Global inequities and the international health scene

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Gustav Nossal was born in Bad Ischl, Austria, in 1931, and came to Australia with his family in 1939. He studied Medicine at The University of Sydney and, after two years' residency at Royal Prince Alfred Hospital, moved to Melbourne to work at The Walter and Eliza Hall Institute of Medical Research, where he has spent most of his research career in immunology. He has written seven books and over 530 scientific articles in this and related fields. Nossal has served as President of the Australian Academy of Science, President of the International Union of Immunological Societies, Chairman of the Victorian Health Promotion Foundation, Chairman of the committee overseeing the Global Programme for Vaccines and Immunization of the World Health Organization, Chairman of the Strategic Advisory Council of the Bill and Melinda Gates Foundation's Children's Vaccine Program and Deputy Chairman of the Council for Aboriginal Reconciliation. He was knighted in 1977, made a Companion of the Order of Australia in 1989 and has received numerous honours from 16 countries. In 2000 he was appointed Australian of the Year. He is currently Professor Emeritus, Department of Pathology, The University of Melbourne and a Principal of Foursight Associates Pty Ltd.

All young people should be deeply concerned at the global inequities that remain, and nowhere is this more clearly seen than in international health. Particularly we in the lucky country need to be mindful of this as we enjoy some of the best health standards in the world (with the notable exception of Aboriginal and Torres Strait Islander Australians). After decades of neglect, there are rays of hope emerging over the last 10-15 years. This brief essay seeks to outline the dilemma and to give some pointers to future solutions.

Mortality statistics

A stark example of the health gap is shown in Table 1, which shows that life expectancy at birth has risen markedly in the richer countries in the last 50 years, but has actually gone backwards in some countries, the situation being worst in Sub-Saharan Africa. As a result, life expectancy is now less than half of that in industrialised countries.

Deaths in children under five is widely used as a rough and ready measure of the health of a community, and also of the effectiveness of health services. Table 2 shows some quite exceptional reductions in the richer countries over half a century, but a bleak picture in many developing countries. India is doing reasonably well, presumably as a result of rapid economic growth, although the good effects are slow to trickle down to the rural poor. The Table shows the toll of communicable diseases and it is clear that at least two-thirds of these premature deaths are preventable.

We can total up these deaths, and note that the total comes to 20 million in 1960 and less than 8 million in 2010. Much of this improvement is due to international aid. One can do some optimistic modelling, and if we project the downward trend to 2025, deaths will be around 4.5 million. This would mean a total of 27 million extra child deaths prevented, chiefly though better treatment of pneumonia, diarrhoea and malaria; better newborn care practices; and the introduction of several new vaccines.

Table 1. *Life expectancy at birth in years. [1]*

Country	1960	2011
Sweden	73	81
Australia	71	82
USA	70	78
Japan	68	82
Zambia	45	39
Angola	33	38

2011 worst to best: 46%

A final chilling set of statistics is presented in Table 3. This concerns the risk of a mother dying in childbirth. As can be seen, this is now exceedingly rare in industrialised countries. With few exceptions, those rare deaths are in mothers who have some underlying serious disease not connected with their pregnancy. In contrast, deaths in childbirth are still common in poor countries. Once again, the chief causes, obstructed labour, haemorrhage and sepsis, are largely preventable. It is unconscionable that a woman is 400 times more likely to die in childbirth than in the safest country. In some villages with high birth rates and high death rates a woman's lifetime chance of dying from a pregnancy complication is one in seven!

International aid is increasing but must go higher

Properly deployed and in full partnership with the developing country, international aid can really help. At the prompting of the former Prime

Table 2. *Deaths under five years per 1,000 live births. [2]*

Country	1960	2011
Singapore	28.6	2.3
Japan	25.8	2.8
Australia	19.8	4.7
USA	25.4	6.3
Angola	199.9	180.2
Zambia	126.6	101.2
India	140.1	30.1
Nigeria	164.0	94.3

2009 mortality worst to best: 78%
Last decade world improvement: 2.8% per annum
Pneumonia 1.5 million; Diarrhoea 740,000; Malaria 670,000

Table 3. *Maternal mortality per 100,000 live births. [3]*

Country	1960	2011
Italy	7.4	3.9
Sweden	6.3	4.6
Australia	6.3	5.1
Japan	11.7	6.8
USA	16.6	11.5
Afghanistan	1261.0	1575.1
Sierra Leone	1044.2	1032.7
Nigeria	473.4	608.3
India	523.3	253.8

2008 mortality worst to best: 404%
Last 20 years improvement: 1.4% per annum

Minister of Canada, Lester Pearson, the United Nations mandated that the rich countries should devote 0.7% of their gross national income (GNI) to development assistance. Only five countries have reached or exceeded that goal, namely Denmark, Norway, Sweden, The Netherlands and Luxembourg. The global total is only 0.32% of GNI, or US$128.5 billion in 2010. Australia, presently at $4.8 billion, is pledged to go to 0.5% of GNI by 2015. The health component of aid varies from 7-15%.

Major new programmes speed progress in health

In the last 10-15 years, and for the first time, major health programmes have come forward where the budgets are measured in billions rather than millions. One with which I am particularly familiar is the GAVI Alliance, a global alliance for vaccines and immunisation. I had the honour of being involved in the "pre-history" of GAVI when I acted as the Chairman of the Strategic Advisory Council of the Bill and Melinda Gates Children's Vaccine Program from 1997-2003. Alerted to the fact that Bill and Melinda Gates wished to make a major donation in the field of vaccines a working party with representatives from the World Health Organization (WHO), UNICEF, The World Bank, and the Gates and Rockefeller Foundations engaged in a series of intense discussions with all stakeholders throughout 1998 and 1999, prominently including the Health Ministers of developing countries. GAVI was launched at the World Economic Forum in Davos in January 2000 with an initial grant of $750 million from the Gates Foundation. Its purpose is to bring vaccines to the 72 poorest countries in the world, including newer vaccines, and to sponsor research and development of still further vaccines. As regards the six traditional childhood vaccines, namely those against diphtheria, tetanus, whooping cough, poliomyelitis, measles and BCG (for tuberculosis), 326 million additional children have been immunised and the coverage has been increased from 66% to 82%. Some 5.5 million deaths have been averted. Sturdy progress has been made in deploying vaccines against hepatitis B, one form of meningitis and yellow fever. More ambitiously, programmes are now being rolled out against pneumonia, the worst form of viral diarrhoea, cervical cancer and german measles. The budget of the GAVI Alliance is now over $1 billion per year, but it will have to rise as further vaccines are included. There are still 19 million children unimmunised each year. One GAVI strategy is to demand some co-payment from the affected country, requiring it to give a higher priority to health and encouraging sustainability.

Two separate large programmes are addressing the problem of HIV/AIDS, arguably the worst pandemic the world has ever faced. They are the Global Fund for AIDS, TB and Malaria and PEPFAR, the US President's Emergency Fund for AIDS Relief. Together these programmes spend an astonishing US$12 billion per year. As a result, highly active antiviral therapy (HAART) is reaching 6.5 million people in low and middle income countries, not only prolonging their lives indefinitely but also lowering the virus load in their blood, thus diminishing their capacity to transmit the virus. There is good evidence that the epidemic has peaked with the number of new cases going down each year. In addition, special effort is going into the prevention of mother to child transmission of HIV.

The search for an AIDS vaccine continues. An encouraging but vexing result emerged from a clinical trial of Sanofi-Pasteur's vaccine in Thailand, involving 16,000 volunteers. The vaccine gave 31.2% protection from HIV infection, clearly not sufficient to go forward with mass immunisation, but enough to warrant further investigation in what has previously been a rather discouraging field.

Progress in malaria has been substantial. Insecticide-impregnated bednets turn out to be a powerful weapon, causing a 5% lowering of mortality where they are used. The Global Fund has distributed 240 million of these, and it is planned to reach a total of 700 million, an astonishing effort. Chemotherapy has been increased, including IPT, intermittent preventive therapy, where a whole population of children receives antimalarials every six months. IPT is also useful in pregnant women. A malaria vaccine is in the late phases of clinical trial. Produced by GlaxoSmithKline, it is known as RTS,S and has proven about 50% effective. It is targeted at the surface of that life-form of the parasite, known as sporozoite, which leaves the mosquito's salivary gland and is injected under the skin when the mosquito feeds. Most experts believe that the final, definitive malaria vaccine will also need to target the liver cell stage, where the parasite goes underground, the blood cell stage, where it multiplies extensively in red blood cells, and perhaps the sexual stages. Good progress is being made in research in all these areas.

Tuberculosis remains a formidable foe particularly as resistance to anti-tuberculous drugs is developing. That being said, the Global Fund is treating 8.7 million tuberculosis patients with DOTS (directly-observed therapy, short term, to assure compliance). Sadly, short term means six months, which is quite a burden. Extensive research is seeking newer drugs able to act in a shorter time frame. As regards vaccines, unfortunately it is clear that the birth dose of BCG, which does a good job of preventing the infant manifestations of TB, namely tuberculous meningitis and widespread miliary tuberculosis, is ineffective in preventing the much more common pulmonary tuberculosis of adolescents and young adults. An impressive body of research is attempting to develop new TB vaccines. Three are in Phase II clinical trial and at least eight in Phase I trial. The chronic nature of tuberculosis makes this a slow and expensive exercise.

The challenge of global eradication of poliomyelitis

Following the triumph of global eradication of smallpox, WHO set itself the challenge of eradicating poliomyelitis. When I was young, this was a most feared disease, with its capacity to kill and maim. The Salk vaccine and then later the oral Sabin live attenuated vaccine brought the disease under control in the industrialised countries with remarkable speed. A dedicated effort in Latin America did the same. But in Africa and the Indian subcontinent it was a different story. For this reason, a major partnership was launched in 1988 between the voluntary organisation Rotary International, WHO and UNICEF, with help from many others, to eradicate polio globally. Five strategies underpinned the venture. The Sabin oral polio vaccine was used to cut costs and ease administration, as oral drops rather than an injection was needed. High routine infant immunisation rates were encouraged. To get to the hard to reach children, national immunisation days were instituted, where all children under five were lined up and given the drops, regardless of previous immunisation history. Strong emphasis was placed on surveillance of all cases of paralysis with laboratory confirmation of suspected cases.

Finally, as control approached, a big effort was made to quell every little outbreak, with two extra doses of vaccine two weeks apart around the index case. As a result of this work, polio cases were reduced by over 99%. In 2011, there were only 650 confirmed cases in the whole world. India deserves special praise. Despite the large population and widespread poverty, the last case in India occurred on

13 January, 2011. There are now only three countries in which polio has never been eradicated, namely Pakistan, Afghanistan and Nigeria. Unfortunately, three countries have re-established polio transmission after prior eradication: Chad, DR Congo and Angola. Furthermore, sporadic cases are occurring in other countries following importation, though most of those mini-outbreaks are quickly controlled. We are at a pivotal point in this campaign. It is costing about $1 billion per year to maintain the whole global apparatus while the public health burden is currently quite small. Cessation of transmission was targeted for end 2012; this deadline is unlikely to be met. But failure to reach the end goal would constitute the most expensive public health failure in history. If we can get there, the economic benefits of eradication have been estimated at US$40-50 billion.

Table 4. *Some further vaccine challenges.*

Type	Challenges
Bacterial	• Protein for meningococcus B • Protein for pneumococcus • Various approaches for Group A streptococcus • Vi-conjugate for *Salmonella typhi* • Live attenuated or subunit vaccines for *Shigella* • Live attenuated or subunit vaccines for *Helicobacter pylori*
Viral	• Dengue (Sanofi Pasteur Phase III end 2012) • Cheaper rotavirus – India prominent (Bharat, Shanta, Serum Institute of India) • Broadly active influenza • Inhalable measles
Parasitic	• More complete malaria vaccine (liver, blood, sexual stage antigens) • Protozoa: leishmaniasis, trypanosomiasis • Metazoa: schistosomiasis, hookworm, onchocerciasis, *Taenia*

Some further vaccine challenges are listed in Table 4. In a twenty year framework success in most of these is not unrealistic. The dividends would be enormous; finding the requisite funds will be a daunting task.

Conclusions

This essay focuses on infections and vaccines, my own area of expertise, but plentiful pathways for progress exist in other areas. New drugs for all the above diseases; clever biological methods of vector control; improved staple crops with higher micronutrients and protein through genetic technologies; stratagems for improved antenatal care and obstetrics; a wider array of contraceptive measures tailored to particular cultures; in time thrusting approaches to non-communicable diseases including cardiovascular disease, diabetes, obesity, hypertension and their consequences; and greater recognition of the importance of mental health with depression looming as a very grave problem. As young people contemplating a career in medicine, I commend all of these areas to you. In particular, consider spending some months or a few years in joining this battle to provide better health to all the world's citizens. There are plenty of opportunities and the relevant travel will certainly prove enriching. A new breeze is blowing through global health. The thought that we can build a better world has taken firm hold. It is your generation, dear readers, who can turn dreams into realities and make the twenty-first century one truly to remember.

References

[1] World Life Expectancy: Country Health Profiles [Electronic Database]; 2012 [cited 2012 15 March 2012]. Available from: http://www.worldlifeexpectancy.com/world-health-rankings.
[2] Mortality rate, under-5 (per 1,000) [Electronic Database]: World Bank, United Nations; 2012 [cited 2012 15 March 2012]. Available from: http://data.worldbank.org/indicator/SH.DYN.MORT.
[3] Hogan MC, Foreman KJ, Naghavi M, Ahn SY, Wang M, Makela SM, *et al.* Maternal mortality for 181 countries, 1980-2008: a systematic analysis of progress towards Millennium Development Goal 5. Lancet 2010;375(9726):1609-23.