Dr. Leon Speroff, Professor Emeritus and former Chair of Obstetrics and Gynecology at the Oregon Health & Science University School of Medicine and former Arthur H. Bill Professor and Chairman of the Department of Reproductive Biology at the Case Western Reserve University School of Medicine, is being recognized as a Giant in Obstetrics and Gynecology.

Leon has made seminal contributions to reproductive endocrinology, including key concepts in the regulation of the human menstrual cycle, the role of prostaglandins in ovulation, induction of myometrial contractility, induction of labor, and midtrimester termination of pregnancy in addition to the development of radioimmunoassays for primary prostaglandins and their metabolites. Moreover, he described the role of prostaglandins in endotoxic shock and the use of clomiphene in ovulation induction and made contributions that advanced hormone replacement therapy for perimenopausal women as well as steroid hormones for contraception, which changed the practice of medicine.

Leon, with Nathan Kase and Robert Glass, and subsequently with Marc Fritz, wrote the book *Clinical Gynecologic Endocrinology and Infertility* (Figure 1), a true medical best-seller, which has been a vademecum and has taught generations of physicians. Now in its eighth edition, the book has sold nearly 300,000 copies throughout the world.

**Leon’s early life in the Midwest**

Leon was born and raised in Ohio, where he also attended college and medical school. His family came from Macedonia, and his grandparents were mountain people in what is now the northwest corner of Greece. Leon grew up speaking Macedonian and little English until he went to grade school in Lorain. Leon’s father was a barber until he bought a tavern and restaurant in Akron. Leon spent his undergraduate years at Denison University, a liberal arts college in Granville, 30 miles east of Columbus.

**Education in obstetrics and gynecology and steroid hormones**

Leon decided to become a physician in his senior year of college. The Dean of Admissions at the Case Western Reserve University School of Medicine came to interview Leon and offered him a position at the conclusion of the interview. His decision to become an obstetrician was made after he read a book, *Childbirth Without Fear,* about natural childbirth by British obstetrician Grantly Dick-Read. Yale University had the only academic Department of Obstetrics and Gynecology in the United States that promoted natural childbirth, so Leon spent a month as a subintern in New Haven during the summer before his senior year at medical school. Consequently, Yale was the only residency to which he would apply: this proved to be a pivotal decision that influenced the rest of his professional career.

In the beginning of Leon’s year as chief resident, Nathan Kase brought him into his office and said, “Now, let’s think about what’s going to follow.” Once Leon completed a two-year tour of duty in the U.S. Air Force, Nate helped him arrange to become a Fellow in the steroid training program at the Worcester Foundation for Experimental Biology. Following that training, Leon accepted a fellowship with Raymond Vande Wiele at Columbia University. A fascinating observation emerged from that research—mathematical modeling of the hormones produced during the menstrual cycle. Jeff Bogumil, an engineer, and Dr Vande Wiele, using mathematical analyses based on physiologic data pulled from the literature by Leon, predicted that hormones would be secreted in short spurts, a pulsatile manner (Figure 2). This was subsequently confirmed by empirical observations by Robert Jaffe at the University of Michigan.

**Academic career and authorship in reproductive endocrinology**

Leon intended to spend two years at Columbia University, but after his first year, Nate, who had become Chair at Yale in
1969, asked Leon to return, which he did during the summer of 1970. He went on to gain national and international stature because of his clarity of thought, eloquence, and impeccably delivered lectures in reproductive endocrinology. Leon became director of the residency program and, eventually, vice chairman of the department.

One day, Robert Glass stopped Leon in the corridor and asked, “Nate and I are writing a book on endocrinology. Would you like to join us?”

Leon jumped at the chance, met with Bob and Nate, and asked, “Well, what have you done so far?”

They replied, “Nothing.” So Leon took over the project, wrote most of the book, and became the first author of what would be Clinical Gynecologic Endocrinology and Infertility. The first edition was published in 1973; the price was $17 for a book of 266 pages.

Research in prostaglandins and editor of Prostaglandins
Leon’s research at Yale focused on prostaglandins. He recruited Burt Caldwell from the Worcester Foundation to develop radioimmunoassays for prostaglandins, assembled a team that explored the role of prostaglandins in every facet of reproduction, and founded the journal Prostaglandins, which he edited with Burt Caldwell and Gerry Anderson. John Hobbins and Harold Behrman also became important members of the team.

The result was an extremely prolific period of applied research in which the team published extensively on the role of prostaglandins in ovulation, luteolysis, and midtrimester termination of pregnancy as well as induction of labor (Figure 3) and the role of prostaglandins as a cause of preeclampsia, which was validated many years later by the demonstration that aspirin (which blocks prostaglandin production) reduces the frequency of pre-term preeclampsia.

Leon and his group were the first to demonstrate that indomethacin prevents ovulation in the rabbit, and he was the first to report that prostaglandins increase the production of progesterone by the corpus luteum.

Chair at Oregon and Cleveland
Leaving New Haven was difficult, but Leon had decided that he wanted to become a Chair; in the summer of 1976, he accepted a position as Professor and Chair of the Department of Obstetrics and Gynecology at the Oregon Health & Science University School of Medicine in Portland.

Leon introduced daily morning obstetrical rounds. The department’s budget was derived from the Medical School, and faculty members negotiated their salaries with the Chair. In other words, faculty salaries were guaranteed, and the faculty did not have to see a certain number of patients or perform a certain number of procedures, which meant that they had time to teach, do research, and be clinicians. But all that gradually changed with a growing emphasis on finances.

During a recession in 1983, the plans for a desperately needed new labor and delivery unit were canceled, so when the Chair at Leon’s alma mater became available, the temptation to move back to where Leon still had family proved too great. He left Oregon and took a position as Chair of the Department of Reproductive Biology at Case Western Reserve University in Cleveland and was charged with turning around the finances of the MacDonald Women’s Hospital, which was several million dollars in the red.

Leon accomplished this feat in approximately four years, mainly from the income generated by the faculty he had recruited, to the point that the hospital was now $2-$3 million in the black. Subsequently, Leon called a meeting with...
the chief executive officer of the hospital, the dean, and the chief financial officer, presented the new financial situation, and requested that some of the funds be used to develop and support the academic enterprise and research of the department. The leadership was not favorable to this proposal, and Leon thus decided to return to Oregon.

A new approach to contraception
Executives of the Parke-Davis Pharmaceutical Company approached Leon in 1983 and asked for his advice on how to compete with the multiphasic oral contraceptives that were popular at the time. Leon conceived a new approach, using graduated doses of estrogen, with the aim being a beneficial impact on the lipid profile (a hope that did not work out) and better support of the endometrium, an effect that did yield reduced estrogen symptoms (including menstrual and breakthrough bleeding), with the eventual commercial product, Estrostep. The approach was called estrophasic dosing and was published in the Journal in 1999 (Figure 4).16

In addition, Estrostep, with its low androgenicity, proved to be effective for the treatment of acne and was approved for that purpose by the Food and Drug Administration.28 Around the same time, Leon convinced Parke-Davis that the components of its oral contraceptives, ethynyl estradiol and norethindrone acetate, if used in significantly reduced doses, would provide effective postmenopausal hormone therapy. He organized the pilot studies that yielded the commercial product FemHRT.17-19
Leon neither filed patents on his designs nor requested financial compensation from Parke-Davis, but the company spontaneously and graciously volunteered to provide his department an annual grant for the rest of his professional career. In this arena, Leon made a major contribution in the evolution of oral contraception with the use of a low dose of estrogen; additionally, he was instrumental in eliminating the age of 35 years as an upper limit for the use of oral contraceptives.

Hormone replacement therapy and the Women’s Health Initiative Study
After the first publication of the Women’s Health Initiative that reported the clinical trial results with postmenopausal hormone therapy, Leon was one of an intrepid few who offered critical analyses that highlighted the flaws of the trials and the study and provided an accurate interpretation of the data that, over the following years, proved to be correct.20,21,29

Looking back over those years, Leon said, “I am proud that, in my lectures and publications, I provided support to clinicians and patients who desired to continue to benefit from the appropriate use of postmenopausal hormone therapy, with doses and durations of treatment adjusted according to their individual needs.”

Leon, an author, outside medicine
Leon indulged his passion and great gift as a storyteller and has written several nonmedical books. He published his first book, Carlos Montezuma, three years before he retired from medicine. It is about the Yavapai Native American doctor and activist, Wassaja, who was given the name Carlos Montezuma by the Italian photographer, Carlo Gentile, who purchased Wassaja for 30 silver dollars from the Pima raiders who had captured him and other children to sell or barter them.

Leon was delighted to discover that the skills needed to write a nonmedical book were the same as those required to write a medical book, including the ability to distill a substantial amount of information into a story.

His second book, The Deschutes River Railroad War,31 explores the history of railroads in the Pacific Northwest, specifically about the contest between two railroad magnates, James J. Hill of the Great Northern and Edward H. Harriman of the Union Pacific, to extend railroad services from the Columbia River to Bend, Oregon, up the Deschutes River.

Leon’s next book was closer to home: a biography of Gregory Pincus,32 the man who invented the combined birth control pill. Pincus had died a year before Leon arrived at the Worcester Foundation, the institution Pincus had
founded, and so Leon interviewed his relatives and many others who knew Pincus personally for the book. Leon’s story recounts not only how the pill affected the lives of women around the world but also the emotional reactions to it, especially from the Catholic Church.

Then came two books about senior softball: the first, A Slow-pitch Summer: My Rookie Senior Softball Season, described Leon’s new passion; the second, Slow-Pitch Therapy: Playing Senior Softball Through Aches, Pains, and Illness, is the very personal story of how softball got Leon through the ordeal of chemotherapy for lymphoma.

Leon at leisure: softball world champion
Along with fly fishing, reading is one of Leon’s great passions, and he reads a great deal, both fiction and nonfiction. It is difficult for him to pick out favorites, so he focused on books he had read in the last few years. In the nonfiction category, he especially likes two books that he believes to explain so much about human behavior: Sapiens, a Brief History of Humankind by Yuval Noah Harari, and The Meaning of Human Existence by Edward O. Wilson. Among fiction, his recent favorites include A Gentleman in Moscow by Amor Towles and Birds Without Wings by Louis de Bernieres.

The metaphorical fork in the road for Leon came at the point in his life when it was time to consider retirement. He was 75 years old and still enjoying medicine, especially traveling and lecturing to clinicians; people with Leon’s energy, inquisitiveness, and zest for life never retire (well, not completely).

Fortunately, Leon had found a new passion when he started playing softball at the age of 71 years, so he became Professor Emeritus in 2009, and for the last seven years, he has played in three leagues every summer (which means three double-headers every week); in the winter, he has batting practice twice a week. His new passion helped him face a battle in 2012 when he was diagnosed with a lymphoma and had to undergo three months of chemotherapy. On the day his oncologist told Leon that he was in complete remission, his wife asked him, “Do you think you could have done this without softball?”

“I can’t answer that question with certainty,” Leon reflected. “But this much I do know: each time I came to the ballpark throughout that difficult summer, I gained strength from my interactions with the other ballplayers. My teammates’ cheers after a good hit, or their encouragement after a weak grounder, lifted my spirits.”

In October 2016, Leon played in the World Senior Games in St George, Utah. There were more than 11,000 athletes aged 50 years or older from 34 different countries. The softball tournament is the largest in the world—nearly 4000 ball players. There were nine teams in Leon’s division of players 80 years old or older, and his team won the gold medal.
Advice: passion is the key to a meaningful life

Leon has no regrets. “Not one! I mean, I am so grateful I went to Yale; it opened up the rest of my life to me. Every person, every place, everything I’ve done: I’ve loved it. No regrets. I have been fortunate enough, after I retired, to find a new passion in playing senior softball, so that principle of having a passion continues to be a part of my life.”

And that has always been Leon’s advice to students and residents: “You have to have a passion.” Leon even loved his internship and residency when he worked every day and every other night for five years. “I loved it. I loved every minute of it. If you don’t have that passion, then you need to make a change.”

The current state of clinical academic medicine concerns Leon. One reflection, he pointed out, is that 60–70% of the articles in American clinical journals come from abroad: “There needs to be a fundamental change in the way academic medicine is funded because full-time faculty spend their entire day seeing patients, so they do not have time to teach or do research. I do not see that change coming, but I do see it in other countries. The reason we have such good research from Denmark, Sweden, and other countries is that academic medicine is independently funded and not dependent on clinical earnings. I have also read articles raising concern that our residents are not adequately trained, surgically, for example. Our young people need to become proactive and bring about much-needed change.”

Leon has five children and three grandchildren, including a one-year-old granddaughter. Leon choked up as he told me, “Her middle name is Leonova, which is Macedonian and means daughter of Leon.” Despite being charismatic, insightful, generous, talented, and world renowned, Leon is humble and has both a great sense of humor and a memorable laugh. His passion for life is contagious, and he has inspired so many of us to be better physicians, scientists, and human beings.

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Leon enjoys the sport of fly fishing

Leon’s passion for playing softball