

Biologics: How Animal Testing Has Improved the Treatment of Ulcerative Colitis

I walked into the kitchen; blood was splattered on the floor. I yelled for my parents but the house was empty. I followed the blood to the back door and out into the garage, where I saw my parents pulling away, my dad holding a rag to his hand. Twenty minutes later I received a phone call. My mom told me my dad had punctured his wrist while working on the roof. He was given a prescription for the antibiotic Keflex and six stitches. We thought everything was fine. Within five days of taking the Keflex my dad became very sick. Within six weeks, he had lost almost twenty pounds, could no longer go to work, and was hospitalized for dehydration. He was tested twice for Clostridium Difficile (C. Diff), and both tests came back negative. When he was released from the hospital, he switched to a new doctor. The new doctor re-ran the C. Diff test. The test came back positive.

A C. Diff infection occurs when good bacteria in your intestines is killed off causing harmful C. Diff bacteria to overgrow. Most healthy people do not develop C. Diff from antibiotics. However, my dad developed C. Diff because he has Ulcerative Colitis (UC), which makes him susceptible to a C. Diff infection. UC is an autoimmune disease that causes ulcers to develop in a patient's colon. Physicians first described UC in the late 1800's. At the time of discovery, UC had a mortality rate of 30-60% (ScienceDirect). Although UC was identified approximately 150 years ago, there are still minimal medicinal treatment options for severe cases and no definitive cure other than surgical removal of the colon. The goal of most medical therapies is to force the disease into remission. Until the 1950's, UC patients suffered due to lack of options. With the development of corticosteroids through animal testing, there was a new treatment option for forcing UC into remission. Upon the introduction of steroids, the mortality

rate dropped to 1% (ScienceDirect). However, patients who remain on steroids for long periods of time suffer severe side effects. Researchers had to work on developing new treatment options. By chemically inducing colitis in animals, biologics were created. Biologics are medications made out of real life materials, such as proteins and nucleic acids. One of the original biologics was Remicade, which was approved by the FDA in 2005. Since then additional biologics have been approved for the treatment of UC, such as Entyvio and Humira.

My dad was prescribed two rounds of Vancomycin (another antibiotic), which treated the C. Diff. However, the C. Diff infection increased the severity of his UC. For the past year, my dad has tried various medical therapies to force the disease into remission. He first used Prednisone, a corticosteroid. The corticosteroid decreases inflammation and suppresses the immune system. These drugs have improved his symptoms but not forced him into remission. He then tried Remicade, which is an anti-tumor necrosis factor agent. This drug blocks the development of a protein called tumor necrosis factor (TNF-alpha) that causes inflammation in the body. Remicade did not, however, trigger remission. In the next two weeks my dad will try a new biologic, called Entyvio. Entyvio is meant for people who did not respond to anti TNF-alpha agents. Entyvio prevents the interaction of an integrin receptor with a protein, which blocks inflammatory cells from moving into the gastrointestinal tract.

All of the medications described above: Keflex, Vancomycin, Prednisone, Remicade, and Entyvio have been tested on animals. With respect to biologics, researchers chemically induce colitis in animals, specifically mice, which allows them to understand the functions of the disease and target certain proteins or cells to fight off the disease. Mice are valuable tools in research because their DNA is similar to humans. However, many are concerned with the safety and

welfare of animals being tested. They are concerned that animal testing is cruel, invasive, and causes pain. The Animal Welfare Act of 1966 was enacted to protect lab animals. In addition many research labs have their own moral and ethical standards, which includes providing pain relief for animals receiving treatments. Without animal testing to target treatments, and analyze the effectiveness of medication, researchers would be unable to determine how drugs affect a whole living body, which is much more complicated than the individual parts. The discovery of new drugs, such as biologics, through animal testing has given hope to all patients with Ulcerative Colitis, such as my dad.

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