Duchenne Muscular Dystrophy and the Heart

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Natural history of Duchenne Muscular Dystrophy

Birth
Age 1 - Delayed walking, frequent falling
Age 2-3 - Difficulty climbing
Age 5-6 - Average age of diagnosis
Age 8-12 - Weakening and wheelchair use
• 25% EKG changes

Age 14-17 - Worsening scoliosis and discomfort
• Echocardiogram may be abnormal
• 33% have cardiac hypertrophy (wall thickening)

Age 16-20 - Breathing problems, pneumonia, tracheostomy
• Echocardiogram begins to show worsened heart function, but no symptoms yet

Age 18-25 - Fully ventilator dependent
• Cardiomyopathy worsens and may progress to heart failure

Age 27-28 - Average lifespan for patients
• (With excellent care, may live to 30s or 40s)
THE GOOD NEWS:
• Patients with DMD are living longer
• Medical technology is advancing quickly
• Treatments are continuing to improve

WHAT DOES THIS MEAN?
• The medical teams are now seeing the later complications of Duchenne Muscular Dystrophy (because patients are living longer)
• Heart failure from cardiomyopathy is becoming a major cause of death in older DMD patients
Duchenne Muscular Dystrophy happens because dystrophin, a protein that is very important for muscle function, is abnormal or missing.

- Because of this, the muscles in the body become weak:
  - **Skeletal (movement) muscles** - arms and legs
  - **Respiratory (breathing) muscles** - chest wall and diaphragm
  - **Cardiac (heart) muscle** - The entire heart is a muscle!
Questions about DMD and the heart

1. What is cardiomyopathy?
2. What is the difference between cardiomyopathy and heart failure?
3. When should my child see a cardiologist?
4. How can we make sure my child’s heart stays healthy?
5. What symptoms should I watch out for at home?
6. What treatments are available?
7. What can I expect from the future?
What is cardiomyopathy?

Dilated cardio-myo-pathy is the term used to describe the abnormal changes in the heart which enlarges as it becomes weaker

Cardio = heart
Myo = muscle
Pathy = disease

There are several types of cardiomyopathy, so cardiologists describe this specific heart condition as “dilated” to be more specific.
What is cardiomyopathy?
What is cardiomyopathy?
Who gets cardiomyopathy?

• Almost all patients who have Duchenne Muscular Dystrophy (>97%)
• 2/3 of patients with Becker Muscular Dystrophy
• 1/10 of females with the DMD gene (even if they aren’t weak)
• Patients with other muscular dystrophies
  – Limb Girdle Muscular Dystrophy (types 2C, 2D, 2E, 2F)
  – Congenital Muscular Dystrophies (some)
  – Facioscapulohumeral Muscular Dystrophies (rarely)
Heart failure is a consequence of dilated cardiomyopathy -

- We start to talk about heart failure when dilated cardiomyopathy becomes significant enough to affect how the heart functions.
- **Heart failure** DOES NOT mean the heart has failed

- **PATIENTS CAN LIVE LONG LIVES WITH HEART FAILURE**
What is the difference between cardiomyopathy and heart failure?

• There are several levels of heart failure, classified by the New York Heart Association (NYHA):
  – **NYHA Class I**: Heart function is decreased on echocardiogram, but the patient does not have any symptoms *(DMD patients 10-15 years old)*
  – **NYHA Class II**: Patient is comfortable at rest but ordinary activity causes breathlessness, fatigue, or palpitations *(15-20 years old)*
  – **NYHA Class III**: Comfortable at rest, but smaller activities cause symptoms *(15-20 years old)*
  – **NYHA Class IV**: Unable to do any physical activity without discomfort. Symptoms are present at rest *(>20 years old)*
When should my child see a cardiologist?

• The American Academy of Pediatrics (AAP) recommends that patients with DMD or BMD should begin to see a cardiologist as soon as the diagnosis is confirmed.

• Because significant cardiomyopathy does not typically occur before 10 years old:
  – See cardiologist at least once every two years until age 10
    • Or more frequently if there are concerns or symptoms
  – See cardiologist once a year after age 10
    • Or more frequently if there are concerns or symptoms
  – Before any major surgery
How can we make sure my child’s heart stays healthy?

These tests are helpful to make sure your child’s health stays healthy:

• **Echocardiogram** - Ultrasound of the heart to look for dilation (cardiomyopathy) and heart function.

• **EKG** - Record rhythm of the heart to make sure it looks normal

• **Holter Monitor** - a longer monitor worn at home to record heart rhythm over several days.

• **Cardiac (heart) MRI** - MRI to get more information about the heart muscle and function.
Echocardiogram - Ultrasound of heart

• **Advantages** -
  – Can be done quickly in clinic
  – No radiation

• **Disadvantages** -
  – Younger patients may not want to lie still
  – Quality of pictures get worse as patients get older
  – Not accurate to check function of right ventricle
Echocardiogram

- Echocardiogram
  - At CHLA, we perform an initial echocardiogram at time of diagnosis
  - Every 2 years until age 10
  - Every year for patients >10 years old
  - More frequently if there are concerning symptoms, signs of dilated cardiomyopathy or heart failure
**EKG and Holter Monitor**

**EKG** - with 9 stickers, we check the heart rhythm over several seconds

**Holter Monitor** - We use a ZioPatch, which can check the heart rhythm for up to 2 weeks! **AND, no WIRES!**
EKG and Holter Monitor

• **EKG**
  – At CHLA, we typically perform an EKG at time of diagnosis
  – Every 2 years until age 10
  – Every year for patients >10 years old
  – More frequently if there are concerning symptoms, signs of dilated cardiomyopathy or heart failure

• **Holter Monitor (ZioPatch)**
  – We consider placing a ZioPatch if there are symptoms of dizziness, fainting, palpitations (abnormally fast heart beats), or other reasons to worry about abnormal heart rhythm.
Cardiac (heart) MRI - As patients get bigger and less mobile, it may be hard to get accurate images by echocardiogram.

**Advantages** -
- Detailed images of heart
- Accurate assessment of function
- Additional information (fibrosis, preclinical cardiomyopathy)
- No radiation involved

**Disadvantages** -
- Need to lie down in MRI scanner for a longer time
- Usually involves placing an IV
- Small space
- Expensive
Cardiac (heart) MRI

- It is a good idea to get a baseline cardiac MRI between 8-10 years old
  - Patient doesn’t typically need anesthesia
  - Patient’s heart may be starting to develop subtle changes of cardiomyopathy around this time (tonic contraction)
- Repeat MRI every 3-5 years after first MRI
  - Depends on development of cardiomyopathy seen by echocardiogram
  - Depends on how well the heart can be seen by echocardiogram
What symptoms should I watch out for at home?

• Your cardiologist may ask about:
  – Tiredness (fatigue) and weakness
  – Decreased ability to exercise
  – Abdominal pain
  – Nausea or decreased appetite

These symptoms happen because the heart is not pumping enough blood to keep up with what the body needs
What symptoms should I watch out for at home?

- Your cardiologist may ask about:
  - Shortness of breath (dyspnea)
    - during activities
    - when lying down
  - Needing to sleep on more pillows or sitting up
  - Persistent cough or wheezing

_These symptoms happen because the left side of the heart is not pumping blood well, and so there is blood backing up into the lungs._
What symptoms should I watch out for at home?

• Your cardiologist may ask about:
  – Swelling (edema) in legs or feet
  – Swelling in abdomen (ascites)

These symptoms happen because the right side of the heart is not pumping blood well, and so there is blood backing up into the body.
What symptoms should I watch out for at home?

- Your cardiologist may ask about:
  - Chest pain
  - Fast or irregular heartbeats
  - Dizziness
  - Fainting or near-fainting

*These symptoms happen because the heart is stretched and so the electrical system isn’t working properly.*
What treatments are available?

- It is important to start medication **before** dilated cardiomyopathy develops (prophylaxis)!
  - Many studies show that prophylactic treatment slows down the development of cardiomyopathy and heart failure
  - Together, the cardiologist and parents should decide when to start medication (not too early, but before development of cardiomyopathy)
  - Typically at CHLA, the first medication is started around 8 years old
Heart Function over time

Blue: early treatment with ACE inhibitor

Heart Size over time

Red: no early treatment

**Statistical Notes:**
- Mean Z = -0.06 (p = 0.01)*
- Mean Z = -0.52 (p = 0.008)*
- Mean Z = -1.17

*compared with mean LVId of 11 to 15 year age group
What treatments are available?

• Medications:
  – Angiotensin Converting Enzyme Inhibitor
    • Also known as ACE inhibitor
    • *This is the medication we use for prophylaxis (prevention)*
    • **Enalapril** - comes in liquid form, but has to be given twice a day
    • **Lisinopril** - a small pill that can be given once a day
    • Lowers blood pressure
    • Side effect: cough, dizziness from lower blood pressure
  – Beta blocker
    • Once heart failure develops, we may start this
    • **Propranolol, carvedilol, atenolol**
    • Lowers blood pressure and slows heart rate
    • Also can be used to control abnormal heart rhythms
    • Side effect: decreased energy, low heart rate, dizziness
What treatments are available?

- Because **ACE inhibitors** and **beta blockers** lower blood pressure, the decrease the workload of the heart.
What treatments are available?

• **Medications:**
  – *Spironolactone (a.k.a. Aldactone)*
    • Once heart failure develops, we may start this
    • Typically taken once or twice a day
    • Side effect: mildly increased urination, increased breast tissue
  – *Diuretics*
    • Used for symptoms of heart failure caused by fluid accumulation (shortness of breath, coughing, swelling of abdomen or legs)
    • *Furosemide (Lasix)* - given 1-3 times/day
    • *Chlorothiazide (Diuril)* - given 1-3 times/day
    • Side effect: increased urination
What treatments are available?

- **Medications:**
  - Others - depends on symptoms
    - Angiotensin receptor blockers (ARB):
      - **Losartan**
    - Phosphodiesterase-5 inhibitors (PDE-5 inhibitor):
      - **Sildenafil (Revatio)**
      - **Tadalafil (Adcirca)**
    - Antiarrhythmics
    - Anticoagulation
      - **Aspirin**
      - **Warfarin (Coumadin)**
      - **Low molecular weight heparin (Lovenox)**
What treatments are available?

• Future directions:
  – There is exciting research on gene-repair strategies for DMD
    • Stop codon read-through and exon skipping
  – Currently gene therapies show promise to strengthen skeletal muscle, but do not seem likely to affect heart muscle.
  – Researchers are exploring possibilities to combine gene replacement therapy with medications that lessen workload on the heart
    • Example: combination gene therapy + ACE inhibitor
Duchenne Muscular Dystrophy: Life expectancy

Average life expectancy of a patient with DMD:

In 1960 - 15 years old
In 1990 - 20 years old
In 2010 - 27 years old

What will the future bring?