DUCHENNE 101: UNDERSTANDING THE EFFECT OF DUCHENNE ON THE BODY & SYSTEMS
WHAT IS DUCHENNE?

Duchenne muscular dystrophy is caused by mutations to the largest known human gene, dystrophin. Most commonly, one or more portions of the gene are missing, and the remaining segments don’t fit together properly.

Because of this error in the genetic instructions, cells cannot make dystrophin, one of a highly complex group of proteins that is found in all muscle cells throughout the body.

Dystrophin keeps muscle fibers strong and working together to protect them from injury as they contract and relax.
Duchenne’s Effect on Muscles

Without dystrophin, muscle cells are damaged, and, over time, are replaced with scar tissue and fat in a process called fibrosis.

Healthy Muscle Tissue

Muscle Tissue with Duchenne Muscular Dystrophy
WHAT IS DYSTROPHIN?

Think of a person's body as their house, and the dystrophin proteins are the nails, mortar and cement.

It's these important fasteners that bind the framework, materials, electrical, and plumbing systems together. Dystrophin gives the house its strength, stability, and ensures that all individual parts work together.
The Role of Dystrophin

When people with Duchenne lack these vital proteins, cracks and voids are formed in between the body’s various building blocks. Without its connective fasteners and “glue,” the house as a whole loses its strength and stability.

Individual parts and systems are no longer connected, communicating or working cohesively. In time, the overall structure fails and can no longer withstand the stresses of everyday use.
FEMALE CARRIERS OF DUCHENNE

Humans have two chromosomes, X and Y, that combine to determine a person’s sex. Males inherit one X chromosome from their mother, and one Y chromosome from their father, making them (XY). Females get one X chromosome from each parent, giving them (XX).

Because the Duchenne dystrophin gene mutation is found on the X chromosome, it primarily affects males, as they inherit just one X from their mother. Females are typically unaffected carriers having a second normal X chromosome. However, some female carriers experience varying ranges of physical symptoms including skeletal muscle weakness, cardiac changes, and problems with learning and behavior.
Duchenne is not just a disease of the muscles. It affects every system in the human body.
MUSCLES

There are more than 600 muscles in the human body. Major muscles, such as those in the trunk, arms, and legs, are responsible for large movements like walking or lifting something heavy. Smaller muscles, such as those in the hands and face, are responsible for tasks like writing with a pen, or drinking out of a straw.

MUSCLES WORK BY EXPANDING AND CONTRACTING TOGETHER IN PRECISION, ALLOWING THE BODY TO MOVE AND PERFORM EVERYDAY TASKS.
SKELETAL MUSCLES

Healthy Function: Skeletal muscles are voluntary muscles, which means a person can control what they do. Skeletal muscles attach to and work with bones to allow for body movement by contracting and relaxing in coordination.

Symptoms: In Duchenne, the lack of dystrophin causes damaged muscle cells to be replaced by scar tissue and fat, which causes progressive weakness over time, as muscles can no longer contract properly.

Treatments: Steroids are used to help maintain muscle strength for as long as possible. Physical therapists can prescribe safe exercise, stretching routines, and mobility and assistive devices to keep muscles working their best.
BONE & JOINTS

The skeletal system includes the bones and a network of tendons, ligaments, and cartilage that connects them. Taking steroids may impact bone health in Duchenne. In addition, as people living with Duchenne become less ambulatory, joints may also be affected over time.

THE SKELETAL SYSTEM IS RESPONSIBLE FOR SUPPORT OF THE BODY, MOVEMENT, AND PROTECTION OF THE VITAL ORGANS.
BONES

**Healthy Function:** Bones provide a framework for the body, protection for organs, and store calcium to grow and strengthen—as well as to supply the rest of the body.

**Symptoms:** Taking steroids can decrease bone mineral density, causing them to become thinner and weaker, known as osteoporosis. If untreated, it puts a person at high risk for fractures, including those in the spine.

**Testing & Treatments:** DEXA scans measure bone density, and can assess whether osteoporosis is present. Lateral spine X-rays can check for vertebral compression fractures. If osteoporosis is found, diet modification including calcium and vitamin D supplementation can help to optimize bone health and prevent fractures. Bisphosphonates or other bone sparing medications may be prescribed to increase bone density.
JOINTS

Healthy Function: Joints are located where two or more bones meet and allow for body movement. Tendons and ligaments are the tough connective tissue that attach muscles and bones and provide support and movement at joints.

Symptoms: As people with Duchenne become less ambulatory, muscles, tendons, and ligaments become shorter and less flexible. This can pull joints into a flexed position, known as a contracture. The spine is also made up of a series of joints and weakened muscles can lead to scoliosis, or curvature of the spine.

Testing & Treatments: Stretching routines, ankle-foot orthoses, and supportive seating/wheelchairs can help keep joints flexible and prevent contractures. If contractures of the ankles or spine (scoliosis) develop, serial casting or surgery may correct the problem.
CARDIOVASCULAR SYSTEM

The cardiovascular system is made up of the heart muscle and the circulatory system, an intricate network of blood vessels, called arteries and veins. The heart works to pump blood through these vessels to all cells of the body. Arteries deliver oxygen and nutrients throughout the body, while veins carry waste products away.

THE HEART MUSCLE IS RESPONSIBLE FOR PUMPING BLOOD, RICH IN OXYGEN AND NUTRIENTS, TO EVERY ORGAN, TISSUE, AND CELL IN THE BODY.
THE HEART

Healthy Function: The heart is made up of four chambers that work together to fill with blood and contract, squeezing and pushing blood out to the cells in the body. Each squeeze, or heartbeat, is controlled by an electrical system in the heart.

Symptoms: As a muscle, and lacking dystrophin from Duchenne, the heart develops fibrosis, affecting both the electrical system and the strength of the "squeeze."

Testing & Treatments: A cardiologist should perform echocardiograms, cardiac MRIs, and ECGs annually to evaluate the structure and squeeze of the heart, the rate and rhythm of heartbeats, and measure fibrosis. ACE-inhibitor medication should be started at the onset of fibrosis, abnormal test results, or by age 10, even if heart function is normal. Beta blockers, diuretics, and antimineralcorticoids (Eplerenone, Spironolactone) are also commonly used.
PULMONARY SYSTEM

The pulmonary system, responsible for oxygen intake, is made up of the lungs and muscles that help to breathe and cough. The diaphragm beneath the lungs is responsible for breathing. Accessory muscles between ribs and in the abdomen work with the diaphragm to move air in and out of the lungs, as well as to initiate coughing.

MUSCLES REQUIRED TO BREATHE AND COUGH ARE ALL AFFECTED BY THE LACK OF DYSTROPHIN THAT OCCURS IN PEOPLE WITH DUCHENNE.
**VENTILATION**

**Healthy Function:** Air is inhaled through the nose and mouth, and travels through the trachea into bronchial tubes, which pass the air throughout the lungs. The diaphragm works by contracting downward to pull air into the lungs, and relaxing upwards to deflate the lungs. The intercostal muscles, located between the ribs, expand the rib cage allowing space for the lungs to inflate as a person breathes air in.

**Symptoms:** Over time, the diaphragm and intercostal muscles grow weak and less elastic, which leads to shallow breathing known as hypoventilation.

**Testing & Treatments:** A pulmonologist should assess changes using Pulmonary Function Testing (PFT) at least annually. At first signs of decline, a technique called breath stacking (or lung volume recruitment) can help keep muscles flexible, preserving respiratory volume and function.
GAS EXCHANGE

Healthy Function: In the lungs, a process known as gas exchange occurs. Oxygen from the air passes into the blood so it can be used by the body for energy. Carbon dioxide, which is a waste product of the body, passes from the blood back into the lungs to be removed from the body through exhalation.

Symptoms: Hypoventilation can affect gas exchange in the lungs, and results in decreased oxygen in and carbon dioxide out. The imbalance of gasses in the blood can cause many side effects such as fatigue and headaches during the day.

Testing & Treatments: A sleep study, ordered by a pulmonologist, will measure oxygen and carbon dioxide levels at rest. Non-invasive breathing support (i.e. BiPAP) can be prescribed to help normalize the gas levels in the blood, and improve sleep quality.
Coughing

Healthy Function: Air passages produce mucous to trap allergens, bacteria, pollutants, and viruses found in the air before they reach the lungs and cause damage or infection. Coughing protects the lungs by removing mucous filled with harmful substances.

Symptoms: The diaphragm, intercostal, and abdominal muscles, responsible for coughing, weaken over time, leading to an ineffective cough or even the inability to cough. As a result, it becomes difficult to remove mucous from the airway passages, which increases the risk for lung infections or pneumonia.

Testing & Treatments: A pulmonologist will evaluate coughing strength through a Peak Cough Flow (PCF) measurement. If the peak cough flow level is too low, an assisted cough, either with a Cough Assist machine or manually, may be recommended.
DIGESTION

Comprised of both skeletal muscles, used in chewing and swallowing, and smooth muscle tissues that move food through the intestines, the digestive system, or gastrointestinal (GI) tract, is responsible for transporting, breaking down, and absorbing nutrients from food to fuel the body.

**These GI muscular tissues are all affected by the lack of dystrophin that occurs in Duchenne.**
CHEWING

Healthy Function: Multiple muscles of the jaw work together to grind food into small pieces so it can be safely swallowed.

Symptoms: Over time, these chewing muscles can weaken, and dental arches and other mouth structures may be affected. Changes in bite force, speech, and other dental abnormalities can affect how well food can be ground down and swallowed.

Treatments: Regular dental visits can keep teeth at optimal health and functioning at their best.
SWALLOWING

**Healthy Function:** Muscles in the mouth, such as the tongue, and muscles in the throat work together to transfer food down through the esophagus toward the stomach.

**Symptoms:** Because it’s a muscle, the tongue may become enlarged and weakened over time. Weakened swallowing muscles extending down through the esophagus may impact safe and complete swallowing, also known as “dysphagia.”

**Treatments:** If swallowing problems are suspected, your doctor can refer you to a Speech Language Pathologist (SLP) for evaluation.
ESOPHAGUS & STOMACH

**Healthy Function:** Muscles in the esophagus move food toward the stomach. A muscular “sphinicter” connects the esophagus to the stomach allowing food in and functions as a barrier to keep stomach acids contained.

**Symptoms:** As the muscular sphincter weakens, gastroesophageal reflux (or heartburn) occurs when stomach fluids move back up into the esophagus. Steroids can increase gastric acid, compounding the problem. Delayed emptying of the stomach into the small intestine causes slow and uncomfortable digestion.

**Treatments:** These problems can be improved with diet modifications and medications prescribed by your doctor.
**SMALL & LARGE INTESTINE (BOWEL)**

**Healthy Function:** Abdominal wall muscles and smooth muscles in the small and large intestine (bowel) are responsible for absorbing nutrients in food.

**Symptoms:** Slowed smooth muscle movement delays digestive movement, and as people become increasingly less active, bloating and constipation can become problematic.

**Treatments:** Maintaining a healthy diet with plenty of fiber and liquids can prevent constipation and keep the digestive system functioning at its best. Guidance from a Registered Dietician (RD) and taking consistent measurements of height, weight, and BMI will help ensure that a healthy weight is maintained.
Evidence suggests that there are changes in dystrophin levels in specific brain structures associated with learning, behavior, and emotional responses. This can lead to challenges that affect day-to-day activities at school, work, and at home. In addition, steroid treatments can exacerbate these behaviors.

People living with Duchenne may experience cognitive or learning difficulties, neurodevelopmental disorders, and problems with emotional adjustment.
COGNITIVE FUNCTION

**Symptoms:** People living with Duchenne may experience cognitive or intellectual issues, including language delays, learning disabilities, and problems with working memory or processing information.

**Treatments:** Early evaluation from a professional – such as a clinical neuropsychologist, child psychologist, or special education expert – is recommended to properly diagnose specific conditions and can recommend interventions to help with school performance.
NEURODEVELOPMENTAL

**Symptoms:** Individuals living with Duchenne have an increased risk for neurodevelopmental disorders such as attention-deficit/hyperactivity disorder (ADHD), autism spectrum disorders (ASD), oppositional/defiant or aggressive behavior, or sensory processing disorder.

**Treatments:** It is recommended to consult with a mental health or behavioral therapist about neurodevelopmental disorders. Therapy, behavioral modification plans, and in some cases, medication can help with these behaviors and improve school and home and social routines.
**EMOTIONAL**

**Symptoms:** People living with Duchenne may be at risk for emotional problems including anxiety, OCD, and depression.

**Treatments:** Depression and anxiety are serious conditions and should be treated by mental health professionals. Psychotherapy and medication, if recommended, can help people suffering from emotional problems and improve quality of life.
GROWTH & DEVELOPMENT

The Endocrine System is a series of glands that produce chemical messengers, called hormones, that are responsible for regulating many of the body’s systems. In Duchenne, steroids are considered the gold standard of treatment as they can improve muscle strength and function. However, over time, using these steroid medications can lead to endocrine issues.

Although you can’t physically see hormones, they are responsible for growth, puberty and sexual development, glucose metabolism, and more.
CORTISOL

Healthy Function: Cortisol, known as the stress hormone, is produced by the adrenal glands in response to serious injuries or infections. It controls many body functions, including blood sugar levels, regulating metabolism, and reducing inflammation.

Symptoms, Treatments & Risks: The benefits of steroid medications often outweigh the risks associated with side effects, and are usually prescribed to be taken daily. Steroids are synthetic versions of cortisol, and can cause side effects such as weight gain, weak bones, and delayed growth and puberty.

If these side effects are unmanageable, other dosing regimens (for example, weekend dosing) may be explored. Over time, the body stops making its own cortisol. Thus, it’s dangerous to suddenly stop taking steroids, miss daily doses for more than 24 hours, or fail to take a stress dose when indicated.
GROWTH HORMONE

**Healthy Function:** Growth hormone, produced by the anterior pituitary gland located in the brain, acts on the body to promote growth and development in children.

**Symptoms & Treatments:** Steroid medications prescribed for Duchenne have the potential to affect growth hormone in some people, which results in slowed or stopped linear growth. It’s important to monitor a person’s height and weight at each clinic visit to track growth over time.

If growth is slowing, or a person has a short stature, it’s important to visit an endocrinologist for a growth hormone test. If a person is found to deficient in growth hormone, supplemental growth hormone (GH) may be discussed. GH can improve growth, but does not guarantee normal height.
TESTOSTERONE

Healthy Function: Testosterone is produced by the reproductive organs and is responsible for pubertal development in boys. Testosterone also increases bone density to strengthen bones in men.

Symptoms: Prescribed steroid medications have been shown to negatively affect testosterone production in boys living with Duchenne, causing delays in puberty and sexual development.

Treatments: If puberty is delayed past age 14, or if the person living with Duchenne is distressed over the lack of sexual development, a referral to an endocrinologist is recommended. If testosterone levels are found to be low, testosterone replacement therapy may be recommended.
YOUR BODY’S LIKE A HOUSE

Duchenne is multi-systemic, affecting not only body mechanics and movement, but also breathing, heart health, digestion, growth, mental health, even learning and behavior. There is a lot to understand as a new patient or caregiver and it’s easy to become overwhelmed.

Parent Project Muscular Dystrophy is here to help.

TO LEARN MORE ABOUT CARING FOR DUCHENNE, CURRENT RESEARCH AND ADVOCACY EFFORTS, PLEASE VISIT www.endduchenne.org
JOIN THE FIGHT.
END DUCHENNE.
Emergency Information

www.parentprojectmd.org/supportmaterials

STERIODS
Remember to tell your doctor if your child is on steroids. If severe trauma or unable to take daily corticosteroids for 48 hours, go to the ER and ask that IV corticosteroids are given until pills by mouth are tolerated (6 mg of deflazacort equals 5 mg of Prednisone). Bring the PJ Nicholoff Steroid Protocol (parentprojectmd.org/pj). Stress doses may be needed for moderate/severe stress on the body.

ANESTHESIA PRECAUTIONS
If possible, inhaled anesthesia should be avoided. IV anesthesia is considered safe with close monitoring. Succinylcholine should NEVER be used. Local anesthesia and nitrous oxide are generally safe for minor dental procedures.

GENERAL RECOMMENDATIONS
- Keep immunization up to date & get influenza (flu) vaccine annually. Always wear seat belts in the car AND in chairs/wheelchair/scooter/shower chairs.
- 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:

NEUROMUSCULAR CENTER EMERGENCY NUMBER:
Q&A Panel
Moderated by Jonathan Finder, MD

• Elena Caron, MD (Le Bonheur Children’s Hospital) – Neurology
• Jonathan Finder, MD (Le Bonheur Children’s Hospital) – Pulmonology
• Hugo Martinez, MD (Le Bonheur Children’s Hospital) – Cardiology
• Aravindhan Veerpandiyan, MD (Arkansas Children’s Hospital) – Neurology
• Seth Sorensen, PhD (Arkansas Children’s Hospital) – Neuropsychology