On Rare Disease Day, Lancet's Spotlight Offers Needed Shine

By Jamie Wells, M.D. — February 28, 2019

The theme for this year’s Rare Disease Day is “bridging health and social care” and *The Lancet Diabetes & Endocrinology* [2], in addition to featuring the topic throughout its February issue, provides a worthwhile spotlight on glaring aspects not often addressed. There is a lack of universal awareness that the term “rare disease” does not do the societal impact justice, so it is essential to clarify the surrounding confusion, understand the healthcare and personal burdens and showcase what is hopeful and what is in need of a fix.

As the *journal* [2] accurately reflects,
“More than 6000 rare diseases (80% with a genetic component) affect more than 300 million people worldwide. While an individual disease might be classed as rare (defined as affecting less than 1 in 2000 of the general population in the European Union or fewer than 200,000 people in the USA), the sheer number of rare diseases means that the overall numbers quickly stack up: 3.5 million people in the UK, 30 million across Europe, and 30 million in the USA are affected. Whether a single rare disease affects thousands or just one person, the impact on the affected individual and those around them can be devastating: 50% of rare diseases affect children, 30% of whom will die before age 5 years.”

These conditions can be additionally challenging because there is often little information available on a particular disease, the financial costs are high and patients are often “difficult [3] to diagnose and manage because in their early stages, symptoms may be absent or masked, misunderstood, or confused with other diseases.”

Some background

You may recall President Donald Trump [4] in 2017, while addressing a joint session of Congress, highlighted the presence of 20-year old Notre Dame sophomore Megan Crowley, who is afflicted with Pompe disease. Pompe disease results from mutations in the GAA gene which prompt an inability of the body to break down the complex sugar called glycogen. That resulting buildup, especially in muscles, prevents them from functioning normally. It’s an inherited disease and relatively rare.

According to the National Institutes of Health [5], Pompe disease affects about 1 in 40,000 people in the United States while all glycogen storage diseases affect 1 in 20,000. Compare that to the 40,000 women [6] who will die from breast cancer and you can see why it doesn’t get as much attention. These smaller population “Orphan Diseases” [3], defined as those that affect less than 200,000 people across the nation, include conditions like Cystic Fibrosis, ALS, acromegaly (aka gigantism) and Tourette’s Syndrome. But they collectively impact 25 million Americans [7], a substantial public health issue.

A big reason why rarer diseases get fewer treatments is because we have a regulatory process that forces business decisions to go for the "home run." However, there is already a faster route for "orphan" drugs, which helps to bypass the financial obstacles of getting ordinary approval. President Reagan signed the Orphan Drug Act in 1983 [3] in an attempt to incentivize discovery. And to some extent, it has worked. According to the U.S. Food and Drug Administration (FDA [3]) more than 250 drugs “available to treat a potential patient population of more than 13 million Americans” have become available in the three decades since it became law. But is about 9 a year really good? Some have argued that the regulatory process is still crippling discovery because of the government hurdles before human trials can begin. Patient advocacy groups have emerged—especially in these decades—and served to increase awareness while directly advancing the research (1).
Fortunately, this appears to be a priority of the current FDA Commissioner Scott Gottlieb as one of his earliest actions in the job involved eliminating a backlog of roughly 200 orphan drug designation requests that were pending review. To learn more, read *FDA Closing Loopholes That Game Orphan Drug Act* [8]. To understand further why these conditions are so important to understand, raise awareness about and divert resources for in order to advance therapeutic and potentially curative research, read *Pompe Disease, Newborn Screening And Inborn Errors Of Metabolism* [9].

**What Lancet Gets Right**

The authors [2] aptly address the many struggles individuals and families endure,

> "While coordination between health and social care undoubtedly needs to be improved, radical new strategies to fund research and do clinical trials for rare diseases that affect only a handful of patients (too small a market to be commercially viable) need to be developed, repurposing of existing drugs for the treatment of rare diseases must be maximised, and the situation where drugs are developed but no one can afford them avoided. Above all else, we should recognise that, although these diseases might be individually rare, the challenges they pose for patients, families, and carers are common to millions of people worldwide."

In their call-to-action [2], they “address the unmet need for subspecialty training” [10] in adult rare (inherited metabolic) diseases, which is crucial given that 50% of rare diseases present in adulthood and children surviving rare diseases eventually transition to adult care.” This response is actually good news. Modern medical advances have impacted survival rates in many instances. Whereas in the past, a patient might not have made it into adulthood, now this is happening - enough to be hopeful, not enough to be complacent. So, pediatricians often are tasked with treating adults with such rare diseases since they are the most knowledgeable on the subject matter. With respect to these types of disorders, it is quite common for adult practitioners never to have met a patient with a particular condition. Or, for a patient (and family) to incur great expense and inconvenience to access care by the one person in their region who treats a particular disease.

**In the end**

There is a lot of promising attention currently focused on this topic and a shifting pendulum appears to be emphasizing expediting diagnosis and treatments. But, this is a marathon not a sprint. As we take the day to value the many achievements, we must gear up for a continued, arduous multi-system battle to make even more meaningful strides.

**Note:**

(1) It doesn't take a president. Sometimes national attention comes from other parts of culture. Though Parkinson’s disease was long known, it got a highly visible champion when a young Michael J. Fox, in the prime of his career, was diagnosed with it. Since 2000, his foundation has raised and spent $700 million
an amount only superseded by the government and private sector.

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