In Memoriam: Edwin D. Kilbourne, MD, 1920–2011

Jeffery K. Taubenberger,1 David M. Morens,2 Richard M. Krause,3 and Anthony S. Fauci2

1Viral Pathogenesis Section, Laboratory of Infectious Diseases, 2Office of the Director, and 3Division of Intramural Research, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland

“Having entered the field as a physician, I have always sought practical applications of my work, yet in every instance, such applications have led me to seek further answers in basic research as new questions arose” [1]. So wrote Edwin Dennis Kilbourne, MD, the preeminent influenza virologist who died at age 90 on 21 February 2011.

Efforts to understand and control human influenza virus infections span the 78 years since the first isolation of the virus in 1933 [2]; Ed Kilbourne (Figure 1) was one of the pioneers of this field. His influential and wide-ranging publications on influenza virus biology, immunology, epidemiology, and vaccinology spanned 8 decades—and 62 of those 78 years [3, 4]. His lifelong commitment to understanding influenza arose from frustrations as a physician caring for patients during a severe epidemic in 1947, and in the following decades led him to important discoveries on the molecular biology of the virus, to correlates of the host immune response, and to seminal contributions to the development of influenza virus vaccines. At every step, Ed remained the consummate bench-to-bedside physician-scientist [5], whose life work directly connected cutting-edge science to clinical care, prevention, and public health.

His enduring impact on almost every aspect of influenza research and control was profound. He trained, influenced, and collaborated with 3 generations of scientists, among them many of the leaders in influenza virology today. He was an advisor to presidents and a friend to anyone interested in understanding and controlling influenza disease. He developed and applied the technology to produce the first genetically engineered influenza vaccines (high yield reassortants [6]), which have been used for the last 41 years as “backbones” to develop the annual inactivated influenza vaccines [7, 8]. Over these decades, these vaccines have saved countless lives. At retirement, he left to future generations a meticulously catalogued collection of important viral and vaccine strains and reagents. Ed authored a classic textbook on influenza [9] and was also a distinguished academic epidemiologist who coauthored a highly influential public-health text [10]. He was a leader in characterizing the first pandemic in the era of virus isolation (1957 H2N2 “Asian” influenza) and in understanding its pathogenic basis [11–13]. He expanded our fundamental understanding of influenza virus biology and immunity by demonstrating that the hemagglutinin and neuraminidase glycoproteins were encoded on separate viral gene segments [14], and he pioneered efforts to characterize the molecular determinants of immunity [15] and their roles in mitigating disease [16, 17]. He was also among the first to hypothesize a zoonotic origin for human influenza viruses and to attempt to understand zoonotic emergence [18].

During the 1976 swine flu outbreak at Fort Dix, New Jersey, in which the sudden and unprecedented cluster of infections with a 1918-like swine influenza virus in military recruits led to predictions of an emerging pandemic [19], Ed lent his respected voice to the almost-unanimous scientific recommendation that an anti-pandemic vaccine should be made and deployed on an urgent basis [20]. The 1976 pandemic never materialized, but the idea that a pandemic virus of swine origin might emerge was proven correct 33 years later when a different swine virus, containing an HA antigenically very similar to that of 1976 [21], emerged to cause the 2009–2010 pandemic. It is both an irony and a fitting tribute to Ed that the 1976 swine flu vaccine, made using Ed’s technology and administered to over 43 million people in the United States [20], may have prevented illness and saved many lives among its recipients 3 decades later, in 2009 [22]. Those who knew Ed are above all grateful that, even in failing health, he lived to witness and...
understand the events of 2009–2010, and even to make, in the last months of his life, important contributions to understanding the antigenic relationships among human and swine viruses [4].

Ed Kilbourne was born on 10 July 1920 in Buffalo, New York. After spending his early childhood in the Dominican Republic and later in Ridgewood, New Jersey, he received AB (1942) and MD (1944) degrees from Cornell University. After residency at The New York Hospital—Cornell Medical Center, he served 2 years as a captain in the US Army Medical Corps. As assistant chief of medicine at the hospital in Fort Monmouth, New Jersey, he observed the almost total failure in 1947 of a newly developed influenza vaccine. It soon became clear that he had observed firsthand a key influenza virus phenomenon, namely viral escape from population immunity by antigenic change, a process now accepted as characteristic of human influenza virus evolution.

This event prompted Ed to pursue a career in influenza virology, starting with 3 years at the Rockefeller Institute with Frank L. Horsfall, Jr. (1906–1971), learning the new technologies that were then revolutionizing virology. After a stint as professor of medicine at Tulane University, in 1955 Ed was appointed professor of public health and director of the Division of Virus Research at his alma mater, Cornell University Medical College. In 1969, he went to the Mount Sinai School of Medicine as founding chairman of the Department of Microbiology and distinguished service professor. He then continued his long academic career at New York Medical College, eventually being appointed emeritus professor. Ed’s devotion to public health led to active service on important commissions and committees, prominently including the Influenza Committee of the Armed Forces Epidemiology Board, at the time the most powerful organization directing and supporting influenza research. His impact was reflected in a number of prominent awards, honorary degrees, and election to such honorific societies as the Association of American Physicians (1962), the U.S. National Academy of Sciences (1977), and the American Philosophical Society (1994). In private life, Ed was a devoted fisherman and conservationist, and an athlete who bowled regularly and played competitive tennis into his late 80s.

Ed was both a rigorous scholar and a wry and witty dreamer. To students he must have appeared stern and intimidating. He held strong opinions, always backed up by solid science, and had an uncanny knack of drawing the right conclusions from complicated data. He could be taciturn but was never shy about expressing opinions, even those that were unpopular. He liked to follow the trail of rigid experimental data to practical conclusions, and everything he did, even work at the molecular level, was aimed directly at helping real people in the real world.

But there was another side of Ed that surprised and bemused those who knew him only as a scientist. Throughout his life Ed wrote and published humorous, often bawdy, poems designed to elicit laughs either by their wit or by the intentional torturing of language, or frequently both [23]. In a 1997 keynote address on avian influenza [24], he closed with this observation:

We haven’t heard the final word,
On which came first, the egg or bird,
So how can we expect to find
An answer of another kind
Hitchcockian though it may be –
To fear the birds, or they fear we? […]
But then we learn the bottom line
Is putting perils before swine.

Figure 1. Edwin Dennis Kilbourne, MD (1920–2011). The photograph is believed to have been taken around 1970.
Ed Kilbourne was the last of a generation of influenza pioneers, of bench-to-bedside physicians who led us from the early days of virology into the modern molecular era. As was true of many other colleagues who knew this unforgettable man, in different capacities and at different times in his career, each of us has been influenced by him in different but important ways, and each has cherished memories of this extraordinary teacher, colleague, and friend. His legacy is large, and the shadow he cast stands tall even after his passing.

Funding

Funding for this study was provided by the National Institute of Allergy and Infectious Diseases, National Institutes of Health.

References