

DIA Then and Now: A Half-Century Odyssey

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As I considered potential topics for this Editorial, the first one written since attending our Americas Annual Meeting in Chicago in June (our publishing schedule required my July article to be written before the meeting even though it appeared in print afterwards), my excitement from multiple aspects of the meeting remained palpable. Something else remaining fresh in my memory was the brief discussion in my July article¹ of FDA's Dr Frances Kelsey and her role in the early 1960s in preventing the drug thalidomide from receiving marketing approval in the United States. Her story is deserving of more detail here, not just for its importance in the history of regulatory oversight of drug safety and marketing decisions but also for its role in the founding of DIA. The title of this article therefore suggested itself.

Dr Frances Kathleen Oldham Kelsey was born in 1914 in Canada.² She obtained her Bachelor and Master of Science degrees from McGill University and her PhD from the University of Chicago. She joined the FDA in 1960. After just 1 month at the agency, and still on her first assignment, she declined to approve the marketing of thalidomide in the United States as a result of becoming concerned by data that suggested untoward effects in individuals taking the drug repeatedly. Despite considerable pressures, she continued to withhold marketing approval.

In November 1961, reports from Germany and the United Kingdom started to emerge that mothers who had taken thalidomide during pregnancy were having babies with severe birth defects. Thalidomide was first marketed in 1956 in Germany for the treatment of insomnia and vomiting in early pregnancy. During 1961, a sizeable increase in the incidence of certain congenital birth defects was observed. The defects were typically an absence or reduction of the long bones of the limbs with normal or rudimentary hands and feet. The association of these conditions with the drug was not recognized for several years after the drug was marketed in Europe, and hence several thousand affected babies were born. Dr. Helen Taussig, perhaps best known as the founder of pediatric cardiology for her innovative work on "blue baby" syndrome and who had her own distinguished career including teaching at Johns Hopkins University,³ learned of the tragedy and traveled to Europe to investigate. Upon her return to the United States she testified before the Senate, helping Dr Kelsey to cement her initial efforts by permanently preventing the drug from being indicated for morning sickness. (Thalidomide is currently approved and indicated for the treatment of multiple myeloma and severe

erythema nodosum leprosum, but its prescribing information contains a boxed warning for embryo-fetal toxicity and venous thromboembolism: the drug also has an associated Risk Evaluation and Mitigation Strategy.⁴)

On August 7, 1962, Dr Kelsey was awarded the President's Award for Distinguished Federal Civilian Service by President John F. Kennedy: this is the highest honor given to a civilian in the United States. The President commented as follows: "Her exceptional judgment in evaluating a new drug for safety for human use has prevented a major tragedy of birth deformities in the United States. Through high ability and steadfast confidence in her professional decision she has made an outstanding contribution to the protection of the health of the American people."² Shortly thereafter, on October 10, 1962, President Kennedy signed into law the Kefauver-Harris Amendments to the US Federal Food, Drug, and Cosmetics Act of 1938. These Amendments had been under consideration for some time, and the thalidomide tragedy was instrumental in them being finalized.

DIA was founded just two years later, in 1964, as a "neutral global membership association dedicated to improving communication and collaboration in drug development."⁵ It was realized by a small group of 30 pharmaceutical professionals, medical writers, and academics that thalidomide was an example of a global issue for which no organization at the time "could foster cooperative efforts across the entire world," and hence they created DIA as a fully independent, unbiased, non-profit association.⁵ Fast forward a half-century, and DIA is now a vibrant worldwide organization with thousands of members. The global nature is reflected by regional offices covering the Americas, Europe, Asia, the Middle East, and Africa. The neutral posture of DIA encourages active participation: it is the only global organization dedicated to bringing health care professionals together in a trusted, global, neutral environment to share insights and drive action in health care product development and life cycle management. Because membership spans all aspects of health care product development and life cycle management, members are free to collaborate fully as they explore fresh ideas and think outside of their traditional fields.⁵ And, with regard to annual meetings, three statistics from June's meeting (a fourth will follow shortly) testify to our success: we had 132 scientific posters presented, we held 252 sessions, and over 40 spotlights were published in leading industry publications.

After commenting on “then” and “now,” let’s also consider some of the things that occurred during that time: the potential list is enormous, and so I’ll limit myself to examples from scientific and educational domains (with the exception of noting that Elvis Presley visited President Richard Nixon in the White House in December 1970!). Thanks to incredible scientific work, Neil Armstrong and Edwin “Buzz” Aldrin landed on the moon in July 1969. Following that came fiber optics, the personal computer, large-scale integrated circuit development and supercomputers, the Internet and the worldwide web, and the launch of the iPhone in June 2007. The interconnectedness facilitated by these electronic developments leads nicely to the fourth statistic about June’s meeting: we had over 20 million touchpoints on social media.

The transition to educational considerations occurs fairly naturally here since the two individuals I’ll mention are also scientists: we’ll consider their scientific accomplishments first. During the last 10 years I have had the privilege and pleasure of meeting two Nobel Laureates, Dr Richard Roberts (who shared the prize in Physiology or Medicine in 1993 for the discovery of split genes)⁶ and Dr Robin Warren (who did so in 2005 for the discovery of the bacterium *Helicobacter pylori* and its role in gastritis and peptic ulcer disease).⁷

In the mid-1970s, it was generally accepted that genes existed as continuous segments within a DNA molecule. This view changed radically with the discovery in 1977 that, in higher (eukaryotic) organisms, an individual gene can comprise multiple DNA segments separated by chunks of noncoding DNA, that is, there are protein-coding (exon) and noncoding (intron) regions within a gene. A typical human gene has 8 to 10 introns lying between the exon coding sections. (At the extreme end of the scale, the human gene dystrophin is spread across approximately 2.4 million base pairs and has 79 introns separating the coding sections.) An elegant editing process called RNA splicing removes non-coding chunks of genetic material and connects the relevant segments together to create messenger RNA. Messenger RNA then ensures that amino acids are successfully made. Amino acids are joined together in various sequences to make proteins.

After their independent discoveries of split genes in 1977, Dr Roberts and Dr Philip Sharp waited 16 years until receipt of the Nobel Prize. Such a wait is not atypical (and is by no means the longest: Frederick Reines detected the neutrino in 1957 and shared the Nobel Prize in Physics 38 years later in 1995, while Ernst Ruska invented the electron microscope in 1932 and waited over fifty years to share the Nobel Prize in the same category in 1986).⁸ No matter how brilliant and subsequently influential a discovery is, that influence has to become widely acknowledged before prizes are awarded (even James Watson and Francis Crick had to wait 9 years following their proposal of the structure of DNA in 1953⁹ before sharing the 1962 prize in Physiology or Medicine with Maurice Wilkins). As was noted in the Award Ceremony

Speech before Drs Roberts and Sharp received their awards in Stockholm in 1993, “The discovery of split genes was revolutionary, triggering an explosion of new scientific contributions. Today this discovery is of fundamental importance for research in biology as well as in medicine.”⁶ This statement continues to ring true, not least in the field of biopharmaceutical medicine.

Dr Warren shared the 2005 prize with his collaborator Dr Barry Marshall. Their groundbreaking work is also aptly and succinctly captured in the respective Award Ceremony speech: “Against prevailing dogmas, you discovered that one of the most common and important diseases of mankind, peptic ulcer disease, is caused by a bacterial infection of the stomach. Your discovery has meant that this frequently chronic and disabling condition can now be permanently cured by antibiotics to the benefit of millions of patients. Your pioneering work has also stimulated research all around the world to better understand the link between chronic infections and diseases such as cancer.”⁷ (See also Marshall and Warren¹⁰ and Marshall and Adams.¹¹)

I met Dr Warren when he traveled from Australia to give a talk at North Carolina State University. Dr Roberts and I met via fund-raising activities conducted in the United States for our common alma mater, the University of Sheffield (United Kingdom): many alumni and individuals who “studied abroad” live here and are keen to support current students. At my request, Dr Roberts has spoken to students at two universities in North Carolina. These Nobel Laureates share two defining qualities: transcendent humility in the face of scientific immortality, and a great desire to inspire and encourage the next generation of scientists via their active support of educational activities.

What have we (and others before us) at DIA learned in the last half-century? We have learned that there is a great appetite worldwide for our educational offerings and scientific endeavors, both of which influence the next generation of individuals who will work for better health worldwide.

Fifty-three years and counting: the Odyssey continues.

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