Dr. Andrew Onderdonk is proudest of three things he accomplished in his work. First, his research, especially on the role of *Clostridioides difficile* in pseudomembranous colitis. Second, the people he has mentored in science and medicine. Third, his time as Editor in Chief of the *Journal of Clinical Microbiology* and how he raised the standards at the journal, improving the quality of the papers and the national and international stature of the journal.

Dr. Onderdonk grew up in rural Connecticut, surrounded by apple orchards and tobacco farms. He had six sisters and one brother, all of whom he still visits and talks with frequently. His mother was busy at home and his father was a successful structural engineer with his own firm, where he designed the Bank of Bermuda, with a tricky lower floor below sea level, and many of the dormitories at the University of Connecticut. Dr. Onderdonk's interest in science came early. He received a microscope from his aunt and uncle when he was 10 years old and investigated the microorganisms in pond water. He was keenly interested in nature, so he brought home a mass of frog eggs to keep in an aquarium and, later, a praying mantis egg case. The frog's eggs hatched and the tadpoles were easily dealt with. It was more challenging when the praying mantis egg case...
hatched. “You’ve got a problem in your room,” his mother said, and the future Dr. Onderdonk went into his bedroom to find “10,000 little-bitty praying mantises crawling all over the place.” Later, he took an outstanding college course, “The Protists,” at MacMurray College in Jacksonville, Illinois, which sparked his interest in microbiology. While still in college, he began working in a clinical microbiology laboratory at a small hospital, also in Jacksonville, where he first became interested in clinical microbiology. He later attended the University of Missouri, where he got his Ph.D., followed by a clinical fellowship in the Infectious Diseases Service at University of California Los Angeles.

Following his Ph.D. work, Dr. Onderdonk joined Dr. Sherwood Gorbach’s research group for postdoctoral research, initially at the University of California Los Angeles and, soon thereafter, at Tufts University in Boston. It was with Dr. Gorbach’s group that he began the research that continues to this day. The unifying theme of Dr. Onderdonk’s research has been the role of the microbiota, particularly obligate anaerobic bacteria, in health and disease. His initial work was on a pressing issue at the time, the cause of antibiotic-associated colitis. The discovery of *C. difficile* as the cause of antibiotic-associated colitis proceeded very quickly, beginning when Dr. Onderdonk was 27 years old. In 1975, representatives of the Upjohn Company contacted Dr. Gorbach, asking him to investigate the colitis that followed treatment with clindamycin in many patients. Dr. Gorbach asked Dr. Onderdonk to work on this with Dr. John Bartlett at Tufts University School of Medicine and suggested that an animal model was needed. Dr. Onderdonk reviewed the literature and decided that hamsters would be the best small-animal model, as they develop fatal colitis when given lincomycin or clindamycin. Dr. Onderdonk and colleagues demonstrated that treatment with vancomycin prevented mortality in similarly treated animals and, furthermore, reduced the number of clostridia in stool (1). A virologist and collaborator, Dr. Te Wen Chang, had found that stool filtrate from patients with antibiotic-associated colitis caused a cytopathic effect in tissue culture, suggesting that the cause of this disease was a virus or, as Dr. Onderdonk thought, a bacterial toxin. In a subsequent paper the same year, they found that colitis could be caused by transferring cecal contents or cell-free filtrate of cecal contents from hamsters treated with clindamycin to untreated hamsters (2). Dr. Onderdonk recalls that, “within 3 months, I had the bug.” It was an isolate of *Clostridiodes* species recovered from a hamster with clindamycin-induced colitis. A cell-free supernatant of the isolate caused colitis when administered intracecally to healthy hamsters. Gas gangrene antitoxin, presumably containing antibodies to clostridial toxins, could neutralize the ability of cecal contents from affected hamsters from causing disease upon intracecal transfer to healthy hamsters, further supporting the hypothesis that a toxin-producing species of *Clostridiodes* was the cause of clindamycin-associated colitis in this animal model. These results in hamsters were linked to antibiotic-associated pseudomembranous colitis in humans in a subsequent paper in which cytotoxicity of samples from clindamycin-treated hamsters and a patient with pseudomembranous colitis following antibiotic treatment was found to be neutralized by clostridial antitoxin (3). Finally, in a paper in the *New England Journal of Medicine* in 1978 on which Dr. Onderdonk is the senior author, stool samples from four patients with pseudomembranous colitis following antibiotic treatment and one patient with antibiotic-associated diarrhea were found to cause cytotoxicity in cell culture and enterocolitis in hamsters (4). These effects could be neutralized by pretreatment of the samples with antitoxin for gas gangrene. Cell-free broth from cultures of *C. difficile* isolated from most of these samples also caused cytotoxicity and enterocolitis in hamsters, firmly linking toxin-producing *C. difficile* to antibiotic-associated pseudomembranous colitis in humans. Dr. Onderdonk vividly remembers when the work was presented at the American Society for Microbiology (ASM) meeting, with several thousand people in attendance. Dr. Lynn Bry, Associate Medical Director in the Clinical Microbiology Laboratory at Brigham and Women’s Hospital, wrote, “Not only did Andy discover *C. difficile* as the cause of pseudomembranous colitis, but he developed the first diagnostic tests and animal models that would enable specific diagnosis of disease and also support mechanistic studies to define how commensals modulate disease.”
After working as a postdoctoral fellow at Tufts University for a few years, Dr. Onderdonk decided he should look for a faculty position. At the time, Tufts University was starting a new school of veterinary medicine. “That sounds like an opportunity,” Dr. Onderdonk thought, so he contacted the newly appointed Dean of the Cummings School of Veterinary Medicine, who appointed him as the second faculty member at the nascent school. There, he built the veterinary clinical microbiology laboratory “from scratch.” The comparative biology and microbiology “were very, very helpful to me in a lot of different ways throughout my career, so I did that for about a decade,” Dr. Onderdonk recalls. In 1990, he was asked to join the Brigham and Women’s Hospital as the Director of the Clinical Microbiology Laboratory, which he did, while also building a highly successful research laboratory at the Channing Laboratory, which was affiliated with the hospital. “It was a good opportunity to swim in a pond with the big fish,” Dr. Onderdonk recalls. When he joined the Brigham and Women’s Hospital, he was appointed as Associate Professor of Pathology at Harvard Medical School, followed by promotion to Professor of Pathology in 2000.

At the Channing Laboratory, Dr. Onderdonk’s research built on his previous work and expanded it to include new collaborations and subjects while continuing in the general area of the role of the anaerobic microbiome in health and disease. He developed a model for intra-abdominal sepsis, demonstrating that abscess formation occurred when facultative anaerobic and obligate anaerobic bacteria were both present but not when only one of these was present (5). This model was successfully used to evaluate treatment of abdominal infections by a variety of antibiotics (5–7). Another major area of investigation was the vaginal microbiome. As with all good science, the first step was to develop an accurate method of quantification using the best technology available, which, at the time, was bacterial culture (8). Initial descriptive studies determined the vaginal microbiota of adults and children (9, 10). This work progressed to include work on the role of the vaginal microbiota in toxic shock syndrome (11–13), bacterial vaginosis (14, 15), and preterm delivery (16–18). Another major area of inquiry for Dr. Onderdonk, pursued in collaboration with Dr. Dennis Kasper, was the role of the capsule in the virulence of Bacteroides fragilis. Encapsulated, but not unencapsulated, strains caused abscess formation in the intra-abdominal sepsis model; furthermore, purified capsule also caused abscess formation (19). Subsequent work demonstrated the potential for immunization with B. fragilis capsule in protection from infection and, surprisingly, that this protection was mediated by T lymphocytes (20). The zwitterionic capsular polysaccharide was found in a series of studies to activate T lymphocytes and mediate both abscess formation and immune protection (21).

Dr. Onderdonk’s research into the microbiome is highly respected by his colleagues. Dr. Wendy Garrett, Irene Heinz Given Professor of Immunology and Infectious Diseases in the Departments of Immunology and Infectious Diseases and of Molecular Metabolism at the Harvard Chan School of Public Health, said that “Andy’s identification of C. difficile as a causative agent for antibiotic-associated diarrhea and colitis remains a landmark discovery for microbiology and gastroenterology. I firmly believe that he is a founder of the current human microbiome studies field and his fervor for culture has fueled the current resurgence of interest for a wide swathe of biologists in anaerobes.” In 2006, an obligate anaerobic bacterium, Alistipes onderdonkii, was named “to honor Andrew B. Onderdonk… for his contribution to increased knowledge about intestinal microbiota and anaerobic bacteria” (22). Dr. Onderdonk recalls that Dr. Sydney Finegold (23) called and said, “You know, I isolate and characterize these new bacteria. I’d like name one after you. The one I want to name after you is really smelly.” Dr. Onderdonk replied, “That fits me perfectly. Go for it.” There are now two subspecies of A. onderdonkii, A. onderdonkii subsp. vulgaris and A. onderdonkii subsp. onderdonkii (24).

Dr. Onderdonk performed several research projects related to his work directing the busy clinical microbiology laboratory at Brigham and Women’s Hospital. These included studies of innovative methods for culture of obligate anaerobic bacteria (25, 26), improved data analysis for pulse-field gel electrophoresis (27), antibiotic resistance in Streptococcus
pyogenes (28), and molecular detection of methicillin-resistant *Staphylococcus aureus* (29). In total, his remarkable publication record includes over 200 original research articles and over 50 review articles. He has authored chapters in influential clinical texts, including chapters on *Laboratory Diagnosis of Infectious Diseases* in *Harrison’s Principles of Internal Medicine* and on *Gas-Liquid High Performance Chromatographic Methods for the Identification of Organisms and Clostridium* in the *Manual of Clinical Microbiology*. A key to his success is described by Mary Delaney, M.A., who worked with Dr. Onderdonk for 36 years. She wrote that “There is one phrase that I heard repeatedly over the years: ‘We can do that.’ It is a simple 4-word phase that summarizes the type of scientist, researcher, and individual that he is. Andy has a passion for learning and for sharing his knowledge and imparts his enthusiasm to empower his team to produce successful outcomes.” In other clinical work, Dr. Onderdonk has been a consultant to a remarkable number of small and large biotechnical companies, all with the goal of making clinically useful technology available for patient care.

Many of those who sent me reflections on their work with Dr. Onderdonk stressed his importance as a mentor. Here, I include myself. Dr. Onderdonk was my mentor in clinical microbiology during my residency in clinical pathology and for several years while I worked as Assistant Director in the microbiology laboratory at Brigham and Women’s Hospital. He decided I was ready to run my own laboratory before I did and encouraged me to apply for a job as Medical Director at a neighboring hospital. To prepare me, he asked me a difficult interview question about whether a specific test should be used in the clinical laboratory. I answered as best I could, but my answer was, frankly, lame. He cheerfully said, “That’s great, that’s great, Alex. You might also say that…” and then gave me a detailed framework for explaining what steps I would take to decide whether to implement the test. I followed his advice and got the job.

Dr. Manfred Brigl, who also trained in clinical pathology at the Brigham and Women’s Hospital, where he has succeeded Dr. Onderdonk as the Director of the Clinical Microbiology Laboratory, wrote that “What stands out to me about Andy is his dedication to being a mentor and teacher, be it for residents, students, medical directors or technologists in the micro lab: he always cares to know what you want to do or become and helps you get there.” Dr. Raina Fichorova, Distinguished Chair in Obstetrics, Gynecology, Brigham and Women’s Hospital, said of her 2-decades-long collaboration with Dr. Onderdonk that “Andy was light years ahead of the field investigating and teaching the importance of what we call now the vaginal holobiont. Andy most generously and wholeheartedly opened his microbiology ‘kitchen’ not just to me, but also to countless young investigators. What I learned helped me start a novel *in vitro* human vaginal colonization model widely utilized today. He is a true encyclopedia in clinical microbiology and the best mentor ever.” Dr. Garrett said of Dr. Onderdonk that “Professor Onderdonk is an exceptional mentor. I will be eternally grateful for his generosity in spirit and knowledge-sharing. I personally and the field of microbiome studies in general owe Andy an enormous debt of gratitude for his mentorship and contributions. Andy’s joy for bacteria is truly infectious.” Despite his success as a mentor (and scientist), Dr. Onderdonk is unassuming. Dr. Lawrence C. Paoletti, now retired as Associate Professor of Medicine at Brigham and Women’s Hospital, wrote that “Andy never took himself too seriously, yet he was dead serious about how research was designed, performed, and evaluated. He was an accommodating, down-to-earth, easy-going, unassuming scientist who led by example.”

Dr. Onderdonk served as the Editor in Chief of the *Journal of Clinical Microbiology* from 1999 to 2009, after having been an Editorial Board member from 1989 to 1993 and an Editor from 1993 to 1999. His first order of business as Editor in Chief was to improve the quality of the journal by raising the standards for accepting manuscripts for publication. “I said we’re going to have two criteria for publication. First, good science and second, clinical relevance. Then I brought in some editors who were like minded,” he recalls. Dr. Yi-Wei Tang was one of the editors appointed by Dr. Onderdonk, and he remembers that during his appointment “Andy promised to walk me through the complicated, manual manuscript editing process after hearing both my excitement and hesitation. I remember that
several months later, during an international meeting in Cancun, he made good on his promise, patiently spending an afternoon with me and skipping the sightseeing opportunity. He also generously shared his invaluable experience on numerous unusual cases. He emphasized several times to me his guiding principle for acceptance in JCM of ‘good science with clinical relevance.’ Dr. Peter Gilligan (30), another Editor appointed by Dr. Onderdonk, wrote, “I was indebted for his mentoring when I was chosen to be an editor of JCM. There really is no playbook for that. Andy always had a steady and encouraging hand. He made me feel I was competent even when I was worried that I was not.” As the standards for manuscripts rose, the acceptances fell from approximately 50% to approximately 30%, and journal metrics rose in turn. Dr. Onderdonk is proud that they brought the journal “into the forefront as a major scientific journal.” When ASM Journals began the transition to a web-based system for handling manuscripts, Dr. Onderdonk volunteered the Journal of Clinical Microbiology to pilot the new system, and he successfully led the journal through the challenging transition. In 2001, following the attacks in which spores of Bacillus anthracis were mailed to media companies and congressional offices, the ASM asked the National Academy of Sciences to organize a meeting of biomedical publishers to discuss how to handle publications with information that could be used in terrorist attacks. Dr. Onderdonk was one of the representatives from ASM at that meeting, and he was an author on the PNAS paper that set out the principles by which such manuscripts should be handled (31). I think, as a former Editor and the current Editor in Chief, that Dr. Onderdonk brought the Journal of Clinical Microbiology to the position it has today as the leading journal in clinical microbiology. After his term as Editor in Chief ended, he returned for 10 more years as an Editor of the journal, during which he handled manuscripts, wrote several Biographical Feature articles (32–34), and helped design the very popular Brief Case feature (35). His various appointments at the journal spanned 31 years. Dr. Onderdonk also served in editorial roles at several other journals, including Infection and Immunity, Reviews of Infectious Diseases, mBio, Anaerobe, and Clinical Microbiology Reviews.

Dr. Onderdonk has held a large number of administrative leadership positions and has received numerous honors. He was the Chair of the Faculty Council at Tufts University School of Veterinary Medicine. After moving to Harvard Medical School, he served as the Chair of the Committee on Microbiologic Safety (COMS), which is the Institutional Biosafety Committee at Harvard Medical School and several affiliated hospitals. Rebecca Caruso, the Director, COMS Office of Biological Safety at Harvard Medical School wrote, “Andy helped ensure that the work occurring in Harvard-affiliated institutions only began after careful review of the safety procedures put in place to support the science. Due to his incredible expertise in microbiology, we still call on him from time to time to provide scientific reviews as an external reviewer.” He was the Chair of the organizing committees for several meetings, including the Society for Microbial Ecology and Diseases, and the three separate World Congresses on Anaerobic Bacteria and Bacterial Infections. Dr. Onderdonk was elected President of the Society for Microbial Ecology and Disease and President of the International Society for Anaerobic Bacteria. In 1981, he was elected as a Fellow of the American Academy of Microbiology of ASM. He also received the Distinguished Alumni Award from MacMurray College in 1999.

Dr. Onderdonk is proud of the family that he and his wife, Juliet (Wherry) Onderdonk, raised together. He and Jill were introduced by family friends just before beginning college. “We hit it off right away,” he recalls and they were married in 1969, following graduation. Mrs. Onderdonk worked as the Housing Coordinator for the Westwood Housing Authority, where she increased access to affordable housing in their community. She was also very active in politics with the local Democratic Party and worked on several local and national campaigns. She and Dr. Onderdonk were members of St. John’s Episcopal Church in Westwood, Massachusetts, where they both held roles in church leadership. Sadly, Mrs. Onderdonk passed away in 2019, when they had been married nearly 50 years. They had three children, Mark Onderdonk, who teaches special education at the League School of Greater Boston; Sara Jastrem, a Senior Project Manager NASDAQ; and Abby De Molina, now the Head of Private Client...
and Select Program at Santander Bank. Dr. Onderdonk has three grandchildren, Ayden, Teddy and Andrew, who is named after Dr. Onderdonk. All three of Dr. Onderdonk’s children live near him, and he sees them and their families often.

In retirement, Dr. Onderdonk has hardly slowed down at all. Today, Dr. Onderdonk is Professor of Pathology, Emeritus, at Harvard Medical School. He continues to teach microbiology to the pathology residents and clinical microbiology fellows at Brigham and Women’s Hospital, to consult for the Food and Drug administration, to collaborate on research on the microbiome, and as a consultant to a start-up technology company that is working on a product to improve microscopy. When I spoke with him recently, he was deeply tan and as cheerful, boisterous, and kind as ever. He has touched and brightened the lives of his family, his colleagues, those he has mentored, the clinical microbiology community, and, most importantly, countless patients.

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