

# Women and Myopathies

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## INTRODUCTION

Neuromuscular disorders (NMD) range from mild peripheral neuropathies to rapidly progressive autoimmune or degenerative diseases. More than 40 specific genetic and sporadic diseases are considered to have their anatomic localization in the neuromuscular system. Incidence and prevalence data for each of these individual diseases are difficult to estimate. In the United States, 75,000 patients are seen at Muscular Dystrophy Association clinics annually suggesting a prevalence of approximately 3 per 10,000. This estimate is likely low as it doesn't include many patients who are followed exclusively by primary care physicians. While none of these diseases is unique to women, there are specific consequences for women associated with many of them. Here, we discuss the diagnosis, and management of these diseases and specific implications for women with these diseases.

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## DIAGNOSIS OF NEUROMUSCULAR DISORDERS

### *History*

The symptoms of weakness and or fatigue are most common in the history of women with neuromuscular disorders. It is important to determine the pattern of weakness and the duration of the fatigue. For example, a patient with a peripheral neuropathy may complain of tripping over her feet, suggesting distal ankle weakness. In contrast, a patient with a myopathy will report difficulty lifting objects or difficulty walking up steps, suggesting proximal weakness. Likewise, the complaint of difficulty with speech, swallowing, or diplopia should lead one to consider myasthenia.

Fatigue is a symptom difficult to pinpoint but is often clarified by looking at the time course of the fatigue and which muscle groups are involved. Fatigue is not a minor or insignificant symptom and it is potentially very manageable if it is understood by the physician and patient. A woman with myasthenia gravis will complain of fatigue toward the end of the day. In contrast, a patient with a mitochondrial myopathy may have fatigue which was present all day. Women need to understand fatigue and be educated about how this will impact their overall quality of life. Energy conservation and exercise parameters need to be discussed in order to help each patient manage this symptom.

### *Physical Examination*

**Mental status** – Depression may be a common comorbid problem with women with any chronic disease and it is important to ask both general and specific questions regarding depression. In older women, memory should also be tested directly. While older individuals with muscle disease are not any more prone to degenerative brain disorders than healthy women, dementia or pseudodementia should be considered at each visit [2, 3].

**Cranial nerve examination** – Particular attention should be given to extraocular muscles, facial strength, and bulbar function. Patients with myasthenia often have limitation of extraocular muscles. Bulbar weakness is manifest by weak voice or difficulty eating or swallowing and is common in myotonic dystrophy and myasthenia.

**Motor tone** – Muscle tone is generally reduced in neuromuscular disorders. An exception is ALS where tone is often increased. This is important, as tone will affect function. Increases and decreases in tone can also be helped to a significant degree. For example, foot deformities may develop which may develop as part of the neuromuscular disorder, or as a consequence of pregnancy, can be dramatically improved with foot orthotics. Medical treatment with muscle relaxants may relieve some spasticity associated with ALS.

**Muscle strength** – Strength can be tested using the modified MRC scale [4]. The Medical Research Council scale is as follows: 0 (no visible movement); 1 (just detectable movement); 2 (movement with gravity eliminated); 3 (movement against gravity); 4 (movement against some resistance); and 5 (movement against full resistance). A somewhat ambiguous part of this scale is the difference between 4 and 5. We use quantitative strength testing using a hand held manometer, as this method is superior for judging improvement in weakness. Fatigue requires additional specific tests including a) having the women hold her arms abducted for two minutes, and b) standing from a low lying step stool 5 times.

**Muscle stretch reflexes** – In general, peripheral causes of weakness lead to reduced or absent reflexes. However, if a distal neuropathy occurs, distal reflexes alone may be lost.

**Gait analysis** – This involves not only assessing the safety of the gait but also careful analysis for joint position. For example, valgus or various deformities of ankles may be corrected with orthotics. This may prevent joint deterioration years later.

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## MEDICAL MANAGEMENT OF NEUROMUSCULAR DISORDERS

### *Management Considerations of Specific Diseases*

**Myasthenia Gravis** – This disease tends to wax and wane but good medical management should allow most women to have full, active lives. Some, however, will have very specific, often focal weakness, which may be permanent. For some this may involve bulbar or eye muscles. The symptom of fatigue rather than fixed weakness must be considered. Acetylcholine esterase antagonists must be timed carefully to give maximal benefit. Pyridostigmine, the most commonly used acetylcholine esterase inhibitor, is usually given 3-4 times a day. If spaced too closely or given to too high doses, side effects including diarrhea, nausea, and increased saliva are common. If spaced too far apart there will be recurrence of myasthenic symptoms.

Immunosuppressive medication and therapies such as intravenous immunoglobulin and plasma exchange are commonly needed when the diagnosis is first established, particularly if generalized weakness is present [5]. While the role of thymectomy has never been resolved with a blinded study, most experts agree that early thymectomy leads to marked improvement or even remission in many patients with generalized myasthenia gravis [6].

**Myopathies and Dystrophies** – For most patients with myopathies or dystrophies the weakness is proximal more than distal. This means, for example, that lifting and walking may be affected earlier and more severely than hand use. While many myopathies are not progressive, most dystrophies are. Major changes in body weight will affect both groups. Thus weight management is very important. Development of contractures can also have a major impact on function in women with myopathies and dystrophies. Both weight and contractures must be monitored closely at each visit. Weakness may not change. However, contractures or weight gain may put the joints at a mechanical disadvantage leading to loss of function.

**Neuropathies** – Cranial nerves are usually spared in patients with peripheral neuropathies. Electrophysiology should distinguish the two most common types of neuropathy - - axonal or demyelinating. The most important reason to distinguish these is that some demyelinating neuropathies are acquired and therefore potentially treatable with immunosuppressive therapy. Therefore, if the onset of weakness is subacute, electrophysiological examination is needed. Treatable causes for relatively distal weakness include chronic inflammatory demyelinating polyneuropathy, (CIDP), neuropathies associated with myelin associated glycoprotein autoantibodies (MAG neuropathy), and lower motor neuron syndromes associated with ganglioside (e.g. GM1) autoantibodies.

**Carriers of Duchenne muscular dystrophy, Emery Dreifuss Muscular Dystrophy, and myotubular myopathy** – These three muscle disorders are x-linked and therefore predominately affect males. However, manifesting female carriers do exist and they may have a course that is more slowly progressive or may have specific features. For example, recently it has been recognized that a cardiomyopathy may develop in mothers of boys with Duchenne MD [7-9]. This cardiomyopathy may or may not be asymptomatic. As these women often act as the primary caretaker for the boys with Duchenne MD, they should be evaluated carefully for possible cardiomyopathy. This may involve both an echocardiogram and EKG. Mothers of boys with Emery Dreifuss MD should be also be evaluated carefully for cardiac arrhythmias [10-14]. Recently a carrier of myotubular myopathy was found to have significant weakness with respiratory involvement and dysphagia[15]

### *Health Care Team*

As illustrated above, there are relatively few medical treatments for many neuromuscular disorders. Therefore, the “management” of these diseases often involves trying to treat symptoms or compensate for loss of function that is not expected to return. Treatment may include medications, physical therapy, occupational therapy, speech therapy, exercise, diet, flu and pneumonia vaccines, and psychological support (both formal and with support groups). Sensitive issues such as incontinence, mechanical ventilation, death and dying issues need to be specifically addressed by physicians, as many patients may not bring them up during the visit.

The most important prerequisite for delivering good health care to women with neuromuscular disabilities is a well-informed health care team. Because issues at each visit may vary from difficulty swallowing to difficulty walking, many individual specialists are required. The first component of this team is the primary care physician. Most women are also followed by a neurologist, who works directly or indirectly with physical, occupational, and speech therapists, orthotists and equipment specialists. Access to each of these is critical. The Muscular Dystrophy Association (MDA) affiliated clinics often have many of these health professionals available on site. In addition, representatives from the MDA are a valuable resource for advice about other services and support groups[1].

### *Exercise*

The use of exercise among patients with neuromuscular disorders is not well understood and somewhat controversial [16-19]. A moderate plan of exercise is reasonable for avoiding the negative effects of disuse or inactivity. The overall activity level of the patient should be assessed at each visit. If she is an active individual (e.g. a mother caring for small children or a woman employed outside the home), an exercise program may become detrimental in that it will cause additional fatigue, rather than improve strength and energy. One rule of thumb is to instruct the patient to evaluate her overall strength and fatigue after she has exercised. If exercise appears to prevent her from performing normal activities of daily living, or if fatigue occurs a couple of hours after exercise, she is probably doing too much. Exercise programs will have to be adjusted to account for fluctuations in the patient's schedule. For example, on a busy day no additional exercise would be recommended.

Stretching and flexibility programs are very beneficial across all diagnostic types. As strength is lost, joint mobility is adversely affected which can greatly impact overall function. Joint contractures are a common occurrence in patients with neuromuscular disorders. They may be due to inactivity and weakness, or may be part of the disease process itself as in muscular dystrophies. An independent or assisted range of motion (ROM) program should be implemented early on and carried out throughout the patient's lifetime. This will need to be taught to the patient or caregiver because third party payers provide little or no coverage for physical therapy for chronic conditions. Physical therapy intervention can be justified with any change in the patient's condition, but will only be funded on a short-term basis.

### *Equipment*

Equipment needs vary by individual as well as stage of illness. The woman may need something as simple as an assistive device for ambulation such as a cane or walker. With more severe weakness, mobility devices such as scooters and manual or motorized wheelchairs will be required. Equipment to assist with activities of daily living might include dressing aides, feeding aides, grooming aides, and toileting aides. Advice about these and how to get them should be given at the visit to the neuromuscular specialist. More complicated issues involving home accessibility and home safety may require a home visit. This home visit allows the occupational therapist to determine needs as simple as grab bars to hold on to or as complex as patient lifts, stair glides, or elevators. Other advice given during the clinic visit may include advice about orthotics (hand splints, leg braces, trunk braces) or assisted ventilation (invasive vs. non-invasive).

Someone on the treatment team should be familiar with resources to not for acquiring these items but also to help the family identify sources of funds to pay for them.

Well-chosen equipment can be extremely beneficial. Various therapists can be of great help. Difficulties with ambulation may require the use of a cane or walker for stability or balance disorders. They do not prevent falls from lower extremity weakness, however, and a discussion about the risks of falls needs to occur. Prolonged recovery following an orthopedic injury can lead to irreversible weakness and increased disability. Orthotics (short and/or long leg braces) can be introduced when falls are occurring with daily frequency; getting up from the floor independently is impossible; climbing stairs is impossible. Lightweight plastic materials are ideal in this patient population. An orthotist familiar with neuromuscular disorders is important in order to address the unique issues that will arise. These will include changes in limb morphology with muscular atrophy, joint contractures and abnormal gait patterns that are “normal” in this population. The progression of each disease must also be understood.

Assisted mobility via a scooter, manual or motorized wheelchair can be introduced as an energy conservation measure or when long distance ambulation is difficult. It is important to work with an experienced therapist or rehabilitation specialist familiar with neuromuscular disorders, when discussing or prescribing these types of equipment. Special consideration for each diagnosis must be given in order to recommend the appropriate equipment. This can involve such considerations as:

- Is the disease likely to progress slowly or quickly? If rapidly progressive, a device that can be readily adapted may be necessary.
- Is there trunk weakness as well as limb weakness? A customized seating device may be required.
- How many hours a day will she be using her scooter or wheelchair? If individuals will sit for long periods, they will need pressure relief systems such as recline or tilt-in-space.
- How will she be controlling (driving) her scooter or wheelchair? The amount of strength will determine if she will need a joystick, head control, or special electronics.
- Will he need to transport other equipment such as a ventilator? Do she have the means to transport their scooter/wheelchair within the community?
- Is the home environment accessible to such a device? If not, what kinds of modifications would be needed and what resources are available to pay for these modifications?
- How will repairs be handled? Will a loaner scooter/wheelchair provided?

Equipment to assist with activities of daily living can be introduced as necessary in order to keep each patient as independent as possible, or to assist their caregiver and make their task easier. Bathing, toileting [20] and grooming [21] problems are common issues with all patients with NMD. An experienced occupational therapist can help determine what equipment and aides may be needed for each patient. Many patients are reluctant to bring these sensitive issues up; therefore the physician should specifically question the patient about these areas. Sometimes a home evaluation is necessary in order to solve

problems that may be unique. Long-term solutions also need to be discussed. For example, does the family plan to stay in their present home, modifying it as they need to? Do they need to consider a more accessible home which may be more cost beneficial in the long run? What is their caregiver situation? If there is a paid caregiver, what are their financial resources, now and long term?

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## CHILD BEARING AND REARING

Many neuromuscular disorders are inherited and the patterns of inheritance vary from autosomal recessive, to autosomal dominant to autosomal dominant with anticipation. This last category is important because the child's disease may be much worse than the mother's. One example is myotonic dystrophy [22-24]. Prior to considering pregnancy we recommend a meeting with a genetic counselor. For some disease the genes are well known and carrier status can be determined. For others the "counseling" becomes a statistical estimate. In addition to these genetic issues, there are many specific problems, which must be considered [25-27].

First, there is likely to be difficulty during pregnancy due to weak trunk/abdominal muscles. For some, this may advance weakness and there may be worse disability post partum. This means women must ask themselves if they are willing to sacrifice their current level of function and or independence to carry a baby. At the time of the delivery, there may be a decreased ability to "push" though this will vary with specific diseases. For example, women with neuropathies may have no difficulty. Women who already have weak abdominal muscles are likely to be most affected.

Second, the hormonal effect on joints and ligaments may lead to new onset of musculoskeletal pain. In non-progressive or very slowly progressive conditions it may be possible to treat these changes with orthotics or other assistive devices. However, for some women, these changes may not be reversible.

Third, specific diseases require specific considerations. For immune-mediated diseases such as myasthenia gravis, dermatomyositis and inflammatory myopathies, the medications needed to treat the mother may have to be changed or eliminated during pregnancy and while breast-feeding. Of these, myasthenia gravis, an antibody-mediated disease can be passively transferred to the infant. The infant is transiently weak at birth and in some cases, this weakness is severe enough that hospitalization is required. There is also an increased incidence of gestational diabetes in disorders predisposed to blood sugar problems. Freidrich's ataxia and myotonic dystrophy are two such examples. For some inherited diseases the risk to the infant is more serious than the risk to the mother. For example, mothers with myotonic dystrophy (autosomal dominantly inherited) are likely to have infants who are not only more severely weak but are likely to have significant mental retardation as well.

Parenting issues require specific planning. Specific tasks from how to diaper an infant to how to move a child to safety must be considered. In general, if the mother has severe disability, the non-disabled parent or attendant must be willing to take on disproportionate responsibility for these tasks. Through the Looking Glass is a nonprofit organization in Berkeley, CA that receives federal funding to serve as a National Resource Center for Parents with Disabilities[28]. The physician must be aware of resources to help with these issues[27]. Certainly, if these issues are understood from the outset, the rewards of parenthood are tremendous[25].

### *Other Medical Management Issues*

Perhaps the most important “treatment” issue is to remember that women with neuromuscular disorders are still at risk for other health issues that affect all women. Several health issues merit specific comments:

**Osteoporosis** may be more severe or have an earlier onset in women with NM disorders [3, 19, 29, 30]. This is in part because they do not have the benefits of weight bearing and also because some of the medications (e.g. prednisone) required to treat the condition put women at increased risk.

**Depression** must be considered. Specific questions regarding mood, appetite and sleep patterns should be part of the review of systems questions at each visit. These issues may not be brought up by the patient. In our experience depression can be treated very effectively with medication and or counseling and support. Others have also shown that specific support benefits patients with disability [2].

**Routine medical care** including screening for breast and cervical cancer must not be neglected. A recent epidemiological study suggests that lack of screening may put women with disabilities at a higher risk for these diseases[31].

**Pain** usually occurs as a secondary symptom, primarily due to musculoskeletal imbalances and joint wear-and-tear. However, it can often be managed with non-steroidal anti-inflammatory medications. Again, early attention to joints in slowly progressive diseases can prevent problems later. It is important that early education about joint care be part of the evaluation and discussion at each visit. In some cases, using assistive devices such as a wheel chair for long distances can protect joints and prevent pain.

**Bowel and bladder dysfunction** are not usually a direct result of the neuromuscular disease. However they may be a secondary problem due to decreased mobility. Bladder control is usually preserved but weak abdominal muscles may make emptying of the bladder more difficult. Decreased GI motility secondary to decreased walking may also develop. Symptomatic treatment including stool softeners and increased fiber is usually effective. In rare cases, periodic enemas are required.

**Menses** can be difficult to manage with decreased mobility. For women with severely decreased hand/arm strength and dexterity consideration for hormonal treatment to limit menses may be very helpful. However, there is no generalized consensus on the relative benefit versus risk of this hormonal treatment and therefore the decision must be individualized.

**Hormonal influences** on ligaments can have an adverse effect on joints, which are already vulnerable secondary to weakness of normally stabilizing muscles. This may be a particular problem with pregnancy.

### *Education*

Educating others about neuromuscular disorders is paramount for better understanding of patient's issues. For example, especially school (high school or college) personnel dealing with young women need to be aware that individuals with hand weakness may require additional time for tests. Employers need to know that a woman with myasthenia may require additional breaks because of fatigue. The MDA provides a wealth of educational materials, both for those afflicted as well as caregivers, educators,

health care providers, etc. It is also a great source of support for the patient via its publications, web site, chat rooms, and community support groups.

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## CONCLUSION

To provide excellent care to women with neuromuscular disorders requires a multi-disciplinary approach. The physician's role is complicated but must first focus on current symptoms and then on being aware of resources and other health care professionals who may be able to help. As with all good medical care, careful history and examination will direct therapy.

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