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Contributions to International Health

The great majority of the essays in this book are, very properly, about research work carried out by staff of the School in the laboratory, the clinic or the field. But as we mention in Part I and summarize in Appendix VII, in Part III, academic staff of the School, especially the more senior staff, were also involved in a great number and variety of activities that contributed to the promotion of their branch of science, by service in national and international scientific societies, on editorial boards of journals and on important national governmental committees. In addition, two staff members, Gordon Ada and Frank Fenner, had the opportunity to be deeply involved in important programs of the World Health Organization (WHO). The two essays which follow summarize these contributions to international health.

Association with the World Health Organization (WHO), 1964–1991

by Gordon Ada

Howard Goodman, a well-known American immunologist, was appointed Director of an Immunology Section at WHO, Geneva, in the early 1960s, and he immediately began to organize small specialist international meetings on important new immunological topics. I attended two of these meetings in Prague, in 1964 and 1969, and was rapporteur at one in Geneva in late 1969.

WHO had established an Agency, The International Agency for Research on Cancer (IARC) at Lyon, France, in the 1960s, to specialize in epidemiological aspects of cancer. Each year the Agency awarded a number of scholarships for such studies. In 1971, I was appointed to the Scholarship Selection Committee. After interviewing candidates in the Western Pacific region, the Committee met in Lyon to choose the suc-

cessful candidates. It was at the first of these meetings that I met Henri Isliker, Rolf Zinkernagel's chief in Lausanne, and this led to Rolf coming to the JCSMR. In 1973 I was appointed to the IARC Scientific Council, and was its Chairman in 1975 and 1976. Two of its major interests were to see if epidemiological data could be obtained to show that aflatoxin was a significant cause of human liver cancer (this was subsequently shown to be the case) and the reason for the high incidence of breast cancer in Iceland.

In 1976, Gustav Nossal had helped to establish a new, independently funded, Tropical Diseases Programme at WHO in Geneva. A temporary advisory committee met annually for the first three years and I was appointed to it in 1978. In 1979, this

was succeeded by the Scientific and Technical Advisory Committee (STAC), of which I was a member for six years. STAC was responsible for the distribution of funds to the different components of the Programme to support research, mainly on epidemiological studies, drug and vaccine development for six major tropical diseases. Committees to review progress were established at four yearly intervals and during this period, I chaired those on Leprosy and Malaria and on Research Capability Strengthening in Developing Countries.

In 1981, I was appointed for a four year term to the Global Advisory Committee on Medical (later Health) Research, a small high-powered Committee on which Macfarlane Burnet, John Eccles and Gustav Nossal had previously served. From 1984, I chaired for another four years a Committee reviewing Technology Transfer to Developing Countries. From 1985 to 1989, I was a member of the WHO Western Pacific Regional Committee on Health Research, which met annually in Manila. These august bodies had no administrative powers but discussions ranged very widely over the activities of the Organization. I benefited greatly by getting to know a wide range of top people in the international health area.

In 1984 the Director-General of WHO made funds available to initiate a new Programme for Vaccine Development.

Although several diseases were to be targeted, a major activity would be 'trans-disease' technology – supporting research on new approaches, such as the use of peptides or chimaeric live vectors, viruses or bacteria. I was appointed chairman of the governing body, the Scientific Advisory Group of Experts (SAGE) for the first six years. Fortunately, the Rockefeller Foundation decided to support this new initiative. Because of this Programme's 'central' role in this area of WHO activities, I was appointed to the Vaccine Committee of the Human Reproduction Programme and became a member (1987–89) of the Research and Development Group of the Expanded Programme of Immunization. My last meeting at WHO on a vaccine project was in 1991.

These experiences influenced my research activities back in Canberra, which increasingly became directed towards studying the different immune responses to viral infections, especially influenza. What were the immune correlates of protection, what was the sequence of their appearance in an infected tissue, and how long did different responses persist (see p. 333). When I retired in 1987, vaccine development and vaccination practices were set to remain a major interest for the remainder of my working life as a Visiting Fellow in JCSMR.

Contributions to the Intensified Smallpox Eradication Programme

by Frank Fenner

In May 1965 I accepted an invitation to serve on the WHO Expert Advisory Panel on Virus Diseases and I have continued to be a member of this Panel. In consequence, I regularly receive a number of WHO publications and was asked to serve on various committees concerned with viral diseases. The most important of the early meetings

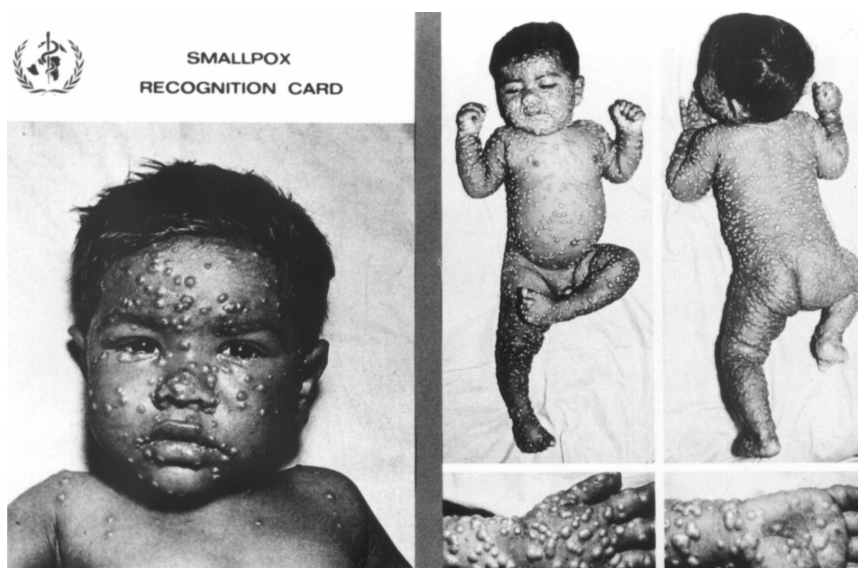
was the invitation to go to Moscow in March 1969 to a meeting of an 'An Informal Group on Monkeypox and Related Viruses.' This had been called by the Dr D.A. Henderson, Chief of the Smallpox Eradication Unit in Geneva, to investigate the possibility that there might be an animal reservoir of smallpox virus, the existence of which

would have made global eradication impossible. The very next year it was discovered that monkeypox virus, up to then only seen in monkeys in laboratories in Europe and the United States, caused a severe disease very like smallpox in humans in Central and West Africa. A few years later some Russian virologists claimed that monkeypox virus, which produces pocks with a haemorrhagic centre on the chorioallantoic membrane, was indeed the animal reservoir of smallpox virus, which, they claimed, was a white pock mutant of monkeypox virus. My experience with rabbitpox virus (see p. 390) convinced me that they were wrong, because all their 'white pock' mutants were identical and indistinguishable from an Indian strain of smallpox virus. Later they conceded that their 'mutants', and four isolates from wild African mammals, were contaminants.

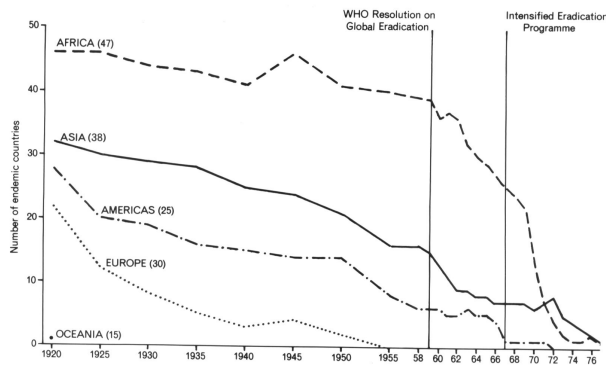
I continued to serve on this committee, first as rapporteur and later as Chairman. In the course of these meetings, which were usually held at WHO Headquarters in Geneva, I came to know the members of the

Smallpox Eradication Unit very well and learned more about the magnitude and importance of the job that they had undertaken. At this stage it will be useful to outline the task and how it was being tackled.

Smallpox has possibly killed more people over the last 2,000 years than any other infectious disease. It is a generalized infection and even in India, where it had been endemic for some 2,000 years, had a case-fatality rate in unvaccinated subjects of 20-25%. The incubation period was 12-14 days, after which a pustular rash developed and the patient died or gradually recovered with crusting of the lesions and sometimes residual pock marks or blindness. No sub-clinical cases occurred, although in persons vaccinated a long time before infection the disease may be relatively mild. It was the first disease for which a vaccine was developed; cowpox virus, discovered by Edward Jenner in 1796, and vaccination was effectively used to eliminate endemic smallpox from Europe, North America and Japan by about 1950. In 1958 the Soviet Union persuaded the World Health Assembly to



Smallpox patient at the height of development of the rash. This 'Smallpox Recognition Card' was used in surveillance in India and in investigations carried out in preparation for certification. It shows the distinctive nature and distribution of the rash. Similar cards with an African child were used in African countries. (Courtesy of the World Health Organization, Geneva, with permission.)



Numbers of countries in which smallpox was endemic between 1920 and 1978, arranged by continent. The figures in brackets indicate the numbers of countries involved. (Courtesy of the World Health Organization, Geneva, with permission.)

attempt the global eradication of smallpox by a campaign to vaccinate at least 80% of the population in endemic countries.

By 1966 it was clear that this approach, while working well in small countries, was making little impression on the disease in Africa and the Indian subcontinent. In 1967, when it was estimated that there were 31 endemic countries, with 20 million cases and two million deaths annually, an Intensified Smallpox Eradication Programme was launched by WHO, and a small Smallpox Eradication Unit was established in Geneva to oversee the project. In addition to routine vaccination, surveillance and containment was introduced as a major strategy and steps were taken to ensure that there were adequate stocks of potent freeze-dried vaccine. Gradually the number of endemic countries was reduced and a method was devised of certifying elimination of the disease from a country or region by stipulating that at least two years of intensive follow-up had occurred before an independent 'Certification Commission' visited the country and satisfied itself that there had been no transmission of smallpox there for at least two years.

In April 1977 I was asked to serve on and act as rapporteur for the International Commission for India, which was the key country as far as global eradication was concerned. I spent a most interesting two weeks journeying through Rajasthan and Himachal Pradesh and discussing findings

with other members of the Commission, each of whom had gone to different states. I was involved in three other International Commissions, for South Africa and Namibia in February 1978, for Southeastern Africa in March 1978 and for China in July 1979.

In October 1977 I was asked to act as Chairman of a large Consultative Committee appointed to advise the Director-General of WHO on procedures needed to be able to declare that smallpox had been eradicated globally and to develop recommendations for actions in a post-smallpox world. The next year the Consultative Committee was converted to the Global Consultation on the Certification of Smallpox Eradication and I served as its Chairman in October 1978 and December 1979. At the 1979 meeting it was agreed that the transmission of smallpox had been interrupted globally, and I announced this to the World Health Assembly in May 1980; the Report and its 19 recommendations were accepted unanimously.

This was not the end, for a small Committee on Orthopoxvirus Infections was set up to oversee implementation of the 19 recommendations and again I was asked to act as Chairman. By this time I had reached retirement age and joined JCSMR again as a Visiting Fellow. I was immediately attracted by the recommendation that a suitable book should be written on the project, which is regarded as the most important achievement of WHO in the field of preventive medicine.

Since I now had no other obligations, I thought that I could do this in three years. In fact it took seven years and four co-authors to produce what is the most satisfying book that I have ever written (I can say this only because everything went through my word processor, a Wang, which was one of the first personal computers in the School, purchased with WHO funds). It involved five or six visits of at least two weeks each year to Geneva and often to Baltimore, where D.A. Henderson, former Chief of the WHO Smallpox Unit and at the time Dean of the Johns Hopkins School of Public Health, was the key figure in writing the all-important operational chapters.

The early meetings of the WHO Committee on Orthopoxvirus Infections were concerned with ensuring that WHO had an adequate store of vaccine, kept in appropriate conditions, and that all countries destroyed their stocks of smallpox virus or transferred material to one of the two WHO laboratories, in Atlanta, USA, and Moscow,

USSR. By 1990, having ensured that all known stocks were now lodged in one or other of these laboratories, the Committee recommended that they should be destroyed. This recommendation met with opposition from some virologists, on the grounds that smallpox virus 'might hold the key to curing cancer or AIDS'. Although at this time the virus had been available at CDC for over ten years, not one of these virologists has sought to work with it. Then, in 1992, came the revelation that the Soviet Union had used the declaration of eradication in 1980 as a reason to bring smallpox virus into their enormous biological warfare program. This has delayed destruction of known stocks and called for continuing meetings and some research in USA and Russia, funded by the United States government, but the World Health Assembly recommended in 1996 that all known stocks should be destroyed by 31 December 2002.

Further Reading

Alibek, K. with Handelman, S. (1999). *Biohazard*. Random House, London.

Fenner, F., Henderson, D.A., Arita, I., Jezek, Z. and Ladnyi, D.I. (1988). *Smallpox and its Eradication*. World Health Organization, Geneva.