Overview of Myotonic Dystrophy Symptoms and Pathology

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Myotonic Dystrophy Type-1 Pathogenesis

- Autosomal dominant disorder
- CTG repeat expansion in DMPK on chromosome 19q13.3 leads to MBNL sequestration

![Diagram showing the pathogenesis of Myotonic Dystrophy Type-1.]
Core Symptoms

• Distal muscle weakness and wasting
  – Progressive hand and foot weakness
• Myotonia (delayed muscle relaxation)
• Early onset cataracts
A Multisystemic Disorder

- **Cardiac arrhythmias**
  - Increase with age and weakness
  - Progressive heart block, prolonged QRS and PR interval
  - Often require a pacemaker

- **Gastrointestinal symptoms**
  - Abdominal pain, constipation, diarrhea, fecal incontinence
  - Dysphagia

- **Endocrine abnormalities**
  - Glucose intolerance, thyroid dysfunction, testosterone deficiency
A Multisystemic Disorder

- Cognition impaired
  - Executive function and visual spatial processing deficits
  - Global cognitive dysfunction
  - Avoidant personality disorder
- Prominent daytime sleepiness and fatigue
  - Number one symptomatic issue
  - Combination of OSA and central hypoventilation
- Respiratory
  - Respiratory failure
  - Anesthesia risks
- Increased risk of neoplasms
  - Increased risk of endometrial, brain, ovarian, and colon
Epidemiology of Myotonic Dystrophy

• Prevalence 1:8000 (most common adult muscular dystrophy)
• Average age of death 53
• Cause of Death (n=20)
  – Cardiac arrhythmias or heart failure (6)
  – Infection (4)
  – Neoplasm (2)
  – Stroke (2)
  – Unspecified (6)
## Relative Risk of Comorbidities

<table>
<thead>
<tr>
<th>Co-morbidity</th>
<th>Relative Risk</th>
<th>P-value</th>
<th>Mean Age at Diagnosis of Comorbidity (years) (SD; range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac Conduction Disorder</td>
<td>60.2 (29.9, 108.6)</td>
<td>&lt;0.0001</td>
<td>39.6 (11.3; 18-48)</td>
</tr>
<tr>
<td>Obstructive Sleep Apnea</td>
<td>9.8 (5.6, 15.8)</td>
<td>&lt;0.0001</td>
<td>45.4 (13.4; 22-74)</td>
</tr>
<tr>
<td>Central Sleep Apnea</td>
<td>66.1 (11.7, 208.1)</td>
<td>&lt;0.0001</td>
<td>*</td>
</tr>
<tr>
<td>Intellectual Disabilities</td>
<td>9.0 (1.6, 28.4)</td>
<td>0.02</td>
<td>*</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>2.6 (1.1, 5.1)</td>
<td>0.03</td>
<td>51.5 (21.8; 27-79)</td>
</tr>
<tr>
<td>Any Cataract</td>
<td>6.23 (4.08, 9.15)</td>
<td>&lt;0.0001</td>
<td>41.3 (12.4; 20-59)</td>
</tr>
</tbody>
</table>

* -- indicates that the exact number is below 5 and cannot be reported due to data confidentiality
# Routine Care in DM

<table>
<thead>
<tr>
<th>Organ system</th>
<th>Screening test</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart</td>
<td>Routine ECG</td>
<td>Once yearly or symptomatic</td>
</tr>
<tr>
<td>Respiratory</td>
<td>Supine FVC</td>
<td>At diagnosis and symptomatic</td>
</tr>
<tr>
<td>Sleep (CNS)</td>
<td>Polysomnogram</td>
<td>Symptomatic</td>
</tr>
<tr>
<td>Eye</td>
<td>Slit lamp exam</td>
<td>Once yearly or symptomatic</td>
</tr>
<tr>
<td>Ear</td>
<td>Audiometry</td>
<td>Symptomatic</td>
</tr>
<tr>
<td>Endocrine</td>
<td>HbA1c, TSH, lipid panel</td>
<td>At diagnosis and once yearly</td>
</tr>
<tr>
<td>Malignancy</td>
<td>Routine surveillance for age + consider CNS tumors, endometrial tumors</td>
<td>Symptomatic</td>
</tr>
</tbody>
</table>