

Foreword: Introduction to Neglected Diseases

Improvements in social conditions and healthcare have transformed life in the developed world over the last century where, for example, life expectancy has increased dramatically. Indeed, some babies born today can expect to live into the next century! These advances are undoubtedly due to a combination of improved hygiene, social conditions and lifestyle, but some 40% is estimated to result from new medicines. A clear example is heart disease: hypertension is now well controlled and cardiovascular risk reduced using safe and effective medicines. Similar breakthroughs have been seen in other areas: for instance, deaths due to HIV/AIDS have been brought under control in most developed countries. These advances have involved a significant investment, not only by the pharmaceutical industry (US biopharmaceutical companies spent over US\$65bn on R&D in 2009) but also by academic groups in science and clinical research. Even with the extremely high prices for some medicines in the West, such healthcare expenditure is not sustainable and is under increasing pressure, so how can we address serious diseases in less advanced countries where safe food and water supplies may be more pressing priorities?

Nowhere is the divide more apparent than for HIV/AIDS, where 70% of the 33 million sufferers are located in sub-Saharan Africa, with limited access to effective drugs that are priced at US\$10,000/year in the US. Even generic alternatives that may be more than 10-fold cheaper are beyond many patients' reach and in some countries, life expectancy has dropped to below 40 years. However, all is not lost and "where there is a will, there is way" as seen by previously successful worldwide collaborations to eradicate smallpox and polio. There is now a similar sense of social responsibility in some developed nations that high mortality and unnecessary suffering, particularly amongst

children, cannot continue, and that we should mobilise international collaborations to control neglected diseases, reduce mortality and improve quality of life.

The George Institute for International Health estimates that total R&D spending on neglected diseases was US\$3.1 billion in 2008, although AIDS, malaria and TB consumed almost 75%. Funding was strongly led by the US NIH (\$1.1 billion) and the generosity of the Bill and Melinda Gates Foundation (\$0.64 billion), followed perhaps surprisingly by the biopharmaceutical sector (\$0.39 billion). Pharmaceutical companies have long recognised their responsibility to shareholders rather than non-profitable markets, but management has become increasingly receptive to persuasive lobbying from research scientists that neglected diseases must be addressed. Consequently, the tide has turned over the past decade where, for example, GSK and Novartis have established dedicated research centres to tackle diseases of the developing world while various bio- and pharmaceutical-companies have also invested directly, or in kind. Innovative Public Private Partnerships (PPPs) have been established, including MMV, TB Alliance, OneWorldHealth and DNDi, and are starting to bear fruit.

I first became involved with neglected diseases in 1999 by answering an advertisement in *Nature* and offering my services to the nascent WHO/TDR malaria initiative which I recall had only 2 or 3 staff members. However, we created an Expert Scientific Advisory Committee, where I served as the inaugural chair, and our first Call for Proposals overwhelmed us with more than 100 responses. Ten were selected for funding and we were on our way! A couple of years later, the Medicines for Malaria Venture was formally established as a Swiss charity, which today has over 50 employees with an annual budget of \$55 m. More importantly, this investment is now making a significant impact with one new medicine launched, 2 more in registration and an R&D portfolio of over 20 innovative projects. When these achievements are scaled across the overall research activities against neglected diseases, we can be proud and confident that we are taking important strides against some of today's scourges that cause so much suffering, deteriorating social conditions and economic disaster. It has been estimated that in 2008, Africa lost over \$12 billion GDP to malaria, and yet control of the disease was possible in 1914 in Panama, and was a key factor in completing canal construction. Surely, such game-changing scenarios must instil an even greater sense of urgency into our own research and access efforts.

Encouragingly, participation by academia, PPPs, pharmaceutical and biotech companies, together with other research organisations in the fight against neglected diseases has led to an enhanced sense of collaboration and camaraderie across the sector. Probably for the first time, pharmaceutical companies have provided their compound files for third-party screening, and in some cases hit structures have been placed in the public domain to encourage community exploitation. Projects with similar targets have joined forces to avoid duplication, prioritise objectives and identify development candidates as rapidly and

efficiently as possible. Provision of resource in kind from large and small organisations has been outstanding.

Of course, there are still major economic, scientific and political challenges that must be faced and overcome. Despite continued generosity from many donors, world economies face increasing pressures, which we must appreciate, but which should not deter continued and focussed fundraising. We have an unusual responsibility for the transparent use of funds and clearly communicating objectives, progress and issues to our stakeholders. It is essential we help funders appreciate the importance of maintaining a robust discovery pipeline even as successful projects move into the more expensive development phase. Scientifically, we are dealing with dangerous organisms where attack, evasion, and resistance are the norm, such that a continuous pipeline of novel agents suitable for combination therapies will be required for most of the diseases we are addressing. Some pose additional challenges, such as drug penetration and 6-month compliance for TB, while a \$1, 3-day treatment for malaria has significant cost of goods issues. Target validation is a continuing problem where genomic approaches have not yet blossomed, but whole cell screening is enjoying considerable success by providing attractive lead series for innovative medicinal chemistry follow on. Political will and stability will obviously have a major effect on drug distribution and treatment campaigns, where a key issue is how patients who subsist on a \$1/day could ever access and afford modern, effective medicines.

I am delighted to offer an introduction to this excellent volume in the RSC series, which I am sure will be well received by researchers and lay folk alike. I am particularly impressed by the breadth and depth of topics covered by such acknowledged scientific experts. Surely, this volume is a fitting testament to the dedication and commitment of the editors, authors, colleagues, funders and everyone else involved in the collective fight against neglected diseases. We have started to make meaningful progress, but the best is yet to come!

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