



Harley W. Moon

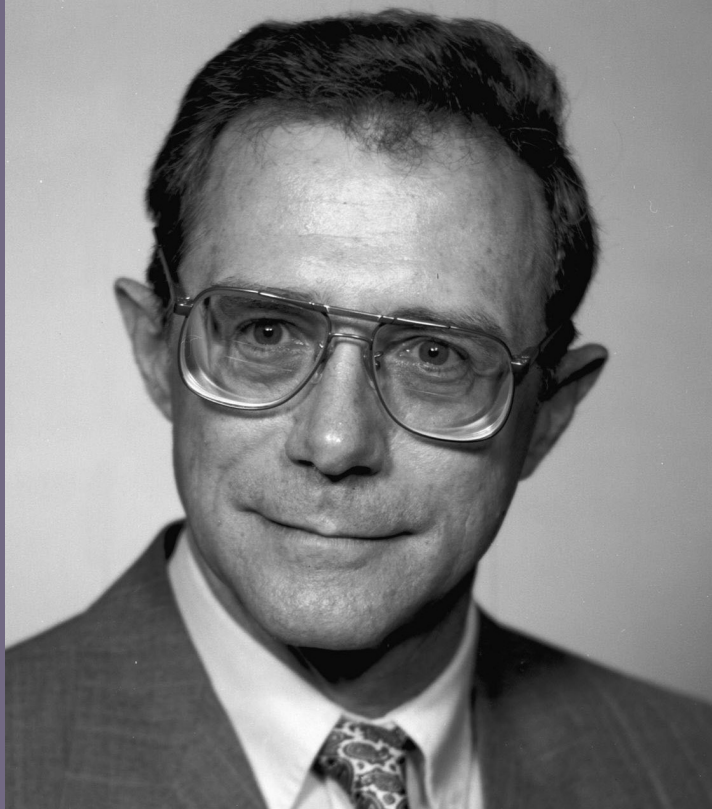
1936–2018

BIOGRAPHICAL

Memoirs

*A Biographical Memoir by
Edward Hoover
and Béla Nagy*

©2023 National Academy of Sciences.
Any opinions expressed in this memoir
are those of the authors and do not
necessarily reflect the views of the
National Academy of Sciences.



NATIONAL ACADEMY OF SCIENCES

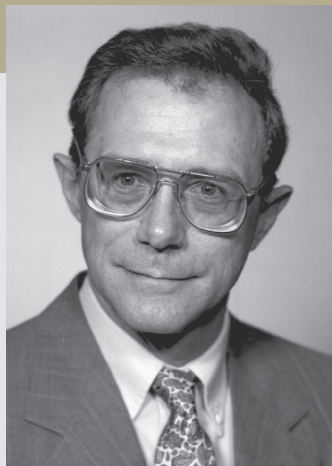
HARLEY WILLIAM MOON

March 1, 1936–October 7, 2018

Elected to the NAS, 1991

Harley William Moon was an outstanding scientist whose translational research reshaped both our understanding of and the treatment of intestinal disease in animals and humans. Equally impactful, he was an inspiring and formative mentor and collaborator who seeded and guided the research careers of many young scientists and colleagues. He earned a D.V.M degree in 1960 and a Ph.D. in 1965 from the University of Minnesota.

Moon was an effective leader in his roles as director, respectively, of the National Animal Disease Center of the USDA's Agricultural Research Service; the Plum Island Animal Disease Center; and the Veterinary Research Institute at Iowa State University, as well as professor in the Department of Veterinary Pathobiology at Ohio State University. In total, Harley Moon had a formative and lasting impact in the United States and the world.



Photography by NADC, ARS, USDA

*By Edward Hoover
and Béla Nagy*

Harley W. Moon was born on a farm in southwest Minnesota on March 1, 1936, during the Great Depression. He lost his father in World War II in 1945. Thereafter he was mentored by his stepfather, farmer Melvin Lien. Harley's innate curiosity, sharp intellect, and the desire to understand and prevent intestinal disorders was prompted by the fatal intestinal diseases he witnessed in piglets and calves. He earned a D.V.M in 1960 and a Ph.D. in 1965 from the College of Veterinary Medicine at the University of Minnesota. His PhD doctoral thesis focused on enteric colibacillosis of piglets, which led to his life's work.

In 1956 Harley married his first love in high school, Irene Casper. Their marriage was blessed with four children, and the young family went with Harley to his postdoctoral studies at the Brookhaven National Laboratory, and then at the University of Saskatchewan.

In 1968, he joined the Department of Agriculture's Agricultural Research Service, working at the National Animal Disease Center (NADC) for more than 25 years, serving for several years as research veterinarian and research leader and directing the center from 1988 to 1995 (Fig. 2). Harley then directed the USDA Plum Island Animal Disease Center for a year, before being named to the F.K. Ramsey Endowed Chair and as director of the Veterinary Research Institute at Iowa State University from 1996 to 2003. He took sabbaticals as a professor in the Department of Veterinary Pathobiology at Ohio State University in 1973 and traveled in 1979 to Canberra, Australia, to study immunology. During his three decades of leadership at the NADC, Harley engendered and guided the work of many highly capable scientists in the USA; he also had an international impact on intestinal disease research through his collaborations with many European veterinarians, physicians, and biologists. He generously and formatively shared his knowledge, laboratory, and professional network with these scientists many of whom became later significant contributors to their area of science in Europe.

Harley's long-term scientific interests were many, but always returned to his first focus and search—understanding the deadly enterotoxigenic *E. coli* (ETEC) infection of pigs, calves, and then also a similar disease in children. His work in the newborn pig model brought breakthroughs in ETEC, unveiling the events central to the pathogenesis of fatal colibacillosis by identifying the key events of *E. coli* mucosal adhesion and enterotoxin production.¹⁻⁵ These studies also led to the discovery of bacterial colonization factors that were also essential in imparting host species specificity and were key to successful vaccine development.⁶⁻¹⁰

Harley's research on *E. coli* in animals had an immediate impact on human enteropathogenic *E. coli* (EPEC) and enterohemorrhagic *E. coli* (EHEC) diseases, the latter now known as one of the most feared foodborne zoonotic infections. His work demonstrated that the pathogenic mechanisms of EPEC and EHEC could be studied in rabbits and pigs.^{11,12,13} and that the EHEC disease was mediated by a Shigella-like enterotoxin. For EPEC and EHEC, Harley and coworkers coined the term “attaching effacing *E. coli*” (AEEC).¹⁴ This work led to the elucidation of the processes of bacterial colonization and persistence, and, ultimately, to its prevention.¹⁵⁻¹⁸



Fig.2- Harley W. Moon at his microscope.
(Photography by NADC, ARS, USDA.)

In all, Harley's work changed forever our understanding and treatment of *E. coli* intestinal disease and is a prototype of translational research.

The third realm of Harley's work focused on the zoonotic protozoan cryptosporidia—the cause of cryptosporidiosis in calves and other species, including humans. These pioneering studies established *Cryptosporidium* parvum as an important opportunistic pathogen in immunosuppressed animals and humans and included development of mouse models. Typifying Harley's approach to science, he conducted his work in collaboration with colleagues in Europe and the USA.^{19,20,21}

Perhaps most vivid and cherished by the authors of this memoir, Harley Moon was a warm, inquisitive, enthusiastic, and energetic person who could attract and inspire students, counsel young faculty, and offer his empathy to them and others who needed help. (Fig.3). One of us (EH), then a young assistant professor who wanted to be a veterinary pathologist and biomedical investigator, had the good fortune to have an office next to Harley's and benefitted from all of his contagious traits. Harley demonstrated daily that these things were possible, and that this writer was already doing it—something he has never forgotten. We (EH, BN) also learned through Harley a deep respect for farming and the importance of high-quality and humane treatment of all animals with which we work. We also appreciated his emphasis on writing and reporting results, and not overlooking alternate explanations and implications of negative results. All of this helped young scientists believe that all was not wrong, badly done, or lost, and that there were always other possibilities. In this way, Harley's energy and enthusiasm were contagious and could be saving.



Fig.3- Harley W. Moon with colleagues and collaborators in Ames, IA.

(Photography by B. Nagy, 1990.)

In recognition of his numerous contributions to investigative translational microbiology and pathology, Harley received many awards. To name just a few, he was entered into the USDA Science Hall of Fame in 2000 and into the American Association of Science in 2003. His international impact was recognized by the title of 'Doctor Honoris Causa' in the University of Zürich (1995) and the University of Liege (2001). He was also named an Honorary Member of the Hungarian Society for Microbiology in 1995. Harley also served on expert panels with the World Health Organization, the National Institutes of Health and the National Academy of Sciences.

He advised the U.S. Senate regarding use of antibiotics in livestock feed, and, as chair of the National Research Council's Committee on Agricultural Bioterrorism, discussed threats to agriculture.²²

Harley and his wife, Irene, hosted and helped several colleagues and their families traveling to work with him for extended periods of time. He remained intellectually influential in their lives and careers. He was elected to the National Academy of Sciences in 1991, where he had a continued influence and was treasured as a colleague up to the time of his death on October 7, 2018, when he was 82. Irene died six years before Harley and they are survived by four children and four grandchildren.

The authors are grateful to Oxford University Press and to coauthors of BN for the opportunity of using the data and parts of this text.²³

REFERENCES

1. Moon, H. L. 1971. Epithelial Cell Migration in the Alimentary Mucosa of the Suckling Pig. *Proceedings of the Society for Experimental Biology and Medicine* 137:151-154.
2. Bertschinger, H. U., S. C. Whipp, and H. W. Moon. 1972. Association of *Escherichia coli* with the small intestinal epithelium. I. Comparison of enteropathogenic and nonenteropathogenic porcine strains in pigs. *Infect. Immun.* 5:595-605.
3. Donta, S. T., H. W. Moon, and S. C. Whipp. 1974. Detection of heat-labile *Escherichia coli* enterotoxin with the use of adrenal cells in tissue culture. *Science* 183:334-336.
4. Moon, H. W. 1978. Mechanisms in the pathogenesis of diarrhea: A review. *J. Am. Vet. Med. Assoc.* 172:443-448.
5. Lee, C. H., S. L. Moseley, H. W. Moon et al. 1983. Characterization of the gene encoding heat-stable toxin II and preliminary molecular epidemiological studies of enterotoxigenic *Escherichia coli* heat-stable toxin II producers. *Infect. Immun.* 42:264-268.
6. Moon, H. W., B. Nagy and R. E. Isaacson. 1977. Intestinal colonization and adhesion by enterotoxigenic *Escherichia coli*: ultrastructural observations on adherence to ileal epithelium of the Pig. *J. Infect. Dis.* 136:124-129.
7. Nagy, B., H. W. Moon, and R. E. Isaacson. 1977. Colonization of porcine intestine by enterotoxigenic *Escherichia coli*: selection of piliated forms in vivo, adhesion of piliated forms to epithelial cells in vitro, and incidence of a pilus antigen among porcine enteropathogenic *E. coli*. *Infect. Immun.* 16:344-352.
8. Isaacson, R. E., P. C. Fusco, H. W. Moon, and C. C. Brinton. 1978. In vitro adhesion of *Escherichia coli* to porcine small intestinal epithelial cells: pili as adhesive factors. *Infect Immun.* 21:392-397.
9. Nagy, B., T. A. Casey, S. C. Whipp and H. W. Moon. 1992. Susceptibility of porcine intestine to pilus-mediated adhesion by some isolates of piliated enterotoxigenic *Escherichia coli* increases with age. *Infect. Immun.* 60:1285-1294.
10. Moon, H. W. and T. O. Bunn. 1993. Vaccines for preventing enterotoxigenic *Escherichia coli* infections in farm animals. *Vaccine* 11(2):213-220.
11. Moon, H. W., S. C. Whipp, R. A. Argenzio, et al. 1983. Attaching and effacing activities of rabbit and human enteropathogenic *Escherichia coli* in pig and rabbit intestines. *Infect. Immun.* 41:1340-1351.

12. Mainil, J. G., C. J. Duchesnes, S. C. Whipp, et al. 1987. Shiga-like toxin production and attaching and effacing activity of *Escherichia coli* associated with calf diarrhea. *Am. J. Vet. Res.* 48:743-748.
13. Pospischil, A. J. G. Mainil, G. Baljer, and H. W. Moon. 1987. Attaching and effacing bacteria in the intestines of calves and cats with diarrhea. *Vet. Pathol.* 24:330-334.
14. Moon, H. W., S. C. Whipp, R. A. Argenzio, et al. See Ref 11.
15. Moon, H. W. and W. C. Cray, Jr. 1995. Experimental infection of calves and adult cattle with *Escherichia coli* O157:H7. *Appl. Envir. Microbiol.* 61:1586-1590.
16. Dean-Nystrom, E. A., B. T. Bosworth, H. W. Moon, and W. C. Cray, Jr. 1997. Pathogenicity of *Escherichia coli* O157:H7 in the intestines of neonatal calves. *Infect. Immun.* 65:1842-1848.
17. Dean-Nystrom, E. A., L. J. Gansheroff, M. Mills et al. 2002. Vaccination of pregnant dams with intimin_{O157} protects suckling piglets from *Escherichia coli* O157:H7 infection. *Infect. Immun.* 70:2414-2418.
18. Pruiimboom-Brees, I. M., T. W. Morgan, M. R. Ackermann, and H. W. Moon. 2000. Cattle lack vascular receptors for *Escherichia coli* O157:H7 Shiga toxins. *Proc. Natl. Acad. Sci. U. S. A* 97:10325-10329.
19. Pohlenz, J., W. J. Bemrick, H. W. Moon, and N. F. Cheville. 1978. Bovine cryptosporidiosis: a transmission and scanning electronmicroscopic study of some stages in the life cycle and of the host-parasite relationship. *Vet. Pathol.* 15:417-427.
20. Heine, J., H. W. Moon and D. B. Woodmansee. 1984. Persistent *Cryptosporidium* infection in congenitally athymic (nude) mice. *Infect. Immun.* 43:856-89.
21. Harp, J. A. and H. W. Moon. 1991. Susceptibility of mast cell-deficient W/W^w mice to *Cryptosporidium parvum*. *Infect. Immun.* 59:718-720.
22. Moon, H. W., C. Kirk-Baer, M. Ascher, R. J. Cook et al. US Agriculture Is Vulnerable to Bioterrorism. *J. Vet. Med. Educ.* 30:96-104.
23. Bertschinger, H. U., C. J. Duchesnes, J. G. Mainil et al. 2020. Harley William Moon (1936-2018). *FEMS Microbiol. Lett.* 2020, 367: fnz012.

SELECTED BIBLIOGRAPHY

- 1971 Epithelial Cell Migration in the Alimentary Mucosa of the Suckling Pig. Proceedings of the Society for Experimental Biology and Medicine 137:151-154.
- 1972 With H. U. Bertschinger and S. C. Whipp. Association of *Escherichia coli* with the small intestinal epithelium. I. Comparison of enteropathogenic and nonenteropathogenic porcine strains in pigs. *Infect. Immun.* 5:595-605.
- 1974 With S. T. Donta and S. C. Whipp. Detection of heat-labile *Escherichia coli* enterotoxin with the use of adrenal cells in tissue culture. *Science* 183:334-336.
- 1977 With B. Nagy and R. E. Isaacson. Intestinal colonization and adhesion by enterotoxigenic *Escherichia coli*: ultrastructural observations on adherence to ileal epithelium of the Pig. *J. Infect. Dis.* 136:124-129.
- With B. Nagy and R. E. Isaacson. Colonization of porcine intestine by enterotoxigenic *Escherichia coli*: selection of piliated forms in vivo, adhesion of piliated forms to epithelial cells in vitro, and incidence of a pilus antigen among porcine enteropathogenic *E. coli*. *Infect. Immun.* 16:344-352.
- 1978 Mechanisms in the pathogenesis of diarrhea: A review. *J. Am. Vet. Med. Assoc.* 172:443-448.
- With R. E. Isaacson, P. C. Fusco, and C. C. Brinton. In vitro adhesion of *Escherichia coli* to porcine small intestinal epithelial cells: pili as adhesive factors. *Infect Immun.* 21:392-397.
- 1978 With J. Pohlenz and W. J. Bemrick. Bovine cryptosporidiosis: a transmission and scanning electronmicroscopic study of some stages in the life cycle and of the host-parasite relationship. *Vet. Pathol.* 15:417-427.
- 1983 With C. H. Lee, S. L. Moseley, et al. Characterization of the gene encoding heat-stable toxin II and preliminary molecular epidemiological studies of enterotoxigenic *Escherichia coli* heat-stable toxin II producers. *Infect. Immun.* 42:264-268.
- With S. C. Whipp, R. A. Argenzio, et al. Attaching and effacing activities of rabbit and human enteropathogenic *Escherichia coli* in pig and rabbit intestines. *Infect. Immun.* 41:1340-1351.
- 1984 With J. Heine and D. B. Woodmansee. Persistent *Cryptosporidium* infection in congenitally athymic (nude) mice. *Infect. Immun.* 43:856-89.

- 1987 With J. G. Mainil, C. J. Duchesnes, and S. C. Whipp. Shiga-like toxin production and attaching and effacing activity of *Escherichia coli* associated with calf diarrhea. *Am. J. Vet. Res.* 48:743-748.
- With A. Pospischil, J. G. Mainil, and G. Baljer. Attaching and effacing bacteria in the Intestines of calves and cats with diarrhea. *Vet. Pathol.* 24:330-334.
- 1991 With J. A. Harp. Susceptibility of mast cell-deficient W/Ww mice to *Cryptosporidium parvum*. *Infect. Immun.* 59:718-720.
- 1992 With B. Nagy, T. A. Casey, and S. C. Whipp. Susceptibility of porcine intestine to pilus-mediated adhesion by some isolates of piliated enterotoxigenic *Escherichia coli* increases with age. *Infect. Immun.* 60:1285–1294.
- 1993 With T. O. Bunn. Vaccines for preventing enterotoxigenic *Escherichia coli* infections in farm animals. *Vaccine* 11(2):213-220.
- 1995 With W. C. Cray, Jr. Experimental infection of calves and adult cattle with *Escherichia coli* O157:H7. *Appl. Envir. Microbiol.* 61:1586-1590.
- 1997 With E. A. Dean-Nystrom, B. T. Bosworth, and W. C. Cray, Jr. Pathogenicity of *Escherichia coli* O157:H7 in the Intestines of Neonatal Calves. *Infect. Immun.* 65:1842-1848.
- 2000 With I. M. Pruiimboom-Brees, T. W. Morgan, M. R. Ackermann, et al. Cattle lack vascular receptors for *Escherichia coli* O157:H7 Shiga toxins. *Proc. Natl. Acad. Sci. U S A* 97:10325–10329.
- 2002 With E. A. Dean-Nystrom, L. J. Gansheroff, and M. Mills. Vaccination of pregnant dams with intimin_{O157} protects suckling piglets from *Escherichia coli* O157:H7 infection. *Infect. Immun.* 70:2414–2418.
- 2003 With C. Kirk-Baer and M. Ascher, et al. US Agriculture Is Vulnerable to Bioterrorism. *J. Vet. Med. Educ.* 30:96-104.

Published since 1877, *Biographical Memoirs* are brief biographies of deceased National Academy of Sciences members, written by those who knew them or their work. These biographies provide personal and scholarly views of America's most distinguished researchers and a biographical history of U.S. science. *Biographical Memoirs* are freely available online at www.nasonline.org/memoirs.