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Biographical Feature

Clyde Thornsberry, Ph.D.

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Weep no more, my lady, Oh! Weep no more today! We will sing one song For the old Kentucky home, For the old Kentucky home, far away. —Stephen Collins Foster, "My Old Kentucky Home, Good Night"

A s this writer set out to draft the biographical feature on Dr. Clyde Thornsberry following various bibliographic surveys and personal interviews, the lyrics and music of this classical 19thcentury American ballad resonated continuously. On the basis of *curriculum vitae* status, one can easily ascertain the prominent influence that Thornsberry imprinted on the field of microbiology. However, salient "down-home" and "laid-back" personality traits and sentiments further contributed to his success in the field. During a conversation that this writer was privileged to experience with Dr. Thornsberry, on more than one occasion an important reflection was preceded by the phrase "Now this may sound hokey, but. . . ." Gary V. Doern, Ph.D. (1), editor in chief emeritus of *Journal of Clinical Microbiology*, described Thornsberry as being "near the top of the list of all-time good guys in the realm of microbiology and infectious diseases" as well as "a good ol' boy from Kentucky." Ronald N. Jones, M.D., president of JMI Laboratories, not only proclaimed that Thornsberry is "an enjoyable person to be around and share in social events, not because of the microbiology itself, but because he has so many experiences to share" but moreover stated that he "taught me how to drink Jack Daniel's."

Clyde Thornsberry was born in 1930 in Pippa Passes, KY, and had the great fortune ("one of the better things that happened to me in my life") to attend Alice Lloyd College in the same community. At that time, the institution was a 2-year college that also

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operated a grade school. Thornsberry's parents, a coal miner and a stay-at-home mother of 12, understood the value of a quality education and resided in Pippa Passes for the sole purpose of school enrollment. This academic setting fostered the highestquality education by hiring faculty from across the United States (Thornsberry noted that a majority of elementary school instructors possessed a master's degree) and further distinguished itself from other school systems by provision of cultural opportunities (including music and theater) and an emphasis on student teaching experience for students at the collegiate level. Thornsberry excelled in his early education; he tells the story of not only being graduated from high school at age 14 but also of spending a total of 10 minutes in third grade before "the teacher picked me up out of my chair and placed me into the next grade." Following his graduation, Thornsberry taught public school for 5 years before serving at the Eighth Army Headquarters in Seoul, South Korea, for 16 months during the Korean Conflict. Thornsberry remarked that his commission was with the colloquially termed "Remington (typewriter) Raiders" division in a largely administrative role.

Recalling his earlier days in education, Thornsberry reported being a good student in everything but taking a particular interest in science. In a self-effacing tone, Thornsberry reminisced about the bout of pyelonephritis that likely set the tone for his career as a microbiologist. "When I was 14, I came up with a severe kidney infection. They sent me to a hospital in Huntington, West Virginia. I never found out what the organism was . . . but they treated me with streptomycin and penicillin successfully. That really fascinated me and kept me going." Following his service in South Korea, Thornsberry completed a baccalaureate degree in microbiology at the University of Kentucky and undertook microbiology doctoral studies at the same institution, with minors in genetics and biochemistry. The focus of Thornsberry's doctoral research and dissertation was actually immunologic hypersensitivity; however, his graduate school tenure also saw him working as a clinical laboratory technician at Good Samaritan and St. Joseph Hospitals and as an instructor of microbiology at both the University of Kentucky and Transylvania University (all in Lexington, KY).

Groundwork for Thornsberry's first professional position following completion of his graduate studies (Streptococcus Unit, Bacteriology Division at the Centers for Disease Control and Prevention [CDC], Atlanta, GA) was largely paved by previous University of Kentucky graduates such as Drs. Phil Edwards and Bill Cherry, who were integral in his 1966 recruitment. Although the career of Thornsberry is being recognized by this publication in Journal of Clinical Microbiology, he has never described himself as a clinical microbiologist. "Heavens, no. They just let me claim to be a clinical microbiologist." In spite of this "vocational status," Dr. Doern stated that Thornsberry "certainly has influenced the practice of clinical microbiology." In 1971, George Douglas, M.D., chief of the now-defunct CDC Microbiology Branch of the Bureau of Laboratories, upon return from a World Health Organization (WHO) conference that described an emerging threat of worldwide antimicrobial resistance, appointed Thornsberry as chief of the newly founded Antimicrobics Investigations Branch at CDC. Thornsberry embraced this opportunity, stating "I could build the lab the way I wanted it . . . I wanted to make marks for the United States and the rest of the world and I was able to do that."

With respect to major contributions of Thornsberry to the field of clinical microbiology, Daniel F. Sahm, Ph.D., chief scientific

officer of IHMA, Inc., credits him for "shepherding in standardization of antimicrobial susceptibility testing and [doing] much in his career to keep it on track." Dr. Doern added, "in vitro susceptibility testing, as it's done today, is the result of Thornsberry's work." Listening to Thornsberry chronicle the events around standardization of in vitro susceptibility testing procedures was not only very interesting and insightful but also encyclopedic. "Maybe this is how I got associated with the clinical microbiology people," Thornsberry deadpanned. He proceeded to credit Drs. William Kirby and John Sherris (2) for leading the first efforts to standardize disk diffusion susceptibility testing in the early 1960s in the context of appropriate medium, incubation interval, and results interpretation. Moreover, Thornsberry cited early-1960s involvement of the U.S. Food and Drug Administration (FDA) toward delivery of precise antimicrobial agent concentrations into disks as a tremendous step toward achieving standardization of the assay. Such interaction resulted in federal litigation between the FDA and commercial disk manufacturers, with eventual adjudication favoring the FDA. Thornsberry realized the significance of this precedent. "If they [the FDA] could control the disk, they could control everything else." The FDA subsequently adopted the disk diffusion method and published it in the Federal Register.

Dr. Jones, at that time a managed health care system laboratory director in Oregon, recalled that his first introduction to Clyde Thornsberry was in 1973 at a demonstration for a dilution device utilized to create panels for broth microdilution susceptibility testing. Thornsberry had already implemented the device at CDC, and Dr. Jones was reaching out to him for advice with respect to the novel system. The few microbiologists in the United States who were utilizing broth microdilution at that time (including Thornsberry and Drs. Jones, Arthur Barry, Thomas Gavan, Hugh Gerlach, Peter Fuchs, and Herbert Summers) subsequently formed the Collaborative Antimicrobial Susceptibility Testing (CAST) group. The focus of this collaboration was to assess quantitative susceptibility testing technologies and to determine clinical application. These investigations were often concomitant with the introduction of novel anti-infective agents. According to Dr. Jones, the mid-1980s were especially significant for the CAST group, with the introduction of a variety of carbapenems and extended-spectrum cephem agents. Drs. Thornsberry and Jones collaborated on more than 130 peer-reviewed publications between 1977 and 1989 on behalf of the CAST group. Dr. Jones additionally credited Thornsberry for being "able to bring government, academia, and Pharma together to talk and work toward a common goal." Work advancing the broth microdilution method additionally served as a bridge into automated systems of commercially available antimicrobial susceptibility testing.

Thornsberry noted that laboratories directed by the likes of himself and Drs. Jones, Gavan, and Barry subsequently investigated means to "make these tests better and to demonstrate how they should be done." These efforts were subsequent to the establishment of the National Committee for Clinical Laboratory Standards (NCCLS; predecessor to today's Clinical and Laboratory Standards Institute) by Dr. Russell Eilers in the mid-1960s for the purpose of test standardization in the clinical pathology laboratory. Thornsberry became involved in the NCCLS in 1971 (holding membership in the Subcommittee on Disk Diffusion Antimicrobial Susceptibility Testing, the Subcommittee on Antimicrobial Susceptibility Testing of Anaerobes, and the Subcommittee on Dilution Antimicrobial Therapy) and served this organization for the next 41 years. Dr. Doern remarked that the early work of Thornsberry and these subcommittees "developed and promulgated the standards that are still in place today." In essence, fundamental susceptibility testing concepts that are not only employed today in clinical microbiology laboratories but also discussed in clinical laboratory science training programs and undergraduate medical microbiology curricula emanated from Thornsberry's work and were published as seminal NCCLS documents (3–5).

A second major contribution by this pioneer to the field of clinical microbiology is summarized by Ian A. Critchley, Ph.D., vice president of clinical microbiology for Allergan, Plc, who recalled Thornsberry's philosophy that "once an antibiotic is discovered, your job is not done. You need to monitor your product for development of resistance and do surveillance." Dr. Doern credited Thornsberry for inventing the wheel of bacterial antimicrobial surveillance while at CDC, starting with enteric Gramnegative bacilli and then moving on to respiratory pathogens [Haemophilus influenzae, Streptococcus pneumoniae, and Moraxella (Branhamella) catarrhalis] and Neisseria meningitidis. As time moved on, Thornsberry anticipated internal promotion from his position at CDC to one involving more administration and less laboratory. Citing sentiments that "I really didn't want to move up at CDC" and that "maybe I should go out and try the rest of the world," Thornsberry resigned his position in 1989 and became director of the Institutes for Microbiology Research in Franklin, TN, from 1989 to 1993 and chief scientific advisor at MRL Pharmaceutical Services/Focus Technologies/Eurofins from 1993 until his retirement in 2012. During this period, he founded a national database called The Surveillance Network (TSN), which has come to be known by many as the Thornsberry Surveillance Network. This entity is designed to collect quantitative and qualitative real-time antimicrobial resistance test results from clinical microbiology laboratories across the United States and is claimed to be the only source of passive surveillance data accepted by the FDA and other scientific audiences (http://www .eurofins.in/pharma/laboratory-testing-capabilities/global -infectious-disease-services/the-surveillance-network.aspx). Over 300 subscribing laboratories now have access to surveillance data dating back to 1998 with respect to nearly 600 bacterial taxa and over 100 antimicrobial agents, allowing them to ascertain and compare local antimicrobial resistance activity on a temporal and geographic basis.

Thornsberry's career embodies service to the microbiology community. Positions held include fellowships in the American Academy of Microbiology and the Infectious Disease Society of America; Foundation for Microbiology lecturer (American Society for Microbiology); councilor, vice chair, and chair terms of service in the American Society for Microbiology Division C (clinical microbiology); consultant to the FDA, U.S. Pharmacopeia, and WHO concerning antimicrobial agents, susceptibility testing, and resistance to antimicrobial agents; and editorial board activities for Journal of Clinical Microbiology, Antimicrobial Agents and Chemotherapy, Antimicrobics and Infectious Diseases Newsletter, and Manual of Clinical Microbiology (5th edition). In addition, he has been bestowed with the U.S. Army Commendation Ribbon with Metal Pendant and the Public Health Service Superior Leadership Award (the highest award from the Public Health Service to noncommissioned personnel). However, as cited by Dr. Critchley, service to the Interscience Conference on Antimicrobial Agents

and Chemotherapy (ICAAC) from 1980 to 1995 is one of Thornsberry's greatest legacies. Thornsberry himself stated that, on a professional basis, "ICAAC was the love of my life . . . the best infectious diseases meeting in the world" and that his 3-year term as program chair was "the best thing I ever did." He spoke at length about the opportunities to interact with experts during multiple terms on the program committee and the ability to review cutting-edge abstracts on an annual basis. Finally, Thornsberry has accumulated over 330 PubMed-indexed peer-reviewed publications and has coauthored a number of NCCLS standards in proposed, tentative, and approved forms.

Paramount to Thornsberry's success as a microbiology laboratory director and public health officer was his acumen in dealing with people, providing encouragement and counsel. Dr. Sahm referred to Thornsberry as a "common kind of guy and very approachable. He believes in doing the right thing, treating people the right way." James Karlowsky, Ph.D., medical director of clinical microbiology for Diagnostic Services Manitoba, recalled that Thornsberry was "never too big for his britches. He was never the first one to jump into a conversation. He always crafted a very thoughtful answer. He takes the time to listen to people; it's a very useful skill to have when you direct laboratories." Dr. Critchley noted that Thornsberry was very collegial, cooperative, and "a champion for folks interested in antimicrobials." Dr. Jones pegged Thornsberry as "the guy who could reach across the aisle [to pathologists] and brought us all together to make things happen." On top of that, several spoke to Thornsberry's knowledge and experience. Dr. Karlowsky noted that Thornsberry "still pulls things from the 1950s and 1960s that are still relevant." The trustworthy and easygoing nature of Thornsberry made him a highly sought-after speaker around the world. Taken together with his position at CDC, he used this platform to disseminate advances in accurate, clinically relevant antimicrobial susceptibility testing.

Clyde Thornsberry is currently enjoying life in Macon, GA, with Glenda, his wife of 63 years. His residence is local to three children, eight grandchildren, and three great-grandchildren. He now has increased time to enjoy more theater with his wife; he also plays bluegrass guitar on a daily basis, as "thirty minutes of guitar is equal to 6 hours of psychiatry." In addition, he tries to "keep a hand in" by reviewing manuscripts for Journal of Clinical Microbiology and Antimicrobial Agents and Chemotherapy. Thornsberry has always maintained an interest in athletics, having once coached Pop Warner football ("you take your most aggressive player and make him the center; then you take your next best player and make him the quarterback—most teams cannot even manage the center/quarterback snap") and Little League baseball. Baseball is his main sport, because "when you grow up in eastern Kentucky, your team is the Cincinnati Reds." When Thornsberry started employment at CDC, he and his wife became die-hard Atlanta Braves fans and follow them to this day. Finally, Thornsberry ensures his audience that University of Kentucky men's basketball will be sufficiently reloaded for this season.

In conclusion, this short biographical feature can only begin to encapsulate the career and tremendous influence of Dr. Clyde Thornsberry as well as the warmth of the man himself. His legacy may be best captured by the writing of Dr. Doern. "During his long and productive career, Clyde Thornsberry made enormous contributions to our current understanding of antimicrobial resistance—mechanisms of resistance, the epidemiology of resistance, and *in vitro* susceptibility testing. But beyond his uncommon level of scholarly productivity, the thing that really distinguished Dr. Thornsberry was the manner in which he conducted himself. Simply put, Clyde Thornsberry was always planted firmly above the fray. He saw things differently than everyone else, with greater clarity; he was a 'forest from the trees' kind of guy. Perspective was his watchword. The discipline of clinical microbiology is hugely indebted to this consummate laboratory professional."

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