Orphan Diseases: where are we now

By Heather Claverie

IT'S 1980 AND Adam Seligman has just hit a wall. At the time, the drugs necessary to treat the teen's Tourette's syndrome were unavailable in the United States. So Seligman turned to our neighbors to the North, ordering the medication from a Canadian doctor. When the drugs were seized at the border, Seligman's mother contacted her congressman, Rep. Henry Waxman, D-Calif., and relayed her son's story.[1] Soon, the cause of rare diseases, or so-called orphan diseases, made its way from California to Capitol Hill, and a mother's crusade to help her son receive some much-needed medicine morphed into quite the Hollywood story.

Before awareness-raising events like the Ice Bucket Challenge and social media, many of the diseases Americans are now familiar with were completely foreign. These so-called orphan diseases — primary immunodeficiency, chronic inflammatory demyelinating polyneuropathy (CIDP), polymyositis, Sjögren's syndrome, Lou Gehrig's disease and many more — were, and still are, so rare that few companies were willing to dedicate resources to develop the pricey drugs that were bound to yield low profit margins. While scientists had discovered some promising treatments, companies declined to seek approval from the U.S. Food and Drug Administration (FDA). As such, these potential treatments, or orphan drugs, sat abandoned, and the rare diseases they were designed to help were soon referred to as orphan diseases.

Orphan diseases are defined as any disorder affecting fewer than 200,000 Americans. An orphan drug is one that is intended to treat fewer than 200,000 Americans or one that treats a disease that affects more than 200,000 people but the company developing and marketing the drug doesn't expect to recoup the costs of research and development.[2] There are currently between 6,000 and 7,000 orphan diseases affecting nearly 30 million Americans, or less than 1 percent of the population.[3] And, half of the diseases affect children.[4]

The Orphan Drug Act of 1983

Before 1983, individuals suffering from rare diseases stood at a dead-end road. Because such a small percentage of the population suffers from these diseases — some affect as few as 150 Americans — pharmaceutical companies before 1983 were reluctant to invest time and resources to develop these pricey prescriptions, which can cost hundreds of thousands of dollars per year. Still, the obscure topic wasn't exactly a hot-button issue. Enter Seligman and Rep. Waxman. Seligman's story tugged at the congressman's heartstrings, so Rep. Waxman convened a hearing to learn more about the issue.

A reporter from the *Los Angeles Times* was the only media presence at the hearing. After his story ran, it caught the eye of Jack Klugman, star of the 1980s crime drama "Quincy, M.E." and co-star of "The Odd Couple." Klugman and his brother, Maurice, a writer and producer who suffered from a rare form of cancer, decided to use their show as a platform for awareness, writing Tourette's syndrome and the orphan drug problem into an episode of Quincy.[5] Klugman then headed to Washington, D.C., to testify before Congress, where his prowess shined a spotlight on the issue and *The New York Times* ran a front-page article on orphan drugs, turning the previously little-known topic into national news.

During the hearings, at which witnesses from FDA, National Cancer Institute, Pharmaceutical Research and Manufacturers of America and many drug companies testified, it was discovered that there were 134 drugs developed for rare diseases, yet only 47 were approved for use by FDA, and only 10 had been developed and marketed solely by pharmaceutical companies. One witness in particular, Dr. J. Richard Crout, then director of the U.S. Bureau of Drugs, testified that the major problems with orphan drugs were patentability and liability. In essence, because the drugs were designated for such a small population, developing them was a risk for companies since so few individuals were available for clinical trials.[6]

Eventually signed into law by President Reagan on Jan. 4, 1983, the Orphan Drug Act of 1983 provides financial incentives to drug companies willing to develop treatments for rare diseases or conditions. If a drug is granted orphan status, the act provides the following: federal funding of grants and contracts for clinical trials, a tax credit of 50 percent of clinical testing expenses paid or incurred during the year, and exclusive marketing rights for seven years from the date of FDA approval.[7]

Today, more than 3,000 products are designated as possible treatments for orphan diseases, with more than 450 approved by FDA for clinical use, according to the National Organization of Rare Disorders (NORD), a nonprofit dedicated to assisting individuals with rare diseases through advocacy, education and research.

Orphan Disease Obstacles

More than three decades have passed since the signing of the Orphan Drug Act, yet many obstacles remain for individuals suffering from orphan diseases. "I think the challenge for all of us in the community now is to figure out how we translate this great research into safe, effective treatment for patients," said Mary Dunkle, vice president of communications for NORD. "There's a great sense of urgency in the community. In many cases, the patients are children, so there's always this feeling that the clock is ticking."

Spending years hopping from physician to physician is the hallmark of patients suffering from rare diseases. Many are misdiagnosed, and some, like Barbara Fowkes, are even told it's a mental, not a physical, issue. "They diagnosed me with rheumatoid arthritis, Sjögren's and fibromyalgia, and 'it's all in your head,'" said Fowkes.

When the Pennsylvania resident one day found herself so weak she was unable to open her car door, she knew it had to be something else. Fowkes was eventually diagnosed with CIDP. "You have to be your own advocate throughout the whole process," she said. "Even after your diagnosis, I tell people 'never stop being your own advocate.'"

Fowkes, who serves as a liaison for the GBS/CIDP Foundation International, said that since there are so few individuals suffering from these orphan diseases, it's paramount to seek out an organization that specifically serves the communities associated with these rare diseases. And, she encourages anyone having a difficult time receiving a diagnosis to head to a teaching hospital in an urban area. Since teaching hospitals are affiliated with a university, physicians tend to be more open to possibilities and have more experience with rare diseases.

The Future of Orphan Diseases

It's still too early to say exactly how the Affordable Care Act will impact those suffering from orphan diseases. Eliminating discrimination of those with pre-existing conditions is one aspect of the law that helps those with orphan diseases. But, there are many concerns as to how the Act will affect the research and development of these pricey drugs. Still, there is some good news. The plummeting cost of sequencing DNA could lead to the development of more drugs and help drop prices. In addition, some companies have found a way to turn major profits from the development of orphan drugs, which is likely to entice more pharmaceutical companies.[8] And, because the pool of insured individuals has increased under the new law, these niche drugs are bound to become more commercially viable, enticing current and future developers of orphan drugs.

In the meantime, organizations like NORD will continue to promote awareness through a variety of outlets. The nonprofit funds between five and 10 research grants a year. On the last day of February, Rare Disease Day is staged.

On the legislative front, Congress launched the initiative 21st Century Cures in April, with the goal of accelerating the pace of cures and medical breakthroughs in America. NORD has provided personal testimony for the initiative, bringing the issues of orphan diseases to the congressional table. ■

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