University of Colorado's longest serving chair of neurology and pioneering neurovirologist Donald H. Gilden, MD, FAAN, died August 22, from an aggressive form of renal cancer. But in interviews with Neurology Today, friends, family, and colleagues painted a portrait of a man who led his life fast — and with passion and purpose.

Indeed, they said, there was something about Don Gilden that made everyone feel that they lost a best friend, a mentor, and a larger-than-life man with a tremendous dose of enthusiasm (for everything and everyone) that was in itself as infectious as the viruses he studied.

In his final days, Dr. Gilden called on his colleagues to ensure that his grants would continue funding his research team and that the decades of advances he had made in unraveling the nature of the varicella zoster virus would continue. As a clinician, he was so astute about what this virus can do once it makes its way into the brain that he very recently admitted a dying patient to Hadassah for his own sabbatical. The tissue from patients who died with a fatal condition. Arteritis is traditionally involved his discoveries of how VZV (in spinal ganglia, later he would also find it in trigeminal ganglia. Those discoveries would send him down a path lead to two very different phenotypes — an all-body attack of chicken pox in childhood and a localized infection of shingles much later in life?

Dr. Gilden was the first on many VZV fronts. He found the virus in the morgue samples in normal human ganglia. He saw its structure in latent VZV DNA and would later identify latent VZV transcripts, finding the virus was latent only in human ganglionic neurons.

In 1985, he was recruited to the University of Colorado to chair the department of neurology and continue his lab and clinical work. He was known to be a generous teacher.

“He was interested in VZV because it is a model of a persistent infection,” said Howard L. Lipton, MD, FAAN, professor at the University of Illinois College of Medicine. They met when they were young men at Hopkins together. They became friends over a fastball. Dr. Lipton also played baseball. He was a catcher.

Dr. Lipton said that his colleague went on to discover that there was a certain inflammatory profile in the arteries that could cause problems in the brain and in the heart: giant cell arteritis.

Earlier this year, he and his colleagues found VZV in the gut of a patient with a fatal condition. Artentis is traditionally treated with steroids, but if the Colorado scientists are right then antivirals could be a more direct and effective treatment, said Dr. Lipton.

“Tis a lot more to do, but I think he is right,” he added. Many of Dr. Gilden’s more than 420 scientific papers involved his discoveries of how VZV works in human disease.

Dr. Gilden’s research changed the way the field thinks about VZV and disease, added Neurology Today Associate Editor Kenneth Tyler, MD, FAAN, the Reuler-Lewin family professor and chairman of neurology at University of Colorado. Dr. Tyler, who also specializes in central nervous system infections, said that the Gilden lab showed that

**He was hard-charging in every part of his life. He was consumed by things he loved.**

**FRIENDSHIPS AND SCIENCE**

Oded Abramsky, MD, PhD, FAAN, a professor of neurology at the Hebrew University Hadassah Medical School, was taking a sabbatical at the University of Pennsylvania when he first met Dr. Gilden in July of 1976. Dr. Gilden, then a young professor, took to the stage to greet the new residents that year. “Who was this guy who lit up the stage with his green bowtie?” Dr. Abramsky remembers thinking. After the talks, the two neurologists were introduced, and Don Gilden reached up and hugged and kissed the visiting professor. “He seemed to know everything about me. He gave me his heart.”

They remained the best of friends, and four years later Don Gilden was invited to Hadassah for his own sabbatical. The American neurologist spent his time in Israel working with Yochiel Becker, PhD, a virologist focusing on herpes simplex virus, there he learned the latest molecular and genetic techniques, using them to map VZV. There were so many questions. What is its structure? Why is it latent? How is it reactivated? How can the virus lead to two very different phenotypes — an all-body attack of chicken pox in childhood and a localized infection of shingles much later in life?

**‘He was hard-charging in every part of his life. He was consumed by things he loved.’**

**DR. DONALD H. GILDEN**

1937-2016
Calculated supplements may raise the risk of dementia in elderly women with cerebrovascular disease, according to a five-year Swedish study reported in the August 17 online edition of Neurology.

Stroke and white matter lesions, which often co-exist, are already known markers of generalized cerebrovascular disease with different types of vessel pathology, the authors of the population-based study said. But while earlier studies have demonstrated that cerebrovascular disease can heighten the risk of dementia, calcium supplementation appears to augment this risk, the study authors said.

Researchers reported an increased risk for dementia, Study Finds

**ARTICLE IN BRIEF**

Researchers reported an associated risk between calcium supplementation and the development of dementia in women with cerebrovascular disease. But the study authors and independent experts said the five-year population-based study sample was too small and the findings are premature and need to be replicated in a larger study.

Calcium supplements may raise the risk of dementia in elderly women with cerebrovascular disease, according to a five-year Swedish study reported in the August 17 online edition of Neurology.

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However, they cautioned that confirmation of these results would be advisable due to the relatively small patient sample and the observational methodology of the study.

The researchers noted that the small sample size led to a low statistical power in some of the subgroups; for example, the number of individuals with pure VaD (vascular dementia) was too small for separate analyses, which required us to merge this group with that of mixed dementia. However, both these entities had a history of stroke and are expected to share the same vulnerability to calcium supplements, they wrote.

“Our findings need to be replicated before any recommendations can be made,” Silke Kern, MD, PhD, principal co-author and consulting neurorologist at the University of Gothenburg in Gothenburg, Sweden, told Neurology Today. “Meanwhile, women with cerebrovascular disease can discuss this new information with their clinicians and assess the risks versus the benefits.”

**STUDY METHODOLOGY**

The study — drawing from the Prospective Population Study of Women and H70 Birth Cohort Study in Gothenburg, Sweden — involved 700 women, aged 70-92, who were free of dementia at the outset. At baseline in 2000–2001 and at follow-up in 2005–2006, psychiatric research nurses assessed participants for psychiatric symptoms as well as conducted physical exams and mental and memory tests at a geriatric outpatient clinic in Gothenburg, and in home visits.

Researchers stratified the sample into women with a history of stroke (108) and those without a history of stroke (592), and found that calcium supplementation intake correlated with development of dementia in groups with a history of stroke or presence of white matter lesions, but not in patients without these conditions.

Continued on page 9
In memoriam: Donald H. Gilden, M.D.

Howard L. Lipton¹ · Ken Tyler²

Donald Harvey Gilden, M.D., died on August 22, 2016, in hospice care surrounded by his family in Denver, Colorado. He was 78 and had battled renal cell cancer for 16 months yet worked regularly on research almost to the end. Donʼs commitment to and passion for research was celebrated with his Pioneer in NeuroVirology Award in 2007. His dedication to future research and his colleagues was evident in the detailed, written instructions left regarding his NIH Program Project grant on the molecular pathogenesis of varicella zoster virus (VZV) infection that he had directed for 28 years. Don also prided himself in being a practical yet thorough clinical diagnostician, and he displayed unconditional, positive regard for his patients.

Don was an inveterate optimist with a fiercely independent mindset who was also quick to question what he viewed to be dogma. Professionally, he will be remembered for being the Chairman of the Department of Neurology at the University of Colorado School of Medicine for nearly a quarter of a century until 2009 when he stepped down and was recognized for his clinical teaching and his research on VZV. His research focused on VZV latency and clinical manifestations upon reactivation. Donʼs talents were not confined to the medical profession. He played semi-professional baseball the summer before entering college, was a life-long, expert skier, and was a dedicated violinist who practiced each morning before work and performed at professional gatherings.

Don received his undergraduate education at Dartmouth, his medical degree at the University of Maryland, and completed residency training in Neurology at the University of Chicago before becoming a postdoctoral neurovirology fellow with Neal Nathanson at The Johns Hopkins School of Public Health. He excelled in medicine and research and later received the University of Chicagoʼs Alumni Award for Distinguished Service, election to the Johns Hopkins Society of Fellows and the Medical Association of the University of Marylandʼs Honor Award and Gold Key.

After fellowship Don joined the faculty of the Wistar Institute and the University of Pennsylvania Department of Neurology, attaining the rank of Professor. Don was mentored by the Instituteʼs Director Hilary Koprowski with whom he developed a friendship and shared a love for classical music. In 1986, Don became the Chair of Neurology at the University of Colorado, a position he held with distinction. After retiring as Chair, Don continued to direct his productive virology research group.

Don published over 400 papers, reviews, and chapters in the medical and scientific literature. Early on, Don believed that multiple sclerosis was caused by a persistent viral infection, and he worked on this possibility for many years. The issue of viral persistence led him to begin working on VZV infection. Perhaps no other individual contributed more to our understanding of VZV and its role in clinical diseases than Don. He and his colleagues established that VZV DNA was present in normal human cranial and dorsal root, as well as autonomic ganglia, throughout the neuraxis. They showed that latent VZV DNA is circular and is associated with histone proteins.
that help regulate virus gene expression in human ganglia. Don and his colleagues established simian varicella virus infection in monkeys as the only animal model that accurately recapitulates human VZV primary infection, latency, and reactivation. Don also identified *zoster sine herpete* (shingles pain without rash) as a clinical entity. Don showed that productive VZV infection in cerebral arteries produced strokes, or VZV vasculopathy—a separate entity from VZV encephalitis. In the last few years, he expanded the spectrum of VZV vasculopathy to include giant cell (temporal) arteritis and granulomatous aortitis. From this experience, Don assumed that the full spectrum of multi-system disease caused by VZV is yet to be discovered.

We know he will be missed by his family but also by his many students, trainees, colleagues and friends.
In Memoriam: Donald H. Gilden, MD (1937-2016)

Kenneth L. Tyler, MD; Maria Nagel, MD

Donald H. Gilden, MD, passed away at the age of 79 years on August 22, 2016, after a long battle with renal cell carcinoma. He remained active as the director of a major National Institutes of Health–funded research laboratory in the Department of Neurology at the University of Colorado School of Medicine until the time of his death. Don had previously served as the second chair of the University of Colorado’s Department of Neurology, a position he held for nearly a quarter of a century (1985-2009) before relinquishing his administrative duties to devote his full-time efforts to his research program on the biology of varicella-zoster virus (VZV). During his tenure, the department grew into one of the nation’s leading academic neurology programs.

Don was a Dartmouth undergraduate, a University of Maryland medical student, and completed his neurology residency training at the University of Chicago. His interest in neurovirology was fostered during his postdoctoral years (1969-1971) at Johns Hopkins where he worked closely with Neal Nathanson, MD, who would later become chair of Microbiology at the University of Pennsylvania. After completing his neurovirology fellowship, Don joined the faculty of the Wistar Institute and the University of Pennsylvania, where he rose rapidly to the rank of professor. At the Wistar, he developed a close personal and professional friendship with the director, Dr. Hilary Koprowski, which would last until Koprowski’s death in 2013. Like Koprowski, Don cultivated a plethora of interests outside of science and medicine. He was an accomplished athlete who played catcher for Israel’s softball team in the XItth Maccabiah Games (1981). He was an expert skier who loved treacherous double black diamond runs and mogul fields and an accomplished classical musician who never traveled without his beloved Amati violin. His violin performances were a regular feature of many departmental and professional society gatherings.

Don left an extraordinary legacy of accomplishment at every institution with which he was affiliated and subsequently received honors from each, including the University of Maryland Medical Association Honor Award and Gold Key in 2008, the University of Chicago’s Alumni Award for Distinguished Service (1991), and election to the Johns Hopkins Society of Fellows (2000). Don’s retirement as chair of Neurology was marked by a symposium in his honor attended by many of his trainees and colleagues (2010), and by the establishment of an annual “Gilden Lectureship” hosted by the Department of Neurology. In addition to these awards, Don received the “Outstanding Teacher” award of the Neurology residents he trained 4 times (a departmental record), was elected to the Association of American Physicians (1994), and to fellowship in the American Association for the Advancement of Science (2003). He was the recipient of the International Society of Neurovirology (ISNV) Pioneer Award and the Drexel Hilary Koprowski Prize in Neurovirology (2014). He was a member of numerous journal editorial boards including those of Neurology and Annals of Neurology. He was elected to honorary membership in the American Neurological Association (2007) and served on their council and as a Second Vice President.

Don was the author of more than 400 papers, reviews, and chapters. His most notable contributions were in neurovirology and in particular in the field of VZV. Don arguably produced more seminal contributions to our understanding of the biology and neurological diseases caused by this virus and their mechanism(s) than any other individual. Among his many contributions were the demonstration that VZV DNA could be found in normal human dorsal root ganglia and that this was the site of viral latency,1,2 that the latent VZV DNA was in the form of a circular episome in ganglia,3 and that specific viral transcripts were expressed during viral latency.4 Don’s clinical studies of VZV, included establishing zoster sine herpete (shingles pain without rash) as a true clinical entity,5 and the seminal demonstration that VZV produced a “vasculopathy” and that this, rather than simply viral infection of neurons, was the critical component of the pathogenesis of “VZV encephalitis.”6 His groundbreaking studies of VZV were continuing at the time of his death. His most recent work established an association between VZV infection and temporal (giant cell) arteritis by showing that the majority of arteries form patients with this enigmatic disorder contained virion particles, viral antigen, and viral DNA.7 The implication of this discovery for the pathogenesis of temporal arteritis, as well as its diagnosis and treatment, is currently being actively investigated by his research group. True to form, Don left them a detailed handwritten “roadmap” of how he wanted them to proceed in these studies, written in the late stage of his illness.

With Don’s passing, neurology lost an extraordinary individual and a truly “larger-than-life” figure who excelled in all aspects of academic life. He gave 100% to everything he did both personally and professionally and expected the same from everyone he worked with. His passing leaves a tremendous void for his many lifelong colleagues and friends. He will be greatly missed by these friends and by the family he was so extra-
ordinarily proud of and devoted to including his wife, Audrey, and their 3 sons, Adam, Paul, and Daniel, and their families.


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Short communication

Donald H. Gilden, M.D.

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A R T I C L E   I N F O

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On August 22, 2016, the field of clinical and basic neurology and neurovirology lost a great leader when Donald H. Gilden died of renal cell carcinoma in Denver, Colorado, surrounded by his family. Dr. Gilden's obtained an undergraduate degree from Dartmouth College, a medical degree from the University of Maryland, a neurology residency from the University of Chicago and a postdoctoral neurovirology fellowship from The Johns Hopkins School of Public Health. He subsequently became a Professor in Neurology at the University of Pennsylvania and The Wistar Institute followed by an appointment as the Louise Baum Endowed Chair and Professor of Neurology at the University of Colorado, which he served with great distinction for 25 years. During his career, Dr. Gilden served as an Army physician at Walter Reed National Medical Center for 2 years, as a reviewer and expert consultant for the National Institute of Health and as editor for numerous books and journals. His efforts as a clinician and scientist produced more than 400 publications, chapters and books highlighting remarkable clinical cases spiced with a foray as a professional baseball pitcher and with adventures in skiing and violin performances.

Dr. Gilden had a long interest in the role of viruses in central nervous system (CNS) demyelinating disease and devoted much of his early academic career to the isolation and culture of novel disease-relevant viruses from multiple sclerosis (MS) brain tissue (Friedman et al., 1975; Warren et al., 1977). Although these early studies did not identify a disease-specific pathogen, they led to the development of tools used to successfully isolate a novel parainfluenza virus and herpes simplex virus from human nervous system tissue. Dr. Gilden returned to investigation of MS in the early 1990’s, convinced that the persistence of cerebrospinal (CSF) IgG oligoclonal bands was a vital clue to the underlying nature of disease. Using modern molecular approaches, he initiated the construction of cDNA libraries from active MS lesions, their screening with MS CSF IgG and the sequencing of MS plaque IgG transcripts. The latter studies led to one of the first descriptions of B cell clonal expansion and somatic hypermutation in MS lesions and contributed to a renewed interest in the role of B cells in MS pathogenesis (Owens et al., 1998; Smith-Jensen et al., 2000). To further study clonal B cell responses in MS and other CNS inflammatory diseases, as well as to recapitulate their binding properties, his laboratory developed tools to analyze immunoglobulin V region segments at the single-cell level from both CSF-sorted plasma blasts and plasma cells microdissected from CNS tissue. Using this technology, Dr. Gilden and colleagues: 1) confirmed clonal expansion as a prominent feature of MS CSF B cell responses; 2) showed that expansion occurred early in the disease process; and 3) found an overriding bias for use of VH4 heavy chain gene segments that was not present in naïve or memory peripheral blood B cell repertoires (Owens et al., 2003, 2007; Ritchie et al., 2004; Haubold et al., 2004), indicating strong selective pressures for B cells migrating to the CNS.

Subsequently, human IgG1 recombinant antibodies (rAbs) were generated from expanded CSF IgG plasma blast clones identified in patients with MS and with other human CNS inflammatory diseases. A series of proof-of-principle studies showed that the majority of CSF and tissue plasma cells infiltrating the CNS of patients with subacute sclerosing panencephalitis are measles virus-specific (Burgoon et al., 2005; Owens et al., 2006). Dr. Jeffrey Bennett, a colleague in the Department of Neurology, successfully applied these approaches to clone disease-relevant AQ4-specific rAbs from CSF of patients with the inflammatory demyelinating disease neuromyelitis optica and demonstrated that they recapitulated pathologic features of the human disease in animal models, including complement-mediated targeted destruction of astrocytes followed by oligodendrocyte death and demyelination (Bennett et al., 2009). Although the specific molecular targets of monoclonal rAbs

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produced from MS CSF plasma blast clones remain elusive (Owens et al., 2009), continuing studies at the University of Colorado have begun to reveal their CNS autoimmune activities and the potential contribution of intrathecal antibodies to MS pathogenicity (Blauth et al., 2015). Dr. Gilden's hypothesis of a viral etiology for MS never wavered and the approaches and tools he set in place to study the intrathecal B cell response continue to enhance our understanding of their role in human inflammatory demyelinating disease.

Early in his MS studies, Dr. Gilden realized that if a causative virus were found, he needed to develop tools and techniques for its analysis. He chose varicella zoster virus (VZV) to develop highly specific and sensitive techniques to study a neurotropic virus that is acquired early in life, establishes latency and can reactivate decades later. Dr. Gilden's lab was among the first to apply modern techniques to analyze the state of VZV DNA in human neurons obtained at autopsy. They cloned the virus genome, constructed cDNA libraries enriched for virus transcripts, and developed transcriptional arrays and multiplex PCR assays to detect virus in human ganglia (Cohrs et al., 1996, 2003; Nagel et al., 2013a). His lab went on to show that in human neurons, VZV DNA is circular (Clarke et al., 1995), present at low copy numbers (Cohrs and Gilden, 2007) and that virus gene transcription is associated with euchromatin marked histones (Gary et al., 2006), depending on the time between death and tissue harvest (Cohrs et al., 2000; Nagel et al., 2011a; Ouwendijk et al., 2012). The function and regulation of many of these VZV genes have been analyzed (Cohrs et al., 1998, 2002). An example of Dr. Gilden's success at combining various research areas was the use of the rAb technology developed by the MS group to construct plasmids expressing humanized rAbs that recognize specific phosphorylation sites (Mueller et al., 2008, 2009, 2012) and tertiary configurations of VZV proteins (Birlea et al., 2013). Although initiated as a model to study virus latency in neurons, Dr. Gilden's work continues to expand the VZV field by describing virus and host interactions in cultured neurons over extended time periods (Goodwin et al., 2013; Cohrs et al., 2016) and to analyze vanishingly small amounts of virus DNA:protein complexes and gene transcripts in a vast excess of host material.

Realizing the limitations of human autopsy material, Dr. Gilden and his team set out to develop an animal model that mirrors all stages of VZV infection. Gilden was of the firm conviction that any animal model of VZV latency must fulfill several criteria for varicella latency, including: the ability to reactivate; the presence of viral DNA in ganglia but not in other tissues; limited viral gene transcription; and restriction of ganglionic infection predominantly to neurons. Like many other researchers in the VZV field, Gilden found that inoculation of mice, rats and rabbits with VZV elicits an antibody response but not the necessary triad of primary infection, latency and disease following reactivation. Thus, in 1990, Dr. Gilden turned to primates as a possible animal model of VZV infection, personally inoculating monkeys at the Tulane National Primate Research Center intracerebrally with VZV-infected cells. Unfortunately, VZV did not infect monkeys. However, Gilden and his lab found that: 1) infection of monkeys with simian varicella virus (SVV), a primate counterpart of human VZV, disseminates as does varicella in immunosuppressed humans, with lung and liver most severely affected (Dueland et al., 1992); 2) SVV infection of multiple organs including ganglia precedes appearance of rash (Mahalingam et al., 2001); establishes latency in ganglionic neurons, and; 3) reactivates with immunosuppression to produce clinical disease similar to humans (Mahalingam et al., 2007, 2010).

In the last two decades, Dr. Gilden's lab established three models of experimental infection of monkeys with SVV. The first model was intracerebral inoculation of African green and cynomolgus monkeys with SVV (White et al., 2002a, 2002b). SVV DNA and transcripts corresponding to all classes (immediate-early, early and late) of SVV genes were found in liver, lung and ganglia at multiple intervals for one year after inoculation, resembling a persistent infection (White et al., 2002a). During primary infection, virus was also found to infect alveolar macrophages and/or dendritic cells in lungs and memory T cells in blood (Ouwendijk et al., 2013a). SVV-infected T cells were detected in ganglia, lymph nodes and in skin lesions close to blood vessels (Ouwendijk et al., 2013a). In the second model (Messaudi et al., 2009), intranuclear inoculation of rhesus macaques with SVV produced varicella rash followed by establishment of latency in ganglia. Virolological and immunological features of primary SVV infection and latency in these monkeys were similar to those of VZV infection in humans. In addition, T cell proliferation was detected starting at 7 days post infection (dpi), peaking at 14 dpi. Virus-specific CD4+ T cells also peaked at 14 dpi and reached stable levels at 73 dpi. Granzyme-B-expressing CD4+ and CD8+ memory T cells, indicative of cytotoxic potential, appeared at 7 dpi and remained at high levels for at least 28 dpi. Using both the second and the third model, i.e., natural SVV infection by exposure of African green and cynomolgus monkeys to those previously inoculated intratracheally (Mahalingam et al., 2002), Dr. Gilden and his lab showed that SVV can be experimentally reactivated in African green monkeys, cynomolgus and rhesus macaques (Mahalingam et al., 2007, 2010; Traina-Dorge et al., 2015), and that a transient T cell infiltration in ganglia during reactivation correlated with expression of CXCL10, a chemokine that recruits activated T and NK cells (Ouwendijk et al., 2013b). Recently, Dr. Gilden and his lab demonstrated for the first time that abundance of all T cell subsets decreased, except for CD8 effectors which peaked 2 weeks before zoster in monkeys, and that PD-1 expression increased at reactivation (James et al., 2014).

While Dr. Gilden's basic research kept him busy in the lab, his primary devotion was to patients. His open-mindedness led to the significant expansion of the clinical spectrum of VZV, as well as the characterization of key features, laboratory and imaging abnormalities, diagnostic tests and treatment guidelines for disease caused by VZV reactivation. Historically, the clinical manifestations of VZV were thought to include only varicella (chickenpox) during primary infection and herpes zoster (shingles) with rare complications of associated stroke. In 1996, Gilden et al. (1996) described the first definitive case of stroke produced by productive VZV infection of cerebral arteries (VZV vasculopathy) in a patient with waning and waxing vasculitis without zoster rash (Case Records of the Massachusetts General Hospital, Case 5–1995, 1995). In 2002, Gilden described a patient with left sacral distribution zoster and VZV vasculopathy verified by intrathecal synthesis of anti-VZV IgG antibodies, demonstrating that VZV can reactivate from multiple ganglia with peripheral spread of virus to skin in one ganglion, as well as central spread to cerebral arteries in another remote ganglion (Gilden et al., 2002). In 30 patients with virologically confirmed VZV vasculopathy, he demonstrated the presence of brain imaging abnormalities in the majority of cases, with characteristic grey-white matter junction lesions and involvement of both large and small vessels; furthermore, rash and CSF pleocytosis were absent in one-third of cases, and time from rash to neurological symptoms/signs was 4.2 months, alerting clinicians to this challenging diagnosis (Nagel et al., 2008). He showed that detection of anti-VZV antibodies in the CSF was more sensitive than detection of VZV DNA by PCR for diagnosis of VZV vasculopathy due to the chronic nature of disease (Nagel et al., 2007, 2008). In 2011, Gilden and colleagues (Nagel et al., 2011b) described the morphological features of arteries from patients with VZV vasculopathy, i.e., a thickened intima composed of myofibroblasts, a disrupted internal elastic lamina, and a paucity of smooth muscle cells in the media. Neutrophils characterized early VZV vasculopathy, while T cells and macrophages predominated later in disease (Nagel et al., 2013b).

During a prolific career, Dr. Gilden described many more cases of VZV reactivation beyond rash and vasculopathy to include dermatomal distribution pain without rash (zoster sine herpete; reviewed in Gilden et al., 1994a), postherpetic neuralgia due to chronic VZV ganglionitis (Gilden et al., 2003), VZV myelitis (Gilden et al., 1994b) and VZV-associated cognitive impairment (Silver et al., 2012; Gilden et al., 2016a). Finally, Dr. Gilden's most significant and novel contributions expanded on...
the clinical presentation of VZV vasculopathy to include giant cell arteritis (Gilden et al., 2016b), the most common form of systemic vasculitis in the elderly, and granulomatous aortitis (Gilden et al., 2016c). His findings of VZV antigen in arteries of the majority of these patients has opened the field for further studies on mechanisms of VZV-induced inflammation and potential use of antiviral reagents in these often refractory and progressive diseases. Dr. Gilden’s clinical contributions in the past decades have expanded our knowledge of VZV disease, educated numerous clinicians and scientists, and improved lives of countless patients through improved patient care, diagnosis and treatment of multi-system diseases caused by VZV. (See Fig. 1.)

Dr. Gilden was a Renaissance man, engaged in translational medicine before it was a field. He successfully united clinical observations with basic science to help treat many previously idiopathic diseases. Don will be remembered as an individual of great ability who truly loved life.

Statement of interest

The authors declare no conflict of interest.

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