth, with muscle length strongly influenced by the number of hours per day that muscles are in shortened or lengthened positions.^{36–38}

Muscle extensibility impairments, contracture, and deformity

Muscle hypoextensibility, muscle hyperextensibility, contracture, and deformity can develop from the chronic alterations in posture and positioning that result from weakness³⁹ and can further compromising muscle function, effective movement, positioning, and comfort. Contracture and deformity occur in accordance with severity of weakness, age of onset and duration of weakness, extent of imbalanced muscle activity, and intervention used or not used to minimize contracture and deformity.^{28,37} Muscles that cross two or more joints are at increased risk of early contracture.²⁸ With severe early weakness, the unopposed force of gravity has the most profound effect on positioning and the development of contracture and deformity, as in SMA.⁴⁰ With moderate to mild weakness, muscle imbalance across joints has an increased role in the development of contracture and deformity, as in DMD.^{28,37} Immobilization of muscle from chronic positioning in any diagnosis can lead to changes in fiber length and extensibility, sarcomere number, sarcomere length, length-tension curves, collagen concentration and orientation, ratio of tissue to muscle fiber, stiffness, and changes in ratio of tendon length to muscle belly,^{36,38} with muscle plasticity responsive to both deforming and corrective forces.

Positional tendencies in individuals with infantile-onset Pompe disease lead to early contracture of iliotibial (IT) bands, followed by hip and knee flexion contractures, and contracture of plantarflexors and plantar fascia. Classic areas at risk for abnormal muscle extensibility, contracture, and deformity in the infantile-onset form are listed in Table 1.^{1,2} Risk of contracture and deformity is also present in late-onset Pompe disease, including scoliosis and lordosis,¹ but presence and severity may vary due to greater variation in weakness. Additional detail is covered in the electronic version of this article.

Osteopenia/osteoporosis

Osteopenia and osteoporosis have recently been recognized as complications of Pompe disease and osteopenia has been identified in infants as young as four months of age.⁴¹ Femoral and vertebral fractures have been identified in patients with infantile-onset disease⁴¹ and vertebral fracture has been reported in late-onset disease⁴² (see Pompe Disease Diagnosis

and Management Guideline in this issue for details regarding osteopenia and osteoporosis).

Gross motor function

Infants with infantile-onset disease historically did not achieve motor milestones of independent sitting, creeping, standing, or walking,^{1,2,43,44} a fact that is changing with ERT, with some children on ERT now walking independently.^{2,5,6} In a study of physical disability in children spanning infantile and late-onset forms and ranging from age six months to 22 years, 2/3 were non-ambulatory, 3/4 used a ventilator, and age did not correlate with level of disability.⁴⁵

Individuals with late-onset disease characteristically experience gradual difficulty with motor function, noted initially in walking, running, and activities of elevation against gravity such as climbing stairs, rising from the floor, getting up out of a chair, and lifting the arms overhead.²⁴ The use of mobility devices such as canes, walkers, manual wheelchairs, and powered mobility are usually added gradually, often used part-time at first, for long distance community mobility or on uneven terrain.²⁴ Progression of weakness and increased risk of falls may lead to ambulation only possible or practical indoors on level surfaces for short distances in safe environments such as home; with a manual or motorized wheelchair or scooter used in all other environments.²⁴ Mean age at which use of a wheelchair is initiated has been reported as 46 years²⁴ and mean age at which ambulation is lost as 50 years.³

PHYSICAL THERAPY MANAGEMENT

Physical therapy (PT) management of Pompe disease, as in all motor unit diseases, should provide comprehensive, anticipatory, and preventative management based on an understanding of the pathophysiology and pathokinesiology of disease presentation and evolution, and on individual assessment.^{28,33,46} The key to management lies in understanding the interaction between the presence, progression, and potential remediation of weakness; the biomechanics of efficient movement; the risks for development of contracture and deformity and strategies for prevention and remediation; the risks and possible remediation of osteoporosis; and function. Muscle weakness presents and progresses in generally predictable patterns with predictable compensations used to cope with weakness.^{1,2,28} Secondary muscle tightness, contracture, and deformity occur in predictable patterns without intervention.²⁸ Intervention is focused on breaking or slowing this predictable, self-perpetuating cycle of events whenever possible²⁹ so that strength and endurance are maximally achieved and maintained, contracture and deformity are minimized, and compensations can be used to maximize function without leading to increased disability. PT intervention is designed to optimize and preserve motor and physiological function as much as possible within the limits of the disease; to minimize the clinical impact of the disease process; to prevent or minimize secondary complications; to promote and maintain the maximum level of function, functional independence, and participation; to optimize quality of life; and to maximize the benefits of enzyme replacement or

other treatments as they become available. PT should address all domains of the World Health Organization (WHO) International Classification of Functioning, Disability, and Health (ICF),⁴⁷ as well as the interaction between these domains; and evaluation and intervention should reflect current standards of care and management.⁴⁸ Selected PT assessment tools are listed in Appendix A of the Pompe Disease Diagnosis and Management Guideline in this issue. PT may be provided in a variety of settings, depending on the needs and preferences of the individual and family (see Pompe Disease Diagnosis and Management Guideline in this issue for details regarding service delivery and funding sources).

Management of skeletal muscle function (strengthening and enhancing motor function)

Guidelines for muscle strengthening are not established for individuals with Pompe disease. Studies of the effect of strengthening in individuals with Pompe disease have been few, with small numbers, limited to late-onset form, and recommend aerobic and sub-maximal exercise, reporting that sub-maximal exercise may stimulate the degradation of some of the glycogen that accumulates in the cytosol¹⁵ and that aerobic exercise combined with optimal nutrition may help clear glycogen from muscle with accompanying gains in strength and function.^{49,50} Concern exists, however, about excessively strenuous strengthening, consistent with precautions in disorders characterized by muscle degeneration in which strenuous exercise contributes to weakness by increasing muscle degeneration.³⁴ Awareness of general precautions with exercise in the presence of myopathy and cardio-respiratory impairment is important as well as the potential, theoretical concern in Pompe disease that excessive muscle contraction could increase leakage of glycogen from lysosomes or cause lysosomal rupture.¹¹ Studies of the effects of strengthening and exercise including strengthening and exercise with ERT are needed. If structural and physiological integrity in muscle is re-established with ERT due to a decrease in abnormal glycogen accumulation, more normal capacity for exercise may emerge. There is early evidence in animals that enzyme replacement may clear glycogen from cardiac and type I muscle fibers more efficiently and more fully than from type II fibers which may impact strengthening emphasis and results.⁵¹ Until more definitive studies are completed, caution and moderation in exercise are recommended.

Recommendations regarding strengthening of fragile muscles include precautions and guidelines from other degenerative muscle diseases³⁴ with an emphasis on the use of sub-maximal and aerobic exercise, avoidance of excessive resistive and eccentric exercise, use of functional activities for exercise, and appropriate monitoring of cardiopulmonary and respiratory response to activity, to exercise, and even to different positions (especially supine). Monitoring with pulse oximetry is recommended during initial examination and treatment, with changes in status and activity, and as needed based on medical stability. Exercise programs should consider fragility due to possible loss of contractile mass and contractile protein content and the possibility of abnormal force transmission within the muscle cells due to accumulation of non-contractile glycogen.¹² Consideration of physiological fragil-

ity should include cardio-respiratory impairment and potentially decreased oxidative capacity resulting in decreased ATP availability for muscle contraction.²¹

Intervention for enhancing muscle function should include strategies to optimize biomechanical advantage for movement, minimize contracture against which weak muscle must work, allow practice and strengthening within limits of physiological stability, avoid overwork weakness, avoid disuse atrophy, use energy conservation techniques, and avoid excessive fatigue (Table 3). Although excessively strenuous exercise should be avoided, gentle sub-maximal exercise is believed to be important to allow practice of new motor skills and patterns of functional movement, especially in children; to allow strengthening within physiological limits; to avoid additional disuse atrophy, especially in muscles that might not be used spontaneously because of biomechanical disadvantage and relative weakness compared to other muscles; and to avoid secondary decrease in cardiopulmonary function and deconditioning from inactivity.

Infantile-onset Pompe disease

Weakness in infants can be profound. Medical stability and ranges of cardiopulmonary safety should be established prior to initiation of therapeutic activity and cardiopulmonary response to activity and to position changes should be monitored. Self-initiated rests should be respected and rests should be established as needed to insure medical stability, avoid overwork weakness, and conserve energy. Positioning and support to maximize biomechanical advantage, decrease the impact of

gravity, and minimize the development of contracture against which weak muscles must work can allow easier, less strenuous use of weak muscles, increasing the possibility of appropriate practice of developmental skills and avoidance of additional disuse atrophy. Strategies of support during functional exercise should include well-known motor control principles including control of degrees of freedom to allow permissive conditions for the emergence and practice of movement that might not be possible without support. The buoyancy of water in a tub/pool⁵² can provide opportunities for movement while guarding against overexertion, as long as aquatic precautions are followed, especially regarding medical stability and the effects on respiration of the hydrostatic pressure of water on the trunk. Prolonged exposure to excessively heated pools should be avoided in myopathies in order to avoid fatigue. Gentle facilitation of movement with active, graded assistance and with assisted practice of movement in all medically safe positions may allow additional practice of developmental skills and strengthening of muscle within physiological limits and may maximize the benefits of ERT as it becomes available. Specific therapeutic activities making use of the above principles can be used to maximize head and trunk control, facilitate weight shift and transition between positions, facilitate sitting skills and floor mobility such as rolling and creeping on hands and knees, and facilitate standing and walking in children with the capability for these skills.^{5,6,10} Details (Figs. 1, 2) regarding therapeutic intervention for these tasks are presented in the online version of this article. Coordination with the rest of the team should occur regarding bone density and integrity, levels of osteoporosis, hip joint status, and potential precautions regarding weight bearing.

Late-onset Pompe disease

For older individuals, and those with more residual strength, gentle sub-maximal and aerobic functional exercise, such as swimming and cycling without excessive resistance, with active assist as needed, and functional activities, performed with respect for the limitations of cardiopulmonary and muscular endurance are generally considered beneficial.^{15,34,49,50,52} and may maximize the benefits of ERT as it becomes available. Excessive resistive and eccentric exercise is considered contraindicated in most neuromuscular diseases characterized by muscle degeneration, although debate exists over details of appropriate guidelines for many disorders.³⁴ Sub-maximal, graded, regularly scheduled exercise is considered beneficial in optimizing strength and avoiding additional disuse atrophy.³⁴ Excessive stair climbing is generally considered an activity to avoid in disorders characterized by muscle degeneration because of excessive concentric demands when ascending stairs and excessive eccentric demands when descending stairs. Energy conservation techniques assist in avoiding excessive exertion which may lead to overwork weakness.

Management of respiratory muscle function and pulmonary status

Respiratory/pulmonary management should follow current established guidelines for neuromuscular disorders,⁵³ and

Table 3

Physical therapy management—movement and strengthening

Establish medical stability and ranges of cardiopulmonary stability
Optimize biomechanical advantage for movement
Provide positioning and support to increase biomechanical advantage
Optimize influence of gravity
Use positioning that optimizes length-tension relationships in muscle
Minimize contracture against which muscles must work
Control degrees of freedom to provide permissive conditions for optimal movement and for the emergence of new movement
Allow practice and gentle strengthening within limits of physiological stability, following precautions and guidelines from other degenerative muscle disease
Use sub-maximal, aerobic exercise
Use active assistance where needed
Avoid overwork weakness and excessive fatigue
Avoid excessive resistance during exercise
Avoid eccentric exercise
Establish rests as appropriate and respect self-initiated rests
Use appropriate cardiopulmonary monitoring during exercise
Avoid disuse atrophy
Use energy conservation techniques

Fig. 1. Classic positioning and facilitation of strengthening and increased function in sitting and quadruped. A) Classic positioning and weakness/hypotonia in infantile-onset Pompe disease. B–G) 14 month old child with infantile-onset Pompe disease on ERT. B) Sitting posture with straight back, but lower extremities in typical flexion, abduction, external rotation (provides stability but prevents weight shift and transition out of sitting). May lead to scooting in sitting for mobility, rather than creeping on hands and knees, if creeping is not facilitated. C) Facilitation of weight shift, protective extension, and weight bearing through upper extremity in sitting, with lower extremity positioning controlled to allow transition to another position. D) Stabilization of lower extremities and facilitation of weight shift in sitting for more active beginning trunk rotation, reaching across midline and outside of the base of support, with weight bearing through the other upper extremity. E) Facilitation of quadruped with support at shoulders and hips. F) Facilitation of quadruped with support only at hips. G) Facilitation of forward weight shift and reaching in quadruped.

Fig. 2. Facilitation of standing and function with children with infantile-onset Pompe disease on enzyme replacement therapy: A) Facilitation of sit-to-stand and supported standing at a support with 14-month-old child. B) Facilitation of standing with hand support with 14-month-old child. C) Twenty-one-month-old child using adapted tricycle with shoe holders. D) Twenty-one-month-old child using stander for experience in standing, to provide weight bearing in good alignment, and to prevent/minimize contracture into hip flexion, knee flexion, ankle plantarflexion-elongates gastrocnemius muscles across knee and ankle joints simultaneously. E) Independent stair climbing.

specific guidelines for Pompe disease as outlined in the Pompe Disease Diagnosis and Management Guideline in this issue. Respiratory and pulmonary care is supported by PT management of respiratory/pulmonary function, including recognizing the effects of positioning on respiratory function, maximizing respiratory function and efficiency, use of airway clearance and pulmonary hygiene techniques (potentially including chest PT, active cycle breathing, autogenic breathing, positive expiratory pressure and flutter, intrapulmonary percussive ventilation, high frequency chest wall oscillation (HFCWO) with the use of vests, manually and mechanically assisted coughing with a mechanical in-exsufflator, and appropriate exercise, depending on age, level of involvement, and capabilities of the individual),⁵⁴ maintenance of rib cage mobility, and inspiratory muscle training as appropriate and as established in other neuromuscular disorders. Monitoring of oxygenation levels in different positions, and during activity and exercise with pulse oximetry is recommended.

Prevention of secondary musculoskeletal impairments

Secondary musculoskeletal impairments, including contracture and deformity, should be prevented by counteracting deforming forces in accordance with principles of developmental biomechanics³⁵ using gentle forces over time with daily stretching, correction of positioning, splinting and orthotic intervention, provision of adequate support in all positions, support in standing as appropriate, use of adaptive equipment and assistive technology, and education of patients and families (Table 4).^{55,56} Increased incidence of osteopenia and osteoporosis, and increased risk of fracture⁴¹ must be considered in application of forces. Interventions with the potential to contribute to bone strength and integrity, including weight bearing in PT and standing devices, shown to be associated with increased bone density in individuals with neuromuscular diagnoses,⁵⁷ should be considered, but even normal forces have the capacity to lead to fragility fractures⁵⁸; in osteoporotic bone, and care must be taken in force application. The natural evolution, and effective principles for treatment, of contracture and deformity in neuromuscular disorders are well established^{28,55} and should be followed in intervention for individuals with Pompe disease.

If adequate strength for more normal and complete anti-gravity movement is available early through ERT, and if motor milestones are achieved at relatively typical ages with a normal amount of movement throughout the day, the forces that lead to contracture and deformity may not occur and prevention of secondary musculoskeletal impairment may occur spontaneously through normal movement, as in typically developing children. However, monitoring and protection of the musculoskeletal system during ERT is critical so that secondary impairments such as contracture and deformity do not occur and limit the benefits of enzyme replacement.

Stretching should be initiated preventatively, done daily when there is a risk of contracture due to weakness and chronic positioning, and is best augmented by follow-up positioning including positional supports, splints and orthotic devices, and adaptive equipment.^{56,59} Stretching should include areas iden-

Table 4

Physical therapy management-prevention of contracture and deformity

Optimize alignment and positioning
Minimize deforming force of gravity
Stretching:
Passive stretching should be done daily and is best augmented by:
Active assistance if possible
Joint mobilization as needed
Modalities as appropriate (gentle heat, warm bath)
Stretch the structures that are at risk, and those identified by individual assessment:
Iliotibial bands
Hip and knee flexors
Hamstrings
Plantarflexors
Plantar fascia
Elbow flexors
Forearm pronators
Wrist/finger flexors
Anything else at risk by exam: individual joints, rib cage, spine
Follow-up with active movement as possible and prolonged positioning
Orthotic intervention (orthoses, casting)
Lower extremity binders (thigh binders)
Knee immobilizers/knee splints
Spine jackets
Wrist/hand/finger flexor splints
Standers or wheelchairs with standing capability
Adaptive seating and mobility devices (specialized strollers and manual and motorized wheelchairs with custom seating and motorized positional changes)

The number of hours per day in a given position determines the development/prevention of contracture and deformity. Standing may be important to minimize contracture and osteopenia/osteoporosis.

tified by individual assessment and areas of classic risk including hip flexors, IT bands, tensor fascia lata, hamstrings, long and short plantarflexors, posterior tibialis, plantar fascia, forearm pronators, and long wrist and finger flexors; with isolated stretching into hip and knee extension and ankle dorsiflexion. A stretching program is easier to establish as part of the daily routine if it is begun before muscle tightness/contracture is established and before stretching is painful. Stretching should be done gently and physiologically, with an awareness of the risks of fragility fractures⁵⁸ in the presence of osteopenia. Positional supports to augment stretching are detailed in the electronic version of this article and orthotic intervention is outlined below.

Measures to prevent and reduce contracture and deformity require diligence over time and are important to minimize the resistance and biomechanical disadvantage against which weak

muscles must work and to allow motor function and progression. Consideration must be given to the number of hours per day that a muscle is in a shortened position, as this will determine the risk for the development of contracture and deformity as well as determining successful prevention.^{36–38}

Adaptive equipment and orthotic intervention

Adaptive equipment and orthotic intervention can be used to support function, provide positioning to control contracture and deformity, and allow changes in position and pressure relief for maintenance of skin integrity.

Orthotic intervention (Fig. 3) may include ankle foot orthoses (AFO's) for prevention of plantarflexion contractures,⁵⁶ thigh binders for prevention of IT band contractures, and wrist/hand/finger splints to prevent shortening of long wrist/finger flexors over multiple joints and flexion contracture at the wrist or in individual finger joints. Knee extension splints may be used to prevent knee flexion contractures and maintain hamstring extensibility.

Seating systems in adapted strollers or wheelchairs are used to assist in preventing or minimizing contracture and deformity, especially spinal deformity, and should include solid seat, solid back, hip guides, lateral trunk supports, knee adductors, and head support as needed. Head support should be in place if the seating system is used during transport in a motor vehicle. Adapted car seats and specialized seat belts, harnesses, and vests can be used for safe support in vehicles, and those designed for infants with poor head control should be used for safe transport of fragile infants.

Supported standing may be beneficial in neuromuscular disease for prevention or minimization of osteoporosis⁵⁸ as well as for contracture control. Recommendations regarding the use of standers are detailed in the electronic version of this article.

The use of positioning, splinting, and standing devices should be coordinated with medical specialists in pediatrics, pulmonary medicine, cardiology, and orthopedics in consideration of potential contraindications in terms of cardiac or pulmonary status, osteoporosis, the risk of fracture, hip subluxation or dislocation, and prohibitive hip and knee flexion contractures.

Function

At every age, and every stage, appropriate function and maximal levels of independence should be supported as allowed by levels of medical stability, including participation in all aspects of life in which the individual is interested. Functional developmental activities and participation as well as maximal independence in activities of daily living should be supported. Practice, adaptation for function, and family education should be included. Appropriate adaptive equipment and assistive technology should be used to assist in activities of daily living, to maximize function and functional independence, to provide safety in transfers and transport for access. Technology may be the key to function and freedom in many situations, including motorized mobility (with power positioning controls such as tilt, recline, elevating leg rests, seat elevation, seat to floor mobility, and standing) with ventilator trays if needed; power lifts (including portable patient lifts, ceiling lifts, stand-pivot lifts, stair climbers, van lifts); computers (including

Fig. 3. Prevention of secondary musculoskeletal impairments: A) Assessing/stretching iliotibial bands; B) thigh binder for preventing/minimizing iliotibial band contractures; C) AFOs (ankle foot orthoses) to prevent/minimize plantarflexor hypoe extensibility and provide improved distal support and alignment for standing/supported standing; and D) AFOs and thigh binder used simultaneously to optimize overall lower extremity alignment.

voice activated systems, adapted keyboards, microswitches, hand-held computer devices); internet access; environmental control units; ramps and portable ramps; bathing and bathroom equipment that fosters ease and independence such as specialized bath and shower chairs, hand-held showers, roll-in showers; power-operated adjustable beds with hand-held remote and alternating pressure pad with pump for pressure relief and maintenance of skin integrity; and all aspects of emerging technology. Motorized mobility should be considered early enough to allow functionally independent mobility at developmentally appropriate ages, reported as early as 20 months of age in SMA.⁶⁰ Recommendation and training in the use of assistive technology at home, school, and work are important. Driving may be appropriate.

CONCLUSION

The clinical manifestations of Pompe disease are beginning to change with the advent of ERT with greater opportunity for potential improvement in motor status, function, and survival than ever before.^{5–10} With the potential of ERT as a treatment for Pompe disease, provision of comprehensive clinical management is important in maximizing clinical and functional benefits of ERT. The purpose of this article is to increase the understanding of the pathology and pathokinesiology of motor function in Pompe disease, and to provide an overview of physical therapy management. Physical therapy is an important component of management and should be included in the multidisciplinary team for care for individuals with Pompe disease.

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