WHO and health research – some personal reflections

G. J. V. Nossal

WHO's health research effort is reviewed through the eyes of an outside supporter. Drawing on his 30 years of experience with particular WHO programmes and the Advisory Committee on Health Research, the author highlights some of the important changes that have occurred, and his own involvement in bringing them about.

In any organization devoted to change and progress, creative tensions are almost inevitable. In WHO the tension is frequently between health care delivery and health research. There are many good public health officials who believe WHO's central goal must be to catalyse the delivery of today's health technologies to as many countries and people as possible. There are many others, equally good, who believe that some diseases will be conquered only when new and sharper tools are available to fight them. According to them, the pathway to the development of those tools and to their effective deployment is health research, comprising biomedical research, clinical research and associated areas of epidemiology and health services research.

Neither group has a monopoly on the truth. Optimally, robust dialogue between them will lead to policies embodying a judicious compromise. In WHO's 50th anniversary year, we should applaud the Organization for not choosing the soft option and leaving all research on world health to others. WHO has had a substantial involvement in research from the beginning, one which has changed with the decades and managed to mobilize resources and produce programmes of global significance. I have been asked to offer some personal reflections which may highlight, albeit in a fragmentary way, the imaginative manner in which the Organization has harnessed huge amounts of talent from around the globe to join in the fray. I make no apology for the fact that many of the examples will involve my own field, which is immunology; this brief article is not a formal history but a non-academic account of one person's experience. I hope it may encourage others to highlight the great work done in different fields.

It is important to state at the outset that WHO is not, and does not seek to be, a substantial performer of research in its own right. Rather, its role is primarily in three areas: setting strategic research goals and devising mechanisms for attaining these through global coordination; encouraging training and institution-strengthening for research in developing countries; and funding appropriate research.

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The Expert Advisory Panel on Immunology

I first became aware of WHO’s interest in research in the early 1960s through my “boss”, Sir Macfarlane Burnet, then Director of The Walter and Eliza Hall Institute of Medical Research in Melbourne. He was a member of WHO’s Advisory Committee on Medical Research and its Expert Advisory Panel on Immunology. The latter responsibility, involving, as I recall, a couple of visits to Geneva, occupied him greatly, in part because a deep-thinking colleague in theoretical immunology, the Danish-born scientist Niels K. Jerne, was the secretariat person in charge. Jerne forced Burnet and many other prominent biologists to ponder on the benefits the new immunology, properly exploited, could bring to the world.

My own interest in this question took a leap forward in 1964, when a fellow-immunologist from the National Institutes of Health in the United States informed me he was changing career direction. This was Howard Goodman, a prominent clinician and scientist, who replaced Jerne and proceeded to build up the relevant section of WHO considerably. In 1967, he asked me to join the Expert Advisory Panel on Immunology. An important focus of its work was the establishment of a network of immunology research and training centres, to give up-to-date training in this burgeoning science to workers in various developing countries. I became particularly familiar with the training centres in Kenya, Nigeria and Singapore.

(How hard it is to recall that 30 years ago Singapore was still a “developing country”! An excellent training course was also set up in Geneva, and a WHO Laboratory was started in Lausanne. Many hundreds of developing country scientists benefited from these initiatives, and some of them are now in positions of prominence in their own countries. The colleagues who supported Goodman in this effort included Georgio Torrigiani, David Rowe, Zdenek Trnca, Vaqek Houba and Alex Szenberg, and they made a great team. Under a young Norwegian, Dr Tore Godal, another very promising effort was under way. This was the scientific working group on the immunology of leprosy, known for short as IMMLEP, which was thinking through the central problems of developing a leprosy vaccine, and provided modest seed funding for the relevant research. Sitting at the feet of this group was not a bad way to get familiarized with the perils and possibilities of research on diseases prevalent in developing countries.

Research on human reproduction—HRP

In 1973, my interest in WHO was further enhanced from quite a different direction. One of the mentors who influenced me most as a young hospital resident was a brilliant Australian obstetrician, Rodney P. Shearman. I heard that he was soon to join the WHO staff for a year of sabbatical leave from his post at the University of Sydney. He would be working for a new kind of programme, known then as Human Reproduction. Dr Alex Kessler had become so impressed with the urgency of the world population problem that he built up a research programme devoted to the discovery of novel methods of birth control. The programme was to come up with a variety of methods that
took into consideration ethnic, religious and social differences between peoples.

Research was to be conducted around the world, but coordinated from Geneva. Funding was arranged from outside WHO’s regular budget. It was the first example of a so-called Special Programme, with considerable input into research design by outside experts, and equally considerable influence on programme management by the various international donor agencies who pledged their contributions quite independently of obligations related to membership of WHO.

Shearman was so inspired by the intellectual and humanitarian challenge of this work that he very nearly decided to devote his whole career to the venture. Kessler took WHO into the “big time” of world medical research through this programme, and brought in a model which, with variations and improvements, served as the prototype for WHO’s continuously increasing involvement in research. Previously, WHO Directors had only been in a position to allocate small research grants to collaborators in developing countries, using decision-making processes internal to WHO. With the special programme on human reproduction it became possible to make substantial grants, including many to scientists in industrialized countries, but using outside peer review as the decision-making tool. This was a significant departure from previous patterns, and not all WHO staff were comfortable with it.

Advisory Committee on Medical Research. This, at the time, met for a week in Geneva in June of each year, and drew its membership from leaders in both developing and industrialized countries. Four Nobel laureates in medicine participated, as did brilliant scientists from China, India, Kenya, Nigeria and many other countries.

It was certainly an opportunity to forge interesting associations and lasting friendships, but the work was in some ways disappointing. Most of the agenda was devoted to presentations by the secretariat of numerous worthy but small research endeavours. The programme on human reproduction was hardly mentioned, as the mechanism that governed it was outside the mainstream. Furthermore, it was difficult to determine what this high-powered committee was actually supposed to do. It had no budget and, it seemed to me, only a moderate degree of influence.

In corridor discussions, a few of us came to the conclusion that a great opportunity was being missed. Recombinant DNA technology had just been discovered and was likely to revolutionize biology. Immunology was booming. Cell biology and protein chemistry were making great strides. Yet few of the leaders of the new biology were in any way within WHO’s orbit. The new knowledge being generated was clearly relevant to disease control, but few had pondered its significance for the

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major public health problems of the tropical countries. We included Howard Goodman in these discussions. Initially, the idea was floated that ACMR should create a greatly expanded role for him in an enlarged programme called Immunology, Cell Biology and Genetics. But more

sober discussions with the secretariat made it clear that something as abstract as this would not be likely to fly, either with the donor community or with the Director-General.

What were the root evils of tropical pathology that had been left essentially untouched by the new biology? It soon became apparent that a great deal more could be done in the field of parasitic diseases.

**The Special Programme for Research and Training in Tropical Diseases – TDR**

Over the next couple of years, the concept of a Special Programme for Research and Training in Tropical Diseases gradually took hold. Those involved in the discussions decided to restrict the proposed research to the five worst groups of parasitic diseases: malaria, schistosomiasis, filariasis, trypanosomiasis and leishmaniasis. There then remained the question of what to do with the highly promising pilot programme on the immunology of leprosy. Though leprosy is a bacterial disease, it was added to complete “the big six”.

A couple of thorny issues still had to be resolved. In the field of agriculture, a successful programme known as CGIAR – the Consultative Group on International Agricultural Research – had been launched. It consisted chiefly of one free-standing international research institute for each major crop variety. Could this serve as a model? The Deputy Director-General of WHO, Dr Lambo, was rather taken by the idea of starting a major medical research institute of this kind in Africa. He was actually offered space in a hospital in Ndola, Zambia, which had been built but was surplus to current requirements. I was on a team which visited this facility to assess its potential. The more we looked at the question, the more it appeared that a network of collaborating laboratories made more sense than one or more large new institutes. The Ndola facility could indeed be used for clinical and field research, but for a variety of reasons it proved to be quite unsuitable for basic research. Following the site visit, we realized that training and institution strengthening were vitally important in the affected countries and needed to be a substantial part of the programme, but it seemed best to deliver these in the context of existing institutions rather than new ones.

The second thorny issue arose a little later. Because of the devastating effects of falciparum malaria in sub-Saharan Africa, because of Tom Lambo’s forceful advocacy, because of the high profile of the proposed Ndola centre, and because African sleeping sickness and river blindness were such dramatic examples of trypanosomiasis and filariasis respectively, TDR (as the planned tropical disease
research programme came to be universally known) was seen by many as an African programme. This had never been the case – everyone, starting with Lambo himself, had in mind a truly global programme – but donors' perceptions are sometimes hard to shift. For example, I had to argue very hard with the Australian authorities to disabuse them of this view.

In 1976, I took a year off from my job as Director of The Walter and Eliza Hall Institute in Melbourne to work full time on the planning of TDR, preparatory to a major donor meeting at the end of that year. Howard Goodman, the founding Director, and so essential to the birth of the concept, had moved on to become the head of all research promotion and development for WHO, but had built up a wonderful team, which I joined. David Rowe, Georgio Torrigiani, Richard Wilson, George Peterson, Ed de Maar, Jan Lilienfeld and others welcomed me to Geneva, and soon the distinguished public health academic from the University of Ibadan in Nigeria, Professor Adetokunbo Lucas, came to head the effort. While planning was shared by everyone, my main task was to show where basic science could fit in, and to promote the programme with the global academic community and the more prominent donors.

We soon reached consensus on the following principles. The controlling power on funds disbursement would lie not with WHO officials (including ourselves) but with scientific working groups using stringent peer group review criteria and a transparent, widely advertised grant application process. These groups would have a think-tank function as well, helping to define research strategies and pinpoint gaps and special opportunities. This helped to give the research programme both the "top down" and the "bottom up" approaches that were felt to be desirable.

Secondly, scientists from developing countries had to be full partners in every phase of the research programme. Thirdly (as already mentioned), heavy emphasis was put on training and institution strengthening. Many of these features resembled those of HRP, but I think it is fair to say that TDR was more fully integrated into the mainstream of WHO's continuing work on public health. For example, officials charged with control of malaria or trypanosomiasis acted as joint secretaries of Scientific Working Groups side by side with staff directly employed by TDR. Furthermore, later in the development of the programme, TDR officers were prominent in the different regions of WHO, as well as at headquarters.

In the event, the donor meeting at the end of 1976 was a great success – not by chance but as a result of a lot of hard work! After 10 years of commitment and superb leadership, Lucas moved on to a chair of public health at Harvard, and Tore Godal came from Norway to become the third Director. Few would dispute the claim that, 21 years on, TDR is among the two or three most respected programmes of WHO. Of course, we were not alone in seeing the power of the new biology. The Rockefeller Foundation's Great Neglected Diseases programme, the MacArthur Foundation's

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parasitology programme, and the work of the Wellcome Trust and the Edna McConnell Clark Foundation all helped to change world opinion on tropical diseases.

Medical research, health research and the regions

Two further developments of the 1970s are worth mentioning. When Professor Sune Bergström took up the chairmanship of the Advisory Committee on Medical Research, he was very keen to see more practical developments, and believed this would be helped by setting up a regional

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ACMR in each of WHO’s six regions. To underscore the importance of these regional bodies, their chairmen were to become members of the Global ACMR. To my delight, I was elected founding Chairman of the Western Pacific Regional ACMR. This gave me a further four years on the global body, double the normal term.

Clearly, these regional efforts were bound to have a more field-oriented, clinical and epidemiological focus. This natural movement downstream from biomedical research also responded to a second trend of these years. Led largely by the Canadian academic John Evans, the Global ACMR began to take a greater interest in health services research and the wider issues of how to optimize health care delivery. This was seen not as competing with the conventional medical research effort but rather as complementing it. So strongly felt were these two elements of change that the ACMR was renamed as ACHR – the Advisory Committee on Health Research rather than medical research.

This is by no means a trivial issue. Health research is very broad. It spans fields as diverse as molecular and cellular science; disease-specific disciplines such as pathology, pharmacology, medicine and surgery; applied research, development and demonstration; epidemiological and field research; programme evaluation and cost–benefit and risk–benefit analysis; community and sociological research, and many other areas. Nor is this a simple linear progression. In fact, the sectors interact in a very dynamic fashion. Organizational patterns around the world tend to reflect an older, simpler era of science when “biochemistry”, “public health” and “health economics” could be put into separate boxes. It is worth putting a great deal of effort into extensive communication between the different research sectors, and between researchers and health care professionals. Only an intellectual continuum will achieve an optimal harnessing of research outcomes to public well-being. This realization has illuminated my present involvement with WHO.

The Global Programme for Vaccines and Immunization and the Children’s Vaccine Initiative

After eight years on the ACMR/ACHR and, somewhat later, three years on the Scientific and Technical Advisory Committee of TDR; and after building up a splendid immunoparasitology unit at the Hall Institute under the inspired leader-
ship of Graham Mitchell (with excellent funding from WHO, the Rockefeller Foundation, the MacArthur Foundation and the Australian Government), I thought it was time to step into the background as far as WHO was concerned. However, fate decreed otherwise.

I was inveigled into the so-called Scientific Advisory Group of Experts (SAGE) of a small but elite programme devoted to research on new and improved vaccines. This programme was headed by an old friend, Dr Paul Henri Lambert, who had taken over responsibilities for immunology within WHO. I had thought that this would represent only a modest commitment of time to a very important cause. Tragically, not long after I joined, the distinguished German virologist Fritz Deinhardt, who was the Chairman of this group, died. Under the circumstances, I could not refuse the request to take over as Chairman.

Then, in 1993, the Director-General of WHO took a critical decision: the programme on vaccine research was merged with one of WHO’s major flagships, the Expanded Programme on Immunization (EPI). Furthermore, a new group was added, to work towards ensuring the availability everywhere of an adequate supply of vaccines that are of good quality and affordable. These three efforts were to constitute the new Global Programme for Vaccines and Immunization. A new Scientific Advisory Group of Experts was created, and I was asked to chair it.

The same advisory group was also charged with the responsibility of guiding the scientific strategy of the Children’s Vaccine Initiative. Dr J.W. Lee was appointed to head both the Global Programme for Vaccines and the Children’s Vaccine Initiative, with Dr Roy Widdus as his right hand man in the latter endeavour. The Children’s Vaccine Initiative is the umbrella body, embracing the whole of the wide constituency of supporters of global immunization, with special responsibilities for advocacy and long-term strategy. Under this structure, I now find myself with heavy responsibilities in what has been termed an “end to end” mission. The Scientific Advisory Group of Experts has to deal with all the issues, starting with basic molecular and cellular research, moving to applied research and development – which demand a very close working relationship with industry – and ending with actual vaccine deployment, including all that this requires in interaction with member countries and field workers.

So far, this work “from laboratory bench to bush” seems to be proceeding well; I have certainly had a great deal of positive feedback. Of course, an immense amount more needs to be done. We hope to achieve the global eradication of poliomyelitis by the year 2000, after which measles will be the next big target. We need to achieve wider deployment of the existing excellent vaccines against hepatitis B, yellow fever and Haemophilus influenzae. We need to prepare the way for a panoply of new vaccines for diarrhoeal and acute respiratory diseases. We need to promote research on simplifying vaccine delivery, including entirely new approaches. We need to mobilize far more resources for the struggle.
In the Global Programme on Vaccines we have something that closely approximates to the united, multi-pronged programme which John Evans was advocating so many years ago in the Advisory Commit-

tee on Medical Research. Very recently, the International Vaccine Institute, a new endeavour based in Seoul, Republic of Korea, has been launched as an independent international body. I have been asked to be Deputy Chairman (under Dr Barry Bloom) of the Board of Trustees. This body will work in close collaboration with WHO and the Children’s Vaccine Initiative. As this article goes to press, the search for a Founding Director has begun.

WHO is not alone in seeing health research as an urgent priority. Recently, much effort has gone into raising awareness of the potential of health research within the whole United Nations system, and in the eyes of governments, foundations and other decision-making groups. This process has been driven by an Ad Hoc Committee on Health Research headed by Tore Godal, Dean Jamison and James Tulloch. It has been vigorously supported by The World Bank under the leadership of Dr Richard Feachem.

During my 30-year association with WHO, the prominence of health research in the Organization’s work has increased dramatically. From being viewed as a luxury somewhat peripheral to its main mission, health research is now woven into the fabric of WHO and many of its programmes. WHO has learnt that the moral force of its noble goal gives it free access to the best brains in the world. Few hesitate to come when WHO calls. This has resulted in the building up of extensive networks of support in academia. WHO’s role in coordinating global research is respected by national bodies with much larger budgets. Its funding, though often modest, unlocks much greater national and private sector resources because of its prestige. Its continuing endeavours in training and capacity-building are bearing fruit.

As scientists, we should critically assess the yield from all this work, but that is very difficult to do. By its very nature as a coordinating body and a technical think-tank, WHO is never a single player in health research. It is critically dependent on its many collaborators and supporters. That being said, I have no doubt that WHO’s input has been important in focusing attention on developing countries’ research needs, and in providing powerful new tools to fight disease. Progress may be slow, but it is steady. In the field I know best, communicable diseases, WHO’s achievements have been monumental. As we celebrate WHO’s 50th Anniversary, as we prepare to usher in a new Director-General, as we contemplate the enormous health challenges in a new millennium, let us not just rejoice in the triumphs of the past, but resolve to do much more in the future.