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Obituary

In Memoriam: Ira Shoulson, MD

E. Ray Dorsey[a,*] and Karen E. Anderson[b]
[a]*Department of Neurology, University of Rochester Medical Center, Rochester, NY, USA*
[b]*Department of Psychiatry & Department of Neurology, Georgetown University School of Medicine, Washington, DC, USA*

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Ira Shoulson, MD (1946 – 2024)

Dr. Ira Shoulson, an academic and organizational genius who helped make Huntington disease (HD) treatable, died from bladder cancer on May 12. He was 78.

In Dr. George Huntington's 1872 description of the disease, he wrote, "I have never known a recovery or even an amelioration of symptoms in this form of chorea; when once it begins it clings to the bitter end. No treatment seems to be of any avail, and indeed nowadays its ends is so well-known to the sufferer and his friends, that medical advice is seldom sought. It seems at least to be one of the incurables." A century later, Ira launched a 50-year effort to end this nihilism, relieve its symptoms, and find treatments that make a difference.

Ira's tie to HD was forged when he met the researcher and advocate, Dr. Nancy Wexler. For over a decade, Dr. Wexler, Dr. Anne Young, Ira, and a generation of HD researchers travelled annually to Lake Maracaibo in northwest Venezuela to evaluate a remote and isolated population affected by a condition known locally as "el mal." The bad disease ran in families and caused the previously healthy to move incessantly, behave erratically, think irrationally, and die prematurely.

After tracing through family trees that covered walls and collecting thousands of blood samples, they, led by the geneticist Dr. James Gusella, found the genetic marker for the disease in 1983. A decade later, an expansion in *huntingtin* was identified as its cause. Along with cystic fibrosis, HD was one of the first conditions to be identified as a monogenetic illness, and its discovery ushered in efforts to map the entire human genome.

With a cause in hand, Ira organized an academic network to find treatments. In 1994, one year after the genetic discovery, Ira and the late Dr. Jack Penney founded the Huntington Study Group. The result of the first meeting in Baltimore, Maryland, was to meet again, and among its first outputs was an outcome

*Correspondence to: Ray Dorsey, 265 Crittenden Blvd, CU 420694, Rochester, NY 14642. E-mail: ray.dorsey@chet.rochester.edu.

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measure – the Unified Huntington Disease Rating Scale – that is still in use today. Ira and his colleagues soon put the scale to use in clinical trials.

No one tried harder or failed more to develop therapies for HD than Ira. Ira investigated the GABAergic imidazole-4-acetic acid in 1975 ("failure"), muscimol in 1978 ("therapeutic failure"), baclofen in 1989 ("not favorably influenced"), fluoxetine in 1997 ("failed to exert substantial clinical benefits"), ethyl-EPA in 2008 ("not beneficial"), minocycline in 2010 ("suggested futility"), and coenzyme Q_{10} in 2017 ("does not slow the progressive functional decline").

For Ira, however, failure was only a prerequisite to success. Success came in 2006 when chorea, which Dr. Huntington had never seen ameliorated, was lessened by tetrabenazine. The randomized controlled trial conducted by the Huntington Study Group led the U.S. Food and Drug Administration to approve the first therapy for HD in 2008. Since then, two related therapies – deutetrabenazine in 2017 and valbenazine last year – have been approved. Today, George Huntington's therapeutic nihilism is dead. Dozens of clinical trials for HD are ongoing, and medical advice for the condition is frequently sought at numerous centers around the world.

Ira knew that genetic disorders carried their own burdens. In Rochester, New York, Ira worked closely with the late Congresswoman Louise Slaughter to pass the Genetic Information Nondiscrimination Act (GINA) of 2008. GINA prohibits discrimination in employment and health insurance based on an individual's genetic information, family history, or – Ira's contribution – participation in clinical research. Senator Ted Kennedy hailed it as the "first major civil rights bill of the new century."

Ira also recognized the importance of engaging with regulators to help them understand the needs and challenges of developing therapies for neurodegenerative diseases, especially rare ones like HD. He was the founder and director of the Center of Excellence in Regulatory Science and Innovation at Georgetown University in Washington, DC. This center, funded by the Food and Drug Administration, worked to reimagine how drugs and medical devices are reviewed and evaluated.

His final body of work was to prioritize the role of patients in drug development. To this end, he founded a company, Grey Matter Technologies, to amplify patient voices in research and drug development. With the Huntington Study Group, he developed "myHDstory," an online platform that included the Huntington Disease Patient Report of Problems, a tool for verbatim collection of patients' most bothersome problems. He also founded the Making Patients Heard Foundation to study how patients describe and prioritize their problems.

An incredibly kind and active mentor, Ira guided hundreds of students, residents, fellows, clinicians, and professionals during his long career. Despite a packed schedule, he was generous with his time, even with the most junior of his mentees. To be his trainee was to be his friend. He remembered personal details and asked about family events, children, and pets. He delighted in hearing about children getting into colleges and mourned the deaths of family members with many of us. When a colleague died unexpectedly, Ira reached out to the family. At conferences, even when he was ill and fatigued from chemotherapy, he hosted dinners to foster collaborations and friendships. He worked across disciplines and was a strong advocate for all members of care teams, including social workers, nurses, psychologists, and genetic counselors. He ensured that coordinators were recognized at meetings and provided them leadership roles in the HSG. He was famous for his "offer you can't refuse" calls when he volunteered someone for a new opportunity. It was hard not to get excited about such projects once Ira pitched it with his infectious optimism.

Far beyond his relationships with colleagues, protégés, and disciples, Ira was sustained by his loving family and often recounted how this foundation enabled his success. He is survived by his wife of 41 years, Josie (Paskevich) Shoulson; his sister, Jolene Kellner; his son Zachariah; his daughter Amanda and son-in-law Richard Friedrich; and two adoring grandchildren, Noah and Emma.

Few, very few, have done more to reduce the burden of HD than Ira. With friends, he pursued its single cause. He cared for hundreds. He evaluated and found treatments for tens of thousands. He helped forge policies that protect millions. He trained and inspired countless individuals, including us. His fingerprints are everywhere. For fifty years, he gave his best.

However, he knew that more remained to be done. Much more. It is now up to a new generation of scientists, clinicians, students, advocates, friends, and families to find treatments that make a difference. Ira would take enormous delight in those who bring an end to this terrible disease either through prevention, slowing its progression, or cure.