

Giants in Obstetrics and Gynecology Series: a profile of Mary Lake Polan, PhD, MD, MPH



Roberto Romero, MD, DMedSci

Dr Mary Lake Polan is a physician-scientist, clinician, educator, and academic leader who has produced pioneering work on the role of cytokines and inflammation in reproduction, specifically in implantation and ovulation. She served as Professor and Chair of the Department of Obstetrics and Gynecology at Stanford University, promoted clinical excellence, and established a unique program to treat women with obstetrical fistulas and to train surgeons in the East African country of Eritrea. Dr Polan is an elected member of the National Academy of Medicine, an author, and a humanist. For her many contributions that have changed the lives of women, Dr Polan is recognized as a Giant in Obstetrics and Gynecology.



Dr Mary Lake Polan

Early life

Born in Las Vegas, New Mexico, Mary Lake was the eldest child of a first-generation Lithuanian father, an ophthalmologist then serving in the United States Army, and a first-generation Protestant, Wisconsin-born mother of Norwegian descent. Her parents had met and married while her father was a resident and her mother a nurse at the University of Wisconsin teaching hospital. Mary Lake was born during the Second World War while her father was stationed in New Mexico before his posting overseas for two years in a military hospital in the Azores.

Mary Lake spent her early life in Huntington, West Virginia—an idyllic small town stretched out along the Ohio River—where the front doors were left unlocked, children walked to and from school with friends, and lunch was eaten at home. On the weekends, since Mary Lake was nine years old, her father took her and her younger brother Chuck into the mountains of West Virginia where they shot bottles off

tree stumps with their .22 rifles. From an early age, she found “the world beyond the coalmines and mountains magnetic,” as she describes in her 2016 book, *A Doctor’s Journey: What I Learned about Women, Healing and Myself in Eritrea*¹.

Her large Jewish family in Huntington comprised her father’s relatives. She recalls being raised among her two younger siblings and a dozen cousins, whose fathers, unlike her physician father, were connected to the Polan family business where they manufactured bombsights during World War II, and subsequently, optical lenses. The mothers of all the children were surrogate mothers to all the cousins. When it came to issues of discipline, “they would paddle you or correct you regardless of who your parents were,” Mary Lake recalls. The cousins were more like siblings and have remained so throughout their lives.

Mary Lake’s interest in medicine came quite naturally—her father often took her with him on Sunday mornings for rounds on surgical patients at the hospital. Her first job at the age of 17 was as a summer ward clerk at the local hospital, where she managed the phones and paperwork on a surgical ward. Mary Lake says that her father was loving and supportive and made her feel that she could achieve anything to which she aspired.

It all sounds pretty idyllic, except for one thing. Mary Lake perceived a much more rewarding and exciting world outside the Appalachian region of the country, in part because her father had often exposed their family to the more metropolitan and cosmopolitan regions of the country, which included periodic trips to New York City, Miami, and the Caribbean islands. In addition to being the already voracious reader she has remained throughout her life, Mary Lake knew that she had a great deal to learn from the wider world. “I would have done anything to get out of West Virginia” and “If there’s some way to get there, I’m ready to go anywhere” are two of a number of her utterances that begin to describe the life of Mary Lake Polan.

Her chance came during the ninth grade in Huntington. At Mary Lake’s request, her parents surveyed several Southern boarding schools, but ultimately, they sent her to the Emma Willard School—a private school for girls in Troy, New York, founded in 1814. At first, Mary Lake told me that she felt more like the Appalachian girl she wished to leave behind. Her fellow classmates were, at least in her

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mind, more sophisticated and worldly than she envisioned herself. For example, in class one day, her French pronunciation of the Battle of Agincourt was corrected by her teacher. In that moment, she promised herself that she would learn French and never again be embarrassed by mispronouncing a French word. And she did learn, spending her junior year of college in Paris with the Smith College Junior Year Abroad Program. Mary Lake's talent to live up to her father's expectations soon showed itself as an indicator of what life thereafter would be like for her. The Emma Willard School and its student life became something that she came to enjoy and admire. Years later, her devotion to the merits of all-girls schooling caused her to remain both supportive of the School and connected to its leadership and her classmates.

An education in Connecticut: college and graduate school

Mary Lake attended Connecticut College, then a private liberal arts women's college, in New London. The school was supportive of students charting their own educational course, and Mary Lake began after her freshman year, spending a summer in Switzerland with the "The Experiment in International Living" program. That summer trip was quickly followed by her junior year in Paris. After graduating from Connecticut College with a major in chemistry, Mary Lake migrated 50 miles down the Connecticut coastline to the Department of Molecular Biophysics and Biochemistry at Yale University, where she completed her PhD in molecular biophysics and biochemistry, followed by a postdoctoral fellowship in the Department of Biology in the laboratory of Dr Joseph Gall. Dr Gall, who developed *in situ* hybridization, was awarded the Albert Lasker Award in 2006 and is known for encouraging women to pursue a career in science. His trainees include Dr Joan Steitz (Lasker-Koshland awardee for pioneering contributions to RNA biology) and Dr

Elizabeth Blackburn (Nobel Laureate for her discoveries of the molecular nature of telomeres). Mary Lake's work focused on the isolation and characterization of the circular mitochondrial DNA of *Drosophila melanogaster*² (Figures 1 and 2).

Yale University Medical School: residency and fellowship

At this juncture, medical school seemed to be a better idea than a laboratory career—Mary Lake found that talking to colleagues about the experiments was more fun than actually doing the research. Yale Medical School offered a logical path to medicine, as there were no exams and it only required a passing grade on Boards Part 1 and 2 and a thesis project to graduate. Having completed her PhD thesis at Yale, Mary Lake finished medical school in three years—an important bonus, because her father had told her that he was not willing to pay for medical school.

FIGURE 1

Behold the fruit fly: molecular revelations of MtDNA

ISOLATION AND CHARACTERIZATION OF MITOCHONDRIAL DNA FROM *DROSOPHILA MELANOGASTER*

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While working in the laboratory of Dr Joseph Gall at Yale University in the 1970s, Dr Mary Lake Polan analyzed and described unique genetic aspects of the fruit fly, reported in the study "Isolation and characterization of mitochondrial DNA from *Drosophila melanogaster*."²

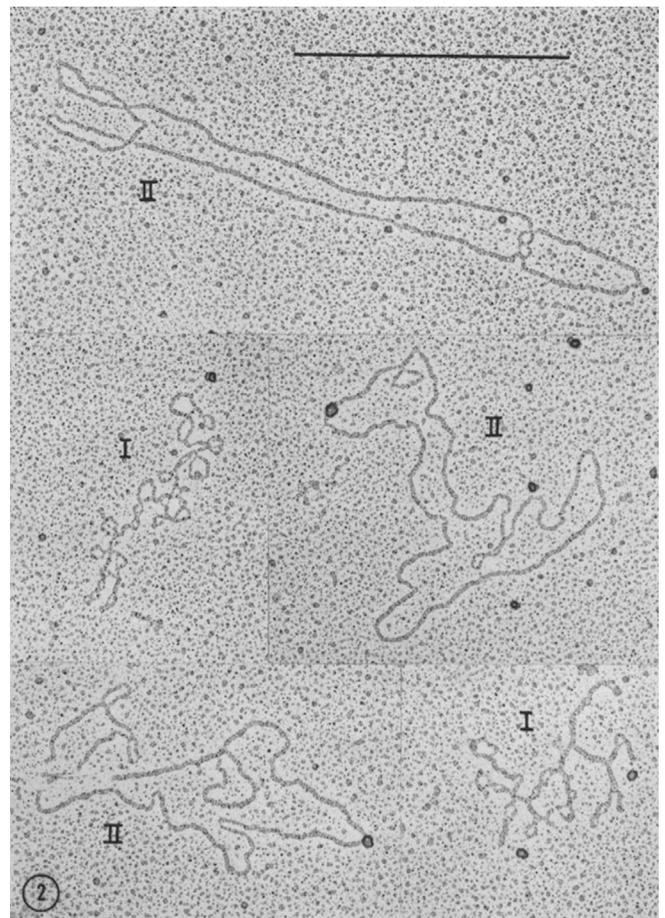
©1973 by The Rockefeller University Press. Polan et al.²

MtDNA, mitochondrial DNA.

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FIGURE 2

Microscopy revealed distinctive circular forms in MtDNA



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FIGURE 3

Mary Lake and her son Scott visiting Tehran, Iran



Photo courtesy of Dr Mary Lake Polan.

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Undertaking only three years of tuition was critical, and she spent her two preclinical years of medical school working part-time as a laboratory technician in Dr Gall's lab to support herself.

There were two other major advantages to staying in New Haven. First, the Yale curriculum was flexible, allowing Mary Lake to spend three months at the University of Oxford, England in the Radcliffe Infirmary and the John Radcliffe Hospital completing her obstetrics and gynecology and pediatric clinical clerkships during her third year of medical school. Second, while conducting research in the Department of Dermatology for her doctoral thesis at Yale, she met her future husband, Dr Joseph Smith McGuire, Professor of Dermatology.

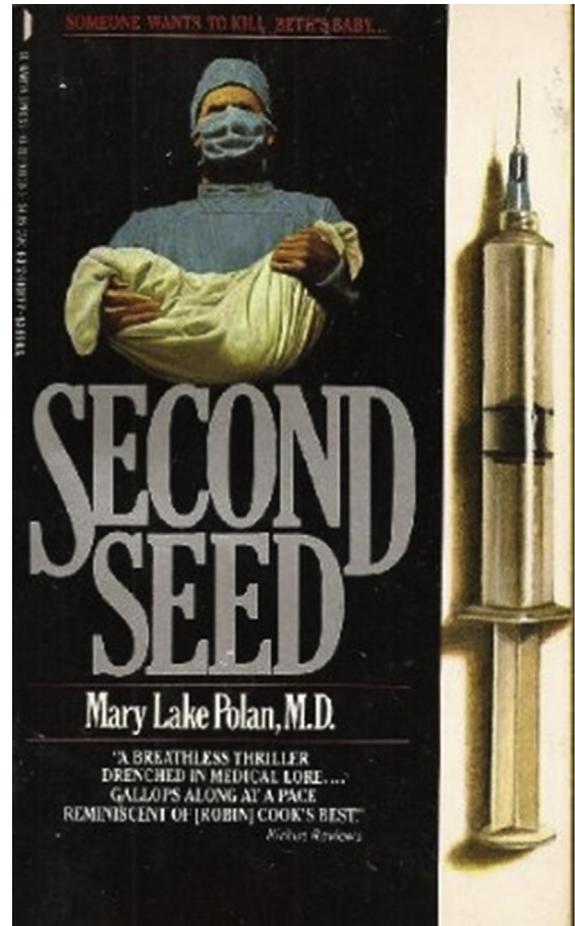
Mary Lake remained at Yale for her residency. Indeed, she was the first woman to graduate from the residency program in the Department of Obstetrics and Gynecology. She had the opportunity to spend three months as an elective during the last year of residency in the hospitals in Shiraz—the “City of Roses”—in southern Iran. The Iranian spring included trips to Isfahan and Persepolis—a UNESCO World Heritage Site located 60 kilometers from Shiraz; its ruins date back to 515 BC. Mary Lake's fascination with Iran continued—in 2005, she returned to Tehran to participate in an IVF Scientific Meeting with her son Scott (Figure 3). The mystique of Persia was translated into Mary Lake's medical mystery novel, *SECOND SEED*, published in 1987³ (Figure 4).

A Fellowship in Reproductive Endocrinology and Infertility

Louise Brown, the first in vitro fertilization baby, was born on July 25, 1978. The excitement of the new infertility technologies drew Mary Lake to a reproductive endocrinology and infertility fellowship with Drs Nathan Kase and Alan DeCherney, who worked with Drs Harold Behrman and Richard Hochberg conducting bench research in

FIGURE 4

Bridging science, history, and the literary arts



Inspired during a visit to the historic city of Shiraz in southern Iran, Dr Polan wrote a medical mystery novel *Second Seed*.³

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endocrinology.⁴ The fellowship was followed by a faculty appointment as Assistant Professor at Yale, where she initiated a National Institutes of Health-sponsored research program on the hormonal function of human granulosa-luteal cells.^{5,6}

Yale also brought priceless opportunities for relationships and mentors. There, she married Dr McGuire, a distinguished physician and teacher who, remarkably, came from Mary Lake's native West Virginia. From his early life as a coal miner's son, Joe became a highly regarded Professor of Pediatric Dermatology at Yale and later at Stanford. As a mentor, he encouraged Mary Lake to fully realize her potential in the world of medicine. Her other mentors at Yale were Drs Joan Steitz, Florence Haseltine, and Leon Speroff, along with Drs DeCherney and Kase. The latter three physicians, previously recognized as Giants in Obstetrics and Gynecology, have been important mentors to many in obstetrics and gynecology.⁷⁻⁹

FIGURE 5

An innovative study in implantation

Single Blastomeres within Human Preimplantation Embryos Express Different Amounts of Messenger Ribonucleic Acid for β -Actin and Interleukin-1 Receptor Type I*

JAN S. KRÜSSEL[†], HONG-YUAN HUANG[‡], CARLOS SIMÓN, BARRY BEHR, ANDREA R. PAPE, YAN WEN, PETER BIELFELD, AND MARY LAKE POLAN

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A study of importance emerged during her tenure at Stanford University, reflecting a significant research interest in implantation.²²

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Throughout her residency and fellowship, which included time as a fellow in gynecologic oncology, she met and worked for Dr John McLean Morris, a Yale gynecologist who had been raised in China. The child of Christian missionaries, Dr Morris—world renowned for his discovery of testicular feminization and postcoital contraception (morning-after pill)—introduced Mary Lake to the Yale-China Program, which had sponsored Yale undergraduates to teach English to middle-school students in Changsha, a city of five million people in central Hunan Province, since 1914. As a junior faculty member, Mary Lake, her husband Joe McGuire, and their two children—seven-year-old Joshua and five-year-old Lindsay, spent four months in 1986 at the Second Affiliated Hospital in Changsha teaching students and residents. After enrolling the children in a Chinese daycare, Mary Lake, then four months pregnant with their third child, taught, lectured, and performed infertility surgeries. On returning to Yale,

her research interests expanded to include cytokines and the relationship of interleukin (IL)-1 to reproductive function.^{10–12}

Professor and Chair at Stanford University School of Medicine

In 1990, Mary Lake moved to Palo Alto, California with her husband and their three young children to become the Chair of the Department of Obstetrics and Gynecology as the Katherine Dexter McCormick and Stanley McCormick Memorial Professor at Stanford University School of Medicine. This appointment opened an even wider world of interest and service with regard to women's health for Mary Lake. During her 16 years in that capacity, she joined the boards of Wyeth—a prestigious pharmaceutical company and Quidel—a maker of rapid diagnostic tests; she was elected to The Institute of Medicine (now the National Academy of Medicine) and

FIGURE 6

A murine study of molecular mechanisms in implantation

Interleukin-1 receptor antagonist prevents embryonic implantation by a direct effect on the endometrial epithelium

Carlos Simón, M.D.,* Diana Valbuena, M.D.,[†] Jan Krüssel, M.D.,[†] Alejandra Bernal, Ph.D.,* Christopher R. Murphy, Ph.D.,[‡] Tim Shaw, Ph.D.,[‡] Antonio Pellicer, M.D.,[†] and Mary Lake Polan, M.D., Ph.D.[†]

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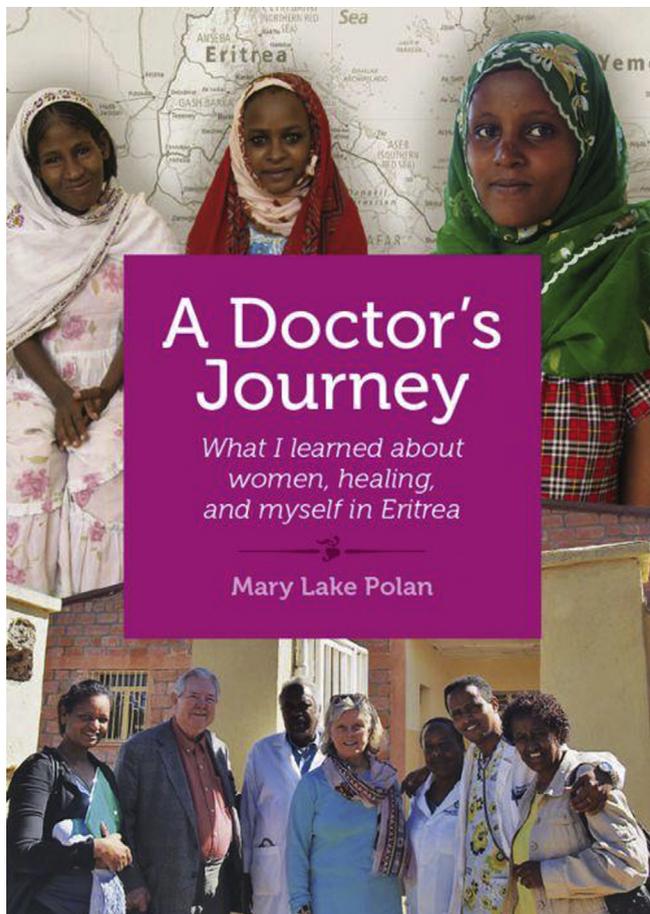
A novel finding in implantation that informed our field came forth from Dr Mary Lake Polan's laboratory at Stanford University in the late 1990s.²³

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served on its Governing Council and on numerous National Institutes of Health and other professional association committees; she lectured and testified broadly about women's health issues. During a sabbatical, Mary Lake returned to school at the University of California, Berkeley, where she obtained a Master's in Public Health degree and became interested in obstetrical fistulae. Significantly, in 2002, she founded the Eritrean Women's Project, as described earlier, resulting in novel reports of surgical techniques and social interventions to prevent and treat obstetrical fistulas resulting from birth trauma.^{13–15}

FIGURE 7
Sabbatical: reflections on women's reproductive healthcare in Eritrea¹



Author Mary Lake Polan chronicles her sabbatical in Eritrea, relating the significant outcomes for pregnant women and their children affected by obstetrical fistulas and other birth traumas and the restorative surgeries performed by an international medical team, in her 2016 memoir, *A Doctor's Journey: What I Learned about Women, Healing and Myself in Eritrea*.¹

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A role for interleukin-1 in ovulation and implantation

Ovulation is a sterile inflammatory process, and a role for the IL-1 system was envisioned in the early 1990s after the identification of the cytokine in human follicular fluid^{16,17} and the characterization of the human intraovarian IL-1 system.¹⁸ Mary Lake's studies showed that the production of IL-1 by peripheral blood monocytes and ovarian cells increases during the luteal phase of the menstrual cycle and produces a midcycle IL-1 surge in humans.¹⁹ Her laboratory at Stanford demonstrated the presence of the IL-1 system in the mouse ovary during follicular growth, ovulation, and lutealization²⁰ and of time-dependent inhibition of ovulation by the natural IL-1 receptor antagonist.²¹ Much of this work was done in collaboration with Professor Carlos Simón, a member of her team at Stanford, who has now become a towering figure in reproductive endocrinology and infertility. The focus then turned to the role of IL-1 in implantation after showing that the blastocysts produce IL-1^{22,23} (Figure 5) and that the administration of the natural IL-1 receptor antagonist prevented embryonic implantation by a direct effect on the endometrial epithelium²⁴ (Figure 6).

Mary Lake Polan, the author

Several years after writing her novel *Second Seed*, Mary Lake published *A Doctor's Journey: What I Learned about Women, Healing, and Myself in Eritrea*¹—a story of friendship between physicians in the United States and doctors and nurses in Eritrea, which began on a winter night in 2002 (Figure 7). With this first trip to East Africa, Mary Lake initiated the Eritrean Women's Program, created to surgically treat women with obstetrical fistulas and to train Eritrean surgeons to repair the fistulas; it was an endeavor lasting nearly two decades. This excerpt is Mary Lake's description of her first arrival in Asmara, which is the capital of Eritrea—a small country in the Horn of Africa on the Red Sea, tucked between Sudan, Ethiopia, and Djibouti:

“After the plane had hopscothed from San Francisco to Frankfurt to Jeddah, Saudi Arabia, the pilot's announcement—‘We're descending for our landing in Asmara’—was an electric jolt waking me from the intermittent dozing of the twenty-four-hour trip. Deprived of sleep, hair uncombed, I tried unsuccessfully to separate excitement from anxiety.

“The airplane door swung inward. Freezing night air washed over me. In my *Out of Africa*-influenced imagination, it should have been hot, but on this January night, I shivered in my cotton jacket as we descended the roll-up staircase onto a cracked concrete runway. Asmara Airport read the sign on the wall of a two-story building a couple of hundred yards away, visible in the yellow glow from the airport windows.

“I’d been dreaming of this moment for a long time. This trip was the goal I had worked toward over the last two years, ever since the idea of bringing American surgeons to treat women injured in childbirth became the focus of my sabbatical studies in international public health. I was then Chair of the Ob-Gyn department at Stanford University, and I had become fascinated by the problem of obstetrical fistula—a terrible situation caused by prolonged labor which left a woman with a stillborn baby and constantly leaking urine from a hole torn in her bladder.

“Five American gynecologists, including me, were here because of my efforts. After months of work and planning, I had finally persuaded two foundations to support this two-week trip to Eritrea....

“The heavy metal door to the terminal clanged open and we followed an animated group of Eritrean men and women into a bare room, painted a dull brown. The room was lit by hanging bulbs and smelled of stale cigarette smoke. Two unsmiling officials sat behind glass panels at the far end, the sleeves of their uniform shirts rolled up to the elbow. They were slowly and systematically examining documents handed to them by the incoming passengers. The Eritrean passengers chatted excitedly as they greeted one another and the border control guards behind the glass. Tired, we held back until one of the guards beckoned. One by one, we handed over our passports and visas to be stamped and were ushered into the Customs area. We waited as the boxes of donated medical sutures, antibiotics, and surgical retractors were brought from the plane and piled up around us.

“I began to sweat. *What if nobody comes to meet us?*

“We were here because *I* wanted to work in Africa. I was drawn to this strange and unknown world. I felt acutely responsible for the three other women docs and for the single man in the group. I silently prayed we would be able to accomplish our goal of successful surgeries and, equally important, that we’d be safe in this very foreign country....

“Please, God, let someone be here to tell us what to do and take care of us.”¹

An international presence

Before COVID-19 interfered with world travel, Mary Lake encouraged her second husband, Frank Bennack Jr, (Figure 8) to take trips that he probably would not have taken without her urging. They first journeyed in 2008 with the New York Philharmonic Orchestra to Pyongyang, Democratic People’s Republic of Korea, when Frank served as Chairman of New York’s Lincoln Center for the Performing Arts. Several years later, they traveled to Havana, Cuba, in October 2016, again with a group from the Lincoln Center.

FIGURE 8

A memorable day



Mary Lake and her husband Frank at their wedding, standing on a bluff overlooking the ranch.

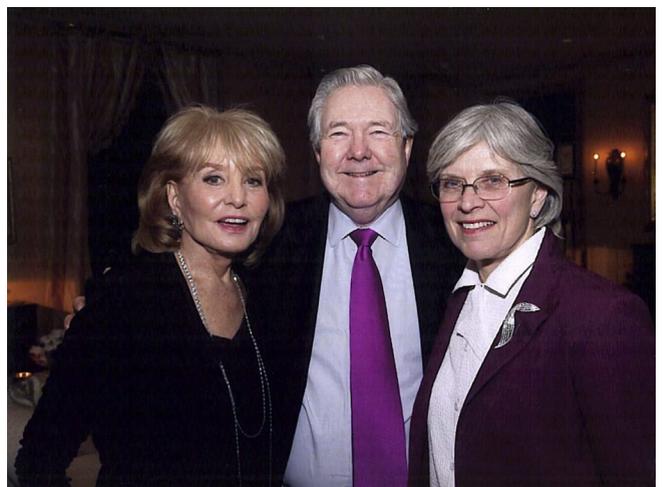
Photo courtesy of Dr Mary Lake Polan.

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With Mary Lake’s planning, the couple also collaborated on family trips of up to 40 children, spouses, significant others, and grandchildren to Kenya and South Africa, to the glacial waters of Alaska, and to the beaches of the Galapagos Island, to name a few of their excursions.

FIGURE 9

Visiting with a well-known personality in broadcasting



Barbara Walters hosted the Hearst affiliate ABC’s talk show *The View* from 1997 until 2014. L-R: Ms Barbara Walters, Mr Frank Bennack Jr, and Dr Mary Lake Polan. Photo courtesy of Dr Mary Lake Polan.

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FIGURE 10

Encountering a legend in television, film, and publishing



Oprah Winfrey is editor-in-chief of *O, The Oprah Magazine*, published by Hearst. L-R: Dr Mary Lake Polan, Ms Oprah Winfrey, and Mr Frank Bennack Jr. Photo courtesy of Dr Mary Lake Polan.

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Remarkably, Mary Lake was destined to meet prominent political leaders and media luminaries (Figures 9-11). Her husband Frank is Executive Vice Chairman and former Chief Executive Officer of Hearst, one of the nation's largest publishing companies, and an accomplished author.

FIGURE 11

Attending a History Channel symposium, 2019



L-R: William J. Clinton, former US president; Mr Frank A. Bennack Jr; Dr Mary Lake Polan; and George W. Bush, former US president.

Photo courtesy of Dr Mary Lake Polan.

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After her marriage to Frank, Mary Lake moved to New York City, accepting an appointment as Visiting Professor at Columbia University School of Medicine. Subsequently, coming full circle, she returned to Yale in 2014 as Professor of Clinical Obstetrics, Gynecology, and Reproductive Sciences in the School of Medicine.

Having contributed to the field of women's health in the laboratories, clinics, and operating rooms of the United States, Iran, China, and Eritrea, Mary Lake says, "Living in a different country, working with physicians from other cultures, with very different training, forces you to be flexible, open to new techniques and, importantly, new ways to relate to people. Unconstrained by familiar social hierarchies, you are thrown back on yourself—who you essentially are—and you discover unexpected capabilities. It is a freedom to give back that becomes addictive, and it has been a guiding theme throughout my life, facilitating friendships between colleagues here at home and in countries around the world. Yes, it has allowed me to help women, but as importantly, it has enriched my life." In the full spirit of giving, Mary Lake and Frank have endowed Chairs at Stanford and Yale, both dedicated to the area of gynecologic oncology in the respective Departments of Obstetrics and Gynecology.

The *American Journal of Obstetrics and Gynecology* recognizes Dr Mary Lake Polan's professional contributions as a physician, scientist, leader, and role model.

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