DMD STANDARDS OF CARE

PPMD 2019 END DUCHENNE TOUR

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February 2, 2019

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

DMD STANDARD OF CARE GUIDELINES

- 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

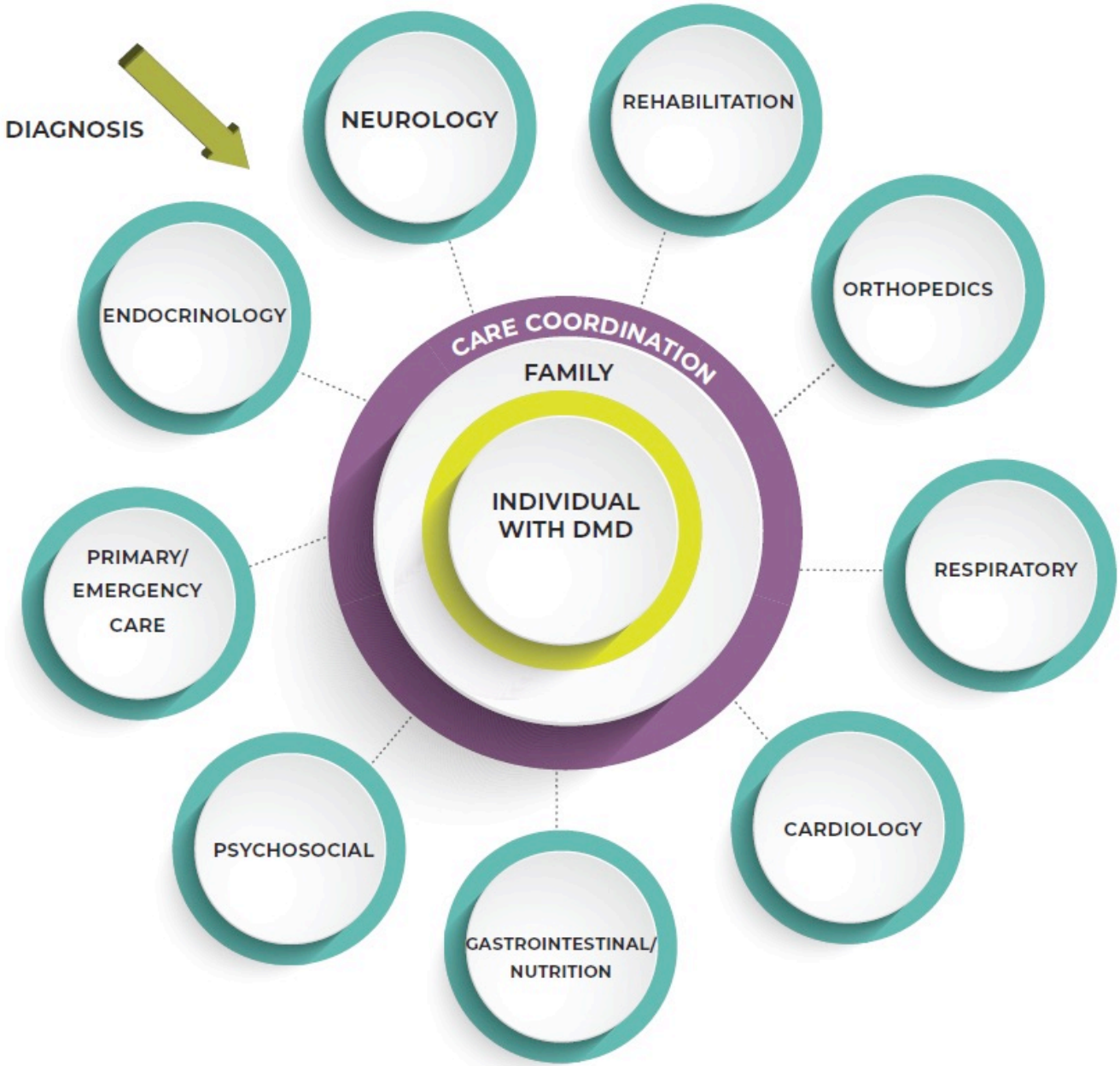
PROCESS OF CONSENSUS BUILDING

- 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

Lancet Neurology January 2018

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


DIAGNOSIS
NEUROLOGY
REHABILITATION
ENDOCRINOLOGY
ORTHOPEDICS
CARE COORDINATION
FAMILY
INDIVIDUAL WITH DMD
PRIMARY/ EMERGENCY CARE
RESPIRATORY
PSYCHOSOCIAL
CARDIOLOGY
GASTROINTESTINAL/ NUTRITION

DMD CARE IS DEPENDENT ON PROGRESSION

Stage 1: Presymptomatic	Stage 2: Early ambulatory	Stage 3: Late ambulatory	Stage 4: Early non-ambulatory	Stage 5: Late non-ambulatory
Can be diagnosed at this stage if creatine kinase found to be raised or if positive family history	Gowers' sign	Increasingly laboured gait	Might be able to self propel for some time	Upper limb function and postural maintenance is increasingly limited
Might show developmental delay but no gait disturbance	Waddling gait	Losing ability to climb stairs and rise from floor	Able to maintain posture	
	Might be toe walking		Might develop scoliosis	
	Can climb stairs			

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

ENDOCRINE—ADRENAL CRISIS

- 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

- 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 → testosterone replacement

CARDIAC

- 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

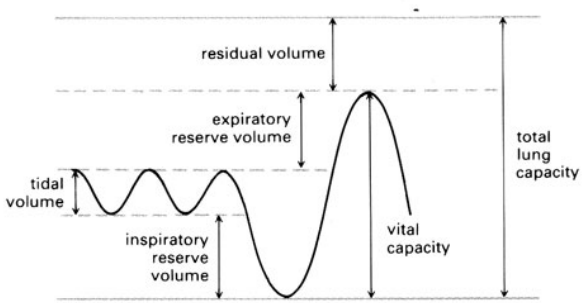
- Cardiac surveillance for female carriers
  - Assessment at baseline and 3-5 years

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 CO_2
- Cough Assist
  - FVC<50%, peak cough flow <270L/min, or MEP <60 cmH_20
- Nighttime BiPAP
  - With symptoms of hypoventilation or sleep disordered breathing
  - FVC<50%, peak cough flow <,70L/min, or MIP <60 cmH_20, pCO2 >45mmHg



BONE HEALTH

- 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

BONE HEALTH—INTERVENTIONS

- 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

PRIMARY CARE

- 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.

The settings for my Cough Assist are:

Inspiratory Pressure: cm H_2O

Expiratory Pressure: cm H_2O

Inspiratory time: sec; Expiratory time: sec; Pause: sec;

If my oxygen saturations are less than 94% then I need more frequent Cough Assist and possibly BIPAP (IPAP 12-20 cm H_2O; EPAP 3-6 cm H_2O) or nasal mask non-invasive ventilation (assist controlled volume ventilation).

Using just oxygen to treat low oxygen saturations can mask and cause CO_2 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:

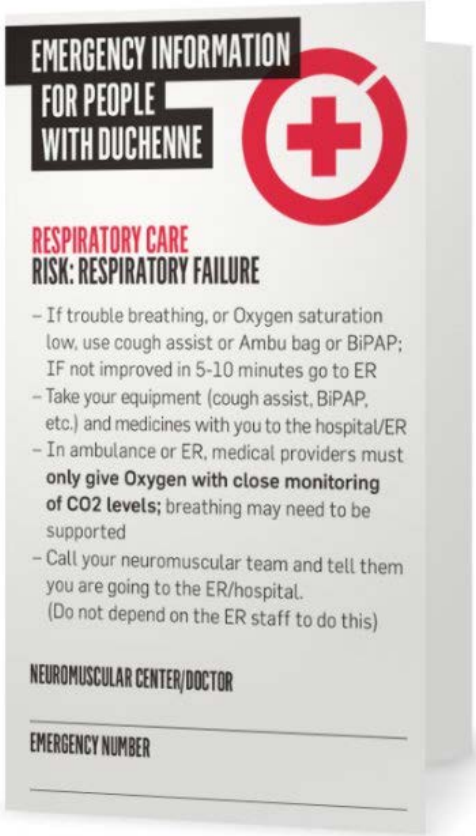
Contact #:

Cardiologist is:

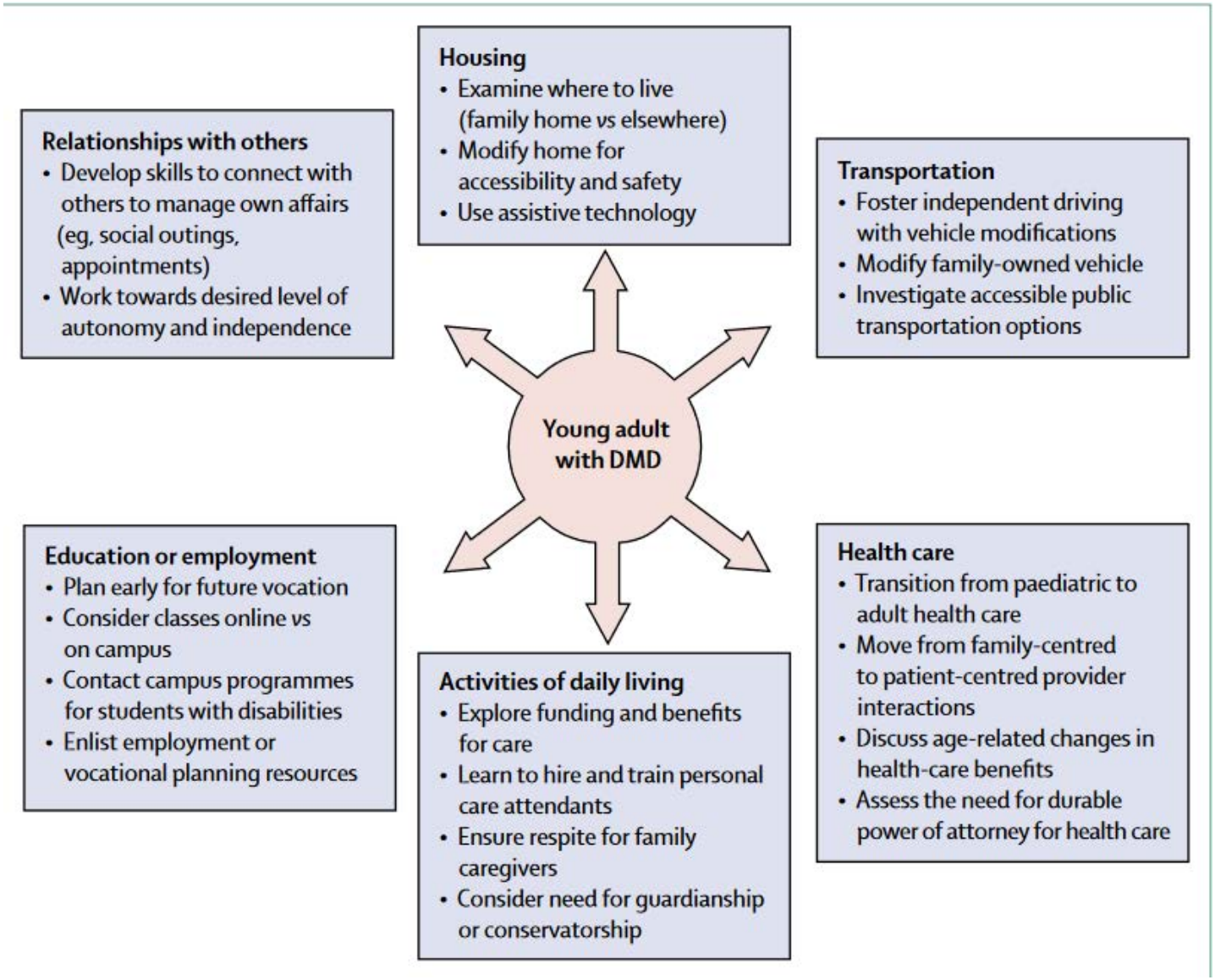
Contact #:

Respiratory Therapist is:

Contact #:



TRANSITIONS (TO ADULTHOOD) IN DMD



QUESTIONS/COMMENTS