Incidence

- Estimated prevalence ranging from 2.4-7.3 per 100,000 (Becker) to 0.07 per 100,000 (LGMD2D, E) to 0.43 per 100,000 (LGMD2I)²
- Pompe disease has an estimated incidence of 1 in 40,000⁵

Inheritance

- Most subtypes of LGMW are autosomal recessive (LGMD2A-Q, Pompe)⁴
- Several rare subtypes are autosomal dominant (LGMD1A-E)⁴
- A few myopathies are X-linked (Becker, EDMD-X1, -X2)⁴

Overview

Limb-girdle muscle weakness (LGMD) is a term describing the weakness pattern encompassing a group of diseases associated with weakness and wasting of predominantly proximal muscles of the pelvic and shoulder girdles. Diagnosis is challenging as many symptoms, like progressive muscle weakness in the shoulders, pelvis, and lower limbs, as well as elevations in creatine kinase, can overlap.¹ LGMW encompasses a heterogeneous group of disorders (limb-girdle muscular dystrophies (LGMDs), and other myopathies) that vary in severity and age of onset and can be classified into 2 main groups, depending on the inheritance pattern: LGMD1 is autosomal dominant, and LGMD2 is inherited in an autosomal recessive pattern.² There are very few pathognomonic features of LGMDs that clearly identify one from the other, or even from other diseases characterized by muscle weakness.

Late Onset Pompe Disease (LOPD) shares considerable phenotypic overlap with the LGMDs, presenting with progressive proximal weakness (particularly pelvic girdle), scapular winging, feeding/swallowing difficulties and respiratory insufficiency. Pompe is an autosomal recessive disorder, caused by mutations in the GAA gene and should be considered in the differential diagnosis of LGMDs.³,⁴

Diagnosis

When a diagnosis of LGMD is suspected, ruling out other diseases, such as Pompe disease, can shorten the diagnostic delay.²,⁴

The following evaluations may support a diagnosis of limb-girdle muscle weakness:

Clinical Findings

- A medical history to determine age of onset and a family history, along with a physical examination can distinguish patterns of weakness specific to certain LGMD subtypes⁶

Laboratory Testing

- Serum creatine kinase levels are typically elevated secondary to muscle degeneration/regeneration⁶,⁷
- Next-generation sequencing (NGS) allows for the rapid sequencing of multiple genes in parallel and can more easily determine LGMD subtypes⁶
- Muscle biopsy: Morphology, immunostaining/immunoblotting and biochemical testing may be helpful or diagnostic, though many providers are electing to use NGS testing panels before more invasive testing

Other

- Electrophysiology and MRIs may be useful in the differential diagnosis and to rule out other neuromuscular diseases⁴
- Electromyography (EMG) findings suggestive of LGMD include myotonic or pseudomyotonic discharges. EMG in LGMD may show short-duration, small-amplitude motor units with early recruitment in weak muscles; findings may be subtle in mild cases²
- Pulmonary function testing including spirometry and maximal inspiratory/expiratory force in the upright and supine positions may help narrow the differential diagnosis²
Some of the laboratories offering gene panels for limb-girdle muscle weakness are listed below. There may be other gene panels appropriate for your patient and this is not an endorsement of any one lab. Other testing options can be found at [www.concertgenetics.com](http://www.concertgenetics.com) or [www.ncbi.nlm.nih.gov/gtr](http://www.ncbi.nlm.nih.gov/gtr). Consult each laboratory for a full range of options. Content is current at time of printing and tests may not be available in all states; please call laboratory to confirm test availability, sample shipping information, and all other logistics. Sanofi Genzyme does not review or control the content of non-Sanofi Genzyme websites. These listings do not constitute an endorsement by Sanofi Genzyme of information provided by any other organizations.

<table>
<thead>
<tr>
<th>Lab</th>
<th>Test name (Test Code)</th>
<th>Sample Requirements</th>
<th>Avg TAT</th>
<th>Test Details</th>
<th>Kits</th>
<th>Billing</th>
<th>Mobile Blood Draw</th>
<th>Contact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Centogene</td>
<td><strong>Muscular Dystrophy Panel</strong></td>
<td>WB: 1ml EDTA (lavender) tube; extracted DNA: 2 μg; DBS: 10 spots; saliva: Oragene; buccal swab</td>
<td>&lt; 25 days</td>
<td>74 genes. Includes Pompe, LGMDs, hereditary neuropathies, myasthenic syndromes and muscular dystrophies</td>
<td>Buccal, DBS</td>
<td>Inst, Ins (prior auth required), Self-Pay</td>
<td>Yes</td>
<td>P: 617-580-2102 E: <a href="mailto:customer.support-US@centogene.com">customer.support-US@centogene.com</a> W: <a href="http://www.centogene.com">www.centogene.com</a></td>
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<tr>
<td>EGL Genetics</td>
<td><strong>LGMD Sequencing Panel (MM212)</strong></td>
<td>WB: 2-10 ml EDTA (lavender) tube (volume varies with age)</td>
<td>6 wks</td>
<td>34 genes for LGMDs and Pompe</td>
<td>Blood, DBS, Saliva</td>
<td>Inst, Ins, Self-Pay</td>
<td>No</td>
<td>P: 855-831-7447 E: <a href="mailto:eqlcs@egl-eurofins.com">eqlcs@egl-eurofins.com</a> W: <a href="http://www.eqlcgs.com">www.eqlcgs.com</a></td>
</tr>
<tr>
<td>GeneDx</td>
<td><strong>LGMD Panel (890)</strong></td>
<td>WB: 2-5 ml EDTA (lavender) tube; buccal swabs</td>
<td>4 wks</td>
<td>30 genes for LGMDs and Pompe</td>
<td>Blood, Buccal, Oral rinse</td>
<td>Inst, Ins, Self-Pay</td>
<td>Yes</td>
<td>P: 301-519-2100 E: <a href="mailto:genedx@genedx.com">genedx@genedx.com</a> W: <a href="http://www.genedx.com">www.genedx.com</a></td>
</tr>
<tr>
<td>Greenwood Genetics Center</td>
<td><strong>Neuromuscular Disorders Sequencing Panel</strong></td>
<td>WB: 5-7 ml EDTA (lavender); extracted DNA also accepted</td>
<td>8-10 wks</td>
<td>144 genes. Includes Pompe, LGMDs, nuclear-encoded mitochondrial genes, select storage disorders, hereditary neuropathies, myasthenic syndromes and muscular dystrophies</td>
<td>Blood</td>
<td>Inst, Ins, Self-Pay</td>
<td>No</td>
<td>P: 800-473-9411 E: <a href="mailto:labgc@ggc.org">labgc@ggc.org</a> W: <a href="http://www.ggc.org">www.ggc.org</a></td>
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<tr>
<td>Invitae</td>
<td><strong>LGMD Panel (03304)</strong></td>
<td>WB: 3 ml EDTA (lavender) tube; Saliva/assisted saliva (per Oragene kit)</td>
<td>10-21 d</td>
<td>31-34 genes for LGMDs and Pompe</td>
<td>Blood</td>
<td>Inst, Ins, Self-Pay</td>
<td>No</td>
<td>P: 800-436-3037 E: <a href="mailto:clinconsult@invitae.com">clinconsult@invitae.com</a> W: <a href="http://www.invitae.com">www.invitae.com</a></td>
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<tr>
<td>The Lantern Project (performed at PerkinElmer Genomics)</td>
<td><strong>Focused Neuromuscular Diseases Panel (SAN002)</strong></td>
<td>WB: 3-5 ml EDTA (lavender) tube, DBS card: 5 circles, saliva: Oragene</td>
<td>3 wks</td>
<td>66 genes including LGMDs, Pompe and other inherited myopathies, dystrophies and myasthenic syndromes</td>
<td>Blood, DBS, Saliva</td>
<td>No charge*</td>
<td>Yes</td>
<td>P: 866-354-2910 E: <a href="mailto:genomics@perkinelmer.com">genomics@perkinelmer.com</a> W: <a href="http://www.lanternprojectdx.com">www.lanternprojectdx.com</a></td>
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<tr>
<td>Prevention Genetics</td>
<td><strong>LGMD Sequencing Panel (10401)</strong></td>
<td>WB: 3-5 ml EDTA (lavender) or ACD (yellow) tube; DNA also accepted; saliva: Oragene/GenefIX</td>
<td>18 d</td>
<td>34 genes for LGMDs and Pompe</td>
<td>Blood</td>
<td>Inst, Ins, Self-Pay</td>
<td>No</td>
<td>P: 715-387-0484 E: <a href="mailto:clinicaldnatesting@preventiongenetics.com">clinicaldnatesting@preventiongenetics.com</a> W: <a href="http://www.preventiongenetics.com">www.preventiongenetics.com</a></td>
</tr>
<tr>
<td>University of Chicago, Genetic Services Laboratory</td>
<td><strong>LGMD Sequencing Panel (3106)</strong></td>
<td>WB: 3-10 ml EDTA (lavender) tube; saliva (Oragene)</td>
<td>8 wks</td>
<td>31 genes for LGMDs and Pompe</td>
<td>No</td>
<td>Inst, Self-Pay</td>
<td>No</td>
<td>P: 888-UC-GENES (824-3637) E: <a href="mailto:ucgslabs@genetics.uchicago.edu">ucgslabs@genetics.uchicago.edu</a> W: <a href="https://dnatesting.uchicago.edu">https://dnatesting.uchicago.edu</a></td>
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*Testing is performed at no charge; local charges may apply for sample collection, processing, or shipping.

avg TAT = average turnaround time; d = days; DBS = dried blood spot; DMD = Duchenne muscular dystrophy; Ins = insurance; Inst = institution; WB = whole blood; wks = weeks.

References: