

Health Plans: Lacking Cure, a New Tack on a Muscle Disease

Mark Lyons for The New York Times, 20th February 2008

Anthony Hoel, now 18, walking with the aid of leg braces at Cincinnati Children's Hospital. On the most recent telethon, which was staged in Las Vegas and raised \$63.8 million, the "Law and Order" actress Mariska Hargitay spoke of patients' "hope that M.D.A. research will lead to treatments and cures." Mr. Lewis, who has never disclosed why he chose this disease as his cause, once again closed the broadcast with an emotional rendition of the song "You'll Never Walk Alone."

But for all the money collected toward a cure, Duchenne muscular dystrophy, the most common form of the disease, still confines thousands of boys in this country to wheelchairs in their early teens. Many do not live past their 20s. It is a stark reminder of how American medicine — with its focus on breakthrough treatments — can sometimes fail a complex, rare and stubbornly incurable disease. Single-minded in their pursuit of a cure, doctors and researchers for years all but ignored the necessary and unglamorous work of managing Duchenne (pronounced doo-SHEN) as a chronic condition.

The approach is changing at a few medical centers, which are focused on making better use of available therapies to eke out longer lives for their patients. Rather than concentrate only on a cure, some researchers are now intent on developing drugs that may alleviate the effects of the disease. But, absent a cure, too many doctors around the country still assume there is little or nothing that can be done for the muscle-wasting condition, parents and specialists say. "We're in a stone age with Duchenne," said Dr. Linda H. Cripe, a pediatric cardiologist at the Cincinnati Children's Hospital Medical Center. She describes Duchenne patients as "a group of kids that pediatric medicine had forgotten, a group of lost boys."

Among those is Josh Winheld, who years ago served as the Muscular Dystrophy Association's poster boy in Southeastern Pennsylvania. Now, at age 29, Mr. Winheld is among the oldest Duchenne patients seen at the Children's Hospital of Philadelphia, in part because of the unusually close oversight of his doctors. But the recent discussion of new drugs, however promising, holds little hope for him because he is already almost completely paralyzed. "I feel totally lost," he said. Using a ventilator to help him breathe and a defibrillator to regulate his heart, and nourished by a feeding tube, he is able to move his head and operate his motorized wheelchair with a slight movement of his fingers. He lives outside of Philadelphia with his parents and requires around-the-clock care. His medical expenses are covered by a combination of his parents' private insurance and state assistance.

Duchenne is caused by a mutation of the gene for dystrophin, a protein in muscle. The disease occurs almost exclusively in males, about once in every 3,500 live births, and occurs about a third of the time when there is no family history of the disease. With the discovery of the gene in 1986, most of the research attention and financing focused on gene therapy — coming up with a way to cure the disease by replacing the defective gene. "There was great hope at the time," recalled Mr. Winheld, who has his own blog (winheldsworld.blogspot.com) and is publishing his memoirs. "We always thought 'cure.'" But the size of the gene and the variety of mutations have made even diagnosis problematic and researchers are now looking elsewhere for an answer. The lack of interest in the mundane has also slowed progress in knowing what available therapies are the most useful. Large pharmaceutical companies often ignore a rare disease like Duchenne, and they are unwilling to undertake further research into treatments like steroids, where any benefits they show are shared by other

manufacturers. "The economics aren't there," said Charles Farkas, head of the health care practice in the Americas for Bain & Company.

The current focus has changed to trying to identify the patient's mutation and then using a cocktail of different drugs tailored for that specific mutation. "For too long, I was stuck on it as the home run or nothing," said H. Lee Sweeney, a professor and medical researcher at the University of Pennsylvania School of Medicine, who is among the researchers now taking a different approach. "The home run may skip the next two generations of these kids," he said. Others are pushing doctors to focus on making the best use of what therapies are now available. "For a very long time, this disease was no hope and no help," said Patricia Furlong, founding president of Parent Project Muscular Dystrophy, a nonprofit group in Middletown, Ohio, who lost two sons to the disease. Her group has been instrumental in prodding doctors to concentrate on helping existing patients.

And it is often the parents who insist the doctors keep trying. Two years ago, a 16-year-old Duchenne patient named Anthony Hoel stopped walking. His doctors in Minneapolis assumed there was nothing they could do and told Anthony's father, Tom, to accept the fact that his son would be in a wheelchair. The doctors "were content to follow the old rule book," said Tom Hoel. About a week after corrective surgery and extensive rehabilitation at Cincinnati Children's Hospital, Anthony, now 18, walks with the aid of leg braces. "He is a real success story," said Dr. Brenda Wong, Anthony's doctor at Cincinnati.

The challenge for Josh Winheld's doctor, Richard Finkel, in caring for someone whose disease is advanced is to keep a close watch on his patient so he can quickly address any problems. During a recent visit, for example, a nutritionist went over Josh's diet, making sure he got enough calories but not too much liquid to stress his heart, while Dr. Finkel examined Josh carefully and tried to determine if there were any changes in his condition.

Dr. Finkel is also among the doctors studying a new drug aimed specifically at a mutation that causes about 15 percent of the cases. Clinical trials for the drug, PTC124, are expected to begin enrolling patients early this year. To date, the greatest progress has been through the use of steroids. But exactly when steroids should be started, which work best and how best to manage the side effects still remain unclear. And unlike their counterparts in cystic fibrosis, a disease where specialists have successfully stretched life expectancy for patients well into their adulthood, doctors have been slow to develop clear standards of care and aggressively track the results of varying treatments to determine how best to manage the disease. "We've had the tools, and we haven't used them as effectively," acknowledged Dr. Finkel. The result is that patients are often treated much later than they should be, with some doctors referring a patient to a cardiologist only after he has developed heart failure or waiting too long to start a patient on steroids.

The Muscular Dystrophy Association, which raises tens of millions each year through Jerry Lewis's telethon and other efforts, has also been criticized for a lack of focus on the specific needs of patients with Duchenne. The organization finances some 225 clinics across the country, including the one at Children's Hospital of Philadelphia. While Duchenne is the most common of the dystrophies, the association also raises money and provides services for more than three dozen conditions, including amyotrophic lateral sclerosis, or Lou Gehrig's disease. The association has no direct oversight of the clinics, some of which may have little experience in treating a patient with Duchenne. Dr. Valerie A. Cwik, the association's medical director, says the group is now working to create a formal research network to gather and share information about Duchenne. "People have recognized there are gaps in our knowledge of this disease," she said.

There is also a federal effort under way to draft recommendations to treat Duchenne. The Centers for Disease Control and Prevention says these recommendations are likely to be made public late this year or early next year. "That is going to go a long way to standardize care," Dr. Cwik said. And even as experts say there is significant promise in some of the new drugs being studied, doctors like Dr. Wong at Cincinnati say they need to remain committed to making the seemingly small advances that buy patients like Anthony Hoel more time on his feet, or give Josh Winheld a chance to complete his graduate degree once his memoirs are published. "The outcome can be changed if you tweak little, little details," Dr. Wong said.