

Special Feature

Gates, GAVI, the glorious global funds and more: All you ever wanted to know

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Summary Global immunization programmes have achieved some remarkable successes. In 1977, Frank Fenner's Commission declared smallpox to have been eradicated by an 11-year-long intensive campaign. The Expanded Programme on Immunization encompassed six important childhood vaccines and reached over three-quarters of the world's children. Polio eradication has gone remarkably well, with only 10 out of 200 countries reporting residual cases. But amidst all the good news, there is also bad news. Coverage is variable; infrastructure is crumbling; and newer vaccines are not being incorporated in many country programmes. The Bill and Melinda Gates Foundation has introduced a new dynamic here. From their initial gift of \$100 million in December 1998, their commitment to date is US\$1.5 billion – and rising. At the centre is a Global Children's Vaccine Fund which permitted the launch, in January 2000, of the Global Alliance for Vaccines and Immunization. This is targeted to the 74 poorest countries of the world and is designed to improve vaccination infrastructure, to purchase newer vaccines and to support research and development.

Even before we know how successful this programme will be, it has had its imitators. The Global Fund to Fight AIDS, TB and Malaria borrowed many concepts from GAVI. The Global Alliance for Improved Nutrition announced in May 2002 does so as well, and is heavily supported by Gates. Highly effective parasite control programmes antedate all this but will be much strengthened. However, we still face a sizeable budgetary gap both for research and for bringing the best advances to all people who need them.

Key words: Expanded Programme on Immunization, Global Alliance for Vaccines and Immunization.

Introduction

As scientists and health professionals we understand the tremendous hardships that diseases bring and of course the burden falls unduly on the tropical developing countries. What is not so often appreciated is the impact of poor health on economic development. Over the last decade, an increasing body of evidence has accumulated supporting this contention. To the degree that economic development (in the long run) can bring nations out of poverty and despair it could also fairly be argued that economic development can aid global stability and health reform makes its own valuable contribution.

The relationship between economic status and health outcomes starkly illustrates the point. In the least developed countries, the income per head of population is US\$296.00 per annum, average life expectancy is 51 and, shockingly, the under-five mortality per 1000 live births is 159. In contrast, for the high-income countries, the average income per head is US\$25 730.00, life expectancy now 78 and under-five mortality 6 per 1000 live births. The intolerable 27-year difference in life expectancy and 26-fold excess of deaths in early childhood forms the focus of much of the health work of the United Nations system.

Under the chairmanship of Dr Jeffrey D Sachs, the Commission on Macroeconomics and Health convened by the Director-General of the World Health Organization reported some startling statistics in December 2001. It concluded that essential interventions against infections and nutritional deficiencies would cost US\$34.00 per person per year. It calculated that such extra expenditure could be achieved globally with additional donor support of US\$30 billion per year, admittedly a large sum in comparison with present funding flows. However, if the spend rate could rise to this level say within 10–15 years, it would be expected to save 8 million lives per year. The direct economic benefit was calculated at US\$186 billion per year, a six-fold return on the investment! The Commission also believed that a new global health research fund should be created, disbursing US\$1.5 billion per year.

The role of immunization

Infectious diseases continue to be the leading cause of mortality, particularly in children. Of the 3.5 million deaths per year from acute respiratory diseases, nearly 2 million occur in children under five, and the number of diarrhoeal diseases is only slightly smaller. Malaria and measles each cause nearly 1 million deaths per year in the same age group. AIDS of course is rising but still exercises its main mortality in adults (running at 2.3 million per year in 2001). Some of these diseases are vaccine preventable; in others there is an intensive global effort of research into new and improved vaccines.

The fact that concerted global action can achieve dramatic results is illustrated by the smallpox eradication campaign. An intensive effort over an 11-year period eradicated this disease from the world, although sadly the virus still exists in storage and could be used for bioterrorism.

Expanded Programme on Immunization (EPI)

The success of the smallpox programme eradication campaign encouraged the World Health Organization, in collaboration with UNICEF and others, to embark on the Expanded Programme on Immunization (EPI) which initially was designed to offer to all the children of the world immunization against six diseases, namely diphtheria, pertussis, tetanus, tuberculosis, poliomyelitis and measles. Lack of funds meant that the Program got off to a slow start in the late 1970s, but the combined strong efforts of UNICEF Chief Jim Grant and WHO Director-General Halfdan Mahler meant that universal childhood immunization coverage rates moved from 20% to nearly 80% in the decade of the 1980s, an incredible achievement saving millions of lives. The decade of the 1990s, however, was somewhat disappointing for the EPI. Despite World Health Assembly resolutions, the addition of hepatitis B and yellow fever vaccines to the Program proved disappointingly slow, and coverage in the poorer countries, those with a GDP per head of less than US\$1000 per year, actually fell from about 55% to about 42% with the strong possibility that both figures were over-reported. At the same time, infrastructure for the maintenance of the cold chain was crumbling, and human and financial resources devoted to immunization were grossly suboptimal in many countries. In part this may have been due to 'donor fatigue' with health priorities of the major UN Agencies shifting to other directions.

Plans for the resuscitation of EPI in the 21st century are described below:

Eradication of poliomyelitis

While the EPI was going so well, WHO espoused another very ambitious goal, namely to eradicate poliomyelitis completely. This plan involved four linked strategies. High routine infant immunization rates were essential and have in fact been achieved in many countries. This alone, however, did not suffice. Mass vaccination campaigns known as National Immunization Days had to be instituted. These involved a great degree of social mobilization, with help from governments, the media and community groups, whereby all children under five, regardless of previous immunization history, were lined up and given the oral Sabin antipoliomyelitis vaccine on the same day. Financial and volunteer human contributions of Rotary International have been critical to the success of this programme. So too has been acute flaccid paralysis identified. Surveillance was particularly important where the disease was coming under control. In such areas, 'mop up' campaigns represented the last step – intensive dwelling-to-dwelling visits by vaccinators in areas surrounding the last few index cases. These measures are intensive both in terms of vaccine usage (over 2 billion doses of Sabin vaccine were used in 2001) and also in human resources. As a matter of fact, polio eradication has become the largest health initiative ever.

While polio has not yet been eradicated, the campaign has to be termed a considerable success so far. The last wild cases of polio occurred in the Western Hemisphere in 1991, in the Western Pacific Region in 1997 and in the European Region in 1998. Efforts over the next year or two are directed at 10 countries, five of which suffer from extreme poverty and very dense populations, so-called 'Reservoir' countries; and five being countries of conflict, in the midst of civil or actual wars. Hopes are still high for success over the next couple of years despite the tremendous difficulties. If so, it will be vital to use the infrastructure and the human resources that have been built up for other immunization purposes.

Role of the Gates Foundation in the Global Alliance for Vaccines and Immunization

1998 proved to be an important year for global immunization. In March, the President of The World Bank Mr James D Wolfensohn convened a 'World Bank Summit' in an attempt to bring to the table all parties interested in revivifying EPI and getting universal childhood immunization back on track. He got the support of the new, dynamic Director-General of the World Health Organization, Dr Gro Harlem Brundtland, and also the Executive Director of UNICEF, Ms Carol Bellamy, as well as keen enthusiasm from the leaders of the academic community and a reasonable degree of support from the pharmaceutical industry, with the caution that sizeable funds would be needed if the dreams were to be turned into realities. A great deal of work was done to plan for a second Summit which was duly held in Bellagio, Italy, under my chairmanship in March 1999. In the meantime, however, a major new dynamic entered the field in the shape of the Bill and Melinda Gates Foundation. In December of that year they announced a grant of US\$100 million for the Children's Vaccine Program but this was only the beginning. As the months rolled by the generosity of the Foundation kept astounding the world community. There were major research initiatives in malaria, tuberculosis, diarrhoeal diseases, measles, hookworm and meningococcal vaccines. There was a strong contribution to both polio eradication and AIDS research. All of this together totalled approximately three-quarters of a billion dollars, but the most dramatic grant was towards the establishment of a Global Children's Vaccine Fund, with another three-quarters of a billion dollars, thus total grants being US\$1.5 billion.

This generosity really provided the underpinning of the Global Alliance for Vaccines and Immunization (GAVI) which was launched at the World Economic Forum in Davos in January 2000.¹ In the meantime, the Vaccine Fund has received other grants and pledges and stands at well over US\$1 billion. The Global Alliance is targeted to the 74 poorest countries of the world, those with a GDP per head of population of less than US\$1000 per annum. It has three closely linked purposes. The first is to improve the infrastructure for vaccination and to increase the safety of injections through a programme aimed at rewarding countries financially for extra children immunized in excess of those immunized the previous year. The second is to purchase, or aid in the purchase of, vaccines beyond the traditional six, which the countries could not themselves afford. These include hepatitis B, Hib, yellow fever, newer combination vaccines and in some

cases single injection vaccines. The third purpose is to support the research and development. This could be for existing vaccines, for example to do epidemiological and disease burden studies, to institute vaccine trials, to attempt to set priorities and to gauge community acceptance. It could also be to support development of vaccines where much research has already been done but where some further applied work is needed, for example in areas like rotavirus, pneumococcus, meningococcus A and eventually hopefully other and more difficult vaccines. The degree to which this develops will depend very much on further contributions to the Fund. Already in its third year, heavy emphasis is being placed on sustainability, and work is being done to persuade countries to assume a bigger share of the financial burden for vaccine purchases themselves, in a phased manner. At October 2002, more than two-thirds of the countries have availed themselves of GAVI, more than 50 million doses of vaccine have been shipped and more than 30 million have already been administered.

The Global Fund to Fight AIDS, TB and Malaria

Already quite early in its history, GAVI has prompted some imitators. The largest and the most contentious is the Global Fund to Fight AIDS, TB and Malaria. This initiative has the personal backing of the Secretary-General of the United Nations Mr Kofi Annan and has won considerable support from the G7 group of rich nations. The UN itself has estimated that the Fund will have to reach US\$7–8 billion per year to make a truly major impact and some have estimated that it might even need US\$20 billion by 2007. A recent meeting of the Board of the Fund heard sobering comments from the poor countries and received the first detailed outlines of how much demand there is likely to be. The present realities, however, are somewhat different. Pledges to date total US\$2 billion over five years and the first round of grants made in April 2002 went to 40 countries with awards totalling US\$616 million. A second round of grants will be awarded in January 2003. Much of the program will purchase drugs but appropriate prevention strategies will also be underwritten. The fact that antiretroviral therapy needs to be continued indefinitely obviously means that there will be enormous pressure on the Fund. At the moment, the lion's share of the pledges have come from the aid agencies of industrialized countries, with so far quite modest contributions from foundations and corporations. The distinguished public health specialist Dr Richard Feachem is the Director of the Global Fund and a young Australian, Dr Kate Taylor, is coordinating the private sector input from the large corporations via the World Economic Forum which is the main private sector partner in the initiative.

The Global Alliance for Improved Nutrition

The Gates Foundation once again stepped into the breach on 9 May 2002, when the Global Alliance for Improved Nutrition (GAIN) was announced. Details of this initiative still have to be worked out; there will be a major involvement of Canada, and the most important elements will be vitamin A and iron supplementation.

Control of parasitic diseases

Vaccines, of course, are not the only effective public health tools. There have been sizeable triumphs through the use of drugs at the population level. For example, the disease river blindness is due to *Onchocerca volvulus*. The vector of this filarial parasite is the appropriately named black fly *Simulium damnosum*. The larval stage of the black fly breeds in the fast-flowing river water and where the disease is rife, those farming fertile riverside land are at great risk. The onchocerciasis control program in sub-Saharan Africa (where 30 countries are at risk from the disease) initially concentrated on aerial spraying of fly laticide, which, despite expense and environmental problems, did achieve a certain degree of success. However, annual treatment with Ivermectin on a population basis represents a more appropriate tool. This drug has been given free of charge by Merck Inc. As a result, the disease is coming under control in 35 countries, 40 million people have been protected from onchocerciasis and 25 million hectares of fertile riverside land have been resettled with agricultural production sufficient to feed 17 million people each year.

Another potential success story is the control of lymphatic filariasis due to the parasite *Wucheraria bancrofti*. This is another filarial worm where the adult blocks lymphatic vessels causing elephantiasis. Lymphatic filariasis threatens one billion people in 73 countries and there are 120 million actually infected. The 20-year plan for global elimination involves mass administration of Ivermectin (Merck) and Albendazole (Glaxo-SmithKline). The idea is to take 15 years for elimination and then five more years for certification. The Alliance against lymphatic filariasis was formalized in 1997 and already by 2001 coverage reached 39.8 million people in 27 countries. One could cite other examples, such as the control through public health measures of guinea-worm or the very substantial reduction of leprosy via chemotherapy. Consolidated and concerted world action can achieve remarkable goals.

Very substantial challenges remain for the vaccine research community

Again some statistics gathered on this occasion by the Global Forum for Health Research provide helpful insights. The current annual spending on health research in the world is US\$73 billion, but less than 10% of this is directed at 90% of the world health problems. Combining public and private sector initiatives, 10% only goes to health problems in the developing countries, and of this only one-fifth is devoted to AIDS, TB, malaria, acute respiratory diseases and diarrhoeal diseases. The Global Forum for Health Research has termed this the '90–10 gap'. No-one doubts that the challenge of developing an effective vaccine against the 'big three', namely AIDS, TB and malaria, is an enormous one. However, if we do not put in the resources, we cannot hope to achieve the results. Let us hope that the deliberations of this Tenth Fenner Conference will come forward with some pertinent strategies in this regard.

Reference

- 1 Nossal GJV. The Global Alliance for Vaccines and Immunization – a millennial challenge. *Nat. Immunol.* 2000; 1: 5–8.