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Limb Girdle and Fascioscapulohumeral Dystrophies

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Objectives

1. Identify the hallmark symptoms of Limb Girdle and FSH dystrophies.

2. Recognize the current research findings about persons with Limb Girdle and FSH dystrophies and how to apply those findings to treatment.

3. Identify 3 treatments which would be appropriate for persons with Limb Girdle and FSH dystrophies.

Limb Girdle Muscular Dystrophy

Limb-girdle muscular dystrophy (LGMD) isn’t really one disease. It’s a group of disorders affecting voluntary muscles, mainly those around the hips and shoulders (limb-girdles). It affects more proximal muscles first. Caused by a mutation in any of at least 15 different genes that affect proteins necessary for muscle function.
Causes/Genetics

Insufficient function of a protein in the extracellular matrix — the substance in which each muscle fiber is embedded.

This protein, known as alpha-dystroglycan, must not only be structurally sound but must also undergo a specific type of sugar-coating, or glycosylation, to carry out its key role in connecting the muscle fiber to its surroundings.

Causes/Genetics

Type 1 LGMDs are dominantly inherited, requiring only one mutation for symptoms to result. 8 types.

Type 2 LGMDs are recessively inherited, requiring two mutations — one from each parent — for symptoms to appear. 16 types.

Some LGMD subtype names:

- Bethlem myopathy (collagen 6 mutation; dominant)
- Calpainopathy (calpain mutations; recessive, LGMD2A)
- Desminopathy (desmin mutation; recessive, LGMD1E)
- Dysferlinopathy (dysferlin mutations; recessive; LGMD2B)
- Myofibrillar myopathy (mutations in desmin, alpha-B-crystallin, myotilin, ZASP fiberin C, BAG3 or SEPN1 genes; all dominant except desmin type, which can be dominant or recessive)
- Sarcoglycanopathies (sarcoglycan mutations; recessive, LGMD2C, LGMD2D, LGMD2E, LGMD2F)
- ZASP-related myopathy (ZASP mutation; dominant, a form of myofibrillar myopathy)


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Symptoms LGMD

Symptoms may include:

- Proximal voluntary muscle weakness
- Large and muscular-looking calves, pseudohypertrophy, abnormal waddling walk
- Loss of muscle mass
- Low back pain
- Shoulder weakness
- Weakness of the muscles in the face
- Weakness in the muscles of the lower legs, feet, lower arms, and hands (eventually)
Progression

Progression in each type of LGMD can’t be predicted, although knowing the underlying genetic mutation can be helpful. i.e.: 2B slower progression
Some forms of the disorder progress to loss of walking ability within a few years and cause serious disability, while others progress very slowly over many years and cause minimal disability.
LGMD can begin in childhood, adolescence, young adulthood or even later. Both genders are affected equally.
When limb-girdle muscular dystrophy begins in childhood, the progression is usually faster and the disease more disabling.
When the disorder begins in adolescence or adulthood, it’s generally not as severe and progresses more slowly.

Exercise

If they have [types 2A, 2C, 2A, 2B, 2C, 2D, 2E, 2F, 2I, and 2Q] that’s related to muscle-fiber membrane maintenance or repair. from animal studies that you can speed the injury to muscle by doing certain kinds of exercise.
So, avoid eccentric exercise, weight training program.
Teach patients when fatigued, stop. If pain, stop.
If CK (creatine kinase) is over 5,000, no strengthening exercises

If they’re in the other categories [of LGMD] don’t discourage them from exercise. No evidence that there is harm from exercise in these other forms.

Exercise

Signs of muscle damage or impending muscle damage are:
- cramping in muscles (probably related to insufficient energy supply for muscles);
- pain in muscles;
- weakness of exercised muscles
- dark urine that looks like cola (indicating the presence of myoglobin protein), hours after exercising (seek medical care immediately if this occurs); Type 2l in particular

LGMD types 1A, 1B, 1C, 1E, 2C, 2E, 2F, 2G, 2I, and 2M are known to involve the heart.
LGMD Research

1. Gene therapy—restore the expression of proteins, has shown promise in a pilot trial in people with the alpha-sarcoglycan-deficient form of LGMD.
2. Exon skipping—Restore the expression of proteins, clinical trials are underway of compounds that coax cells to snip out these error-containing DNA regions.
3. Stop codon read through—a bridge to achieving a full length dysferlin protein, the stop-codons cause cells to stop reading genetic instructions.
4. Myostatin blocking—Myostatin puts a halt to muscle growth.
5. Stem Cells.

LGMD

http://www.youtube.com/watch?v=uc5VJMrE0mc – getting off the ground

Fascioscapulohumeral Dystrophy

Genetic muscle disorder in which the muscles of the face, shoulder blades and upper arms are among the most affected.
Later, weakness can spread to abdominal muscles and sometimes hip muscles.
Usually begins before age 20.
Some experts divide FSHD into adult-onset and infantile-onset forms. The adult-onset (which includes FSHD that begins in adolescence) is far more common.
FSHD usually progresses very slowly and rarely affects the heart or respiratory system. Most people with the disease have a normal life span.
Symptoms

The age of onset, progression and severity of FSHD vary a great deal. Usually, symptoms develop during the teen years, with most people noticing some problems by age 20, although weakness in some muscles can begin as early as infancy and as late as the 50s. FSHD doesn’t cause learning disabilities or other cognitive impairments, nor does it affect sensation, ability to control the bladder and bowels, or sexual function. In most people with FSHD, the disease progresses very slowly. It can take as long as 30 years for the disease to become seriously disabling, and that doesn’t happen to everyone. Estimates are that about 20 percent of people with FSHD eventually use a wheelchair at least some of the time.

FSH Causes

FSHD may be inherited through either the father or the mother, or it may occur without a family history. It is almost always associated with a genetic mutation that leads to a shorter than usual segment of DNA on chromosome 4. No genes were found in the region of chromosome 4 that’s shortened in people with FSHD. Instead, the shortened strip of DNA is found in a part of the chromosome where there are no genes. The segment isn’t part of any particular gene, but it nevertheless seems to interfere with the correct processing of genetic material.

Genetic testing is very accurate.

Surgery

In this procedure, the scapulae are fixed to the ribs so that they don’t move. The patient gains some leverage with the arm on the side that’s had the operation, since the scapulae no longer slide around. Although this type of surgery may actually decrease the arm’s range of motion (since the shoulder blade can no longer rotate normally), the ability of the arm to function may be better, since the arm’s leverage point is now stable.
FSH Exercise

Since the precise underlying defect that causes muscle loss in FSHD isn’t yet understood, it’s hard to make precise recommendations about exercise.

However, physical therapists who have observed people with FSHD for many years say that moderate exercise appears to do no harm and may even be helpful, at least for muscles that haven’t severely weakened.

The program should emphasize exercising muscles that are still relatively strong and resting those that have weakened.

FSH Research

In 2009, MDA-supported researchers found that pieces of a gene called DUX4 are abnormally activated in FSHD-affected cells, leading to production of potentially toxic proteins.

Blocking the erroneously activated genes or the proteins made from them seems a likely pathway for the eventual treatment of FSHD.

Treatment for both

- Corsets, braces for lordosis, AFOs
- Wheelchairs, walkers, scooters
- Home safety, home set up
- Safe ROM
- Adaptive equipment: reacher, long handled sponge/brush/comb
- Shower/bathing equipment, toileting equipment
- IADL tasks
- Leisure
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