Comprehensive Duchenne Care
Duchenne is not just a disease of the muscles. It affects every system in the human body.
• Duchenne Family Guide
  – Partnered with MDA, Treat-NMD, and WDO
  – Includes the Duchenne Care Considerations in an “easier to digest” format

• New Diagnosis and Early Care Guide
  – Introduction to Duchenne/Becker and genetic testing, adjusting to the diagnosis and support, early care, and introduction to clinical trials

• Imperatives for Healthcare Providers
  – One-page fact sheets for healthcare providers unfamiliar with Duchenne
  – Versions for pediatric and adult patients
  – Also available in Spanish

• Education Matters
  – Comprehensive guides for parents and teachers
Emergency Care Information

- PPMD App
  - Includes Duchenne emergency information
- PPMD emergency information cards
  - Also available in Spanish
- PPMD large weatherproof emergency information cards for wheelchairs, scooters, and backpacks
- PJ Nicholoff Steroid Protocol
  - Guide for families and healthcare providers to navigate steroid stress dosing, tapering, and what to do in the case of a missed dose
- Online Resources
  - Emergency care and hospital checklists
  - Caring for the Flu
  - Fracture management

#EndDuchenne
<table>
<thead>
<tr>
<th>Specialty</th>
<th>Name</th>
<th>Affiliation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuromuscular Care</td>
<td>Erika Finanger, MD</td>
<td>Oregon Health &amp; Science University</td>
</tr>
<tr>
<td></td>
<td>Meganne Leach, MSN, PPCNP-BC</td>
<td>Oregon Health &amp; Science University</td>
</tr>
<tr>
<td>Pulmonary Care</td>
<td>Courtney Goshue, DO</td>
<td>Oregon Health &amp; Science University</td>
</tr>
<tr>
<td>Endocrine Care</td>
<td>Lindsey Nicol, MD</td>
<td>Oregon Health &amp; Science University</td>
</tr>
<tr>
<td>Physical Therapy</td>
<td>Kirsten Zilke, PT</td>
<td>Shriners Hospital for Children</td>
</tr>
<tr>
<td>Cardiac Care</td>
<td>Aaron Olson, MD</td>
<td>Seattle Children’s Hospital</td>
</tr>
<tr>
<td>Genetics</td>
<td>Ann Martin, MS, CGC</td>
<td>Parent Project Muscular Dystrophy</td>
</tr>
</tbody>
</table>
Duchenne Muscular Dystrophy
Pediatric Neuromuscular Research Program

Meganne Leach, MSN, PPCNP-BC
Instructor, Oregon Health & Science University
Consultant, Shriners Hospitals for Children Portland

September 12, 2020
PPMD End Duchenne Tour – Portland, OR
Neuromuscular Clinic Team at Shriners

- Care Coordinator/Nursing
- Neurology
- Orthopedic Surgery
- Genetics/Genetic Counseling
- Pulmonary
- Physical Therapy
- Occupational Therapy
- Speech Language Pathology
- Social Work
- Orthotics
- Nutrition
- Research Coordinators
- Psychology
  - Cardiology
  - Endocrinology
  - Palliative Care
Role of Neurology

1) Diagnose and treat DMD
2) Coordinate with other health care providers (not just doctors-physical therapists, occupational therapists, respiratory therapists, school nurses, etc)
3) Evaluate and discuss clinical trials/research in DMD
4) Serve as a guide for the management of DMD
5) Be a good listener...
6) Be an advocate for patient and family...
7) Be a resource for patients and their families!
Standards of Care in DMD

- Guidelines updated in 2018
- Care considerations based on stage of disease as well as body system/subspecialty
- www.parentprojectmd.org
Duchenne Muscular Dystrophy
Pediatric Neuromuscular Research Program

Erika Finanger, MD
Associate Professor, Oregon Health & Science University
Consultant, Shriners Hospitals for Children Portland
Director, Neuromuscular Clinic

September 12, 2020
PPMD End Duchenne Tour – Portland, OR
Importance of Clinical Research

• **Clinical research** is what allows doctors to decide how to best treat patients. It is what makes the development of new medicines, new procedures and new tools possible. Without **clinical research**, we would not be able to decide if new treatments are better than our current treatments. (from NIH website)

• Outcomes in DMD have improved with aggressive supportive care, but there is much more progress to be made...
Types of Clinical Research

• Natural history/Registry studies

• Interventional studies:
  – Phase 1: safety
  – Phase 2: safety, dosing
  – Phase 3: efficacy
HDAC inhibitors
Clinical Trials—Active, enrolling

**NS Pharma (Racer 53):**
- A Phase 3 Randomized, Double-blind, Placebo-controlled, Multi-center Study
- DMD with dystrophin deletion amenable to exon 53 skipping
- Ambulant boys; 4 to <8 years with DMD

**FGCL-3019-079 (Fibrogen):**
- Phase 3, Randomized, Double-Blind, Trial of Pamrevlumab (FG-3019) or Placebo in Combination with Systemic Corticosteroids in Subjects with Non-ambulatory Duchenne Muscular Dystrophy (DMD)
- > 12 years old, non-ambulatory, FVC 45-85% predicted, LVEF >50%

Clinical Research Contact:
- Shriners: 971-544-3377
- OHSU: 503-418-8297
Clinical Trials—Active, not enrolling

PTC124-GD-016 (Ataluren):
• Phase 3 – Open Label, DMD Male, DMD dx, received ataluren in previous PTC trial, on stable dose of steroids

PTC124-GD-041 (Ataluren):
• Phase 3, DMD Nonsense point mutation, > 5 years old, on stable dose steroids, DMD dx

CAT-1004-302 (GalaxyDMD)
• Phase 3, DMD Steroid naïve, completed MoveDMD, age 4-8 years old, DMD dx

CAT-1004-301 (PolarisDMD)
• Phase 3, DMD No steroids w/in 24 weeks of screening, age 4-7 years old, ambulatory, sit to stand in < 10 sec, able to swallow pills, DMD dx

FGCL-3019-079 (Fibrogen)
• Phase 2, DMD Non-ambulatory, > 12 years old, wheelchair dependent < 5 years, stable dose of steroids, DMD dx

Sarepta 4045-301
• Phase 3, DMD Exon deletion amenable to exon 45 or 53 skipping, ambulatory, 7-13 years old, stable dose of steroids, DMD dx

Sarepta 4045-302, DMD
• Completed Sarepta 4045-301 trial, deletion amenable to exon 45 or 53 skipping, stable dose of steroids, DMD dx

DSC/14/2357/48 (Italfarmaco)
• Givinostat, DMD Ambulatory, > 6 years old, stable dose of steroids for > 6 months, Platelet count above the Lower Limit of Normal, DMD dx
Respiratory health in DMD
Role of the Pulmonologist

- Ask questions / uncover subtle symptoms
- Prevent / treat problems related to breathing
- Address questions and concerns
What to expect during the visit

- Breathing test
- Questions!
- Examination
- Discuss studies
- Agree on plan together

Forced vital capacity
- Cough flow
- Carbon dioxide (CO2)
- Mean inspiratory/expiratory pressures (MIP/MEP)
Thank You
Lindsey Nicol, MD

Associate Professor
Director of Pediatric Bone Health
Pediatric Endocrinology
Oregon Health & Science
What can a pediatric endocrinologist do for you?

- Delayed puberty assessments and treatment
- Bone health/Osteoporosis monitoring and treatment
- Adrenal insufficiency management and recovery
- Insulin resistance assessment and treatments
How to get our help...

- We can work directly with your PCP through consultation
- Referral to OHSU pediatric endocrinology
- Through the Portland Shriners Neuromuscular Clinic
Duchenne Muscular Dystrophy
Physical Therapy and Rehabilitation Considerations

Kirsten Zilke PT - Shriners Hospitals for Children - Portland
September 12, 2020
PPMD End Duchenne Tour – Portland, OR
General Considerations and Philosophy

- Rehabilitation practice based on the 2018 DMD Care Considerations and 5 stages of DMD (Diagnosis/Early Ambulatory/Late Ambulatory/Early Non-ambulatory/Late Non-Ambulatory)
- Individualized care based on the family and child’s specific needs
- Honest and compassionate guided discussions at each stage that attempts to anticipate needs and set expectations for future function. **AVOID SURPRISES!!**
- Work closely with school and community therapists to support families where they live
- Close communication with all Muscular Dystrophy clinic providers which is continuous.
Assessments

**Comprehensive PT and OT Assessments** – typically occur outside of the clinic visit

- Diagnosis
- Significant change in function
  - Disease progression
  - Injury

**Needs-based Assessments** – occur during clinic visits every 6 months

- Standardized Tests of Function
  - 6-minute walk test
  - NSAA (North Star Ambulatory Assessment)
  - 10-meter walk/run
  - Timed rise from floor
  - PUL (Performance of upper limb module)

- Adaptive Equipment
- Orthotic Intervention
- Fall risk
Interventions

Initiate a prescribed course of PT/OT
  To address a specific goal or concern
  To trial or train with adaptive equipment
  Post fracture rehabilitation
  Serial casting

Recommendations for “exercise” or as I prefer, ACTIVITY
  Be active regularly, getting heart and breathing rate higher than at rest
  Avoid over exertion, performing exercise sub-maximally in most instances
  Avoid repetitive eccentric exercise
  Respect the need for rest

Focus on incorporating activity into daily routines
  Create opportunities for family activities
  Passive ROM through static joint positioning throughout the day
  Engage in recreational activities with disabled and non-disabled peers
References


Cardiac complications of DMD

Aaron Olson, M.D.
Seattle Children’s Hospital
Overview

- **Cardiac involvement**
- **Screening**
  - When
  - How
- **Therapies**
Cardiac involvement

- Dilated cardiomyopathy
  - enlarged left ventricle with decreased function

- Arrhythmias
  - ECG changes
  - Arrhythmias—potentially life threatening
Cardiac involvement

- Unusual before age 10 years*
- Nearly universal at age 20 years
- Cause of death in 25%
Heart failure symptoms uncommon

- Altered sleep
- Pronounced fatigue
- Unexplained weight loss or gain
- BMD can have typical symptoms
Overview

- Cardiac involvement
- **Screening**
  - »When
  - »How
- Therapies
Screening
Why

Changes in heart function occur without obvious symptoms
Screening

When

- At diagnosis
- Yearly thereafter
- Every 4-6 months with initiation of meds or significant myocardial dysfunction
Screening

How

- Echocardiogram/cardiac MRI
- ECG
- Holter monitor. Palpitations or significantly reduced function
### Echocardiogram vs. MRI

#### Cardiac function

<table>
<thead>
<tr>
<th></th>
<th>Positives</th>
<th>Negatives</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Echocardiogram</strong></td>
<td>Fast study</td>
<td>Images become worse in teens</td>
</tr>
<tr>
<td></td>
<td>Rapid results</td>
<td></td>
</tr>
<tr>
<td><strong>MRI</strong></td>
<td>Clear images in all ages</td>
<td>Long study</td>
</tr>
<tr>
<td></td>
<td>Assess for fibrosis</td>
<td>Have to lay still</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Claustrophobia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>May need an IV</td>
</tr>
</tbody>
</table>
DMD Carriers

Echocardiogram or MRI every 5 years after age 18 years
Overview

- Cardiac involvement
- Screening
  - When
  - How
- Therapies
Indications

- Abnormal heart function
- Scarring on MRI
- Age 10 years with normal cardiac exam
Therapies

- Standard heart failure medicines
- Slow the rate of decline in heart function
Therapies

- ACE Inhibitors - 1st choice
- Carvedilol (non-selective β and α1 blocker) - 2nd choice
- MRAs - 2nd choice (spironolactone)
- Diuretics
- Newer heart failure meds (Entresto, ivabradine)
Conclusions

- Cardiac involvement is nearly universal by adulthood
- Regular screening with cardiologist
- Medications commonly used