

Chapter 2

The GND Years

Warren was an immediate beneficiary of the changing philanthropic principles that Knowles began to introduce at the RF and, with his customary drive, he immersed himself in the opportunities that arose from this redefined strategy. One of Knowles' first acts was to add the title of Health to the foundation's Population Programme, which subsequently became known as Population and Health. Previously, under the presidency of the biologist George Harrar, health programmes, with the notable exception of the St. Lucia schistosomiasis research, had grown peripheral to the core concerns of the foundation, which were oriented toward agricultural development.¹ The Conquest of Hunger Programme of the Agricultural Sciences Division fostered the so-called "Green Revolution" for which one of its officers, Norman Borlaug, received the Nobel Peace Prize in 1970. When Warren arrived at the RF in July 1977, annual expenditures in the area of health, other than those related directly to the Population Programme, were less than 2% of the foundation's disbursements. The appointment of Warren, a tropical medicine specialist, marked a watershed departure from recent policy; however, at the same time, it adhered to the traditional interests of the RF. After all, its philanthropic genealogy can be traced to the success of the Rockefeller Sanitary Commission in 1913 and the inauguration of a major global hookworm control campaign. Key international public health activities followed in the 1930s and 1940s when the foundation played a significant part in the control of malaria and yellow fever, for which a foundation officer—Max Theiler—received the Nobel Prize in 1950 for developing the yellow-fever vaccine.²

Knowles had hired Warren for a specific purpose—to focus on the debilitating infectious diseases of the forgotten three quarters of the world's people in devel-

¹The Conquest of Hunger Programme of the Agricultural Sciences Division fostered the so-called "Green Revolution," for which one of its officers, Norman Borlaug, received the Nobel Peace Prize in 1970. The prize was awarded to Borlaug for his pivotal role in helping modernise agriculture in the developing world, an effort known as the "Green Revolution." The phrase was first used in 1968 by William S. Gaud, former director of United States Aid for International Development (USAID).

²J. P. Kreuer (ed.), *Malaria, Immunology and Immunization*, Academic Press, 1980, p. 336.

oping countries. It was a concrete problem, and 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.”³ Warren adopted a numerical view of global health and was firm in his belief that the lives of children in poor countries mattered just as much as those of children in richer geographies. Everyone scored the same in terms of the metrics of importance with the aim to achieve good health care at low cost. Through his constant exposure to and interaction with other medical scientists, Warren became greatly interested in diarrheal and respiratory diseases (the biggest killers of children), neonatal death, and the delivery of vaccines. His great project, which was a unique idea at the time, was to combine known excellent active groups already working on tropical medicine, with an emphasis on tropical diseases, especially parasites, with other scientists in the nascent fields of immunology and molecular biology. Although this latter group may have had no previous experience in tropical disease research, Warren recognised the achievements of the founding fathers of the discipline of parasitology and had indeed been inspired by them to enter the field. However, scientific medicine after World War II had greatly accelerated as a result of the increased professionalisation of research. Of course, fine work was still being performed in parasitology, but for Warren the discipline had somehow remained immune to the infusions of excitement, experimental advance, and forward momentum that were occurring in biology. Revolutionary developments were happening in molecular and cell biology, but parasitology was not transformed in the same way as virology had been for example. Furthermore, the experts who had a profound understanding of specific tropical diseases lived and worked in countries where the infrastructure for first-class research was poor or non-existent. As the celebrated Australian research biologist, Gus Nossal, who first met Warren in 1976, noted, “It is no disrespect to many fine parasitologists to say that, in the third quarter of the twentieth century, their discipline slipped behind the times.” Now with the financial backing of the RF, Warren’s vision was to apply this “new biology” to parasitic diseases, particularly malaria and schistosomiasis, in the developing world. It would not be too much to say that Warren wanted to change the world’s structure.⁴

The Rockefeller years marked the high-water point of Warren’s career. In the 1960s and 1970s, the RF had been in the business of growing crops, slowing population growth, and providing public-health initiatives around the world while at the same time consciously attempting to avoid becoming entangled in the internal politics of beneficiary countries.⁵ This philosophical position became a point of internecine contention that underscored the profound differences within the RF about the value and the role of Western science in the developing world. Warren entered the debate wholeheartedly on the side of those who continued to advocate

³J. 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.

⁴Gustav Nossal, personal communication.

⁵Kenneth Prewitt, personal communication.

for the role of Western science in ameliorating the social problems of developing countries. Although some contended that this view bore all the marks of hubris and that true salvation should come through the alleviation of poverty, which was the true root of the burden of disease, Warren believed there was no time to waste in waiting for such conditions to come about. As such, the RF offered him, in his own words, a “truly unique” opportunity to fulfill his visions. He had great freedom within the organisation, and providing he could read the prevailing policy mood, he could build on the great American tradition of scientific philanthropy by coupling science and scholarship to foster the RF’s noble ambition to promote the “good of mankind throughout the world.” Indeed, Warren’s belief in science formed a historical precedent with the legendary RF officer Warren Weaver, who for a generation had been the architect of programmes in the natural sciences.⁶ Weaver had been brought into the foundation in the early 1930s to apply the ideas and methods of the physical sciences in biology. Weaver, like Warren, was a taxonomist and is credited with the first use of the term “molecular biology.” He too eschewed peer review in favour of his own personal selection of grantees, just as Warren would do.

Inside the offices of the RF on the Avenue of the Americas in New York, the atmosphere was conducive, as it had been in the 1920s, to the idea that the foundation’s primary purpose was to facilitate the programmes of its directors. These directors played a pivotal role in the working of the organisation, acting as a bridge between the foundation’s trustees and field programmes. Experts in their own specialties, these officers, including Warren and the head of Agricultural Sciences, Norman Borlaug, were autonomous and trusted custodians of their divisions, well respected in their fields, and accountable only to the RF board. On occasion, members of the board were well-informed individuals, e.g., when Theodore “Ted” Hesburg, President of Notre Dame, was chairman of the RF. However, in general, they were not experts on parasitic diseases or geographic medicine, and there was little in the way of peer-review adjudication of new internally conceived research projects. This did not mean that programmes in Warren’s Health Sciences Division were not the end result of rigorous debate and intellectual examination. John Knowles wanted what he called “scholar activists” on his staff: people who had deep knowledge of their programme’s subject matter, who were respected for their own research and scholarship, and who had a vision of how this research and scholarship might be applied to solve social problems worldwide. Warren unreservedly embraced this ideal, feeling it was incumbent upon him to remain active to the best of his ability in his field of scholarship, to keep up to date with the literature, and indeed to continue to contribute to this body of knowledge.

In August 1978, the philosopher John Bruer was interviewed for the post of Visiting Research Fellow and became the first person to be hired by Warren as Director of the Health Sciences Division. “At the interview Ken said that he *needed* a philosopher. He believed in the ideals of scholarship and he encouraged others to follow his example, which I think was admirable of him and the RF at that time.

⁶*The Rockefeller Foundation 1913–1988*. RF publication, p. 12.

Also, Ken brought his knowledge and vision to one of the most important positions in international philanthropy and health. He taught us to make a good programme, the importance of finding the best advisors and grantees, and how to build an intellectual and institutional infrastructure to support new research areas. As a grant-maker, Ken was both entrepreneurial and enthusiastic—two rare traits.”⁷

Warren may have believed that he “needed” a philosopher for three specific purposes. First, he valued the humanities and saw the benefit of recruiting a non-scientist scholar into his circle. Another primary reason was Warren’s awareness of the ethical issues surrounding health and population work in the developing world. Third, a more tangential reason lay in his interest in information and information systems. Bruer had previously worked in quantum mechanics and had some abilities in lattice and graph theory. Graph theory has provided the analytical background for much work in bibliometrics as well as complex systems research. In 1988, Warren and his colleague, William Goffman, published a bibliometric analysis of the papers published by the Great Neglected Diseases of Mankind Programme.

This commitment to science owed much to the contemporary self-confidence of the scientific community and the growing sense that science and medicine increasingly had the capabilities to mediate all kinds of previously intractable social ills, an ambitious and optimistic mindset exemplified by the publication of the Yarrowborough report in 1970 that advanced a strategy for the “means and measures necessary to facilitate success in the treatment, cure and elimination of cancer—at the earliest possible date.”⁸ Warren embraced the ‘can-do’ attitude, and placed himself in the slipstream of the feel-good factor that was deeply entrenched at the RF in the 1970s. The foundation was still riding the wave of its Green Revolution, and its enormous historical accomplishments, so why couldn’t the future be an intimation of the past? Why couldn’t there be a breakthrough in male contraception, in vaccine discovery, and in the mechanisms of parasitic diseases?

Genesis and Recruitment

Warren was faced with a scientific and administrative challenge—how to attract outstanding scientists in the burgeoning fields of molecular biology, immunology, and biochemistry to work on the great neglected diseases in the developing world. He began by sketching the outline of a new programme that would target such illnesses by harnessing and funding the collective talent of leading scientists from around the world.

In December 1977, Warren presented his proposal to the Board of Trustees of the RF. The document suggested how the great neglected diseases of mankind could be addressed by the creation of “a network of high-quality investigators who would constitute a critical mass in the field, attract the brightest students and

⁷John Bruer, personal communication.

⁸National Programme for the Conquest of Cancer, *Report of the National Panel of consultants on the Conquest of Cancer*, US Government Printing Office, 1970.

conduct research of excellence.”⁹ The great neglected diseases were described as “great” in terms of prevalence and “neglected” because they affected neglected people. Warren wanted to remodel the historic ideals of the foundation to couple philanthropy and basic science to help address the disproportionate inequity of the global poor. In particular, the synthesised programme would target diarrheal and respiratory diseases, malaria, schistosomiasis, African sleeping sickness, hookworm, and many other infectious diseases. An essential component was the establishment of research units in the mainstream of modern biomedical investigation housed within universities, medical schools, and great scientific institutions. Importantly, the programme affirmed one of Warrens’ sacrosanct ideals, that “a significant part of the investigator’s efforts would be spent in applied collaborative research with colleagues in developing countries.”¹⁰ In this sense the project would establish global networks linking “the bench to the bush.”¹¹

The idea of attracting numerous groups of carefully selected researchers in both developed and developing countries to focus on parasitic diseases was both innovative and controversial. Focusing on “neglected” diseases certainly proved provocative. For some, the word was suggestive of the fact that errors had been made in how and where financial and intellectual capital had previously been channelled.¹² Yet Warren was unapologetic in attempting to reorient and reinvigorate the field. Although outstanding work had been performed in descriptive parasitology earlier in the century, by the 1970s the discipline had failed to adopt the revolutionary changes that had been taking place in molecular and cell biology, genetics, and immunology. By emphasizing the collaborative and interdisciplinary fusion of research from around the globe, Warren’s GND network was poised to revolutionise the ways in which infectious tropical diseases were investigated by representing the first attempt to apply modern biomedical technology in the elucidation of mechanisms of disease prevalent in developing countries and bringing research on the latter to the mainstream of medicine in developed countries. The project was also a departure from tradition in terms of how it would be funded. As a researcher himself, Warren knew only too well the frustrations of writing grant applications, the trepidation of not having a grant renewed, and the general administrative obstacles to actually getting on with the work. To avoid these strictures and to smooth the progress of research, he advocated that all of the GND grants would be guaranteed for a period of 8 years, an unusually long period of time that gave researchers financial security and freedom.

⁹K. 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.

¹⁰K. 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.

¹¹G. F. Mitchell, 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. 49.

¹²Hans Wigzell, personal communication.

Warren successfully sold the idea to the RF board by emphasising the foundation's long history in international health and that the time was now ripe for new ground to be broken. The formal tenets of the new undertaking were as follows:

- Research would range from the basic level in highly sophisticated laboratories through clinical investigation and field epidemiology and anthropology.
- Research would be investigator-initiated in terms of the problems approached, which could be any aspect of any of the "great neglected diseases."
- Support would be for at least 8 years and would be flexible, although emphasis would be on the development of young investigators and on international collaborative research.
- The units would be gathered into a global network for communication and collaboration fostered by annual meetings. Fourteen foundational units were to be recruited and established with the only mandatory requirement being that high-quality collaborative science was undertaken and that members would attend annual meetings of the GND.

Thus, the Great Neglected Diseases of Mankind Network was born. With the concept and research objectives in place, Warren spent the best part of a year persuading some of the world's leading scientists to bring their chosen specialties into tropical medicine. In addition to persuading several American colleagues to join the GND, he established collaborations with scientists across the world in Egypt, Israel, Australia, Thailand, Sweden, England, and Mexico. It was a truly interdisciplinary group bound together by Warren's ability to persuade good scientists to work on diseases in which he was interested and, in some cases, in which they had shown scant curiosity. He achieved this with a combination of bonhomie, enthusiasm, and the mutual respect of those working with him.¹³ Of course, there was no peer-review committee and no consensus; the entire group was selected single-handedly by Warren.

The impetus to get the project off the ground relied almost entirely on Warren's strength of character and his personal evolution as a scientist. For Warren, four distinct elements were necessary: (1) to tempt some of the best minds in medical science into the field of tropical medicine; (2) to apply the most sophisticated methods and ideas to the work; (3) to expose these teams recruited from outside traditional tropical medicine to the realities of the diseases in the field; and (4) to create intellectual and personal connections between the different teams, to fuse them into a strike force whereby the whole was greater than the sum of its parts. To achieve this, Warren used his inherent strengths as a catalyser, proselytiser, and matchmaker. He prided himself on his personal network, on knowing *everyone*.

Key to the recruitment process was to convince outstanding individuals who were not currently working in tropical medicine that they should consider a change of direction. This Warren did with consummate ease. Antony Cerami, the world-renowned biomedical scientist, was at Rockefeller University in 1977 and

¹³Keith McAdam, personal communication.

looks on his first meeting with Warren as career defining: “The first time I met Ken was a memorable and unique experience. Over lunch, Ken painted in broad strokes but very bright colours, this vision of what was to be subsequently known as the GND. The dedication of Ken to the field of parasitology and the poor people of the world is an aspect of the GND that I will never forget. He managed to instill these thoughts in everyone. It was the most important lunch of my life, since it launched me into new unknowns with a group of dedicated people that I am proud to be associated with.”¹⁴ Many of the enlisted “high-class investigators” echoed this sentiment and recognised that the GND had a profound influence on their careers and personal values.

To advise the network on immunology, Warren courted a giant of translational immunology, the President of Israel’s Weizmann Institute, and President of the International Union of Immunology, Michael Sela. Perhaps it was their shared Jewishness—although Warren didn’t wear his Jewishness on his sleeve and was highly secularised—or their internationalism, or a commitment to using science to alleviate suffering, but there was an immediate empathetic understanding between the men. Sela found Warren to be an “infinite charmer” and they became close friends almost immediately. Sela believed that the idea of the GND was “terrific” and that the people selected “were not only good scientists, nice people, but also had the quality to collaborate together... which was all part of the success.” Sela admired Warren’s ideas, the zeal he brought to the project, and he particularly valued another trait of Warren’s from which he benefited personally: “Ken was what is called in Yiddish a ‘shadkhen’, a matchmaker, and matchmaking is very important. I met Shelley [Sheldon] Wolff through Ken and he became a great friend. When I finished my ten years as head of the Weizmann, I moved to Tufts in Boston, where Shelley was Chairman of the Department of Medicine. Shelley was very important: he was a leader, and while I was an advisor on immunology, Shelley performed the same role for infectious diseases [as part of the GND network].”¹⁵

One of the outstanding physicians already on Wolff’s staff at Tufts was Gerald “Jerry” Keusch, who went on to become director of the Fogarty International Centre for Global Health at the NIH. Jerry had finished his training in infectious disease in 1970 and hoped to pursue a career in what is known today as “global health.” After spending some time in Bangkok trying to understand the mechanisms of cholera, he later became interested in the relationship between malnutrition and the susceptibility of children to recurrent infection. By the time he was recruited to Tufts in 1978, he was a pioneering physician in the nascent field of molecular medicine. At the time, there was no formal relationship between the RF and Tufts, and so Wolff set up an appointment for Jerry to meet Warren in the hopes that they might join the network and secure much-needed funding. In many respects, Keusch fulfilled the criteria that Warren was looking for: He had experience of working in the field; he

¹⁴Anthony Cerami, personal communication.

¹⁵Michael Sela, personal communication.

would be mentored by his friend Shelley Wolff; and he fully intended to make his career studying infectious diseases in developing countries. Still, there was a lot riding on the meeting, and Jerry felt a sense of trepidation when he learned that their get-together would take place at the Infectious Diseases Society Conference in New York, in October 1978: “We met, and he sits me down in the middle of a staircase, where everybody is going up and down. Kind of a classic Ken move; he’s conducting an interview and people are walking by, everybody who wanted one of the RF grants was stopping and tapping him on the shoulder in a ‘remember me?’ way. Anyway, I guess I passed [the interview] because we got the award and took the job in January 1979.”¹⁶

In a similar fashion, Warren also persuaded Hans Wigzell to join the group. Wigzell at the time was working on the immunology of murine malaria at Uppsala University in Sweden. Just how unorthodox the GND programme was seen to be was evident from the men’s first meeting. Warren travelled to the Karolinska Institute in Stockholm where Wigzell introduced him to the institute’s president, Sune Bergstrom, himself a Nobel laureate. Wigzell remembers Bergstrom’s bafflement at the GND concept as he asked his colleague, “This strange American, what is he actually doing? It’s strange...?” Bergstrom was unable to visualise how the new programme would work in the context of traditional research methods.¹⁷

Warren was also keen to recruit a specialist in molecular medicine and quickly convinced the Oxford-based physician–scientist David Weatherall (at the time working on inherited disorders of haemoglobin in the tropics) and his team to join the network. Indeed, the new link would prove fortuitous for Oxford medicine in general because the university’s leading reputation in international health for developing long-term north–south research partnerships and capacity building in tropical medicine can be traced to a seemingly innocuous meeting between Weatherall and Warren on a dark misty evening in 1977. The two men met in London, and as Weatherall admits, “when Ken first told me about the GND programme over an excellent dinner at a slightly decadent hotel near Victoria, I was quite sceptical. [But] in the words of the poet Oliver Goldsmith, ‘fools who came to scoff remained to pray.’ When he told me that the Rockefeller would offer research support for a minimum of eight years and that the only stipulation was that we met annually with the other groups to exchange information, I decided to go ahead.”¹⁸

With the majority of the key players selected, Warren’s Great Neglected Diseases project began operation. The network would eventually span five continents and placed Warren at the forefront of tropical medical research. Each unit was deliberately situated within existing departments of medicine so as not to be divorced from clinical skills and clinical understanding in terms of pathogenesis and mechanisms of disease—essentially the science of identifying vaccine

¹⁶Gerald Keusch, personal communication.

¹⁷Hans Wigzell, personal communication.

¹⁸David Weatherall, personal communication.

candidates, drug targets, and diagnostics. Initial components of the GND included divisions of geographic or tropical medicine at Case Western Reserve University, Tufts University, the University of Virginia, the University of Washington, Oxford University, and the Biomedical Research Centre for Infectious Diseases in Cairo, Egypt. Immunology units were established at Harvard University, the Walter and Eliza Hall Institute in Australia, the universities of Stockholm and Uppsala in Sweden, and the Weizmann Institute, whereas pharmacology units were in action at Rockefeller University, Case Western Reserve University, the Centro de Investigación y de Estudios Avanzados in Mexico City, and Mahidol University in Bangkok, Thailand. All of the groups were to spend approximately 30% of their time in collaborative research in the developed world with countries such as Kenya, Egypt, Sudan, India, Guatemala, Brazil, Malaysia, Gambia, Indonesia, and Papua New Guinea. The investigators worked mainly on bacterial diarrheas and helminth and protozoan infections.¹⁹

The Network in Action

The first meeting of the GND was held at the Abby Aldrich Rockefeller Hall, New York, in 1978. It was an unforgettable experience. Warren had invited two giants of British parasitology, George Nelson and Philip Marsden, to the event to elaborate on the new possibilities of applying modern specialties to the old field of parasitology. The two men were great raconteurs, full of mind-expanding stories gathered over decades working in the tropics and thrilled the group by signposting the ways in which the new biomolecular sciences might affect old diseases. Marsden was a legendary figure in tropical medicine with research interests in insect-borne protozoal disease. He worked in both Africa and South America and was a professor of medicine at the University of Basilia for 17 years. In Gambia, West Africa, he performed one of the first longitudinal studies of tropical child health, which led to his doctoral thesis. One event that occurred while he was a medical officer in Gambia colourfully describes his idiosyncratic and highly adaptive remedial style: “While water surfing in the Atlantic the Governor trapped a large *Physalia* jellyfish between his chest and the surf-board. I was fishing off the beach at Mile 5 and they brought him to see me. The red wheals were already visible on his chest from the discharged nematocysts on the tentacles. Fortunately I had a full bladder, so immediately I urinated on his chest to wash off the residual nematocysts and had people throw sand on his chest while I ran to the car to get some morphia. After much pain he made an uneventful recovery.”²⁰ Meanwhile, George Nelson was one of the world’s most distinguished parasitologists; a former medical officer in Uganda and researcher at the division of insect-borne diseases in Nairobi, he ended his academic career in parasitology at the Liverpool School of Tropical Medicine. The friendship,

¹⁹Warren described parasitology as, “a biological discipline concerned largely with two separate groups of organisms—single-celled protozoa and the multi cellular metazoan of which the helminths form the most important group”.

²⁰A *Jubilee Scrapbook 1947–1997. An anthology of tales and photographs depicting 50 years of the MRC in The Gambia. Collected by A. Greenwood, J. Foster, H. Pickering and M. Weber*, p. 10.

camaraderie, and sense of fun that existed between Warren and Nelson are borne out in an exchange of letters between the two men:

Dear George, What a pleasure to receive your enthusiastic letter about 'a marvelous safari' in the Sudan and Kenya. Sylvia and I had the great pleasure last March of going up to Lake Turkana by land, an incomparable experience. I also had another incomparable experience and that was developing chronic diarrhea which I brought to China with me and back before I realised that it was our old friend the Giardia...²¹

For the uninitiated, Nelson and Marsden gave a perspective that none of the GND team possessed because they had spent decades in the tropics coping with parasitic assault. Moreover, at the time, British parasitology was far ahead of the discipline anywhere else in the world, and in addition to being full of inspiring stories, Nelson and Marsden knew the field's literature intimately. Keith McAdam attended the meeting at the Abby Aldrich Hall as part of Shelly Wolff's team from Tufts: "Marsden and Nelson were two eccentric champions of tropical medicine. They taught a week's course on parasitology which was quite something for a group of biomedical scientists who were into the new age of immunology and molecular biology. They just thrilled us with all the possible involvement of new skills in developing answers to the diseases they described."²²

With only three or four scientists from each of the units present, the meeting was characterised by its intimacy and held in an atmosphere that oscillated between excitement, optimism, apprehension, and relaxed creativity. It marked the fulfillment of an audacious ambition: to bring new bio-molecular scientists to the field of parasitology, to create intellectual and personal connections between the different units, to stimulate competition as well as collaboration, and, ultimately, to improve the human condition. In a wider context, the subsequent flowering of invention within the GND was partially attributable to the breadth of intellectual perspective that informed the scientific work during the period. The group represented an interdisciplinary ideal that was the very antithesis of the divided world described by C.P. Snow in 1959 as a 'society split into the two titular cultures—namely the sciences and the humanities'.²³ Warren prided himself on his undergraduate studies at Harvard and was eager to point out that it was not always necessary to have a first-class degree in biochemistry to be a physician. There were other backgrounds that would be helpful, and several of his GND colleagues had backgrounds in the liberal arts, which played perfectly into one of Warren's favorite aphorisms: "there are many rooms in the house of medicine."²⁴

Each year the meetings became bigger and more rambunctious. Close friendships were established between many outstanding researchers, and the annual event became rather like a reunion or perhaps a family gathering. At one of the early

²¹Letter from K. S. Warren to G. S. Nelson, Department of Parasitology, Liverpool School of Tropical Medicine, Pembroke Place, Liverpool, England. March 17, 1987.

²²Keith McAdam, personal communication.

²³C. P. Snow, Rede Lecture, 7 May 1959.

²⁴John Bruer, personal communication.

meetings in the US, David Weatherall's team was invited to give a series of papers. The Oxford team had built up a strong partnership with the thalassaemia group in Thailand, which was led by Prawase Wasi, who had a habit of giving his lectures squatting on the floor in Buddhist style. Weatherall wanted his colleague to emphasise in his talk the importance of the RF to their work, and "not in the least because of the financial implications, I asked Prawase if he would lay on the thanks very thickly at the end of the lecture. He did say that he had had some success with the control of thalassaemia in Thailand but now they had been blessed in their endeavors because God had brought them Ken Warren. My immediate reaction to this rather excessive praise was to try and put my head under the seat!"²⁵ Later meetings took place in locations as far afield as Woods Hole, Massachusetts, a game park in Kenya, a hotel in Tel Aviv, a ski resort in Canada, and an Oxford college but with the continuing unifying objective to report on the past year's work, progress, and developments, to share knowledge, ideas, and doubts, and to create a sense of common goals and joint destiny. As observed first-hand by Sylvia Warren, the atmosphere was conducive to a huge degree of productivity: "They got an enormous amount accomplished at their meetings, and then they got on with their work afterwards because there were no impediments; they had long-term funding, so they didn't need to waste time filling in grant applications. It allowed them to produce, and how! (Fig. 2.1)".²⁶

Of course, there were occasions when things did not run smoothly. In 1979, the second meeting of the GND programme was held at The Queen's College, Oxford. David Weatherall hosted the meeting and had gone to great lengths to provide an exciting scientific programme for the delegates and to make their stay in the city memorable. However, after spending one night in the historic but Spartan undergraduate accommodation, Shelly Wolff, muttering disquiet about the far-distant bathroom, decamped to the refined comfort of the Randolph Hotel! Similar dissatisfactions were expressed about the catering provision because the Gothic setting was accompanied by a diet rich in carbohydrate and which had changed little since the days of Henry VIII. After the second day, with nobody showing up for college meals, David Weatherall was forced to make an appeal to his colleagues' humanitarianism, entreating them to "come to breakfast in the morning," because "the chef has threatened to commit suicide if nobody shows up."²⁷

Research was at the heart of the GND's workings. Warren's philosophy was to develop the science, line it up with the clinical problems, and move between the laboratory and the clinic—the clinic, in the case of the GND, being the developing world. This was translational medicine in a developing world setting: the long road back and forth between the bedside, the laboratory, and the community. The main focus of each GND unit continued to be an examination of the mechanisms of

²⁵David Weatherall, personal communication.

²⁶Sylvia Warren, personal communication.

²⁷Gerald Keusch, personal communication.



Fig. 2.1 Early 1980s meeting of the GND network at Woods Hole. Courtesy of Peter Hotez

disease, i.e., finding out how things worked. The innovative nature of the programme relates to a combination of applying genetic engineering technology to problems of parasitism; a belief that without fundamental investigations of the biology of these organisms as the major causes of disease, it would be very difficult to make progress in finding ways to control the disease. Importantly, the flexibility of the financial support allowed researchers to perform field work that would have been completely impossible under any other form of research grant. In this respect, the programme was prodigiously successful with groundbreaking work undertaken on the workings of numerous parasitic diseases including hookworm and schistosomiasis, although vaccines to such infections remain elusive even to this day. Rather, perhaps the most enduring legacy of the GND can be found in the transformations brought about in the financial modeling of such projects and the concomitant capacity to incubate new talent and collaborative work. The actuarial model of Warren's RF programme achieved remarkable results with only modest resources. During the 8-year period of its funded existence, the project involved 161 scientists and clinicians and 360 trainees, of which 150 were from the developing world, and resulted in the publication of 1800 papers. This was all accomplished at the cost of approximately \$15 million (\$55 million in 2015 values)—a prodigious rate of return on the investment by any standards.²⁸

²⁸K. S. Warren & C. C. Jimenez (eds), *The Great Neglected Diseases of Mankind Biomedical Research Network: 1978–1988*. New York: The Rockefeller Foundation, 1988, p. 2.

The funding policy of the RF transformed some of the units in the network from small laboratories working on model systems in mice into large bustling units with a stunning cadre of investigators who could attract additional resources. This was certainly the case at The Walter and Eliza Hall Institute of Medical Research, Melbourne, led by Graham Mitchell. Receiving GND funding enabled the Institute to expand its parasitology work by recruiting new researchers who would take part in the annual GND meetings alongside carrying out world-leading laboratory investigations. One such beneficiary was the immunochemist Emanuela Handman, who worked on leishmania. As a young, relatively inexperienced post-doctoral fellow at the time, Handman found inclusion into the GND network an “inspirational” experience that allowed her to rub shoulders with some of the greatest scientists of the era. She remembers these encounters as “open, friendly, and encouraging,” while “the meetings opened new vistas of biology of which I knew nothing. This gave me the impetus and the confidence to move into new areas of research. As I moved on in my career, I started to realise how unusual the GND Network was. There was a sense of openness; the fact that junior or senior scientists did not hesitate to present the entire, uncensored data to all of the other participants. There was no sense of competition or secrecy; everything was on the table.”²⁹ Being a recipient of GND support also meant that institutions were far more competitive when seeking other forms of external funding. Handman was the beneficiary of long-term funding from the NIH, WHO, and the Australian Society for Medical Research, all of which she acknowledges would “not have been possible were it not for the GND’s seed funding. Moreover, the type of high-risk high-return work that we were undertaking would not have been fundable even for established parasitologists let alone newcomers Fig. 2.2”.³⁰

GND funding thus played a crucial 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 and beyond. A brilliant cohort of scientists—including John David, Adel Mahmoud, Anthony Cerami, James Kazura, Gerald Keusch, Richard Guerrant, and Peter Hotez—were enticed by Warren to work on tropical diseases who otherwise might not have done so. In turn, all of these investigators have made a lasting contribution to disease control and human health, both as part of the GND programme and in subsequent years. Part of the reason why the network became such a formative experience in the lives of so many scientists was Warren’s insistence that an important part of working in tropical medicine was to study in the field. This became a crucial component of the GND programme and in many cases a career-defining moment for those involved.³¹

²⁹Emanuela Handman, personal communication.

³⁰Emanuela Handman, personal communication.

³¹K. S. Warren, “The bench and the bush in tropical medicine,” *Am J. Trop. Med. Hyg.* 30: 1149–1158, 1981.



Fig. 2.2 Graham Mitchell and his boss, Gus Nossal (sitting), in the lab in Melbourne, Australia. Courtesy of The Walter and Eliza Hall Institute of Medical Research

Warren's own contribution to the story of schistosomiasis had revealed the crucial interplay between the "bench and the bush,"³² and as the network developed and expanded, he encouraged his scientists to productively combine knowledge of the developing world with the powerful new tools of the "bench" into an effective synthesis. The benefits of this approach were clearly demonstrated by Anthony Cerami's experiences in the GND. Cerami ran his own laboratory in medical biochemistry at Rockefeller University, and through one of his MD/PhD students,

³²In the tropics, clinical studies in hospitals and epidemiological studies in villages and among school children had shown the silent nature of the infection, even in patients with relatively advanced disease. The field investigation, which included the development of better parasitological methods for diagnosis, resulted in the collection of relatively large banks of parasitologically and clinically characterised sera. Meanwhile, work at the bench on the pathogenesis of schistosomiasis resulted in the development of an animal model, the characterisation of the parasite factor (egg) responsible for the disease, the essential role of the host inflammatory cell-mediated immunological response, and the occurrence of suppression of the host response by way of serum antibodies.

Steve Meshnick, he became interested in parasitic diseases in Africa. This led Cerami to spend time in Kenya observing the presence of cachexia in animals and people infected with parasites, work that marked the beginning of Cerami's search for the mechanism of this common occurrence of chronic disease, which is now known to be a macrophage protein produced in response to infection. On the back of this research, Cerami would later go on to co-write the patent that has become a landmark document in the history of anti-tumor necrosis factor (TNF) therapies.³³ Anti-TNF treatment of rheumatoid arthritis, Crohn's disease, and psoriasis has helped to improve the lives of millions of patients throughout the world.³⁴ Cerami's work was a vindication of Warren's concept of the scientific endeavour—Choose good people, fund them well, and let them rip!

Life in the field, however, did not always run smoothly. On one occasion, the native New Yorkers, Cerami and Meshnick, were taking in the local sites in Kenya. Unwisely, Steve thought that it would be a good idea to take his boss on a whirlwind safari at Nairobi National Park in his ancient Datsun. Within a short time they witnessed one of nature's most dramatic events: a lion killing and devouring its prey. The men got out of their car and cautiously took photographs of the scene. When they returned to the Datsun, however, it was stuck fast in the deep ruts in the road. Both men looked at each other and across at the blood-splattered lion. Cerami, the tenured professor, broke the silence: "Do you want to get out and push...?" Salvation came in the form of a Maasai tribesman, who, accustomed to the ways of the bush, walked across the open land, passed the salivating lion, and with the two laboratory-trained scientists looking on, perfunctorily eased the car out of the fissure to safety.³⁵

Aberrations aside, Cerami readily acknowledges that the GND years were the most important in his life in science. His reflections capture the subtle equipoise between sacrifice and achievement that many biomedical scientists will recognise: "The annual meeting of the GND offered to each of us an opportunity to recharge our batteries to continue the hard, lonely work associated with science. The GND became a family dedicated to improving the well-being of mankind. The family aspects of belonging to a group had unique sociological effects. Every group wanted to show that they had established new and important scientific findings. Everyone wanted to look their best."³⁶ Perhaps most importantly, the meetings proved a focal point where researchers from geographically disparate parts of the globe could meet to collaborate across continents.³⁷ For young talented researchers at the beginning of their careers, it was exhilarating to talk, learn, and interact with

³³A. Cerami, "A Surprising Journey in Translational Medicine," *Molecular Medicine* Vol. 20 (Supplement 1) 2014, p. s4.

³⁴M. Feldmann, "Translating molecular insights in autoimmunity into effective therapy," *Ann. Rev. Immunol.* 27: 1–27, 2009.

³⁵Steven Meshnick, personal communication.

³⁶Anthony Cerami, personal communication.

³⁷Keith McAdam, personal communication.

some of the world's brightest and most creative biomedical scientists including Michael Sela, David Weatherall, Gus Nossal, Peter Pearlman, and Shelley Wolff. This intellectual nexus brought professional recognition, that much needed antidote to the inevitable disheartening failures and loneliness of laboratory research. Acknowledgement and professional respect, experienced early in a scientific career, can have a life-long influence and strengthen resolve in difficult times.

Although the various units within the GND worked on very different aspects of parasites, from ecology, epidemiology, and immunology to infection and the genetics of host responses, the meetings offered an opportunity to foster new connections, particularly between researchers from the global north and south, as Warren had originally envisaged. An embodiment of the success of this ideal was the research on early childhood diarrhoea and enteric infections, undertaken by Dick Guerrant at the University of Virginia and Manasses Fonterles in Fortaleza, the capital of one of the poorest states in northeast Brazil. When Dick Guerrant attended the GND meeting in Oxford in 1979, he was 26 years old. He had trained as a paediatrician, just like his grandfather, and had begun his career in tropical medicine in the Congo before moving to Dhaka, Bangladesh, where the NIH ran a cholera programme. Working on cholera-stimulated oral-rehydration therapy (ORT), Guerrant sought to understand the mechanisms of secretory toxins to make ORT work more effectively, and it was this research that had brought him to Warren's attention. When Guerrant attended the meeting in Oxford, he invited along a stellar cast of colleagues: an expert on amoebic dysentery, Jonathan Ravdin; Ferid Murad, who would win the Nobel Prize in 1998; and the pharmacologist, Manasses Fonterles.³⁸

For both Guerrant and Fonterles, the meeting marked the cementing of a working relationship, managed by Warren, that would endure for the next 35 years. Fonterles, a pharmacologist, possessed a good scientific genealogy, having worked with both Raymond Ahlquist and later with Julius Cohen in Rochester, New York, and had begun to work on the receptors that had important effects on the kidney and the gut. This research dove-tailed perfectly with Guerrant's own work on ORT, and so began the decades-long collaboration on enteric and diarrheal infections between the University of Virginia, the Makenzie Presbyterian University in Sao Paulo, and the village of Pakatuba in Fortelaza. This extended programme produced ground-breaking discoveries that would not have been made had it not been for the initial RF funding.³⁹ Guerrant is adamant that, far more important than any of his work on guanylate cyclase or adenylyl cyclase, was the discovery that high rates of chronic enteric and diarrheal infection lead to, on average, an 8-cm growth shortfall and a ten-point IQ deficit by the time children are 7–9 years old. With ORT, a child

³⁸Ferid Murad shared the Nobel Prize in Physiology or Medicine in 1998 for showing that nitroglycerin and related drugs worked by releasing nitric oxide into the body, which relaxed muscles by elevating intracellular cyclic GMP.

³⁹R. L. Guerrant, G. D. Fang, N. M. Thielman & M. C. Fonteles, "Role of platelet activation factor in the intestinal epithelial secretory and Chinese hamster ovary cell cytoskeletal responses to cholera toxin," *Proc. Natl. Acad. Sci.* Sept 27; 91 (20): 9655–9658, 1994.

will not die; mortality, although still high, has been decreasing, but morbidity is not. The collective work of Guerrant and Fonterles revealed the human and societal costs of diarrheal infection to the world's populations who continue to live in extreme poverty: It was a true translational partnership that successfully linked the laboratory to the clinic.

Warren, who retained a keen fascination with Brazil, having experienced his first true encounter with the “bush” there in Bahia in 1962–1963 while working on hepatosplenic *Schistosomiasis mansoni*, was the catalysing force that ensured the success and longevity of the partnership.⁴⁰ As a young researcher at the time, Guerrant admits to being “scared to death” at the beginning of the GND, but with Warren acting as a “masterful mentor,” he was encouraged to follow his “wildest dreams.”⁴¹ Similarly for Manasses Fonterles, it was a chance encounter in Oxford with the colourful American who had opened his eyes to the possibility that his own scientific training could be used to help to identify the mechanisms of diarrheal disease in his native Brazil: “He made me believe that under his leadership a programme would not die and we started building bridges. He was a tremendous man, very energetic in defence of his ideas, in defence of the neglected diseases. At the time no one wanted to put money into them [neglected diseases] because the amount of return that you have will always be small ... So for me, he was one of the most tremendous human beings that I ever met. The GND was the turning point in my life.”⁴²

A similar personal renaissance connected to Warren was experienced by Onesmo ole-MoiYoi, who grew up in a Maasai village in Kenya. His destiny as the community's cattle herder was irreversibly redirected by the power of education. More interested in books than being a trusted custodian of cattle roaming the edges of the Serengeti, Onesmo was sent by his father to school, where his dedication eventually won him an Aga Khan scholarship to Harvard. Reminiscent of Warren's own curriculum at the same university, Onesmo took a humanities degree before entering Harvard Medical School and specialising in immunology and molecular biology. Today, he is one of Africa's leading scientists and a forceful advocate for the application of more biomedical research to the continent's indigenous infectious diseases. Although Onesmo was never formally part of the GND network, he attended most of their meetings. Crucially, he had jettisoned the pathway of a conventional medical career for the study of infectious diseases after attending a lecture at Harvard in 1977 given by a proselytising Ken Warren: “Ken was talking about the idea of a network connecting leading institutions in the West with scientists in the developing countries, and in that lecture he mentioned the disproportionate amount of money spent on cardiovascular disease, diabetes and cancer, diseases considered important to the West, compared to the miniscule amount of

⁴⁰K. S. Warren, “The bench and the bush in tropical medicine,” *Am. J. Trop. Med. Hyg.* 30: 1149–1158, 1981.

⁴¹Richard Guerrant, personal communication.

⁴²Manasses Fonterles, personal communication.

money spent on diseases of the developing world which affected millions of people.”⁴³ At the time, ole-MoiYoi was working on the mechanism of hypertension, nothing to do with infectious disease, but the lecture, rather like his earlier disenchantment with herding cattle, brought unimagined change: “Meeting Ken was really a turning point in my life, because the numbers he gave showed that with minimal investment you could make a huge change in helping people to live healthier lives. Ultimately, a friend of Ken’s, Barry Bloom, wrote a paper that mentioned a disease of livestock which transforms lymphocytes to become cancerous and kill the animal in three weeks. That caught my attention. Three years later, one of my professors, Donald Fawcett, went to Nairobi to set up an electron-microscopy laboratory in what is now called The International Laboratory for Research on Animal Diseases (ILRAD). A year later I went to Nairobi to work on the microbiology of this disease that transforms the lymphocytes to become cancerous. Meeting Ken, and listening to his lecture, was one of the things that led me to work on trypanosomiasis and malaria.”⁴⁴ Indeed, the RF had a long-standing track record of supporting agriculture and animal care in the developing world. As early as 1943, CIMMYT, the International Maize and Wheat Improvement Centre, was established in collaboration with the Mexican Department of Agriculture to increase food crop production through research and development. Thirty years later, John Knowles was instrumental in providing the institutional framework for Onesmo ole-MoiYoi’s career in East Africa by providing financial support for livestock research at ILRAD in Nairobi.

Warren and the GND

Warren remained very much at the epicentre of the network’s activities, often by sheer force of his personality. Excitement, enthusiasm, and a sense of fun were the sentiments with which Warren infused his nascent recruits. His message was simple: Hubris and perfection are two of the enemies of getting things done, but enjoy the thrill of the science, and if you’re lucky you will have some relevance to the people who suffer from infectious diseases. This he championed with great energy, and he found it difficult to take “no” for an answer. As one of his obituary notices observed, “this caused some to hide out until we were quite sure he was fully engaged in another project.”⁴⁵

Warren was certainly a “larger than life figure,” an inherently charismatic and charming man, who in the words of Allen Cheever (who worked with him at the NIH in 1960), “was many things but never unenthusiastic and never modest. Ken saw what he wanted and got it.”⁴⁶ He could also be bombastic, eccentric and swashbuckling, with a knack for “telling it the way it was ... and sometimes

⁴³Onesmo ole-MoiYoi, personal communication.

⁴⁴Onesmo ole-MoiYoi, personal communication.

⁴⁵R. Selzer, Kenneth S. Warren, M. D. June 11, 1929–September 11, 1996, *Molecular Medicine*, Vol. 2, No. 6, November 1996.

⁴⁶John Cheever, personal communication.

rubbing people up the wrong way.”⁴⁷ However, these perceived components of his personality were tempered by the recognition that he had a great vision for tropical medicine and the delivery of health services in the tropics. A more nuanced understanding of Warren’s character is offered by his wife, Sylvia: “He did rub people up the wrong way, but somebody like that is bound to. 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.”⁴⁸ John Bruer also recognised that Warren could be perceived as confrontational but that the loquaciousness, noise, and excitement could be open to misinterpretation: “He certainly didn’t mind ruffling feathers, but I wonder if he even noticed that he was doing it ... I don’t think he set out to irritate people, I just think it was a function of his enthusiasm and drive. There was a single-mindedness to him, and that blinded him to problems and obstacles along the way. But Ken was always very kind personally, helping us younger people with our careers, and while he might get angry with Shelley Wolff or Ken Prewitt, he never got angry with us. There was that kindness that I think was at his core. He did some admirable things—you have to be in awe of the guy—but like all of us there were glaring deficiencies that got in his way.”⁴⁹

Warren was not helped in this department by the fact that the GND network’s ethos and philosophical underpinning were at odds with many of the established ways of getting things done. At the outset of the programme, Warren ruffled feathers in particular at the World Health Organisation (WHO) by criticising the commendable but unobtainable goals for total primary health care for every human being (set out in a WHO declaration in 1978) and instead advocated a selective assault on those few diseases that caused the highest mortality among the world’s poor.⁵⁰ In a similar fashion, he was also critical of the focus of the WHO’s Tropical Diseases Research Programme (TDR), which he believed wrongly targeted diseases that did not cause the greatest suffering to the greatest number of people. Moreover, the GND sought to understand the mechanisms of disease by way of the use of molecular sciences, whereas the TDR’s original mission was to use immunology to develop new tools and strategies to combat tropical diseases. Understandably then, there was some initial bureaucratic friction between the free-enterprise ethos of the RF and the more politically sensitive WHO. However, resistance soon turned to (competitive) acceptance: Warren invested emotional capital each year by attending WHO meetings, and the GND and TDR programmes continued to run in parallel for a decade. Scott Halstead, Warren’s colleague at the RF in the 1980s, concludes of their professional co-existence, “I think if you had gotten Ken in a reflective mood he would have said, ‘No, TDR is a good thing.’ After all, while the TDR diseases were fewer, they were many of the same ones that we were supporting.”⁵¹

⁴⁷Scott Halstead, personal communication.

⁴⁸Sylvia Warren, personal communication.

⁴⁹John Bruer, personal communication.

⁵⁰Richard Peto, personal communication.

⁵¹Scott Halstead, personal communication.

There is little doubt that, building on the foundations laid by an earlier generation of scientists, the GND programme transformed parasitology from a lower technical endeavour to one that was at the forefront of the biotechnology revolution. And yet the GND was viewed by some as being peopled by “Johnny-come-latelies” with Warren evaluated alternatively as an “upstart” or a “new kid on the block.”⁵² These views may have evolved in response to the fact that the GND *was* indeed an exclusive club and was recognised as such by those both inside and outside its sphere of influence. Hans Wigzell was conscious of this situation and believed that it emanated from those who possibly felt threatened by microbiology and the new technologies that were being applied to the field. The rumblings from the establishment were subdued rather than overt, but they were unambiguously felt by Wigzell: “It was somehow that unless you had contracted malaria, or any other parasitic diseases yourself, or that you had been swinging in the jungle or been getting infected, you were not really a true person to be working in tropical diseases. I wouldn’t call it vehement, but it was an *uppish* kind of treatment, with Ken treated like an underdog who was doing things that were ‘not completely proper’.”⁵³

The disparaging view that Wigzell detected was not held by everyone. Bridget Ogilvie attended some of the GND meetings as an independent adjudicator and eschewed belligerence for a more balanced evaluation of Warren’s contribution to neglected diseases: “I greatly admired and respected what Ken did—a lot of strengths in parasitology in the US now are because of Ken. But what I objected to with his GND was that everything that the Wellcome Trust or the MRC or anybody else funded, he took the credit for. He would give a group, who the Wellcome Trust was spending £1 million on, \$50,000 or \$100,000, and then take credit for everything that came out of it. I really objected to that. I thought it was beyond tolerance....”⁵⁴ This propensity to “big himself up” had been noted before. As a grant-maker, Warren was both entrepreneurial and enthusiastic. Kerr White, his Deputy Director at the RF, used to say that when a horse and rabbit stew was about to be made, Ken was there with his rabbit. But after the stew had been made, everyone believed that Ken had brought the horse.⁵⁵ Joe Cook had also encountered this exact phenomenon on several occasions; nonetheless, the sense of injustice was attenuated by the feeling that the investment had been shrewd of perception and profound in legacy: “Ken learned to use power very well, that was part of his genius, and when it came to funding schistosomiasis and the Molecular Parasitology Course at Woods Hole, I guess he probably did bring the rabbit and I brought the horse. But the course was very important for bringing people into parasitology research.”⁵⁶ Even those who were outside the GND orbit were often

⁵²Keith McAdam, personal communication.

⁵³Hans Wigzell, personal communication.

⁵⁴Dame Bridget Ogilvie, personal communication.

⁵⁵John Bruer, personal communication.

⁵⁶Joe Cook, personal communication.

quick to acknowledge the programme's strengths. In the 1970s, for instance, there were only two laboratories in the world working with cellular immunology on schistosomiasis: Ken Warren's in Cleveland and Dan Colley's in Nashville. Dan was not invited to be a part of the GND network and never attended any of their meetings, even though Ken Warren knew him well and had helped him at the beginning of his career. Inevitably Dan felt neglected and left out of the camaraderie, spirit of optimism, and collective endeavour that defined the annual meetings. Nevertheless, he recognised the subtle link between the network's prodigious success and the human condition: "The reason people really liked the GND was the sense of *recognition*. Bringing scientists together and showing respect for what they do is important, because scientists don't often get that. That was probably the telling thing. Certainly, getting some money doesn't hurt, nor does meeting important people from other fields ... but simply having a group to identify with is part of what I think it did."⁵⁷

The GND programme forms an important chapter in the anthropology of tropical diseases. The interdisciplinary approach led to a great leap forward in understanding pathogenesis and represented the first attempt to apply modern biomedical technology in the elucidation of the mechanisms of disease that were prevalent in developing countries. At the same time, it gave renewed vitality to parasitology and elevated the status of tropical medicine by developing new tools and methods for the control of what were the great neglected diseases.

As the architect of the GND network, Warren tried to pull off a difficult balancing act: using modern, expensive molecular science developed in the West to bring a greater understanding of the diseases that were devastating the lives of the poorest people on the planet. This involved funding researchers at two of the world's leading centres of biomedical science, the University of Oxford and the Karolinska Institute, which inevitably led to accusations of elitism. Funds were paid directly to the respective institutions and then channeled to the specific groups. The first RF grant arrived in Sweden in September 1979, and the research unit consisted of two closely collaborating research teams within the Departments of Immunology at the University of Stockholm and the Karolinska Institute. The unit also worked in close association with the department of Medical Genetics (Uppsala University) and the Department of Infectious Diseases (Karolinska Institute). Certainly both Peter Perlmann and Hans Wigzell in Sweden were brilliant immunologists: Perlmann had particularly wide scientific interests, ranging from developmental biology to the importance of delineating the function of individual lymphocyte subsets and the co-operation of cells in understanding immunity. His recruitment into the GND marked a new, highly productive phase in his career in which he made contributions to the pathogenesis of cerebral malaria, whereas his department's training of a succession of doctoral students from malaria-endemic countries led him to become

⁵⁷Dan Colley, personal communication.

a member of the Malaria Vaccine Steering Committee for many years.⁵⁸ GND funding also transformed the fortunes and directions of the wider institutions, and much of the seed-corn funding given by the RF continues to have a long-term impact today. The creation of the Chair of Parasitology at the Karolinska Institute was a direct consequence of Warren's programme: While looking at parasitic research in his own country and across the other foundational units, Hans Wigzell suggested that "seldom before has such relatively little money had such an impact on the course of research in tropical medicine."⁵⁹ Meanwhile, in Oxford the RF's funding came as a financial lifeline at a time when support for science in general, and for work in the developing world in particular, had decreased in the UK. GND support enabled Oxford medicine to develop enduring links with a number of centres in the developing world: An encounter "over a good bottle of scotch" at the inaugural GND meeting in New York between David Weatherall and the director of the Wellcome Trust, Peter Williams, gave birth to a series of partnerships between British universities and centres in the tropics.⁶⁰ This meeting led to the establishment of the Oxford–Wellcome Trust unit in Thailand in 1979 and began a programme that altered the concept of tropical medicine to medicine in the tropics. This template was subsequently expanded to encompass partnerships in India, Indonesia, Vietnam, Sri Lanka, Laos, and Jamaica. In addition to producing international leaders in tropical medicine research, these connections led to important developments in the management of common diseases such as malaria. Weatherall's contribution to understanding the cause of thalassemia, and his lifelong contribution to the control of tropical diseases in poor countries, was recognised in 2010 when he was awarded the Lasker Prize.

Even those who criticised the GND's perceived elitism acknowledged that Warren's selectivity was perhaps a necessary byproduct of the quest to attract the best investigators and to supercharge the field. The immunologist Alan Sher spent much of his scientific life at the NIH, and early in his training he was the beneficiary of a Research Career Development Award in Geographic Medicine from the RF. At the end of the 1980s, he perfectly captured the calibrated balance of forces and interests that Warren recognised to be inherent but inescapable dichotomies of his plans: "Although I have criticised the GND programme for its elitism in terms of institutions and groups supported and neglect of talented investigators already in the field of parasitology, its overall impact has been nothing short of outstanding. It has helped to bring parasitology into the modern age, made it a fashionable subject for the basic scientist, provided many investigators with a chance to enter the field and helped launch their careers (e.g. myself)."⁶¹ There is no doubt that Warren made the

⁵⁸P. Perlmann in M. Coluzzi & D. Bradley, *Parasitologia. The Malaria Challenge after one hundred years of malariology*, Rome: Lombardo, 1999, p. 7.

⁵⁹K. S. Warren & C. C. Jimenez (eds), *The Great Neglected Diseases of Mankind Biomedical Research Network: 1978–1988*. New York: The Rockefeller Foundation, 1988, p. 37.

⁶⁰David Weatherall, personal communication.

⁶¹K. S. Warren & C. C. Jimenez (eds), *The Great Neglected Diseases of Mankind Biomedical Research Network: 1978–1988*. New York: The Rockefeller Foundation, 1988, p. 309.

careers of a generation of biomedical scientists in the US and across the world. John David, Hans Wigzell, Peter Perlmann, Michael Sela, James Kazura, Dick Guerrant, Adel Mahmoud, Gerald Keusch, Tony Cerami, Peter Hotez, Adolfo Martinez-Palomo, and many others were brought into the field of infectious diseases by the charm, vision, and sheer force of Warren's personality.

In 2014 an article in *The Lancet*, looking back at a century of the RF's existence, described the GND network as an example of its "excellent philanthropic work."⁶² For a variety of reasons, Warren was a more influential figure than has generally been appreciated. His ideas were ahead of their time as he defined a new field of study and its lingua franca. Christopher Murray, now Director of the Health Institute for Health Metrics and Evaluation in Seattle, met Warren in the mid-1980s and recognises that his concepts still have a resonance today: "I think the GND programme had a great effect. He coined the term and it has stuck, and now people compete to call their disease 'neglected.' There is [now] a bit of a war about what the borders are, what is in and what is not. Is leprosy neglected? Is rabies? There are a lot of different definitions of what is neglected, and I think that the concept can reasonably be traced back to Ken."⁶³

As well as taking the field in a new direction, Ken Warren's aim was for the GND to make a major impact on reducing the burden of disease while at the same time infusing young scientists with the immense importance, fascination, and potential of tropical disease research. For many investigators, meeting Ken Warren was a turning point in their lives that took them in new, previously unimagined destinations. One such scientist was Gerald "Jerry" Keusch, a former Director of the Fogarty International Centre for Global Health at the NIH and a world-renowned researcher in tropical diseases. After securing a grant for a decade from the GND, he then followed it up with a further 10-year grant from the RF, which was used to establish a partnership with the Christian Medical College in Vellore, India, which itself became a leading infectious-disease center. Jerry recognised that Warren had great skill at creating programmes and mobilizing money but also that he was greatly admired by the cadre of young scientists who had been so carefully selected. Warren created an environment where highly competitive research scientists in the real world could lower the antenna and interact in a collective way: "At the annual meetings, everybody participated, and you wanted to present your best work. There was a true sense of collaboration. I have not seen that in any other group that I've been part of. I think that most of us who were there would say that that period of time was probably the best in our scientific career. Ken's legacy is the network itself. We metastasised and spawned a new revolution in tropical diseases; it goes from the very molecular, upstream, down to the delivery of health care and health

⁶²L. C. Chen, "China Medical Board: a century of Rockefeller health philanthropy," *The Lancet*, 384: 717–719, 2014.

⁶³Christopher Murray, personal communication.

care systems. That has really come out of the drive that Ken imparted to it. It is quite remarkable.”⁶⁴

In addition to the benefits envisaged and hoped for, the GND had many unforeseen positive influences. In Oxford, for instance, the GND legacy helped to influence research in tropical medicine to the more general benefit of the subject: attracting excellent young clinicians into the field, both from the UK and from the developing world, stimulating undergraduates to spend elective periods in the Third World, and leading to the establishment of an undergraduate teaching programme in tropical medicine. It also had a major influence on the format of the Oxford Textbook of Medicine, which, probably more than any other standard medical textbook, deals with problems in the developing world.

The GND was not the sole focus of Warren’s activities at the RF. In 1977, when he was appointed Director of Health Sciences, he was responsible for distributing \$100 million over a decade in three major areas: In addition to biomedical research by way of the GND, he also was responsible for the development of the International Clinical Epidemiological Network (INCLEN) and the creation of efficient, low-cost medical- and health-information systems. These new challenges would require all of Warren’s drive, ingenuity, salesmanship, and passion to make them succeed. One momentous undertaking that had been incubating for many years came to the fore in the early 1980s: the campaign to immunise the world’s poorest children against killer diseases. Warren knew the field well, having helped to establish the WHO’s Programme for Vaccine Development and their Scientific Advisory Group of Experts (SAGE). In the words of his colleague, Scott Halstead, “‘vaccines’ was every other word that came out of Ken’s mouth.”⁶⁵ Overlapping with, and leading on from, the GND era, vaccines were to be Warren’s next great project.

⁶⁴Gerald Keusch, personal communication.

⁶⁵Scott Halstead, personal communication.

Kenneth Warren and the Great Neglected Diseases of
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