DMD STANDARDS OF CARE

PPMD 2019 END DUCHENNE TOUR

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DISCLOSURES

- Scientific advisory board: Sarepta Therapeutics, Biogen, PTC Therapeutics
- Active clinical trials: PTC Therapeutics, Sarepta Therapeutics, Pfizer, Biogen,
- Funding:
  - NIH/NINDS: K08, CureSMA, CDC
OBJECTIVES

- Outline changes to standard of care guidelines published in 2018
  - Discuss how the care guidelines are developed
  - Focus on things that are new in 2018
First published January 2010 Lancet in 2 parts
- Updated care guidelines published 2018
- PPMD, MDA, PPMD, TREAT-NMD and the CDC
- Follow-up on previously addressed topics and literature review
- Three new topics
  - Primary and emergency care
  - Endocrine management
  - Transitions of care across a lifetime
PROCESS OF CONSENSUS BUILDING

- RAND/UCLA Appropriateness Method
  - “Experts” from various fields
  - Reviewed all relevant literature (updates from 2010)
  - Consider different clinical scenarios with recommendations
    - Rate interventions for “appropriateness” or “necessity” at different stages of the condition
    - Appropriate = expected benefit outweighs risk (does not include financial consideration)
  - Iterative process with final agreement on “necessary” and “appropriate” or “inappropriate” interventions
  - NOTE: There is a significant lack of good literature supporting decision-making
    - Recommendations are largely based on consensus of experts
Diagnosis and management of Duchenne muscular dystrophy, an update

- Part 1: Diagnosis, neuromuscular, rehabilitation, endocrine, and gastrointestinal and nutritional management
- Part 2: Respiratory, cardiac, bone health, and orthopedic management
- Part 3: Primary care, emergency management, psychosocial care, and transitions of care across the lifespan
DMD CARE IS DEPENDENT ON PROGRESSION

Stage 1: Presymptomatic
- Can be diagnosed at this stage if creatine kinase found to be raised or if positive family history
- Might show developmental delay but no gait disturbance

Stage 2: Early ambulatory
- Gowers’ sign
- Waddling gait
- Might be toe walking
- Can climb stairs

Stage 3: Late ambulatory
- Increasingly laboured gait
- Losing ability to climb stairs and rise from floor

Stage 4: Early non-ambulatory
- Might be able to self propel for some time
- Able to maintain posture
- Might develop scoliosis

Stage 5: Late non-ambulatory
- Upper limb function and postural maintenance is increasingly limited
STEROID

- Benefits
  - Loss of ambulation at a later age, preserved upper limb and respiratory function, and avoidance of scoliosis surgery

- Initiation
  - Before substantial physical decline—Usually between 3-4 yrs old
  - Preferred after completion of 5 yr old immunizations
  - Careful discussion of discussion of side effects
    - Behavior and weight gain are the most important practically speaking
  - Nutrition consultation

- Prednisone 0.75mg/kg/day or deflazacort (Emflaza) 0.9mg/kg/day
  - If side-effects decrease dose by 25-33-%
  - If persistent side-effects, consider alternative dosing schedule, ie. weekend dosing

- Continue steroid after loss of ambulation with reduced dose to manage side effects
Long term treatment with corticosteroids suppresses the adrenal glands
- Cortisol is produced by the adrenal glands in response to stress, illness etc.

Adrenal insufficiency
- Confusion, rapid heart rate, loss of appetite, sweating, vomiting, fever
- Can occur if steroid is stopped suddenly, or patient under increased “stress”
- Under typical dosing for DMD, this low risk
  - Risk increased if dosing is below physiological levels or stopping suddenly

PJ Nicholoff Steroid Protocol
- Stress dosing with hydrocortisone for patients at risk for adrenal insufficiency
- We are working with endocrinology to develop a protocol
  - For most patients this will include a stress dosing protocol, and prescription for hydrocortisone
Endocrine complications of DMD
- Impaired growth
- Delayed puberty,
- Adrenal insufficiency

Monitor growth and development
- Human growth hormone to treat DMD related growth failure NOT recommended
- Absence of pubertal development by 14 years requires referral
  - Hypogonadism \(\rightarrow\) testosterone replacement
Recommendations
- Cardiology referral at diagnosis
- Annual follow-up including EKG and imaging echocardiogram/cardiac MRI
  - Previously was every 2-3 years until age 10 and annually thereafter
- Start medication by age 10 even with normal heart function
  - ACE inhibitors (lisinopril, enalapril) or ARB (losartan, valsartan)
- Echocardiography vs. cardiac MRI
  - MRI becoming more routinely used—identifies fibrosis at earlier age than echo
  - Ejection fraction—EF

Cardiac surveillance for female carriers
- Assessment at baseline and 3-5 years
PULMONARY

- Weakness in respiratory muscles results in poor airway clearance and hypoventilation
  - Diaphragm
  - Chest wall
- Usually becomes a problem in non-ambulatory stage
- Pulmonary complications are major cause of morbidity and mortality
  - Mucus plugging, atelectasis, pneumonia, respiratory failure
- Contributing factors: stiff noncompliant chest walls, scoliosis, weak cough efforts, immobility
- Vaccinations are critical to respiratory health
  - Influenza annually
  - Pneumonia (2)
    - Most people receive PCV13 in the first year (3 doses)
    - PPSV23 for certain sensitive groups (including DMD) and elderly
      - 2 doses five years apart
PULMONARY TESTING AND SURVEILLANCE

- Anticipatory approach decreases respiratory complications, improves quality of life, prolong survival

- Pulmonary Function Test (PFT)
  - Annually in ambulatory and twice yearly in non-ambulant
    - FVC, MIP, MEP, peak cough flow
    - Transcutaneous CO₂

- Cough Assist
  - FVC<50%, peak cough flow <270L/min, or MEP <60 cmH₂O

- Nighttime BiPAP
  - With symptoms of hypoventilation or sleep disordered breathing
  - FVC<50%, peak cough flow <70L/min, or MIP <60 cmH₂O, pCO₂ >45mmHg
Ostopenia (low bone density) is common to any person with muscle weakness

Chronic steroid use in boys with DMD may exacerbate osteopenia

Fracture risk increases with age
- May occur with relatively minor trauma
- Risk for fat embolism with long bone fracture
- Vertebral fracture may be asymptomatic
- Early mobilization is key to treatment to maintain function

Scoliosis is common and may require treatment with spinal fusion
- Follow spinal XR ray
Ensure adequate vitamin D intake
- 1000-2000 IU per day

Annual vitamin D level

Spine films
- Annual if on steroid
- Every 2-3 years not on steroid

Treatment with IV bisphosphonate if >2 fractures (not explained by obvious trauma)

DEXA scan (for bone density)

Scoliosis
- Risk decrease by use of steroid
- May require spinal fusion to treat
  - Goal to treat early
Good primary care is essential for routine care and follow up of issues that arise

Coordinate with MD Care Center

Immunizations
  - Flu and pneumococcal vaccines

Nutrition/growth

Standardized screening
  - Hearing/vision
  - Mood disorders
  - Substance abuse
  - Etc.

Medical Home Portal
EMERGENCY CARE

- PPMD app for emergency care considerations for families
- Oxygen can be given but ONLY if CO2 monitored → hypercapnia
  - If patient needs oxygen, should always consider ventilation (BiPAP)
- Awareness of potential for cardiac problems
- Anesthesia
  - Risk for malignant hyperthermia—selection of correct drugs
- Adrenal Crisis
  - Steroids are stopped suddenly
  - Doses are missed for any reason
  - The body is under extreme “stress” (severe illness, surgery, or trauma)
- Fat embolism syndrome with fracture
  - Onset within 24 hours
  - Altered mental status, respiratory distress, tachycardia
**About Me**

Hi! My name is:

I have:

When I have a respiratory infection or pneumonia, my weak cough makes it difficult to keep mucus from building up in my lungs. I use a Cough Assist Device to help bring up the mucus.

<table>
<thead>
<tr>
<th>The settings for my Cough Assist are:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inspiratory Pressure: cm H₂O</td>
</tr>
<tr>
<td>Expiratory Pressure: cm H₂O</td>
</tr>
<tr>
<td>Inspiratory time: sec; Expiratory time: sec; Pause: sec;</td>
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</tbody>
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If my oxygen saturations are less than 94% then I need more frequent Cough Assist and possibly BIPAP (IPAP 12-20 cm H₂O, EPAP 3-6 cm H₂O) or nasal mask non-invasive ventilation (assist controlled volume ventilation).

**Using just oxygen to treat low oxygen saturations can mask and cause CO₂ retention and respiratory acidosis! As a general rule, oxygen without BIPAP should be avoided!**

BIPAP and nasal mask non-invasive ventilation can reverse hypoxemia and respiratory acidosis AND prevent the need for intubation.

**My Muscular Dystrophy Neurologist is:**

Contact #:

**Pulmonologist is:**

Contact #:

**Cardiologist is:**

Contact #:

**Respiratory Therapist is:**

Contact #: 

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**Emergency Information for People with Duchenne**

**Respiratory Care Risk: Respiratory Failure**

- If trouble breathing, or Oxygen saturation low, use cough assist or Ambu bag or BIPAP; IF not improved in 5-10 minutes go to ER
- Take your equipment (cough assist, BIPAP, etc.) and medicines with you to the hospital/ER
- In ambulance or ER, medical providers must only give Oxygen with close monitoring of CO₂ levels; breathing may need to be supported
- Call your neuromuscular team and tell them you are going to the ER/hospital. (Do not depend on the ER staff to do this)

**Neuromuscular Center/Doctor**

**Emergency Number**
TRANSITIONS (TO ADULTHOOD) IN DMD

**Relationships with others**
- Develop skills to connect with others to manage own affairs (e.g., social outings, appointments)
- Work towards desired level of autonomy and independence

**Housing**
- Examine where to live (family home vs. elsewhere)
- Modify home for accessibility and safety
- Use assistive technology

**Transportation**
- Foster independent driving with vehicle modifications
- Modify family-owned vehicle
- Investigate accessible public transportation options

**Education or employment**
- Plan early for future vocation
- Consider classes online vs. on campus
- Contact campus programmes for students with disabilities
- Enlist employment or vocational planning resources

**Activities of daily living**
- Explore funding and benefits for care
- Learn to hire and train personal care attendants
- Ensure respite for family caregivers
- Consider need for guardianship or conservatorship

**Health care**
- Transition from paediatric to adult health care
- Move from family-centred to patient-centred provider interactions
- Discuss age-related changes in health-care benefits
- Assess the need for durable power of attorney for health care
QUESTIONS/COMMENTS