BIOGRAPHICAL MEMOIRS

Edward A. Hoover

November 18, 1942–March 1, 2023
Elected to the NAS, 2014

A Biographical Memoir by Sue VandeWoude, James Mullins, and Candace Mathiason

Figure 1 Edward A. Hoover.

Edward "Ed" A. Hoover was a preeminent figure in the field of veterinary virology and prion research, as well as an outstanding educator and mentor. He is best known for his development of one of the first FeLV vaccines, which has protected millions of cats worldwide against the leukemia-causing retrovirus and is an example of a successful retroviral vaccine. He was also part of the research group that discovered the transmission method of chronic wasting disease in deer populations. Throughout his prolific career, he conducted studies that interrogated the relationship between exposure to pathogens and disease outcome, with goals of understanding the basis of viral and prion disease pathogenesis and developing vaccine and other therapeutic modalities for some of the most virulent diseases of humans and animals.

Early Life and Training

Ed Hoover was born on November 18, 1942, to Marian Brunn Hoover and Edward Hoover in Chicago, Illinois. He spent his childhood living out many Hardy Boys-like adventures and exploring the "Near North" neighborhood of Chicago around Wrigley Field, the home of his beloved Cubs, and near Lake Michigan. His home above the McKillip Animal Hospital, home to Buzzy the McCaw, undoubtedly imprinted his eventual career choice. Although the kennel of barking dogs below his bedroom did not bother him at the time, it may have led to his adult "flight or fight" responses upon hearing a dog barking in distant neighborhoods.

Ed attended Our Lady of Mount Carmel Academy and the Albert Grannis Lane Technical High School. Upon graduation, he trained for one year at the Illinois Institute of Technology, intending to become an architect. After determining his artistic visions were best expressed in two—versus three—dimensions, Ed took his curiosity to the University of Illinois, where he received his bachelor's and then doctor of veterinary medicine degree in 1967. He then entered graduate school at the Ohio State University, completing a doctoral degree in 1970 and completing a residency and earning board certification in veterinary pathology in 1972. He launched his research career by studying the

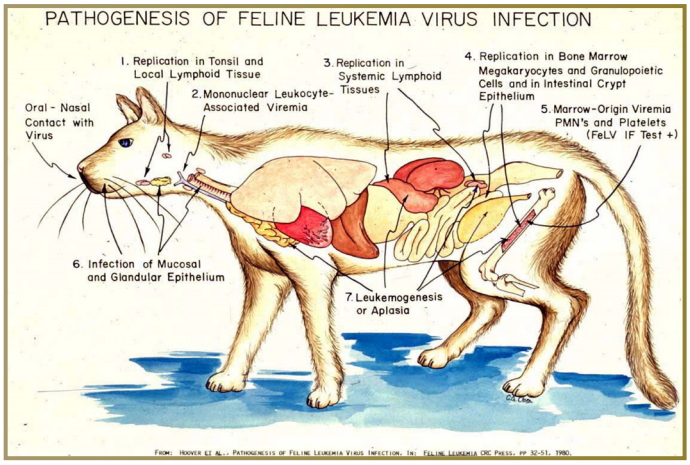

Figure 2 CRC Press figure of transparent cat.

viruses of cats, and his early publications included studies of pathogenesis of feline rhinotracheitis, herpesvirus, picornavirus and calicivirus. Ed focused his early scientific career efforts on feline leukemia virus (FeLV) while participating in studies supported by the National Institutes of Health's "War on Cancer." In 1981, he became head of the Department of Pathology at Colorado State University and moved to Fort Collins, Colorado. Following the 1987 discovery of a lentiviral infection of cats that caused an AIDS-like disease, Ed's laboratory began studies on feline immunodeficiency virus (FIV) pathogenesis in the early 1990s. In the last twenty years of his prolific research life, his laboratory pivoted to studies of chronic wasting disease in deer and other protein misfolding disorders.

Feline Leukemia Virus (FeLV): The First Successful Retroviral Vaccine

Ed's work on FeLV was both extensive and highly beneficial to the world. Of great note are his studies of the natural history of infection, strain-specific disease specificity, and vaccine development.[1–4] His studies of the natural history of infection included demonstration of horizontal transmission[5] and the importance of the age of cats in infection susceptibility, as well as the early pathogenesis and progression of the virus infection through the body (the figure of the transparent cat was particularly memorable).[6] [Figure 2]

Ed also showed the importance of virus strain to tissue tropism and disease specificity, defining viruses and genetic determinants of aplastic anemia and an AIDS-like disease (FeLV-FAIDS),[7] and anti-retroviral therapies that interrupt FeLV disease progression.[8,9,10] Ed made important contributions to the development of retrovirus vaccines[11] by demonstrating the importance of FeLV vaccine strains to the success of prevention versus enhancement of infection by vaccines.

Feline and Simian Immunodeficiency Virus Studies

Ed's was one of the first laboratories to study pathogenesis, transmission, and immunopathology of feline immunodeficiency virus (FIV). His laboratory revealed that FIV was harmful to the developing fetus and could be transmitted from dam to offspring during pregnancy, establishing a natural model for studies to help mitigate HIV in utero transmission.[12–15]

He and coworkers characterized a highly pathogenic strain of FIV (FIV-CPG) subsequently used in studies to assess FIV receptor usage, mucosal transmission mechanisms, and disease course.[16–20]

Ed and co-workers also described neurotropic properties of FIV and documented the intravaginal route of transmission. His laboratory validated several anti-retroviral agents as therapeutic modalities for lentiviral disease.[21]

His work with Steve O'Brien and Sue VandeWoude characterized infection of domestic cats with FIV strains isolated from nondomestic felids, demonstrating diminution of susceptibility to species-adapted FIV during coinfection.[22]

Ed's work branched from AIDS-like disease in cats to SIV pathogenesis and vaccinology in nonhuman primates. Work in his laboratory demonstrated tissue tropism and infection kinetics of the virulent SIVsmmPBj14 strain. Additional studies demonstrated partial immune resistance to lentiviral infection and partial protection from virulent disease in the SIV model following recombinant vaccination with subunit Env glycoproteins.[23–26]

Chronic Wasting Disease and Prion Pathogenesis

In the late 1990s, following the persistent suggestion of then-graduate student Christina Sigurdson, Hoover took up studies of chronic wasting disease (CWD) of deer, the fatal neurodegenerative prion disease now found in cervid populations of North America, Scandinavia, and Asia. By the mid 2000s, his laboratory became an international center for research on this disease, resulting in the establishment of CSU's Prion Research Center.

Studies conducted in the Hoover laboratory employing rodent and native cervid hosts have been instrumental in defining CWD pathogenesis and transmission dynamics of the disease.[27–31] The first of many studies conducted in Ed's lab demonstrated that fawns were susceptible to CWD infection in as little as two months post oral dosing with CWD-positive material.[32] Further investigations conducted by Ed's group defined CWD pathogenesis and revealed early and persistent CWD accumulation within lymphoid and peripheral organs prior to CWD deposition within the central nervous system.[33] To better understand how CWD is transmitted among cervids, Ed's group studied the native white-tailed deer host to demonstrate the presence of the infectious prion

agent within bodily fluids and excreta ("secreta") throughout the longitudinal disease course.[34,35] Their findings provided evidence that direct sharing of secreta among cervids, as well as indirect contact with secreta shed to the environment, contain sufficient infectivity to initiate and progress CWD infections and supported earlier studies monitoring CWD infections in free-ranging populations. Hoover's more than twenty years of study in the native cervid host also provided less invasive sample targets for the development of antemortem diagnostics, a goal that Ed held as an important component to his work.[36] The development of longitudinal studies in a native host for CWD infections continues to support ongoing vaccine development,[37] prion strain[38,39,40] and vertical transmission studies,[41] and studies to unravel the mysteries of interspecies transmission[42] and prion protein polymorphisms[43] on disease susceptibility. These studies continue in the laboratory of Candace Mathiason and others in the Prion Research Center at CSU.

Legacy of Mentorship for Veterinary Researchers

Over his more than forty-year career at CSU, Ed built the tradition of multidisciplinary biomedical research training for veterinarians. Ed considered as his most treasured accomplishment serving as primary mentor for twenty-seven mostly D.V.M. Ph.D. students. As of 2023, twenty-two received NIH funding as trainees, fourteen have received the NIH Career Development (K) Award, fifteen have received university faculty appointments, and several have gone on to serve as a department head, associate department head, or associate dean.

In addition to providing mentorship to this distinguished collective, Ed was primary investigator on training grants that provided funds for post-D.V.M. Ph.D. training for over three dozen individuals and was instrumental in national recognition for CSU's combined D.V.M.-Ph.D. training program, one of the first veterinary dual-degree programs to receive an NIH Medical Scientist Training Program award. Ed's legacy will continue to live on through his inspiration to his many trainees, their trainees, and a network of inspired learners.

Awards and Recognition for an Incredibly Productive Career

Ed retired in August 2022 at the age of seventy-nine and reflected at his retirement party in the lobby of Colorado State's pathology building, the site where he spent more than forty years of his incredibly productive career, that his motivation for his long career centered on his relationships with the faculty, staff, and students he cherished.

Reflective of this dedication, Ed was named CSU's researcher of the year in 1990 and was named one of twelve University Distinguished Professors at Colorado State University in 2004. He was named distinguished alumnus at both Ohio State University and the University of Illinois and received the American Association of Veterinary Medical College researcher of the year in 2012. He was elected to the National Academy of Sciences in 2014 and over his lifetime he accrued more than $50 million in extramural funding for his laboratory's work and published more than 280 papers.

Ed co-developed the first highly effective vaccine against FeLV and led the study of the first demonstration of the attenuation of SIV infection by a vaccine in macaques. He held multiple patents for FeLV vaccines and licenses and was posthumously awarded a patent for a process for prion blood detection. In recognition of this work, he was elected to the National Academy of Inventors in 2016.

The Man Beyond the Science

These accolades illustrate the sum of Ed's scholarship and tremendous legacy in the scientific community, but this does not capture the nature of his life force. The creativity that his scientific colleagues knew was reflected equally, or in greater quantity, in his meandering conversational constructs. His unique, relentless curiosity included many topics: the beauty and form of structures, the way art and science intersect, and the force of human nature and behavior, for example. To a person, those that have known Ed recall how a conversation with him would inevitably wander from the initial topic into a cavernous maze of typically humorous associations. Ed recounted some of his life's philosophies in an interview conducted by two aspirational podcasters (Sarah Schweickart and Hannah Walls) in April 2022, just a few months before his diagnosis of stage-four lung cancer.[44] Several of the mantras captured in this wide-ranging dialogue, which will be familiar to many colleagues fortunate to have been privy to Ed's private conversation, include:

> "What is unique about a university job? Why would you want to be a veterinary scientist who works on how things work, and what we can do about it? Because you get to work with students. You get to work with young people who have ideas that you might not have and who are willing to search with some guidance."
>
> ***
>
> "One of the things that I love about veterinary medicine is that it applies in many ways, and you can do many things, and you can think about, 'how could this exist in the world in general and with all the species? How do we effect this? What is our responsibility and capability? How much do we change things by what we do?'"

Figures 3a, 3b, and 3c Hoover's doodles, from left to right: diamonds and lines, fat trees, and lumpy cat abstract.

"[Art and science] are both us trying to figure out, 'who are we? Why are we here? How do things work? How do people work? How do animals work?' Artists and scientists are trying to figure out the same things."

***

"If you're a pathologist, as am I, you're just fascinated by the art that's in everything. That's the stuff you can see though, with a high-powered microscope or such. But you don't need one, you can just look at the grace of animals, you can look at how beautifully all their parts are constructed, how they have these amazing abilities."

***

"I think what stands out to me the most is the interactions and relationships I've developed with colleagues and students, former students. The single thing I'll miss most is the interactions with people."

***

"Don't ever lose the wonder of the world, and everything that's in it, and how we can keep it."

Ed's nonscietific obsessions were too numerous to count: trees, very specific coffee preparation, daily exercise regimen, correct grammar, beautifully addressed package return labels, low-fat meals, fashionable and/or comfortable clothes within his limited color wheel, dental hygiene, automobile type and maintenance, shoes (for himself and family members), ample stores of tape in well-organized boxes, love of surf yet fear of drowning, watering the hell out of plants, the perfect seat in the restaurant, and optimization of life in all ways (for this, he earned the affectionate nickname "Mr. Picky-Poo" from stepdaughter Sarah).

Following his family and friends, Ed's next greatest love was trees. He planted well over 100 trees of all varieties in the foothills of Loveland at his Spring Glade home, most requiring pickaxe and pry bar for planting. In his later years, Ed developed a particular fondness for oaks, planting more than a dozen at his last home in Applewood (on Apple Drive) and sprouting acorns in an experiment designed to determine if the floating characteristics of these seeds correlated with germination.

Ed was famous for his doodles. He never attended a seminar without a particular type of pen and a particular type of notebook. The uninitiated would think that Ed was taking copious notes, but those in the know realized he was penning one of his characteristic abstract-ish line drawings [Figure 3]. Each of these drawings was fascinating and different than all others. Repeating characters included stick figure Ed, Noseman, and a variety of cats based upon Leon and Goodies. His drawing talent was extraordinary, and many felt he could have had an equally successful career as an artist.

Family and Final Notes

Ed loved his three children, Susan, Matthew, and Karen, entertaining them with sock puppets, crazy driving, and

word play in early years, indoctrinating them with a love of cats and imagination of the secret lives of cats, and instilling a sense of service, sustainability, and the joy of absurdity. In his later years, he so looked forward to his weekend phone calls to discuss the latest bike rides, home improvements, and cat antics. Ed also cherished his three stepchildren, Eric, Eston, and Sarah, who were introduced to Tales of Noseman, the very plainest types of crackers, and hijinks card shuffling by Ed. His brightest moments were when all six of them were together comparing notes. We would all do well to observe and emulate Ed's love of all things of beauty, his relentless pursuit of the perfect, and his deep recognition of the value of relationships above success and fame.

Acknowledgments

With thanks to Sarah Schweickart for editing and reference formatting.

References

1 Hoover, E. A., et al. 1977. Horizontal transmission of feline leukemia virus under experimental conditions. *J. Natl. Cancer. Inst.* 58(2):443–444.

2 Hoover, E. A., et al. 1981. Determinants of susceptibility and resistance to feline leukemia virus infection. I. Role of macrophages. *J. Natl. Cancer. Inst.* 67(4):889–898.

3 Hoover, E. A., et al. 1987. Experimental transmission and pathogenesis of immunodeficiency syndrome in cats. *Blood* 70(6):1880–1892.

4 Hoover, E. A., et al. 1996. Efficacy of an inactivated feline leukemia virus vaccine. *AIDS Res. Hum. Retroviruses* 12(5):379–383.

5 Hoover, E. A., et al. 1976. Feline leukemia virus infection: age-related variation in response of cats to experimental infection. *J. Natl. Cancer. Inst.* 57(2):365–369.

6 Rojko, J. L., et al. 1979. Pathogenesis of experimental feline leukemia virus infection. *J. Natl. Cancer. Inst.* 63(3):759–768.

7 Quackenbush, S. L., J. L. Mullins, and E. A. Hoover. 1996. Replication kinetics and cell tropism of an immunosuppressive feline leukaemia virus. *J. Gen. Virol.* 77(Pt 7):1411–1420.

8 Zeidner, N. S., et al. 1989. Treatment of FeLV-induced immunodeficiency syndrome (FeLV-FAIDS) with controlled release capsular implantation of 2',3'-dideoxycytidine. *Antiviral Res.* 11(3):147–160.

9 Hoover, E. A., N. S. Zeidner, and J. I. Mullins. 1990. Therapy of presymptomatic FeLV-induced immunodeficiency syndrome with AZT in combination with alpha interferon. *Ann. N. Y. Acad. Sci.* 616:258–269.

10 Hoover, E. A., et al. 1991. Early therapy of feline leukemia virus infection (FeLV-FAIDS) with 9-(2-phosphonylmethoxyethyl)adenine (PMEA). *Antiviral Res.* 16(1):77–92.

11 Hoover, E. A., and J. I. Mullins. Prototype FelV isolates for use in disease models and vaccines. U.S. patent US6042835A, filed 22 April 1994, and issued 28 March 2000.

12 Burkhard, M. J., et al. 2002. Kinetics of early FIV infection in cats exposed via the vaginal versus intravenous route. *AIDS Res. Hum. Retroviruses* 18(3):217–226.

13 O'Neil, L. L., et al. 1995. Vertical transmission of feline immunodeficiency virus. *AIDS Res. Hum. Retroviruses* 11(1):171–182.

14 O'Neil, L. L., et al. 1997. Regression of feline immunodeficiency virus infection. *AIDS Res. Hum. Retroviruses* 13(8):713–718.

15 Allison, R. W., and E. A. Hoover. 2003. Covert vertical transmission of feline immunodeficiency virus. *AIDS Res. Hum. Retroviruses* 19(5):421–434.

16 Diehl, L. J., et al. 1995. Induction of accelerated feline immunodeficiency virus disease by acute phase virus passage. *J. Virol.* 69(10):6149–6157.

17 Diehl, L. J., et al. 1996. Plasma viral RNA load predicts disease progression in accelerated feline immunodeficiency virus infection. *J. Virol.* 70(4):2503–2507.

18 de Rozières, S., et al. 2004. Characterization of a highly pathogenic molecular clone of feline immunodeficiency virus clade C. *J. Virol.* 78(17):8971–8982.

19 Obert, L. A., and E. A. Hoover. 2000. Feline immunodeficiency virus clade C mucosal transmission and disease courses. *AIDS Res. Hum. Retroviruses* 16(7):677–688.

20 Obert, L. A., and E. A. Hoover. 2000. Relationship of lymphoid lesions to disease course in mucosal feline immunodeficiency virus type C infection. *Vet. Pathol.* 37(5):386–401.

21 Dow, S. W., M. J. Dreitz, and E. A. Hoover. 1992. Feline immunodeficiency virus neurotropism: Evidence that astrocytes and microglia are the primary target cells. *Vet. Immunol. Immunopathol.* 35(1-2):23–35.

22 VandeWoude, S., et al. 2002. Nonpathogenic lion and puma lentiviruses impart resistance to superinfection by virulent feline immunodeficiency virus. *J. Acquir. Immune Defic. Syndr.* 29(1):1–10.

23 Israel, Z. R., et al. 1993. Early pathogenesis of disease caused by SIVsmmPBj14 molecular clone 1.9 in macaques. *AIDS Res. Hum. Retroviruses* 9(3):277–286.

24 Mossman, S. P., et al. 1996. Protection against lethal SIVsmmPBj14 disease by a recombinant Semliki Forest virus gp160 vaccine and by a gp120 subunit vaccine. *J. Virol.* 70(3):1953–1960.

25 O'Neil, S. P., et al. 1999. Virus threshold determines disease in SIVsmmPBj14-infected macaques. *AIDS Res. Hum. Retroviruses* 15(2):183–194.

26 O'Neil, S. P., et al. 1999. In vivo cell and tissue tropism of SIVsmmPBj14-bcl.3. *AIDS Res. Hum. Retroviruses* 15(2):203–215.

27 Hoover, C. E., et al. 2017. Pathways of prion spread during early chronic wasting disease in deer. *J. Virol.* 91(10):e00077-17.

28 Henderson, D. M., et al. 2015. Longitudinal detection of prion shedding in saliva and urine by chronic wasting disease-infected deer by real-time quaking-induced conversion. *J. Virol.* 89(18):9338–9347.

29 Seelig, D. M., et al. 2011. Chronic wasting disease prion trafficking via the autonomic nervous system. *Am. J. Pathol.* 179(3):1319–1328.

30 Mathiason, C. K., et al. 2009. Infectious prions in pre-clinical deer and transmission of chronic wasting disease solely by environmental exposure. *PloS one* 4(6):e5916.

31 Mathiason, C. K., et al. 2006. Infectious prions in the saliva and blood of deer with chronic wasting disease. *Science* 314(5796):133–136.

32 Sigurdson, C. J., et al. 1999. Oral transmission and early lymphoid tropism of chronic wasting disease PrPres in mule deer fawns (Odocoileus hemionus). *J. Gen. Virol.* 80(Pt 10):2757–2764.

33 Sigurdson, C. J., et al. 2002. PrP(CWD) lymphoid cell targets in early and advanced chronic wasting disease of mule deer. *J. Gen. Virol.* 83(Pt 10):2617–2628.

34 Denkers, N. D., et al. 2020. Very low oral exposure to prions of brain or saliva origin can transmit chronic wasting disease. *PloS one* 15(8):e0237410.

35 McNulty, E. E., et al. 2020. In vitro detection of haematogenous prions in white-tailed deer orally dosed with low concentrations of chronic wasting disease. *J. Gen. Virol.* 101(3):347–361.

36 Bartz, J. C., et al. 2024. Chronic wasting disease: State of the science. *Pathogens* 13(2):138.

37 Goñi, F., et al. 2015. Mucosal immunization with an attenuated *Salmonella* vaccine partially protects white-tailed deer from chronic wasting disease. *Vaccine* 33(5):726–733.

38 Haley, N. J., et al. 2012. Sensitivity of protein misfolding cyclic amplification versus immunohistochemistry in ante-mortem detection of chronic wasting disease. *J. Gen. Virol.* 93(Pt 5):1141–1150.

39 Kurt, T. D., et al. 2011. Alteration of the chronic wasting disease species barrier by in vitro prion amplification. *J. Virol.* 85(17):8528–8537.

40 Angers, R. C., et al. 2010. Prion strain mutation determined by prion protein conformational compatibility and primary structure. *Science* 328(5982):1154–1158.

41 Nalls, A. V., et al. 2021. Detection of chronic wasting disease prions in fetal tissues of free-ranging white-tailed deer. *Viruses* 13(12):2430.

42 Bian, J., et al. 2017. Prion replication without host adaptation during interspecies transmissions. *Proc. Natl. Acad. Sci. U. S. A.* 114(5):1141–1146.

43 Haley, N. J., and E. A. Hoover. 2015. Chronic wasting disease of cervids: Current knowledge and future perspectives. *Annu. Rev. Anim. Biosci.* 3:305–325.

44 Schweickart, S., and H. Walls-Scott. Edward A. Hoover Memorial 2023, streamed live on May 16, 2023, YouTube video, 6:04, https://www.youtube.com/watch?v=lGS8oHtryMQ.

Selected Bibliography

1967 With R. G. Olsen et al. Feline leukemia virus infection: Age-related variation in response of cats to experimental infection. *J. Natl. Cancer Inst.* 57(2):365–369.

1986 With J. I. Mullins and C. S. Chen. Disease-specific and tissue-specific production of unintegrated feline leukaemia virus variant DNA in feline AIDS. *Nature* 319(6051):333–336.

1987 With J. I. Mullins, S. L. Quackenbush, and P. W. Gasper. Experimental transmission and pathogenesis of immunodeficiency syndrome in cats. *Blood* 70(6):1880–1892.

1995 With L. J. Diehl et al. Induction of accelerated feline immunodeficiency virus disease by acute phase virus passage. *J. Virol.* 69(10):6149–6157.

With L. L. O'Neil, M. J. Burkhard, and L. J. Diehl. Vertical transmission of feline immunodeficiency virus. *AIDS Res. Hum. Retroviruses* 11(1):171–182.

1996 With L. J. Diehl, C. K. Mathiason-DuBard, and L. L. O'Neil. Plasma viral RNA load predicts disease progression in accelerated feline immunodeficiency virus infection. *J. Virol.* 70(4):2503–2507.

With S. P. Mossman et al. Protection against lethal SIVsmmPBj14 disease by a recombinant Semliki Forest virus gp160 vaccine and by a gp120 subunit vaccine. *J. Virol.* 70(3):1953–1960.

1999 With C. J. Sigurdson et al. Oral transmission and early lymphoid tropism of chronic wasting disease PrPres in mule deer fawns (*Odocoileus hemionus*). *J. Gen. Virol.* 80(Pt 10):2757–2764.

2000 With J. I. Mullins. Prototype FelV isolates for use in disease models and vaccines. U.S. patent US6042835A, filed April 22, 1994, and issued March 28, 2000.

2006 With C. K. Mathiason et al. Infectious prions in the saliva and blood of deer with chronic wasting disease. *Science* 314(5796):133–136.

2020 With N. D. Denkers et al. Very low oral exposure to prions of brain or saliva origin can transmit chronic wasting disease. *PloS one* 15(8):e0237410.

2024 With J. C. Bartz et al. Chronic wasting disease: State of the science. *Pathogens* 13(2):138.