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Kenneth Warren and the Great Neglected Diseases of Mankind Programme

The Transformation of Geographical
Medicine in the US and Beyond

CONRAD KEATING

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Programme

The Transformation of Geographical
Medicine in the US and Beyond

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Cover Photo: Ken Warren Photo. Ken Warren circa 1979. Courtesy of Sylvia Warren.

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Foreword

This is the story of the life and work of a remarkable clinical scientist, Kenneth Warren. After describing Warren's early successes in medical research, mainly in the fields of parasitology, the story goes on to discuss his major achievement, which was the founding of a programme called the Great Neglected Diseases of Mankind. He achieved this by approaching leaders of research groups in several parts of the world, the work of which focused on diseases of the tropical belt. With the support of the Rockefeller Foundation, he offered financial help to each of the groups, and his only requirement was that they would meet together at least once each year to present their work to each other. In this way he was able to evolve valuable partnerships between workers in different but related fields. This remarkable programme lasted from 1978 to 1987 after which, sadly, it was terminated by the foundation.

There is no doubt that this programme had a very important effect on the evolution of research on many neglected diseases, particularly those of the tropical countries. Here is just one example: At the first and highly successful meeting of the chosen research groups in New York in 1978, there were several observers who were not related directly to the programme. One of them was Dr. Peter Williams, who at that time directed the Wellcome Trust in London, a medical research charity that later became one of the richest in the world. After the first day of the meeting was over, Dr. Williams invited me to his room and, stimulated by the day's programme, discussed how we could change the "field of tropical medicine" to "medicine in the tropics." In other words, how could partnerships be developed for research and capacity-building between rich and poor countries that not only would cover tropical disease but would also provide expertise and support in all aspects of medical research and care? The end result of this discussion was the development of highly successful partnerships between Oxford University and Thailand, Vietnam, and East Africa that are still fully active at the present time.

There is no doubt that although Kenneth Warren could be rather eccentric and difficult at times, his overall influence in developing ways to improve the health of poor countries, particularly those in the tropics, was extremely successful. It is a

great pleasure to introduce this largely untold story while at the same time being able to thank Kenneth Warren and the Rockefeller Foundation for their personal support during the years of the Great Neglected Diseases of Mankind programme.

October 2015

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“One of the commitments of our foundation is to secure the stories of scientists whose defining purpose is to develop breakthrough solutions to human suffering. Ken Warren’s contributions to the health of people in the developing world had been forgotten; we hope that this biography will help to underscore his role in helping to transform the global health agenda.”

Ann Dunne

“This book is in memory of my dear friend Ken Warren, who gave me the courage to trust my scientific insights, and march against the consensus.”

Anthony Cerami

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About the Author

Conrad Keating is the Writer-in-Residence at the Wellcome Unit for the History of Medicine at the University of Oxford. He is the author of the widely-acclaimed biography of the British epidemiologist Sir Richard Doll, *Smoking Kills: The Revolutionary Life of Richard Doll*. His most recent publication, *Great Medical Discoveries: An Oxford Story*, accompanied the exhibition ‘Great Medical Discoveries: 800 Years of Oxford Innovation’ which he curated for the Bodleian Library. He lives in Oxford.

Introduction

In 1996, the dynamic medical researcher, Kenneth S. Warren, did a very rare thing: He spoke at his own memorial service.¹ In fact, the occasion was not a formal memorial event but rather the presentation of an honorary degree in recognition of his contributions to biomedical science and neglected tropical diseases. However, all of those in attendance, including Warren himself, knew that he did not have long to live. Perhaps, driven by the energy and scientific curiosity that were his lifeblood, he might well have echoed the sentiment of the physician William Osler, who in recognition of his own impending death, was heard to say, “I wish I could be there for the autopsy!”² The ceremony took place in June at the Picower Institute for Medical Research on Long Island, New York. Warren died of metastatic melanoma less than 3 months later on 18 September 1996.

Warren’s career in medicine will be remembered for three enduring achievements: his efforts to introduce modern biomedical science to the study of infectious diseases in the developing world; the proselytising energy he brought to the ethical challenge of how to provide the most cost-effective health care to the world’s poorest people; and his tenure as the Director of Medical Sciences at the Rockefeller Foundation (RF). Never short of grandiose ideas or audacious undertakings, Warren, while at the RF, played a pivotal role in shaping some of the most important campaigns to reduce the global burden of disease. His outstanding ability was his use of metrics to articulate health as an investment, not simply as expenditure. Furthermore, in the language of modern philanthropy, Warren had “convening power,” which he used to mobilise powerful people, agencies, and institutions on behalf of the poor and the sick.

For Warren, and indeed for us all, life is lived with inevitable forward momentum, but very often the arc of its trajectory is only more properly understood in its final chapters. Certainly in Warren’s case, much about his life scientific can be gleaned from the reactions to his death. In one of his obituary notices, he was

¹Ann Dunne, personal communication.

²Bryant Boutwell, personal communication.

described in this unusual way: “Ken Warren has died. He was a boy of sixty-seven. I say ‘boy’ because he retained throughout his life all the enthusiasm and energy that he must have had at seventeen. If his body aged and was at last to betray him, his mind remained lively, sparkling, and faithful to the end.”³ The combination of boundless energy, intelligence, and being “inherently charismatic” enabled Warren to become a powerful force in global medicine in the second half of the twentieth century.⁴ Even today, 20 years after his death, his contributions to the science of parasitology and the public-health strategies he championed are simultaneously lionised and questioned.

This equivocal perception can be better understood by recognising the polarising influence that Warren’s personality and *modus operandi* had on his supporters and detractors. Warren was an iconoclast, yet he was both an establishment as well as a non-conformist figure. The celebrated immunologist, Michael Sela, encapsulates the anthropological paradox that Warren embodied: “[For me] with Ken it was love at first sight, because of his ideas and energy; but he was the most WASP-ish person I’ve ever met who had had a bar mitzvah!”⁵ A driven, “larger than life character”⁶ who had studied Literature at Harvard College “because he wanted to have subjects that he could talk to girls about,”⁷ Warren developed a lifelong love of literature and poetry before going on to Harvard Medical School. Following the example of the British epidemiologist Jerry Morris, Warren was a devotee of the “three A’s”: analyst, agitator, and activist.⁸ Possessing a contagious personality, he was full of charm and conviction, a straight-shooter who was allergic to concession and undeterred by confrontation. Equally, his ability to make friends as well as powerful adversaries began early. While a medical student at Harvard, and coming to the end of his studies, Warren sought career advice from Tom Weller, the virologist and Nobel laureate (Weller shared the Nobel Prize in 1954 for his work on poliomyelitis viruses). Receiving Weller’s suggestion to go into public health and sanitation rather than tropical medicine, Warren took the opposite course, setting up years of future friction between the men.⁹ Subsequently Warren and Weller were to take their disagreements over how to implement the most cost-effective form of medical treatment for infectious diseases into many public forums.

Outside of his immediate family, the closest person to Warren was Adel Mahmoud. A self-confessed “adopted son” of Ken and Sylvia Warren, Mahmoud forged his prodigious career under his mentor’s influence and witnessed first-hand

³R. Selzer, “Obituary. Kenneth S. Warren, M.D. June 11, 1929–September 11, 1996”. *Molecular Medicine*, Vol. 23, No. 6, November 1996.

⁴Don Bundy, personal communication.

⁵Michael Sela, personal communication.

⁶David Weatherall, personal communication.

⁷Adel Mahmoud, personal communication.

⁸Jerry Morris, personal communication.

⁹Adel Mahmoud, personal communication.

the polarising personality traits: “Early in his career Ken was widely respected as a scientist because he opened up the idea of mechanisms of disease in schistosomiasis. But his main stumbling block was his personality. If you could get along with him, you are in great shape. But if you’re on the other side, and Ken is attacking you, and you’re trying to attack him, you are going to have a hard time.”¹⁰ Others, such as Anthony Bryceson, who spent much of his life working on leishmaniasis in Africa, saw Warren as a man of quiet charm, who, while expecting people to go along with his ideas, would reward them with interest and praise.¹¹ Warren was certainly capable of being bombastic, eccentric, and swashbuckling, but these at-times-divisive components of his personality were tempered by the recognition in the minds of many that he had a great vision for tropical medicine and the delivery of health services in the tropics. On occasion, his enthusiasm sometimes bordered on the unrealistic, but the force of his will succeeded in carrying others with him. Warren’s powers of persuasion were strengthened by the recognition, as noted by one of his colleagues, that “Ken was all heart. Above all he had the heart of an ox.”¹² Physically, Warren was of average size, always well-dressed, hair groomed, very presentable but not showy—in the style of an American academic. The constants were a big smile and huge glasses.¹³ He would walk very quickly and always had a full schedule of meetings to which he was hurrying, talking all the while about new ideas and possibilities.¹⁴ He was fun to be with; not overly jovial but upbeat and animated.¹⁵ In the words of his wife, Sylvia, “Enthusiastic was probably the best way to describe him. Very focused, very sure of what he wanted to do, and very adept at finding the best way to do it.”¹⁶

The constant leitmotif running through Warren’s work, and which, it could be argued, provided an apologia for his tendentious stance, was his dedication to the field of parasitology and to the poor people of the world whose lives were blighted by infectious diseases. For him, taking the numerical view of global health, substituting emotion with metrics, and achieving good health care at low cost would be achieved by the application of medical statistics and epidemiology, which he unsentimentally described as “medicine with the tears wiped off.”¹⁷ Warren was a man of science, and he knew that he ought to have no wishes or affections but instead a Darwinian heart of stone. Nevertheless, his own conversion to thinking globally about disease control came as an epiphany: “I was driving on a back road

¹⁰Adel Mahmoud, personal communication.

¹¹Anthony Bryceson, personal communication.

¹²Gus Nossal, personal communication.

¹³Anthony Bryceson, personal communication.

¹⁴Julia Walsh, personal communication.

¹⁵Howard Klein, personal communication.

¹⁶Sylvia Warren, personal communication.

¹⁷K. S. Warren, “The Alma-Ata Declaration: Health for All by the Year 2000?”, *Britannica Book of the Year, Encyclopedia Britannica*, Chicago, 1988. From a collection of Warren’s private papers, p. 21.

in the Rift Valley of Kenya when I passed a large, apparently unruly crowd of Maasai who were attempting to wave me down. My first impulse was to put my foot on the accelerator, but in my rear view mirror I noticed what appeared to be several limp children in their arms. I turned back, and five men and women carrying four unconscious children jumped into the car while others tried to force their way in as well. As we drove frantically to the nearest aid station, about eight kilometres away, the adults moaned and cried while taking mouthfuls of cow's blood and milk from their gourds and blowing it on the children and all over the interior of the car. I don't think I've ever felt such a concentrated message of despair as those people evinced. Receiving that message, I suddenly realised how hardened I had become to the deaths of infants and children in the less developed world, and how I had assumed that the high death rates similarly inured parents to loss ... Each day, tens of thousands of children die in the world's less developed countries for lack of adequate health care."¹⁸ The experience was transforming for Warren: He felt very strongly that the deaths of children in poor countries mattered just as much as the deaths of children in rich countries and were a lot easier to prevent. For Warren, everyone scored the same in terms of importance.¹⁹ He had identified a concrete problem, and he sought a scientific mechanism for its alleviation.

His ambitious plan was to create a scientific programme that would harness the new biological sciences to help alleviate the old parasitic diseases indigenous to the developing world. The idea had been incubating in Warren's mind for some time and was a direct result of his own laboratory work, much of which was undertaken at Case Western Reserve University (Cleveland, OH, USA) and had established his status as a renowned investigator in schistosomiasis.²⁰ This work was an early attempt to apply modern biomedical technology to the understanding of the mechanisms of disease prevalent in developing countries. With more than 3 billion people in those countries suffering from infectious diseases, Warren set himself the objective of finding the most cost-effective form of medical intervention to help reduce the sequence of "exposure, disability and death."²¹ He was particularly interested in diarrheal and respiratory diseases (the biggest killers of children), neonatal death, and the delivery of vaccines. His path in life was set. The eminent Australian research immunologist, Gustav "Gus" Nossal, first met Warren in 1976 and was impressed by his ambitious vision: "His passion was to bring the fruits of the new biology, genetics and molecular biology to bear on tropical diseases,

¹⁸K. S. Warren, "The Alma-Ata Declaration: Health for All by the Year 2000?", *Britannica Book of the Year, Encyclopedia Britannica*, Chicago, 1988. From a collection of Warren's private papers, pp. 21–30.

¹⁹Richard Peto, personal communication.

²⁰K. S. Warren, "Pathophysiology and pathogenesis of hepatosplenic schistosomiasis mansoni." *Bull. N.Y. Acad. Med.* 44: 280–294, 1968.

²¹J. A. Walsh & K. S. Warren, "Selective primary health care: an interim strategy for disease control in developing countries". *N. Engl. J. Med.* 301: 967–74, 1979.

which had been the domain of the older generation who had been out in Africa for twenty years, divorced from the new biology.”²²

Warren’s vision was to establish a network of laboratories that would apply this “new biology” to the parasitic diseases prevalent in the developing world, particularly malaria and schistosomiasis. The opportunity for him to realise his global ambition came in 1977. Warren resigned from Case Western Reserve, where he had taught both in the medical school and in library sciences, and took up the post of Director of Health Sciences at the Rockefeller Foundation. Established in 1913, the Rockefeller charter states a noble objective: “to promote the well-being of mankind throughout the world.” It was at the RF that Ken Warren forged his reputation for propagating the importance of scientific research to human well-being, and in so doing, made an enduring contribution to the transformation of disease control and global health. In December 1977, the RF Board of Trustees agreed, at Warren’s suggestion, to establish the Great Neglected Diseases of Mankind (GND) programme, a project that would create “a network of high-quality investigators who would constitute a critical mass in this field, attract the brightest students and conduct research of excellence.”²³ The idea was to bring together several research groups working on the more basic aspects of diseases of the developing world. The great neglected diseases were described as “great” in terms of prevalence and “neglected” in terms of the involvement of major international scientists and financial support. Warren, now with the financial backing of the RF, was going to roll out his synthesised programme, which would target diarrheal and respiratory diseases, malaria, schistosomiasis, African sleeping sickness, hookworm, and many other infectious diseases. The programme affirmed one of Warren’s sacrosanct beliefs, i.e., that “a significant part of the investigator’s efforts would be spent in applied collaborative research with colleagues in developing countries.”²⁴ In this sense, the project would establish global networks that would link what he termed from “the bench to the bush.”

The GND marked the fulfillment of an audacious undertaking to bring new biomolecular scientists to the field of parasitology, to create intellectual and personal connections between the different units, and to mould them into a strike force that was greater than the sum of its parts. This created an excitement about the science and a truly collaborative spirit. Keith McAdam joined the GND as part of Sheldon Wolff’s team at Tufts University School of Medicine, and was immediately conscious of the scientific and social cohesion of the GND family: “Everyone had to go to the annual meeting, which helped to forge the GND into a major force that identified with the subject of parasitology, with Ken Warren and with the

²²Gus Nossal, personal communication.

²³K. S. Warren & C. C. Jimenez (eds), *The Great Neglected Diseases of Mankind Biomedical Research Network: 1978–1988*. New York: The Rockefeller Foundation, 1988, p. 1.

²⁴K. S. Warren & C. C. Jimenez (eds), *The Great Neglected Diseases of Mankind Biomedical Research Network: 1978–1988*. New York: The Rockefeller Foundation, 1988, p. 1.

RF.”²⁵ The programme also played a role in expanding the horizons of parasitology by funding a talented group of young researchers who reinvigorated the status of tropical medicine in the United States. A brilliant cohort of scientists—including John David, Adel Mahmoud, Anthony Cerami, James Kazura, Richard Guerrant, and Gerald Keusch—was persuaded by Warren to work on tropical diseases; otherwise, they might not have done so. Furthermore, the network brought research, education, and studies of diseases of the developing world to the mainstream of medicine in developed countries. Carlos Gitler, of the Weizmann Institute of Science in Israel, attended the inaugural meeting of the GND at Rockefeller University and was persuaded to transfer his research efforts to the understanding of diseases caused by parasites. At that meeting, held at the Abby Aldrich Rockefeller Hall in 1978, Gitler heard for the first time the famous Warren dictum: “Helminths are different from all other parasites in that they do not multiply in the host.”²⁶

Warren was a catalyser; his expertly delineated exhortations described how molecular science had the capacity to improve the human condition anywhere in the world, even in areas of great poverty at the edge of development. In many ways, this vision was prescient in that it took the study of neglected tropical diseases (NTDs) into the modern scientific age, and the network itself was very much a forerunner of contemporary disease-control practice. According to one of Warren’s colleagues at the foundation, “Ken was an entrepreneur and an impresario. He was good at moving pieces around. He left his fingerprints all over that programme. He lived and breathed it.”²⁷

The GND Programme brought a stellar cohort into the field of parasitology, and their contributions to understanding the mechanisms of disease, improving human health, and transforming health outcomes are still relevant today. Warren’s work has, according to his former colleague, Julia Walsh, “saved millions of children’s lives.”²⁸ His enduring role, according to Walsh, stems from their controversial study, “Selective Primary Health Care: An Interim Strategy for Disease Control in Developing Countries” (SPHC).²⁹ The paper advocated, contrary to the WHO view of total primary health care, a new turn toward selective and achievable goals by way of targeted assaults on specific diseases as implemented by the GND network. This approach had an enormous impact on health policy. For the first time, a study listed the diseases people died of so as to identify the biggest killers. It established a metric that could be used by donors, governments, and bilateral agencies for measuring the impact of the programme. It asked the fundamental question, “Is the programme that you plan to implement going to improve health in any way?”

²⁵Keith McAdam, personal communication.

²⁶C. Gitler in K. S. Warren & C. C. Jimenez (eds), *The Great Neglected Diseases of Mankind Biomedical Research Network: 1978–1988*. New York: The Rockefeller Foundation, 1988, p. 75.

²⁷Joyce Moock, personal communication.

²⁸Julia Walsh, personal communication.

²⁹J. A. Walsh & K. S. Warren, “Selective primary health care: an interim strategy for disease control in developing countries”. *N. Engl. J. Med.* 301: 967–74, 1979.

Within a couple of years, USAID declared that it would focus on child survival and implementing the policies of immunisations, oral rehydration, and breast feeding in line with the SPHC thinking described in the article by Warren and Walsh.³⁰ The policy's influence has been so far-reaching that "it massively changed the investment and resource allocation at UNICEF, at the WHO, USAID, [and] the World Bank."³¹

Ken Warren was a passionate communicator, a scientist with a feel for language, who embraced new technology as a way to get scientific information to make a difference. One of his favourite places in New York was The Century Association, a club for artists and amateurs in the arts, where he would hold post-work meetings to develop new programme ideas.³² He was a friend and benefactor of the physician and writer Lewis Thomas, and Thomas's final collection of essays, *The Fragile Species*, was edited and published at Scribner under Warren's supervision. The art and practice of writing was close to Warren's heart, particularly because among his many fervently held ambitions had been to find ways for health workers in the developing world to have access to the most up-to-date biomedical knowledge. While at high school, Warren became fascinated by prose and poetry, and at Harvard, where he read American History and Literature, this developed into a love of books and writing.³³ His ambition to write may have been given metaphysical affirmation when, as a student at Harvard Medical School in the early 1950s, he double-dated with a friend, Richard "Dick" Norton, whose date was Sylvia Plath.³⁴ Dick and Ken were at Harvard Medical School together, but Dick didn't have a car, and Ken offered to drive him to Smith College in Northampton, Massachusetts, where Sylvia Plath studied, on the condition that he could be part of a double date. It is widely acknowledged that Dick Norton influenced the character of Buddy Willard in Plath's book, *The Bell Jar*, which was published in 1963.

Warren's creative energy aligned to an enviable command of the English language, which enabled him, according to his co-author Adel Mahmoud, "to write incredibly well."³⁵ In a professional career that spanned three decades, Warren wrote hundreds of scientific papers, numerous book chapters, 14 books, and, in 1994, he co-founded the journal *Molecular Medicine*, after a lifetime dedicated to expanding the frontiers of tropical and geographical medicine.

In many ways, Warren perfectly embodied the characteristics described by Isaiah Berlin in his 1953 essay, *The Hedgehog and the Fox*. In it the philosopher divided writers and thinkers into two categories: hedgehogs, who know one thing, and foxes who have many interests. Tellingly, in 1996, reflecting on his own personality and

³⁰Julia Walsh, personal communication.

³¹Julia Walsh, personal communication.

³²John Bruer, personal communication.

³³R. Selzer, "Kenneth S. Warren" (obituary), *Molecular Medicine*, Vol. 2, No. 6, November 1996.

³⁴Howard Klein, personal communication.

³⁵Adel Mahmoud, personal communication.