Transcript Details
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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Duchenne Muscular Dystrophy Management: Analyzing Current Approaches

Announcer:
This is *NeuroFrontiers* on ReachMD. On this episode, we'll discuss current treatment options for Duchenne muscular dystrophy with Dr. Nancy Kuntz. Dr. Kuntz is an attending physician at the Ann and Robert H. Lurie Children's Hospital of Chicago and the Medical Director of the Mazza Foundation Neuromuscular Program. Let's hear from her now.

Dr. Kuntz:
There are two categories of treatment for Duchenne muscular dystrophy. The first is just general symptomatic treatment that isn't directed toward the specific gene mutation. So, for example, we can keep boys active and exercising to prevent contractures developing at heel cords, which cause them to toe walk and be less stable at the knees and hips in response to the proximal weakness that gives them lordosis and a crouch in the posture. The flexion of those joints allows a child to keep their center of gravity over their feet and decreases the chance of falling, so we use physical therapy and exercise to stretch the heel cords and keep the muscles as toned as possible. And then it turns out we can use a corticosteroid therapy to decrease the inflammation that is caused by the leakage of the muscle membrane.

But one of the most exciting things in recent years has been the development of some disease-targeted therapies that are very specific to the exact mutation. So currently, one of the most important things that you can do once you suspect a diagnosis is to get the gene mutation analysis done, because there are certain treatments that are appropriate for certain types of mutation and not others. In addition, there are some exon-skipping mutations that can take groups of mutations—of the many hundreds of different types of mutations that are seen in Duchenne muscular dystrophy—that might respond to taking out another exon, either at the beginning or ending of that string of absent exons. And what that can sometimes do is reinstate the reading frame so that you will be able to get a protein, even if it's a slightly shortened one. And so exon skipping started with exon 51 skipping, which about 15 percent of the mutations respond to, and it has progressed so that we now have commercially available exon 51, exon 53, and exon 45 skipping. And there are several other exon-skipping agents that are being studied in clinical trials right now.

And then finally, there are five scientific teams around the world who are looking at ways of generating a microdystrophin that can be used for gene replacement therapy. One of these has been commercially approved, and the other four are being studied actively right now. The reason I said microdystrophin is that the very best technique that people have for gene replacement involves viral vectors, and the largest viral vector that has been developed successfully for this purpose is something that can only hold one third of the volume of the entire dystrophin gene. So the microdystrophin types are created by selecting what scientific groups think are the most important functional portions of the dystrophin gene.

There are some mutations that cannot have the gene replacement because there is an increase in immunogenicity between that particular deletion and the replacement gene product. And, in addition, if children already have natural immunity from community exposure to the viral vector that's been used to develop the replacement gene, they cannot have the dosing, which would involve treatment with one times ten to the fourteenth times their weight in kilograms of vector genome copies, creating an unacceptable and overwhelming immune response. So we're still in the infancy where there's a lot of science and promise, but we do not yet have a cure for Duchenne muscular dystrophy.

Announcer:
That was Dr. Nancy Kuntz discussing the therapies currently available for Duchenne muscular dystrophy. To access this and other episodes in our series, visit *NeuroFrontiers* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!